EGE KLİNİKLERİ TIP DERGİSİ
MEDICAL JOURNAL OF AEGEAN CLINICS

Cilt /No: 60 **Sayı**/No: 2 August/ 2022

İÇİNDEKİLER/CONTENTS

KLİNİK ÇALIŞMALAR/ CLINICAL TRIALS

OLGU SUNUMLARI/CASE REPORTS

EGE KLİNİKLERİ TIP DERGİSİ
THE MEDICAL JOURNAL OF AEGEAN CLINICS

«EGE KLİNİKLERİ TIP DERGİMİZ HAKEMLİ BİR DERGİDİR»

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

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

Dr. İlgül BİLGİN
Dernek Başkanı
Chairman of the society

Sorumlu Müdür /Director in charge
Dr. Tuncay KIRIŞ

Yönetim Adresi/ Administration address

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

Dökümantasyon ve Tasarım
Documentation and Design
Aslı GİRİT

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

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

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

Dergimizin Eski Adı: İzmir Atatürk Eğitim Hastanesi Tıp Dergisi' dir. (1964-2012)

DANIŞMA KURULU/ADVISORY BOARD

Prof. Dr. Murat AKSUN-*İ.K.Ç.Ünv.A.E.A.Hast., Anesteziyoloji Reanimasyon Kliniği*
Prof. Dr. Galip AKHAN-*İ.K.Ç.Ünv. A.E.A.Hast., Nöroloji Kliniği*
Prof. Dr. Enver ALTAS -*İ.K.Ç.Ünv. A.E.A.Hast., KBB Kliniği*
Doç. Dr. Mehmet Reşit ASOĞLU-Bahçeci Tüp Bebek Merkezi
Uzm. Dr. H. Mücahit ATALAY- *İ.K.Ç.Ünv. A.E.A.Hast., Nükleer Tıp*
Doç. Dr. Çetin AYDIN - *İ.K.Ç.Ünv. A.E.A.Hast. Kadın Doğum Kliniği*
Prof. Dr. Cengiz AYDIN- Sağlık Bakanlığı Üniversitesi Tepecik Eğitim ve Araştırma Hastanesi,Genel Cerrahi A.B.D.
Doç. Dr. Kaan BAL - *İ.K.Ç.Ünv. A.E.A.Hast. Üroloji Kliniği*
Doç. Dr. Alkan BAL -Celal Bayar Üniversitesi Tıp Fakültesi Çocuk Acil
Doç. Dr. Uğur BALCI - *İ.K.Ç.Ünv. A.E.A.Hast. Üroloji Kliniği*
Dr. Öğr.Gör. Mehtap BALABAN *Yıldırım Beyazıt Ünv. Radyoloji A.B.D.*
Doç. Dr. Korhan Barış BAYRAM- *İ.K.Ç.Ünv. A.E.A.Hast. Fizik Tedavi ve Reh. Kliniği*
Uzm. Dr. İlgül BİLGİN- *İ.K.Ç.Ünv. A.E.A.Hast ., Dermatoloji Kliniği*
Prof. Dr. Yeşim BECKMANN- *İ.K.Ç.Ünv. A.E.A.Hast., Nöroloji Kliniği*
Prof. Dr. Şahin BOZOK- Recep Tayyip Erdoğan Ünv. Kalp Damar Cer. A.B.D.
Doç. Dr. Mehmet BULUT -Antalya Eğitim ve Araştırma Hastanesi Göz Kliniği
Doç. Dr. Tuğrul BULUT -İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Ortopedi ve Travmatoloji A.B.D.
Doç. Dr. Umut CANBEK - Muğla Sıtkı Koçman Ünv. Tıp Fakültesi Ortopedi ve Travmatoloji A.B.D.
Prof. Dr. Erdem CANDA-Koç Üniversitesi Üroloji A.B.D
Prof. Dr. Fulya ÇAKALAĞAOĞLU- *İ.K.Ç.Ünv.A.E.A.Hast., Patoloji Labaratuvarı*
Doç. Dr. Mehmet ÇELEBİSOY- *İ.K.Ç.Ünv. A.E.A.Hast., Nöroloji Kliniği*
Prof. Dr. Etem ÇELİK -Ankara Eğitim ve Araştırma Hastanesi Kardiyoloji Kliniği
Dr. Öğrt. Gör. Hüseyin ÇETİN -*Yıldırım Beyazıt Ünv. Radyoloji A.B.D.*
Doç. Dr. Nihal DEMİREL-*Etlik Zübeyde Hanım Kadın Hast. Çocuk Hast., Yenidoğan*
Doç. Dr. Çetin DİNÇEL-*Bozyaka Eğitim ve Araştırma Hastanesi Üroloji Kliniği*
Prof. Dr. Giuseppe DODİ-*Padua University Hospital, First General Surgery Unit*
Doç. Dr. Tuba EDGÜNLÜ- *Muğla Sıtkı Koçman Ünv., Tıbbi Biyoloji ABD.*
Yrd. Doç. Dr. Nazile ERTÜRK *– Muğla Sıtkı Koçman Ünv., Çocuk Cerrahisi ABD.*
Doç. Dr. Demet ETİT-*İ.K.Ç.Ünv. A.E.A.Hast., Patoloji Labaratuvarı*
Prof. Dr. Hamza DUYGU -Yakın Doğu Üniversitesi Hastanesi Kardiyoloji A.B.D.
Doç. Dr. Orhan GÖKALP- İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Kalp Damar Cer. A.B.D.
Prof. Dr. Serhat GÜRPINAR- Süleyman Demirel Ünv. Araş. Ve Uygulama Hastanesi Adli Tıp A.B.D.
Doç. Dr. Kemal GÜNGÖRDÜK- *Muğla Sıtkı Koçman Ünv., Kadın Hast. ABD.*
Prof. Dr. Mehmet HACIYANLI- *İ.K.Ç.Ünv. A.E.A.Hast.,Genel Cerrahi Kliniği Kliniği*
Prof. Dr. Erdinç KAMER-*Tepecik.E.A.Hast.,Genel Cerrahi Kliniği Kliniği*
Doç. Dr. Volkan KARAÇAM- *Dokuz Eylül Ünv. Hastanesi, Göğüs Cer. ABD.*
Doç. Dr. Kenan KARBEYAZ- Eskişehir Osmangazi Ünv. Adli Tıp A.B.D.
Doç. Dr. İbrahim KARAMAN -Erciyes Üniversitesi Ortopedi ve Travmatoloji A.B.D.
Prof. Dr. Ali KARAKUZU- *İ.K.Ç.Ünv. A.E.A.Hast., Dermatoloji Kliniği*
Doç. Dr. Kaan KATIRCIOĞLU- *İ.K.Ç.Ünv.A.E.A.Hast., Anesteziyoloji Reanimasyon Kliniği*
Uzm. Dr. Uğur KOCA - *İ.K.Ç.Ünv. A.E.A.Hast Anesteziyoloji ve Reanimasyon ABD.*
Doç. Dr. Kuntay KOKANALI -SBÜ Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi
Prof. Dr. Gülnihal KUTLU *– Muğla Sıtkı Koçman Ünv., Nöroloji ABD.*
Prof. Dr. Mehmet KÖSEOĞLU- *İ.K.Ç.Ünv. A.E.A.Hast., Biyokimya Labaratuvarı*
Prof. Dr. Mehmet KIZILKAYA- *İ.K.Ç.Ünv. A.E.A.Hast., Anesteziyoloji Ve Reanimasyon Kliniği*
Prof. Dr. Yakup KUMTEPE-*Erzurum Atatürk Ünv., Kadın Doğum Kliniği*
Doç. Dr. Levent METE- *İ.K.Ç.Ünv. A.E.A.Hast., Psikiyatri Kliniği*
Prof. Dr. Okay NAZLI- *Muğla Sıtkı Koçman Ünv., Genel Cerrahi ABD.*
Prof. Dr. Haşim OLGUN- *Muğla Sıtkı Koçman Ünv., Çocuk Kardiyoloji ABD.*
Prof. Dr. Orhan OYAR- *İ.K.Ç.Ünv. A.E.A.Hast., Radyoloji*
Doç. Dr. Ali ÖLMEZOĞLU- *Celal Bayar Ünv. Tıp Fakültesi Radyasyon Onkoloji*
Prof. Dr. F. Esra ÖZER -*Muğla Sıtkı Koçman Ünv, Neonataloji Kliniği*
Prof. Dr. Behzat ÖZKAN- *İstanbul Medeniyet Ünv., Çocuk Endokrinoloji*
Prof. Dr. Peter PETROS- *UNSW Academic Dept. Of Surgery St Vincent's Clinical School, University of Western Australia*
Prof. Dr. Ercan PINAR- *İ.K.Ç.Ünv. A.E.A.Hast., KBB Kliniği*
Dr. Öğrt. Üyesi Ercan SARUHAN *- Muğla Sıtkı Koçman Ünv., Tıbbi Biyokimya AD.*
Prof. Dr. İlknur AKYOL SALMAN -Atatürk Üniversitesi Araştırma Hastanesi Göz Kliniği
Doç. Dr. Taylan Özgür SEZER -Ege Ünv. Tıp Fakültesi Genel Cerrahi A.B.D.
Prof. Dr. İbrahim Muhittin ŞENER- *İ.K.Ç.Ünv. A.E.A.Hast, Ortopedi Kliniği*
Uzm. Dr. Atilla ŞENCAN- *İ.K.Ç.Ünv. A.E.A.Hast.,Anesteziyoloji ve Reanimasyon Kliniği*
Op. Dr. Bekir TATAR- *İ.K.Ç.Ünv. A.E.A.Hast., KBB Kliniği*
Doç. Dr. Fatma TATAR- *İ.K.Ç.Ünv. A.E.A.Hast., Genel Cerrahi Kliniği*
Doç. Dr. Mesut TAHTA- İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Ortopedi ve Travmatoloji A.B.D.
Prof. Dr. Yusuf TAMAM- Dicle Ünv. Tıp Fakültesi Hastanesi Nöroloji Kliniği
Doç. Dr. Cengiz TAVUSBAY- *İ.K.Ç.Ünv. A.E.A.Hast., Genel Cerrahi Kliniği*
Doç Dr. Cihan TUĞRUL- Hitit Ünv. Kadın Hast. A.B.D
Doç. Dr. Tuba TUNCEL- İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Çocuk Alerji ve İmmünoloji Bilim Dalı
Doç. Dr. Nesrin TÜRKER- *İ.K.Ç.Ünv. A.E.A.Hast., İntaniye Kliniği*
Op. Dr. Dilek UYSAL- *İ.K.Ç.Ünv. A.E.A.Hast., Kadın Doğum Kliniği*
Prof. Dr. Harun ÜÇÜNCÜ- *Muğla Sıtkı Koçman Ünv.,KBB ABD.*
Prof. Dr. Erden Erol ÜNLÜER- *Uşak Ünv. A.E.A.Hast., Acil Tıp ABD.*
Prof. Dr. Nurettin ÜNAL- *İ.K.Ç.Ünv. A.E.A.Hast.Çocuk Kardiyolojisi*
Prof. Dr. Bülent ÜNAL -Osman Gazi Üniversitesi, Genel Cerrahi A.B.D.
Dr. Öğr. Üyesi Mustafa Gökhan ÜNSAL -Adnan Menderes Ünv. Tıp Fakültesi Genel Cerrahi A.B.D.
Dr. Öğr. Üyesi İlkin YERAL - Kırıkkale Ünv. Kadın Hast. A.B.D.
Doç. Dr. Aşkın YILDIZ- *İ.K.Ç.Ünv. A.E.A.Hast., Kadın Doğum Kliniği*
Doç. Dr. Seyran YİĞİT- *İ.K.Ç.Ünv. A.E.A.Hast., Patoloji Labaratuvarı*
Doç. Dr. Süreyya GÜL YURTSEVER- *İ.K.Ç.Ünv. A.E.A.Hast., Mikrobiyoloji Labaratuvarı*
Doç. Dr. Derya ARSLAN YURTLU- İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Anestezi ve Reanimasyon A.B.D.

GENEL BİLGİLER

Ege Klinikleri Tıp Dergisi, İzmir Hastanelerine Yardım ve Bilimsel Araştırmaları Teşvik Derneği'nin süreli yayın organıdır. Yılda üç sayı olarak yayımlanır. Basım ayları Nisan, Ağustos ve Aralık'tır. Dergide, tıbbın her dalı ile ilgili prospektif, retrospektif ve deneysel araştırmalar, olgu sunumu, editöre mektuplar ve derlemeler yayınlanır. Yayınlanan makalelerde konu ile ilgili en yüksek etik ve bilimsel standartlarda olması ve ticari kaygılarda olmaması şartı gözetilir. Yayın için gönderilen çalışmalar; orijinal, başka bir dergide değerlendirme sürecinde olmayan ve daha önce basılmamış olması koşullarıyla kabul edilir.

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

BİLİMSEL SORUMLULUK

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

ETİKSEL SORUMLULUK

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

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

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

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

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

İSTATİSTİKSEL DEĞERLENDİRME

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

YAZIM DİLİ

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

TELİF HAKKI BİLDİRİMİ

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

YAZI TİPLERİ

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

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

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

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

YAZI GÖNDERİMİ

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

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

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

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

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

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

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

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

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

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

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

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

Dergi makaleleri için örnek

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

Komite veya yazar grupları için örnek

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

Kitaptan konu için örnek

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

Kitap için örnek

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

İLETİŞİM

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

MAKALE GÖNDERİM KURALLARIMIZ

• Telif Hakkı Devir Formu tüm yazarlar tarafından imzalanılmalıdır.

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

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

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

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

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

• Kapak sayfası ekteki örnekte olduğu gibi tasarlanılmalıdır.

EGE KLİNİKLERİ TIP DERGİSİ

TELİF HAKLARI DEVİR FORMU

Yazının Başlığı:

Sorumlu Yazarlar:

Yazarların sorumlulukları:

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

Yazar Adı Soyadı **İmza** **Tarih**

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

Klinik İzole Sendromda Multipl Skleroza Dönüşümde Manyetik Rezonans Görüntülemenin Belirleyici Rolü

Ali BİGE*0000-0212-4446-0717

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

**

***

Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532

e-mail adresi: alibige@gmail.com

GENERAL INFORMATION

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

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

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

SCIENTIFIC RESPONSIBILITY

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

ETHICAL RESPONSIBILITY

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

STATISTICALLY EVALUATION

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

LANGUAGE

The official languages of the Journal are Turkish and English. Turkish dictionary published by Turkish Language Institution (www.tdk.gov.tr) should be predicated on Turkish manuscripts. All spelling and grammar mistakes in the submitted articles, are corrected by the editor without changing the data presented.

It is the authors' responsibility to prepare a manuscript that meets spelling and grammar rules.

COPYRIGHT STATEMENT

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

ARTICLE TYPES

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

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

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

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

MANUSCRIPT SUBMISSION

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

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

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

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

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

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

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

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

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

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

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

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

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

Format for journal articles:

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

Format for Committees and Groups of Authors:

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

Format for Chapter from a book:

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

Format for Books and Monographs:

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

COMMUNICATION

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

OUR ARTICLE SUBMITTING RULES

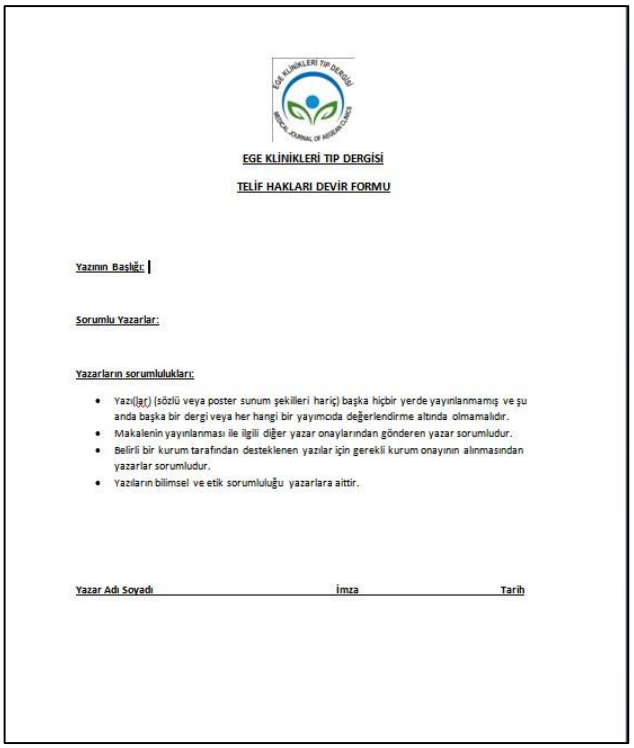
• Copyright Transfer Form must be signed by all authors.

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

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

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

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



EGE KLİNİKLERİ TIP DERGİSİ

TELİF HAKLARI DEVİR FORMU

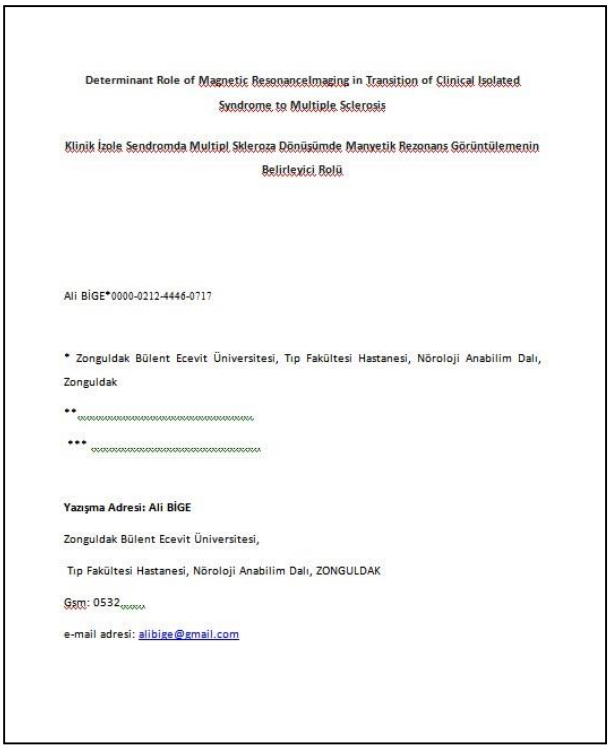
Yazının Başlığı:

Sorumlu Yazarlar:

Yazarların sorumlulukları:

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

Yazar Adı Soyadı İmza Tarih



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

Klinik İzole Sendromda Multipl Skleroza Dönüşümde Manyetik Rezonans Görüntülemenin Belirleyici Rolü

Ali BİGE*0000-0212-4446-0717

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

**

***

Yazışma Adresi: Ali BİGE

Zonguldak Bülent Ecevit Üniversitesi,

Tıp Fakültesi Hastanesi, Nöroloji Anabilim Dalı, ZONGULDAK

Gsm: 0532

e-mail adresi: alibige@gmail.com

İÇİNDEKİLER/CONTENTS

KLİNİK ÇALIŞMALAR/ CLINICAL TRIALS

OLGU SUNUMLARI/CASE REPORTS

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 84-87

Is The Repeat Co-Testing After One Year Enough in the 30 Years Old and Over Women Who Are Cytology Negative, But Other High Risk Human Papillomavirus Infection Positive?

Sitoloji Negatif, Ancak Diğer Yüksek Riskli Human Papillomavirus Enfeksiyonu Pozitif Olan 30 Yaş ve Üzeri Kadınlarda Bir Yıl Sonra Yapılan Tekrar Co-Test Yeterli midir?

Çetin AYDIN* 0000-0001-7597-5572
Ayşegül GÜLBAHAR* 0000-0001-6533-6195
Hakan ÇÖKMEZ* 0000-0002-8912-328X

*İzmir Atatürk Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İzmir.

Yazışma Adresi : Hakan ÇÖKMEZ
İzmir Atatürk Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Basın Sitesi Mah. Hasan Tahsin Cad. No: 143. PK: 35150 Karabağlar/İzmir.
Email: hakancokmez@hotmail.com

Abstract

Objective: Our aim in this study was to compare the colposcopic biopsy results in cytology negative patients in terms of human papilloma virus (HPV) type.

Methods: The study was retrospectively made in women ≥ 30 years of age with positive HPV deoxyribonucleic acid (DNA) sampling and negative smear cytology.

Results: Cervical intraepithelial neoplasia (CIN) II and CIN III prevalence is significantly high in the HPV type 16-18 positive group (respectively, 88.2%; 82.0%) compared to the other high risked group (respectively, 11.8%; 10.0%) ($p<0.05$). High grade squamous intraepithelial lesion (HGSIL) prevalence rate in HPV type 16-18 positive group (83,7%) was found significantly high according to the other high risk group (16,3%) ($p<0.05$).

Conclusion: In colposcopic biopsy, we observed less HGSIL in females over 30 years of age with negative cytology but positive other high risk HPV therefore Co-testing repeating a year after may be satisfactory.

Keywords: Cervical intraepithelial neoplasia, colposcopy, human papillomavirus, vaginal smears.

Öz

Amaç: Bu çalışmadaki amacımız, sitoloji negatif hastalarda kolposkopik biyopsi sonuçlarını human papilloma virüsü (HPV) tipi açısından karşılaştırmaktır.

Yöntem: Çalışma, pozitif HPV deoksiribonükleik asit (DNA) örneklemesi ve negatif yayma sitolojisi olan 30 yaş ve üzeri kadınlarda retrospektif olarak yapıldı.

Bulgular: Servikal intraepitelyal neoplazi (CIN) II ve CIN III prevalansı, HPV tip 16-18 pozitif grupta (sırasıyla %88,2; %82,0) diğer yüksek riskli gruba göre (sırasıyla %11,8; %10,0) anlamlı derecede yüksektir ($p<0.05$). HPV tip 16-18 pozitif grupta yüksek dereceli skuamöz intraepitelyal lezyon (HGSIL) prevalans oranı (%83,7) diğer yüksek risk grubuna göre (%16,3) anlamlı yüksek bulundu ($p<0,05$).

Sonuç: Kolposkopik biyopside, sitoloji negatif ancak diğer yüksek riskli HPV pozitif olan 30 yaş üstü kadınlarda daha az HGSIL gözlemledik, bu nedenle bir yıl sonra tekrar Co-test yapmak tatmin edici olabilir.

Anahtar Kelimeler: Servikal intraepitelyal neoplazi, kolposkopi, human papilloma virüsü, vajinal smear.

Geliş Tarihi: 16/02/2022
Kabul Tarihi: 30/06/2022

Introduction

Today HPV is emphasized as the most important etiological agent for cervical cancer. The lifelong HPV infection risk for sexually active females and males worldwide was reported as 50% (1). HPV type 16 and 18 were found to be the most important factor in the cervical cancer etiology, other high risk types (31, 33, 45) follow this. In the situation of negative cytology while colposcopy was only suggested for patients who positive HPV type 16 or 18 results according to American Society for Colposcopy and Cervical Pathology's (ASCCP) Guide, repetition of HPV DNA test a year later is recommended in other HPV DNA positivities. If HPV DNA of the patient is still present in the repetition made a year later or deterioration is observed in cytology, colposcopy is suggested (1). Pap smear test is the first scanning test used to decrease cervical cancer incidence and related mortality. On the other hand, the sensitivity ratio changes between 55% and 94% depending on laboratory and expertise experiences in recognizing high-degree lesions (2,3).

The aim of this study was to determine the agreement between HPV type and cervical biopsy results for negative cytology smear results so as to inform the appropriate follow-up method of other high-risk HPV-positive patients.

Material and Method

We retrospectively evaluated the medical records of patients who underwent colposcopic cervical biopsy in Izmir Ataturk Training and Research Hospital Department of Gynecology and Obstetrics between January 1, 2018 and December 31, 2019. The study was approved by the local ethics committee (#44-2017). The study was performed in accordance with the ethical standards described in an appropriate version of the 1964 Declaration of Helsinki, as revised in 2013. Because of the retrospective design of the study and anonymized data used in the analyses, informed consent was not obtained from the patients.

Patient ≥ 30 years of age who underwent colposcopic cervical biopsy with a positive high-risk HPV DNA sampling test and negative Papanicolaou smear were included in the study. Those who had received previous treatment for cervical pathology (e.g., loop excision, electrosurgical procedure, or cold knife conization) were excluded. In addition patients who used hormone replacement therapy (HRT), oral contraceptive pills (OCP) or Levonorgestrel intrauterine device or had cervical pathology based on the cytology were excluded from the study.

We used the Cobas 4800 HPV test (Roche Molecular Systems, Pleasanton, CA, USA) which detects HPV DNA. The patients were separated into two groups as those with HPV type 16-18 positive and the other high-risk HPV positive patients. The patients were divided into subgroups according to their colposcopic biopsy results.

Subgroups based on CIN classification;

CIN I: Cell sequence and structural defect in the 1/3 lower part of epithelium (mild dysplasia)

CIN II: Cell sequence and structural defect in the 2/3 part of epithelium (medium dysplasia)

CIN III: Cell sequence and structural defect in nearly all epithelium (severe dysplasia)

CIS: If the dysplastic changes include whole epithelium; carcinoma in situ

Subgroups based on Bethesda (4) classification;

Squamous cell abnormalities;

Atypical squamous cells (ASC): of undetermined significance (ASC-US) and cannot exclude HSIL (ASC-H)

Low grade intraepithelial lesion (LSIL)

High grade intraepithelial lesion (HSIL)

Squamous cell carcinoma

Glandular cell abnormalities;

Atypical glandular cells (AGC): Endocervical (AGUS), endometrial or other glandular cells of undetermined significance.

Adenocarcinoma in situ (AIS)

Adenocarcinoma

Biopsy results of the patients were evaluated based on both groups.

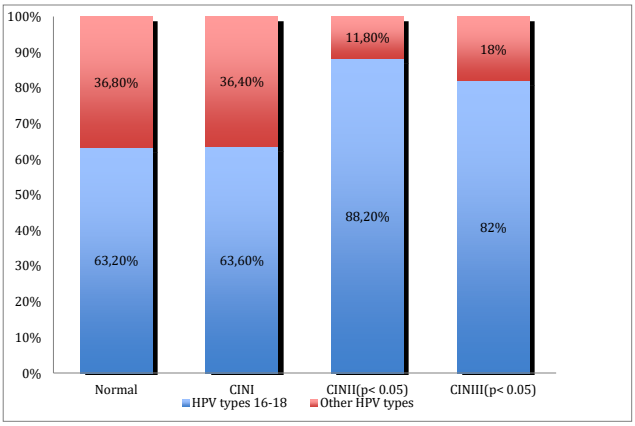
Continuous data were expressed as mean ± standard deviation and categorical data were expressed as numbers and percentages. Categorical data were compared using Pearson's chi-squared tests. All calculations are based on IBM SPSS Statistics for Windows, Version 20.0. (IBM Corp., Armonk, NY). Significance was evaluated at a minimum level of $p<0.05$.

Results

Average age of the population in the study is 42 ± 8.1 and the number of patients included in the study is 375. While 257 of the patients (68.5%) are HPV type 16-18 positive, 118 are (31.5%), the other high risk group HPV positive.

The distribution of the patients in both groups in order was normal biopsy (156; 63.2%), CIN I (21; 63.6%), CIN II (30; 88.2%), CIN III (50; 82%) for HPV type 16-18 and normal biopsy (91; 36.8%), CIN I (12; 36.4%), CIN II (4; 11.8%), CIN III (11, 18%) for other high risk group HPV ($p< 0.05$). While no statistical significance was observed when we compared both groups according to normal biopsy (63.2%, 36.8%) and CIN I (63.6%, 36.4%) classification ($p>0.05$), CIN II and CIN III prevalence is statistically significantly high in HPV type 16-18 positive group compared to the other high risked group ($p<0.05$) (Graphic 1).

Graphic 1: Comparing subgroups based on CIN classification

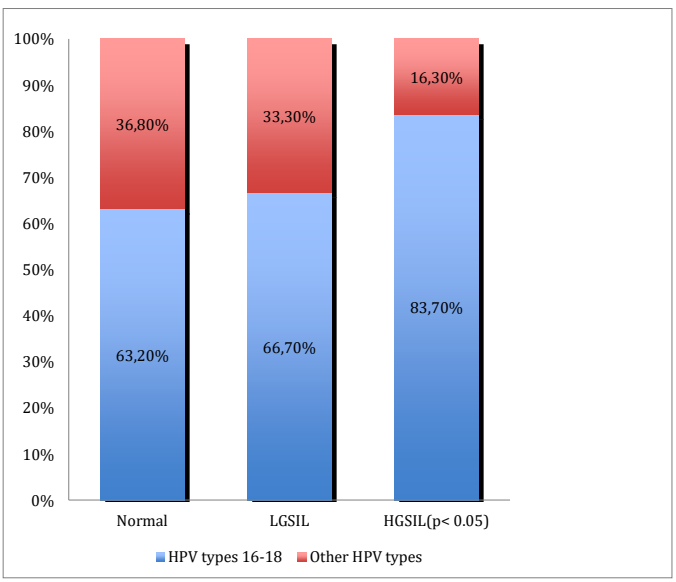


According to Bethesda classification, the distribution of the patients in both groups in order was normal biopsy (156, 63.2%), LGSIL (24, 66.7%), HGSIL (77, 83.7%) for HPV type 16-18 and normal biopsy (91, 36.8%), LGSIL (12, 33.3%), HGSIL (15, 16.3%) for other high risk group HPV (p<0.05).

The distribution of the total of 36 patients in LGSIL group based on CIN classification was CIN I (33, 91.6%) and CIN II (3, 8.4%) and in HGSIL group of a total of 92 patients CIN II (31, 33.7%) CIN III (61, 66.7%) according to CIN classification (p<0.05).

While no statistical significance was observed among normal biopsy and LGSIL rates in both groups when subgroup analyses were made in line with these data (p>0.05), HGSIL prevalence rate in HPV type 16-18 positive patient group was found statistically high and significant according to the other high risked group (p<0.05) (Graphic 2).

Graphic 2: Comparing subgroups based on Bethesda classification



Discussion

Our most important finding was that CIN II, CIN III and HGSIL prevalence is significantly high in the HPV type 16-18 positive group compared to the other high risk group. While HPV types in the high risk group for cervical cancer formation are as 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82 in order, HPV type 16 and 18 constitute the most common cause of invasive cervical cancer with a ratio of 70% (5,6). Therefore referral for direct colposcopy is recommended if the test result is positive for HPV-16 and HPV-18 in cytology negative patient group, co-test repetition 12 months later is recommended in other group HPV positivities. It was reported by ASCCP that CIN2 and progressive pathology occurred in 21% in a year in HPV-16 and HPV-18 positive patients and CIN3 will occur in a few years in 10% of these patients (7). In many study, HPV 16 and/or 18 prevalence was reported as higher in females with CIN II/III or more severe lesions than CIN I (8-10). In a meta-analysis on females from different countries in Europe, the prevalence of HPV 16 or 18 was reported as 29.4% in CIN I lesions, 61.4% in CIN II/III and 76.2% in invasive cervical carcinoma (11). In another study, HPV positivity was found 70% in Turkish females with invasive cervical cancer and CIN lesion. In this study, HPV positivity was detected as 77.8% in CIN I lesions, 28.6% in CIN II lesions, 91.7% in CIN III lesions and 68.2% in invasive carcinoma. The most common HPV types were found HPV 6/11, HPV 16 and HPV 18 (12). In contrast, follow-up is recommended for other high risk HPV if the cytology is negative because other high risk HPV positive patients do not have a strongly correlated relationship with high-grade cervical lesions (13).

Most HPV infections are harmless, and additional tests are required to identify women with progressing infections or precancerous lesions (14). In a 2018 study by Sole-Sedeno et al., 143 women with a first diagnosis of HPV infection (16, 18 and other high risk HPV) and assessed for progression or regression of their cervical lesions. At the end of the 2-year follow-up, the regression rate was 53.6% in the HPV 16 group and 75.4% in the other high risk HPV group (15). Consistent with these studies (14,15), our study showed significantly fewer advanced cervical lesions among other high risk HPV patients with negative cytology compared to patients with HPV 16 or 18. In Turkey, 3,29% of patients with HPV detected by a cervical cancer screening program and other high risk HPV infection represents 70.9% of all HPV types detected. In this study, when cytological results of HPV DNA positive women were examined, 66.52% of the patients had negative cytology were observed (16).

The strength of our study is that the colposcopic biopsy materials were evaluated by the same gynecological pathology team. However, our study has several limitations. Our study had a retrospective design and small sample size owing to our strict inclusion and exclusion criteria. In line with all these data, we think that wider prospective studies are required in our country to detect the HPV prevalence and type distribution in cervical lesions and for making a management algorithm specific to our country.

As a result, it has been observed to be satisfactory that co-testing is repeated a year after in women over 30 years of age with negative cytology but positive other high-risk HPV as stated in the ASCCP management guideline.

References

1. American Society for Colposcopy and Cervical Pathology. Algorithms, Updated Consensus Guidelines for Managing Abnormal Cervical Cancer Screening Tests and Cancer Precursors, 2013.
2. Andrae B, Andersson TM, Lambert PC, et al. Screening and cervical cancer cure: population-based cohort study. BMJ 2012;344:e900.
3. Dillner J. Primary human papillomavirus testing in organized cervical screening. Curr Opin Obstet Gynecol 2013;25:11-6.
4. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002; 287:2114-9.
5. Smith EM, Ritchie JM, Levy BT, et al. Prevalence and persistence of human papillomavirus in postmenopausal age women. Cancer Detect Prev 2003;27:472-80.
6. Castle PE, Glass AG, Rush BB, Scott DR, Wentzensen N, Gage JC, et al. Clinical human papillomavirus detection forecasts cervical cancer risk in women over 18 years of follow-up. J Clin Oncol 2012;30:3044-50.
7. L. Stewart Massad, Mark H. Einstein, Warner K. Huh, Hormuzd A. Katki, Walter K. Kinney, Mark Schiffman; 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors; American Society for Colposcopy and Cervical Pathology Journal of Lower Genital Tract Disease, Volume 17, Number 5, 2013;1-27.
8. Illades-Aguiar B, Cortés-Malagón EM, AntonioVéjar V, Zamudio-López N, Alarcón-Romero Ldel C, Fernández-Tilapa G, et al. Cervical carcinoma in Southern Mexico: Human papillomavirus and cofactors. Cancer Detect Prev 2009;32(4):300-7.
9. Sandri MT, Riggio D, Salvatici M, Passerini R, Zorzino L, Boveri S, et al. Typing of human papillomavirus in women with cervical lesions: prevalence and distribution of different genotypes. J Med Virol 2009;81(2):271-7.
10. Dursun P, Senger SS, Arslan H, Kuşçu E, Ayhan A. Human papillomavirus (HPV) prevalence and types among Turkish women at a gynecology outpatient unit. BMC Infect Dis 2009;9:191.
11. De Vuyst H, Clifford G, Li N, Franceschi S. HPV infection in Europe. Eur J Cancer 2009;45(15):2632- 9.
12. Yavuzer D, Karadayı N, Erdağı A, Salepçi T, Baloğlu H, Dabak R. HPV Typing with PCR in cervcal cancerous and precancerous lesions. Kartal Eğitim Araştırma Tıp Dergisi. 2009;20(1):1-6.
13. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis. 2013;17:S1-S27.
14. Wentzensen N, Schiffman M, Palmer T, Arbyn M. Triage of HPV positive women in cervical cancer screening. J Clin Virol 2016;76 Suppl 1:49-55.
15. Solé-Sedeno JM, Mancebo G, Miralpeix E, Lloveras B, Bellosillo B, Alameda F, et al. Utility of human papillomavirus genotyping in the management of low-grade squamous intraepithelial lesions. J Low Genit Tract Dis 2018;22:13-6.
16. Kan O, Gorkem U, Baris A, Kocak O, Togrul C, Yildirim E. Evaluation of the frequency of human papillomavirus (HPV) in women admitted to cancer early diagnosis and screening training centers (KETEM) and analysis of HPV genotypes. Turk Hij Den Biyol Derg, 2019; 76(2): 163-168.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 88-93

The Effect of Hypericium Perforatum Oil on Tissue Adhesion in Experimental Subtotal Thyroidectomy Model

Deneysel Subtotal Tiroidektomi Modelinde Hypericium Perforatum Yağının Doku Yapışıklığı Oluşumu Üzerine Etkisi

Mehmet GÜLMEZ* 0000-0001-8803-6160
Can SARAÇOĞLU 0000-0002-8047-1296**
Esma ÇINAR* 0000-0002-7993-1056**
Tugrul KESİCİOĞLU** 0000-0002-9263-5032**
Mert GÜNGÖR*** 0000-0001-5006-9565**
Ali AKTEKİN**** 0000-0003-3540-2686**

** Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey*
***Department of General Surgery, Giresun University Training and Research Hospital, Giresun, Turkey*
****Department of Pathology, Giresun University Faculty of Medicine, Giresun, Turkey*
*****Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey*
****** Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey*
******* Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey*

Corresponding author: Mehmet GULMEZ
Department of General Surgery, Giresun University Faculty of Medicine, Giresun, Turkey
Debboy Mevkii P.K 28200
e-mail: mehmetgulmez86@hotmail.com

Geliş Tarihi: 14/03/2022
Kabul Tarihi: 20/06/2022

Abstract

Objective: The risk of developing any of the known complications from thyroid surgery, such as recurrent laryngeal nerve injury and persistent hypoparathyroidism, increases significantly after re-operative thyroid surgery. The literature contains few clinical and experimental studies that address the prevention of adhesions after thyroidectomy. We aimed to determine whether Hypericum perforatum, which is thought to be effective for wound healing, has traditionally been used by the public, and of which many species are endemic to our country, had a positive effect on preventing the formation of tissue adhesions after thyroidectomy.

Materials and methods: The study included 24 male Wistar-Albino rats that were divided into three groups, each containing eight rats: Group 1: the control group, Group 2: the olive oil group, and Group 3: the H. perforatum oil group. On the postoperative day 14, the rats were sacrificed and difference between the groups were evaluated both macroscopically and histopathologically.

Results: There were no statistically significant differences in the macroscopic evaluations between the groups in terms of the type and degree of adhesions. However, the mean scores of the collagen and chronic inflammation parameters were statistically lower in the olive oil group than in the control and H. perforatum oil groups ($p<0.05$). In other parameters, no statistically significant differences were found between the groups.

Conclusions: As a result of these evaluations, there was no evidence that H. perforatum oil had a positive effect on postoperative adhesion formation when compared to the other groups.

Keywords: Hypericium perforatum, Adhesions, Thyroid

Öz

Amaç: Reoperative tiroid cerrahisi sonrası rekürren laryngeal sinir yaralanması ve kalıcı hipoparatiroidizm gibi tiroid cerrahisinin bilinen komplikasyonlarının riski önemli ölçüde artmaktadır. Literatürde tiroidektomi sonrası meydana gelen yapışıklıklar ve bunları önlemek için yapılan klinik ve deneysel çalışmalar oldukça sınırlıdır. Biz de yara iyileşmesi üzerine etkinliği düşünülen, geleneksel olarak halk arasında sıkça kullanılan ve ülkemizde de birçok türünün endemik olduğu H. Perforatum (Sarı Kantaron)'un deneysel olarak tiroidektomi ameliyatı sonrası doku yapışıklığı oluşumunu önlemede olumlu etkisinin olup olmadığını tespit etmeyi amaçladık.

Gereç ve yöntemler: Çalışmada 24 adet erkek Wistar-Albino ratlar her biri 8 rat içeren 3 gruba ayrılarak kullanıldı. Grup 1: Kontrol grubu, Grup 2: Zeytinyağı grubu, Grup 3: Hypericium Perforatum grubu. Postoperatif 14. günde ratlar sakrifiye edilerek makroskopik ve histopatolojik olarak gruplar arasında fark olup olmadığı değerlendirildi.

Bulgular: Gruplar arasında makroskopik inceleme neticesinde yapışıklığın tipi ve derecesinde istatistiksel fark saptanmadı. Bununla birlikte kollajen ve kronik inflamasyon parametrelerinin ortalama sokarları H. Perforatum grubuna göre zeytinyağı kullanılan grupta istatistiksel olarak daha düşük tespit edildi ($p<0.05$). Diğer parametrelerde gruplar arasında istatistiksel olarak fark saptanmadı.

Sonuçlar: Bu değerlendirmelerin sonucunda, H. Perforatum yağının diğer gruplar ile kıyaslandığında postoperatif yapışıklık oluşumu üzerine pozitif etkisi olduğuna dair kanıt elde edilememiştir.

Anahtar Kelimeler: Sarı kantaron, Adezyon, Tiroid

Introduction

Conditions requiring re-operative surgery in thyroid disease leave surgeons with great difficulties. The indications for re-operative thyroid surgery are detection of cancer in the trachea after the first surgery, symptomatic nodular or multinodular recurrence after surgery for benign thyroid disease, development of cancer in the residual thyroid tissue, or paratracheal, jugular, or lateral nodal recurrence in the neck (1).

Removal of some or all of the thyroid gland in the first surgery causes anatomical disorders. Further deterioration occurs, ranging from postoperative tissue changes to fibrosis and scar formation. The risk of complications increases because of scar tissue that makes it difficult to recognize and protect structures such as recurrent laryngeal nerves or vascular roots of the parathyroid gland (1). Therefore, the risk of developing any of the known complications from thyroid surgeries, such as recurrent laryngeal nerve injury and persistent hypoparathyroidism, increases significantly after re-operative thyroid surgery (2-4).

The literature includes experimental studies on the prevention of tissue adhesion that develops after surgery. However, these studies mainly address intra-abdominal adhesions, and studies evaluating the changes in the neck structures after thyroidectomy are very limited.

Hypericum species include plants that have been known for about 2,000 years and are widely used for medicinal purposes, and there are studies that evaluate the effectiveness of H. perforatum for wound healing as well as its antidepressant, anti-inflammatory, and antibacterial properties. In our study, we also aimed to determine whether H. perforatum, which is thought to be effective on wound healing, has traditionally been used by the public, and of which species are endemic in our country, had a positive effect on preventing the formation of tissue adhesions after thyroidectomy.

Materials and Methods

The study was conducted in Giresun University Experimental Research and Animal Laboratory after approval was obtained from the Giresun University Experimental Animals Ethics Board (approval no: 2020/27). In the study, 24 male Wistar-Albino rats, four-to-six months of age, with adult weights ranging from 250–300 g were used. The rats were kept in separate cages and followed up on a 12-hour day-night cycle, keeping the temperature at 20–22^{0}C. During the experiment, the animals were given standard rat chow and water and were cared for according to the principles of the National Institutes of Health publication, “Guide for Care and Use of Laboratory Animals”.

Surgery

The rats were anesthetized by intraperitoneal administration of 80 mg/kg ketamine (Ketalar, Pfizer, Turkey) and 10 mg/kg xylasine hydrochloride (Rompun, Bayer, Turkey). The neck of each rat was cleaned with 10% povidone-iodine solution, and all surgical procedures were performed under aseptic conditions. The thyroid lodge was entered with a 2 cm horizontal incision in the midline of the necks of the rats. Subtotal thyroidectomy was performed after reaching the trachea by lateralizing the submaxillary glands and muscle tissues (Figure 1). The rats were randomized into three groups:

Group 1: Control group (after subtotal thyroidectomy, the surgical sites were closed without any material being placed in them).

Group 2: Olive oil group (1 ml of pure olive oil was added to the surgical sites. Hypericium perforatum oil was obtained through a maceration method, by putting the plant in a jar containing pure olive oil and draining it for a certain period of time. With this group, the effectiveness of pure olive oil on tissue adhesion formation was measured without the effect of the H. perforatum plant).

Group 3: Hypericium perforatum group (1 ml of H. perforatum oil was added to the surgical site, and the efficiency of the H. perforatum plant for the formation of tissue adhesion was measured using this group). After the procedure, the muscle and gland structures were placed in their normal positions, and the skin was closed with non-absorbable 5/0 polyprolene sutures. On the postoperative day 14, the rats were sacrificed, and tissue adhesion was evaluated macroscopically. After this evaluation, the thyroid and surrounding tissues were removed en bloc, including the trachea and strep muscles, for histopathological examination.

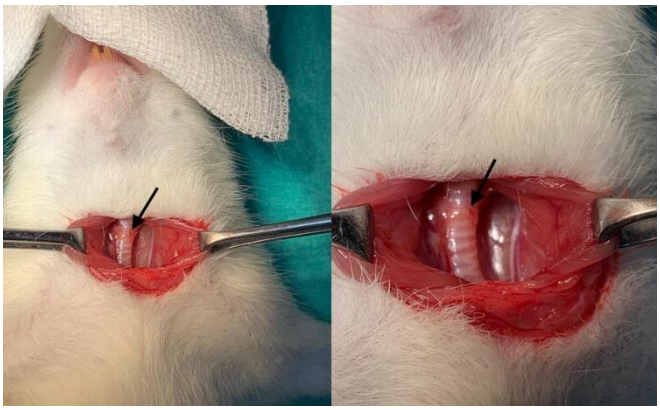
Macroscopic examination

The type of adhesion for each rat was scored by a surgeon who did not know the groups and was a different surgeon from the one who had performed the procedures, according to the scoring described by Zühlke et al. (5) (Table 1). Thus, the extent and nature of adhesions were evaluated.

Table 1. Evaluation of adhesion (Zühlke et al.)

Type	Definition
1	Firmly adhesion which can be easily separated by blunt dissection
2	Hard adhesion which can be separated by blunt dissection and partial sharp dissection at the start of vascularization
3	Strong vascularized adhesion which can be separated by only sharp dissection
4	Very strong adhesion which can be separated only by sharp dissection causing damage on organs

Figure 1. Images of surgical plane and trachea with strap muscles, arrow shows thyroid gland



Histopathological examination

The histopathological examinations were evaluated blindly by a pathologist. All of the samples that were extracted were placed in separate boxes and fixed in 10% buffered formaldehyde solutions for 48 hours. The samples were then placed in separate cassettes and embedded in paraffin after tissue follow-up. Five micron sections were prepared and stained with Hemotoxylin-Eosin (H&E) and evaluated under light microscope in terms of fibrosis, fibroblast, collagen, granulation tissue, histiocyte, giant cell, chronic inflammation, polymorphonuclear leukocyte, erythrocyte extravasation and vascular proliferation parameters. Granulation tissue, histiocyte, giant cell, chronic inflammation, polymorphonuclear leukocyte and fibroblast parameters were evaluated as criteria in terms of 'foreign body reaction'; fibrosis, fibroblast and collagen were evaluated as criteria in terms of 'adhesion formation'; and erythrocyte extravasation was evaluated as criterion in terms of 'presence of bleeding'. Fibrosis scores were determined by using a semi-quantitative scale by the pathologist (Table 2). Other parameters such as fibroblast, collagen, granulation tissue, histiocyte, giant cell, chronic inflammation, polymorphonuclear leukocyte, erythrocyte extravasation and vascular proliferation were scored with a separate scale as 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Figure 2 and 3 show the microscopy images of histopathological analysis.

Table 2. Scale for microscopic assessment of fibrosis

Grade	Histopathological Signs
0	No fibrosis
1	Thin bunches of a cellular fibrosis
2	Wide areas of fibrosis with reduced vascularization
3	Areas of fibrosis formed by thick bunch of collagen

Figure 2. Microscopy images of histopathological analysis: (a) Grade 1 fibrosis and chronic inflammation (H&Ex20), * indicates cartilage (b) Grade 3 fibrosis and chronic inflammation (H&Ex10), (c) Grade 2 fibrosis and chronic inflammation (H&Ex20) and (d) Granulomatous reaction (H&Ex40), arrow shows foreign-body giant cell

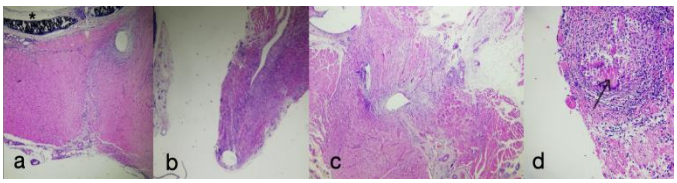
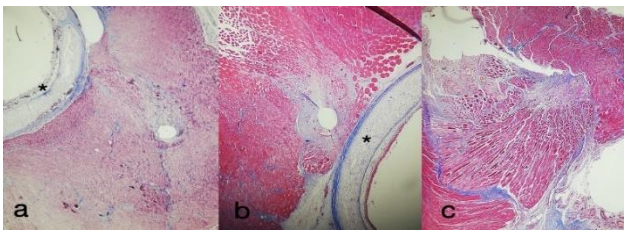


Figure 3. Microscopy images of histopathological analysis: (a) Grade 1 fibrosis (MTx40), (b) Grade 2 fibrosis (MTx40), and (c) Grade 3 fibrosis (MTx40), * indicates cartilage in all images



Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS for Windows, Version 15.0, Chicago, Illinois). Kruskal-Wallis and Mann-Whitney U tests corrected with Bonferroni were used. A value of $p < 0.05$ was regarded as significant.

Results

There was no statistically significant difference between the groups in terms of the type and degree of adhesion, macroscopically. Average scores were calculated for each of the histopathological parameters in each group (Table 3). The mean scores of collagen and chronic inflammation parameters were statistically lower in the olive oil group compared to the control and H. Perforatum oil groups ($p<0.05$). A point of interest to us was that in all three groups, severe vascular proliferation was observed in all rats, erythrocyte extravasation was found in all rats in the control group, while it was found to be lower in the other treatment groups without reaching statistical significance. In other parameters, no statistically significant difference was found between the groups.

Table 3. Scores for histopathologic parameters in the groups

Histopathologic Feature	Control (n= 8)	Olive Oil (n = 8)	H. Perforatum Oil (n=8)
Fibrosis	1,75 ± 0,70	2,37 ± 0,51	2,25 ± 0,88
Collagen	2,12 ± 0,35	2,87 ± 0,35[a]	2,50 ± 0,75
Granulation	2,37 ± 0,51	2,75 ± 0,46	2,62 ± 0,74
Histiocyte	2,87 ± 0,35	2,75 ± 0,46	2,62 ± 0,74
Giant cell reaction	2,62 ± 0,51	2,62 ± 0,51	2,62 ± 0,74
Chronic inflammation	2,87 ± 0,35	2,00 ± 0,75[a]	2,50 ± 0,75
PMNL	0,37 ± 1,06	0,00 ± 0,00	0,37 ± 1,06
Eritrocyte extravasation	3,00 ± 0,00	2,25 ± 0,88	2,37 ± 0,74
Vascular proliferation	3,00 ± 0,00	3,00 ± 0,00	3,00 ± 0,00

Values are given as mean ± standard deviation.

[a]$p < 0,05$; significant when compared with Control group.

Discussion

Adhesion is the formation of abnormal fibrotic connections between tissues and organs as a result of inflammatory events, such as surgical trauma, infection, and bleeding. It is one of the most common problems in modern surgery. Although minimally invasive techniques are adopted to reduce trauma, which is a cause of adhesions and may occur during surgical procedures, surgical techniques are not sufficient to reduce postoperative adhesions and related complications (6).

Many drugs and adhesion barriers have been developed to prevent or minimize postoperative adhesions. Although these substances have been shown to reduce intra-abdominal adhesions in animal models, very few of them can be used in clinical practice because of their potential side effects (7, 8).

Most studies aimed at preventing postoperative adhesion aim to prevent conditions such as intra-abdominal adhesions, intestinal obstruction, and infertility (9, 10). Adhesions at the surgical site after thyroid surgeries also pose a significant problem. Although there are relatively few indications for re-operative thyroid surgery, it is a difficult surgery to perform. The risk of major complications, such as recurrent laryngeal nerve injury and permanent hypoparathyroidism, increases because of fibrosis, scar tissue formation, and deterioration of the normal anatomy. In addition, adhesions that develop after thyroid surgery cause some neck dysfunctions, such as pulling sensation during neck extension or swallowing difficulty.

In the literature, there are limited clinical (11) and experimental studies on preventing adhesions after thyroid surgery (12-15). In one such study, Yiğit et al. evaluated the effectiveness of the anti-adhesive barriers Seprafilm® (Genzyme Corporation, USA) and Interceed® (Jonhson & Jonhson, USA) and found that both these materials improved the parameters affecting fibrosis histopathologically (12). Hypericium species have been used by the public as healing herbs for centuries. These herbs have several medicinal effects because of their high metabolite content.

H. perforatum (HP) oil, which is widely used in Turkish traditional medicine, is produced from olive oil using the maceration method. The flowers of the plant are collected and placed in a jar containing pure olive oil at a 1:5 ratio. The mixture is shaken at regular intervals and kept under sunlight for 15 days. At the end of this period, the mixture is filtered through cotton. While this homemade mixture is topically used for dermal damage and wounds, it is orally used for stomach diseases and as an antidepressant because of its sedative effect. Many experimental and clinical studies have evaluated the effects of HP oil on wound healing (16-20). These studies have revealed that HP oil increases epithelialization in the early period of primary and secondary wound healing (16, 18). Another experimental study evaluating the effects of topical application of HP oil on wound healing did not demonstrate a positive effect of HP oil on wound healing in the palatal mucosa of rabbits in comparison with olive oil, the main ingredient of HP oil; however, it revealed that HP oil could be effective in the late periods of wound healing (21).

Similarly, in their clinical study, Samadi et al. found that HP oil reduced scar formation after cesarean section in 144 women (22). Abnormal peritoneal healing and adhesion formation due to insufficient fibrinolytic activity can occur during the wound healing process. The sequence of events that initiate adhesion begins with the induction of an inflammatory response by peritoneal trauma caused by mechanical, chemical, or thermal factors or foreign bodies. Thromboplastin (tissue factor) is released along with inflammatory mediators into the wound site, initiating the coagulation process that results in fibrin formation. If fibrin is not sufficiently degraded, a fibrotic condition occurs. This is followed by the migration of fibroblasts to the wound site, collagen accumulation, edema, and the formation of granulation tissue with small blood vessels, and subsequently, tough adhesions (23).

Anti-inflammatory drugs have been used to suppress inflammatory reactions at the wound site in order to prevent peritoneal adhesions. We aimed to evaluate the effect of HP oil, which is known for its anti-inflammatory properties and wound healing effects, on adhesion formation in a thyroidectomy model.

Fibroblasts play an important role in the proliferative phase of wound healing that ends with scar formation. They also play a role in the synthesis of collagen and other adhesion molecules. Flavonoids and xanthones present in H. perforatum increase the percentage of fibroblasts and the stimulation of collagen synthesis and affect epithelial cell proliferation and migration (24).

To our knowledge, in the literature, there is no study on the effect of HP oil on adhesion formation in a thyroidectomy model. Only one study evaluated the effect of HP oil on adhesion; in this study, the researchers assessed the effects of HP oil on intra-abdominal adhesion formation but could not find any beneficial effect (25). In the present study, macroscopic examination of the effect of HP oil on adhesion formation in the experimental thyroidectomy model revealed no beneficial effects in terms of histopathological parameters in comparison with the other groups.

The present study has some limitations. As HP oil was topically applied to evaluate its effectiveness in preventing adhesions, we were unable to determine its properties for systemic use. Another limitation was related to the timing of adhesion formation and the assessment period. As it has been frequently used in intra-abdominal adhesion models, we planned to perform the assessment in terms of adhesion formation on the 14th day; however, this period may have been insufficient. Longer periods may be needed to evaluate the effectiveness of HP oil in preventing adhesions, especially in terms of histopathological parameters.

A substance effective in preventing adhesion formation after thyroidectomy will be useful in preventing many complications, considering that this is a common surgery. We believe that more studies will be needed in the future for this purpose.

References

1. Shaha AR. Revision thyroid surgery–technical considerations. Otolaryngologic Clinics of North America. 2008;41(6):1169-83.
2. Hardman JC, Smith J, Nankivell P, Sharma N, Watkinson J. Re-operative thyroid surgery: a 20-year prospective cohort study at a tertiary referral centre. European Archives of Oto-Rhino-Laryngology. 2015;272(6):1503-8.
3. Wilson DB, Staren ED, Prinz RA, McHenry C, DeJong SA. Thyroid reoperations: Indications and risks/Discussion. Am Surg. 1998;64(7):674.
4. Chao T-C, Jeng L-B, Lin J-D, Chen M-F. Reoperative thyroid surgery. World journal of surgery. 1997;21(6):644-7.
5. Zühlke HV, Lorenz EM, Straub EM, Savvas V. [Pathophysiology and classification of adhesions]. Langenbecks Arch Chir Suppl II Verh Dtsch Ges Chir. 1990:1009-16.
6. Liakakos T, Thomakos N, Fine PM, Dervenis C, Young RL. Peritoneal adhesions: etiology, pathophysiology, and clinical significance. Digestive surgery. 2001;18(4):260-73.
7. Yeo Y, Highley CB, Bellas E, Ito T, Marini R, Langer R, et al. In situ cross-linkable hyaluronic acid hydrogels prevent post-operative abdominal adhesions in a rabbit model. Biomaterials. 2006;27(27):4698-705.
8. Song Z, Zhang Y, Shao H, Ying Y, Mei L, Ma X, et al. Effect of xanthan gum on the prevention of intra-abdominal adhesion in rats. International journal of biological macromolecules. 2019;126:531-8.
9. Hellebrekers BW, Trimbos-Kemper TC, Trimbos JBM, Emeis JJ, Kooistra T. Use of fibrinolytic agents in the prevention of postoperative adhesion formation. Fertility and sterility. 2000;74(2):203-12.
10. Tokita Y, Satoh K, Sakaguchi M, Endoh Y, Mori I, Yuzurihara M, et al. The preventive effect of Daikenchuto on postoperative adhesion-induced intestinal obstruction in rats. Inflammopharmacology. 2007;15(2):65-6.
11. Chung YS, Lee KE, Kim HY, Choe J-H, Youn Y-K, Park WS, et al. Anti-adhesive effect and safety of sodium hyaluronate and sodium carboxymethyl cellulose solution in thyroid surgery. Asian Journal of Surgery. 2010;33(1):25-30.
12. Yigit O, Uslu Coskun B, Coskun H, Yilmaz B, Alkan S, Cinar U, et al. Efficacy Of Anti-Adhesive Barriers in Secondary Thyroidectomy: An Experimental Study. The laryngoscope. 2004;114(9):1668-73.
13. Cimen SG, Atila K, Cimen S, Sozmen MK, Canda T. Impact of polyethylene glycol and dextran 70 treatment on adhesion formation after subtotal thyroidectomy. Int J Surg Res. 2013;2:8-12.
14. Makay O, Isik D, Erol V, Yenisey C, Kose T, Icoz G, et al. Efficacy of simvastatin in reducing postoperative adhesions after thyroidectomy: an experimental study. Acta Chirurgica Belgica. 2017;117(2):77-83.
15. Idiz O, Aysan E, Firat D, Ersoy YE, Cengiz MB, Akbulut H, et al. Efficacy of glycerol and flax seed oil as anti-adhesive barriers after thyroidectomy. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2014;20:1090.
16. Altıparmak M, Eskitaşçıoğlu T. Comparison of systemic and topical Hypericum perforatum on diabetic surgical wounds. Journal of Investigative Surgery. 2018;31(1):29-37.
17. Arsić I, Žugić A, Tadić V, Tasić-Kostov M, Mišić D, Primorac M, et al. Estimation of dermatological application of creams with St. John's Wort oil extracts. Molecules. 2012;17(1):275-94.
18. Süntar I, Akkol EK, Keleş H, Oktem A, Başer KHC, Yeşilada E. A novel wound healing ointment: a formulation of Hypericum perforatum oil and sage and oregano essential oils based on traditional Turkish knowledge. Journal of ethnopharmacology. 2011;134(1):89-96.
19. Farsak M, Özdağli G, Özmüş D, Çömelekoğlu Ü, Yalın S, Gen R, et al. Effects of Hypericum perforatum on an Experimentally Induced Diabetic Wound in a Rat Model. Wounds: a Compendium of Clinical Research and Practice. 2017;29(2):E10-E7.
20. Gul MO, Akyuz C, Sunamak O, Ogunc AV, Sehirli AO. Effects of Saint John's Wort extract on intestinal injury and apoptosis. Annals of Medical Research. 2021;28(9):1725-30.
21. Gunpinar S, Kilic OA, Duran I, Tosun M, Firat T, Soyler G. Evaluation of the effect of topical Hypericum perforatum oil on excisional palatal wound healing in rabbits. Journal of Investigative Surgery. 2018.
22. Samadi S, Khadivzadeh T, Emami A, Moosavi NS, Tafaghodi M, Behnam HR. The effect of Hypericum perforatum on the wound healing and scar of cesarean. The Journal of Alternative and Complementary Medicine. 2010;16(1):113-7.
23. Nayak S, Nalabothu P, Sandiford S, Bhogadi V, Adogwa A. Evaluation of wound healing activity of Allamanda cathartica. L. and Laurus nobilis. L. extracts on rats. BMC complementary and alternative medicine. 2006;6(1):12.
24. Öztürk N, Korkmaz S, Öztürk Y. Wound-healing activity of St. John's Wort (Hypericum perforatum L.) on chicken embryonic fibroblasts. Journal of ethnopharmacology. 2007;111(1):33-9.
25. Hızlı D, Hızlı F, Köşüş A, Yılmaz S, KöŞüŞ N, Haltaş H, et al. Effect of Hypericum perforatum on intraperitoneal adhesion formation in rats. Archives of medical science: AMS. 2014;10(2):396.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2):94-100

Factors Affecting the Cost of Emergency Service in Occupational Injuries Applying to the Emergency Department

Acil Servise Başvuran İş Kazalarında Acil Servisteki Maliyete Etki Eden Faktörler

Mustafa Oguz TUĞCAN*0000-0002-1200-9198
Önder YEŞİLOĞLU0000-0003-0149-8456**
Arif AKSU*0000-0001-8987-0640
Yagmur TUĞCAN*0000-0002-9112-5030**
Ali İlker ÖZER* 0000-0002-8884-1650
Ozan DEMİR* 0000-0001-5713-0496
Akkan AVCI* 0000-0002-4627-0909

* Health Science University, Adana City Research and Training Hospital, Department of Emergency Medicine, Adana, Turkey
** Gaziantep 25 Aralik State Hospital, Emergency Medicine Clinic, Gaziantep, Turkey
***Cukurova University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Adana, Turkey

***Corresponding Author:** Mustafa Oguz TUGCAN
Health Science University, Adana City Research and Training Hospital, Department of Emergency Medicine, Adana, Turkey
e-mail: oguztugcan@gmail.com

Geliş Tarihi: 17/03/2022
Kabul Tarihi: 27/05/2022

Öz

Amaç: İş kazaları, hem tıbbi hem de diğer giderler nedeniyle bireysel işletmelere yılda önemli ölçüde mali yük getirebilir. Bu çalışmada, iş kazası nedeniyle hastaneye başvuran hastaların mesleki yaralanmalarının finansal maliyeti ile komorbid bozuklukları arasındaki ilişkiyi araştırmayı amaçladık.

Materyal-metot: Çalışma retrospektif gözlemsel vaka serisi olarak yapıldı. İşyerinde çalışırken, yöneticileri tarafından görevlendirilerek işyerinden başka bir yerde iken veya işyerine giderken gerçekleşen yaralanma nedeni ile başvuran 18 yaş ve üzeri yedi yüz üç hasta çalışmaya dahil edildi.

Bulgular: Acil servise iş kazası nedeniyle başvuran yedi yüz üç hasta çalışmaya dahil edildi. Yüzde otuz hastada (n=211) en az bir komorbidite vardı. En az bir komorbiditesi olan hastalarda en sık görülen komorbidite görme sorunlarıydı. Diabetes mellitus varlığının 7,2 (OR=7,180; %95 CI: 1,366-37,743) kat, künt yaralanma varlığının 1,7 (OR= 1,157; % 95CI: 1,157-2,351) kat ve diğer yaralanmaların varlığı 16.2 (OR= 16.222, %95 GA: 1.800-146.195) hasta maliyetlerini artırdığı tespit edildi (p<0.05).

Sonuç: Her bir komorbid hastalık ile mesleki yaralanmaların maliyet sonuçları arasındaki ilişkiyi belirleyerek, ek araştırmalar yapılabilir ve farklı hasta gruplarını hedefleyen daha iyi eğitim programları uygulanabilir.

Anahtar Kelimeler: Maliyet; mesleki yaralanmalar; komorbidite; acil tıp.

Abstract

Background: Workplace injuries can cause individual businesses significant financial burden per year in due to both medical and other expenses. In this paper we discuss the link between financial cost of occupational injuries and comorbid disorders of patients admitted to the hospital because of the workplace related trauma.

Methods: The study was performed as a retrospective observational case series. Seven hundered and three patients aged 18 and over who applied to the emergency department of our hospital with occupational injuries where at work or on the way to work or somewhere other than the workplace as appointed by the manager or were included in the study.

Results: Seven hundered and three patients who applied to the emergency department due to occupational injuries were included in the study. Thirty percent patient (n=211) had at least one comorbidity. The most common comorbidity among patients with at least one comorbidity was vision problems. It was determined that the presence of diabetes mellitus has an effect of 7.2 (OR=7,180; %95 CI: 1,366-37,743) times, the presence of blunt injury 1.7 (OR= 1,157; % 95CI: 1,157-2,351) times, and the presence of other injuries 16.2 (OR= 16,222, %95 CI: 1,800-146,195) times increasing the costs of the patients (p<0.05)

Conclusion: Identifying the association between each comorbid disease and cost outcomes of occupational injuries, additional research can be conducted and better educational programs targeting different patient groups can be implemented.

Keywords: Cost; occupational injuries; comorbidity; emergency medicine

Introduction

Workplace injuries can cause individual businesses significant financial burden per year in due to both medical and other expenses. Estimates presented by European Agency for Safety and Health at Work (EU-OSHA) together with the International Labour Organization for the cost of occupational injuries and ilnesses show a global cost of 2 680 billion euros, which is 3.9 % of global GDP [(1)]. There are a number of studies amongst different countries conducted with national and regional data to help identify the elements influencing cost consequences of occupational accidents. Last year alone, there were 10.89 workers per 1.000.000 working hours and 2.45 workers per 100 full time workers suffered workplace injuries in Turkey, showing the pressing need to identify the causes and factors possibly associated with these alarming rates [(2)]. Comorbid conditions, with their potential complications like sensory impairment and sudden incapacitation, might result in traumatic injuries and, as a result, higher costs. While workplace norms have custom job prospects and impose special regulations for employees with comorbid disorders such as diabetes mellitus, the financial impact of these workers' injuries is yet unknown. In this paper we discuss the link between financial cost of occupational injuries and comorbid disorders of patients admitted to the hospital because of the workplace related trauma.

Material and Method

The study was initiated after the approval of the XXXXX Training and Research Hospital Non-Invasive Clinical Research Ethics Committee.

Seven hundered and three patients aged 18 and over who applied to the emergency department of our hospital with occupational injuries where at work or on the way to work or somewhere other than the workplace as appointed by the manager or were included in the study. Patients younger than 18 years of age and whose information could not be reached were not included.

The study was performed as a retrospective observational case series. The files of the patients in the emergency department, consultation notes in the hospital system and reports of occupational injuries were reviewed retrospectively. We recorded the demographic data (age, gender), additional diseases, health insurance, outcomes in the emergency department, whether they had emergency surgery, the department they were hospitalized, the time they spent in these clinic, the outcomes of the inpatient, the total service costs in the hospital system throughout this process of the cases.

In addition, we looked that Injury mechanisms, body parts affected by this accident, types of imaging performed in the emergency department.

Statistical Evaluation

SPSS 23.0 package program was used for statistical analysis of the data. Categorical measurements are summarized in terms of “numbers and percentages”. On the other hand, “mean, deviation, and minimum-maximum” are used for continuous measurements. Pearson's Chi-squared test was used to compare categorical variables. Multiple logistic regression model was used to determine the factors affecting the cost. The statistical significance level was taken as 0,05 for all tests.

Results

Seven hundered and three patients who applied to the emergency department due to occupational injuries were included in the study. Eighty-five point six (n=602) of the patients were male and 14.4% (n=101) were female. Seventy percent (n=492) of the applied patients did not have a comorbidity, 30.0% (n=211) had at least one comorbidity. The most common comorbidity among patients with at least one comorbidity was vision problems (%33.2, n=70) (Table 1).

Injury mechanisms were examined: the most common was blunt injuries 64% (n=446) (Injuries in the blunt injury group are being caught/squeezed into a machine, heavy object falling on body, hitting any part of the body against any somewhere, stuck any part of the body between two object, falling from own level, falling from high, falling of an object to the extremity, sprains, straining, traffic accident, beating). 24% (n=171) of all injuries were in the penetrating injury group (Injuries in the penetrating injury group are; injuries by cutting/penerating tools, cutting the eye, firearm injuries), 12% (n=86) of the patients were in the other injuries group (Injuries in the other injury group are; biological agent exposure, caustic substance exposure, burn, non-traumatic causes, animal bites, electric shock, other) (Table 1).

Table 1. Distribution of Patients by Gender, Presence of Comorbidity and Mechanism of Injury

	Frequency (n)	Percentage (%)
Sex		
Male	602	85,6
Female	101	14,4
Comorbidity		
No	492	70,0
Yes	211	30,0
Comorbidites		
Dibetes Mellitus	15	7,1
Hypertension	17	8,1
Coronary Artery Disease	17	8,1
Chronic Obstructive Pulmonary Disease	3	1,4
Asthma	21	10,0
Visual Disorders	70	33,2
Hearing Disorders	3	1,4
Renal Colic	46	21,8
Anxiety	15	7,1
Vertigo	34	16,1
Migraine	14	6,6
Epilepsy	4	1,9
Other	23	10,9
Injury Mechanisms		
Penetrating injuries	171	24
Blunt injuries	446	64
Other injuries	86	12

The most frequently injured body part was extremity injuries(67.4%, n=474). The rates of other injuries were as follows; 15.5% (n=109) head injuries, 13.2% (n=93) eye injuries, 7.7% (n=54) spinal injuries, 7% (n=49) thoracic injuries, 2% .4 (n=17) abdominal injuries, 2.3% (n=16) pelvis injuries, 1.3% (n=9) neck injuries. No imaging was performed in 29% (n=204) of the patients. Only direct radiographs were taken in 39.8% (n=280) patients. Only ultrasonography was performed on 0.4% (n=3) patients. Only computed tomography was performed in 12.8% (n=90) of them. Both direct radiography and computed tomography were performed on 17.8% (n=125) patients. Both direct radiography and ultrasonography were performed to 0.1% (n=1) patients (Table 2).

Table 2. Distribution of Patients' Affected Body Part and Imaging Tests

	Frequency (n)	Percentage (%)
Affected Body Part		
Head	109	15,5
Neck	9	1,3
Thoracic	49	7,0
Abdomen	17	2,4
Pelvis	16	2,3
Eyes	93	13,2
Spinal	54	7,7
Extremities	474	67,4
Other	3	0,4
Imaging Tests		
N/A	204	29,0
Direct Radiography(DG)	280	39,8
ULTRASOUND(USG)	3	0,4
Computed Tomography(CT)	90	12,8
DG + CT	125	17,8
DG + USG	1	0,1

Ninety point nine percent (90.9%, n=639) of the patients who applied to the emergency department were discharged from the hospital, 6.5% (n=46) of the patients were hospitalized, 1.3% (n=9) of the patients were referred to an external center because they need to be hospitalized or need an emergency operation, 1.1% (n=8) did not accept the treatment and left the emergency room without permission, 0.1% (n=1) of the patients died in the emergency department. 93.5% (n=657) of the patients were discharged from emergency department. Among the hospitalized patients, the most hospitalization was given to the orthopedics department (39%, n=18). Sixty-five percent of the inpatients (n=30) were admitted to the service, 35% (n=16) of the inpatients were admitted to the intensive care unit. Four point six percent of the patients (n=32) who applied were operated in our hospital. Ninety-eight percent (n=45) of the hospitalized patients were discharged, and 2% (n=1) died (Table 3).

Table 3. Outcomes of the Patients

	Frequency (n)	Percentage (%)
Outcome in Emergency Department		
Discharged	639	90,9
Hospitalized	46	6,5
Sent to Another Hospital	9	1,3
Refused Treatment	8	1,1
Exitus	1	0,1
Department of Hospitalization		
Orthopedics and traumatology	18	2,6
General Surgery	4	0,6
Brain and Nerve Surgery	7	1,0
Thoracic Surgery	2	0,3
Burn Unit	4	0,6
Otorhinolaryngoloji	1	0,1
Plastic and Reconstruction Surgery	1	0,1
Ophthalmology	7	1,0
Anesthesiology and Reanimation	1	0,1
Cardiovasculer Surgery	1	0,1
Type of Unit Hospitalized		
Service	30	65
Intensive Care Unit	16	35
Has The Patient Had Surgery?		
No	670	95,3
Yes	32	4,6
The Patient's Outcome In The Hospitalization Department		
Discharged	45	98
Exitus	1	2
	Avg±sd	**Med (Min-Maks)**
Time of Stay of The Patient In The Hospital	0,55±5,0	0 (0-105)
Cost	137,9±233,5	69,5 (14,6-3443,9)

The cost findings of the patients were analyzed in two different groups as the median value <69.5 and ≥69.5. The parameters in table 4 were included in the cost-increasing factors in the examination.

According to our analysis; It was determined that the presence of diabetes mellitus has an effect of 7.2 (OR=7,180; %95 CI: 1,366-37,743) times, the presence of blunt injury 1.7 (OR= 1,157; % 95CI: 1,157-2,351) times, and the presence of other injuries 16.2 (OR= 16,222, %95 CI: 1,800-146,195) times increasing the costs of the patients (p<0.05) (Table 4).

Table 4. Analysis of Factors Affecting Cost in Emergency Service

	B	S.E.	Wald	df	p	Odd Ratio	95% C.I.for EXP(B)	
							Lower	Upper
Sex (Female)	-,390	,234	2,778	1	0,096	,677	,428	1,071
Presence of Comorbidity	-,040	,412	,010	1	0,922	,960	,429	2,152
Presence of Dibetes Mellitus	1,971	,847	5,420	1	**0,020***	7,180	1,366	37,743
Presence of Hypertension	1,357	,709	3,657	1	0,056	3,883	,967	15,597
Presence of Coronary Artery Disease	,092	,607	,023	1	0,879	1,097	,334	3,607
Presence of COPD	-,892	1,691	,278	1	0,598	,410	,015	11,270
Presence of Asthma	-,268	,552	,236	1	0,627	,765	,259	2,257
Presence of Visual Disorders	-,053	,447	,014	1	0,906	,949	,395	2,277
Presence of Hearing Disorders	-1,561	1,556	1,007	1	0,316	,210	,010	4,428
Presence of Renal Colic	-,116	,444	,068	1	0,794	,890	,373	2,127
Presence of Anxiety	,507	,635	,638	1	0,424	1,660	,479	5,759
Presence of Vertigo	,032	,495	,004	1	0,949	1,032	,392	2,722
Presence of Migraine	,129	,621	,043	1	0,836	1,138	,337	3,840
Presence of Epilepsy	-1,142	1,302	,769	1	0,380	,319	,025	4,096
Presence of Other	1,008	,598	2,838	1	0,092	2,740	,848	8,851
Penetrating Injuries			12,194	2	**0,002****			
Blunt Injuries	,500	,181	7,647	1	**0,006****	1,649	1,157	2,351
Other Injuries	2,786	1,122	6,170	1	**0,013***	16,222	1,800	146,195
Constant	1,216	1,481	,674	1	0,412	3,373		

* p<0,05, **p<0,001, a. Variable(s) entered on step 1: COPD: Chronic Obstructive Pulmonary Disease

Discussion

Work-related injuries can impose significant costs on employers, bussinesses and the government, causing a major economical impact on the whole community. In order to create proper prevention measures and allocate limited health-care resources, a thorough understanding of injury costs must be necessitated. In the year 2020 alone, the number of occupational accidents occurred in Turkey is approximately 384.000, with almost three million and half work days lost as result [(2)]. Due to the evaluation of different cost components and varied methodologies used, comparing the costs of work related injuries in Turkey with statistics of other countries would not be fruitful, but given about 270 million work-related injuries and almost two million deaths occur worldwide each year [(3)], studies evaluating the work related injuries from both developed and developing countries are needed. While literature research shows there are numerous studies focusing on financial burden of work-related injuries, few of these evaluate a possible association between injury costs and ongoing chronical illness of the injured employee. From most common comorbid diseases such as diabetes mellitus and hypertension to neurological and sensorial disorders, many chronic condition has the potential to cause temporary incapacity in the workplace. Therefore, in our study we aimed to investigate the relationship between financial burden of occupational injuries and comorbid diseases in patients admitted to the hospital due to occupational injuries.

There are a number of factors influence the cost claims of occupational injuries; type of injury and demographical variables are just a few of them. Back, knee, and shoulder injuries are suggested as the most expensive single injury types with high frequency and high average cost of workers' compensation claims in terms of percentage across all claims, according to Mroz et al [(4)]. Results of our study regarding injury types also showed that bone and soft tissue trauma of extremities as the most common injury zones, and the inpatient clinic with the highest hospitalization ratio was the orthopedic and traumatology ward. Injured workers included in our study also show a relatively similar distribution regarding injury mechanism compared with national statistical data [(2)], with most frequent injury type being contact with sharp points, followed by trappings and crushings. Vast majority of patients included in the study were male (85,6 %), and discharged from the hospital without need for hospitalization (93.5), again, consistent with yearly national work injury reports.

Our results showed no significant difference between any comorbidities and costs related to workplace injuries with the exception of patients with diabetes mellitus. While these results provide some reassurance, the cost and risk of injuries should be evaluated as seperate entities.

Our results showed no significant difference between any comorbidities and costs related to workplace injuries with the exception of patients with diabetes mellitus. While these results provide some reassurance, the cost and risk of injuries should be evaluated as seperate entities.

It's worth noting that eye illnesses and visual impairment (n=70) were the most frequent group of comorbid disorders among the employees in our survey, accounting for 33.2 percent of the total. We have found no statistically significant increase in occupational accident expenses in the patients with eye disorders. One reason for this result might be the requisite credentials, such as good visual acuity, in job categories that demand specialist workers such as law enforcement, driver, and vehicle operator, in order to qualify for the job in the first place.

It has been reported that hypertension has a detrimental impact on the outcomes of trauma patients brought to the hospital, with longer hospitalization days in the intensive care unit [(5)]. In another study, while the data is limited, cardiovascular diseases such as hypertension did not appear to be associated with increased risks **[(6)]**. There seem to be different outcomes regarding the injury risk of hypertensive patient, both inside the work environment and outside, but as far as literature search goes, no studies evaluate the link between hypertension and cost of occupational injuries. Our study suggests no statistical difference regarding costs of work related injuries between hypertensive patient and control group, however, relatively small (n=17) sample of patients with hypertension demonstrates the need for further studies.

Our research found no evidence of neurological disorders, even those with complications that can entail job loss and a has relatively higher risk of harm such as epilepsy, had any negative influence on costs. In a cohort study conducted by Cornaggia et al. with 600 epilepsy patients, writers suggest a 2.5 fold higher increase of occupational harm [(7)]. Meanwhile, a case-control study of 160 epilepsy patients found no evidence of injury caused directly by a seizure, and none of the patients had been consulted about epilepsy or its complications hundred days prior to injury, indicating that there is no statistically significant link between epilepsy and work-related injury [(8)]. Epilepsy is a cost effective disorder by itself. According to a systematic review about cost of epilepsy which includes studies from 13 countries over 17 years period, main contributers to direct costs of eplipesy are anti epileptic drugs and hospitalization related costs such as diagnostics, transportation, physician services and similar, while main culprit of indirect costs are productivity loss and work days lost due to unemployment and hospital visits and/or admissions **[(9)]**. Results vary among the different studies, but again work-related injuries are not taken into consideration as a seperate factor. The only comorbid disease in our study that had a statistically significant impact on direct expenses of patients with work-related injuries was diabetes mellitus. Literature review suggests diabetes is one of the comorbid conditions whose relationship with occupational injuries is better researched. Sprince et al. found that there was no increased risk for work related injury among employees with diabetes after conducting a survey with 195,284 adult employees over an eight-year period, with the exception of select subgroups such as patients who do not use insulin or oral medications and have had diabetes for at least 13 years **[(10)]**.

Li et al. conducted a similar study in the Canadian context, observing an association between diabetes and risk of experiencing a serious injury during working hours or traveling to and from work, in a retrospective analyze of yearly national cross-sectional survey results **[(11)]**.

Another study conducted with 1020 diabetes cases in Finland revealed different results according to genders, stating incidence of workplace injury in diabetic women is higher, and there was an association between insulin-treated diabetes and commuting injury in men **[(12)]**. Diabetes can cause further harm due to its various long term complications. Poor mobility, as well as cognitive and visual impairment, are one of the key risk factors for motor vehicle accidents in diabetic patients **[(13)]**. Peripheral nerve damage, visual impairment, and kidney dysfunction are also common risk factors related to fall injuries **[(14)]**. Despite the fact that the findings regarding the association between diabetes and workplace injuries show regional differences, different diabetic subgroups are emphasized to be at risk. Unlike some other comorbidities, diabetes in known to impair the immun system and tissue healing by a number of patophysiological pathways such as weakening structure of collagen by formation of advanced glycation end products (AGEs), erroneous down regulating of inflammation due to increased TNF levels, and increased levels of reactive oxygen species negatively effecting bone healing **[(15)]**. This in return can further impacting the medical costs by delaying the recovery period of the injured employee. Furthermore, hyopglicemia, a rather common and life-threatening complication of insulin or oral antidiabetic treatment, has a high risk of sudden incapacity and can be considered a workplace hazard by itself, with the potential to cause major traumatic injuries which could further increase medical costs. When assessing occupational risks in diabetic workers it's critical to conduct an individualized assessment of the worker and take hypoglycemic risk factors into account [(16)].

Limitations

One of the main limitations of our research is the absence of data regarding indirect costs. Direct costs included medical care such as payments for hospital, physician, allied health services and workers' compensation while indirect costs include wage and productivity losses, higher consumer prices, and nonworkers' compensation costs borne by the medical insurance systems. In our study, only direct costs are taken into account, however, based on factors taken into account, indirect costs can grossly outweigh medical claims **[(17)]**. Another important limitations on the analysis was the lack of information regarding management of comorbid diseases; since the risk of trauma can differ greatly according to how succesful these diseases is managed on patient level; such as compliance to medical treatment and physician recommendations, or frequency and severity of complications which may effect the cost outcomes.

Conclusion

While comorbidities are often pre-existing and not directly included in a claim, they can have a significant impact on claim costs and the injured employee's recovery. Diabetes mellitus seems to negatively effect these cost outcomes, with its complications not only pose significant burden as a risk factor for trauma, but also a heavy financial burden for the country economy In addition to lifestyle changes such as diet and exercise, these diabetic workers may also benefit from a number of workplace policy changes such as consistent meal times, more frequent breaks to eat and take medication, continuous monitoring of blood glucose levels, specifically tailored work shifts and job requirements, public awareness campaigns, and similar.

In conclusion, by identifying the association between each comorbid disease and cost outcomes of occupational injuries, additional research can be conducted and better educational programs targeting different patient groups can be implemented.

References

1. Elsler D, Takala J, Remes J. An international comparison of the cost of work-related accidents and illnesses. European Agency for Safety and Health at Work. 2017 September, ISSN: 1831-9343.
2. 2020 Yıllık Bölüm 3-1 İş Kazası ve Meslek Hastalığı İstatistikleri. http://www.sgk.gov.tr/wps/portal/sgk/tr/kurumsal/istatistik/sgk_istatistik_yilliklari
3. International Labour Organization. Safety in numbers: pointers for the global safety at work. Geneva; 2003.
4. Mroz TM, Carlini AR, Archer KR, Wegener ST, Hoolachan JI, Stiers W, Shore RA, Castillo RC. Frequency and cost of claims by injury type from a state workers' compensation fund from 1998 through 2008. Arch Phys Med Rehabil. 2014 Jun;95(6):1048-1054.e6. doi: 10.1016/j.apmr.2013.11.025. Epub 2014 Jan 28. PMID: 24480333.
5. Jaclyn N. Portelli Tremont, Brian Orleans, Paula D. Strassle, Elizabeth B. Dreesen, Michelle R. Brownstein, Hypertension in the Young Adult Trauma Population: Rethinking the Traditional "Incidentaloma", Journal of Surgical Research, Volume 256, 2020, Pages 439-448, ISSN 0022-4804, https://doi.org/10.1016/j.jss.2020.07.013.
6. K T palmer, E C harris, D coggon. Chronic health problems and risk of accidental injury in the workplace: A systematic literature review. Occup Environ Med. 2008 November ; 65(11): 757–764. doi:10.1136/oem.2007.037440.
7. Cornaggia CM, Beghi M, Moltrasio L, et al. Accidents at work among people with epilepsy. Results of a European prospective cohort study. Seizure. 2006; 15:313–319. [PubMed: 16632385]
8. Palmer KT, D'Angelo S, Harris EC, Linaker C, Coggon D. Epilepsy, diabetes mellitus and accidental injury at work. Occupational Medicine (Oxford, England). 2014 Sep;64(6):448-453. DOI: 10.1093/occmed/kqu079. PMID: 24964785; PMCID: PMC4431610.
9. Strzelczyk A, Reese JP, Dodel R, Hamer HM. Cost of epilepsy: a systematic review. Pharmacoeconomics. 2008;26(6):463-76. doi: 10.2165/00019053-200826060-00002. PMID: 18489198.
10. Sprince, Nancy L., et al. "Occupational Injuries Among Workers With Diabetes: The National Health Interview Survey, 1997-2005." *Journal of Occupational and Environmental Medicine*, vol. 50, no. 7, Lippincott Williams & Wilkins, 2008, pp. 804–08, http://www.jstor.org/stable/44997592.
11. Li AK, Nowrouzi-Kia B. Impact of Diabetes Mellitus on Occupational Health Outcomes in Canada. Int J Occup Environ Med. 2017 Apr;8(2):96-108. doi: 10.15171/ijoem.2017.992. PMID: 28432371; PMCID: PMC6679613.
12. Kouvonen A, Kivimäki M, Pentti J, Aalto V, Oksanen T, Virtanen M, Vahtera J. Diabetes and risk of occupational injury: a cohort study. Diabet Med. 2017 Nov;34(11):1629-1636. doi: 10.1111/dme.13423. Epub 2017 Aug 14. PMID: 28703867.
13. Seeger R, Lehmann R. Driving ability and fitness to drive in people with diabetes mellitus. *Ther Umsch.* 2011;68:249–52.
14. Schwartz AV, Hillier TA, Sellmeyer DE, Resnick HE, Gregg E, Ensrud KE, et al. Older women with diabetes have a higher risk of falls: A prospective study. *Diabetes Care.* 2002;25:1749–54.
15. Jiao H, Xiao E, Graves DT. Diabetes and Its Effect on Bone and Fracture Healing. *Curr Osteoporos Rep*. 2015;13(5):327-335. doi:10.1007/s11914-015-0286-8
16. Gerbo RM, Jin CF, Clark K. Diabetes in the Workplace: the Hazards of Hypoglycemia. Curr Diab Rep. 2019 Nov 4;19(11):119. doi: 10.1007/s11892-019-1234-2. PMID: 31686223.
17. Leigh JP. Economic burden of occupational injury and illness in the United States. Milbank Q. 2011 Dec;89(4):728-72. doi: 10.1111/j.1468-0009.2011.00648.x. PMID: 22188353; PMCID: PMC3250639.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 101-107

Covid-19 Pandemi Hastanesinde Görevli Sağlık Çalışanlarında Anksiyete, Uyku Kalitesi, Algılanan Sosyal Destek ve Çalışanların Stresle Başa Çıkma Tarzları Arasındaki İlişki

The Relationship Between Anxiety, Sleep Quality, Perceived Social Support and Coping Styles with Stress in Health Care Workers at the Covid-19 Pandemic Hospital

Nazan DOLAPOĞLU* 0000-0003-1400-7580
Rıza Gökçer TULACI ** 0000-0003-2113-5855
Adil Ozan GÖKUÇ * 0000-0001-6195-3823**

* Balıkesir Üniversitesi, Tıp Fakültesi Hastanesi, Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Balıkesir
** Sağlık Bilimleri Üniversitesi, Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Ankara
*** Özel Hekim, Balikesir

Yazışma Adresi: Nazan DOLAPOĞLU
Balıkesir Üniversitesi, Tıp Fakültesi Hastanesi,
Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Balıkesir
e-mail adresi: nazandolapoglu@yahoo.com

Geliş Tarihi: 20/04/2022
Kabul Tarihi: 20/07/2022

Öz

Giriş: Covid-19 salgını sırasında Türkiye'deki bir pandemi hastanesinde çalışan sağlık çalışanlarındaki anksiyete prevalansı ile uyku kalitesi, sosyal destek algısı ve stresle başa çıkma yöntemleri arasındaki ilişkiyi değerlendirmek amaçlanmıştır.

Gereç ve Yöntemler: 878 sağlık personeli çalışmaya alınmıştır. Verilerin toplanmasında sosyodemografik veri formu, Yaygın Anksiyete Bozukluğu Ölçeği (YAB-7), Pitsburg Uyku Kalitesi İndeksi (PUKİ), Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ), Stresle Başa Çıkma Tarzları Ölçeği (SBTÖ) kullanılmıştır.

Bulgular: Katılımcıların YAB-7'ye göre %13.2'sinde klinik olarak önemli derecede anksiyete belirtileri, PUKİ'ye göre %53.6'sında kötü uyku kalitesi saptandı. Çalışma arkadaşlarında Covid-19 tanısı olanlarda, geçmişte ruhsal hastalık öyküsü olanlarda, sosyal medyada Covid-19 ile ilişkili haberlerle ilgilenme süresi uzun olanlarda anksiyete puanı anlamlı derecede yüksekti. Hastaya direkt bakım veren grupta, Covid-19 şüphesi yaşayanlarda, yeterli kişisel koruyucu ekipmana sahip olmadığını düşünen çalışanlarda kötü uyku kalitesi oranı anlamlı olarak yüksekti. Katılımcıların anksiyete düzeyi arttıkça uyku kalitesinin bozulduğu saptandı. Belirgin anksiyetesi olan grupta algılanan sosyal destek daha düşük olarak saptandı. Algılanan sosyal destek arttıkça uyku kalitesi iyileşiyordu. Çalışanlar kullandıkları başa çıkma stilleri açısından karşılaştırıldığında klinik düzeyde belirgin anksiyetesi olanlarda çaresiz yaklaşım, klinik düzeyde belirgin anksiyetesi olmayanlarda ise kendine güvenli yaklaşım ve iyimser yaklaşım puanları yüksekti.

Sonuç: Sağlık personelinin korku ve kaygılarını direkt anlatabilecekleri psikolojik destek birimlerinin oluşturulması, çalışanlara stresle baş etme tekniklerine yönelik olarak eğitim verilmesi, hem çalışanların iyilik halinin sürdürülmesi hem de sağlık hizmetinin aksamadan yürütülmesi ve ayrıca gelecekteki olası pandemilerde yol gösterici olması açısından önemlidir.

Anahtar Kelimeler: Anksiyete; Covid-19; Uyku Kalitesi

Abstract

Introduction: It was aimed to evaluate the relationship between anxiety prevalence with sleep quality, perception of social support and methods of coping with stress during the Covid-19 outbreak in healthcare workers working in a pandemic hospital in Turkey.

Materials and Methods: 878 healthcare personnel were recruited. Sociodemographic data form, General Anxiety Disorder Scale (GAD-7), Pitsburg Sleep Quality Index (PSQI), Multidimensional Scale of Perceived Social Support (MSPSS) and Stress Coping Strategy Scale (SCSS) were used to collect data.

Results: Clinically significant anxiety symptoms were found in 13.2% of the participants according to GAD-7 and poor sleep quality was detected in 53.6% according to PSQI. The anxiety score was significantly higher in those who had a covid diagnosis in their colleagues, had a history of mental illness in the past, and spent a long time with covid-related news on social media. The rate of poor sleep quality was significantly higher in the group that provided direct patient care, having Covid-19 suspicion, employees who think that they did not have sufficient personal protective equipment. It was found that the sleep quality deteriorated as the anxiety of the participants increased. Perceived social support was found to be lower in the group with significant anxiety. Sleep quality was improved as perceived social support increased. When the employees were compared in terms of the coping styles they used, scores of helpless approach were higher in those with clinical significant anxiety and self-confident approach, optimistic approach scores were higher in those without clinical significant anxiety.

Conclusion: Establishing psychological support units where healthcare personnel can directly express their fears and anxieties, providing training on stress coping techniques are important for maintaining the well-being of employees and providing healthcare services without interruption.

Keywords: Anxiety; Covid-19; Sleep Quality

Giriş

Aralık 2019'da Çin'in Wuhan kentinde yeni bir koronavirüs salgını başladı. Daha sonra Çin'in diğer bölgelerine ve diğer ülkelere hızla yayıldı. 11 Mart 2020'de Dünya Sağlık Örgütü (WHO) tarafından Covid-19 pandemi olarak ilan edildi. Türkiye'de de ilk vaka aynı tarihte Sağlık Bakanlığı tarafından bildirildi (1).

Hastalığın yayılması, vaka sayısının hızla artması sağlık sistemleri için zorluklar yarattı. Covid-19 ile ilişkili morbidite ve mortalite oranlarının yüksek olması, enfekte olma riski, virüsü yakınlarına bulaştırma korkusu, meslektaşlarını kaybetme gerçeği, yorucu çalışma koşulları gibi stres faktörleri sağlık çalışanları için güçlükler oluşturdu (2).

Covid-19 salgını sırasında sağlık çalışanlarında, uykusuzluk, anksiyete, depresyon, somatizasyon bozukluğu ve obsesif-kompulsif bozuklukta yüksek yaygınlık oranları saptanmıştır (3).

Anksiyete, sağlık çalışanlarının bulaşıcı hastalık salgınları sırasında yaşadığı yaygın bir olumsuz duygudur. Uyku kalitesi sağlığın önemli bir göstergesidir ve bu açıdan anksiyetenin uyku kalitesi üzerindeki etkisi önceki çalışmalarla gösterilmiştir (4).

Ruhsal sağlık ve uyku kalitesi birçok sosyo-kültürel faktörden etkilenir. Sosyal destek algısı, insanların diğer kişilerden aldıklarını düşündüğü bakım ve desteği ifade eder. Yeterli sosyal desteğin ruhsal sağlık ve uyku işlevi üzerinde olumlu bir etkisi olduğu daha önce bildirilmiştir (5).

Stresle karşılaşıldığında, kişilerin stresle başa çıkma stilleri farklılık göstermektedir. Olumsuz başa çıkma stilleri anksiyete ve depresyon gibi ruhsal hastalıklarla ilişkili olabilir (6)

Biz bu çalışmada Covid-19 salgını sırasında Türkiye'deki bir pandemi hastanesinde sağlık çalışanlarının anksiyete prevalansı ile uyku kalitesi, sosyal destek algısı ve stresle başa çıkma yöntemleri arasındaki ilişkiyi değerlendirmeyi amaçladık.

Bu çalışmanın hipotezleri, pandemi döneminde sağlık çalışanlarında anksiyete prevalansında artış olacağı, uyku kalitesinde bozulmaya yol açacağı, algılanan sosyal desteğin artmasının ve olumlu başa çıkma stillerinin anksiyete ve uyku bozukluğu belirtilerinin azalması ile ilişkili olacağı şeklindedir.

Yöntem

Katılımcılar ve İşlem: Bu kesitsel çalışma 22 Haziran-22 Temmuz tarihleri arasında, bir pandemi hastanesinde görev yapan ve çalışmaya katılmak için gönüllü olan sağlık çalışanları ile gerçekleştirildi. Hastanedeki tüm bölümlerdeki çalışanlara birim sorumluları aracılığı ile ulaşıldı, çalışma ile ilgili bilgi verildi ve çalışmaya katılmak için gönüllü olan 900 sağlık çalışanı çalışma için değerlendirildi. Araştırmaya dahil olma kriterleri; 18-65 yaşları arasında olmak, aktif olarak görev yapıyor olmak ve dışlama kriterlerinin herhangi birisine sahip olmamak şeklinde belirlendi. Şizofreni, bipolar bozukluk, alkol ve madde kullanım bozukluğu olmak, multiple skleroz, son 3 ay içerisinde tekrarlayan nöbet geçiren epilepsi ve geçirilmiş serebrovasküler olay gibi ağır nörolojik bozukluğu olmak, ölçekleri doldurmasına engel olan görme problemi olmak dışlama kriteri olarak kullanıldı. Çalışma, katılmaya gönüllü olan, dışlama kriterlerine sahip olmayan ve ölçekleri tam olarak dolduran %40.4 (355)'i hastaya direkt bakım veren (doktor, hemşire, sağlık memuru), %59.6 (523)'ü ise direkt bakım vermeyen (sekreter, temizlik personeli, güvenlik görevlisi) toplam 878 sağlık personeli ile gerçekleştirildi. Çalışmada uzun süreli ve yakın temasın önlenmesi, bulaş riskinin azaltılması için benzer birçok çalışmada olduğu gibi kendini değerlendirme araçları kullanıldı. Değerlendirme öncesi, bilgi ve aydınlatılmış onam formu kullanılarak katılımcılardan aydınlatılmış onamları alındı. Katılımcılara onam formu ve kendini değerlendirme ölçekleri birim sorumluları tarafından ulaştırıldı, 1 hafta süre verildi ve 1 haftanın sonunda formlar toplandı. Bu çalışma Helsinki İlkeleri Deklerasyonu'na uygun olarak hazırlanmış ve T.C. Sağlık Bakanlığı Sağlık Hizmetleri Genel Müdürlüğü Bilimsel Araştırma Kurulu'nun onayı sonrasında, Üniversite Hastanesi Tıbbi Araştırmalar Etik Kurulu'ndan onay alınmıştır (Evrak Tarih ve Sayısı: 19.06.2020-E.5338).

Veri Toplama Araçları

Sosyodemografik Veri Formu

Yaş, cinsiyet, eğitim durumu, medeni durum, sosyal destek, meslek, çalıştığı birim, covid ve bulaşma yolları ile ilgili yeterli eğitimi alıp almadığı, kendisinin ya da yakınlarının covid tanısı alıp almadığı ya da izolasyon uygulanıp uygulanmadığı, covid ile ilgili yayınlar için sosyal medyada ne kadar zaman harcadığı gibi bilgiler elde edilmiştir.

Yaygın Anksiyete Bozukluğu Ölçeği (YAB-7)

Katılımcıların anksiyete şiddetini ölçmek için kullanılmıştır. YAB-7 tanısal geçerlilik ve güvenilirliği nedeni ile klinik pratikte ve araştırmalarda anksiyete bozukluklarının taraması, tanısı ve şiddetinin ölçülmesi için yaygın bir şekilde kullanılmaktadır. 7 madden oluşmaktadır ve her maddeye 0 -3 arasında puan verilebilmektedir. Toplam puan 0-21 arasında değişmektedir. (0-4) normal, (5-9) hafif şiddette anksiyete, (10-14) orta şiddette anksiyete ve (15-21) şiddetli anksiyete olduğunu göstermektedir. YAB toplam puanı ≥10 muhtemel anksiyete kesme değeri olarak kullanılmaktadır (7).

Pitsburg Uyku Kalitesi İndeksi (PUKİ)

Son bir ay içerisindeki uyku kalitesi ve uyku bozukluğunun şiddetini değerlendirmek için kullanılmaktadır. 24 soru ve öznel uyku kalitesi, uykuya dalma süresi, uyku süresi, alışılmış uyku etkinliği, uyku bozukluğu, uyku ilacı kullanımı ve gündüz işlev bozukluğunu değerlendiren 7 faktörden oluşmaktadır. Her faktör 0-3 arasında puanlanmaktadır ve toplam skor 0-21 arasındadır. Alınan puanın yükselmesi uyku kalitesinin bozulduğunu göstermektedir. PUKİ toplam puanı ≥5 kötü uyku kalitesi olarak değerlendirilmektedir (8).

Çok Boyutlu Algılanan Sosyal Destek Ölçeği Gözden Geçirilmiş Form (ÇBASDÖ)

Kişiler tarafından algılanan sosyal desteğin öznel olarak ölçülmesinde kullanılır. Zimmet (1988) tarafından geliştirilmiştir ve Türkçe geçerlilik güvenilirlik çalışması yapılmıştır. Aile, arkadaş ve özel biri gibi 3 farklı kaynaktan algılanan sosyal desteği içeren her biri 4 maddeden oluşan 3 ayrı faktörü vardır. Her bir madde 0-7 arasında puanlanmaktadır. Puanların toplamı ölçek skorunu verir. Yüksek puanlar algılanan sosyal desteğin fazla olduğunu gösterir (9).

Stresle Başa Çıkma Tarzları Ölçeği (SBTÖ)

30 maddelik bu ölçek katılımcıların stresli durumlarla başa çıkma tarzlarını değerlendirmek için kullanılmıştır. Folkman ve Lazarus tarafından geliştirilmiş ve Türkçe geçerlilik güvenilirlik çalışması yapılmıştır. Kendine güvenli yaklaşım (7 madde), iyimser yaklaşım (5 madde), çaresiz yaklaşım (8 madde), boyun eğici yaklaşım (6 madde), sosyal desteğe başvurma (4 madde) olmak üzere toplam beş alt boyuttan oluşmaktadır. Toplam puan 30- 120 arasında değişmektedir. Alt boyutlardan alınan puanlar o alt boyuttaki madde sayısına bölünerek o alt boyuta ait puan elde edilir. Alt boyutlardan alınan yüksek puanlar bireylerin o başa çıkma yaklaşımını daha sık kullandığını gösterir (10).

İstatistiksel Analiz

Araştırma verisi SPSS (Statistical Package For Social Sciences for Windows v.22,0, SPSS Inc. Chicago, IL) aracılığıyla bilgisayar ortamına yüklenerek değerlendirilmiştir. Tanımlayıcı istatistikler ortalama (±) standart sapma, ortanca (min-maks), frekans dağılımı ve yüzde olarak sunulmuştur. Verilerin normal dağılıma uyup uymadığı *Kolmogorov-Smirnov* testi kullanılarak değerlendirilmiştir. Sürekli değişkenlerin veri analizinde Mann Whitney-U testi kullanılmıştır. Kategorik değişkenlerin ise Ki-Kare testi, Yates Düzeltmeli Ki-Kare testi ve Fisher'in Kesinlik testi (Fisher's Exact test) ile değerlendirilmiştir. Değişkenler arasındaki ilişki Pearson Korelasyon Testiyle değerlendirilmiştir. İstatistiksel anlamlılık düzeyi $p<0.05$ olarak kabul edilmiştir.

Bulgular

Bu çalışma 878 sağlık personeli ile gerçekleştirildi. Katılımcıların yaş ortalaması 37.2±8.5'ti. Katılımcıların %71.3'ü kadın, %28.7'si erkekti. Çalışanların %40.4'ü hastaya direkt bakım veren (doktor, hemşire, sağlık memuru), %59.6'sı ise direkt bakım vermeyen (sekreter, temizlik personeli, güvenlik görevlisi) çalışanlardı. Katılımcıların %57.9'u covid ile direkt ilişkili birimlerde (covid servis, covid acil, covid yoğun bakım), %42.1'i de covid ile direkt ilişkili olmayan birimlerde çalışıyordu. Katılımcıların %18.2'sinin karantina süreci olmuştu. Çalışanların %80.1'i corona virüs ve korunma yolları ile ilgili yeterli eğitim aldığını, %76.8'i yeterli kişisel koruyucu ekipmana sahip olduğunu düşünüyordu. Katılımcıların sosyodemografik ve klinik verileri tablo 1 de gösterilmiştir.

Tablo-1.Katılımcıların Bazı Sosyo-demografik ve Klinik Verileri

N=878	
Yaş ort±ss	37,2 ± 8,5
Cinsiyet/ kadın n (%)	626 (71,3)
Medeni durum/evli n(%)	634 (72,2)
Çalışma pozisyonu n(%)	
Hastaya direkt bakım verenler	355 (40,4)
Hastaya direkt bakım vermeyenler	523 (59,6)
Çalışma yılı n(%)	
<5 years	383 (43,6)
≥ 5years	495 (56,4)
Geçirilmiş Ruhsal hastalık n(%)	
Evet	154 (82,5)
Hayır	724 (17,5)
Covid-19 testi yapılma durumu n(%)	
Evet	215 (24,5)
Hayır	663 (75,5)
Karantina süreci	
Evet	718 (81,8)
Hayır	160 (18,2)
YAB -7	
Anksiyete var	116 (13,2)
Anksiyete yok	762 (76,8)
PUKİ	
İyi uyku kalitesi	407 (46,4)
Kötü uyku kalitesi	471 (53,6)

Ort:ortalama ss:standart sapma n:sayı %:yüzde YAB-7: Yaygın Anksiyete Bozukluğu Ölçeği PUKİ: Pitsburg Uyku Kalitesi İndeksi

Katılımcıların YAB-7'ye göre %13.2'sinde klinik olarak önemli derecede anksiyete belirtileri vardı. Çalışanların PUKİ ye göre %53.6'sının uyku kalitesi kötü olarak saptandı.

Çalışma arkadaşlarında covid tanısı olanların, çalışma arkadaşlarında covid tanısı olmayanlara göre anksiyete puanı anlamlı derecede yüksekti (p=0,001). Geçmişte ruhsal hastalık öyküsü olan çalışanların YAB-7'ye göre anksiyete puanları geçmişte ruhsal hastalığı olmayanlara göre daha yüksekti (p=0,001). Çalışanların sosyal medyada covid ile ilişkili haberlerle ilgilenme süresine göre anksiyete puanları karşılaştırıldığında gruplar arasında anlamlı fark vardı. 1 saatten az vakit geçirenlerin %9.2' sinde belirgin anksiyete varken, 4 saatten fazla geçirenlerin %31.6' sında klinik olarak belirgin anksiyete saptandı (p=0,005). Covidle direkt ilişkili birimlerde çalışanlar ile direkt ilişkili olmayan birimde çalışanlar arasında anksiyete düzeyi açısından belirgin bir fark saptanmadı (p=0,433). Çeşitli çalışan gruplarının anksiyete düzeylerine göre karşılaştırılması tablo 2 de gösterilmiştir.

Tablo 2. Klinik Olarak Önemli Derecede Anksiyete Yakınması Olan ve Olmayan Sağlık Çalışanlarının Çeşitli Sosyo-demografik ve Klinik Verileri

N=878	Anksiyete yok (YAB<10) n(%)	Anksiyete var (YAB≥10) n(%)	P[a]
Covid ile direkt ilişkili birimde çalışan	325 (86)	45 (14)	0,433
Covid ile direkt ilişkili birimde çalışmayan	437(87,8)	71 (12,2)	
Geçirilmiş ruhsal hastalık var	121 (78,6)	33 (21,4)	0,001
Geçirilmiş ruhsal hastalık yok	641 (88,5)	83 (11,5)	
Hastaya direkt bakım verenler	306 (86,2)	49 (13,8)	0,670
Hastaya direkt bakım vermeyenler	456 (87,2)	67 (12,8)	
Çalışma arkadaşlarında Covid tanısı alan var	246 (81,5)	56 (18,5)	0,001
Çalışma arkadaşlarında Covid tanısı alan yok	516 (89,6)	60 (10,4)	
Covid ile ilgili yeterli eğitimi aldığını düşünenler	619 (88,1)	84 (11,9)	0,27
Covid ile ilgili yeterli eğitimi aldığını düşünmeyenler	143 (81,7)	32 (13,3)	

n:sayı %:yüzde a: Chi-Square tests YAB-7:Yaygın Anksiyete Bozukluğu Ölçeği

Çalışanların çeşitli özelliklerine göre uyku kaliteleri açısından kıyaslandığında hastaya direkt bakım veren grupta (p=0,001), covid şüphesi yaşayan çalışanlarda (p=0,006), covid pozitifliği saptanan iş arkadaşları olanlarda (p=0,023), yeterli kişisel koruyucu ekipmana sahip olmadığını düşünen çalışanlarda (p<0.001), geçmişte ruhsal hastalık tanısı olanlarda (p<0.001), kötü uyku kalitesi oranı anlamlı olarak daha yüksekti (Tablo3).

Tablo 3. Uyku Kalitesi İyi Olan ve Uyku Kalitesi Kötü Olan Sağlık Çalışanlarının Soyo-demografik ve Klinik Verilerinin Karşılaştırılması

N=878	İyi uyku kalitesi (PUKİ<5) n (%)	Kötü uyku kalitesi (PUKİ≥5) n (%)	P[a]
Covid süphesi yaşamayan	308 (49,3)	317 (50,7)	0,006
Covid şüphesi yaşayan	99 (39,1)	154 (60,9)	
Hastaya direkt bakım verenler	141 (39,7)	214 (60,3)	0,001
Hastaya direkt bakım vermeyenler	266 (50,9)	257 (49,1)	
İş arkadaşında Covid tanısı var	124 (41,1)	178 (58,9)	0,023
İş arkadaşında Covid tanısı yok	283 (49,1)	293 (50,9)	
Yeterli kişisel koruyucu ekipmana sahip olduğunu düşünenler	335(49,7)	339 (50,3)	<0,001
Yeterli kişisel koruyucu ekipmana sahip olmadığını düşünenler	72 (35,3)	132 (64,7)	
Geçmişte ruhsal hastalık öyküsü yok	363 (50,1)	361 (49,1)	<0,001
Geçmişte ruhsal hastalık öyküsü var	44 (28,6)	110 (71,4)	
Covid ile direkt ilişkili birimde çalışanlar	241 (47,4)	267 (52,6)	0,452
Covid ile direkt ilişkili birimde çalışmayanlar	166 (44,9)	204 (55,1)	

n:sayı %: yüzde a: Chi-Square tests PUKİ: Pitsburg Uyku Kalitesi İndeksi

PUKİ toplam puanı ile YAB-7 toplam puanı arasında pozitif yönlü istatiksel olarak anlamlı bir ilişki vardı. Katılımcıların anksiyetesi arttıkça uyku kalitesi bozuluyordu (R=0,461, p<0.001) (Tablo4).

Katılımcıların algılanan sosyal destek puanları ile anksiyete düzeyleri karşılaştırıldığında klinik olarak belirgin anksiyetesi olan grupta algılanan sosyal destek daha düşük olarak saptandı (p=0,021). Çok boyutlu algılanan sosyal destek puanı ile PUKİ puanı arasında negatif yönlü istatistiksel olarak anlamlı bir ilişki vardı. Algılanan sosyal destek arttıkça uyku kalitesi iyileşiyordu (R= -0,161 p<0.001) (Tablo4).

Tablo 4. Anksiyete Toplam Puanları, Çok Boyutlu Algılanan Sosyal Destek Puanları ve Pitsburg Uyku Kalite İndeksi Puanları Arasındaki İlişki

		YAB-7 Toplam	ÇBASDÖ-Toplam	PUKİ-Toplam
YAB-7 Toplam	r	1	-0,123	0,461
	p		<0,001	<0,001

r : Pearson korelasyon katsayısı ÇBASDÖ: Çok boyutlu algılanan sosyal destek PUKİ: Pitsburg Uyku Kalitesi İndeksi YAB-7:Yaygın Anksiyete Bozukluğu Ölçeği

Çalışanlar kullandıkları başa çıkma stilleri açısından karşılaştırıldığında klinik düzeyde anksiyetesi olanlarda çaresiz yaklaşım (p= p<0.001) puanları anlamlı olarak daha yüksekti, klinik düzeyde anksiyetesi olmayanlarda ise kendine güvenli yaklaşım (p=0,01) ve iyimser yaklaşım (p=0,017) puanları yüksekti (Tablo5).

Tablo 5. Belirgin Derecede Anksiyetesi Olan/Olmayan Sağlık Çalışanlarının Çok Boyutlu Algılanan Sosyal Destek ve Stresle Başa Çıkma Tarzları Alt Ölçek Puanları

N=878	Anksiyete var (Mean ±sd)	Anksiyete yok (Mean ±sd)	P[a]
(ÇBASDÖ) - Toplam	62,9±18,9	67,9±16,6	**0,021**
(SBTÖ)-KGY	17,3 ±4,2	18,5±4,2	**0,001**
(SBTÖ)-İY	13,9±3,5	14,7±3,3	**0,017**
(SBTÖ)-ÇY	19,9±5,01	17,3±4,5	**<0,001**
(SBTÖ)-BY	13,7±3,7	12,9±3,7	0,056
(SBTÖ)-SDB	10,9±2,5	10,9±2,3	0,954

a : Mann-Whitney-U test ÇBASDÖ: Çok boyutlu algılanan sosyal destek SBTÖ:Stresle başa çıkma tarzları ölçeği KGY: Kendine güvenli yaklaşım İY: İyimser yaklaşım ÇY:Çaresiz yaklaşım BY: Boyun eğici yaklaşım SDB: Sosyal desteğe başvurma

Tartışma

Bildiğimiz kadarıyla bu çalışma Covid-19 salgını sırasında Türkiye'de sağlık çalışanlarındaki anksiyete prevalansı ile uykusu kalitesi, sosyal destek algısı ve stresle başa çıkma yöntemleri arasındaki ilişkiyi beraberce değerlendiren ilk çalışmadır.

Covid-19 salgını sırasında sağlık çalışanlarında daha önce yapılan çalışmalarda anksiyete prevalansının %8.3 ile %44.6 arasında olduğu bildirilmiştir (11,12). Bizim çalışmamızda, katılımcıların %13.2'sinde klinik olarak önemli derecede anksiyete belirtileri saptandı. Görüldüğü gibi Covid-19 salgını sırasında sağlık çalışanlarında anksiyete prevalansı ile ilgili yapılan ulusal ve uluslararası çalışmalarda farklılıklar söz konusudur. Yapılan çalışmalarda anksiyete prevalansının değişen oranlarda saptanması, farklı ölçeklerin kullanılması ya da aynı ölçek kullanılmış olsa bile, farklı kesme değerlerinin kullanımından kaynaklanmış olabilir.

Uyku, iyilik halinin sürdürülmesi için önemlidir. Sağlık çalışanları gibi vardiya veya nöbet usulü çalışma düzenine sahip mesleklere mensup kişilerde, topluma kıyasla uyku bozuklukları daha sık görülmektedir. Huang ve Zhao'nun Covid-19 salgını döneminde yaptıkları çalışmada Çin halkının %18,2'sinin, meslekler arasında da özellikle sağlık personellerinin %23,6'sının kötü uyku kalitesine sahip olduğu saptanmıştır (13). Yuan ve ark.'nın yine Covid-19 salgını sırasında yaptıkları çalışmada da, genel halk içinde en kötü uyku kalitesine sahip olan meslek grubunun sağlık çalışanları olduğu belirlenmiştir (14). Pandemi sırasında sağlık çalışanlarında daha önce yapılan çalışmalarda uyku bozukluğu prevalansını Dong ve ark. %63.9 (PUKI≥5) olarak bildirdi (15). Bizim çalışmamızda ise katılımcıların %53.6'sında (PUKI≥ 5) kötü uyku kalitesi saptandı.

Ayrıca alt analizlerimizde çalışmamıza katılan sağlık çalışanlarında psikiyatrik hastalık öyküsü olması ile anksiyete belirtileri yaşamalarının ilişkili olduğu bulunmuştur. Literatürde de psikiyatrik hastalık geçirmiş olanlarda psikolojik dayanıklılığın daha düşük olduğu, daha yüksek psikolojik dayanıklılığın psikiyatrik hastalığın gelişimini engellediğini gösteren kanıtlar vardır. Travmatik olayların psikolojik dayanıklılığı azaltması ile bu kişilerde psikiyatrik belirtiler görülebilmektedir (16).

Çalışmamızda iş arkadaşlarında covid tanısı olanlarda anksiyete belirtilerinin daha fazla görüldüğü saptanmıştır. Daha önce yapılan bir çalışmada sağlık personelinin %27,7`sinin birinci derece yakınlarından en az birinin Covid-19 tanısı aldığı bildirilmiştir (17). Özdin ve arkadaşları, akrabalarında veya arkadaşlarında covid pozitif olan kişilerde, daha yüksek depresyon ve anksiyete puanları bildirmişlerdir (18).

İnsanların bulaşıcı olabilecek olumsuz duygu ve endişelerini sosyal medya yolu ile sürekli olarak ifade etmeleri nedeniyle yanlış bilgilerin ve temelsiz korkuların toplum içinde hızla yayılma riski mevcuttur. Covid-19 hakkında bilgi almak için sosyal medyanın aşırı kullanımı stres yanıtlarını şiddetlendirebilir, kaygı ve depresyon düzeylerini artırabilir. Bu da, bir kısır döngü içerisinde olumsuz duyguları yatıştırmak amacıyla daha fazla kullanımına yol açabilir ve sosyal medya bağımlılığı için risk oluşturabilmektedir.

Bizim çalışmamızda sosyal medyada covid ile ilişkili haberlerle ilgilenme süresine göre anksiyete puanları karşılaştırıldığında gruplar arasında anlamlı fark vardı. 1 saatten az vakit geçirenlerin %9.2' sinde belirgin anksiyete varken, 4 saatten fazla geçirenlerin %31.6' sında klinik olarak belirgin anksiyete saptandı. Yine pandemi sırasında Çin nüfusunun %82'sinin sıklıkla sosyal medyaya maruz kaldığı raporlanmıştır (19).

Covid-19 pandemisi döneminde aktif görev yapmakta olan sağlık çalışanları üzerinde ruhsal etkiler görülebilir. Geçmişte yapılan araştırmalar, sağlık sektörü çalışanlarının özellikle acil servislerde, yoğun bakım ünitelerinde ve bulaşıcı hastalık servislerinde çalışanlarda psikiyatrik semptom ortaya çıkma riskinin daha yüksek olduğunu bildirmiştir. Lai ve arkadaşları tarafından yapılan araştırmaya göre ön saflardaki sağlık çalışanlarının daha şiddetli anksiyete, depresif belirtiler ve uykusuzluk yaşadıkları bildirilmiştir (14). Diğer yandan Liang ve arkadaşları Covid-19 hastalarına hizmet verilen birimlerde çalışmanın ruhsal belirtileri etkilemediğini belirtmiştir. Ancak bu çalışmanın örnekleminin 59 katılımcı ile sınırlı olduğu göz önüne alınmalıdır (20).

Bizim çalışmamızda covidle direkt ilişkili birimlerde çalışanlar ile direkt ilişkili olmayan birimde çalışanlar arasında anksiyete düzeyi açısından belirgin bir fark saptanmadı. Bu durum covid dışı birimlerde yapılan tarama testlerinde (operayon ve çeşitli girişimler öncesi) covid saptanan hastaların olması, sağlık personelinin yeterli anamnez alınamayan bilinç kapalı hastalara yakın bakım vermesi gereksinimi ve asemptomatik kişilerden de covid bulaşının olabilmesinin covid dışı birimlerde çalışan sağlık personelinin covid ile ilişkili anskiyete yaşamalarına yol açmasından kaynaklanabilir.

Çalışmamızda enfeksiyondan korunmak için yeterli kişisel koruyucu ekipmana ulaşabilmenin anksiyete belirtilerini azalttığı saptanmıştır. Cai ve arkadaşlarının Covid-19 pandemisinde yaptıkları araştırmaya göre efektif kişisel koruyucu ekipmana ulaşabilmek sağlık çalışanlarının yaşadığı stresi azaltmakta, ayrıca motivasyonlarını arttırmaktadır (21).

Pandemi veya salgın hastalıklar aileden sağlanan duygusal ve sosyal desteğin belirgin düzeyde azalmasına yol açmaktadır. Bu durum hem önceki salgınlarda hem de güncel olarak Covid-19 ile mücadele döneminde sıklıkla deneyimlenmiştir. Yapılan araştırmalarda SARS ile mücadele eden Çin ve Kanada'da sağlık çalışanlarının aile üyelerine virüs bulaştırma korkusunun ve anksiyete seviyelerinin yüksek olduğu gözlenmiştir. Sağlık çalışanları virüs bulaştırma korkuları nedeniyle evlerinden ve aile üyelerinden uzun süreler boyunca ayrı kalmayı tercih etmiş, eşleriyle ve çocuklarıyla fiziksel temas olmadan ve genelde telefonla iletişimlerini sürdürmüşlerdir. Bulaşıcı hastalık salgınları sırasında aileden ve arkadaşların göstereceği olumlu tutum ve desteğin stres düzeylerini azalttığı gösterilmiştir (22).

Tüm bu veriler; aile desteğinin ve mevcudiyetinin sağlık çalışanlarının ruhsal durumu açısından koruyucu rol oynadığını, aile desteğinin çalışanlara bir şekilde sağlanmasının ruhsal zorlantılar açısından koruyucu olabileceği ve tüm boyutlarıyla sağlık çalışanlarına sağlanacak sosyal desteğin pandemi ile mücadelede önemli rol oynayacağını göstermektedir (23).

Bizim çalışmamızda katılımcıların algılanan sosyal destek puanları ile anksiyete düzeyleri karşılaştırıldığında klinik olarak belirgin anksiyetesi olan grupta algılanan sosyal destek daha düşük olarak saptandı. Çok buyutlu algılanan sosyal destek puanı ile PUKİ puanı arasında negatif yönlü istatistiksel olarak anlamlı bir ilişki vardı. Algılanan sosyal destek arttıkça uyku kalitesi iyileşiyordu.

Stres durumlarına verilen tepkiler bireylerin, potansiyel stres etkenini nasıl değerlendirdiklerinden ve bu stresli olaylarla başa çıkmak için kullandıkları yöntemlerden büyük ölçüde etkilenmektedir (24). Literatür incelendiğinde bireylerin stresle başa çıkma tarzları ile çeşitli psikolojik bozukluklar arasında ilişki olduğu görülmektedir (25).

Bizim çalışmamızda sağlık çalışanları kullandıkları başa çıkma stilleri açısından karşılaştırıldığında klinik düzeyde anksiyetesi olanlarda çaresiz yaklaşım puanları anlamlı olarak daha yüksekti, klinik düzeyde anksiyetesi olmayanlarda ise kendine güvenli yaklaşım ve iyimser yaklaşım puanları yüksekti. Araştırmamızın tek merkezli olması, kontrol grubunun olmaması ve öz bildirim tarzında ölçekler kullanılması başlıca kısıtlılıklardır. Ayrıca kesitsel bir araştırma olması, nedensellik ilişkisinin kurulmasını ve uzun dönem etkilerini değerlendirebilmeyi güçleştirmektedir.

Sonuçlar

Sonuç olarak Covid-19 pandemisi son 2 yıldır tüm dünya için fiziksel olduğu kadar zihinsel anlamda zorlayıcı bir faktör oldu. Bu anlamda Covid-19 ile mücadelede ön saflarda bulunan birçok sağlık çalışanı psikolojik zorlanma belirtileri yaşadı. Covid-19'un sağlık çalışanları üzerindeki psikolojik etkilerinin belirlenmesi, psikolojik destek birimlerinin oluşturulması, stresle baş etme tekniklerine yönelik olarak eğitim verilmesi, hem çalışanların iyilik halinin sürdürülmesi hem de sağlık hizmetinin aksamadan yürütülmesi ve ayrıca gelecekteki olası pandemilerde de yol gösterici olması açısından önemlidir.

Kaynaklar

1. World Health Organization. Coronavirus disease 2019 (Covid-19) Situation Report, 52. 2020.
2. Hall H. The effect of the Covid-19 pandemic on healthcare workers' mental health. JAAPA 2020 Jul;33(7):45-48.
3. Zhang WR, Wang K, Yin L, Zhao WF, Xue Q, Peng M ve ark. Mental health and psychosocial problems of medical health workers during the Covid-19 epidemic in China. Psychotherapy and Psychosomotics, 2020;89:242-250.
4. Chen XF, Zhang Y, Xu XL, Wang W, Yan H, Li S ve ark. The mediating effects of anxiety, self-efficacy and sleep quality on the relationship between doctor-patient's empathy and inflammatory marker in patients with ulcerative colitis. Med Sci Monit, 2019; 25: 7889–97.
5. Kent de Grey RG, Uchino BN, Trettevik R, Cronan S, Hogan, JN. Social support and sleep: A meta-anal-ysis. Health Psychol, 2018; 37: 787-98.
6. Sliter M, Kale A, Yuan Z. Is humor the best medicine? The buffering effect of coping humor on traumatic stressors in firefighters. Journal of Organizational Behavior, 2014; 35(2):257-272.
7. Kroenke K, Williams J.B.W, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. Arch. Intern. Med. 2006, 166, 1092–1097.
8. Carpenter JS, Andrykowski MA. Psychometric evaluation of the Pittsburgh Sleep Quality Index. J Psychosom Res, 1998; 45: 5-13.
9. Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. Journal of Personality Assessment 1988;52:30-41.
10. Lazarus, R.S. Folkman, S. (1984) Stress, Appraisal and Coping. New York: Springer Publishing Company.
11. Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N ve ark. Factors associated with mental health outcomes among healthcare workers exposed to coronavirus disease. JAMA Network Open Journal, 2020;3(3):e203976.
12. Rossi R, Socci V, Pacitti F, Di Lorenzo G, Di Marco A, Siracusano A ve ark. Mental health outcomes among frontline and second-line health care workers during the coronavirus disease 2019 (Covid-19) pandemic in Italy. *JAMA Network Open Journal, 3*(5), e2010185.
13. Huang Y, Zhao N. Generalized anxiety disorder, depressive symptoms and sleep quality during Covid-19 outbreak in China: A web-based cross-sectional survey. Psychiatry Res, 2020;112954.
14. Yuan S, Liao Z, Huang H, Jiang B, Zhang X, Wang Y ve ark. Comparison of the ındicators of psychological stress in the population of Hubei province and non-endemic provinces in China during two weeks during the coronavirus disease 2019 (Covid-19) outbreak in february 2020. Med Sci Monit, 2020;26:e923767-1.
15. Dong H, Zhang Q, Sun Z, Sang F, Xu Y. Sleep disturbances among Chinese clinical nurses in general hospitals and its influencing factors. BMC Psychiatry, 2017;17:241.
16. Shrivastava A, Desousa A. Resilience: A psychobiological construct for psychiatric disorders. Indian journal of psychiatry, 2016; 58(1): 38.
17.Özdemir İ, Özgen Hergül G, Öztürk M, Arslan A. Covid-19 Pandemi Sürecinde Bir Pandemi Hastanesinde Görev Yapmakta Olan Hemşirelerde, Sosyodemografik Değişkenler, Belirsizliğe Tahammülsüzlük ve Umutsuzluk Düzeylerinin, Algılanan Stres Düzeylerine Etkisinin İncelenmesi. Ankara Eğt Arş Hast Derg, 2021 ; 54(3) : 434-441.
18. Ozdin S, Bayrak Ozdin S. Levels and predictors of anxiety, depression and health anxiety during Covid-19 pandemic in Turkish society: the importance of gender. Int J Soc Psychiatry, 2020;66(5):504-11.
19. Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S ve ark. Mental health problems and social media exposure during Covid-19 outbreak. PLoS One, 2020;15:e0231924.
20. Liang Y, Chen M, Zheng X, Liu J. Screening for Chinese medical staff mental health by SDS and SAS during the outbreak of Covid-19. Journal of psychosomatic research, 2020;133:110102.
21. Cai H, Tu B, Ma J, Chen L, Fu L, Jiang Y ve ark. Psychological Impact and Coping Strategies of Frontline Medical Staff in Hunan Between January and March 2020 During the Outbreak of Coronavirus Disease 2019 (Covid-19) in Hubei, China. Medical science monitor: international medical journal of experimental and clinical research, 2020; 26: 924171-1.
22. Liu Z, Han B, Jiang R, Huang Y, Ma C, Wen J ve ark. Mental health status of doctors and nurses during Covid-19 epidemic in China. Available at SSRN 3551329. 2020.
23. Tuncay FE, Koyuncu E, Özel Ş A. Review Of Protective And Risk Factors Affecting Psychosocial Health Of Healthcare Workers In Pandemics. Ankara Med J, 2020;2:488-501.
24. Folkman S, Lazarus RS. An analysis of coping in a middleaged community sample. Journal of Health and Social Behavior, 1980; 21:219-239.
25. Farley T, Galves A, Dickinson M, Diaz MJ. Stress, coping and mental health: a comparison of Mexican immigrants, Mexican Americans, and Non-Hispanic whites. J Immigr Health 2005; 3:213–220.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2):108-116

Giresun Üniversitesi Prof. Dr. A. İlhan Özdemir Eğitim ve Araştırma Hastanesi Anestezi ve Reanimasyon Yoğun Bakımında Mart 2020-Temmuz 2020 tarihleri arasında Covid-19 Şüphesiyle Yatan Hastaların Klinik, Radyolojik ve Laboratuvar Verilerinin Değerlendirilmesi

Data of Clinical, Radiological and Laboratories of Inpatients with suspected Covid-19 between March 2020-July 2020 elections in Giresun University Prof. Dr. A. İlhan Özdemir Training and Research Hospital Anesthesia and Reanimation Intensive Care

Duygu DEMİRİZ GÜLMEZ* 0000-0002-0874-7067
Azime BULUT*0000-0001-8164-5617
Elvan TEKİR YILMAZ* 0000-0001-8631-2520
Meltem KARAMUSTAFA0000-0002-3496-7354**
Pınar TEKİN*0000-0003-4439-0197
Raziye TURAN0000-0002-6308-4104**
Tuna ALBAYRAK 0000-0002-3611-5569**
Ünal TAŞ* 0000-0001-7440-8971
İlknur YAVUZ* 0000-0003-0247-8772**
Ahmet Melih ŞAHİN* 0000-0003 -3670-7801**

** Giresun Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Ana Bilim Dalı, Giresun, Türkiye*
***Giresun Prof. Dr. A. İlhan Özdemir Devlet Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, Giresun, Türkiye*
****Giresun Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Ana Bilim Dalı, Giresun, Türkiye*

Yazışma Adresi: Duygu DEMİRİZ GÜLMEZ
Giresun Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Ana Bilim Dalı, Giresun, Türkiye
Debboy Mevkii P.K 28200
E-mail: duygudemiriz@hotmail.com

Geliş Tarihi:21/04/2022
Kabul Tarihi:22/07/2022

Öz

Amaç: Yeni koronavirüs hastalığı tüm dünyayı derinden etkileyen, yüzyılda bir görülen bir pandemidir. Hastalardaki klinik bulguların, hafif üst solunum yolu enfeksiyonundan başlayıp solunum yetmezliğinin eşlik ettiği, ölümlerle sonuçlanabilen viral pnömonilere ve çoklu organ yetmezliklerine varan geniş spektrumda olduğu gözlenmiştir. Biz de hastanemiz yoğun bakımında takip edilmiş Covid-19 hastalarının özelliklerinin incelenmesiyle Giresun ilimizin pandemideki yerini ortaya koymak ve yoğun bakım deneyimlerimizi paylaşmayı amaçladık.

Gereç-Yöntem: Bu retrospektif çalışmada Giresun Üniversitesi Hastanesi'nde 15 Mart 2020-1 Temmuz 2020 tarihleri arasında Covid-19 enfeksiyonu şüphesiyle yoğun bakıma başvuran 105 hastanın verilerini inceledik.

Bulgular: Hastaların ortalama yaşı 75.4 ve erkek hasta sayısı daha fazla idi ve %45.7'sinin hipertansiyon (HT) tanısı mevcuttu. Yoğun bakımımızda hastaların %40'ında akut solunum sıkıntısı sendromu (ARDS) gelişirken %38 oranında ikinci sırada akut böbrek yetmezliği (ABY) gözlenmiştir. Çalışmamızda mortalite oranımız %34 olup, laktat dehidrojenaz (LDH), aspartat aminotransferaz (AST) ve laktat yükseliği olanlarda mortalite daha yüksek bulunmuştur ($p < 0.001$).

Sonuç: Çalışmamızdaki veriler ışığında komorbiditeleri olan ve LDH, AST ve laktat değerleri yüksek olan hastalar daha mortal seyretmektedir.

Anahtar Kelimeler: Covid-19, Mekanik ventilasyon, Viral pnömoni

Abstract

Objective: The new coronavirus disease is a once-in-a-century pandemic that deeply affects the whole world. It has been observed that the clinical findings in the patients range from mild upper respiratory tract infection to viral pneumonias with respiratory failure, which can result in death and to multiple organ failures. We aimed to reveal the place of our Giresun province in the pandemic and share our intensive care experiences by examining the characteristics of Covid-19 patients followed in the intensive care unit of our hospital.

Materials and methods: In this retrospective study, we analyzed the data of 105 patients admitted to the intensive care unit with suspected Covid-19 infection between March 15, 2020 and July 1, 2020 at Giresun University Hospital.

Results: The mean age of the patients was 75.4 and the number of male patients was higher. Hypertension was diagnosed in 45.7% of the patients. While acute respiratory distress syndrome developed in 40% of the patients in our intensive care unit, renal failure was observed in the second place with a rate of 38%. In our study, our mortality rate was 34% and mortality was higher in patients with lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and lactate elevation ($p < 0.001$).

Conclusions: In the light of the data in our study, patients with comorbidities and high LDH, AST and Lactate values are more mortal.

Keywords: Covid-19, Mechanical Ventilation, Viral Pneumonia

Giriş

Şiddetli akut solunum sendromu koronavirüs-2 (SARS-CoV-2), ilk olarak Çin'in Wuhan kentinde tespit edilen 2019 koronavirüs hastalığına (Covid-19) neden olan yeni koronavirüstür (1). Çin'de öncelikle deniz ürünlerinden bulaşsa da salgın, kişiden kişiye geçerek insanlık için tehdit oluşturmuştur. Türkiye'de ilk Covid-19 vakası 11 Mart 2020'de avrupadan iş gezisinden gelenlerde tespit edilmiş ve 1 Haziran 2020 itibariyle 201.098 vaka tanı almış ve bunların 5.150'si % 0.02 ölüm oranı ile hayatını kaybetmiştir. Çin ve İtalya'dan gelen ilk raporlar, koronavirüs hastalığının yüksek mortaliteye sahip olduğunu göstermiştir ve ayrıca hastanelerde kritik bakım kapasitesi üzerinde büyük stres yaratmıştır (2,3). Covid-19 'un diğer solunum yolu enfeksiyonları ile benzer klinik semptomları olduğundan ayırıcı tanısı zordur. Bu durumun hastaneler ve özellikle yoğun bakım üniteleri üzerindeki baskıyı arttırdığı gösterilmiştir. Pandemi döneminde kalifiye yoğun bakım ünitesi personeli çok önemlidir. Hastanemizde negatif basınçlı 8 izolasyon odası ile 43 tane seviye-3 yoğun bakım ünitesi yatağı bulunmaktadır. Covid-19 hastaları için yoğun bakım yatak sayısını acil servise kabule göre dinamik olarak belirledik. Giresun'da tespit edilen ilk Covid-19 vakasının ardından 105 vaka 1 temmuz'a kadar Anesteziyoloji ve Reanimasyon Yoğun Bakım Ünitesi'ne yatırıldı. Bu retrospektif çalışmada Giresun'da bir üniversite hastanesinin yoğun bakım ünitesine yatırılan doğrulanmış veya şüpheli Covid-19 hastalarının klinik, laboratuvar ve radyolojik özelliklerini, tedavilerini ve sonuçlarını tanımlamayı amaçladık.

Gereç Ve Yöntem

Bu retrospektif çalışma için Giresun Üniversite Hastanesi'nde 15 Mart 2020 - 1 Temmuz 2020 tarihleri arasında Covid-19 enfeksiyonu şüphesiyle yoğun bakım ünitesine başvuran 105 hastanın elektronik ve yazılı verilerini inceledik. Hastanemizde nefes darlığı ve takipnesi olan (≥30 kez/dk), oksijen satürasyonu düşük (≤ %90, oksijen desteği yok) ve $Pa0_2$/Fi02 (P/F) ≤ 300 mmHg olan hastalar yoğun bakım ünitesinde tedavi edildi. Yüksek akış oksijen desteği ve non-invaziv mekanik ventilasyon uygulamasına rağmen (FiO2≥ %60 ve oksijen akış hızı ≥ %40) hiperkapnik asidoz, hipoksemi ve solunum iş yükünde artma (yardımcı solunum kasları kullanımı, interkostal çekilme) mevcut olan hastalar entübe edilerek invaziv mekanik ventilasyon desteğine alındılar (4). Çalışma Giresun Üniversitesi etik kurulu tarafından 22.05.2020/ 22 karar numarası ile onaylandı.

Hastalardan yoğun bakıma yatışının ilk gününde tam kan sayımı, elektrolitler, böbrek ve karaciğer fonksiyon testleri, fibrinojen, yüksek duyarlı (hs) troponin, d-dimer, laktat dehidrojenaz, C-reaktif protein (CRP), prokalsitonin ve arter kan gazı (AKG) değerleri için kan örneği alındı. Ayrıca tüm hastalara toraks bilgisayarlı tomografi (BT) çekildi.

Klinik sonuçlar (Covid-19 ile ilişkili ölüm, yoğun bakım ünitesinden (YBÜ) taburcu olma, YBÜ'de kalış süresi, mekanik ventilasyon durumu, beslenme durumu, Covid-19'a bağlı organ hasarları) kaydedildi. ARDS Berlin kriterlerine göre tanımlandı (5). ABY KDIGO 2012 (Kidney disease: improving global outcomes definition) kriterlerine göre tanımlandı (6). Çoklu organ disfonksiyon sendromu (MODS) potansiyel olarak geri dönüşümlü iki veya daha fazla organı içeren fizyolojik bozukluk olarak tanımlandı (7).

İstatistiksel Yöntemler

Tanımlayıcı istatistikler için ortalama, standart sapma, medyan, minimum, maksimum değer frekans ve yüzde kullanıldı. Değişkenlerin dağılımı Kolmogorov-Simirnov testi ile kontrol edildi. Nicel verilerin karşılaştırılmasında Mann-Whitney U testi kullanıldı. Nitel verilerin karşılaştırılmasında ki-kare testi kullanıldı. İstatistiksel analizler için SPSS 27.0 kullanıldı.

Bulgular

Hastaların genel dağılımları incelendiğinde %56.2 si erkek, %45.7 si HT tanılı idi (Tablo 1).

Tablo 1. Hastaların klinik ve dermografik özellikleri

		Min-Max	Median	Mean±sd/n-%
YAŞ		21,0 - 97,0	78,0	75,4 ± 13,5
CİNSİYET	KADIN		46	43,8%
	ERKEK		59	56,2%
KOMORBİDİTELER				
Hipertansiyon			48	45,7%
Kardiyovasküler Hastalıklar			27	25,7%
Diyabetes Mellitus			24	22,9%
Serebrovasküler Hastalıklar			37	35,2%
Kronik Obstrüktif Akciğer Hastalığı			18	17,1%
Kronik Böbrek Yetmezliği			12	11,4%
Malignite			9	8,6%
Nöromuskuler Hastalıklar			1	1,0%
Kronik Karaciğer Hastalığı			2	1,9%
SEMPTOMLAR				
Ateş			29	27,6%
Öksürük			18	17,1%
Myalji			4	3,8%
Dispne			89	84,8%
Asemptomatik			5	4,8%

Tablo 2. Hastaların tedavi, komplikasyonlar ve klinik sonuçları

		Min-Max	Median	Mean±sd/n-%	
TEDAVİ					
Plaquanil				65	61,9%
Tami Flu				55	52,4%
Favipavir				41	39,0%
Azitromisin				58	55,2%
Immunplazma				1	1,0%
Tasilizumab				0	0,0%
İntravenöz immunglobulin				2	1,9%
Glukokortikoid Tedavi				3	2,9%
Kaletra				4	3,8%
C Vitamini				5	4,8%
Akut Solunum Sıkıntısı Sendromu				42	40,0%
Akut Böbrek Yetmezliği				40	38,1%
Çoklu organ disfonksiyon sendromu/Şok				29	27,6%
PCR	(+)			31	29,5%
Bilgisayarlı Tomografi	(+)			86	81,9%
Sedasyon	(+)			58	55,2%
Nöromuskuler Blokaj	(+)			8	7,6%
Vazopressör	(+)			59	56,2%
	(-)			49	46,7%
Diürez	100 ml/gün			16	15,2%
	400 ml/gün			40	38,1%
	Enteral			81	77,1%
Nutrisyon	Parenteral			24	22,9%
	M1			73	69,5%
Mekanik Ventilasyon	M2			4	3,8%
	M3			28	26,7%
Sürekli Renal Replasman Tedavisi				15	14,3%
Estrakorporeal Membran Oksijenizasyonu				2	1,9%
Prone Pozisyon				11	10,5%
Mortalite				36	34,3%
Entübasyon				73	69,5%
Hastanede kalış süresi (gün)		1,0 -	116,0	7,0	11,8 ± 15,5
Entübasyon süresi (gün)		0,0 -	116,0	2,0	7,5 ± 14,3

*Mekanik ventilasyon M1: İnvaziv mekanik ventilasyon, M2: Non-İnvaziv mekanik ventilasyon, M3: Basit yüz maskesi

Mortalite olan ve olmayan grupta hastaların yaşları, cinsiyet dağılımı anlamlı (p>0.05) farklılık göstermemiştir. Mortalite olan ve olmayan grupta HT, kardiyovasküler hastalık, diyabetes mellitus (DM), serebrovasküler hastalık (SVO) oranı, kronik böbrek yetmezliği (KBY) oranı, malignite oranı, nöromasküler hastalık oranı, kronik karaciğer hastalık oranı anlamlı (p>0.05) farklılık göstermemiştir. Mortlite olan grupta kronik obstrüktif akciğer hastalığı (KOAH) oranı mortalite olmayan gruptan anlamlı (p<0.05) olarak daha düşüktü (Tablo 3).

Tablo 3. Hastaların klinik ve dermografik özelliklerinin mortalite üzerine etkisi

		MORTALİTE (+)		MORTALİTE (-)		p
		Mean±sd/n-%	Median	Mean±sd/n-%	Median	
YAŞ		74,8 ± 13,2	77,0	76,5 ± 14,0	80,0	0,449 [m]
CİNSİYET	KADIN	31 44,9%		15 41,7%		0,749 [x²]
	ERKEK	38 55,1%		21 58,3%		
KOMORBİDİTELER						
Hipertansiyon		30 43,5%		18 50,0%		0,524 [x²]
Kardiyovasküler Hastalıklar		16 23,2%		11 30,6%		0,412 [x²]
Diyabetes Mellitus		14 20,3%		10 27,8%		0,386 [x²]
Serebrovasküler Hastalıklar		22 31,9%		15 41,7%		0,319 [x²]
Kronik Obstrüktif Akciğer Hastalığı		8 11,6%		10 27,8%		***0,037*** [x²]
Kronik Böbrek Yetmezliği		8 11,6%		4 11,1%		0,941 [x²]
Malignite		8 11,6%		1 2,8%		0,126 [x²]
Nöromuskuler Hastalıklar		0 0,0%		1 2,8%		0,343 [x²]
Kronik Karaciğer Hastalıkları		2 2,9%		0 0,0%		0,545 [x²]
Semptomlar						
Ateş		22 31,9%		7 19,4%		0,176 [x²]
Öksürük		10 14,5%		8 22,2%		0,319 [x²]
Myalji		3 4,3%		1 2,8%		1,000 [x²]
Dispne		58 84,1%		31 86,1%		0,781 [x²]
Asemptomatik		4 5,8%		1 2,8%		0,658 [x²]

[m] Mann-whitney u test/ [x²] Chi-square test

Tablo 4. Hastaların tedavi, komplikasyonlar ve klinik sonuçlarının mortalite üzerine etkisi

		MORTALİTE (+)			MORTALİTE (-)			p
		Mean±sd/n-%		Median	Mean±sd/n-%		Median	
Tedavi								
Plaquanil		45	65,2%		20	55,6%		0,333 x^2
Tami Flu		37	53,6%		18	50,0%		0,724 x^2
Favipiravir		29	42,0%		12	33,3%		0,386 x^2
Azitromisin		38	55,1%		20	55,6%		0,962 x^2
Immunplazma		1	1,4%		0	0,0%		1,000 x^2
Tasilizumab		0	0,0%		0	0,0%		1,000 x^2
intravenöz immunglobulin		2	2,9%		0	0,0%		0,545 x^2
Glukokortikoid Tedavi		1	1,4%		2	5,6%		0,270 x^2
Kaletra		2	2,9%		2	5,6%		0,605 x^2
C Vitamini		4	5,8%		1	2,8%		0,658 x^2
Akut Solunum Sıkıntısı Sendromu		34	49,3%		8	22,2%		***0,007*** x^2
Akut Böbrek Yetmezliği		36	52,2%		4	11,1%		***0,000*** x^2
Çoklu organ disfonksiyon sendromu/Şok		29	42,0%		0	0,0%		***0,000*** x^2
PCR	(+)	26	37,7%		5	13,9%		***0,011*** x^2
Bilgisayarlı Tomografi		58	84,1%		28	77,8%		0,428 x^2
Sedasyon		48	69,6%		10	27,8%		***0,000*** x^2
Nöromuskuler blokaj		8	11,6%		0	0,0%		***0,034*** x^2
Vazopressör		53	76,8%		6	16,7%		***0,000*** x^2
	(-)	24	34,8%		25	69,4%		
Diürez	100 ml/gün	10	14,5%		6	16,7%		***0,001*** x^2
	400 ml/gün	35	50,7%		5	13,9%		
	Enteral	46	66,7%		35	97,2%		
Nutrisyon								***0,000*** x^2
	Parenteral	23	33,3%		1	2,8%		
	M1	63	91,3%		10	27,8%		
Mekanik Ventilasyon	M2	2	2,9%		2	5,6%		***0,000*** x^2
	M3	4	5,8%		24	66,7%		
Sürekli Renal Replasman Tedavisi		13	18,8%		2	5,6%		0,065 x^2
Estrakorporeal Membran Oksijenizasyonu		2	2,9%		0	0,0%		0,545 x^2
Prone Pozisyon		10	14,5%		1	2,8%		0,063 x^2
Entübasyon		63	91,3%		10	27,8%		***0,000*** x^2
Hastanede kalış süresi (gün)		10,5 ±	11,1	7,0	14,4 ±	21,6	6,5	0,471 ^{m}
Entübasyon süresi (gün)		7,2 ±	8,8	3,0	8,1 ±	21,4	0,0	***0,000*** ^{m}

^{m} Mann-whitney u test/ x^2 Chi-square test

Mortalite olan ve olmayan grupta tedaviler arasında anlamlı ($p > 0.05$) farklılık gösterilmemiştir. Mortalite olan grupta ARDS, ABY, MODS görülme sıklığı, PCR pozitiflik oranı, sedasyon, nöromuskuler blokaj ve vazopressör uygulama oranı mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Mortalite olan ve olmayan grupta BT pozitiflik oranı anlamlı ($p > 0.05$) farklılık göstermemiştir. Mortalite olan grupta parenteral beslenme oranı mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Mortalite olan ve olmayan grupta sürekli renal replasman tedavisi (CRRT) oranı, ekstrakorporeal membran oksijenizasyonu (ECMO) oranı, prone pozisyon oranı anlamlı ($p > 0.05$) farklılık göstermemiştir. Mortalite olan grupta entübasyon oranı mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti (Tablo 4).

Mortalite olan ve olmayan grupta hastanede kalış süresi anlamlı ($p > 0.05$) farklılık göstermemiştir. Mortalite olan grupta entübasyon süresi mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti (Tablo 4).

Mortalite olan grupta LDH değeri mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha düşüktü. Mortalite olan grupta AST ve laktat değeri, mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Mortalite olan grupta p/f, PCO_2, ortalama arter basıncı ve kalp atım hızı (P) mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha düşüktü. Diğer laboratuvar değerleri arasında anlamlı bir fark gözlenmedi (Tablo 5).

Entübasyon olan grupta ARDS, ABY, MODS görülme sıklığı, PCR pozitiflik oranı, sedasyon ve vazopressör ihtiyacı oranı entübasyon olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Entübasyon olan ve olmayan grupta BT pozitiflik oranı anlamlı ($p > 0.05$) farklılık göstermemiştir. Entübasyon olan grupta mortalite oranı entübasyon olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Entübasyon olan ve olmayan grupta hastanede kalış süresi anlamlı ($p > 0.05$) farklılık göstermemiştir (Tablo 6).

Entübasyon olan grupta LDH değeri entübasyon olmayan gruptan anlamlı ($p < 0.05$) olarak daha düşüktü. Entübasyon olan grupta Beyaz kan hücresi (BK), C-reaktif Protein (CRP), kreatinin, laktat değerleri mortalite olmayan gruptan anlamlı ($p < 0.05$) olarak daha yüksekti. Mortalite olan grupta p/f, ortalama arter basıncı değeri entübasyon olmayan gruptan anlamlı ($p < 0.05$) olarak daha düşüktü. Diğer laboratuvar değerleri arasında anlamlı bir farklılık görülmedi (Tablo 7).

Tablo 5. Hastaların laboratuvar değerlerinin mortalite üzerine etkisi

	MORTALİTE (+)		MORTALİTE (-)		p	
	Mean±sd	Median	Mean±sd	Median		
BK 10^3(ul)	12,8 ± 10,1	10,9	12,3 ± 8,3	9,0	0,919	m
LYM 10^3(ul)	1,1 ± 1,0	0,9	1,3 ± 1,1	0,8	0,580	m
NLR&RDW-SD %	5,3 ± 3,2	4,7	4,7 ± 2,9	3,6	0,285	m
PLT 10^3 (ul)	208,9 ± 104,9	182,0	238,4 ± 117,3	210,0	0,255	m
CRP (mg/l)	128,4 ± 99,6	109,2	101,1 ± 80,5	96,6	0,232	m
Glukoz(mg/dl)	165,6 ± 150,3	132,0	157,9 ± 70,0	135,0	0,319	m
LDH (ıu/l)	539,2 ± 502,6	412,0	373,8 ± 237,3	312,0	***0,005***	m
Creatine (mg/dl)	1,7 ± 1,6	1,0	1,3 ± 1,3	1,0	0,075	m
BUN (mg/dl)	87,0 ± 64,6	67,0	74,3 ± 46,2	68,0	0,580	m
ALT (ıu/l)	106,4 ± 366,2	23,0	41,0 ± 66,7	24,0	0,478	m
AST (ıu/l)	113,6 ± 334,6	41,0	63,0 ± 153,2	25,0	***0,019***	m
NA (mmol/l)	140,2 ± 8,8	138,0	139,9 ± 8,2	140,5	0,834	m
K (mmol/l)	5,7 ± 10,1	4,3	4,5 ± 0,9	4,4	0,836	m
T.BİL (mg/dl)	1,1 ± 2,7	0,7	0,7 ± 0,5	0,7	0,324	m
D-DİMER NG/ML	2964,4 ± 2467,2	1914,0	3303,8 ± 2552,7	2583,5	0,589	m
PRC µg/L	1,0 ± 1,6	0,5	0,7 ± 1,6	0,3	0,071	m
TROP-T MCG/ML	0,4 ± 1,5	0,1	0,1 ± 0,1	0,0	0,110	m
Fibrinojen (mg/dl)	506,7 ± 209,1	490,0	540,1 ± 201,4	514,0	0,404	m
PH	7,3 ± 0,2	7,4	7,4 ± 0,1	7,4	0,766	m
P/F	134,8 ± 82,9	100,0	182,5 ± 71,5	186,5	***0,001***	m
PCO_2 (mmhg)	39,8 ± 11,4	39,0	44,2 ± 10,7	44,0	***0,035***	m
LAKTAT(mmol/L)	3,6 ± 3,1	2,3	1,6 ± 0,7	1,4	***0,000***	m
Ortalama Arter Basıncı	88,1 ± 20,0	88,0	98,1 ± 23,1	98,0	***0,049***	m
Kalp Atım Hızı	76,8 ± 23,5	72,0	83,5 ± 14,5	85,0	***0,030***	m

[m] Mann-whitney u test

Tablo 6. Hastaların tedavi, komplikasyonlar ve klinik sonuçlarının entübasyon üzerine etkisi

		ENTÜBASYON (-)			ENTÜBASYON (+)			p	
		Mean±sd/n-%		Median	Mean±sd/n-%		Median		
Tedavi									
Plaquanil		20	62,5%		45	61,6%		0,934	x^2
Tami Flu		14	43,8%		41	56,2%		0,241	x^2
Favipavir		11	34,4%		30	41,1%		0,516	x^2
Azitromisin		17	53,1%		41	56,2%		0,773	x^2
Immunplazma		0	0,0%		1	1,4%		1,000	x^2
Tasilizumab		0	0,0%		0	0,0%		1,000	x^2
İntravenöz immunglobulin		0	0,0%		2	2,7%		1,000	x^2
Glukokortikoid Tedavi		1	3,1%		2	2,7%		1,000	x^2
Kaletra		2	6,3%		2	2,7%		0,584	x^2
C Vitamini		1	3,1%		4	5,5%		1,000	x^2
Akut Solunum Sıkıntısı Sendromu		7	21,9%		35	47,9%		***0,012***	x^2
Akut Böbrek Yetmezliği		4	12,5%		36	49,3%		***0,000***	x^2
Çoklu organ disfonksiyon sendromu /Şok		3	9,4%		26	35,6%		***0,006***	x^2
PCR	(+)	5	15,6%		26	35,6%		***0,039***	x^2
Bilgisayarlı Tomografi	(+)	27	84,4%		59	80,8%		0,663	x^2
Sedasyon	(+)	3	9,4%		55	75,3%		***0,000***	x^2
Nöromuskuler Blokaj	(+)	0	0,0%		8	11,0%		0,051	x^2
Vazopressör	(+)	3	9,4%		56	76,7%		***0,000***	x^2
	(-)	22	68,8%		27	37,0%			
Diürez	100 ml/gün	4	12,5%		12	16,4%		***0,008***	x^2
	400 ml/gün	6	18,8%		34	46,6%			
	Enteral	28	87,5%		53	72,6%			
Nutrisyon								0,155	x^2
	Parenteral	4	12,5%		20	27,4%			
	M1	0	0,0%		73				
Mekanik Ventilasyon	M2	4	12,5%		0	0,0%		***0,000***	x^2
	M3	28	87,5%		0	0,0%			
Sürekli Renal Replasman Tedavisi		2	6,3%		13	17,8%		0,119	x^2
Estrakorporeal Membran Oksijenizasyonu		0	0,0%		2	2,7%		1,000	x^2
Prone Pozisyon		1	3,1%		10	13,7%		0,103	x^2
Mortalite		26	81,3%		10	13,7%		***0,000***	x^2
Hastanede kalış süresi (gün)		11,2 ±	20,4	5,5	12,1 ±	13,0	8,0	0,539	m
Entübasyon süresi (gün)		4,8 ±	20,8	0,0	8,7 ±	10,2	4,0	***0,000***	m

m Mann-whitney u test/ X^2 Chi-square test Mekanik ventilasyon M1: İnvaziv mekanik ventilasyon, M2: Non-İnvaziv mekanik ventilasyon, M3: Basit yüz maskesi

Tablo 7. Hastaların laboratuvar değerlerinin entübasyon üzerine etkisi

	ENTÜBASYON (-)		ENTÜBASYON(+)		p
	Mean±sd	Median	Mean±sd	Median	
BK 10^3(ul)	10,5 ± 8,0	7,8	13,6 ± 9,9	11,2	***0,039*** [m]
LYM 10^3(ul)	1,4 ± 1,2	0,9	1,1 ± 1,0	0,8	0,335 [m]
NLR&RDW-SD %	4,8 ± 3,1	3,8	5,2 ± 3,1	4,7	0,431 [m]
PLT 10^3 (ul)	217,7 ± 122,3	203,5	219,6 ± 104,5	200,0	0,770 [m]
CRP (mg/l)	81,2 ± 65,9	61,1	135,7 ± 99,9	130,0	***0,009*** [m]
Glukoz (mg/dl)	154,3 ± 71,6	131,5	166,7 ± 146,5	133,0	0,751 [m]
LDH (ıu/l)	446,9 ± 374,2	299,5	498,2 ± 462,4	402,0	***0,032*** [m]
Kreatinin (mg/dl)	1,2 ± 1,1	1,0	1,7 ± 1,6	1,0	***0,039*** [m]
BUN (mg/dl)	80,8 ± 62,3	62,5	83,4 ± 57,9	68,0	0,411 [m]
ALT (ıu/l)	54,3 ± 96,8	23,0	96,9 ± 354,4	24,0	0,679 [m]
AST (ıu/l)	87,5 ± 189,9	29,5	100,1 ± 320,0	37,0	0,311 [m]
NA (mmol/l)	139,8 ± 8,8	140,0	140,3 ± 8,5	140,0	0,900 [m]
K (mmol/l)	4,5 ± 1,0	4,5	5,6 ± 9,8	4,3	0,894 [m]
T.BİL (mg/dl)	0,7 ± 0,5	0,6	1,1 ± 2,6	0,7	0,314 [m]
D-DİMER NG/ML	3567,2 ± 2612,8	3312,5	2867,6 ± 2421,6	1879,0	0,265 [m]
PRC µg/L	0,7 ± 1,6	0,3	0,9 ± 1,6	0,4	0,342 [m]
TROP-T MCG/ML	0,1 ± 0,2	0,0	0,3 ± 1,5	0,1	0,491 [m]
Fibrinojen (mg/dl)	500,4 ± 219,7	501,5	525,9 ± 201,0	497,0	0,689 [m]
PH	7,3 ± 0,1	7,4	7,3 ± 0,1	7,4	0,282 [m]
P/F	204,4 ± 81,6	208,0	127,8 ± 71,1	100,0	***0,000*** [m]
PCO_2 (mmhg)	42,0 ± 11,6	40,5	41,0 ± 11,3	40,0	0,834 [m]
Laktat(mmol/L)	2,3 ± 2,2	1,4	3,2 ± 2,9	2,0	***0,003*** [m]
Ortalama Arter Basıncı	101,0 ± 21,6	102,5	87,4 ± 20,3	88,0	***0,006*** [m]
Kalp Atım Hızı	80,3 ± 16,5	81,0	78,5 ± 22,8	75,0	0,467 [m]
Ortalama Arter Basıncı/Kalp Atım Hızı	1,3 ± 0,4	1,4	1,2 ± 0,5	1,3	0,325 [m]

[m] Mann-whitney u test

Tartışma

SARS-CoV-2 virüsü halen tüm dünyada mortalite ve morbiditesini sürdürmektedir. Özellikle YBÜ'de takip edilen hastaların seyri virüsün yıkıcı etkisini anlamada önemli rol oynamaktadır. Biz de ilimizde ilk vakanın görüldüğü tarih olan 15 Mart 2020 ile 1 Haziran 2020 arasında ilimiz üniversite hastanesi 3. basamak yoğun bakım ünitesinde yatan hastaların klinik ve laboratuvar verilerini değerlendirdik.

Çalışmamızda diğer çalışmalar ile de paralel olarak erkek hasta sayısı %56 ile kadın hastalardan daha fazlaydı (8). YBÜ'mizde yatan hastaların ortalama yaşı 78 idi ki bu da son zamanlarda yayınlanan çalışmalara baktığımızda daha yaşlı popülasyonu kapsamaktadır (8). Zamanla YBÜ'ye yatan hastaların daha genç olması ülkemizde yaşlı kesimin daha önce aşılanmış olmasından kaynaklanıyor olabilir.

Çalışmamızda YBÜ'ye yatan hastaların %45.7'sinin HT tanısı mevcut ki bu değer malignite, DM, KBY tanılı hastalardan daha fazla olmakla beraber mortalite açısından ek hastalıklar arasında anlamlı bir farklılık bulunmamıştır. Bizim çalışmamız ile paralel olarak yapılan çalışmalar da HT tanısı olan hastaların Covid-19'a daha duyarlı olduğunu göstermiştir (9). Ancak KOAH tanılı hastaların mortalite oranları diğer komorbiditeler ile karşılaştırıldıklarında daha düşüktür. Yani YBÜ'sine yatan KOAH tanılı hastaların %11'i mortal seyrederken %28'i taburcu olabilmiştir. Bizim çalışmamızda diğer kronik hastalara göre KOAH tanılı hastalarda mortalitenin daha düşük olması, hastaların hipoksiye toleransının artmış olmasına bağlanabilir (10). Emami ve arkadaşlarının yayınlamış oldukları bir makalede KOAH tanılı olguların prevalansı diğer kronik hastalıklara oranla daha az bulunmuş olup bunun bir sebebinin KOAH tanısının konulmasındaki zorluk olabileceği söylenmiştir (11).

Yoğun bakımımızda hastaların %40'ında ARDS gelişirken %38 oranında ikinci sırada ABY gözlenmiştir ve %14'ünün CRRT ihtiyacı olmuştur. ABY glişen hastalarda mortalite oranı anlamlı olarak yüksektir.

Bizim çalışmamızla paralel olarak Sreedhar Adapa ve arkadaşlarının 2020 yılında yaptıkları çalışmada Covid-19'un, direk olarak virus hasarı, anjiotensin dönüştürücü enzim 2' nin rolü, immün mediatörlerin böbrek hücrelerine zarar vermesi gibi patogenetik mekanizmalarla ABY gelişimine sebep olup mortaliteyi arttıran bağımsız bir risk faktörü olduğundan bahsetmektedirler (12).

Çalışmamızda mortalite oranımız %34 olup diğer çalışmalar ile karşılaştırdığımızda bu oran düşüktür (8 ,4). Hastalarımızın %69.5'i entübe takip edilmiştir ve entübe olanların mortalite oranı en yüksektir (%91.3, $p<0.05$). Uygulanan antiviral ve immunsupresif tedaviler açısından mortalitede anlamlı bir fark gözlenmemiştir.

Labaratuvar değerlerine baktığımızda LDH, AST, laktat yüksekliği olan hastalarda mortalite daha yüksekti. Ayrıca BK, CRP, LDH ve laktat yüksekliği mevcut hastalarda entübasyon oranlarını da daha yüksek olduğu görüldü. Bu veriler ışığında yoğun bakıma yatışta LDH, AST ve laktat yüksekliğinin mevcut olması kötü prognozun habercisi olabilir.

Sonuç

Türkiye Cumhuriyeti Sağlık Bakanlığı'nın verilerine göre pandeminin ilk zamanlarından beri nüfusa göre en çok vaka görülen illerden biri olan Giresun'da, üniversite hastanemizde 105 hastayı dahil ettiğimiz çalışmamızda başta HT olmak üzere kronik hastalıkların, yatış anında LDH, AST ve laktat yükseliğinin ve invaziv mekanik ventilatör ile takip edilmenin mortaliteyi arttırdığını gözlemledik.

Kaynaklar

1. World Health Organization. Novel coronavirus — China. January 12, 2020
2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; 8(5): 475-481.
3. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. JAMA. 2020; 323(16): 1545-1546.
4. Kocayiğit H, Süner K. Ö, Tomak Y, et al. Characteristics and outcomes of critically ill patients with Covid-19 in Sakarya, Turkey: a single centre cohort study. Turkish journal of medical sciences, 2021; 51(2): 440-47.
5. Task F. A. D, Ranieri V. M, Rubenfeld G. D, et al. Acute respiratory distress syndrome. Jama, 2012; 307(23): 2526-33.
6. WORKGROUP, K. A. K. I. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl, 2012; 2(1): 1-138.
7. ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE, et al. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest, 1992; 101: 1644-55.
8. Ñamendys-Silva, Silvio A., et al. Outcomes of patients with COVID-19 in the intensive care unit in Mexico: A multicenter observational study. Heart & Lung, 2021; 50(1): 28-32.
9. Gasmi A., Peana M, Pivina L, et al. Interrelations between COVID-19 and other disorders. Clinical Immunology, 2021;224: 108651.
10. Halpin DMG, Criner GJ, Papi A, et al. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. The 2020 GOLD Science Committee Report on COVID-19 and Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2021;203(1):24-36.
11. Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of Underlying Diseases in Hospitalized Patients with COVID-19: a Systematic Review and Meta-Analysis. Arch Acad Emerg Med. 2020;8(1): e35.
12. Adapa S, Chenna A, Balla M, et al. COVID-19 Pandemic Causing Acute Kidney Injury and Impact on Patients With Chronic Kidney Disease and Renal Transplantation. J Clin Med Res. 2020 Jun;12(6):352-361.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 117-124

Analysis of Clinical, Laboratory and Radiological Characteristics of COVID-19 Patients Undergoing Hospital Treatment by Gender

Hastanede Tedavisi Sürdürülen COVİD-19 Hastalarının Klinik, Laboratuvar ve Radyolojik Özelliklerinin Cinsiyete Göre Analizi

Halil İbrahim ERDOĞDU* 0000-0001-7755-4931
Mehmet EZER 0000-0003-4422-6768**
Eray ATALAY* 0000-0002-9700-7019
İhsan KAHRAMAN* 0000-0002-1142-105X**

* İç Hastalıkları AD, Sağlık Araştırmaları Merkezi, Kafkas Üniversitesi, Kars, Türkiye.
**Üroloji AD, Sağlık Araştırmaları Merkezi, Kafkas Üniversitesi, Kars, Türkiye.
***İç Hastalıkları AD, Sağlık Araştırmaları Merkezi, Kafkas Üniversitesi, Kars, Türkiye.

Yazışma Adresi : Halil İbrahim ERDOĞDU
İç Hastalıkları AD, Sağlık Araştırmaları Merkezi, Kafkas Üniversitesi, Kars, Türkiye
E-mail: halil-dr@hotmail.com

Geliş Tarihi: 21/04/2022
Kabul Tarihi: 06/06/2022

Abstract

Objective: The aim of this study is to analyze the comorbidity, lung involvement and intensive care requirement of 150 patients hospitalized due to coronavirus disease-2019 (COVID-19) by gender.

Methods: This cross-sectional study was conducted on April 15-30, 2021 in the COVID-19 clinic of Kafkas University Hospital. Patients aged 18 years or older with one or more of the symptoms of cough, shortness of breath, headache, joint pain or chest pain and positive real-time-PCR test were included in the study. Then, demographic, biochemical, clinical and radiological data were collected. Chi-square and Student's t-test were used for statistical analysis of the data. [p value < 0.05 was considered statistically significant (Confidence interval: 95%)].

Results: Of the 150 patients included in this study, 62 were women, and the comorbidity rate was higher than men (64.5% and 47.7%, respectively, p=0.042). On chest computed tomography, females were less affected by diffuse multifocal ground-glass opacities and sub pleural lesions or consolidation on the right and/or left (35.5% and 64.5%, respectively, p=0.016).The female/male ratio in intensive care admissions (ICA) was 6/10, and it was higher in males than females. However, this was not statistically significant (p=0.742). While the average of C-reactive protein level (normal range:0-0.5 mg/dL) was 5.0 mg/dL in men, it was 3.3 mg/dL in women and was higher in men (p=0.028).

Conclusion: Although the rate of comorbidity was higher in women, admission to the intensive care unit and lung involvement levels were not parallel with their comorbidities. Lung involvement, inflammatory response and need for intensive care were higher in men.

Knowing the disease characteristics, clinical features and consequences of COVID-19 will be important to understand the impacts of risk differences for genders.

Keywords: Covid-19, clinical features, radiological findings, laboratory findings, gender.

Öz

Amaç: Bu çalışmanın amacı, koronavirüs hastalığı-2019 (COVİD-19) nedeni ile hastaneye yatırılan 150 hastanın, komorbidite, akciğer tutulumu ve yoğun bakım gereksiniminin cinsiyete göre analiz edilmesidir.

Yöntem: Kesitsel tipte planlanan bu çalışma, 15-30 Nisan 2021 tarihlerinde Kars kafkas üniversitesi hastanesinde yatırılan hastalar ile yapıldı. Çalışmaya, öksürük, nefes darlığı, baş ağrısı, eklem ağrısı veya göğüs ağrısı gibi semptomlardan biri veya daha fazlası ile başvuran ve real-time-PCR testi pozitif saptanan 18 yaş ve üstü COVİD-19 hastaları dahil edildi. Daha sonra demografik, biyokimyasal, klinik ve radyolojik veriler toplandı. Verilerin istatiksel analizinde ki-kare ve student-t testi kullanıldı. [p değeri < 0,05 istatistiksel olarak anlamlı kabul edildi (Güven aralığı: %95)].

Bulgular: Bu çalışmaya 62'si kadın, 88'i erkek olmak üzere 150 hastanın komorbidite oranı sırasıyla 40/62 (%64.5) ve 42/88 (%47.7) olup kadınlarda erkeklere göre daha yüksekti (p =0.042). Akciğer bilgisayarlı tomografisinde, kadınlar sağda ve/veya solda yaygın multifokal buzlu cam opasiteleri, subplevral lezyonlar ve konsolidasyon açısından erkeklere göre daha az etkilenmişti (sırası ile;%35.5 ve %64,5 p=0.016). Yoğun bakıma alınanların kadın/erkek oranı 6/10 olup, erkeklerde kadınlara göre daha yüksekti ancak bu oran istatistiksel olarak anlamlı değildi (p=0,742). C-reaktif protein düzeyi(CRP) erkeklerde 5.0 mg/dL iken, kadınlarda 3.3 mg/dL olup erkeklerde daha yüksekti (CRP normal aralık:0-0.5 mg/dL p=0.028).

Sonuç: Kadınlarda, komorbidite oranı daha yüksek olsa da yoğun bakıma yatış ve akciğer tutulum düzeyleri erkeklere göre daha az idi.

Anahtar Kelimeler: Covid-19, Klinik özellikler, Radyolojik bulgular, Laboratuvar bulguları, Cinsiyet.

Introduction

COVID-19, a microbial disease caused by a novel coronavirus, severe respiratory difficulties have come into the limelight around the world. COVID-19 spread around the world and eventually affected people's health (1,2). In addition, during the pandemic, other diseases of the people remained in the background and caused many health problems (3). On the other hand, the presence of comorbidity in COVID-19 patients is effective on both admission to intensive care and mortality (4).

The appearance of COVID-19 varied from silent cases to severe patients. Fever, nonproductive cough, fatigue, myalgia, and radiological changes in lungs are the common clinical findings of COVID-19 patients. This virus may cause patch-like consolidated areas with the ground-glass appearance, multifocal involvement and bilateral diffuse infiltrates on lung tomography (5). Viral pneumonia with respiratory involvement and the worsening of background diseases are the main causes of death in severe patients (6,7).

COVID-19 causes damage due to uncontrolled adaptive immune response, which is also called 'cytokine storm' in the lung. The disease, which can cause shortness of breath and hypoxemia with an uncontrolled adaptive immune response. Since the number of COVID-19 rises worldwide, there is a need for investigating the laboratory, clinical, and radiological characteristics (5).

The aim of this study was to compare the clinical, radiological, and laboratory characteristics of 150 hospitalized patients with COVID-19 were analyzed to the gender. Potential risk factors and clinical findings associated with COVID-19 patients were investigated.

This is the first study to define the clinical and radiological features of COVID-19 patients in Northeast of Anatolia.

Methods

Study design:

This is a cross-sectional study that was conducted on patients who applied to the Kafkas University Hospital in Kars on April 15-30, 2021.

Patients aged 18 years and older who applied to our hospital with one or more of the symptoms determined for COVID-19 patients such as cough, dyspnea, headache, arthralgia or chest pain and were found to have a positive real-time-PCR test were included in this study. The patients who were discharged from the hospital with a positive real-time-PCR test in the last month and whose above-mentioned complaints continued were included in the study. And also, those who had the stated complaints with the positive real-time-PCR test despite having the COVID-19 vaccine and were included in the study. Those younger than 18 years of age and those with negative real-time-PCR test were excluded from the study.

The patients were diagnosed with COVID-19 by real-time-PCR obtained from nasopharyngeal swabs. Biochemical and clinical data were then collected, including gender, age, comorbidities (diabetes mellitus, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, malignancy, and chronic kidney disease, and other medical conditions). In addition, patients' symptoms (cough, dyspnea, headache, arthralgia, chest pain), arterial oxygen saturation, respiratory rate per minute, blood pressure measurements, and maximum body temperature (°C) were recorded. Patients with missing data are listed below the tables.

All chest computed tomography (CT) examinations for COVID-19 pneumonia screening were performed without the use of contrast material. The lung window setting approach was used for the interpretation of the images. Chest CT images were analyzed for the presence and distribution of the following abnormalities: ground glass opacities, nodules, consolidations, pleural effusion, lymphadenopathy. The number of patients who underwent lung tomography was 143.

The patients were divided into two groups according to their lung attitudes:

First group: Those with no or mild lung involvement includes completely normal lung appearance or with a minimal focal ground glass area on the right and/or left (n:42).

Second group: Those with moderate or severe lung involvement includes diffuse multifocal ground glass area on the right and/or left,or diffuse frosted glass and consolidation on the right and/or left (n:101).

In addition, three of the patients had bilateral pleural effusion and minimal pericardial fluid, and one of these three patients had a mass on the right. Since one of these three patients had extensive metastases from hepatocellular carcinoma, these three patients were excluded from the lung involvement groups because they may have differential diagnosis stages other than COVID-19. However, these patients were included in the independent variable groups in other pairwise comparisons for statistical analysis.

In addition, 12 of the patients were vaccinated with one or two doses (Sinovac) and were not excluded from the study.Vaccination for Covid-19 in our country started 2 months before this study. Although there is not enough time for the formation of sufficient antibody levels for the vaccine response, we wanted to observe whether there are any clinical positive effects in those who have been vaccinated due to the limited data on the efficacy of vaccines worldwide. There was also no statistically significant difference between vaccination rates between women and men (Table 2, p=0.557). For all these reasons, we did not exclude 12 people who were vaccinated from the study.

Those who were given the following antibiotics (levofloxacin or Moxifloxacin or Azithromycin) were determined as the group that received antibiotics. Those who did not receive any antibiotics were named as the group that did not receive antibiotics.

Favipiravir was given to all patients as an antiviral and favipiravir treatment was extended to 5-10 days for those with oxygen saturation below 93, tachypnea, and fever exceeding 38°C. Moreover, patients who were given and not given steroids (Dexamethasone 6 mg or methylprednisolone 60-80 mg) were categorized similarly.

For all inpatients, if d-dimer was ≤1000µg/L, enoxaparin sodium 40-60 mg/0.4-0.6 ml was administered as a single daily dose to all inpatients. If the d-dimer was >1000µg/L, enoxaparin sodium 80-120 mg/0.4-0.6 ml was administered twice daily.

Ethics Committee Approval: The research was conducted according to the Declaration of Helsinki. The protocol was approved by Kafkas University Faculty of Medicine Clinical Research Ethics Committee (Approval number: 80576354-050-99/162-01.07.2021), Kars, Turkey.

Statistical Analysis:

SPSS Statistics of Windows v.21.0 (SPSS; IBM Corporation, New York, USA) was used for statistical evaluation. The normality of distribution was evaluated by the Kolmogorov-Smirnov test. For numerical variables were tested using Student's t-test. In descriptive statistics, continuous variables were considered as mean ± Standard deviation (SD) and categorical variables as frequency (n) and percentage (%). A chi-square test was used in the binary comparison of categorical variables (P <0.05 and 95% CI were considered statistically significant). Mann-Whitney U was used when binary comparison was needed, and variances were not assumed.

Results

The age range of the patients was determined as 23-94. The female-male ratio was 62/88. When Table 1 was followed, 62 of the 150 patients in the study were women. The mean age was higher in women than in men, and it was determined as 60 and 52 years, respectively (p=0.001).

While the CRP level was 5.0±4.9 mg/dL in men and 3.3±4.5 mg/dL in women, there was a statistically significant difference between them (Table1, p=0.028).

Table 1: Analysis Results of Some Laboratory Parameters of Covid 19 Patients by Gender with Student T and Mann Whitney U Test

Variables	Female			Male			P
	n	mean	SD	n	mean	SD	
Age (year)	62	60	13,6	88	52	14,7	**0,001**
Arterial O_2(%)	62	86,8	6,6	88	87,3	7,1	0,688
CRP(mg/dL)(0-0.5)ʸ	62	3,3	4,5	88	5,0	5,1	**0,028**
LDH(U/L)(0-248)ʸ	62	319	117	88	329	120	0,633
D-Dimerˣ(µg/L)(0-500)ʸ	28	749	890	31	813	1722	0,860
CK ˣ (U/L)(0-145)ʸ	57	215	296	79	283	388	0,274
Prothrombin timeˣ (second)(9.7-14.7)ʸ	57	12,7	1,6	83	13,3	2,0	0,065
Albuminˣ(g/dL)(3.5-5.2)ʸ	9	3,5	0,8	18	3,3	0,6	0,458
Hemoglobin(g/dL)(10.8-15.1)ʸ	62	13,6	1,4	88	15,1	1,6	**<0,001**
Leukocytes (10^9/L)(3.7-10.4)ʸ	62	4964	2335	88	5481	2328	0,183
Lymphocyte (10^9/L)(0.9-3.7)ʸ	62	1272	464	88	1204	470	0,385
Platelet ˣ (10^9/L)(149-371)ʸ	62	220.000	79.000	87	214000	93000	0,656
Ürea ˣ (mg/dL)(17-43)ʸ	59	30	12	88	32	11	0,380
	n	**mean rank ***		**n**	**mean rank ***		
ALTˣ (U/L)(0-35)ʸ	61	67		87	79		0,080
Body temperature(°C)	62	65.7		88	82,3		**0,021**
Ferritin ˣ (ng/mL)(11-307)ʸ	61	56,5		87	87,0		**<0,001**

SD: Standard Deviation, CRP:C-reactive protein, ʸ:Normal range,ˣ: Missing data, LDH: Lactic Acid Dehydrogenase, CK: Creatine kinase, ALT: Alanine Aminotransferase, ***:**Mann Whitney -u "mean rank" values of the tested variables

When body temperature was measured, there was a difference between mean values according to gender (Table1, p=0.021). In addition, a statistically significant difference is observed between hemoglobin and ferritin levels by gender (for both parameters, Table1, p<0.001).

When Table 2 was followed, the rate of additional disease was higher in women than in men (40/62 and 42/88, respectively, p=0.042).When lung involvement was analyzed, 35.5% of the patients with moderate or severe lung involvement on chest CT were female and 64.5% were male (p=0.016). In other words, moderate or severe lung involvement was more common in males than females. Therefore, the rate of using favipiravir for more than 5 days was also higher in males (p=0.033).

Table 2: Categorical variables by gender Chi-Square Test Result

Variables		Female n(%)	Male n(%)	Total n(%)	P
Age (year)	<60	36(37.9)	59(62.1)	150(100)	0.261
	≥60	26(47.3)	29(52.7)		
BMI(Kg/m^2) [a]	<30	27(35.1)	50(64.9)	125(100)	0,060
	≥30	25(52.1)	23(47.9)		
Covid-19 Vaccinated[x]	No	58(42.0)	80(58.0)	150(100)	0.557
	Yes	4(33.3)	8(66.7)		
Comorbidity[y]	No	22(35.5)	46(64.5)	150(100)	**0.042**
	Yes	40(48.8)	42(51.2)		
	(Comorbidity rate)	40/62(64.5%)	42/88(47.7%)		
Oxygen support[(up to 2-15ml/min),in the covid 19 clinic and without intubation]	No	33(41.8)	46(58.2)	150(100)	0.908
	Yes	29(40.8)	42(59.2)		
Intensive care support (with or without intubation)	No	56(41.8)	78(58.2)	150(100)	0.742
	Yes	6(37.5)	10(62.5)		
Second hospitalization after discharge [z]	No	54(40.3)	80(59.7)	150(100)	0.456
	Yes	8(50.0)	8(50.0)		
Lung involvement in chest computurized tomography *	None or Mild	23(57.5)	17(42.5)	147(100)	**0.016**
	moderate or common	38(35.5)	69(64.5)		
Antibiotic use **	No	46(42.2)	63(57.8)	150(100)	0.725
	Yes	16(39.0)	25(61.0)		
Number of days favipravir was used	≤5	37(50.0)	37(50.0)	150(100)	**0.033**
	>5	25(32.9)	51(67.1)		
Steroid use ***	No	27(40.9)	39(59.1)	150(100)	0.925
	Yes	35(41.7)	49(58.3)		
Hospitalized (Number of days)	1-3	39(43.8)	50(56.2)	150(100)	0.506
	4-6	16(42.1)	22(57.9)		
	≥7	7(30.4)	16(69.6)		

BMI: Body Mass Index, [a:] Missing data **[x]**:One or two doses of Sinovac vaccine, **[y]:** One or more of any systemic disease (Diabetes Mellitus, Chronic lung diseases, Cardiac diseases, Hypertension, Thyroid diseases, Malignant or Connective tissue diseases etc..),If there is no involvement in the lungs or minimal focal involvement: the none or mild group. Diffuse multifocal involvement or consolidated areas in unilateral or both lungs: moderate or common involvement. ****:** use of any of the quinolones or azithromycin. *****:**Any steroid, preferably Dexamethasone.

When admissions in the intensive care unit were examined, regardless of gender, the rate of hospitalization was 2.9% in patients without comorbidities, and 17.1% in patients with comorbid diseases, and a statistically significant difference was found (p=0.005, Table). 3). The female/male ratio in intensive care admissions (ICA) was 6/10, and it was higher in males than females. However, this was not statistically significant. (p=0.742).

Table 3:Chi-square Test Results of Factors that may Affect Hospitalization in the Intensive Care Unit, Regardless of Gender, in Covid-19 Patients.

Independent variables		Dependent variable: Admission to the Intensive Care Unit(ICU)		Total	P
		No	Yes		
		n (%)	n (%)	n(%)	
Comorbidity [x]	No	66(97.1)	2(2.9)	68(100)	**0.005**
	Yes	68(82.9)	14(17.1)	82(100)	
Gender	Female	56(90.3)	6(9.7)	62(100)	0.742
	Male	78(88.6)	10(11.4)	88(100)	
COVID-19 Vaccinated[y]	No	124(89.9)	14(10.1)	138(100)	0.483
	Yes	10(83.3)	2(16.7)	12(100)	
BMI(Kg/m^2) [a]	<30	67(87.0)	10(13.0)	77(100)	0.937
	≥30	42(87.5)	6(12.5)	48(100)	
Lung involvement in chest computurized tomography [z,a]	None or Mild	39(92.9)	3(7.1)	42(100)	0.601
	Moderate or common	91(90.1)	10(9.9)	101(100)	

[x]: One or more of any systemic disease (Diabetes Mellitus, Chronic lung diseases, Cardiac diseases, Hypertension, Thyroid diseases, Malignant or Connective tissue diseases etc..),[y]: One or two doses of Sinovac vaccine,[a:] Missing data,BMI: Body Mass Index,[z]: If there is no involvement in the lungs or minimal focal involvement: the none or mild group. Diffuse multifocal involvement or consolidated areas in unilateral or both lungs: moderate or common involvement.

Similarly, regardless of gender, those with moderate or severe lung involvement require oxygen support compared to those without or mild involvement, and favipiravir treatment seems to be continued for more than 5 days, and the probability of steroid use increases (respectively p=0.001, p=0.001, p< 0.001, Table 4).

Table 4: Binary Comparison of Lung Involvement Level with some Bio demographic and Treatment Characteristics.

Variables		Lung involvement in chest computerized tomography [x]			
		None or Mild	Moderate or common	**Total**	**P**
		n(%)	**n(%)**	**n(%)**	
BMI(Kg/m^2)	<30	22(30.6)	50(69.4)	72(100)	0.394
	≥30	11(23.4)	36(76.6)	47(100)	
Age (year)	<60	26(28.0)	67(72.0)	93(100)	0.613
	≥60	16(32.0)	34(68.0)	50(100)	
COVID-19 Vaccinated[y]	No	39(29.8)	92(70.2)	131(100)	0.728
	Yes	3(25.0)	9(75.0)	12(100)	
Comorbidity[z]	No	18(27.3)	48(72.7)	66(100)	0.610
	Yes	24(31.2)	53(68.8)	77(100)	
Oxygen support[(up to 2-15ml/min),in the covid 19 clinic and without intubation]	No	32(41.6)	45(58.4)	77 (100)	**0.001**
	Yes	10(15.2)	56(84.8)	66 (100)	
Number of days favipiravir was used	≤5	30(41.7)	42(58.3)	72(100)	**0.001**
	>5	12(16.9)	59(83.1)	71(100)	
Steroid use[a]	No	28(44.4)	35(55.6)	63(100)	**<0.001**
	Yes	14(17.5)	66(82.5)	80(100)	

[x]: If there is no involvement in the lungs or minimal focal involvement: the none or mild group. Diffuse multifocal involvement or consolidated areas in unilateral or both lungs: moderate or common involvement,BMI: Body Mass Index,**[y]:**One or two doses Sinovac vaccine,**[z]:** One or more of any systemic disease (Diabetes Mellitus, Chronic lung diseases, Cardiac diseases, Hypertension, Thyroid diseases, Malignant or Connective tissue diseases etc..),[a]: Any steroid, preferably Dexamethasone.

In Table 5, the comorbidities of the patients by gender are presented. Due to the high diversity of comorbidities, statistical analysis was not performed for each comorbidity.

Table 5: Comorbidities of Hospitalized COVID-19 Patients

Comorbidities	**Female (n)**	**Male (n)**	
HT	9	3	12
DM	6	4	10
DM& HT	3	6	9
CHD	1	2	3
COPD	1	4	5
CHD		1	1
Bronchial asthma	1		1
Hypothyroidism	2	1	3
Hyperthyroidism	1		1
Gilbert syndrome		1	1
Factor V Leiden		1	1
Depression		2	2
Parkinson's disease		1	1
Fibromyalgia		2	2
Colon cancer		1	1
Pharyngeal cancer		1	1
Hepatocellular carcinoma		1	1
Comorbidity:Three or more diseases: [HT/ DM/ /CHF/ CHD/ COPD/ CKD/ AF/ Asthma / Hypothyroidism / Inactive Hepatitis B Virus (normal Alanine aminotransferase, serum HBV DNA negative, HBeAg negative)/Depresyon/ Epilepsi**]**	16	11	27
Total	**40**	**42**	**82**

HT: Hypertension, DM: Diabetes Mellitus (Type 2), CHF: Congestive Heart Failure, CHD: Coronary Heart Disease, COPD: chronic obstructive pulmonary disease, CKD: Chronic kidney disease, AF: Atrial fibrillation.

Discussion

In this study, the results of inpatient COVID-19 cases confirmed by PCR testing were analyzed. The most frequent symptoms were dyspnea, cough, weakness, and myalgia. 55% of the patients presented one or more comorbidities (82/150), common comorbidities were diabetes mellitus, hypertension, and chronic obstructive pulmonary disease(COPD). There was no statistically significant difference between men and women when under 60 years of age and over were categorized (p=0.261, Table 2), and mean age was slightly higher in women (p=0.001, Table1). In the study, no difference was found when the lung involvement of those over 60 years of age and those who were not, regardless of gender, were analyzed (Table 4).

However, this finding isn't coherent with earlier studies, which have shown that older age is an essential prognosticator of serious complications or death in COVID-19 (8-12).Since the elderly population mostly has a fragile immune system, proinflammatory responses may be prolonged and the risk of serious outcomes may be increased (13).

Among the 150 patients in this research, we observed that COVID-19 was more frequently diagnosed in men than women, consistent with previously COVID-19 cases (14,15).In this study, the comorbidity rate was 40/62 (64.5%) in female patients, while it was 42/(88) (47.7%) in males which was lower. Despite this, among those who were treated in the intensive care unit, the female/male ratio was 6/10, slightly lower than that of males. However, this result was not statistically significant (Table 2, p=0.742). Chest CT, it was detected that the presence of diffuse multifocal ground-glass opacities and sub pleural lesions or consolidation on the right and/or left in the form of consolidation was female/male 38/69(107 patients) and it was less common in females than males (p=0.016). In other words, the level of advanced lung involvement was 38/61 (62.2%) in women, while it was 69/86 (80.2%) in men, which was higher than in women (Table 2, p=0.016). In short, although the rate of comorbidity was higher in women, admission to the intensive care unit and lung involvement levels were not parallel with comorbidity.

In the study, although there was more comorbidity in women, the rate of hospitalization in the ICU was lower and moderate or common involvement in the lungs was found less than men. When evaluating this situation, the relatively low number of cases should be taken into account. In a previous study, it was stated that the X chromosome has a role in reducing susceptibility to viral and bacterial infections in women. The observation of susceptibility to infections in males from birth to adolescence suggests that sex chromosomes, not sex hormones, play an important role in sexual dimorphism in innate immunity. Differences between genders have been defined in the expression of pattern recognition receptors of the innate immune response and in the functional responses of antigen presenting cells. Moreover, estrogen and testosterone have been noted to modulate the differentiation, maturation, lifespan, and functions of immune cells, including macrophages, natural killer cells, and dendritic cells (16).

When acute phase reactants were evaluated, CRP and ferritin levels were higher in males and were statistically significant (Table 1).However, the contribution of higher ferritin levels in men and slightly higher hemoglobin averages in men cannot be denied. D-Dimer levels were higher in males, but this was not significant. The missing data of the d-dimer can be considered as the reason for this (Table 1).

While the rate of admission to the ICU was 17.1% in all patients with comorbidities, the rate of admission to the ICU was lower and 2.9% in those without comorbidities. (Table 3, p=0.005).

There was no involvement on chest CT in a 68-year-old female patient who was PCR positive. This patient, who was brought to the emergency room with rapid transitory atrial fibrillation and hypotension, was taken to the cardiology intensive care unit and was discharged after completing his treatment in the COVID-19 clinic after his clinical condition stabilized.

Hypoxemia is a risk factor for higher hospital mortality in COVID-19 patients (17).In this study, the rate of oxygen delivery to those with minimal focal lung involvement was 15.2%, while oxygen support was provided to approximately 85% of those with diffuse multifocal involvement or consolidation in the lungs (p=0.001, Table 4).

Three patients died during their hospital stay. The ages and comorbidities of the patients who died were as follows:91-years old female with hypertension,71-years old male with heart failure, and 48-years old male with liver metastasis due to colon malignancy.

When the complete blood count is evaluated; There was no difference between men and women in leukocyte, lymphocyte, and platelet counts (p>0.05, Table 1). Laboratory findings in COVID-19 have been different however most of the studies report leukopenia and lymphopenia. In a study, laboratory parameters of patients diagnosed with COVID-19 were studied, 63% had lymphopenia, 25% had leukopenia (18,19).

Elder age, comorbidities, lactate dehydrogenase (LDH), high levels of d-dimer, leukocytosis, and low thrombocyte counts were reported as risk factors related to death in hospitals of severe COVID-19 patients (20-22). In the presented study, the presence of diabetes mellitus, hypertension, cardiac disease, and comorbidities including COPD were at similar rates to previous studies (23,24).

The cause of leukopenia and lymphopenia in COVID-19 is not well understood however can be related to lymphocyte sequestration, apoptosis, and suppression of bone marrow. However other respiratory tract viruses can have the same impact on the immune system (25).

Steroid therapy was also used for severe complications in nearly 82.5 % of patients (p=0.001,Table 4).

Severe COVID-19 can lead to lung damage and systemic inflammatory response. It has been suggested that the anti-inflammatory effects of corticosteroids may prevent or reduce these harmful effects. The use of corticosteroids in ARDS (acute respiratory distress syndrome) patients has been evaluated in controlled studies. Meta-analysis of these results demonstrated that, compared with placebo, corticosteroid therapy reduced the risk of all-cause mortality.

The recommendations of the COVID-19 Treatment Guidelines Panel (Panel) regarding the use of corticosteroids in patients with COVID-19 are based on the results of these studies (26).The Panel, based on the RECOVERY trial results, those in need of oxygen therapy support in patients with COVID-19 who are on a mechanical ventilator suggested the use of dexamethasone 6 mg. Prednisone 40 mg, Methylprednisolone 32 mg, and Hydrocortisone 160 mg can be used when Dexamethasone is not available (27).

Although corticosteroid has side effects, the results of a randomized controlled trial showed that dexamethasone treatment resulted in low mortality in COVID-19 patients (26).

In our study, two types of infection treatments were used to heal patients with COVID-19. Antiviral (Favipiravir) and antibiotics (levofloxacin or Moxifloxacin or Azithromycin) were used in 100% (150/150), 27.3% (41/150) of patients, respectively. Antibiotic use in female/male was 16/25 (Table 2, p = 0.725). Favipiravir treatment was extended to 5-10 days regardless of gender for those with oxygen saturation below 93% and respiratory rate exceeding 30/minute (Table 4, p=0.001).

Conclusions

This study was limited due to a low number of patients which may restrict the statistical impact. These restrictions may cause statistical bias and therefore the significant difference identified in demographic and symptomatic characteristics and the laboratory findings between the genders. Missing data on several variables, for instance, information of chest CT images and biochemical parameters, may cause bias in the identification of risk factors for mortality in severe patients.

Analyzing the patient data of the early stages of the pandemic, when vaccination is still very limited, presenting the clinical results according to the comorbidities and gender of the patients, and being the first study in inpatient treatment in our region can be seen as the distinguishing aspects of the study.

As a result, although there was more comorbidity in women, the severity of lung involvement and the rate of admission to the intensive care unit were lower than men. The results of larger studies on this subject should be evaluated.

References

1-Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020;5:536-44.

2- Zhu NA, Zhang D, Wang W, Li X,Yang B, Song J et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382(8):727-33.

3-Çantay H, Anuk T, Doğan G, Eren M.S, Gonullu, D. Effects of Covid-19 Pandemic on General SurgeryEmergency Protocol. KocaeliTıpDergisi 2021:10;(Supp: 1): 56-60.

4-Udell JA, Zawi R, Bhatt DL, Keshtkar-Jahromi M, Gaughran F, Phrommintikul A, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. JAMA 2013;310:1711–20.

5-Ersan G, AkkirazBaç G, YükselÖ, Yıldız FŞ, Papila Ç, Arsu G et al. The Demographic and Clinical Features of 479 COVID-19 Patients: A Single-center Experience. Mediterr J Infect Microb Antimicrob 2020;9:9.

6- Dong X, Cao YY, Lu XX, Zhang JJ, Du H,Yan YQ et al. Eleven faces of coronavirus disease 2019. Allergy 2020;75(7):1699-09.

7- Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). J Gen Intern Med 2020;35(5):1545-9.

8-Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13.

9-Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62.

10-Cao JL, Tu WJ, Cheng WL, Yu L, Liu YK, Hu XY, et al. Clinical features and short-term outcomes of 102 patients with corona virus disease 2019 in Wuhan, China. Clin Infect Dis 2020;71:748–55.

11-Choi KW, Chau TN, Tsang O, Tso E, Chiu MC, Tong WL, et al. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med 2003;139:715–23.

12-Hong KH, Choi JP, Hong SH, Lee J, Kwon JS, Kim SM, et al. Predictors of mortality in Middle East respiratory syndrome (MERS). Thorax 2018;73: 286–9.

13-Opal SM, Girard TD, Ely EW. The immunopathogenesis of sepsis in elderly patients. Clin Infect Dis 2005;41 Suppl 7:S504–12.

14-Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.

15-Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061–1069.

16-Jaillon S, Berthenet K, Garlanda C. Sexual Dimorphism in Innate Immunity. Clin Rev Allergy Immunol 2019;56:308–21.

17- Xie J, Covassin N, Fan Z, Singh P,GaoW,Li G et al. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 2020;95: 1138-47.

18-Terpos E, Ntanasis-Stathopoulos I, ElalamyI,KastritisE,Sergentanis TN, Politou M et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020;95:834-47.

19- Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB et al. Hematologic parameters in patients with COVID19 infection. Am J Hematol. 2020;95(8):E213-15.

20-Wu C, Chen X, Cai Y,XiaJ,ZhouX,Xu S et al. Factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180(7):934-43.

21- Wang K, Zhang Z, Yu M, Tao Y, Xie M. 15-day mortality and associated risk factors for hospitalized patients with COVID-19 in Wuhan,China: an ambispective observational cohort study. Intensive Care Med 2020;46(7):1472-4.

22- Liu Y, Sun W, Guo Y, Chen L,ZhangL,Zhao S et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. Platelets 2020;31(4):490-6

23- Huang C, Wang Y, Li X, Ren L,ZhaoJ,Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan. China. Lancet 2020;395:497-506.

24- Guan WJ, Ni ZY, Hu Y,LiangWH,OuCQ,He JX et al. Clinical characteristics of coronavirus disease 2019 in China. NEngl J Med 2020;382(18):1708-20.

25-Cary GR, Sorrell WB, Kilbourne ED, LourıaDB,Rogers DE. The leukopenia of virus infection-relation to the concentration of virus and the viral lesion. Am J Med. 1955;19(1):137.

26-Alhazzani W, Moller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the managementof critically ill adults with coronavirus disease 2019 (COVID-19). Crit Care Med. 2020;48(6):e440-e469.Available at: https://www.ncbi.nlm.nih.gov/pubmed/32224769

27-RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients withCOVID-19. N Engl J Med. 2021;384(8):693-704. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32678530

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 125-130

Ten-year Infective Endocarditis Data of a Tertiary Centre; Mortality, Causative Agents, Surgery and Complications

Tersiyer Merkezin 10 Yıllık Infektif Endokardit Deneyimi; Mortalite, Etkenler, Cerrahi Tedavi ve Komplikasyonlar

Cenk EKMEKCİ* 0000-0001-7130-4819
Ali Kemal ÇABUK* 0000-0001-5549-3744
Barış ÜNAL* 0000-0002-5087-2574
Barış KILIÇASLAN* 0000-0003-1503-7554
Öner ÖZDOĞAN* 0000-0003-3205-6917

*Tepecik Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İzmir.

Yazışma Adresi: Cenk EKMEKCİ
Tepecik Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İzmir.
E-mail: cenkekmekci@outlook.com

Geliş Tarihi: 13/05/2022
Kabul Tarihi: 01/07/2022

Öz

Amaç: İnfektif endokardit (İE) yüksek mortaliteye sahip bir hastalık olup, epidemiyolojik özellikleri zaman içinde değişim gösterdiğinden gerçek yaşam verileri oldukça önemlidir. Bu amaçla merkezimizde İE tanısıyla yatan hastaları; etiyoloji, klinik özellikler, risk faktörleri ve hastane içi mortalite açısından analiz ettik.

Yöntem: Haziran 2011 ile Kasım 2021 tarihleri arasında İE tanısıyla yatan hastalar retrospektif olarak tarandı. Toplamda 81 hasta, hastane içi ölüm yaşanan (grup 1, 41 hasta) ve yaşayan (grup 2, 40 hasta) olarak gruplandırılarak mortalite ile ilişkili olabilecek tüm faktörler açısından analiz edildi.

Bulgular: Grup 1 hastalar (41 hasta, %50.6) grup 2 hastalardan (40 hasta, %49.4) daha yaşlıydı (61.78±14.33'e karşın 54.27±16.75, p =0.014). Kateter ilişkili İE vaka sayısı (12 hasta [%29.3]'e karşın 4 hasta [%10.0], p =0.029) ve santral sinir sistemine vejetasyon embolisi sayısı grup 1'de anlamlı olarak daha fazlaydı (10 hasta [%24.3]' e karşın 4 hasta [%10.0], p =0.043). Ciddi kapak patolojisi olan (grup 1'de 7 hasta [%17.1], grup 2'de 17 hasta [%42.5], p =0.012) ve cerrahi uygulanan hasta sayısı (grup 1'de 11 hasta [%26.8], grup 2'de 21 hasta [%52.5], p =0.018) grup 2'de anlamlı olarak daha fazlaydı.

Sonuç: Hastane içi mortalite ileri yaş , santral sinir sistemi embolizasyonu olan ve kateter ilişkili İE vakalarında anlamlı olarak daha yüksekti. Ciddi kalp kapak fonksiyon bozukluğu olan hastalarda, muhtemelen erken ve etkin cerrahi yaklaşımla, hastane içi mortalite daha düşüktü.

Anahtar Kelimeler: İnfektif endokardit; mortalite; hastane içi

Abstract

Aim: Since infective endocarditis (IE) has high mortality rate and its epidemiologic characterisitcs have been changed over time, real world data is quite important. For this reason, we analyzed all patients who hospitalized in our institution with diagnose of IE in terms of aetiology, clinical features, risk factors and in-hospital mortality.

Methods: The patients hospitalized with diagnose of IE were searched retrospectively between June 2011 and November 2021. A total of 81 patients were divided into two groups as patients who died in-hospital (group 1, n=41) and who survived (group 2, n=40); and analyzed for all parameters may be related with mortality.

Results: The patients in group 1 (n=41, 50.6%) were older than in group 2 (n=40, 49.4%) (61.78±14.33 vs 54.27±16.75, p =0.014).

Number of catheter related IE (n=12 [29.3%] vs n=4 [10.0%], p =0.029) and central nervous system embolization (n=10 [24.3%] vs n=4 [10.0%], p =0.043) were significantly higher in group 1. In group 2, patients with severe heart valve dysfunction (n=7 [17.1%] vs n=17 [42.5%], p =0.012) and patients who underwent surgery (n=11 [26.8%] vs n=21 [52.5%], p =0.018) were significantly higher.

Conclusion: In-hospital mortality was significantly higher in patients with advanced age, central nervous system embolization and catheter related IE. In patients who had severe heart valve dysfunction, in-hospital mortality was lower probably due to early and effective surgical approach.

Keywords: Infective endocarditis, mortality, in-hospital

Introduction

Epidemiologic studies revealed that infective endocarditis (IE) is a relatively rare disorder with an estimated incidence of 30-40 cases per 1 million per year (1,2). The risk of IE increases in patients with advanced age, prosthetic heart valve or history of IE (3). Particularly, patients with chronic kidney disease or cancer are more likely to have increased frequency of healthcare contact and they have implanted prosthetic vascular access devices (such as hemodialysis/chemotherapy catheters) more frequently which increasing the likelihood of bacteremia and IE (4).

The disease was firstly described by Osler W. (5) in 1885 and its epidemiologic characteristics have been modified from then untill now. It is more prevalent in elderly population nowadays and Staphylococcaceae (staphylococcus aureus 25% and coagulase negative staphylococcus 22%) have been become the predominant microorganisms in aetiology, whereas it was Streptococcaceae previously (6). There are many factors underlying modified epidemiologic and aetiologic characteristics of IE such as decreasing insidence of rheumatic heart disease, inceasing average life span together with comorbidities, increasing the number of patients with prosthetic heart valves, implantable intracardiac devices and recieving hemodialysis. Degenerative heart valve diseases, congenital heart disorders, diabetes mellitus, cancer and intravenous drug usage have been taken the place of rheumatic heart disease in terms of being the predominant risk factor of IE (6). However, rheumatic heart disease remains as the main risk factor for IE in low income countries and the predominant microorganisms are still Streptococcaceae in these regions.

Community-associated IE remains the leading form of the disease; nevertheless, health care accounts for 1/3 of cases in the literature are coming from high-income countries.

The differences observed in epidemiologic characteristics of the disase due to socioeconomic factors are fairly important in terms of management the risk factors and therapeutic approaches (7). We think that more data coming from literature will be able to strengthen the physiciancs' hand in managing the patients with IE.

There fore we decided to investigate all parameters related with IE such as risk factors, causative microorganisms, vegetation location and size, response to medical therapy ± sugery and mortality in patients diagnosed with IE in our tertiary medical centre from 2011 to 2021. To our knowledge, this is one of the largest single institution study regarding real life data for IE in Turkey.

Methods

This was a retrospective single-centre study. We searched recorded data for patients hospitalized with diagnosis of IE in our institution (Tepecik Training and Research Hospital, Izmir) from June 2011 to November 2021. This study was carried out in accordance with the conditions of the declaration of Helsinki and approved by our local ethical committee. We enrolled all patients diagnosed with IE and older than 14 years. The only exclusion criteria was obtaining incomplete information in recorded data for a patient. We analyzed for age, sex, physical examination and echocardiography findings, any cardiac pathology (such as coronary heart disease, heart failure, prosthetic heart valve etc.), intravenous drug usage, comorbidities (such as diabetes mellitus, hypertension, chronic kidney disease ± hemodialysis, chronic obstructive pulmonary disease etc.), any intracardiac device, either it was a nosocomial infection or not, laboratory results (such as fasting glucose, blood urea nitrogen and serum creatinine, C-reactive protein, eritrosite sedimentation rate, alanine aminotransferase, aspartate aminotransferase, rheumatoid factor, haemoglobin, white blood cell, platelet count, blood culture and Wright agglutination test etc.), causative microorganism and antimicrobial therapy, surgery ± complications and in-hospital mortality.

Diagnosis of IE was based on Modified Duke Criteria. All patients who had hospitalization history within 6 months till onset of symptoms were accepted as nosocomial infection. Device and catheter related endocarditis defined as detected vegetation on leads or intravenous catheters with transthorasic/transesophageal echocardiography. All patients were given the appropirate antimicrobial combination in a recommended time period concordant with current guidelines (8). We defined two groups as patients who died (group 1) and patients who survived (group 2) during hospitalization period for purpose of determining the predictors of in-hospital mortality.

Statistical analysis

SPSS version 24.0 (SPSS Inc, Chicago, IL) was used for all statistical analyzes. Categorical variables were demonstrated as number and percentage; and continuous variables were demonstrated as mean ± SD when normally distributed while nonparametric variables were shown as median and the percentiles. Categorical variables were analyzed either by the chi-square test or by Fisher's exact test, as appropriate. Student's t-test was used to compare parameters which were normally distributed. Mann-Whitney U test was used to compare paramaters which were non-normally distributed. All statistical testing was on the basis of a 2-sided α=0.05 significance level.

Results

A total of 81 patients diagnosed with IE were enrolled in this study. Baseline characteristics, risk factors, laboratory and echocardiography findings of patients presented in table 1.

Table 1. Baseline characteristics, risk factors, laboratory results and echocardiographic findings of study population

Features	Patients who died (n=41)	Patients who survived (n=40)	p value
Age, years	61.78±14.33	54.27±16.75	**0.014***
Sex, male (n,%)	29 (70.7%)	25 (62.5%)	0.432
Diabetes mellitus (n,%)	14 (34.1%)	8 (20.0%)	0.152
Hypertension (n,%)	20 (48.8%)	20 (50.0%)	0.913
Chronic obstructive lung disease (n,%)	7 (17.1%)	4 (10.0%)	0.353
Cancer (n,%)	6 (14.6%)	2 (5.0%)	0.146
Solid organ transplantation (n,%)	1 (2.4%)	2 (5.0%)	0.542
Congestive heart failure (n,%)	4 (9.8%)	2 (5.0%)	0.414
Atrial fibrillation (n,%)	8 (19.5%)	6 (15.0%)	0.591
Severe valve dysfunction (n,%)	7 (17.1%)	17 (42.5%)	**0.012***
Device related endocarditis (n,%)	1 (2.43%)	2 (5.0%)	0.432
Catheter related endocarditis (n,%)	12 (29.3%)	4 (10.0%)	**0.029***
Positive blood culture (n,%)	33 (80.5%)	30 (75.0%)	0.553
Vegetation area >10 mm (n,%)	29 (70.7%)	26 (65.0%)	0.581
Cardiac surgery for IE (n,%)	11 (26.8%)	21 (52.5%)	**0.018***
Embolism (n,%)	13 (31.7%)	11 (27.5%)	0.678
Central nervous system embolization (n,%)	10 (24.3%)	4 (10.0%)	**0.043***
Hemodialysis (n,%)	11 (26.8%)	13 (32.5%)	0.576
Coronary artery disease (n,%)	10 (24.4%)	9 (22.5%)	0.841
Blood leukocyte count ($x10^9$/l)	16.36±4.48	15.04±5.06	0.218
Blood thrombocyte count ($x10^3$/µl)	141.39±82.89	156.25±50.61	0.395
Blood haemoglobin level (g/dl)	11.04±1.88	11.47±2.66	0.408
Serum CRP level (mg/l)	111.04±95.05	87.45±94.10	0.265
Serum creatinine level (mg/dl)	1.57±1.14	1.43±1.43	0.595
Vegetation area (cm^2)	1.58±1.25	1.62±1.12	0.645
Ejection fraction (%)..	57.43±6.78	56.90±7.73	0.740

CRP; C-reactive protein.
* Indicates statistical significance.

We found that patients in group 1 (n=41, 50.6%) were older (61.78±14.33 vs 54.27±16.75, p =0.014) and prevalences of catheter-related infective endocarditis (12 [29.3%] vs 4 [10.0%], p =0.029) and central nervous system embolization (n=10 [24.3%] vs n=4 [10.0%], p =0.043) were higher compared to group 2 (n=40 [29.7%]) (Table 1). Blood culture positive patients were 77.8% (n=63) of study population. Predisposing conditions, complaints, clinical and laboratory findings related with IE of whole study population were demonstrated in table 2.

Table 2. Predisposing conditions, complaints, clinical features and physical examination findings of study population

Predisposing conditions	n (%)	Complaints	n (%)
Chronic rheumatic heart disease	15 (18.5)	Fever	51 (62)
Mitral annular calcification	17 (21)	Dyspnea	30 (37)
Degenerative aortic valve disease	6 (7.4)	Fatigue	55 (67.9)
Prosthetic heart valve	10 (12.3)	Arthralgia	27 (33.3)
Chronic kidney disease	42 (51.8)	Headache	8 (12.3)
Chronic obstructive pulmonary disease	11 (13)	Anorexia	38 (46.9)
Intravenous drug user	-	**Physical examination and laboratory findings**	
Cardiac implantable electronic device	5 (6.1)	New murmur	22 (27.1)
Previous infective endocarditis	1 (1.2)	Skin rashes	4 (4.9)
		Roth spot	2 (2.4)
		Central nervous system embolization	14 (17.2)
		Splenic abscess	2 (2.4)
		Congestive heart failure	6 (7.4)
		Elevated C-reactive protein level	73 (90.1)
		Elevated erythrocyte sedimentation rate	67 (82.7)

The most prevalent predisposing conditions were chronic kidney disease (n=42, 51.8%), mitral annular calcification (n=17, 21%), chronic rheumatic heart disease (n=15, 18.5%), chronic obstructive pulmonary disease (n=11, 13%) and prosthetic heart valve (n=10, 12.3%). There weren't any patients with congenital heart disease as a predisposing condition; because our centre sends them to the University Hospitals in our city. The most prevalent complaints were fatigue (n=55, 67.9%) and fever (n=51, 62%); and the most common physicial examination finding was new murmur (n=22, 27.1%). The type of surgical intervention (Table 3) and distribution of causative microorganisms (Table 4) were presented in tables. Vegetation size was >10mm in 55 patients (67.9%), and in 24 cases (29.6% of all patients with vegetation regardless of the size) vegetation emboli occured. Thirty-two patients (39.5%) were underwent surgery (e.g. heart valve surgery, lead extraction).

The patients who underwent surgery were significantly higher in group 2 (n=27, [67.5%]) compared to group 1 (n=14, [34.1%])(p =0.021).We found that Staphylococcaceae were the leading microorganisms in aetiology (33 of 81 cases, 40.7%). In group 1, the causative microorganism was identified in thirty-three of 41 patients (80.4%); and Staphylococcaceae were again the leading microorganism (n=9, 27.7%); followed by Enterococcus spp. (n=6, 18.1%) and Klebsiella pneumoniae (n=5, 15.1%) (Table 5).

Table 3. Type of surgical approach in study groups

	Patients who died (n=41)	**Patients who survived (n=40)**
AVR	2	4
MVR	7	8
AVR+MVR	-	2
Redo AVR	-	1
Tricuspid Surgery	1	1
CABG+MVR	-	1
CABG+ Tricuspid Surgery	-	1
MVR+ Tricuspid Surgery	-	1
Mitral Ring Annuloplasty	1	-
Lead Extraction	-	2
Catheter Extraction	3	6

AVR; aortic valve replacement, MVR; mitral valve replacement, CABG; coronary artery by-pass grafting.

Table 5. Relationship between causative agent and mortatily

Causative Agent	**Total (n)**	**Exitus (n)**	**Mortality (%)**
Brucella melitensis	1	1	100
Acinetobacter	2	2	100
Candida parapsilosis	4	2	50
Klebsiella pneumoniae	5	5	100
Coryneabacterium striatum	1	1	100
ESBL Escherichia coli	1	0	0
Candida albicans	1	1	100
Gemella haemolysans	1	1	100
Enterococcus faecalis	6	4	66.6
Enterococcus gallinarum	2	2	100
Escherichia coli	1	1	100
Streptococcus viridans	1	1	100
Streptococcus mitis	2	1	50
Streptococcus gordonii	1	1	100
Streptococcus gallolyticus	1	1	100
MSSA	9	2	22.2
MRSA	4	2	50
Koa neg staph	6	1	16.6
Staph. hominis	1	0	0
Staph. epidermidis	1	0	0
MRCoNS	12	4	33.3

ESBL; extended spectrum betalactamases, MSSA; methicillin-susceptible Staphylococcus aureus, MRSA; methicillin-resistant Staphylococcus aureus, MRCoNS; methicillin-resistant coagulase-negative Staphylococcus aureus.

Table 4. Causative agents of infective endocarditis in study population

Causative Agent	**Native valve n=68**	**Prosthetic valve n=10**	**Lead n=3**	**Total n=81**
Staphylococcus spp				**33**
MRSA	4	-	-	4
MSSA	6	3	-	9
Staphylococcus epidermidis	-	1	-	1
Coagulase-negative staphylococci (CoNS)	5	1	-	6
MRCoNS	10	-	2	12
Staphylococcus hominis	-	-	1	1
Streptococcus spp				**5**
Viridans Streptococcus	1	-	-	1
Streptococcus Mitis	2	-	-	2
Streptococcus Gordonii	1	-	-	1
Streptococcus Gallolyticus	1	-	-	1
Brucella melitensis	1	-	-	**1**
Acinetobacter baumannii	2	-	-	**2**
Candida spp				**5**
Candida albicans	1	-	-	1
Candida parapsilosis	3	1	-	4
Corynebacterium striatum	1	-	-	**1**
Enterobacteriaceae				**7**
Escherichia coli	1	-	-	1
ESBL Escherichia coli	1	-	-	1
Klebsiella pneumoniae	5	-	-	5
Gemella haemolysans	1	-	-	**1**
Enterococcus spp				**8**
Enterococcus faecalis	6	-	-	6
Enterococcus gallinarum	2	-	-	2
Undefined causative agents	**14**	**4**	-	**18**

Interestingly, we found that severe heart valve disease prevalance was significantly lower in patients who died compared to patients who survived (n=7 [17.1%] vs n=17 [42.5%], p =0.012, respectively). We discussed possible mechanisms of this finding in discussion section.

Discussion

In this retrospective study, we found that in-hospital mortality was related with advanced age and central nervous system embolization in patients with infective endocarditis. Recent trials showed a significant positive correlation between mortality rate and vegetation size and/or embolization (9,10). However, we found in our cohort that the mean of vegetation sizes were similar between study groups. Nevertheless, this finding might be a consequence of our relatively small sample size. In-hospital mortality rate was relatively high in our study compared to existing literature. Our institution is a tertiary centre and accepts mostly complicated IE cases such as with cardiac complication (severe valve dysfunction, device related endocarditis), catheter related endocarditis and patients with vegetation embolization; therefore increased mortality rate was an expected finding for us.

An interesting and probably the most important finding of our study was the higher prevalence of severe valve dysfunction in group 2 compared to group 1. Beside this finding, we observed that number of cardiac surgery was also significantly higher in group 1. This relationship may signify early surgical approach in patients with IE and cardiac complication or large vegetation. We also think that low prevalence of cerebrovascular events in our study was related to higher prevalence of early surgical approach. For instance, Kang et al. (11) showed that mortality was significantly lower with early surgery strategy compared to conventional treatment in a high-risk group of patents with severe heart valve dysfunction and/or large vegetation.

The indications for surgery involve the presence of severe valve dysfunction causing heart failure, local uncontrolled infection resulting in abscess formation or heart block, persistent bacteremia despite appropirate antimicrobial therapy, and IE with fungi or drug-resistant organisms (12). However, we know that in case of major cerebrovascular stroke or intracranial hemorrhage surgery should be delayed for at least four weeks.

IE prevalence was also higher in patients with central venous catheter in our study.

This finding is compatible with the literature. Chaudry et al. (13) showed in their retrospective study which particularly focused on hemodialysis recipients, the incidence of endocarditis in patients with central venous catheters was more than two-fold higher as compared with those with arteriovenous fistulas.

When device related IE is confirmed, the mainstay of treatment have to be antimicrobial therapy and complete extraction of the device and leads. Several studies found improved outcomes in patients who underwent complete device system removal versus those treated only with medical therapy (14,15).

In our cohort there were 3 patients who had device related infective endocarditis. Two of them underwent lead and device extraction in addition to medical therapy. One of them could not be treated surgically due to major cerebrovascular event.

Our study has some limitations. This was a retrospective single-centre study, therefore we had a relatively small sample size and we could speculate about the factors related with prognosis to a certain extent. As a second limitation, we did not have enough informations about post-discharge health status of patients and could not indicate overall survey. Lastly, we send patients with a serious disorder and concomittant congenital heart disease to university hospitals in our city, therefore we did not have a cohort with congenital heart disease in this study.

Conclusion

In this study which we presented the 10-year experience of a tertiary centre, it was shown that in-hospital mortality was higher in patients with advanced age, central nervous system embolization and catheter related IE. In patients who had severe heart valve dysfunction, in-hospital mortality was significantly lower probably due to early surgical approach in addition to medical therapy.

References

1. Lung B. Infective endocarditis. Epidemiology, pathophysiology and histopathology.Presse Med. 2019;48(5):513-521.
2. Cresti A, Chiavarelli M, Scalese M, et al. Epidemiological and mortality trends in infective endocarditis, a 17-year population-based prospective study. Cardiovasc Diagn Ther. 2017;7(1):27-35.
3. Prendergast BD. The changing face of infective endocarditis. Heart 2006;92:879-85.
4. Murdoch DR, Corey GR, Hoen B, et al; International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCS) Investigators. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med. 2009;169(5):463-73.
5. Osler W. Gulstonian lectures on malignant endocarditis. Lancet.1885;1:415-8.
6. Cahill TJ, Baddour LM, Habib G, et al. Challenges in Infective Endocarditis. J Am Coll Cardiol. 2017;69(3):325-344.
7. Wang A, Gaca JG, Chu VH. Management Considerations in Infective Endocarditis: A Review. JAMA. 2018;320(1):72-83.
8. Habib G, Lancellotti P, Antunes MJ, et al; ESC Scientific Document Group. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36(44):3075-3128.
9. Thuny F, Di Salvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. Circulation. 2005;112(1):69-75.
10. Nunes MCP, Guimarães-Júnior MH, et al. Outcomes of infective endocarditis in the current era: Early predictors of a poor prognosis. Int J Infect Dis. 2018;68:102-107.
11. Kang DH, Kim YJ, Kim SH, et al. Early surgery versus conventional treatment for infective endocarditis. N Engl J Med. 2012;366(26):2466-73.
12. Hubers SA, DeSimone DC, Gersh BJ, Anavekar NS. Infective Endocarditis: A Contemporary Review. Mayo Clin Proc. 2020;95(5):982-997.
13. Chaudry MS, Carlson N, Gislason GH, et al. Risk of Infective Endocarditis in Patients with End Stage Renal Disease. Clin J Am Soc Nephrol. 2017;12(11):1814-1822.
14. Athan E, Chu VH, Tattevin P, et al; ICE-PCS Investigators. Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. JAMA. 2012;307(16):1727-35.
15. Le KY, Sohail MR, Friedman PA, et al; Mayo Cardiovascular Infections Study Group. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. Heart Rhythm. 2011;8(11):1678-85.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 131-136

Are YouTube Videos Beneficial for Patients Interested in Cervical Disc Herniation Exercises?

YouTube Videoları Servikal Disk Hernisi Egzersizleriyle İlgilenen Hastalar için Faydalı mı?

Emel ATAR*0000-0002-8373-1196

***Medicana Çamlıca Hospital, Department of Physical Medicine and Rehabilitation, Istanbul, Turkey.

Yazışma Adresi: Emel ATAR
Medicana Çamlıca Hastanesi, Fiziksel Tıp ve Rehabilitasyon Kliniği,
Alemdağ Cd. No: 113, 34767 Üsküdar,
İstanbul, TURKEY
E-mail: drataremel@gmail.com

Geliş Tarihi:27/05/2022
Kabul Tarihi: 22/07/2022

Öz

Amaç: Servikal disk hernisi, yetişkinlerde boyun ağrısına neden olan yaygın bir hastalıktır. Konservatif tedaviler sık kullanılan terapötik müdahalelerdir. Egzersiz tedavisi önemli bir yere sahiptir. Bu çalışmanın amacı, servikal disk hernisi egzersizleri ile ilgili YouTube videolarının güvenilirliğini ve kalitesini araştırmaktır.

Gereç ve Yöntem: 14.07.2021 tarihinde YouTube çevrimiçi kitaplığında "servikal disk hernisi egzersizi", "servikal disk hernisi rehabilitasyonu", "servikal disk hernisi fizik tedavisi" ve "servikal disk hernisi fizyoterapisi" anahtar kelimeleri kullanılarak arama yapıldı. Video parametreleri ile kaynakları kaydedildi. Videoların güvenilirliği ve kalitesi değiştirilmiş DISCERN aracı ve Global Kalite Ölçeği (GKÖ) kullanılarak değerlendirildi.

Bulgular: Çalışmaya toplam 51 video dahil edilmiştir. Global Kalite Ölçeği ve değiştirilmiş DISCERN aracının median değerleri sırayla 3 ve 2 bulundu. GKÖ' ye göre videoların %49' u yüksek kalitede bulundu. Değiştirilmiş DISCERN aracı ile GKÖ değerleri arasında anlamlı pozitif korelasyon saptandı ($p<0.05$). Video güç indeksi değerleri ile video süresi, izlenme sayısı, beğenme sayısı, beğenmeme sayısı, yorum sayısı ve günlük görüntülenme oranı arasında pozitif yönde ve istatistiksel olarak anlamlı korelasyon bulundu ($p<0.05$).

Sonuç: Bu çalışmanın sonuçları servikal disk hernisi egzersizleri videolarının çoğunun yüksek kalitede olduğunu gösterdi. Ayrıca yüksek kaliteli videoların daha iyi güvenirlilik puanına ve daha uzun video süresine sahip olduğu bulundu. Servikal disk hernisi tanısına sahip olan hastaların egzersizleri için daha kaliteli ve güvenilir YouTube videolarına ihtiyaç vardır.

Anahtar Kelimeler: Servikal disk hernisi; Egzersiz; YouTube

Abstract

Introduction: Cervical disc herniation is a common disease that causes neck pain. Conservative treatments are frequently used therapeutic interventions. Exercise therapy has an important place. The purpose of this study is to investigate the the educational reliability and quality of the YouTube videos on cervical disc herniation exercises.

Methods: The YouTube online library was searched on July 14th, 2021 by using the keywords "exercises for cervical disc herniation," "physical therapy for cervical disc herniation," "physiotherapy for cervical disc herniation," and "rehabilitation for cervical disc herniation." Video characteristics and resources were analyzed. The quality and reliability of the videos were assessed using the Global Quality Score (GQS) and the Modified DISCERN tool.

Results: Global Quality Score and Modified DISCERN tool median values of a total of 51 videos included were 3 and 2, respectively. According to the Global Quality Score, 49% of the videos had high quality. Modified DS tool scores and Global Quality Score had a positive and significant correlation ($p<0.05$). Correlation analysis between video power index values and video characteristics showed a positive and significant correlation between video power index values and number of views, number of comments, number of likes and dislikes, video duration, and daily view ratio ($p<0.05$).

Conclusion: The results of this study show that most of the videos presenting exercises for CDH are of high quality. Additionally, high-quality videos were found to have better reliability scores and longer video duration. Patients with CDH need better-quality and reliable YouTube videos on relevant exercises.

Keywords: Cervical disc herniation; Exercise; YouTube

Introduction

Intervertebral disc herniation results from the displacement of the nucleus pulposus beyond the intervertebral disc space and can cause compression of the adjacent nerve roots or the spinal cord (1). Cervical disc herniation (CDH) is a widespread cause of neck pain. Although pain is usually the first symptom in patients in CDH, symptoms can include postural deficiencies throughout the body and fear of falling depending on the location and severity of the prolapse (1). Neck pain imposes a heavy burden on the total cost of healthcare, and chronic diseases make up a large portion of this cost. Different treatment protocols in patients with neck problems are often associated with different costs (2). Exercise therapy is widely used for neck pain relief (2).

Most guidelines for the diagnosis and treatment of neck pain recommend a combination of evidence-based physical therapy modalities including manual therapy, exercise, and training (3, 4). Various modalities of physical exercise are recommended in clinical guidelines including strengthening, stretching, exercises for range of motion, proprioceptive training and motor control and are widely used in the treatment for neck pain. The COVID-19 pandemic and resulting lockdowns have led to the delay or suspension of physical therapy sessions for patients (5). Furthermore, this pandemic has resulted in the decrease in the levels of physical activity (6, 7). To maintain physical therapy services during this period, the use of digital tools including telerehabilitation was initiated (5, 8-10). Digital applications are not used in every country (11) and it is difficult for the most of patients to access these applications immediately (12). Internet is no doubt a significant resource for medical information and health-related research (13, 14).

YouTube (Alphabet, Mountain View, CA) is a well-known online platform and it has more than 1 billion visitors per month. It is used for watching and sharing videos as well as sharing information (14, 15). The vast majority of young adults (nearly 90%) use YouTube worldwide (16). YouTube does not have a control mechanism for the quality of uploaded content, leading to a risk of potential spread of inaccurate and inadequate health information (14, 17). However, appropriate videos can allow learning and deliver exercise the rapies.

To the best of our knowledge, there is no study in the literature has assessed the quality of exercise videos posted on YouTube for patients with symptomatic CDH. The COVID-19 pandemic has made it more important to evaluate the educational quality of the online videos offered on YouTube for CDH patients. This study aims to evaluate the quality of information in the YouTube videos on exercises for CDH.

Methods

Ethics statement

As no human participant or animal was included, no ethics committee approval was required for this study.

YouTube search and video characteristics

This is a study planned in a descriptive pattern that evaluates and reviews public videos available on YouTube. A video search was conducted on YouTube online library on 14.07.2021, using the key terms “exercises for cervical disc herniation,” “physical therapy for cervical disc herniation,” “physiotherapy for cervical disc herniation,” and “rehabilitation for cervical disc herniation.”

The online videos were sorted by their view counts. Over 90 percent of users view videos listed on the first 3 pages (18). Thus, the videos displayed on the first three pages for each key term were saved for evaluation.

Videos in language other than English, no-audio videos, videos matching the key words but providing content unrelated to CDH exercises, videos with different exercise programs, commercial and advertising videos, videos not featuring humans, and duplicate videos were excluded. Videos that met the criteria were evaluated by two independent researchers who were physical medicine and rehabilitation physicians.

For each video, the following variables were recorded: title, video duration (second), video source/uploader, number of views, image quality (pixel), days since upload, number of comments, view ratio (number of views/number of days since upload x 100%), number of likes and dislikes, like ratio (like x 100/ like+dislike) and video power index (VPI). The VPI is an index of video popularity (like ratio x view ratio/100) (14).

Emel ATAR

Video uploaders were categorized into three titles, physician, health-related website, and non-physician health personnel.

Video educational content was assessed using the Global Quality Score (GQS), a five-point Likert scale developed by Bernard et al. (19). GQS evaluates online content based on 5 criteria, and has a maximum score of 5 points. A scoring 4 or 5 is considered good/excellent educational quality, 3 is considered intermediate educational quality, and 1 or 2 is considered poor educational quality.(14, 20, 21) (Table 1).

Table 1. *Global Quality Scale (GQS) and Modified DISCERN*

Global Quality Scale (GQS)
1. Poor quality, information missing, technique misleading, not useful
2. Generally sparse quality, some information provided but majority lacking, technique poor, very limitedly use
3. Moderate quality, important information provided but some lacking, technique mostly ade-quate, limitedly useful
4. Good quality, majority of information provided but some information lacking, technique ade-quate, useful
5. Excellent quality, full information provided, technique adequate, very useful
Modified DISCERN (yes=1 point, no=0 point)
1. Is the video clear, concise, and understandable?
2. Are valid sources cited? (from valid studies, physiatrists)
3. Is the information provided balanced and unbiased?
4. Are additional sources of information listed for patient reference?
5. Does the video address areas of controversy/uncertainty?

The reliability of videos was evaluated using the modified DISCERN tool included of five questions. In the scale, questions are answered with yes (1 point) or no (0 point). The score is ranging between 0-5 points, with higher scores indicating increased reliability.(20). (Table 1).

Statistical analysis

The data analysis was performed using the IBM SPSS Statistics Version 22 (IBM Corp., Armonk, NY). Fisher's Exact test and Chi-square test for trend were used in comparing categorical data between groups; Kruskal–Wallis (Post hoc Bonferroni-adjusted Mann–Whitney U) statistical analysis was used in comparing more than two groups when continuous data were not normally distributed. Spearman's rho and pearson correlation analyzes were used to evaluate the connections between variables. $p < 0.05$ was considered as significant.

Results

A total of 51 videos which was applied the inclusion criteria were examined. The median duration of the videos was 496 (128–1794) seconds, the median view count was 45730 (349–2432204). The median number of likes was 853 (6–51861), number of dislikes was 17 (0–1087), and the like ratio was 97.97 (75–100). The median value of the daily view ratio was 53 (0.82–1752.93) and the VPI was 50.88 (0.82–1729.22). Half of the videos (52.9%, n = 27) had been uploaded by non-physician health care personnel, 35.3% (n = 18) by physicians, and 11.8% (n = 6) by health information websites. Video characteristics are shown in Table 2.

Table 2: *General characteristics of the videos*

		Total sample (n=51)
Video source/uploader	Physicians	18 (35.3)
	Health information websites	6 (11.8)
	Non-physician health care personnel	27 (52.9)
GQS	Poor quality	1 (2.0)
	General poor quality	7 (13.7)
	Intermediate quality	18 (35.3)
	Good quality	20 (39.2)
	Excellent quality	5 (9.8)
GQS	Poor quality	8 (15.7)
	Intermediate quality	18 (35.3)
	Good-Excellent quality	25 (49.0)
Modified DISCERN	1	4 (7.8)
	2	27 (52.9)
	3	16 (31.4)
	4	3 (5.9)
	5	1 (2.0)
GQS		3 (1-5)
Modified DISCERN		2 (1-5)
Duration, second		496 (128-1794)
Number of views		45730 (349-2432204)
Image quality (pixel)		1080 (360-2160)
Number of likes		853 (6-51861)
Number of dislikes		17 (0-1087)
Number of comments		76 (0-2724)
Days online		730 (71-4105)
Daily view ratio		53 (0.82-1752.93)
Like ratio		97.97 (75-100)
VPI		50.88 (0.82-1729.22)

Values are median (minimum-maximum) or n (%). GQS, Global Quality Score; VPI, Video Power Index

Five videos received 5 points which is the highest score on the GQS. The median GQS score was 3, with 2% "poor quality," 13.7% "general poor quality," 35.3% "suboptimal quality," 39.2% "good quality," and 9.8% "excellent quality."

However, on the modified DISCERN (DS) score, there was one video with the highest score. The median modified DS score was 2. According to the modified DS, 7.8% of the videos had a score of 1 point, 52.9% had 2 points, 31.4% had 3 points, 5.9% had 4 points, and 2% had 5 points. Breakdown of scores by GQS and modified DS score is given in Table 2.

Comparison of GQS and video parameters showed a positive and significant correlation between video duration and GQS values ($p<0.05$). Modified DS values and GQS values had a positive and significant correlation. ($p<0.05$) (Table 3).

Table 3: Comparison of global quality score and video parameters

	GQS			X^2	p
	Poor quality	Intermediate quality	Good-Excellent quality		
Modified DISCERN	2 (1-2)	2 (1-4)	2 (2-5)	10.295	***0.006***
Duration, second	263.5 (128-616)	286 (131-1794)	706 (173-1352)	15.604	***0.000***
Number of views	69169.5 (349-409502)	42207.5 (1052-1275829)	63418 (1395-2432204)	1.375	0.503
Image quality (pixel)	1080 (360-1080)	1080 (720-2160)	1080 (720-2160)	1.276	0.528
Number of likes	369.5 (24-10071)	637.5 (6-13689)	1809 (73-51861)	3.954	0.138
Number of dislikes	17.5 (0-154)	10 (1-478)	57 (0-1087)	1.468	0.480
Number of comments	18.5 (2-790)	36,5 (0-856)	249 (0-2724)	5.130	0.077
Days online	562.5 (144-3225)	1234 (335-4105)	629 (71-2806)	3.363	0.186
Daily view ratio	31.83 (0.82-585)	28.55 (1.52-600)	163.45 (4.04-1752.93)	4.713	0.095
Like ratio	97.74 (93.84-100)	97.21 (75-99.46)	98.4 (93.82-100)	4.375	0.112
VPI	30.66 (0.82-576.11)	28.1 (1.14-578)	15846 (4.04-1729.22)	4.800	0.091

Kruskal Wallis H test. Values are median (minimum-maximum). GQS, Global Quality Score; VPI, Video Power Index

Analysis of video parameters, quality, and reliability by video source/uploader revealed no significant difference between groups ($p>0.05$) (Table 4).

Table 4: Comparison of video parameters, quality, and reliability based on source /uploader

	Physicians	Health information websites	Non-physician health care personnel	X^2	p
Duration, second	344.5 (128-1147)	258 (131-1794)	608 (134-1352)	4.145	0.126
Number of views	93821 (349-2432204)	48405.5 (8688-113286)	32757 (577-1275829)	0.325	0.850
Image quality (pixel)	1080 (360-2160)	1080 (720-1080)	1080 (720-2160)	1.375	0.503
Number of likes	1337.5 (6-51861)	832.5 (51-1948)	819 (24-14275)	0.722	0.697
Number of dislikes	27 (0-1087)	25 (1-79)	17 (0-565)	0.248	0.883
Number of comments	223.5 (0-2724)	28.5 (2-214)	76 (0-856)	1.961	0.375
Days online	722.5 (144-4105)	782.5 (335-2831)	803 (71-2806)	0.287	0.866
Daily view ratio	84.5 (0.82-1752.93)	59.5 (3.06-310)	53 (3.84-1242.97)	0.145	0.930
Like ratio	98 (75-100)	96.5 (89.47-98.96)	98.16 (93.82-100)	4.318	0.115
VPI	82.75 (0.82-1729.22)	56.95 (2.73-297)	50.88 (3.84-1195.65)	0.164	0.921
GQS	3 (2-5)	3 (1-3)	4 (2-5)	1.339	0.247
Modified DISCERN	2 (1-4)	2 (2-4)	2 (1-5)	0.048	0.976

Kruskal Wallis test. Values are median (minimum-maximum). GQS, Global Quality Score; VPI, Video Power Index

Correlation analysis between GQS, modified DS and VPI values, and video characteristics showed a positive and significant correlation between GQS values and video duration; a significant positive correlation between modified DS values and GQS values; and a positive and significant correlation between VPI values and video duration, number of views, number of likes, number of dislikes, number of comments and daily view ratio ($p<0.05$) (Table 5).

Table 5: Correlation of video properties with GQS, modified DISCERN and VPI values

	Modified DISCERN		GQS		VPI	
	r	p	r	p	r	p
GQS	0.359	***0.010***	1.000			
VPI	-0.053	0.714	0.264	0.061	1.000	
Duration, second	0.201	0.156	0.585	***0.000***	0.343	***0.014***
Number of views	-0.122	0.394	0.122	0.393	0.923	***0.000***
Image quality (pixel)	0.115	0.421	0.170	0.233	0.166	0.245
Number of likes	-0.101	0.481	0.240	0.090	0.961	***0.000***
Number of dislikes	-0.061	0.671	0.116	0.420	0.921	***0.000***
Number of comments	-0.038	0.790	0.271	0.054	0.910	***0.000***
Days online	-0.101	0.481	-0.161	0.258	0.066	0.643
Daily view ratio	-0.055	0.703	0.259	0.066	1.000	***0.000***
Like ratio	-0.117	0.413	0.218	0.125	-0.148	0.298

GQS, Global Quality Score; VPI, Video Power Index

Emel ATAR

Discussion

This study is possibly the first to investigate the quality and reliability of YouTube videos on exercises for patients with CDH. Former studies have already researched the quality of YouTube videos regarding exercises for lumbar disc herniation, pelvic floor muscle, carpometacarpal osteoarthritis, and ankylosing spondylitis. As 60%–70% of people go online to access health information (22, 23), it is crucial to evaluate videos presenting exercises for CDH. This is primarily because inaccurate information with poor reliability and quality may result in poor outcomes (14). Results of the this study demonstrated that 74% of the videos had medium/high quality. Videos with high quality had longer durations and higher reliability.

According to the GQS, 49% (n = 25) of the videos had high quality, 35.3% (n = 18) had suboptimal quality, and 15.7% (n = 8) had poor quality. Studies in the literature reviewing videos on different diseases have found different results on quality and reliability. In one study that reviewed 77 videos for LDH exercises, Kocyigit et al. found more than a third of the videos (36.4%) were of good/excellent quality (21). Heisinger et al. evaluated 76 videos on LDH exercises and found that 40.8% of the videos were of moderate quality, 6.6% of good quality, and 0% of excellent quality (12). Yıldız et al. analyzed 103 educational videos on YouTube for vestibular rehabilitation and found that they had a relatively low GQS level (24). Villafañe et al. evaluated 10 YouTube videos on thumb exercises for carpometacarpal osteoarthritis and found that their quality was poor (25). Culha et al. assessed the quality of 52 videos containing useful information for pelvic floor exercises and found the quality moderate (26). Rodriguez-Rodriguez et al. analyzed YouTube videos on pelvic floor exercises after prostatectomy surgery and found the quality high (27). In another study evaluating 56 videos providing exercises for ankylosing spondylitis, Kocyigit et al. found the quality of nearly half of the videos (48.2%) high (28). The difference in the results may be attributable to different groups of patients.

The reliability of the videos was evaluated using the modified DS. One study by Kocyigit et al. evaluating videos presenting exercises for LDH found that videos with good/excellent quality had a higher median DS (21). Heisinger et al. found a median DS score of 2 for the videos providing exercises for LDH (40.8%) (12). In their study that analyzed pelvic floor exercises after prostatectomy, Rodriguez-Rodriguez et al. reported a statistically significant correlation between the modified DS and GQS (27). Askin et al. assessed 21 YouTube videos that provide information for Transcranial Magnetic Stimulation used in stroke and they found a significant positive correlation between GQS and modified DISCERN questionnaire scores (29). Another study by Kocyigit et al. evaluating videos on exercises for the treatment of ankylosing spondylitis showed that high-quality videos were also more reliable (28). Similarly, the present study found correlations between the GQS and modified DS scores of the videos. Kocyigit et al. found no correlation between like ratio, the number of daily views, and number of daily comments, and video reliability and quality (21). This result is like to the results of the present study. Additionally, in their study analyzing videos presenting exercises for ankylosing spondylitis, Kocyigit et al. found that the number of daily views, comments and likes were not associated with the quality of the videos (28). These results may interpreted to suggested that internet visitors may have hassle accessing quality and reliable videos.VPI measures popularity of the video based upon the number of likes and views. The present study found a mean VPI value of 50.88, and a significant correlation between VPI and number of views, number of comments, number of likes, number of dislikes, video duration, and daily view ratio. Videos rated as low quality according to the GQS had a median VPI value of 30.66; those with moderate quality had a VPI of 28.1, and high-quality videos had a median VPI of 158.46. Rodriguez-Rodriguez et al. found a mean VPI of 92.28 (27). Additionally, the same study found that videos by a very poor GQS value had a mean VPI of 89.88; videos rated as poor had a VPI of 90.94; a moderate score had a VPI of 93.31; high scores had a VPI of 90.30 and videos rated as very high quality according to the GQS had a VPI of 96.41. Rodriguez-Rodriguez et al. found no statistically significant correlation between video duration and popularity or quality (27). Similar to the research by Aydin et al., this study also found that videos with higher VPI and a longer duration seemed to be related with higher quality scores (30).

The uploaders/sources of the videos were as follows: physicians, health information websites, and non-physician health care personnel. Consistently with our study, Culha et al. on videos presenting pelvic floor muscle exercises found no correlation between video source and quality and reliability (26). However, an association was found between video source and quality by Kocyigit et al. in their study examining ankylosing spondylitis exercises videos, by Rodriguez-Rodriguez et al. in their study that evaluated pelvic floor exercises after prostatectomy, and by Heisinger et al. in their study about LDH exercises videos (12, 27, 28). This difference may be attributable to the relatively small number of videos in the present study. In addition, this study could not find any video uploaded by academic sources. This result supports other studies claiming that healthcare institutions is not sufficient in the publication of videos containing medical information (27, 31).

Some limitations of this study need to be acknowledged. First of all, the number of videos was relatively small. Only English videos were searched in the study. There is no verified tool to control health information on the internet.

Conclusions

The results of this study show that most of the videos presenting exercises for CDH are of high quality. Additionally, high-quality videos were found to have better reliability scores and longer video duration. YouTube is a web platform frequently used by patients for acquiring knowledge and is also the second largest search engine. Therefore, it is crucial to ensure that videos contain high-quality and reliable information. As there is no control mechanism for YouTube, and inaccurate health information is difficult to correct, physicians should refer patients to right sources with high quality on the Internet. Patients with CDH need better-quality and reliable YouTube videos on relevant exercises.

References

1.Wu PH, Kim HS, Jang IT. Intervertebral Disc Diseases PART 2: A Review of the Current Diagnostic and Treatment Strategies for Intervertebral Disc Disease. Int J Mol Sci. 2020;21(6).
2.Safiri S, Kolahi AA, Hoy D, Buchbinder R, Mansournia MA, Bettampadi D, et al. Global, regional, and national burden of neck pain in the general population, 1990-2017: systematic analysis of the Global Burden of Disease Study 2017. Bmj. 2020;368:m791.
3.Parikh P, Santaguida P, Macdermid J, Gross A, Eshtiaghi A. Comparison of CPG's for the diagnosis, prognosis and management of non-specific neck pain: a systematic review. BMC Musculoskelet Disord. 2019;20(1):81.
4.Corp N, Mansell G, Stynes S, Wynne-Jones G, Morsø L, Hill JC, et al. Evidence-based treatment recommendations for neck and low back pain across Europe: A systematic review of guidelines. Eur J Pain. 2021;25(2):275-95.
5.Minghelli B, Soares A, Guerreiro A, Ribeiro A, Cabrita C, Vitoria C, et al. Physiotherapy services in the face of a pandemic. Rev Assoc Med Bras (1992). 2020;66(4):491-7.
6.Violant-Holz V, Gallego-Jiménez MG, González-González CS, Muñoz-Violant S, Rodríguez MJ, Sansano-Nadal O, et al. Psychological Health and Physical Activity Levels during the COVID-19 Pandemic: A Systematic Review. Int J Environ Res Public Health. 2020;17(24).
7.Ammar A, Brach M, Trabelsi K, Chtourou H, Boukhris O, Masmoudi L, et al. Effects of COVID-19 Home Confinement on Eating Behaviour and Physical Activity: Results of the ECLB-COVID19 International Online Survey. Nutrients. 2020;12(6).
8.Falvey JR, Krafft C, Kornetti D. The Essential Role of Home- and Community-Based Physical Therapists During the COVID-19 Pandemic. Phys Ther. 2020;100(7):1058-61.
9.Gitkind AI, Levin S, Dohle C, Herbold J, Thomas M, Oh-Park M, et al. Redefining Pathways into Acute Rehabilitation during the COVID-19 Crisis. Pm r. 2020;12(8):837-41.
10.Prvu Bettger J, Resnik LJ. Telerehabilitation in the Age of COVID-19: An Opportunity for Learning Health System Research. Phys Ther. 2020;100(11):1913-6.
11.da Mata KRU, Costa RCM, Carbone É DSM, Gimenez MM, Bortolini MAT, Castro RA, et al. Telehealth in the rehabilitation of female pelvic floor dysfunction: a systematic literature review. Int Urogynecol J. 2021;32(2):249-59.
12.Heisinger S, Huber D, Matzner MP, Hasenoehrl T, Palma S, Sternik J, et al. Online Videos as a Source of Physiotherapy Exercise Tutorials for Patients with Lumbar Disc Herniation-A Quality Assessment. Int J Environ Res Public Health. 2021;18(11).
13.Diaz JA, Griffith RA, Ng JJ, Reinert SE, Friedmann PD, Moulton AW. Patients' use of the Internet for medical information. J Gen Intern Med. 2002;17(3):180-5.
14.Springer B, Bechler U, Koller U, Windhager R, Waldstein W. Online Videos Provide Poor Information Quality, Reliability, and Accuracy Regarding Rehabilitation and Return to Sport After Anterior Cruciate Ligament Reconstruction. Arthroscopy. 2020;36(12):3037-47.
15.MacLeod MG, Hoppe DJ, Simunovic N, Bhandari M, Philippon MJ, Ayeni OR. YouTube as an information source for femoroacetabular impingement: a systematic review of video content. Arthroscopy. 2015;31(1):136-42.
16.Pew Research Centre. Social Media Usage: 2005-2015. http://www.pewinternet.org/fact-sheet/social-media/. Accessed July 10, 2019.
17.Kunze KN, Cohn MR, Wakefield C, Hamati F, LaPrade RF, Forsythe B, et al. YouTube as a Source of Information About the Posterior Cruciate Ligament: A Content-Quality and Reliability Analysis. Arthrosc Sports Med Rehabil. 2019;1(2):e109-e14.
18.Tolu S, Yurdakul OV, Basaran B, Rezvani A. English-language videos on YouTube as a source of information on self-administer subcutaneous anti-tumour necrosis factor agent injections. Rheumatol Int. 2018;38(7):1285-92.
19.Bernard A, Langille M, Hughes S, Rose C, Leddin D, Veldhuyzen van Zanten S. A systematic review of patient inflammatory bowel disease information resources on the World Wide Web. Am J Gastroenterol. 2007;102(9):2070-7.
20.Singh AG, Singh S, Singh PP. YouTube for information on rheumatoid arthritis--a wakeup call? J Rheumatol. 2012;39(5):899-903.
21.Kocyigit BF, Okyay RA, Akaltun MS. YouTube as a Source of eHealth: Is It Beneficial for Lumbar Disc Herniation Exercises? Journal of Physical Medicine & Rehabilitation Sciences/Fiziksel Tıp ve Rehabilitasyon Bilimleri Dergisi. 2020;23(3).
22.Atkinson NL, Saperstein SL, Pleis J. Using the internet for health-related activities: findings from a national probability sample. J Med Internet Res. 2009;11(1):e4.
23.Madathil KC, Rivera-Rodriguez AJ, Greenstein JS, Gramopadhye AK. Healthcare information on YouTube: A systematic review. Health Informatics J. 2015;21(3):173-94.
24.Yildiz S, Toros SZ. The Quality, Reliability, and Popularity of YouTube Education Videos for Vestibular Rehabilitation: A Cross-sectional Study. Otol Neurotol. 2021;42(8):e1077-e83.
25.Villafañe JH, Cantero-Tellez R, Valdes K, Usuelli FG, Berjano P. Educational Quality of YouTube Videos in Thumb Exercises for Carpometacarpal Osteoarthritis: A Search on Current Practice. Hand (N Y). 2018;13(6):715-9.
26.Culha Y, Seyhan Ak E, Merder E, Ariman A, Culha MG. Analysis of the YouTube videos on pelvic floor muscle exercise training in terms of their reliability and quality. Int Urol Nephrol. 2021;53(1):1-6.
27.Rodriguez-Rodriguez AM, Blanco-Diaz M, Lopez-Diaz P, de la Fuente-Costa M, Sousa-Fraguas MC, Escobio-Prieto I, et al. Quality Analysis of YouTube Videos Presenting Pelvic Floor Exercises after Prostatectomy Surgery. J Pers Med. 2021;11(9).
28.Kocyigit BF, Nacitarhan V, Koca TT, Berk E. YouTube as a source of patient information for ankylosing spondylitis exercises. Clin Rheumatol. 2019;38(6):1747-51.
29.Askin A, Sengul L, Tosun A. YouTube as a Source of Information for Transcranial Magnetic Stimulation in Stroke: A Quality, Reliability and Accuracy Analysis. J Stroke Cerebrovasc Dis. 2020;29(12):105309.
30.Aydin MA, Akyol H. Quality of Information Available on YouTube Videos Pertaining to Thyroid Cancer. J Cancer Educ. 2020;35(3):599-605.
31.Kuru T, Erken HY. Evaluation of the Quality and Reliability of YouTube Videos on Rotator Cuff Tears. Cureus. 2020;12(2):e6852.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 137-142

Oral Beslenme Solüsyonları Gerçekten Etkin Kullanılabiliyor mu? Hastanın Bilgilendirilmesinin Önemi

Can Oral Nutrition Solutions Really be Used Effectively? The Importance of Informing the Patient

Haldun KAR* **0000-0001-7710-0665**
Eda İMECE* **0000-0003-2375-1993**
Buse BAKIR** **0000-0001-5884-5063**
Yeliz YILMAZ BOZOK* **0000-0003-1811-122X**

* İzmir Katip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Beslenme Destek Ekibi, İzmir-Türkiye
** İzmir Katip Çelebi Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, İzmir-Türkiye

Yazışma Adresi: Haldun KAR
Katip Çelebi Universitesi Atatürk Eğitim ve Araştırma Hastanesi, Nutrisyon Destek Ekibi, 35360,Yeşilyurt -Izmir
E-mail: haldunkar@hotmail.com

Geliş Tarihi: 07/06/2022
Kabul Tarihi:30/07/2022

Öz

Amaç: Oral beslenme solüsyonları (OBS) malnutrisyon tedavisinde anahtar role sahiptir. Fakat hastaların bu ürünlere karşı tolerasyon ve uyumu değişkenlik göstermektedir. Bu çalışmada oral beslenme solüsyonlarının kullanımını etkileyen faktörlerin ortaya konması ve bu ürünlere uyumu kolaylaştıracak kuralların geliştirilmesi amaçlanmıştır.

Gereç ve yöntem: Tanımlayıcı ve retrospektif nitelikteki bu araştırma İzmir Kâtip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi Dahiliye ve Genel Cerrahi kliniklerinde OBS order edilmiş olan hastaların dosya incelemesi ile yürütülmüştür.

Bulgular: Çalışmamızda OBS kullanma düzeyi %59,14 olarak bulundu. Bilgilendirme yapılan hastaların OBS kullanım düzeylerinin bilgilendirme yapılmayan hastalara kıyasla daha yüksek olduğu, oral beslenme solüsyonunun tadını beğenmeyen ve bulantısı olan hastaların kullanım düzeylerinin, iştahsız hastalara göre daha düşük olduğu istatistiksel olarak anlamlı bulundu. Karar ağacı modelinde, tadını beğenme durumunun kullanım düzeyi üzerinde en etkili faktör olduğu görüldü.

Sonuç: Oral beslenme solüsyonları order edilmeden önce hastalar ürün içeriği ve yararı konusunda bilgilendirilmelidir. Order edilecek ürün hastalara denetilmeli ve miktar başlangıçta az tutulup hastanın tolerasyon ve uyumuna göre artırılmalıdır.

Anahtar Kelimeler: Enteral beslenme solüsyonları, malnutrisyon, uyum

Abstract

Objective: Oral nutritional solutions (ONS) have a key role in the treatment of malnutrition. However, the tolerance and compliance of patients to these products varies. In this study, it is aimed to reveal the factors affecting the use of oral nutrition solutions and to develop rules that will facilitate compliance with these products.

Methods: This descriptive and retrospective study was conducted by examining the files of patients who were ordered ONS in İzmir Katip Çelebi University Atatürk Training and Research Hospital Internal Medicine and General Surgery clinics.

Results: The level of using ONS was found to be 59.14%. It was found statistically significant that the level of ONS use of the informed patients was higher than the patients who were not informed, and the use levels of the patients who did not like the taste of the oral nutrition solution and who had nausea were lower than those of the patients who had no appetite. In the decision tree model, it was seen that liking the taste was the most effective factor on the level of use.

Conclusion: Before prescribing oral nutrition solutions, patients should be informed about the content and benefits of the product. The product to be prescribing should be tasted by the patients and the amount should be kept low at the beginning and increased according to the patient's tolerance and compliance.

Keywords: Enteral nutrition solutions, malnutrition, compliance

Giriş

Hastaneye başvurularda hastalık ile ilişkili malnutrisyon oranları %20-60 olarak rapor edilmiştir (1). Bu hasta grubunun hastaneye ilk yatışta nutrisyonel tarama yöntemleri ile tespit edilip, beslenme desteğinin başlanması ve yakın takibinin yapılması durumunda hastanede yatış sürelerinin kısalacağı, morbidite ve mortalitenin düşeceği, maliyetin azalacağı ve yaşam kalitesinin artacağı literatürde bildirilmiştir (2,3,4). Oral yol ile beslenebilen malnutrisyonu olan ve/veya malnutrisyon riski altındaki hastalar, günlük kalori ihtiyacının %70'ini mevcut diyeti ile karşılayamadığı takdirde ihtiyacın kalan bölümü oral beslenme solusyonları (OBS) ile karşılanabilir (2,5). OBS hastaların besin ve enerji alımlarını artırmak için kullanılan makro ve mikro besin öğelerini içeren, değişen konsantrasyonlarda hazır beslenme solusyonlarıdır (2). Yapılan çalışmalar ve uluslararası kılavuzlar OBS'nin malnütrisyonlu veya malnütrisyon riski altındaki hastalarda klinik olarak efektif olduğunu göstermiş ve kullanımını desteklemektedir (2,3). OBS kullanımının nutrisyonel tedavide etkinliği, hastaların order edilen ürüne uyumu ile ilgili olarak değişkenlik göstermektedir (6). Yüksek OBS uyumu, enerji alımında ve vücut ağırlığında artış ile ilişkili bulunmuştur (2). Hastaların OBS'ye uyumu ile ilgili birçok faktör tanımlanmış olup Dünya Sağlık Örgütü bu faktörleri hasta ile ilişkili faktörler, sosyal ve ekonomik faktörler, sağlık ekibi ve sistemle ilişkili faktörler, sağlık durumu ile ilişkili faktörler ve beslenme tedavisi ile ilişkili faktörler olarak beş ana grupta toplamıştır (5). Bu çalışmada oral beslenme solüsyonlarının kullanımını etkileyen faktörlerin ortaya konması ve bu ürünlere uyumu kolaylaştıracak kuralların geliştirilmesi amaçlanmıştır.

Gereç ve Yöntem

Tanımlayıcı ve retrospektif nitelikteki bu araştırma İzmir Kâtip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi Dahiliye ve Genel Cerrahi kliniklerinde OBS order edilmiş olan hastaların dosya incelemesi ile yürütülmüştür.

Hastaları tanıtıcı bilgiler (yaş, cinsiyet, eğitim durumu, yattığı klinik, hastalık tanısı), beslenme durumuna ilişkin bilgiler, (NRS 2002-Nutrition Risk Screening 2002- puanı, hastanede verilen rasyon, rasyon tüketim durumu, hastane dışından tüketim durumu) ve OBS'ye ilişkin bilgiler (order edilen ürün ve miktarı, hastanın ürünle ilgili bilgilendirilme durumu, bilgilendirme yapan kişi, hastanın ürünü tüketme/tüketmeme nedeni) dosyalardan kaydedilmiştir.

Tüple enteral beslenen hastalar, terminal dönem kanser hastaları, 18 yaş altı hastalar ve OBS order edilmiş olsa da ürün tüketimine dair bilgileri dosyalarda eksik olan hastalar çalışma dışı bırakılmıştır. Araştırma, 85 hastanın dosya incelemesi ile tamamlanmıştır.

Çalışma Helsinki Bildirgesi'ne uygun olarak tasarlandı ve yürütüldü. Bu çalışma, Katip Çelebi Üniversitesi Klinik Araştırmalar Etik Komitesi'nin onayı ile yapılmıştır (20.01.2022/0603).

Verilerin İstatistiksel Analizi

Araştırma verileri Sosyal Bilimler için İstatistik Paket Programı (Statistical Packag efor Social Sciences, SPSS Inc., Chicago, IL, ABD, Versiyon 21.0) kullanılarak analiz edilmiştir. Çalışma kapsamında ele alınan faktörlerin OBS kullanım düzeyi üzerindeki etkisi Kruskal Wallis testi kullanılarak değerlendirilmiştir. Aynı zamanda karar ağaçları tekniği kullanılarak OBS kullanma düzeyine etki eden temel faktörlerin belirlenmesi amaçlanmıştır. Yapılan analizlerde hata düzeyi 0,05 olarak belirlenmiştir.

Bulgular

Çalışma kapsamında değerlendirmeye alınan 85 hastanın 59'u (%69,4) erkek, 26'sı (%30,6) kadın olup yaş ortalaması 65 (18-95) yıldır. Ortalama OBS kullanım düzeyi %59,14 olarak belirlenmiştir. Hastaların cinsiyet, yaş grubu, eğitim durumu, klinik, tanı ve operasyon durumuna göre OBS kullanım düzeyleri benzer bulunmuştur (p>0,05) (Tablo 1).

Tablo 1. Hastaların genel özellikleri

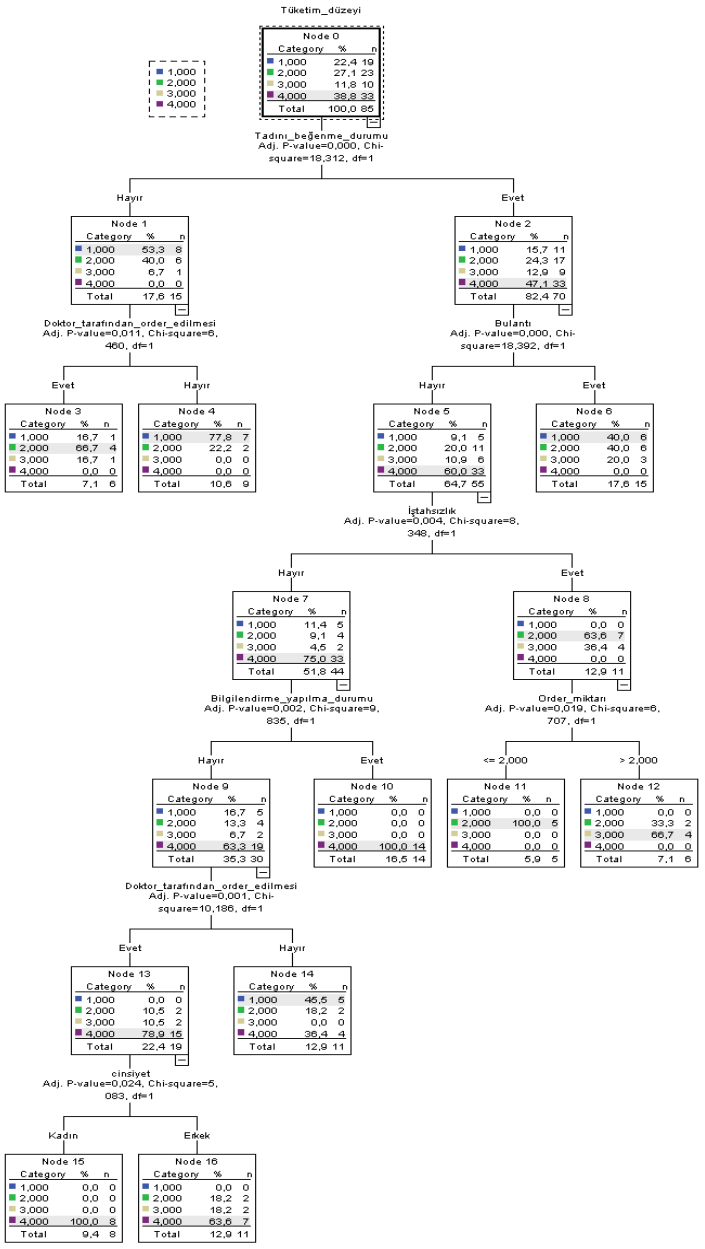
		Hasta Sayısı (n)	OBS Kullanım Düzeyi (%)	p
Cinsiyet				
	Erkek	59	55,25	0,168
	Kadın	26	67,95	
Yaş (Yıl)				
	≤ 50	15	64,44	
	51 – 60	12	63,33	
	61 – 70	23	53,62	0,911
	71 – 80	22	56,06	
	≥ 81	13	64,10	
Eğitim Durumu				
	Okuryazar değil	10	65,33	
	Okuryazar	6	75,00	
	İlkokul	21	57,14	
	Ortaokul	17	53,92	0,930
	Lise	23	57,25	
	Üniversite	8	61,25	
Klinik				
	Göğüs Hastalıkları	4	45,83	
	Nöroloji	8	79,17	
	Palyatif	16	53,13	
	Dahiliye	14	53,57	
	Tıbbi Onkoloji	5	73,33	
	Hematoloji	8	69,58	0,603
	Genel Cerrahi	18	47,22	
	Kulak Burun Boğaz	4	75,00	
	Diğer	8	67,08	
Tanı				
	Kanser	54	52,90	
	Göğüs Hastalıkları	5	70,00	
	Nörolojik Hastalıklar	5	76,67	
	GİS Hastalıkları	9	46,67	0,172
	Kalp-Damar Hastalıkları	3	83,33	
	Hematolojik Hastalıklar	3	83,33	
	Diğer	6	86,11	
Operasyon				
	Operasyon planı yok	68	60,44	
	Preoperatif	8	58,33	0,779
	Postoperatif	9	50,00	

Bilgilendirme yapılan hastaların OBS kullanım düzeylerinin bilgilendirme yapılmayan hastalara kıyasla daha yüksek olduğu (sırasıyla %72,59, %52,87); tadını beğenmeyen (%24,00) ve bulantısı olan (%30,00) hastalarda, iştahsız olan hastalara (%55,56) göre OBS kullanım düzeylerinin daha düşük olduğu belirlenmiştir (p<0,05). Oral beslenme solüsyonu kullanma düzeyi üzerinde diğer faktörlerinin etkili olmadığı görülmüştür (Tablo 2).

Tablo 2. Hastaların beslenme durumu ve OBS'ye ilişkin bilgileri

	Hasta Sayısı (n)	OBS Kullanım Düzeyi (%)	p
Beden Kütle İndeksi (kg/m²)			
≤ 20	15	58,89	0,636
20 – 25	44	62,73	
≥ 25	26	53,21	
NRS 2002 Puanı			
3 – 4	75	61,02	0,253
5 – 6	10	45,00	
Rasyon			
Normal yemek	18	58,33	0,832
Diyet yemeği	67	59,35	
Rasyon Tüketimi			
Tamamı	10	60,00	0,782
Yarısı	36	61,76	
Dörtte biri	25	61,47	
Hiç	14	47,62	
Hastane Dışından Besin Tüketimi			
Evet	28	55,95	0,613
Hayır	57	60,70	
Hastane Dışından Besin Tüketim Miktarı	3	66,67	0,840
Yarısı	21	55,56	
Dörtte biri	4	50,00	
Dörtte birinden az			
Order Edilen Ürün			
Resource Diabet	51	54,44	0,712
Resource 2.0	17	65,69	
Nutrena	7	66,67	
Ensure Plus	4	70,83	
Diğer	6	63,89	
Bilgilendirilme Durumu			
Evet	27	72,59	**0,044***
Hayır	58	52,87	
Bilgilendiren Kişi			
Doktor	9	81,25	0,710
Hemşire	8	71,25	
Diyetisyen	3	68,89	
Nütrisyon Destek	7	61,90	
Ürünü Tüketme Nedeni			
Doktor tarafından verilmesi	40	71,33	0,420
Ürünün yararına inanması	7	78,57	
Tadını beğenmesi	12	76,39	
Enerji ihtiyacını sadece OBS ile karşılaması	8	88,33	
Ürünü Tüketmeme Nedeni			
Tadını beğenmeme	15	24,00	**0,040***
İştahsızlık	9	55,56	
Bulantı	15	30,00	
Diğer	14	36,90	

Karar ağacı modelinde 7 adet değişken etkili değişken olarak belirlenmiştir. Sonuçlar incelendiğinde, tadını beğenme durumunun kullanım düzeyi üzerinde en etkili faktör olduğu görülmüştür. Buna ek olarak; bilgilendirme yapılmasının, solüsyonun doktor tarafından order edilmesinin, hastada görülen bulantı ve iştahsızlığın, order miktarı ve cinsiyetin kullanım düzeyi üzerinde etkili temel faktörler olduğu belirlenmiştir (Şekil 1).



Şekil 1. Karar ağacı

Tartışma

OBS'ye olan yüksek uyum enteral beslenme desteğinin temelini oluşturur (2). Schueren ve arkadaşlarının kemoradyoterapi alan hastalarda OBS'larının beslenme desteğine ve klinik sonuçlara etkisini inceledikleri meta-analizde klinik diyetisyen desteği ve yüksek enerjili OBS kullanımının hastaların vücut ağırlığına pozitif bir etkisi olmadığını rapor etmişlerdir. Bunun sebebini hasta uyumunun yetersizliğinden dolayı hedeflenen kalori değerlerine ulaşılamaması olarak açıklamışlardır (7). Liljeberg ve arkadaşlarının hastaneden taburcu olup OBS ile beslenme desteği verilen hastalarda yaptıkları uyum çalışmasında üç farklı yöntemle OBS uyumunu sırası ile %93, %87 ve %76 olarak bulmuşlardır (5). Lidoroki ve arkadaşlarının çalışmasında ortalama uyum %65±28.3 olarak bulunurken, hastaların ancak %35.9'unun order edilen OBS tam olarak tükettikleri saptanmış (8). Söderström ve arkadaşlarının hastaneden taburcu olan malnutrisyonlu ve/veya malnutrisyon riski altındaki yaşlılarda yaptıkları çalışmada hem diyet önerisi hem de OBS alan malnutre hastalarda %74 ile en yüksek uyum oranını tespit etmişlerdir (9). Hubbard ve arkadaşlarının OBS uyumu ile ilgili sistematik derlemesinde, genel ortalama uyum oranı %78 iken hastanede yatan hastalarda bu oran %67 ile daha düşük bulunmuştur (10). Hastanede yatan hastalarda akut hastalığa bağlı iştahsızlık, mobilizasyon eksikliği ve tedavi süreci ile ilişkili hastaların aç bırakılması gibi faktörler OBS'na uyumun taburcu olan hastalara göre daha düşük olmasının nedenleri olarak gösterilmiştir (10). Çalışmamızda ortalama OBS kullanım düzeyi %59 olarak bulundu. Çalışmanın kesitsel olması, ağırlıklı olarak dahili ve cerrahi kliniklerinde yatan malnütrisyonlu hastaları içermesi, rutin diyetisyen izleminin olmamasının çalışmamızdaki literatüre göre düşük olan uyum oranımıza neden olabileceğini düşünüyoruz.

Hastanın bilgilendirilmesi

Liljeberg ve arkadaşları, hastaların taburculuk öncesinde klinik diyetisyenlerince değerlendirilip, hasta özelinde bir OBS reçetesi verilmesini yüksek OBS uyumu ile ilişkili bulmuşlardır (5). Hashizume ve arkadaşları hastaneden taburcu olup OBS kullanan hastalarda OBS uyumu ile ilgili yaptıkları kesitsel çalışmanın sonucunda, beslenme desteğinin amaçlarının hastaya açıklanması ve hastaların cesaretlendirilmesinin OBS'na uyumu geliştirebileceğini, bunun için de sağlık çalışanlarının desteğine daha fazla ihtiyaç duyulduğunu belirtmişlerdir (2). Wan ve arkadaşlarının çalışmasında, ekonomik kazanç, hasta bakıcılar (eşler ve çocuklar) ve OBS'na karşı gelişen yan etkileri OBS uyumunu etkileyen bağımsız faktörler olarak bulmuşlar ve özellikle hastanın ailesinin günlük diyet bakımına katılması konusunda cesaretlendirilmesinin önemini vurgulamışlardır (11). Hubbard ve arkadaşları OBS başlanacak hastaların daha fazla bilgilendirilmesi, daha fazla vizit yapılması, sağlık çalışanları tarafından hastanın cesaretlendirilmesinin OBS'ye uyumu artırabileceğini bu nedenle kliniklerde bu prensiplerin uygulanması gerektiğini vurgulamışlardır (10). Çalışmamızda literatür ile uyumlu olarak hastaların bilgilendirilmesindeki eksikliğin OBS tüketimindeki düşüşe neden olan en önemli sebep olduğu görüldü.

OBS tadı

Bir gıdanın algılanan lezzetliliği, tadı, ağız duyusu, aroması, kokusu ve görünümü gibi duyusal yönlerle ilgilidir. Bir oral beslenme solusyonunun duyusal yönleri hastanın tercihi, uyumu ve uzun vadeli tüketim için önemli bir hususdur (12). OBS tadını beğenmeme durumunun OBS'ye uyumu azalttığı ve tüketim düzeylerinin düştüğünü gösteren çalışmalar mevcuttur (5,10). Hastalara OBS başlanmadan önce tat testi yapan ve sonuca göre aromayı ve ürünü belirleyen çalışmalarda OBS uyumunun yüksek olduğu görülmüş (5,12). Özçağlı ve arkadaşlarının çalışmasında da tat ve ağız duyusu, OBS tercihi üzerinde en büyük etkiye sahip duyusal özellikler olarak bulunmuştur (12). Lidoraki ve arkadaşları üst gastrointestinal kanser cerrahisi geçiren hastalarda, tadını ve yapısını beğenmemeyi OBS uyumuna engel olan ortak faktörler olarak bulmuşlardır (8). Çalışmamızda Karar Ağacı yöntemi ile değerlendirmede OBS tadının kullanım düzeyi üzerine etkili en önemli faktör olarak bulundu.

Order edilen miktar

Özellikle nutrisyonel desteğe ihtiyacı olan geriatrik hasta gruplarında yapılan çalışmalar enerji dansitesi yüksek OBS'ları daha düşük volumlerde verildiğinde çok daha iyi uyum sağlandığı gösterilmiştir (13). Hubbard ve arkadaşlarının OBS uyumu ile ilgili derleme çalışmasında, enerji dansitesi ≥ 2 kkal/ml olan OBS'na uyumun enerji dansitesi 1-1.5 kkal/ml OBS'larına göre anlamlı olarak yüksek olduğunu bulmuşlardır (10). Yüksek enerjili OBS ile hem daha düşük volumlerde istenilen hedef enerjiye ulaşılmış hem de hasta uyumunu arttırarak israfın önüne geçmek mümkün olmuştur. Wan ve arkadaşları, hastalara reçete edilecek OBS çeşitliliğinin artırılmasını ve daha küçük paketlerde üretim yapılmasını tavsiye etmişlerdir (11). Medication Pass Nutritional Supplement Programı (MEDPass) ile hastalara ilaç seansları sırasında günde üç veya dört kez küçük kaplarda 50 ila 120 ml arasında OBS volumu sağlanmaktadır. Van der Berg ve arkadaşları, MEDpass ve geleneksel öğün aralarında OBS sunumunu karşılaştırdıkları çalışmalarında MEDpass ile OBS verilen grupta uyumun ve tüketimin arttığını bulmuşlardır (14). Krebs ve arkadaşlarının sistematik derlemesinde, hastanede yatan erişkin hastalar ve huzurevi sakinlerinde OBS'ye uyumu artırmak için MEDPass uygulamasını önerilebilir olarak bulmuşlardır (15). Çalışmamızda da literatür ile uyumlu olarak order edilen miktarın tüketim üzerine etkili bir faktör olduğu görüldü. Hastanın uyumuna göre OBS miktarının arttırılmasının servislerde gözlemlediğimiz israfın önüne geçerek daha effektif bir enteral nutrisyon desteği sağlanabileceğini düşünüyoruz.

Bulantı, iştahsızlık

OBS bulantı, kusma, karında şişkinlik ve diyare gibi yan etkilere neden olabilir. Çalışmalarda bu yan etkilerin hastaların OBS kullanmayı bırakmalarına ve/veya uyumsuzluğa yol açabildiği gösterilmiştir (8,11). Van der Berg ve arkadaşları, OBS'larının daha küçük volümlerde daha sık aralıklar ile verildiğinde gastrointestinal yan etkilerin azalacağını ve buna paralel olarak tüketimin artacağını vurgulamışlardır (14).

Çalışmamızda iştahsız hastalara göre, iştahı iyi olup OBS'nın tadını beğenmeyen ve/veya bulantı şikayeti olan hastalarda OBS tüketiminin daha düşük olduğu istatistiksel olarak anlamlı bulundu.

Sonuç

Çalışmamızın sonucunda OBS'larına uyum literatüre göre daha düşük bulunmuş ve uyumu etkileyen en önemli faktörün hastaların bilgilendirilmesindeki eksiklik olduğu belirlenmiştir. Karar Ağacı yöntemi ile değerlendirmede OBS tadının kullanım düzeyine etkili en önemli faktör olduğu saptanmıştır. Bu sonuçlar eşliğinde OBS order edilen hastaların bu ürünler ile ilgili bilgilendirilmesinin, verilecek ürünün hastaya mutlaka denetilmesinin ve başlangıçta düşük miktarlarda verilmesinin ürünlere uyum ve tüketimi artırarak gerekli enerji ve protein ihtiyacının karşılanabileceği kanısındayız.

Teşekkür

Besleme Destek Ekibinde birlikte çalıştığımız ve bizlerden desteklerini esirgemeyen Prof. Dr. Belkıs Ünsal, Doç Dr. Yasin Peker, Diyetisyen Çisem Pehlivan, Nutrisyon Hemşireleri Naciye Günay, Yüksel Karakaya ve çalışmamızın istatistiklerinde yardımcı olan Fatma Güntürkün'e çok teşekkür ederiz.

Kaynaklar

1. Kurmann S, Reber E, Vasiloglou MF, et al. Energy and protein intake in medical and geriatric inpatients with MEDPass versus conventional administration of oral nutritional supplements: study protocol for the randomized controlled MEDPass Trial. Trials. 2021;22(1):210.
2. Hashizume N, Tanaka Y, Fukahori S, et al. Adherences to oral nutritional supplementation among hospital outpatients: An online cross-sectional survey in Japan. PLoSOne. 2019;14(9):e0222972.
3. Nogueira DA, Ferreira LP, Andrade de Lúcia RP, Pena GDG. High frequency of non-compliance with quality indicators during oral nutrition support in hospitalized patients. ClinNutr ESPEN. 2020;40:363-368.
4. Stratton RJ, Elia M. Encouraging appropriate, evidence-based use of oral nutritional supplements. Proc Nutr Soc. 2010;69(4):477-487.
5. Liljeberg E, Andersson A, Blom Malmberg K, Nydahl M. High Adherence to Oral Nutrition Supplements Prescribed by Dietitians: A Cross-Sectional Study on Hospital Outpatients. Nutr Clin Pract. 2019;34(6):887-898.
6. UíDhuibhir P, Collura N, Walsh D. Complete Oral Nutritional Supplements: Dietitian Preferences and Clinical Practice. J Diet Suppl. 2019;16(1):40-50.
7. devan der Schueren MAE, Laviano A, Blanchard H, Jourdan M, Arends J, Baracos VE. Systematic review and meta-analysis of the evidence for oral nutritional intervention on nutritional and clinical outcomes during chemo(radio)therapy: current evidence and guidance for design of future trials. Ann Oncol. 2018;29(5):1141-1153.
8. Lidoriki I, Schizas D, Mylonas KS, et al. Oral Nutritional Supplementation Following Upper Gastrointestinal Cancer Surgery: A Prospective Analysis Exploring Potential Barriers to Compliance. J Am Coll Nutr. 2020;39(7):650-656.
9. Söderström L, Rosenblad A, Bergkvist L, Frid H, Thors Adolfsson E. Dietary advice and oral nutritional supplements do not increase survival in older malnourished adults: a multicentre randomised controlled trial. Ups J Med Sci. 2020;125(3):240-249.
10. Hubbard GP, Elia M, Holdoway A, Stratton RJ. A systematic review of compliance to oral nutritional supplements. Clin Nutr. 2012;31(3):293-312.
11. Wan GY, Yuan H, Xue H, Li HQ, Hu HY, Zhang XY. Assessment of compliance with oral nutritional supplementation and exploration of barriers and facilitators for patients after gastrectomy: A mixed-methods study. J Adv Nurs. 2021;77(6):2845-2859.
12. Ozçağlı TG, Stelling J, Stanford J. A study in four European countries to examine the importance of sensory attributes of oral nutritional supplements on preference and likelihood of compliance. Turk J Gastroenterol. 2013;24(3):266-272.
13. Lombard K, vanSteijn J, Schuur T, et al. Compliance of energy-dense, small volume oral nutritional supplements in the daily clinical practice on a geriatric ward--an observational study. J Nutr Health Aging. 2014;18(7):649-653.
14. van den Berg GH, Lindeboom R, van der Zwet WC. The effects of the administration of oral nutritional supplementation with medication rounds on the achievement of nutritional goals: a randomized controlled trial. Clin Nutr. 2015;34(1):15-19.
15. Krebs F, Uhlmann K, Stanga Z, Kurmann S. Distribution of oral nutritional supplements with medication: Is there a benefit? A systematic review. Nutrition. 2022;96:111569.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 143-149

Comparison of The Number and Results of Colonoscopy Before and After The Covid-19 Pandemic

Covid-19 Pandemisi Öncesi ve Sonrası Yapılan Kolonoskopi Sayılarının ve Sonuçlarının Karşılaştırılması

Ibrahim Ethem CAKCAK*0000-0001-8885-514X
Meltem ERMEYDAN *0000-0001-7877-5007
Leyla ALTÜRK * 0000-000-2523-4001
İrem TÜRKMEN* 0000-0001-7683-0949
Şeymanur GÖKTAŞ* 0000-0003-4349-3258

Medicine Faculty of Trakya University

Abstract

Objective: We aimed to investigate the effects of COVID-19 on colonoscopy and to investigate what should be considered in the following possible epidemic situations.

Material and Methods: In our study, patients who applied to Trakya University School of Medicine and performed colonoscopy between March 2019 and March 2021 were evaluated, retrospectively. Percentages, standard deviation, mean, median, and interquartile range were used as the descriptive statistics. Mann-Whitney U test was used for the variations which are contrary to the normal distribution range in the comparison of two groups. The relations between qualitative variations were studied by the Pearson Chi-Square test and Fisher's Exact test. The significant value was determined as 0.05 for statistical analyses.

Results: In our study, when we compared the pre-Covid and post-Covid periods, we observed that the median age did not change. The number of patients decreased by 63.3%, performing rectosigmoidoscopy (RSS) increased by 8% and patients presenting symptomatic decreased by 8.5%. The rates of malignancies detected after COVID-19 increased statistically significantly. The mean age of the patients with malignancy was 62.8, and with normal result was 54.5(p=0.001). In the post-Covid period, the rate of malignant diagnosis in patients with a previous history of malignant surgery has increased compared to those without a history of surgery(p=0.042).

Conclusion: In such epidemic periods, patients may hesitate to apply to the hospital, which may cause the progression of their disease. More educated patients and planned health services will enable us to achieve much more efficient results.

Keywords : Colonoscopy, Rectosigmoidoscopy, COVID-19

First Author: Ibrahim Ethem CAKCAK
Specialist of General Surgery
General Surgery Department of Medical Faculty of Trakya University/ Edirne
email: ethemcakcak@hotmail.com

Öz

Amaç: COVID-19'un kolonoskopi üzerindeki etkilerini ve bundan sonraki olası salgın durumlarında nelere dikkat edilmesi gerektiğini tespit etmeyi amaçladık.

Materyal Metod: Çalışmamızda Mart 2019-Mart 2021 tarihleri arasında Trakya Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı'na başvuran ve kolonoskopi uygulanan hastalar geriye dönük olarak değerlendirildi. Tanımlayıcı istatistikler olarak yüzdeler, ortalama, standart sapma, ortanca ve çeyrekler arası aralık kullanıldı. İki grubun karşılaştırılmasında normal dağılım aralığına aykırı varyasyonlar için Mann-Whitney U testi kullanıldı. Niteliksel varyasyonlar arasındaki ilişkiler Pearson Ki-Kare testi ve Fisher's Exact testi ile incelenmiştir. Tüm istatistiksel analizler için anlamlı değer 0.05 olarak belirlendi.

Geliş Tarihi:20/06/2022
Kabul Tarihi:30/07/2022

Sonuç: Çalışmamızda COVID-19 öncesi ve sonrasını karşılaştırdığımızda yaş ortalamasının değişmediğini, hasta sayısının %63,3 azaldığını, rektosigmoidoskopi (RSS) yapılan hastaların %8 arttığını ve semptomatik başvuran hastaların %8,5 azaldığını gözlemledik. COVID-19 sonrası tespit edilen malignite oranları istatistiksel olarak anlamlı derecede arttı. Malignite saptanan hastaların yaş ortalaması 62.8, normal sonuç alanların yaş ortalaması 54.5 idi **(p<0.001)**. COVID-19 sonrası dönemde, daha önce malign cerrahi öyküsü olan hastaların malign tanı oranı, cerrahi öyküsü olmayanlara göre arttı.

Tartışma: Bu tür salgın dönemlerinde hastalar hastaneye başvurmaktan çekinebilmekte ve bu durum hastalıklarının ilerlemesine neden olabilmektedir. Daha eğitimli hastalar ve planlı sağlık hizmetleri çok daha verimli sonuçlara ulaşmamızı sağlayacaktır.

Anahtar Kelimeler: Kolonoskopi, Rektosigmoidoskopi, COVID-19

Introduction

A global pandemic has wreaked havoc on healthcare systems worldwide since December 2019, when a local pneumonia epidemic in Wuhan, China, reached an international scale **[1,2]**. The virus responsible for COVID-19, SARS-CoV-2, has caused a global pandemic, with over 114 million cases worldwide as of March 1, 2021 **[3]**. COVID-19 affects the lungs primarily, causing pneumonia and acute respiratory distress syndrome (ARDS), but it can also cause extrapulmonary symptoms, most notably gastrointestinal (GI) symptoms **[4,5]**.

Healthcare workers were quickly identified as one of the groups most at risk of COVID-19 infection with little knowledge of this coronavirus strain **[6]**. Using personal protective equipment (PPE) can significantly reduce the risk of infection associated with caring for SARS-CoV-2 patients **[7]**. However, there have been reports of negative skin reactions caused by healthcare workers' use of PPE **[8]**. The long shifts with the PPE they wear have made the medical personnel's jobs extremely difficult.

Colonoscopy is a diagnostic and therapeutic procedure used to examine the large intestine (colon, rectum, and anus) and the distal portion of the small intestine **[9]**. The primary diagnostic procedure for a wide range of colorectal diseases has been colonoscopy since its introduction in 1969 **[10,11]**.

Colonoscopy plays a significant role in preventing colorectal cancer (CRC) and is the gold standard for detecting and removing adenomas **[12,13]**. There is strong evidence that removing polyps and adenomas by colonoscopy reduces the incidence and mortality of CRC **[12]**.

Because of the virus's increased anxiety and fear, patients have postponed, canceled, or missed routine wellness checkups and screenings, including routine colonoscopies **[2]**. Screenings that are delayed or completely missed caused by COVID-19 have the potential to miss opportunities to detect polyps, diagnose CRC, and seek further treatment for diagnosed patients **[14,15]**.

This study aims to evaluate and investigate the effects of emergencies such as pandemics on colonoscopy (which can be used for scanning and treatment purposes), including indications, the procedure performed, and diagnoses made as due to the procedure.

Material and Method

Ethics

This study was approved by the Scientific Research Ethics Committee of Trakya School of Medicine (Protocol Code: 2022/176).

Patients

his study was approved by the Ethics Committee of the Trakya University and written informed consent was obtained from each participant in accordance with the institutional guidelines. Between March 10, 2019, and March 10, 2021, 404 consecutive patients who underwent colonoscopy or rectosigmoidoscopy were retrospectively recruited from the XXX Hospital.

Inclusion Criteria

The predefined inclusion criteria were as follows: (1) undergoing colonoscopy or rectosigmoidoscopy. (2) Being older than 18. The predefined exclusion criteria were as follows: (1) Being younger than 18.

Statistical Analysis

Normal distribution range was controlled by the Shapiro-Wilk test. The Mann-Whitney U test was used for the variations contrary to the normal distribution range in the comparison of two groups. The relations between qualitative variations were studied by the Pearson Chi-Square test and Fisher's accurate test. Median and quarter values have been given for the quantitative variations and percentage and frequency rates were given for the qualitative variations as descriptive statistic evaluation. Significant value was determined as 0.05 for all statistical analysis. Cut-off values for the quantitative variations were also studied by ROC analysis. All statistical analyses were performed with the TURCOSA (Turcosa Analytics Ltd Co, Turkey, www.turcosa.com.tr) statistical software program.

Results

A total of 403 patients were screened before the COVID-19 Pandemic, and after the first case report in Turkey, 10.03.2020, the number of applications decreased by 63,3%, from 295 to 108 people. The average age of the patients who applied before the pandemic was 56.2, and the average age increased to 58.3 after the COVID-19 pandemic. There was no statistically significant difference between the mean ages before and after the pandemic **(p=0.174) (Table 1)**.

Table1. Average Age of Patients Before and After the **Pandemic**

Before Covid Pandemic		After Covid Pandemic	
Age			
N	*Mean*	*N*	*Mean*
2	56.247	1	58.3889
9	5	0	
5		8	

Note. Within each dependent measure, means with different subscripts differ significantly. (p=0.174)

%68.75 men were diagnosed with cancer before the COVID-19 Pandemic and %71.7 men during the COVID-19 Pandemic. The rate of female patients who underwent colonoscopy was %44.4, but this rate decreased to %37.9 during the COVID-19 Pandemic. The average age of our malignant patients is 62.8, while the average age of our patients with a benign diagnosis or healthy is 54.5.

It was observed that 245 (83%) of the 295 patients who came before the COVID-19 Pandemic came for screening, and 50 (16.9%) patients applied symptomatically. 8 of 108 patients (7.4%) who applied after the COVID-19 Pandemic applied symptomatically, and this rate was found to be lower than before the COVID-19 Pandemic. The number of patients who came for screening increased by 100 (92.5%). The difference was found to be statistically significant **(p=0.016) (Table 2)**.

Table 2. Indication Before and After the Pandemic

	Before Covid Pandemic	After Covid Pandemic	Total
Indication			
Scanning	245(83.05 %)	100(92.59%)	345(85.60%)
Symptomatic Patients	50 (16.94%)	8 (7.40%)	58 (14.39%)
Total	295 (100%)	108 (100%)	403 (100%)

Note. Within each dependent measure, means with different subscripts differ significantly. (p=0.016)

Benign diagnosis was made in 11.1% of 295 patients who applied before COVID-19, and colonoscopy was indicated. Colonoscopy was requested in 30.1% of them considering malignancy. Benign causes were considered in 9.2% of 108 patients who applied after COVID-19, and colonoscopy was ordered from the patient in 37%, considering malignancy.

Before the COVID-19 Pandemic, 21.6% of the patients were diagnosed as malignant, and after the COVID-19, this rate increased to 36.1% and statistically significantly increased **(p=0.005) (Fig. 1)**. The rate of normal pathology reports was 72.2%. It decreased significantly to 62,037% **(Fig. 1)**.

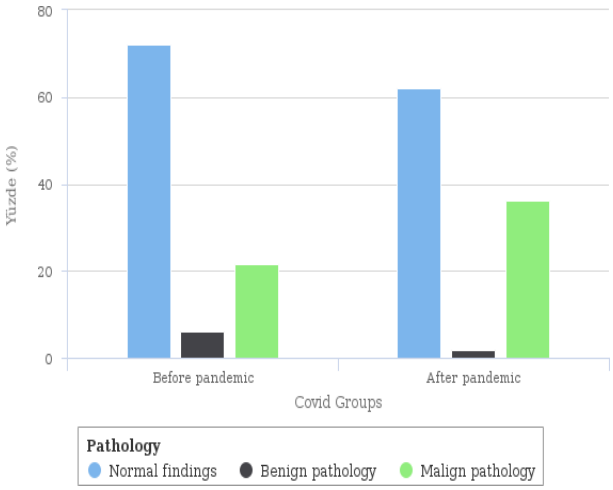


Figure 1. Pathology Result Chart Before and After the Pandemic

No pathology was found in 70.9% of the biopsy taken during colonoscopy from a total of 247 patients who did not have a history of surgery before COVID-19. Benign pathology was found in 5.7% and malignant pathology in 23.5%. In the control colonoscopies of patients who had previously undergone resection for benign lesions, no pathology was found in 12 (85.1%) patients, and benign pathology was found in 2 (14.2%) patients. No malignancy was found in 78.1% of 32 patients who underwent resection for malignancy. 18.7% of them were diagnosed with malignancy again. The difference was found to be statistically significant **(p=0.042) (Table 3)**.

TABLE 3

The Correlation Between the History of Surgery and Pathology, Before and After the Pandemic

	Before Covid Pandemic				*After Covid Pandemic*			
	Pathology							
History of surgery	Normal findings	Benign pathology	Malign pathology	Total	Normal findings	Benign pathology	Malign pathology	Total
No history of surgery	175(70.9%)	14(5.7%)	58(23.5%)	247(100%)	53(64.63%)	1(1.2%)	28(34.1%)	82(100%)
Benign simple procedures	1(50%)	1(50%)	0(0%)	2(100%)	1(100%)	0	0	1(100%)
Benign resections	12(85.17%)	2(14.28%)	0(0%)	14(100%)	1(100%)	0	0	1(100%)
Malign resections	25(78.12%)	1(3.12%)	6(18.75%)	32(100%)	12(50%)	1(4.16%)	11(45.8%)	24(100%)
Total	213(72.2%)	18(6.1%)	64(21.7%)	295(100%)	67(62%)	2(1.85%)	39(36%)	108(100%)

Note. Within each dependent measure, means with different subscripts differ significantly. (p=0.042) (*p=0.749, after the COVID-19 pandemic*)

When we compared the surgical history and control pathology results after the COVID-19 Pandemic, no pathology was found in 64.6% of the 82 patients without a history of surgery. Benign pathology was found in 1.2% and malignant pathology in 34.1%. No pathology was found in the biopsies taken in the control colonoscopy of the patients who had previously undergone benign surgery (resection or simple procedures). However, malignancy was found again in 45.8% of the control biopsies of the patients who had previously undergone resection for malignancy. No pathology was found in 50% of the patients. This difference was not statistically significant **(p=0.749) (Table 3)**.

While the mean age of 103 patients with a malignant pathology report was 62.8, the mean age of 273 patients with a normal result was 54.5. The difference was statistically significant in the Kruskal-Wallis test **(p=0.001) (Fig. 2)**.

Figure of Change of Pathology Result According to Age

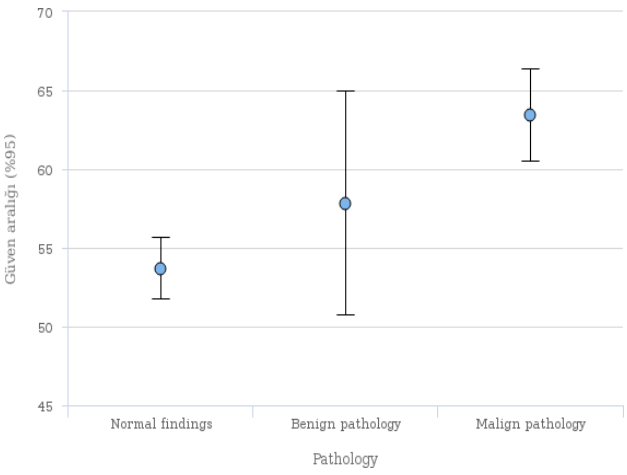


***Fig. 2a**. Before the* COVID-19 *pandemic*

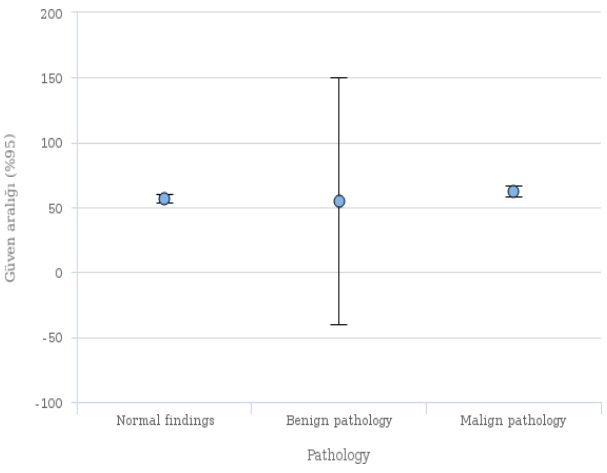


***Fig. 2b**. After the* COVID-19 *pandemic*

The average duration of the total colonoscopy performed without additional procedures before the COVID-19 Pandemic was 9.3, and the longest procedure was 24 minutes. This time increased to 12.4 minutes after the COVID-19 Pandemic, and the longest processing time was 32 minutes. While the duration of rectosigmoidoscopy was 4.4 minutes on average before COVID-19, it increased to an average of 6.7 minutes after the COVID-19 Pandemic.

Discussion

In the year preceding and following the first case of COVID-19 in Turkey on March 11, 2020, the number of patients who underwent colonoscopy at XXX Hospital decreased by %63,389. While this rate was 51.1% in Southern Australia between April-June 2019 and April-June 2020 **[16]**, it was >60% in Italy **[17]** and 41-61% in America **[18]** in the same period. Based on these data, we can conclude that the rate of decrease in the number of patients in our hospital is higher than in South Australia and the United States and similar to Italy.

There is ample data that suggests more cases of colorectal cancer are seen in men than in women **[19]**. Our data also supports this, with %68.7 men diagnosed with cancer before the COVID-19 pandemic and %71.7 men during the COVID-19 pandemic. Although it is more common in male patients, it is also seen in female patients, and colonoscopy is indispensable for diagnosis. However, according to a previous study, the colonoscopy process is very uncomfortable for women, which is why they are hesitant to undergo this procedure, and COVID-19 further decreases the rate of women undergoing this procedure who are already hesitant about colonoscopy **[20]**. This study's findings are consistent with ours. In our hospital, the rate of female patients who underwent colonoscopy was %44.4, but this rate decreased to %37.9 during the COVID-19 Pandemic. We know that developing cancer risk increases with age **[19]**. The average age of our malignant patients is 62.8, while the average age of our patients with a benign diagnosis or healthy is 54.5, indicating that our data is consistent with this information. Comparing the data gathered from the older patients before and after the COVID-19 Pandemic also fits the consensus.

Colonoscopy should be performed in the first three or six months and in the first year to observe whether the tumor has recurred after colorectal cancer surgery because of recurrence of the disease in more than one-third of patients after colorectal cancer surgery (mainly 20-25% of interval cancers are thought to result from incomplete endoscopic resection of adenomas) **[21,22,23,24]**. Similar to other studies in the literature, a severe decrease was observed in the number of colonoscopies performed during the coronavirus pandemic due to hygienic conditions, extra equipment used by doctors, and patients' reluctance to come to the hospital unless they have symptoms **[25]**. According to our study results, while the total number of colonoscopies performed before COVID-19 was 295, the number of colonoscopies for screening purposes was 245 (83%); The total number of colonoscopies performed after COVID-19 was 108, and the number of colonoscopies for screening purposes was found to be 100 (92.5%). According to these results, although the rate of follow-up colonoscopies seems to have increased, they decreased in number with a difference of 145 people.

In the studies of Kim et al., it was observed that the rate of RSS increased in colonoscopies performed after COVID-19 **[26]**. In our study, while 18.8% of colonoscopies performed before COVID-19 were rectosigmoidoscopies (RSS), 26.8% of colonoscopies after COVID-19 were rectosigmoidoscopies. Since the length of the operation period is known to increase the risk of transmission, we can associate this increase with the shortness of the examined section and, therefore, its shorter duration.

When the pathologies in the study of Lantinga et al. were compared, a significant increase in malignancies was observed after the COVID-19 Pandemic **[27]**. In our study, 64 (21.6%) of 295 patients before the COVID-19 Pandemic had a tumor and 18 (6.1%) had a perianal disease; after the COVID-19, 39 (36.1%) tumors and 2 (1.8%) perianal diseases were seen. The increase in malignant pathologies after COVID-19 correlated with other studies and was statistically significant **(p<0.005)**.

When we combined and compared these two data, we came across a more exciting result. While 30.3% of total colonoscopies performed before COVID-19 were malignant, 26.5% were found to be malignant after COVID-19. In addition, when the RSS made were compared, 29.4% of those made in the pre- COVID-19 period were found to be malignant, and 65.5% of the RSS made after COVID-19 were malignant. Since rectosigmoidoscopies are mostly requested secondary to symptoms (constipation, obstruction) or physical examination (rectal examination), the probability of malignancy is higher. Complete colonoscopies are also usually ordered secondary to symptoms of right colon tumors (unexplained anemia). Our study observed an increase in malignancies in RSS due to the decrease in admissions to hospitals with mild symptoms.

Colonoscopy retraction time is the time it takes to pull the colonoscope up to the anus after cecal intubation is performed (Jover et al., 2012) **[28]**. In the absence of additional conditions such as polyp detection, it is recommended to take an average of 6-10 minutes of relapse time, (Barclay et al. (2006) and Simmons et al. This time, which increases in time, increases the probability of detection of polyps and adenomas. Thanks to the prolongation of the retraction time, the anus can be examined in more detail, and a clearer view can be obtained by aspiration (Jover et al., 2012) **[28]**. The mean time for colonoscopy (without additional procedure) was 9.3 minutes, the longest procedure time was 24 minutes due to the procedure. This time for RSS was 4.4 minutes on average. After COVID-19, the average time for a colonoscopy without additional procedure was 12.4 minutes, the procedure The longest colonoscopy time including the This can be explained by the fact that the equipment used with the patient complicates the process, and that the cases become complicated due to late hospital admissions.

In a randomized prospective double-blind study conducted in 2019, the meantime to reach the cecum was found to be 7.49 (±18.3) minutes **[29]**. The average duration of the colonoscopy procedure was 11 (±4.19) minutes, the shortest procedure was 4 and the longest was 30. [29]. When the additional amounts of propofol applied in the same study were compared, no significant difference was found between them **[29]**.

In the literature, complications such as 0.24%-0.33% bleeding and 0.08%-0.19% perforation have been reported after colonoscopy **[30]**. In our clinic, however, no perforation or major bleeding was observed before or after COVID-19.

In epitome, we compared colonoscopy cases from one year before the first confirmed COVID-19 patient in Turkey to one year after. There has been a significant decrease in the number of patients who underwent colonoscopy or RSS after COVID-19. However, with this decrease, the rate of detected malignancy was increased. We found that the average age of patients with malignancy decreased after COVID-19. When we evaluated the patients' indications, we observed that the rate of patients who applied for screening increased. We have seen that rectosigmoidoscopy is applied more after COVID-19 compared to total colonoscopy.

Conclusion

In our clinical life, we observe that patients are afraid of coming to the hospital during the COVID-19 period, so there is a delay or decrease in hospital admissions. The consequences of this delay in terms of long-term patients may lead to an increase in malignancy and worsening of diagnoses. In the same way, the fact that the person performing the procedure cannot work comfortably during the COVID-19 period compared to the past and that the patient and the physician speed up the procedure to reduce contact affects colonoscopy quality.

Therefore, the protection of hospitals against the COVID-19 virus should be increased, an environment should be provided for the patient to apply to the hospital, and a sterile working environment should be provided for the physician. In this way, it can be ensured that patients who hesitate to apply after the pandemic can apply earlier. Our study finds an increase in malignancies, and a decrease in application rates, and with these precautions, we can avoid these problems.

REFERENCES

1. Kim KH, Kim SB, Kim TN. Changes in endoscopic patterns before and during COVID-19 outbreak: Experience at a single tertiary center in Korean. World J Clin Cases. 2021 May 26;9(15):3576-3585. doi: 10.12998/wjcc.v9.i15.3576. PMID: 34046457; PMCID: PMC8130062.
2. Mason MC, Vedhanayagam K, Jernigan JA. Evaluating Patient Adherence to Routine and Symptom Indicated Colonoscopies During the COVID-19 Pandemic. Cureus. 2021 Jul 29;13(7):e16711. doi: 10.7759/cureus.16711. PMID: 34513352; PMCID: PMC8405171.
3. Elmunzer, B. J., Spitzer, R. L., Foster, L. D., Merchant, A. A., Howard, E. F., Patel et al. & for the Study, N. A. A. (2021). Digestive manifestations in patients hospitalized with coronavirus disease 2019. *Clinical Gastroenterology and Hepatology*, *19*(7), 1355-1365.
4. Kopel J, Ristic B, Brower GL, Goyal H. Global Impact of COVID-19 on Colorectal Cancer Screening: Current Insights and Future Directions. Medicina (Kaunas). 2022 Jan 10;58(1):100. doi: 10.3390/medicina58010100. PMID: 35056408; PMCID: PMC8778776.
5. Wu D, Wu T, Liu Q, Yang Z. The SARS-CoV-2 outbreak: What we know. Int J Infect Dis. 2020 May;94:44-48. doi: 10.1016/j.ijid.2020.03.004. Epub 2020 Mar 12. PMID: 32171952; PMCID: PMC7102543.
6. Gholami M, Fawad I, Shadan S, Rowaiee R, Ghanem H, Hassan Khami et al. COVID-19 and healthcare workers: A systematic review and meta-analysis. Int J Infect Dis. 2021 Mar;104:335-346. doi: 10.1016/j.ijid.2021.01.013. Epub 2021 Jan 11. PMID: 33444754; PMCID: PMC7798435.
7. Tabah A, Ramanan M, Laupland KB, Buetti N, Cortegiani A, Mellinghoff J et al.; PPE-SAFE contributors. Personal protective equipment and intensive care unit healthcare worker safety in the COVID-19 era (PPE-SAFE): An international survey. J Crit Care. 2020 Oct;59:70-75. doi: 10.1016/j.jcrc.2020.06.005. Epub 2020 Jun 13. Erratum in: J Crit Care. 2021 Jun;63:280-281. PMID: 32570052; PMCID: PMC7293450.
8. Hu K, Fan J, Li X, Gou X, Li X, Zhou X. The adverse skin reactions of health care workers using personal protective equipment for COVID-19. Medicine (Baltimore). 2020 Jun 12;99(24):e20603. doi: 10.1097/MD.0000000000020603. PMID: 32541493; PMCID: PMC7302613.
9. Stauffer CM, Pfeifer C. Colonoscopy. 2021 Jul 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 32644700.
10. Lee JW, Lee HJ, Kim DS, Yoon J, Hong SW, Hwang HW et al. The Influence of Face Shields on the Quality of Colonoscopy in the Era of the COVID-19 Pandemic. Gut Liver. 2021 Aug 25. DOI: 10.5009/gnl210063. Epub ahead of print. PMID: 34426561.
11. Lee SH, Huh GY, Cheong YS. A case of endoscopic resection of a colonic semipeduncuIated leiomyoma. J Korean Soc Coloproctol. 2011 Aug;27(4):215-9. doi: 10.3393/jksc.2011.27.4.215. Epub 2011 Aug 31. PMID: 21980593; PMCID: PMC3180603.
12. Dik VK, Moons LM, Siersema PD. Endoscopic innovations to increase the adenoma detection rate during colonoscopy. World J Gastroenterol. 2014 Mar 7;20(9):2200-11. doi: 10.3748/wjg.v20.i9.2200. PMID: 24605019; PMCID: PMC3942825.
13. Lee SH, Park YK, Lee DJ, Kim KM. Colonoscopy procedural skills and training for new beginners. World J Gastroenterol. 2014 Dec 7;20(45):16984-95. doi: 10.3748/wjg.v20.i45.16984. PMID: 25493011; PMCID: PMC4258567.
14. Harber I, Zeidan D, Aslam MN. Colorectal Cancer Screening: Impact of COVID-19 Pandemic and Possible Consequences. Life (Basel). 2021 Nov 26;11(12):1297. doi: 10.3390/life11121297. PMID: 34947828; PMCID: PMC8707125.
15. Adams MA, Kurlander JE, Gao Y, Yankey N, Saini SD. Impact of Coronavirus Disease 2019 on Screening Colonoscopy Utilization in a Large Integrated Health System. Gastroenterology. 2022 Jun;162(7):2098-2100.e2. doi: 10.1053/j.gastro.2022.02.034. Epub 2022 Feb 24. PMID: 35219698; PMCID: PMC8867975.
16. Wassie MM, Agaciak M, Cock C, Bampton P, Young GP, Symonds EL. The impact of coronavirus disease 2019 on surveillance colonoscopies in South Australia. JGH Open. 2021 Mar 9;5(4):486-492. doi: 10.1002/jgh3.12525. PMID: 33869788; PMCID: PMC8035475.
17. Maida M, Sferrazza S, Savarino E, Ricciardiello L, Repici A, Morisco F et al. ; Italian Society of Gastroenterology (SIGE). Impact of the COVID-19 pandemic on Gastroenterology Divisions in Italy: A national survey. Dig Liver Dis. 2020 Aug;52(8):808-815. doi: 10.1016/j.dld.2020.05.017. Epub 2020 May 16. PMID: 32425733; PMCID: PMC7229963.
18. Issaka RB, Somsouk M. Colorectal Cancer Screening and Prevention in the COVID-19 Era. JAMA Health Forum. 2020;1(5):e200588. doi:10.1001/jamahealthforum.2020.0588
19. Hultcrantz, R. “Aspects of colorectal cancer screening, methods, age and gender.” *Journal of internal medicine* vol. 289,4 (2021): 493-507. doi:10.1111/joim.13171
20. Bestari MB, Joewono IR. Screening Colonoscopy for Colon Cancer in Women during COVID-19 Pandemic. Acta Med Indones. 2021 Jan;53(1):132-139. PMID: 33818416.
21. Turan, Erkan. "2005-2008 yılları arasında OMÜ Tıp Fakültesinden tanı alan kolorektal kanserli hastalarda sosyodemografik ve klinik özellikler ile risk faktörlerinin değerlendirilmesi." (2009).
22. Dumoulin FL, Hildenbrand R. Endoscopic resection techniques for colorectal neoplasia: Current developments. World J Gastroenterol. 2019 Jan 21;25(3):300-307. DOI: 10.3748/wjg.v25.i3.300. PMID: 30686899; PMCID: PMC6343101.
23. Çetin, Salih Süha. "Kolorektal kanser gelişen hastalarda aynı anda ve sürveyans sırasında lezyona komşu, kanser olmayan tüm kolon mukoza ve lümeninin retrospektif olarak değerlendirilmesi." (2016).
24. Khan R, Tandon P, Scaffidi MA, Bishay K, Pawlak KM, Kral J et al. COVID-19 and Canadian Gastroenterology Trainees. J Can Assoc Gastroenterol. 2020 Oct 24;4(3):156-162. doi: 10.1093/jcag/gwaa034. PMID: 34056533; PMCID: PMC7665532.
25. Miller J, Maeda Y, Au S, Gunn F, Porteous L, Pattenden R et al. Short-term outcomes of a COVID-adapted triage pathway for colorectal cancer detection. Colorectal Dis. 2021 Jul;23(7):1639-1648. DOI: 10.1111/codi.15618. Epub 2021 Mar 29. PMID: 33682302; PMCID: PMC8250907.
26. Kim KH, Kim SB, Kim TN. Changes in endoscopic patterns before and during COVID-19 outbreak: Experience at a single tertiary center in Korean. *World J Clin Cases*. 2021;9(15):3576-3585. doi:10.12998/wjcc.v9.i15.3576
27. Lantinga MA, Theunissen F, Ter Borg PCJ, Bruno MJ, Ouwendijk RJT, Siersema PD; Trans.IT foundation study group. Impact of the COVID-19 pandemic on gastrointestinal endoscopy in the Netherlands: analysis of a prospective endoscopy database. Endoscopy. 2021 Feb;53(2):166-170. DOI: 10.1055/a-1272-3788. Epub 2020 Oct 20. Erratum in: Endoscopy. 2021 Feb;53(2): C11. PMID: 33080630; PMCID: PMC7869035.
28. Arslanca, G. (2019). *Endoskopi hemşireliği hasta bakım uygulamalarının kolonoskopi işlem kalitesi üzerine etkilerinin değerlendirilmesi* (Master's thesis, Sağlık Bilimleri Enstitüsü).
29. Şimşek, L., Yüzkat, N., Soyalp, C., & Gülhaş, N. (2019). Kolonoskopide Ketamin, Fentanil ve Remifentanilin Sedoanaljezi Açısından Karşılaştırılması: Randomize Prospektif Çift Kör Çalışma. *Medical Bulletin of Haseki/Haseki Tip Bulteni*, *57*(1).
30. KOKRMAZ, H., KENDİR, İ. C., & KERPİÇ, O. (2015). Gastroenteroloji ünitemizdeki kolonoskopi sonuçlarımızla birlikte, endikasyonlar komplikasyonlar ve işlem başarısının değerlendirilmesi. *Endoskopi Gastrointestinal*, *23*(1), 9-13.

KLİNİK ÇALIŞMA / CLINICAL TRIAL
Ege Klin Tıp Derg 2022;60 (2): 150-156

Is There a Difference in Incidence of Contrast Induced Nephropathy Between Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors and Other Oral Antidiabetics in Patients With Diabetes Mellitus?

Diyabetik Hastalarda SGLT2 (Sodium-Glucose Cotransporter 2) İnhibitörleri ile Diğer Oral Antidiyabetikler Arasında Kontrast Nefropati Gelişimi Açısından Fark Var mı?

Gizem ÇABUK* 0000-0002-3478-4611

Ali Kemal ÇABUK* 0000-0001-5549-3744

* Tepecik Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İzmir.

Yazışma Adresi: Ali Kemal ÇABUK

Tepecik Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İzmir

E-mail: kardio.80@hotmail.com

Öz

Amaç: Diyabetik hastalarda kontrast nefropati riski daha yüksektir. Yeni çalışmalar SGLT2 (Sodium-Glucose Cotransporter 2) inhibitörlerinin böbrek koruyucu etkilerini ortaya koymuştur. SGLT2 inhibitörlerinin kontrast nefropati gelişimini olası engelleyici etkisini araştırmayı amaçladık.

Yöntem: Bu bir retrospektif tek-merkezli çalışmadır. Ağustos 2020 ile Eylül 2022 tarihleri arasında akut koroner sendrom ve diyabet tanısı ile koroner anjiyografi uygulanan hastalar sıralı biçimde çalışmaya dahil edildi. SGLT2 inhibitörü kullanan hastaları (grup 2, 90 hasta), diğer oral anti-diyabetikleri kullananlarla (grup 1, 110 hasta) kontrast nefropati insidansı açısından karşılaştırdık.

Bulgular: Bazal özellikler açısından (yaş, cinsiyet, risk faktörleri ve ilaç tedavileri) ve laboratuvar bulguları (bazal kreatinin ve eGFR değerleri dahil) iki grup arasında benzerdi. Kullanılan kontrast miktarı iki grupta benzerdi (grup 1= 151.09±68.23; grup 2= 152.11±84.58, *p=0.662*). Grup 1 de, anjiyografiden 48-72 saat sonraki kreatinin ve eGFR değerlerinde ciddi artış olurken; grup 2 de anlamlı fark yoktu. Grup 1'de kontrast nefropati grup 2'ye kıyasla istatistiksel olarak daha fazla görüldü (grup 1=27 [%24.5]; grup 2=7 [%7.8], *p=0.002*). Hastanede yatış süresi grup 1'de (3.93±2.01gün) grup 2'den (2.88±1.31 gün) anlamlı olarak daha uzundu (*p<0.001*).

Sonuç: Kontrast nefropati insidansı ve hastanede yatış süresini, anti-diyabetik tedaviye ek olarak SGLT2 inhibitörü kullanan hastalarda anlamlı olarak daha az bulduk.

Anahtar Kelimeler: Diyabet; kontrast nefropati; SGLT2 inhibitörü

Abstract

Aim: The risk of contrast induced nephropathy (CIN) is higher in patients with diabetes mellitus. Recent trials revealed the renoprotective effects of Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors. We aimed to investigate possible preventive effect of SGLT2 inhibitors against CIN in a high risk population.

Geliş Tarihi:26/04/2022
Kabul Tarihi: 25/06/2022

Methods: This was a retrospective single-centre study. We enrolled patients who were underwent coronary angiography with the diagnoses of acute coronary syndrome and diabetes mellitus consequtively between August 2020 and September 2022. We compared SGLT2 inhibitors (group 2, n=90) with other oral antidiabetics (group 1, n=110) in terms of CIN insidence.

Results: Baseline characteristics (age, sex, risk factors and medications) and laboratory findings (icluding baseline creatinine and eGFR values) were similar between two groups. The means of administered contrast volume were similar (group 1= 151.09±68.23 *vs* group 2= 152.11±84.58, *p=0.662*) between study groups. In group 1 creatinine and eGFR levels rised significantly, whereas in group 2 these parameters were not significantly different 48-72 hours after coronary angiography. We found that CIN occured significantly higher in group1 compared to group 2 (n=27 [24.5%] *vs* n=7 [7.8%], *p=0.002*). Hospitalization time was significantly longer in group 1 (3.93±2.01 days) than in group 2 (2.88±1.31 days) (*p<0.001*).

Conclusion: We found that CIN insidence and hospitalization time were significantly lower in patients using SGLT2 inbitors in addition to anti-diabetic therapy.

Keywords: diabetes mellitus; contrast induced nephropathy; SGLT2 inhibitör

Introduction

Contrast induced nephropathy (CIN) or contrast associated acute kidney injury is an iatrogenic disorder and it is a complication of angiographic procedures using intravascular iodinated contrast media (CM). Although CIN is often regarded as a reversible event (approximately 80% of cases) it portends a variety of short/long-term adverse events, such as longer hospital-stay and in-hospital mortality (1,2). CIN could also result in persistent worsening renal function or renal replacement therapy in a range between 0.7%- 7% (3). The risk of CIN rises with particular baseline factors; such as preexisting renal impairment (eGFR <60 mL/min/m^2) and patients with renal transplant, heart failure with reduced ejection fraction (HFrEF), anemia or procedure-related blood loss, diabetes mellitus (DM), acute myocardial infarction, advanced age (>75 years), periprocedural hypotension or use of an intra-aortic balloon pump (IABP) and risk of CIN rises with administrating higher amount of CM (4).

An evidence-based approach is required for CIN prevention including hydration, administration of low/iso-osmolar CM, minimizing CM volume, pre-treatment with statins and N-acetylcycsteine (with hydration), discontinuation of nephrotoxic drugs (such as cisplatin, amphotericin, aminoglycosides, non-steroidal anti-inflammatory drugs) before CM exposure (5).

As mentioned above, DM is accepted as a non-modifiable risk factor for CIN development particularly in patients with concomitant nephropathy. Diabetes itself may be the independent cause of CIN after CM exposure by means of several mechanisms such as marked alterations in renal physiology including changes in glomerular filtration rate (GFR), enhanced tubular transport activity and oxygen expenditure, intensification of medullary hypoxia and also enhanced generation of reactive oxygen species (6).

Renoprotective effects of a new class of antidiabetic agents — sodium-glucose cotransporter 2 (SGLT2) inhibitors — have recently been demonstrated by several clinical trials (7,8). SGLT2 inhibitors reduce composite renal outcomes (described as doubling of serum creatinine, development of macroalbuminuria, need for dialysis and/or transplantation or kidney death) by 40–70% in patients with type 2 DM (7,8).

It is also known that patients who underwent urgent revascularization procedures due to acute coronary syndrome (ACS) have higher risk for development of CIN compared to patients without ACS (9). Our aim was to investigate the SGLT2 inhibitors' possible protective effect on development of CIN in a high-risk population with DM and ACS.

Methods

Study Design

This was a retrospective and a single-center study. We analyzed recorded data between August 2020 and September 2022 for demographic and clinical characteristics, laboratory and angiographic findings. This study was carried out in accordance with the conditions of the declaration of Helsinki and approved by our local ethical committee.

Study Population

We enrolled patients consecutively in order to eliminate selection bias. The study population comprised of diabetic patients who underwent coronary angiography with diagnose of ACS. We defined two study groups as patients who use any type of oral anti-diabetics and/or insulin (group 1, n=110) and patients who use a SGLT2 inhibitor (empagliflozin or dapagliflozin), at least 1 month, in addition to other anti-diabetic medication (group 2, n=90).

Patients with history of HFrEF (left ventricular EF <40%), preprocedural eGFR <30mL/min/m^2 and acute renal failure or end-stage renal failure requiring dialysis, CM exposure within 15 days, anemia (Hb <10g/dL), abnormal thyroid hormone levels, active infectious disease (including Covid-19), cardiogenic shock and/or use of intra-aortic balloon pump and and excessive exposure to CM (>500 mL) during percutaneous intervention were excluded from the study. Pregnant patients, and patients using nephrotoxic drugs (e.g cisplatin, amphotericin, aminoglycosides, non-steroidal anti-inflammatory drugs, furosemide) or patients who underwent repeated coronary angiography in-hospital (due to a complication such as stent thrombosis or for the purpose of complete revascularization) and patients who were treated by coronary artery by-pass grafting surgery were also excluded.

Laboratory Measurements

Serum creatinine levels were measured by Jaffe assay (IDMS traceable calibration) with Beckman Coulter AU5800 (Beckman Coulter, Inc. Diagnostics Division Headquarters 250 South Kraemer Boulevard Brea, California, USA) before the angiography and after 48-72 hours. We calculated eGFR with the Levey-modified Modification of Diet in Renal Disease (MDRD) formula: (186.3 x serum creatinine $[mg/dl]^{-1,154}$ x age $[years]^{-0,203}$ x (0.742 if female) (10). CIN was defined (which is widely accepted criteria in the literature) by an increase in serum creatinine of ≥0.5mg/dl or an absolute increase of ≥25% from baseline 48 or 72 hours after CM exposure.

Coronary Angiography

All coronary angiography procedures were performed via femoral approach and all patients were given intravenous hydration with isotonic saline infusion (0.9% NaCl, 1 ml/kg/h) which was started at the beginning of angiography and continued at least 12 hours after the procedure. Patients with ST elevation myocardial infarction (STEMI) were immediately taken to the catheter laboratory for percutaneous coronary intervention; and patients with non-ST elevation myocardial infarction (NSTEMI) or unstable angina (UA) pectoris were underwent coronary angiography within 24 hours after admission according to recommendations of recent guidelines (11). We used a non-ionic and low osmolality contrast agent (Optiray© [Ioversol]) and administered manually to all patients.

Statistical Analysis

SPSS 21.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. The Kolmogorov–Smirnov test was applied to the variables to determine whether or not they are normally distributed. Categorical variables were demonstrated as number and percentage; and continuous variables were demonstrated as mean ± SD when normally distributed while nonparametric variables were shown as median and the percentiles. Categorical variables were analyzed either by the chi-square test or by Fisher's exact test, as appropriate.

Student's t-test was used to compare parameters which were normally distributed. Mann-Whitney U test was used to compare paramaters which were non-normally distributed. We tested the significance of the difference of creatinine and eGFR values between before and after coronary angiography with Wilcoxon signed-rank test for both groups. All statistical testing was on the basis of a 2-sided α=0.05 significance level.

Results

Baseline characteristics (age, sex, risk factors and medications) and laboratory findings (including baseline creatinine and eGFR values) were similar between two groups (Table 1). Coronary angiography indications and the parameters related with angiography procedure shown in table 2. While majority of patients in both groups underwent percutaneous coronary intervention (93 of 110 patients [84.5%] in group 1 *vs* 76 of 90 patients [84.4%] in group 2, *p=1.0*), remaining patients were managed medically after coronary angiography. The means of administered contrast volume were similar (group 1= 151.09±68.23 *vs* group 2= 152.11±
84.58, *p=0.662*) between study groups.

Table 1. Baseline characteristics of study population

Parameter	Group 1 (n=110)	Group 2 (n=90)	P value
Age (years)	62.55 (±10.73)	60.38 (±9.94)	0.14
Sex (female) (n,%)	48 (43.6)	37 (41.1)	0.77
Hypertension (n,%)	66 (60)	63 (70)	0.18
Glucose (mg/dl)	213.69±82.34	196.95±66.27	0.12
Urea (mg/dl)	41.98±24.61	40.67 ±13.94	0.65
Creatinine (mg/dl)	1.05 ±0.31	1.01±0.22	0.30
eGFR (ml/min/1.73m^2)	71.40±24.29	69.61±17.17	0.56
Hemoglobin (g/dl)	13.28±1.59	13.70±1.65	0.07
WBC (×10^9/L)	11.15±3.15	11.02±3.01	0.76
Platelet (×10^3/µl)	253.36±75.82	247.00±66.71	0.64
Total cholesterol (mg/dl)	192.64±65.26	200.22±71.25	0.08
LDL (mg/dl)	116.06±43.91	118.96±37.45	0.64
HDL (mg/dl)	41.08±9.32	40.81±9.18	0.90
Trigliseride (mg/dl)	188.40±57.70	200.83±56.85	0.21
HbA1c (%)	7.69±1.74	7.51±1.47	0.67
LVEF (%)	47.14±9.53	47.31±10.70	0.76
Medications (n,%)			
ACE inhibitor	37 (33.6)	42 (46.7)	0.08
ARB	16 (14.5)	16 (17.8)	0.56
Beta blocker	52 (47.3)	49 (54.4)	0.32
Calcium canal blocker	24 (21.8)	11 (12.2)	0.09
Thiazide	24 (21.8)	27 (30)	0.19
Statin	43 (39.1)	32 (35.6)	0.66
Metformin	77 (70.0)	57 (63.3)	0.36
Insulin	37 (33.6)	28 (31.1)	0.76
Thiazolidinedion	19 (17.3)	13 .(14.4)	0.69
Sulfonilurea	24 (21.8)	16 (17.8)	0.59
DPP4 inh	46 (41.8)	44 (48.9)	0.32
Dapagliflozin	-	46 (51.1)	-
Empagliflozin	-	44 (48.9)	-

eGFR; estimated glomerular filtration rate, WBC; white blood cell, LDL; low-density lipoprotein, HDL; high-density lipoprotein, HbA1c; hemoglobin A1c, LVEF; left ventricular ejection fraction, ACE; angiotensin converting enzyme, ARB; angiotensin receptor blocker, DPP4; dipeptidyl-peptidase4.

In group 2, 44 patients (48.9%) were using dapagliflozin, 46 patients (51.1%) were using empagliflozin. We found that CIN occured significantly higher in group1 (n=110) compared to group 2 (n=27 [24.5%] *vs* n=7 [7.8%], *p=0.002*)(Table 3). The distribution of CIN cases in group 2 favored empagliflozin (2 of 7 cases) compared to dapagliflozin (5 of 7 cases), nevertheless this finding could be coinsidental due to limited number of patients and end-points; so, we did not perform a statistical analysis for this finding.

We also analyzed creatinine and eGFR values before and after coronary angiography; and compared seperately in each group. In group 1 creatinine and eGFR levels rised significantly, whereas in group 2 these parameters were not significantly different 48-72 hours after coronary angiography (Table 3).

In group 1, three patients died in-hospital (one of them received dialysis) and three patients needed dialysis due to contrast nephropathy. In group 2, there were not any patients needed dialysis and we did not observe any mortality. Another important finding of our study was the difference in hospitalization time of study groups: It was significantly longer in group 1 (3.93±2.01 days) than in group 2 (2.88±1.31 days) (*p<0.001*)(Table 2).

Table 2. Angiography indications, parameters related with angiography and hospitalization time of study groups

	Group 1 (n=110)	Group 2 (n=90)	p value
Angiography Indication (n, %)			
USAP	25 (22.7)	17 (18.9)	0.67
NSTEMI	34 (30.9)	25 (27.8)	0.16
STEMI	51 (46.4)	48 (53.3)	0.75
PCI	93 (84.5)	76 (84.4)	1.0
Contrast volume (ml)	151.09±68.23	152.11±84.5	0.66
Hospitalization time	3.93±2.01	2.88±1.31	<0.0001*

USAP; unstable angina pectoris, NSTEMI; non-ST elevated myocardial infarction, STEMI; ST elevated myocardial infarction, PCI; percutaneous coronary intervention.
* Indicates statistical significance.

Table 3. Comparison of renal functions and CIN insidence of study groups

	Creatinine (basal)	Creatinine (48-72 h)	p value
Group 1 (n=110)	1.05 ±0.31	1.28±0.87	<0.0001*
Group 2 (n=90)	1.01±0.22	1.04±0.27	0.23
	eGFR (basal)	**eGFR (48-72 h)**	**p value**
Group 1 (n=110)	71.40±24.29	63.32±24.29	<0.0001*
Group 2 (n=90)	69.61±17.17	69.74±19.49	0.92
	Group 1 (n=110)	**Group 2 (n=90)**	**p value**
CIN (n,%)	**27 (24.5)**	**7 (7.8)**	**0.002***

eGFR; estimated glomerular filtration rate, CIN; contrast induced nephropathy.
* Indicates statistical significance.

Discussion

We investigated the possible effect of SGLT2 inhibitors on prevention of CIN in diabetic patients with ACS; and found CIN insidence were significantly lower in patients using SGLT2 inhibitors than did those not using this medication. This finding might be speculated as a new renoprotective effect of SGLT2 inhibitors. Renoprotective effects –as renal outcomes- of SGLT2 inhibitors have already been demonstrated in patients with heart failure, DM (± nephropathy) or coronary heart disease by recent randomized controlled trials (12-14).

Growing evidence indicating favourable cardiovascular and renal outcomes with SGLT2 inhibitors deserved a particular interest on this molecule amoung scientists. Multifactorial mechanisms were described as the renal protective effect of SGLT2 inhibitors in the literature: *a)* Reducing proximal tubular sodium reabsorption, thereby increasing distal sodium delivery to macula densa which activates tubulo-glomerular feedback and leading efferent arteriolar vasodilation and decrease in glomerular hyperfiltration (15); *b)* It is a well-known fact that the reabsorption of electrolyte and organic solutes in the proximal tubule requires much energy (16). The proximal tubule therefore accounts for the largest amount of oxygen consumption in the kidney. SGLT-2 expression is increased in patients with diabetes; therefore, more glucose and sodium are reabsorbed, which increases the oxygen demand of tubular cells. This means, the proximal tubule particularly susceptible to hypoxia in the setting of diabetes mellitus. SGLT-2 inhibition reduces sodium and glucose reabsorption in the proximal tubule, thereby reducing the workload for proximal tubular cells and hypoxia induced proximal tubular damage could lead to improved tubular cell structural integrity and function (17). *c)*

Other effects of SGLT2 inhibitors such as reducing arterial stiffness (18) and serum uric acid levels (20), regulating the systemic and renal neurohormonal systems (20,21), anti-inflammatory, anti-fibrotic effects and reducing oxidative stress (22) may also slow down the progression of renal disease.

Several pathogenetic factors found related with the development of CIN. Increased secretion of vasoactive amins (such as angiotensin, vasopressin, and endothelin) after contrast exposure could be responsible for reduced nitric oxide synthesis, oxidative stress, secretion of proinflammatory cytokines. Interstitial inflammation due to complementary system activation and a tubular obstruction pathogenesis were also proposed as underlying mechasims for the development of CIN (23). Upregulation of SGLT2 in the proximal renal tubules because of hyperglycemia and hyperinsulinemia is a well-known fact in patients with DM. Enhanced action of SGLT2 was found linked to enhanced oxidative stress, mitochondrial dysfunction and inflammation even without hyperglisemia (24). Therefore, these deleterious effects which may contribute to the developement of CIN could be mitigated by SGLT2 inhibitors.

Some preventive strategies in order to avoid the development of CIN have been studied, such as volume expansion with oral and/or intravenous isotonic saline, N-acetylsysteine + isotonic saline, statins, reducing the amount of CM and using low/iso-osmaolar contrast agents. In our study groups all patients were given intravenous saline infusion as a standart protocol of our institution, and there were not statistically significant difference in terms of statin use and amount/type of CM between two groups. The factors effecting the risk of CIN such as heart failure, advanced age, hypotension and baseline eGFR were also similar between study groups (Table 1 and 2). Therefore we could analyze the independent effect of SGLT2 inhibitors on prevention of CIN.

Another important finding of our study was the shorter hospital stay in patients using SGLT2 inhibitors due to lower insidence of CIN. This finding might be speculated as a cost-effectiveness of this medication in patients with DM and ACS. However, this should be studied prospectively in a larger population in order to claim that kind of cost-effective benefit.

Our study had some limitatons. Due to the retrospective design of our study we could not investigate the prognostic value of SGLT2 inhibitors in this particular population. We had a relatively small sample size and limitted number of events (CIN) due to being a single-center study. We could not include patients using canagliflozin because it has not been refunded in our country yet; therefore our findings might not be generalized to all types of SGLT2 inhibitors. Lastly, we could not determine by which mechanism of SGLT2 inhibitors reveal prevention of CIN; future studies should be examined the precise mechanisms of SGLT2 inhibitors for this purpose.

Conclusion

We found in a high-risk patient population who had DM and ACS that CIN insidence and hospitalization time were significantly lower in patients using SGLT2 inbitors in addition to anti-diabetic therapy compared to patients using anti-diabetic regimens without SGLT2 inhibitors.

Teşekkür: Çalışmaya katkılarından dolayı Asistan Doktor **Kutluhan Eren Hazır**'a teşekkür ederiz.

References

1. Finn WF. The clinical and renal consequences of contrast-induced nephropathy. Nephrol Dial Transplant 2006;21:i2–10.
2. McCullough PA, Wolyn R, Rocher LL, et al. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med 1997;103:368–75.
3. Gruberg L, Mintz GS, Mehran R, et al. The prognostic implications of further renal function deterioration within 48 h of interventional coronary procedures in patients with pre-existent chronic renal insufficiency. J Am Coll Cardiol 2000;36:1542–8.
4. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006;100:S11-5.
5. Katsiki N, Athyros VG, Karagiannis A, Mikhailidis DP. Contrast-Induced Nephropathy: An "All or None" Phenomenon? Angiology. 2015;66(6):508-13.
6. Heyman SN, Rosenberger C, Rosen S, Khamaisi M. Why is diabetes mellitus a risk factor for contrast-induced nephropathy? Biomed Res Int. 2013;2013:123589.
7. Neal B, Perkovic V, Mahaffey KW, et al; CANVAS Program Collaborative Group. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017;377(7):644-57.

8. Wheeler DC, Stefánsson BV, Jongs N, et al; DAPA-CKD Trial Committees and Investigators. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021;9(1):22-31.

9. Crimi G, Leonardi S, Costa F, et al. Incidence, prognostic impact, and optimal definition of contrast-induced acute kidney injury in consecutive patients with stable or unstable coronary artery disease undergoing percutaneous coronary intervention. insights from the all-comer PRODIGY trial. Catheter Cardiovasc Interv. 2015;86(1):E19-27.

10. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63(5):713-35.

11. Collet JP, Thiele H, Barbato E, et al; ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42(14):1289-1367.

12. Packer M, Anker SD, Butler J, et al; EMPEROR-Reduced Trial Investigators. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med. 2020;383(15):1413-24.

13. Perkovic V, Jardine MJ, Neal B, et al; CREDENCE Trial Investigators. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. N Engl J Med. 2019;380(24):2295-2306.

14. Wanner C, Inzucchi SE, Lachin JM, et al; EMPA-REG OUTCOME Investigators. Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. N Engl J Med. 2016;375(4):323-34.

15. Vallon V, Gerasimova M, Rose MA, et al. SGLT2 inhibitor empagliflozin reduces renal growth and albuminuria in proportion to hyperglycemia and prevents glomerular hyperfiltration in diabetic Akita mice. Am J Physiol Renal Physiol 2014; 306:F194-204.

16. Gilbert RE. SGLT2 inhibitors: beta blockers for the kidney? Lancet Diabetes Endocrinol 2016;4:814.

17. Sano M, Takei M, Shiraishi Y, Suzuki Y. Increased Hematocrit During Sodium-Glucose Cotransporter 2 Inhibitor Therapy Indicates Recovery of Tubulointerstitial Function in Diabetic Kidneys. J Clin Med Res 2016;8:844-7.

18. Chilton R, Tikkanen I, Cannon CP, et al. Effects of empagliflozin on blood pressure and markers of arterial stiffness and vascular resistance in patients with type 2 diabetes. Diabetes Obes Metab 2015;17:1180-93.

19. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117-28.

20. Cherney DZ, Perkins BA, Soleymanlou N, et al. Sodium glucose cotransport-2 inhibition and intrarenal RAS activity in people with type 1 diabetes. Kidney Int 2014;86:1057-8.

21. Jordan J, Tank J, Heusser K, et al. The effect of empagliflozin on muscle sympathetic nerve activity in patients with type II diabetes mellitus. J Am Soc Hypertens. 2017;11(9):604-12.

22. Zelniker TA, Braunwald E. Mechanisms of Cardiorenal Effects of Sodium-Glucose Cotransporter 2 Inhibitors: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;75(4):422-34.

23. Ruparelia N, Digby JE, Jefferson A, et al. Myocardial infarction causes inflammation and leukocyte recruitment at remote sites in the myocardium and in the renal glomerulus. Inflamm Res 2013;62:515e525

24. Maeda S, Matsui T, Takeuchi M, Yamagishi S. Sodium-glucose cotransporter 2- mediated oxidative stress augments advanced glycation end products-induced tubular cell apoptosis. Diabetes Metab Res Rev. 2013;29:406-12.

OLGU SUNUMU /CASE REPORT
Ege Klin Tıp Derg 2022;60 (1):157-160

Simultaneous Cardio-cerebral Infarction in the Coronavirus Disease

Coronavirüs Hastalığında Eş Zamanlı Kardiyoserebral Enfarktüs

Emel ÖZKAN* 0000-0002-2667-1756
Uğur KOCABAŞ 0000-0002-2667-1756**
Fatma ESİN* 0000-0002-5129-4606**
Ömer PEKERŞEN** 0000-0001-5134-9323**

*İKÇÜ Atatürk Eğitim ve Araştırma Hastanesi Kardiyoloji
** İKÇÜ Atatürk Eğitim ve Araştırma Hastanesi Kardiyoloji
*** İKÇÜ Atatürk Eğitim ve Araştırma Hastanesi Kardiyoloji
**** İKÇÜ Atatürk Eğitim ve Araştırma Hastanesi Kardiyoloji

Yazışma Adresi: Emel ÖZKAN
İKÇÜ Atatürk Eğitim ve Araştırma Hastanesi Kardiyoloji
E-mail: dremelgonul@gmail.com

Abstract

Acute ischemic stroke (AIS) and acute myocardial ischemia (AMI) are the leading causes of morbidity and mortality globally. Simultaneous cerebral and myocardial infarction is named as cardiocerebral infarction (CCI) and is rarely encountered in clinical practice. There are several mechanisms reported in the literature that explain the occurrence of CCI. The anatomic and hemodynamic characteristics of the cardiovascular system direct most emboli towards the central nervous system, the peripheral circulation or coronary arteries. Because of the narrow time window and complex pathophysiology, CCI is challenging to immediately diagnose and treat. Here, we report a case of coronavirus (COVID-19) who had acute inferior myocardial infarction as a result of coronary embolism that developed within 48 hours after acute ischemic stroke.

Keywords: Coronavirus disease, ischemic stroke, myocardial infarction

Öz

Akut iskemik inme (Aİİ) ve akut miyokard iskemisi (AMİ), dünyada başta gelen morbidite ve mortalite nedenleridir. Eş zamanlı serebral ve miyokard enfarktüs, kardiyoserebral enfarktüs (KSE) olarak adlandırılır ve klinik pratikte nadiren karşılaşılır. Literatürde KSE oluşumunu açıklayan birkaç mekanizma rapor edilmiştir. Kardiyovasküler sistemin anatomik ve hemodinamik özellikleri, embolilerin çoğunu merkezi sinir sistemine, periferik dolaşıma veya koroner arterlere yönlendirir. Dar zaman aralığı ve karmaşık patofizyolojisi nedeniyle KSE' nin hemen teşhis ve tedavi edilmesi zordur. Biz burada akut iskemik inme sonrası 48 saat içinde gelişen koroner emboli sonucu akut inferiyor miyokard enfarktüsü geçiren bir koronavirüs (COVID-19) olgusunu sunduk.

Anahtar Kelimeler: Koronavirüs hastalığı, iskemik inme, miyokard enfarktüsü

Introduction

Cerebral and myocardial infarction occuring simultaneously is known as cardiocerebral infarction (CCI) and, it is rarely seen in clinical practice (1). CCI has complex pathophysiology and poses difficulty in diagnosis and treatment. In this manuscript we present a case, who had acute ischemic stroke and coronavirus disease (COVID-19) followed by acute inferior myocardial infarction as a result of coronary embolism that developed in 48 hours. In this case the occlusions of the middle cerebral artery and left anterior descending artery occurred nearly simultaneously and we thought that increased risk of acute myocardial infarction (AMI) and acute ischemic stroke (AIS) was associated with coagulopathic disorder following COVID-19 infection.

Geliş Tarihi: 26/04/2022
Kabul Tarihi: 02/07/2022

Case Presentation

A 72-year-old man with a medical history of hypertension ,suddenly devoloped left-sided body weakness and slurred speech and was transported to our emergency service department 120 min after onset of symptoms. History revealed that he was diagnosed with COVID-19 3 days ago. At initial assessment, his initial blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen (O2) saturation were 120/80mmHg; 110 beats per minute; 18 breaths per minute; 95% at room air, respectively. At neurological examination, he was dysarthric, pupils were nonisochoric, pupils were bilaterally responsive to light, pathologicreflexes were absent and there was no sensory deficit. His NIHSS score was 2. Cerebral parenchymal density was found to be normal in the cranial computed tomography (CCT). Calcific plaques causing less than 50% stenosis were detected in both internal carotid arteries in bilateral carotid CT angiography. Diffusion-weighted magnetic resonance imaging showed signs of acute ischemia at the insular cortex in the right hemisphere (Figure 1). The patient was admitted to the neurology service and dual antiplatelet treatment as acetylsalicylic acid and clopidogrel was initiated. Thirty hours later after admission he started having chest pain and the electrocardiogram demonstrated an ST-elevation at inferior leas consistent with inferior myocardial infarction (Figure 2). His echocardiography showed hypokinesia of inferior basal wall and ejection fraction was estimated as 55%. Serum troponins were elevated. Performing coronary angiography for primary percutaneous angioplasty is decided. In coronary angiography a fresh small thrombus in the distal portion of the left anterior descendant artery (LAD) with total occlusion of distal circulation was found. No stenotic lesions suggestive of atherosclerotic pathology were identified in coronary arteries (Figure 3). Since the thrombus was in the distal end of vessel and the distal vessel diameter was less than 2 mm, coronary intervention was not planned. We continued double antiplatelet therapy and added heparin to the treatment. The patient's rhythm was sinus rhythm in intensive care monitoring and 24-hour Holter monitoring. Contrast-enhanced CT angiography did not reveal any finding in favor of major thrombus in the aorta, but minor thrombus cannot be excluded. During his follow-up, the patient continued to worsen clinically, developing severe hypoxemia, not responding to oxygen therapy, and requiring mechanical ventilation. One week after his admission, he developed asystolic cardiopulmonary arrest and passed away.

Figure 1. Acute ischemia at the insular cortex in the right hemisphere

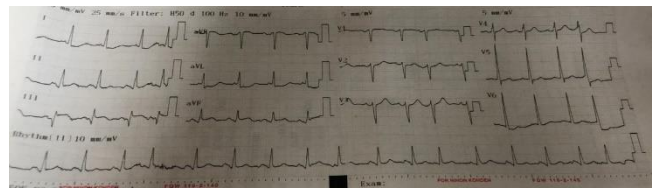
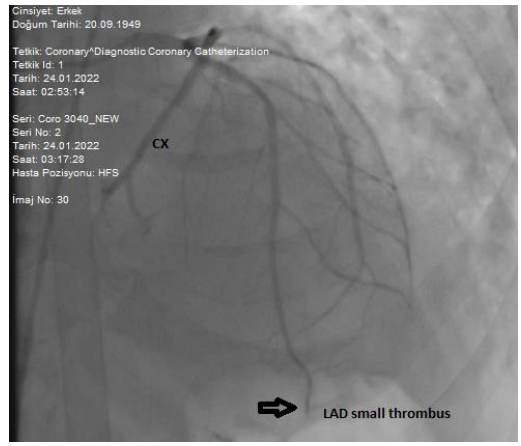
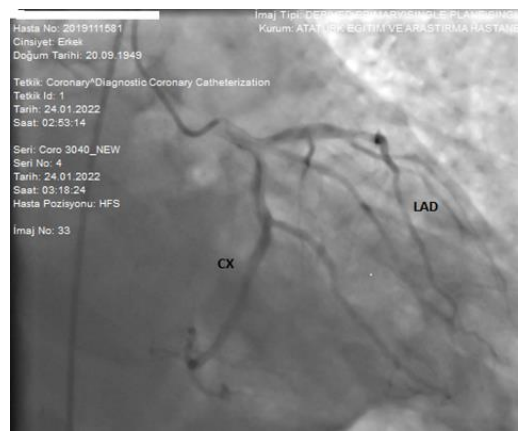


Figure 2. Electrocardiogram showing ST- elevations consistent with inferior myocardial infarction.





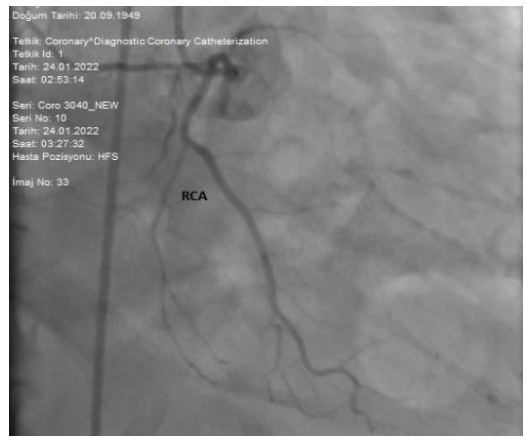


Figure 3. View of coronary angiography showing filling defect in the distal portion of LAD, no stenotic lesions in circumflex artery and right coronary artery

Discussion

AIS and AMI are conditions which require emergency diagnosis and treatment. Cardio-cerebral infarction (CCI), a term introduced by Omar et al. in 2010 , was used to describe the occurrence of AIS and AMI simultaneously. It is seen infrequently, its management is challenging , and the mortality rate is high (1). Chin et al. (2) reported the incidence of CCI as 12.7% in acute stroke patients who were screened for AMI within 72 hours of hospital admission. Global Registry of Acute Coronary Event (GRACE) trial reported -hospital stroke incidence as 0.9% in patients presenting with acute coronary syndrome, and the incidence was much higher in STEMI patients (3).

The Al-Shifa Hospital classified Cardio-Cerebral Infarction Syndrome into 3 types (4):

Type I: Simultaneous cardio-cerebral infarction : Acute myocardial infarction (< 12 hours) with acute ischemic stroke.

Type 2: Acute ischemic stroke (MRI with diffusion-positive lesions in occuring 4.5 hours) after recent myocardial infarction (myocardial infarction in the previous 3 months but more than 12 hours).

Type 3: Acute myocardial infarction (<12 hours) after recent ischemic stroke (ischemic stroke in the previous 3 months but more than 4.5 hours).

The patient we reported had type 3 CCI. Thrombolytics were contraindicated because of recent stroke and need for primary PCI (percutaneous cononary intervention) for the management of STEMI and early invasive strategy for non-STEMI patient is recommended in these type 3 patients.

There are many mechanisms in the literature which explain the occurrence of CCI. AMI with reduced left ventricular function provide a substrate for left ventricular mural thrombus formation . These thrombi in heart are prone to embolisation and may cause simultaneous CCI. Coronary and cerebral artery embolisations have been reported in atrial fibrillation patients (5), there is the possibility of a paradoxical embolus from right side of heart or a vein thrombosis from iliac veins which may pass through a patent foramen ovale. Our patient had also a cerebral infarction of right insular cortex which may cause sympathetic activation resulting in electrocardiogram findings, ST elevation myocardial infarction and cardiac enzyme elevation . Acute ischemic cardiovascular events are also increased due to cytokine mediated hypercoagubility and plaque destabilisation in covid infections (6) .

In conclusion, CCI is rarely encountered and must be immediately diagnosed and treated. There is presently no clinical trial or a consensus guideline for management of CCI. On the basis of current knowledge and experience, the approach to patient management should be individualized.

References

1. Omar HR, Fathy A, Rashad R, Helal E. Concomitant acute right ventricular infarction and ischemic cerebrovascular stroke; possible explanations. Int Arch Med. 2010;3:25.
2. Chin PL, Kaminski J, Rout M. Myocardial infarction coincident with cerebrovascular accidents in the elderly. Age Ageing 1977;6:29-37.
3. Budaj A, Flasinska K, Gore JM, et al. Magnitude of and risk factors for in-hospital and postdischarge stroke in patients with acute coronary syndromes: Findings from a global registry of acute coronary events. Circulation 2005;111:3242-7.
4. Mohammed Habib. Cardio-Cerebral Infarction Syndrome (CCIS): Definition, Diagnosis, Pathophysiology and Treatment. Cardiology and Cardiovascular Research. Vol. 5, No. 2, 2021, pp. 84-93. doi: 10.11648/j.ccr.20210502.15

5. Chlapoutakis GN, Kafkas NV, Katsanos SM, et al. Acute myocardial infarction and transient ischemic attack in a patient with lone atrial fibrillation and normal coronary arteries. Int J Cardiol 2010;139:e1-e4.

6. Jean-Philippe Collet, et al. 2020 Acute Coronary Syndromes (ACS) in Patients Presenting without Persistent ST-Segment Elevation (Management of) Guidelines. European Heart Journal (2021) 42, 12891367.