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AMAÇ VE KAPSAM

Türk Yoğun Bakım Dergisi (eski adı Türk Yoğun Bakım Derneği Dergisi ISSN: 2146-6416), Türk Yoğun Bakım Derneği'nin süreli yayın organı olup yoğun bakım içerikli, yayın dili Türkçe ve İngilizce olan, bağımsız ve önyargısız hakemlik ilkelerine dayanan ulusal, periyodik bir dergidir. Türk Yoğun Bakım Dergisi Mart, Haziran, Eylül, Aralık aylarında olmak üzere yılda dört sayı çıkar. Ayrıca yılda bir kez özel sayı yayınlanır.

Türk Yoğun Bakım Dergisi'nin hedefi nitelikli, sürekli ve yoğun bakım konusunda özgün bir periyodik olarak klinik ve bilimsel açıdan en üst düzeyde derlemeler, olgu sunumları ve araştırmalar yayınlamaktır. Dergi, yoğun bakım alanı ile ilgili olan hekimler, anestezistler, cerrahlar, pediatristler ve bu alanla ilgili diğer uzmanlara yöneliktir.

Türk Yoğun Bakım Dergisi, **Emerging Sources Citation Index (ESCI), ProQuest Health & Medical Complete, EBSCO Database, Gale, Index Copernicus, CINAHL, Tübitak/Ulakbim, Türk Tıp Dizini, Türkiye Atıf Dizini, Hinari, GOALI, ARDI, OARE, AGORA, J-Gate, IdealOnline** ve **Türk Medline**'da indekslenmektedir.

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Açık Erişim, "[hakem değerlendirmesinden geçmiş bilimsel literatürün], İnternet aracılığıyla; finansal, yasal ve teknik engeller olmaksızın, serbestçe erişilebilir, okunabilir, indirilebilir, kopyalanabilir, dağıtılabilir, basılabilir, taranabilir, tam metinlere bağlantı verilebilir, dizinlenebilir, yazılıma veri olarak aktarılabilir ve her türlü yasal amaç için kullanılabilir olması"dır. Çoğaltma ve dağıtım üzerindeki tek kısıtlama yetkisi ve bu alandaki tek telif hakkı rolü; kendi çalışmalarının bütünlüğü üzerinde kontrol sahibi olabilmeleri, gerektiği gibi tanınmalarının ve alıntılanmalarının sağlanması için, yazarlara verilmelidir.

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AIMS AND SCOPE

Turkish Journal of Intensive Care (formerly called Journal of the Turkish Society of Intensive Care ISSN: 2146-6416) is the periodical of the "Turkish Society of Intensive Care" and it covers subjects on intensive care, being published in Turkish and English languages, and is an independent national periodical based on unprejudiced peer-review principles. Turkish Journal of Intensive Care is regularly published four times a year; in March, June, September and December In addition, an annual special issue is published.

The aim of the Turkish Journal of Intensive Care is to publish original periodic research papers of highest scientific and clinical value on intensive care, reviews, case reports. It is directed towards for interested in intensive care, physicians, anesthesists, surgeons, pediatricians, and any other specialists concerned with these fields.

Turkish Journal of Intensive Care is indexed in **Emerging Sources Citation Index (ESCI), ProQuest Health & Medical Complete, EBSCO Database, Gale, Index Copernicus, CINAHL, Tübitak/Ulakbim Turkish Medical Database, Turkiye Citation Index, Hinari, GOALI, ARDI, OARE, AGORA, J-Gate, IdealOnline** and **Turk Medline**.

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Türk Yoğun Bakım Dergisi, Türk Yoğun Bakım Derneği'nin yayın organıdır. Dergi dört ayda bir (Nisan, Ağustos, Aralık) yayınlanan bağımsız, uluslararası hakemli bir dergidir.

Türk Yoğun Bakım Dergisi'ne gönderilen yazılar çift-kör hakemliğe tabi tutulur. Dergi Türkçe ve İngilizce dillerinde makaleler yayınlar.

Türk Yoğun Bakım Dergisi'nin kısa adı "Turk J Intensive Care"dir. Kaynaklarda kullanılırken bu şekilde belirtilmelidir.

Yoğun bakım alanına ilişkin özgün deneysel ve klinik araştırmaları, olgu sunumlarını, yayın kurulu kararı ile istenmiş derlemeleri, editöryal yorumları, editöre mektupları ve ulusal yoğun bakım kongrelerinde sunulan bildiri özetlerini yayımlar. Dergide yayınlanacak yazıların seçimine temel teşkil eden hakem heyeti, dergide belirtilen danışmanlar ve gerekirse yurt içi/dışı otörler arasından seçilir.

Türkçe yazılarda Türk Dil Kurumu'nun Türkçe Sözlüğü ve Yazım Kılavuzu temel alınmalıdır.

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Türk Yoğun Bakım Dergisi makale başvuru ücreti ve ya makale işlem ücreti uygulamamaktadır.

Yazılar sadece online olarak kabul edilmektedir. Yazarların makale gönderebilmesi için web sayfasına (http://www.journalagent.com/tybdd/) kayıt olup şifre almaları gereklidir. Bu sistem online yazı gönderilmesine ve değerlendirilmesine olanak tanımaktadır.

Makale gönderimi yapılırken sorumlu yazarın ORCID (Open Researcher and Contributor ID) numarası belirtilmelidir. http://orcid.org adresinden ücretsiz olarak kayıt oluşturabilir.

Bu sistem ile toplanan makaleler International Committee of Medical Journal Editors (ICMJE), Index Medicus (Medline/PubMed) ve Ulakbim-Türk Tıp Dizini kurallarına uygun olarak sisteme alınmakta ve arşivlenmektedir.

Yayına kabul edilmeyen yazılar, sanatsal resimler hariç geriye yollanmaz.

Editör veya yardımcıları tarafından, etik kurul onayı alınması zorunluluğu olan klinik araştırmalarda onay belgesi (etik onay numarası ile birlikte), talep edilmektedir. Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur.

Yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermelidir. Daha önceki bilimsel toplantılarda 200 kelimeyi geçmeyen özet sunumlarının yayınları, durumu belirtilmek koşulu ile kabul edilebilir. Tüm otörler bilimsel katkı ve sorumluluklarını bildiren toplu imza ile yayına katılmalıdırlar.

Hastalar mahremiyet hakkına sahiptirler. Belirleyici bilgiler, hasta isimleri ve fotoğraflar, bilimsel olarak gerekli olmayan durumlarda ve hasta (ebeveyn veya koruyucu) tarafından yayınlanmasına yazılı olarak bilgilendirilmiş bir onay verilmediği sürece yayınlanmamalıdır.

Bu amaçla, bilgilendirilmiş onay, hastanın yayınlanacak belirli bir taslağı görmesini gerektirir. Eğer gerekli değilse hastanın belirleyici detayları yayınlanmayabilir. Tam bir gizliliği yakalamak oldukça zordur ancak eğer bir şüphe varsa, bilgilendirilmiş onay alınmalıdır. Örneğin, hasta fotoğraflarında göz bölgesini maskelemek, yetersiz bir gizlilik sağlanmasıdır.

Yazarlar, takip edilen standartların, insan deneylerinden sorumlu komitenin (kurumsal ve ulusal) etik standartlarına ve 2013'de gözden geçirilmiş 1964 Helsinki Beyannamesine uygun olduğunu belirtmelidirler. Deney hayvanı ile olan çalışmalarda, yazarlar takip edilen standartların hayvan haklarına (laboratuvar hayvanlarının bakım ve kullanımı için rehber www.nap.edu/catalog/5140.html) uygun olduğunu ve hayvan etik komitesinin onayını aldıklarını belirtmelidirler. Etik kurul onayı ve bilgilendirilmiş onam formu alındığı araştırmanın "Gereç ve Yöntem" bölümünde belirtilmelidir.

Yazıların bilimsel ve etik sorumlulukları yazarlara, telif hakkı ise Türk Yoğun Bakım Dergisi'ne aittir. Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur. Yazarlar, yayın haklarının devredildiğini belirten onay belgesini (Yayın Hakları Devir Formu) yazıları ile birlikte göndermelidirler. Bu belgenin tüm yazarlar tarafından imzalanarak dergiye gönderilmesi ile birlikte yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermiş, bilimsel katkı ve sorumluluklarını beyan etmiş sayılırlar.

Makale Değerlendirmesi

Dergiye yayımlanmak üzere gönderilen tüm yazılar 'iThenticate' programı ile taranarak intihal kontrolünden geçmektedir. İntihal taraması sonucuna göre yazılar red ya da iade edilebilir.

Tüm yazılar, editör ve ilgili editör yardımcıları ile en az iki danışman hakem tarafından incelenir. Yazarlar, yayına kabul edilen yazılarda, metinde temel değişiklik yapmamak kaydı ile editör ve yardımcılarının düzeltme yapmalarını kabul etmiş olmalıdırlar.

Makalelerin formatı Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (http://www.icmje.org/) kurallarına göre düzenlenmelidir.

İncelemeye sunulan araştırmada olası bir bilimsel hata, etik ihlal şüphesi veya iddiasıyla karşılaşılırsa, bu dergi verilen yazıyı destek kuruluşların veya diğer yetkililerin soruşturmasına sunma hakkını saklı tutar. Bu dergi sorunun düzgün biçimde takip edilmesi sorumluluğunu kabul eder ancak gerçek soruşturmayı veya hatalar hakkında karar verme yetkisini üstlenmez.

Yayın Politikası ve Makale Yazım Kuralları aşağıda belirtilen maddeler "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" (2016, http://www.icmje.org/) temel alınarak hazırlanmıştır.

Araştırma makalelerinin hazırlığı, sistematik derleme, meta-analizleri ve sunumu ise uluslararası kılavuzlara uygun olmalıdır.

Randomize çalışmalar için; CONSORT (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285:1987-91) (http://www.consort-statement.org/).

Sistematik derleme ve meta-analizlerin raporlamaları için; PRISMA [Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097] (http://www.prisma-statement.org/).

Tanısal değerli çalışmalar için; STARD (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4) (http://www.stard-statement.org/).

Gözlemsel çalışmalar için; STROBE (http://www.strobe-statement.org/).

Meta-analizleri ve gözlemsel çalışmaların sistematik derlemeleri için; MOOSE [Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting "Meta-analysis of observational Studies in Epidemiology" (MOOSE) group. JAMA 2000; 283: 2008-12].

YAZI ÇEŞİTLERİ

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Yazının tümünün 5000 kelimeden az olması gerekmektedir. İlk sayfa hariç tüm yazıların sağ üst köşelerinde sayfa numaraları bulunmalıdır. Yazıda, konunun anlaşılmasında gerekli olan sayıda ve içerikte tablo ve şekil bulunmalıdır.

Başlık sayfası, kaynaklar, şekiller ve tablolar ile ilgili kurallar bu dergide basılan tüm yayın türleri için geçerlidir.

1) Başlık Sayfası (Sayfa 1)

Yazı başlığının, yazar(lar)ın bilgilerinin, anahtar kelimelerin ve kısa başlıkların yer aldığı ilk sayfadır.

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Türkçe yazılarda, yazının İngilizce başlığı da mutlaka yer almalıdır; yabancı dildeki yayınlarda ise yazının Türkçe başlığı da bulunmalıdır.

Türkçe ve İngilizce anahtar sözcükler ve kısa başlık da başlık sayfasında yer almalıdır.

Yazarların isimleri, hangi kurumda çalıştıkları ve açık adresleri belirtilmelidir. Yazışmaların yapılacağı yazarın adresi de ayrıca açık olarak belirtilmelidir. Yazarlarla iletişimde öncelikle e-posta adresi kullanılacağından, yazışmaların yapılacağı yazara ait e-posta adresi belirtilmelidir. Buna ek olarak telefon ve faks numaraları da bildirilmelidir.

Çalışma herhangi bir bilimsel toplantıda önceden bildirilen koşullarda tebliğ edilmiş ya da özeti yayınlanmış ise bu sayfada konu ile ilgili açıklama yapılmalıdır.

Yine bu sayfada, dergiye gönderilen yazı ile ilgili herhangi bir kuruluşun desteği sağlanmışsa belirtilmelidir.

2) Özet (Sayfa 2)

İkinci sayfada yazının Türkçe ve İngilizce özetleri (her biri için en fazla 200 sözcük) ile anahtar sözcükler belirtilmelidir.

Özet bölümü; Amaç, Gereç ve Yöntem, Bulgular, Sonuç şeklinde alt başlıklarla düzenlenir. Derleme, olgu sunumu ve eğitim yazılarında özet bölümü alt başlıklara ayrılmaz. Bunlarda özet bölümü, 200 kelimeyi geçmeyecek şekilde amaçlar, bulgular ve sonuç cümlelerini içermelidir.

Özet bölümünde kaynaklar gösterilmemelidir. Özet bölümünde kısaltmalardan mümkün olduğunca kaçınılmalıdır. Yapılacak kısaltmalar metindekilerden bağımsız olarak ele alınmalıdır.

3) Metin (Özetin uzunluğuna göre Sayfa 3 veya 4'den başlayarak)

Metinde ana başlıklar şunlardır: Giriş, Gereç ve Yöntem, Bulgular, Tartışma.

Giriş bölümü, çalışmanın mantığı ve konunun geçmişi ile ilgili bilgiler içermelidir. Çalışmanın sonuçları giriş bölümünde tartışılmamalıdır.

Gereç ve Yöntem bölümü, çalışmanın tekrar edilebilmesi için yeterli ayrıntılar içermelidir. Kullanılan istatistik yöntemler açık olarak belirtilmelidir.

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c) Kitap Bölümü: Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk, CN: Appleton and Lange; 1995. p. 361-80.

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e) Elektronik Formatta Makale: Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 1(1):[24 screens]. Available from:s URL:http://www/cdc/gov/ncidoc/EID/eid.htm. Accessed December 25, 1999.

f) Tez: Kaplan SI. Post-hospital home health care: the elderly access and utilization (thesis). St. Louis (MO): Washington Univ; 1995.

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STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/);

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DERLEME / *REVIEW*

Hülya Yücel

Yoğun Bakımda Ergoterapi

Occupational Therapy in Intensive Care

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ÖZ Bu derleme, yoğun bakımda gerçekleştirilen ergoterapi müdahalelerine yönelik literatürün sentezi niteliğindedir. Her yıl, yoğun bakım ünitelerinden taburcu olan milyonlarca kişi, yeni edinilmiş bilişsel bozulma ve/veya işlevsel sakatlık ile karşı karşıya kalmaktadır. Ergoterapi yoğun bakımda bulunan hastaların beslenme, giyinme, erken mobilizasyon, ambulasyon gibi günlük yaşam aktivitelerine; hafıza, dikkat, problem çözme ve çok adımlı görevleri yerine getirme gibi gelişmiş yürütücü işlevlerden oluşan kognitif süreçlerine yönelik çalışmaları içerir. Amaçlı bir davranış ortaya çıkarmak için, uyarılma ve farkındalığı artırmak, uyanıklığı ve erken hareketlilik faaliyetlerine katılımı optimize etmek yoğun bakımda ergoterapi müdahalelerinin amaçlarını oluşturur. Literatürde bu hedeflere ulaşmak için yapılan ergoterapi müdahalelerinin anlamlı sonuçlar ortaya koyduğu görülmektedir. Fakat bu konuda, ergoterapistlerin yakın geçmişte faaliyetler gösterdiğini içeren çalışmalar yetersizdir. Yoğun bakım ünitesinde ergoterapistlerin spesifik müdahalelerini ve rolünü ve bu müdahalelerin etkinliğini netleştirmek için gelecekteki araştırmalara ihtiyaç vardır. Türkiye'de yeni gelişmekte olan ergoterapi ve ergoterapistlik mesleğinin hastanelerin yoğun bakım ünitelerinde faaliyet göstermesi dünyada da yeni bir durumdur. Bu yazı ülkemizde bu konuda yazılmış ilk derleme çalışmasıdır.
Anahtar Kelimeler: Yoğun bakım, nöroloji, kognitif, yenidoğan, ergoterapi

ABSTRACT This review is a synthesis of the literature on occupational therapy interventions in intensive care. Each year, millions of people discharged from intensive care units face newly acquired cognitive impairment and/or functional disability. Occupational therapy includes studies on daily living activities such as feeding, dressing, early mobilization, ambulation, and cognitive processes such as memory, attention, problem solving, and advanced executive functions such as performing multistep tasks. Increasing arousal and awareness, optimizing alertness, and participation in early mobility activities to elicit a purposeful behavior are the goals of occupational therapy interventions in intensive care. In the literature, it is seen that occupational therapy interventions performed to achieve these goals show significant results. However, studies on this subject, which include that occupational therapists have shown intense activities in the recent past, are insufficient. Future research is needed to clarify the specific interventions and role of occupational therapists in the intensive care unit and the effectiveness of these interventions. The occupational therapy and occupational therapist occupation operate in the intensive care units, which is newly developing in Turkey, is also a new situation in the world. This study is the first review written in our country on this subject.
Keywords: Intensive care, neurology, cognitive, neonatal, occupational therapy

Giriş

Yoğun bakım üniteleri (YBÜ) farklı sağlık problemleri olan hastalara özel müdahalelerin yapıldığı bir alandır. Burada kalan ve taburcu olan bireyler, genellikle uzun dönem sonuçları olan fiziksel, kognitif ya da psikolojik bozukluklarla karşılaşabilirler. Engelliliği önlemek veya şiddetini azaltmak için fonksiyonel sonuçlara odaklanarak taburculuk planlaması yapmak gerekmektedir (1,2).

Ergoterapistler bireylerin sağlığını, iyi olma hallerini ve yaşam rollerine katılımını destekleyen anlamlı aktiviteleri gerçekleştirmelerini sağlar (3). Yoğun bakım, ergoterapistler için önemli bir uygulama ortamıdır. Ergoterapistlerin holistik bakım yaklaşımı, kişi-çevre-aktivite etkileşimini temel almaları ve görev analizi becerileri yoğun bakımdaki bireylere fayda sağlar. Yoğun bakımda kalan kişilerle yapılan çalışmalarda günlük yaşam aktivitelerine fonksiyonel katılımın sağlanmasında ergoterapistin rolleri gösterilmiştir (1,2,4).

Ergoterapistler bireylerin mobilite, oryantasyon ve başa çıkma gibi fiziksel, kognitif ve emosyonel becerilerini geliştirmeyi, bireyin yoğun bakımda gerçekleştirdikleri kendine bakım aktivitelerindeki fonksiyonelliği artırmayı, diğer sağlık personelleri ve aile üyeleri/bakım verenleri ile iletişimi hedefleyen müdahaleler planlarlar (5). YBÜ'de ergoterapi uygulamaları; kendine bakım aktivitelerine (banyo yapma, giyinme, kişisel hijyen, beslenme vb.) katılımı, kognitif müdahaleleri (kişi, yer, zaman oryantasyonu ve yürütücü işlevleri geliştirmeyi hedefleyen aktiviteler vb.), depresyon ve anksiyeteyi azaltmak için psikolojik müdahaleleri (kendine bakım becerilerinin yeniden kazanılması, serbest zaman ve sosyal aktivitelerin başlatılması, stresle başa çıkma stratejilerinin öğretilmesi, fiziksel ve sosyal çevrenin uyarlanması vb.) içerir (5). Yoğun bakım ortamındaki iletişim ihtiyaçları için yardımcı teknoloji uygulamaları önemli ölçüde katkı sağlar (6-8). Yoğun bakımda kalan bireyler post-travmatik stres bozukluğu veya hastalık sonrası iyileşmenin çok yönlü etkileriyle başa çıkmak için ruh sağlığı değerlendirmeleri ve müdahale uygulamalarına ihtiyaç duyabilirler ve ergoterapistler bu ihtiyaçlara yönelik çalışmalar yürütmektedirler (9-12). Ayrıca ergoterapistler yoğun bakım sürecinde bireylerin yaşadığı duyusal yoksunluk, hareketsiz kalma, stres ve uzun süreli mekanik ventilasyon ile başa çıkma stratejilerini içeren müdahaleler kapsamında duyu temelli yaklaşımlar, splintleme, disfaji yönetimi, pozisyonlama, transfer yöntemleri ve yardımcı cihazların kullanımına yönelik eğitimler uygularlar (13). Yapılan çalışmalarda yoğun bakımda ergoterapi müdahalelerinin gerekliliği ve etkinliği vurgulanmıştır (5,14).

Ergoterapistler Uluslararası İşlevsellik, Yetiyitimi ve Sağlığın Sınıflandırılması'na (*International Classification of Functioning, Disability, and Health*) göre vücut yapı ve fonksiyonu alt başlığını içeren temel ve acil bakım hizmetleri dışında kalan aktivite ve bireyin rollerine katılımını destekleyen değerlendirme ve müdahalelerde bulunurlar. Bu çalışma alanı ile yoğun bakım hemşirelik hizmeti ve fizyoterapistlikten ayrılırlar. Ergoterapi bir aktivite bilimidir, dolayısıyla yoğun bakımda, günlük yaşam aktiviteleri bağımsızlığını ele alan, yaşam kalitesi odaklı meditasyon, maneviyat, şefkat, aile birlikteliği, akran dayanışması, öykü anlatımı, geçmişte hoşlanarak yaptığı aktiviteleri hatırlatma, müzik terapi gibi konulara odaklanır. Ergoterapi mesleğinde yoğun bakım özelleşilen bir alandır, dolayısıyla lisans müfredatında alınan kardiyopulmoner ergoterapi, kanser ve ergoterapi, pediatride ergoterapi, yenidoğanda duyu bütünleme, duyu/algı/motor yaklaşımları, psikoloji, sosyoloji, yaşam kalitesi, yardımcı teknoloji, sanal gerçeklik gibi derslerin yanı sıra pratik uygulama becerisi de gerektirir.

Ülkemizde yeni gelişmekte olan ergoterapi ve ergoterapistlik mesleğinin hastanelerin YBÜ'lerinde faaliyet göstermesi dünyada da yeni bir durumdur. Bu derlemenin amacı, yoğun bakımda ergoterapistlerin rollerini, yaptıkları uygulamaları ve bu uygulamaların etkinliğini açıklamaktır. Bu konudaki ülkemizde yazılmış ilk derleme çalışmasıdır.

Yoğun Bakımda Ergoterapistin Rolleri

Kapsamlı bir yoğun bakım hizmeti, hastalar için gerekli bakım düzeyine odaklanır ve eksiksiz bakım sürecini ifade eder. Yoğun bakımda ergoterapistler hastaların günlük yaşam aktivitelerindeki bağımsızlığını ve taburculuk sonrası toplumsal katılımlarını en üst düzeye çıkarmalarını sağlamak amacıyla çalışmalar yürütürler. Bu amaca ulaşmak için bireyi, ailesini ve bakım verenlerini değerlendirmeye dahil eden; ilgili herkesin beklentilerine yönelik bilinçli kararlar vermelerine ve tedavi planına dahil olmalarına yardımcı olan kişi merkezli bir yaklaşım benimserler. Ergoterapistlerin müdahale yaklaşımları; fiziksel, mental ve sosyal sağlığı kapsar ve aşağıda açıklandığı üzere üçüncü, ikinci ve birinci basamak sağlık hizmetlerine yönelik olmaktadır (5,15).

Üçüncü Basamak Sağlık Hizmeti

Üçüncü basamak sağlık hizmetlerinde ergoterapistler tarafından ele alınan müdahaleler aşağıda sıralanmıştır.

Komplikasyonların önlenmesi ve organ sistemi yetmezliğinin fizyolojik etkilerine karşı çalışmalar yürütülür (11,15). Bunlar;

a. Kontraktür, eklem deformitesi ve ağrıyı önleyecek şekilde bireyin pozisyonlanması amacıyla; uygun splintleri sağlamak veya yapmak, pasif eklem hareket açıklığı egzersizleri yapmak, bakım hizmeti sağlayan personele pozisyonlama ve transfer teknikleri konusunda tavsiyelerde bulunmak veya teknikleri öğretmek, tekerlekli sandalyeler dahil olmak üzere uygun oturma düzenini değerlendirmek ve sağlamak,

b. Uygun basınç azaltıcı yastıkların kullanımıyla bası yaralarını önlemek,

c. Aktiviteler yoluyla güç, kontrol ve hareket aralığını geliştirmektir.

Hastanın organ sistemi yetmezliği ve işlev kaybının psikolojik etkileri ile baş edebilmek için çalışmalar yürütülür (11,12,15). Bunlar;

a. Bireylere ve bakım verenlerine güvence ve destek sağlamak,

b. Bireylere ve bakım verenlerine kişinin mevcut durumunu anlamada yardımcı olmak ve etkili bir şekilde başa çıkma becerilerine sahip olmalarını sağlamak,

c. İlişkilerdeki olası değişikliklere uyum sağlamada birey ve bakım verenleri değerlendirmek ve yardımcı olmak,

d. Bireylerin stres faktörlerini azaltmalarına ve baş etme stratejileri geliştirmelerine yardımcı olmak (anksiyete yönetimi, gevşeme vb.),

e. Bireyi ve ailesini gelecek için plan yapmaya hazırlamak,

f. Yeniden eğitim ve kompansatuvar tekniklerin kullanımı yoluyla bilişsel ve algısal işlev bozukluğunun etkilerine karşı müdahalede bulunmaktır.

Hastaların hayatlarının kontrolünü ele almaları, fonksiyon kaybına uyum sağlamaları ve günlük görevlerini yerine getirme yeteneklerini en üst düzeye çıkarmaları için çalışmalar yürütülür (13,15). Bunlar;

a. Kendine bakım aktivitelerini değerlendirmek ve yeniden eğitim vermek,

b. Enerji koruma ve yorgunluk yönetimi teknikleri hakkında önerilerde bulunmak,

c. Günlük yaşam aktivitelerine katılıma yardımcı olmak amacıyla ekipman ve çevre uyarlamalarının sağlanması için değerlendirme ve müdahalelerde bulunmak,

d. Bireye duyusal stimülasyon ve hastanede daha yüksek düzeyde anlamlı aktivite sağlama, serbest zaman aktiviteleri ve iş dahil olmak üzere anlamlı bir yaşam tarzının yönetiminde yardımcı olmak,

e. Hastaların ve bakım verenlerin uygun kaynaklara erişimi için gerekli bilgileri sağlamaktır.

İkinci Basamak Sağlık Hizmeti

İkinci basamak sağlık hizmetlerinde yukarıda açıklanan üçüncü seviyedeki tüm müdahalelerin yanı sıra tedaviyi gözden geçirmek ve yeniden derecelendirmek, ameliyat sonrası alınacak önlemler ve günlük aktiviteler konusunda eğitim ve tavsiyeler vermek hedeflenir (5,15).

Birinci Basamak Sağlık Hizmeti

Birinci basamak sağlık hizmetleri, üçüncü ve ikinci seviyedeki tüm müdahaleleri içermekle birlikte aşağıdaki çalışmaların yürütülmesini gerektirir (11,15):

a. Bireyin yaşamının kontrolünü sağlamasını, fonksiyon kaybına uyumunu ve günlük görevleri yerine getirirken güvenliğini en üst düzeye çıkarmasını sağlamak için rehabilitasyona devam etmek,

b. Birey ve bakım verenlerle birlikte hastaneden taburculuğu planlamaya başlamak.

Bireyin iyileşmesini ve fonksiyonlarını en üst düzeye çıkarmak için henüz durumu kritik iken değerlendirme ve müdahalelere başlanmalıdır. Erken ve etkili tedavinin kişinin hastanede kalış süresini ve komplikasyonları çözme maliyetlerini azaltacağı göz önünde bulundurulmalıdır (12,13,15).

Yoğun bakımdaki uygulamaların amacı, genellikle yalnızca hayatı kurtarmak ve organ sistemi yetmezliğini önlemek olarak görülür ve ortaya çıkan fizyolojik ve psikolojik etkiler dikkate alınmayabilir. Bu nedenle yoğun bakımda ergoterapistlerin rolü hemen görülemeyebilir. Ayrıca yoğun bakımda ergoterapinin gerekliliğine ilişkin yayımlanmış araştırmaların yetersizliği ve iyi uygulama örneklerini yaygınlaştırmak için yeterince çalışılmamış olmasına bağlı olarak yoğun bakımda ergoterapistlerin rollerinin bilinmemesi, hastaların ihtiyaçlarını karşılamaya uygun kaynaklara erişimlerini zorlaştırmaktadır (11-13,15).

Yoğun bakımda ergoterapi müdahalelerine aşağıdaki başlıklarda yer verilmiştir.

Yoğun Bakımda Kognitif ve Nörolojik Ergoterapi

YBÜ'lerden taburcu olan kişiler sıklıkla kognitif bozukluklar ile karşı karşıya kalmaktadırlar (16-18). Ergoterapistler, özellikle beyin yaralanması ve inmeli hastalarda, bilişin değerlendirilmesinde ve rehabilitasyonunda rol alırlar; ancak bu konuda YBÜ'lerdeki müdahalelerine yönelik araştırmalar azdır (19,20).

Deliryum, YBÜ'lerde %45-87 oranında insidansı ile sık görülen bir komplikasyondur (21). Deliryum süresinin hastaların hayatta kalmalarını etkilediği ve deliryumun devam ettiği her 48 saatin mortaliteyi %11 oranında artırdığı bildirilmiştir (22). Yapılan bir çalışmada YBÜ'deki yaşlı hastalarda kognitif terapinin uygulanabilirliği ve güvenilirliği araştırılmıştır. Bu çalışmada, YBÜ'deki yaşlı hastalarda ergoterapi müdahalelerinin deliryum süresine, insidansına ve şiddetine etkisinin belirlenmesi; ikincil olarak da hastaların hastaneden taburcu olurken fonksiyonel bağımsızlık, biliş ve kavrama gücüne etkilerinin değerlendirilmesi hedeflenmiştir. Ergoterapi müdahaleleri, duyu stimülasyonunu; ödem ve dekübit ülserlerini önlemek için pozisyonlama ve çevresel uyarlamaları; hafıza, görsel algı, dikkat, oryantasyon, praksi ve problem çözme becerilerini geliştirmeye yönelik kognitif aktiviteleri; üst ekstremitede fonksiyonelliğe yönelik aktiviteleri; günlük yaşam aktiviteleri eğitimini ve aile/bakım veren katılımını içermektedir. Çalışma sonucunda deliryumun azalması, fonksiyonel işlev puanlarının ve kavrama gücünün iyileşmesi ve daha yüksek Mini-Mental

test skorlarının bulunması ile ergoterapinin, yoğun bakımda ventile edilmeyen yaşlı hastalarda deliryum süresini ve insidansını azaltmanın yanı sıra taburculukta işlevselliği artırmak için etkili olduğu sonucuna ulaşılmıştır (23). Yoğun bakımda kalan kişilerde deliryum varlığına bakılmaksızın taburculuk sonrası kognitif bozukluklar olabilmektedir. Ayrıca deliryumun geliştiği hastalarda, uzun süreli kognitif bozukluklar ve fonksiyonel zorluklar yaşandığı görülmüştür. Erken dönemde, hedefe yönelik, çok bileşenli ve çok disiplinli yaklaşımın deliryumlu kişiler için etkili olduğu belirtilmiştir. Bununla birlikte ergoterapi için erken müdahalenin faydalarına ilişkin kanıtlar belirsizliğini koruyor olsa da deliryumun kişiler ve aileler üzerindeki etkisinin tanınması ve bunu azaltmak için stratejiler sağlanması gerektiği belirtilmiştir (20). YBÜ'den taburcu edilen kişilerde kognitif rehabilitasyon ve ergoterapinin problem çözme ve çok adımlı görevleri yerine getirme gibi yürütücü işlevleri geliştirdiği gösterilmiştir (24). Bugüne kadar yapılan girişimsel denemeler; başlangıçtaki fonksiyonel durumu koruyan, deliryum süresini kısaltan ve ölüm veya yeniden hastaneye yatış riskini azaltan erken dönem ergoterapi müdahaleleri ile ilişkilendirilmiştir (25).

YBÜ'de kalan kişilerde erken dönem ergoterapinin taburculuk için gerekli işlevselliği iyileştirdiğine, deliryum epizodlarını azalttığına ve hastaların yatış süresini kısalttığına dair kanıtlar vardır (26,27). YBÜ'de erken dönem kombine fiziksel ve kognitif tedavinin güvenilir olduğu; ancak bu tür müdahalelerin uzun vadeli etkilerinin sonuçsuz kaldığı ve bu konuda yapılacak daha fazla çalışmaya ihtiyaç duyulduğu belirtilmiştir (25).

YBÜ'de kalan kişilerde hareketsizlik ve yatak istirahati ile ilgili kısa ve uzun vadeli komplikasyonlar hasta morbiditesini, mortalitesini, maliyetini ve yaşam kalitesini etkilemektedir. Özellikle nörolojik işlev bozukluğu nedeniyle yüksek hareketsizlik oranı göz önüne alındığında, YBÜ erken mobilizasyon müdahaleleri için ideal bir ortamdır (28). YBÜ'de erken mobilitenin etkili olduğu, yatış süresini kısalttığı ve daha iyi uygun maliyetli sonuçlar sağladığı bilinmektedir (29). Mobilizasyona izin verecek şekilde sedasyonu ve deliryumu azaltmak, hastaların fonksiyonel hareketliliğini iyileştirmek için rehabilitasyon konsültasyonlarının ve tedavilerinin sıklığını artırmak ve hastanede kalış süresi üzerindeki etkilerini değerlendirmek amacıyla mevcut uygulamaların gözden geçirilmesi ve geliştirilmesini içeren kalite iyileştirme programının uygulandığı bir çalışmada ergoterapi müdahalelerini içeren kalite iyileştirme programı sonuçlarında YBÜ deliryumunda ve hastanede kalış süresinde azalma görülürken hastaların fonksiyonel hareketliliğinde iyileşmeler gözlenmiştir (29).

Ergoterapi uygulamaları travmatik beyin yaralanmalarından sonra iyileşmeyi desteklemek için YBÜ'de yer almaktadır. YBÜ'de beyin yaralanması olan bireyler için uygulanan ergoterapi, öncelikle solunum terapisi; kontraktürleri önlemek için pasif yardımcı hareket; duyusal stimülasyon; kuvvet, endurans ve esneklik gibi vücut yapı ve işlevlerine odaklanan çalışmaları içermektedir. Ergoterapi müdahaleleri ayrıca oturma ve/veya ayakta durma pozisyonlarına, mobilizasyon gibi aktivitelere ve kendine bakım veya günlük yaşam aktivitelerine yönelik eğitim uygulamalarını içerir. Terapötik amaç sıklıkla pnömoni veya kontraktür gibi ikincil semptomların önlenmesine, bilincin ve duyusal algının geliştirilmesine ve kasların güçlendirilmesine odaklanır. Genel amaç kendine bakımla ilgili olarak mümkün olan en yüksek düzeyde mobilite ve bağımsızlığa ulaşmaktır (30).

Yoğun Bakımda Mekanik Ventilasyona Bağlı Olan Kişilerde Ergoterapi

Mekanik ventilasyon uygulanan hastaların bakımındaki tıbbi gelişmeler, uzun süreli sağkalım oranlarının artmasını sağlamıştır (27). Buna bağlı olarak kişilerin erken mobilizasyonu ve günlük yaşamlarında işlevsellikleri önem kazanmıştır. YBÜ'de tedavide kullanılan erken mobilizasyon çalışmalarının çoğunun mekanik ventilasyon hastalarına odaklandığı belirtilmiştir (31). Erken mobilizasyon, genellikle mekanik olarak ventile edilen bir hasta rehabilitasyona katılabildiğinde, stabil hemodinamik bir duruma sahip olduğunda ve kabul edilebilir seviyelerde oksijen aldığında mobilite programının başlatılması olarak tanımlanmıştır (32). Sedasyonun kullanıldığı, mekanik ventilasyon uygulanan kişilerde tıbbi YBÜ'deyken mekanik ventilasyona bağlandığı andan itibaren rutin olarak ergoterapi müdahaleleri başlamalıdır (33,34).

Mekanik ventilasyona bağlı yaşlı yetişkinlerde YBÜ ortamında standart bir erken mobilizasyon protokolünün kullanılmasının fizibilitesini araştıran bir çalışmada tedavi için aşamalı bir erken mobilizasyon programı kullanılmıştır. Program, yoğun bakımda mekanik ventilasyona bağlı 65 yaş ve üstü kişilere uygulanmıştır. Çalışmada pozisyonlama, yatakta mobilizasyon, oturma toleransını geliştirme, nefes ve denge egzersizleri, transferler ve ambulasyon çalışmalarına yer verilmiştir. Erken mobilizasyon protokolünün uygulanabilir, güvenli olduğu ve mekanik olarak ventile edilen yaşlı yetişkinler tarafından iyi tolere edildiği sonucuna ulaşılmıştır (35).

YBÜ'de mekanik ventilasyona bağlı kişilerde erken dönemde oturma, ayakta durma ve yürüme aktiviteleriyle başlayıp banyo yapma, giyinme, kendine bakım, tuvalete gitme ve yemek yeme gibi günlük yaşam aktiviteleri eğitimi ile devam eden ergoterapi müdahalelerinin fonksiyonel ve nörobilişsel sonuçları iyileştirdiği ve mekanik ventilasyon süresini kısalttığı gösterilmiştir (33).

Yoğun Bakımdaki Koronavirüs Hastalığı-2019 (COVİD-19) Olan Kişilerde Ergoterapi

COVİD-19 hızla ilerleyen bir enfeksiyondur. COVİD-19'dan kaynaklanan komplikasyonlar pulmoner, kardiyovasküler, renal ve nörolojik sistemleri etkileyerek çoklu organ yetmezliğine ve diğer hastalıklara yol açabilmektedir (36).

COVİD-19 salgın döneminde hastanelerde çalışan ergoterapistler akut ve yoğun bakım ortamlarında ergoterapinin yeri ve etkinliğini araştırmışlardır. Bu tıbbi açıdan karmaşık ortamlarda ergoterapinin özgün ve temel rolünü özetleyen, iyi tanımlanmış görev ve sorumluluklar olmaması nedeniyle birçok ergoterapist COVİD-19 salgın döneminde iş güvencesizliği yaşamıştır (37). Bununla birlikte bu uygulama alanında ergoterapistlerin rolünün tanınabilirliği için yoğun bakım ortamlarında ergoterapi uygulamalarının kapsamının tanımlanması, ergoterapinin kişi merkezli sonuçları, sağlık sistemi sonuçları ve sağlık hizmeti kullanımı üzerindeki farklı etkilerinin tanımlanması ve işbirliğini kolaylaştırmak amacıyla yoğun bakımda çalışan sağlık profesyonelleri için özel ilgi alanlarının geliştirilmesi önerilmiştir (38).

Mekanik ventilasyona ihtiyaç duyan hastalar -özellikle akut solunum yetmezliği olanlar- yoğun bakımdan taburcu olduktan sonraki yıllarda yoğun bakım sonrası sendrom nedeniyle uzun süreli sorunlar yaşamaktadırlar. Yoğun bakım sonrası sendroma benzer şekilde, COVİD-19 ile hastaneye yatırılan hastalar, özellikle ağır hastalık, kas zayıflığı gibi bozukluklar, aktivite limitasyonları, hastaneden taburcu olduktan sonra devam eden ve rehabilitasyon gerektiren katılım kısıtlılıkları göstermektedir. Birçok klinik sürecin uzun süreli hastane kalışını, uzun süreli mekanik ventilasyonu ve çoklu organ yetmezliğini içerdiği göz önüne alındığında, kritik bakıma ihtiyaç duyan COVİD-19 geçiren birçok kişinin yoğun bakım sonrası sendrom yaşamasının muhtemel olduğu düşünülmüştür. Ayrıca fiziksel işlev, günlük yaşam aktiviteleri ve bilişle ilgili yaşanılan zorluklar, kişinin topluma katılımını etkilemekte ve uzun vadede yaşam kalitesini düşürmektedir. Bu nedenle COVİD-19 sonrasında bireylerin işlevsel olarak topluma katılımı için rehabilitasyona olan ihtiyaçları göz önünde bulundurulmalıdır (39).

Salgın döneminin ilk aylarında, kritik durumdaki hastalar için erken dönemdeki ergoterapinin önemi genellikle göz ardı edilmiştir. Dünya bu salgınla karşı karşıya kalmaya devam ederken, kişileri rollerine ve rutinlerine döndürmek için rehabilitasyon ve hayatta kalma ana temalar haline gelmiştir. Yoğun bakımda çalışan ergoterapistler, COVİD-19 hasta popülasyonlarına proaktif bir şekilde en iyi uygulamalarını sunarak ve mesleğin bütüncül ve kişi merkezli bakış açısını birleştirerek ergoterapinin COVİD-19 salgınındaki temel rolünü göstermiştir (39,40). Böylece COVİD-19, yoğun bakım ortamlarında ergoterapi uygulamalarının etkinliğini vurgulama fırsatı sağlamıştır.

Yenidoğan Yoğun Bakımda Ergoterapi

Uzman ergoterapistler güvenli ve etkili uygulamalar için yenidoğanın tıbbi durumu ve yenidoğan yoğun bakım ünitesinde (YYBÜ) bakılan bebeklerde gelişimsel değişkenlikler hakkında gerekli bilgiye sahiptir. Duyusal entegrasyon ve nörogelişimsel müdahale gibi ergoterapi yaklaşımları, YYBÜ'de uygulanabilir. Ancak YYBÜ'de kalan bebekler genellikle fizyolojik olarak hassastır ve çevresel koşullardan kolayca etkilenmektedirler. Zararsız görülebilen bazı etkileşimler ve terapötik müdahaleler, bir bebekte fizyolojik dengesizliği tetikleyebilir ve yaşamı tehdit edebilir. Bu nedenle hassas yenidoğanı çevrenin aşırı veya uygun olmayan duyusal uyaranlarından korumak, genellikle bebekle doğrudan müdahalelerden veya etkileşimlerden daha öncelikli olabilir. Buna göre ergoterapistler yaklaşımlarını bebeğin tıbbi durumuna, fizyolojik homeostazisine, gelişimsel ve aile ihtiyaçlarına göre uyarlar (40).

Ergoterapistler çalışmalarını bebeği YYBÜ'de olan ailelerin ihtiyaçlarına yönelik yürütürler. Bebeğin tıbbi durumu ve sürecin belirsizliği, ebeveyn-bebek ayrılığı ve doğum veya doğumdan sonra annede meydana gelen olası komplikasyonlar aile stresine veya krize yol açabilir. Bu durumlar genellikle optimal bebek gelişimi için gerekli olan ebeveyn-bebek bağlanma sürecini değiştirmektedir. Ailelere en iyi hizmet, yalnızca bebeğin ihtiyaçları hakkında bilgili olan değil, aynı zamanda ailenin koşullarına, önceliklerine, endişelerine ve kültürel inançlarına karşı da duyarlı olan bir ergoterapist tarafından yapılabilir. Ergoterapist, bebeğin optimal gelişimini desteklemek için aile üyeleriyle destekleyici, işbirlikçi ve terapötik ilişkiler kurar (40).

Çevrenin sosyal ve fiziksel yönleri hem bebek hem de aile için stres faktörü olabilir. Ergoterapist, YYBÜ'nün sosyal ve fiziksel özelliklerinin etkileşimini ve bu etkileşimin bebeği, aileyi ve sağlık profesyonelini nasıl etkilediğini inceler. Bu bilgi,

ergoterapi değerlendirmesi için bir temel olarak kullanılır ve etkili müdahale stratejilerine katkıda bulunur. Ergoterapistin önemli bir rolü, YYBÜ ortamının sosyal ve fiziksel sınırları içinde çalışarak, gelişimsel olarak uygun okupasyonların, duyusal-motor süreçlerin ve nörodavranışsal organizasyonun geliştirilmesi dahil olmak üzere, her aileye optimal bebek gelişimini sağlamada yardımcı olmaktır. Ergoterapist, doğrudan gözlem, müdahale, danışma, eğitim ve araştırma yoluyla bebeğe en etkili ve uygun sosyal ve fiziksel ortamı sağlamak için çalışmalar yürütür (40).

Prematüre bebekler yaşadığı davranışsal ve nörogelişimsel bozukluklar nedeniyle çoğunlukla beslenme problemleri yaşarlar (41). Beslenme sırasında yutma yaşamı sürdürmek ve büyüyebilmek için esastır (42). Yenidoğan ve preterm bebeklerde yutma becerisinin zayıf olması nedeniyle ağızdan beslenmeye geçmek zordur. Bebeklerde görülen emme ve yutma problemleri aspirasyona yol açabilmektedir. Aspirasyon görülen bebeklerde ölüm de dahil olmak üzere zatürre, astım gibi solunum problemleri görülebilmektedir (43,44). Bakım verenlerine yönelik eğitimler ile bebeklerin aspire durumundan kaynaklanan ölümlerinde ve hastalıklarında azalmaların olduğu görülmüştür (45). Ergoterapistlerin en yaygın kullandığı müdahaleler arasında taburculuk sonrasında beslenmeye yönelik aile eğitiminin olduğu bildirilmiştir (46).

Prematüre yenidoğanların sinir sistemlerinin olgunlaşmamış olması ve hassasiyetleri nedeniyle nöropsikomotor gelişimlerinde gecikme ve merkezi sinir sisteminde lezyonlar meydana gelebilir (47). YYBÜ'de terapötik pozisyonlandırma ergoterapistlerin erken dönemde başlaması gereken nörogelişimsel müdahalelerdendir. Prematüre yenidoğanların doğru pozisyonlandırılması fizyolojik ve motor stresin azaltılmasına yardımcı olur. Solunum problemi olan bebeklerde pozisyonlamanın önemli olduğu ve pozisyonlama tekniklerinin ve özellikle yüzükoyun pozisyonun oksijenizasyonu artırdığı bildirilmiştir. Ayrıca uygun pozisyonlama ile bebeğin uyku düzeninin sağlandığı gösterilmiştir (48-50).

Sonuçlar

Bu derleme ile ergoterapistlerin YBÜ'de yenidoğan, solunum yolu hastalıkları, kronik hastalıklar, kognitif ve nörolojik bozukluklara yönelik müdahalelerine bir bakış açısı kazandırılmaya çalışılmıştır.

YBÜ'de ergoterapistler hastaya, onun ailesine, bakım verenlerine mesleki kurallara uygun olarak kişi merkezli ve maksimum fayda sağlayabilecek müdahalelerde bulunurlar. Bireyin kontraktürünü önleyecek müdahaleler ve atelleme gibi yardımcı cihazların kullanımında kişiye özgü müdahaleler oluştururlar. Yoğun bakımın zorluk seviyelerine göre görevler üstlenirler. Hastanın yoğun bakım ve yoğun bakım sonrası mevcut rahatsızlığına uygun olarak günlük yaşam aktivitelerini gerçekleştirmelerine yönelik çalışmalar yaparlar.

Hastalarda yoğun bakım sonrası hafıza ve iletişim gibi alanlarda kognitif bozukluklar görülebilir. Ergoterapistler hastaların oryantasyon, hafıza, dikkat ve problem çözme gibi kognitif becerilerini değerlendirip bu becerileri kişinin seviyesine en uygun şekilde geliştirmeye odaklanırlar. Fakat bu çalışmaların uzun vadeli sonuçlarını gösterecek araştırmalara ihtiyaç duyulduğu görülmüştür.

YBÜ'de özellikle yaşlı hastalarda görülen deliryuma yönelik ergoterapi müdahalelerini incelediğimizde ergoterapistin temel amacının sağlık ve refahı geliştirmeye yönelik olduğu görülmüştür. Ergoterapistlerin hastaların kognitif bozukluklarına yönelik değerlendirmeler yaptıkları; uyku hijyeni, günlük yaşam aktiviteleri eğitimleri ve bakım veren eğitimlerinde bulundukları görülmüştür.

Araştırmalarda, COVİD-19 salgınında ergoterapistlerin bireylerin transfer ve ambulasyon gibi temel yaşam aktivitelerine yardımcı oldukları görülmüştür. Ancak bu dönemde hastaların solunum problemlerinde ve yoğun bakımda tedavisi sürdürülen hastalarda ergoterapi yetkinliğine yönelik az bilgiye ulaşılmıştır.

Yenidoğan YBÜ'de ergoterapistler bebeklerin erken doğum, doğum öncesi, sırası ve sonrasındaki komplikasyonlarına yönelik mesleki uygulamalarda bulunmuşlardır. Bebeklerde doğum sonrası görülen beslenme bozukluklarına yönelik uygulamalar yapılmıştır. Ergoterapistler uygulamalarında bebeklerin yaşadığı komplikasyonlara yönelik olarak ve bebeği destekleyici şekilde pozisyonlandırmaya yer vermiştir. Ergoterapistler aynı zamanda bebeğin ailesi ve bakım verenlerine yönelik müdahale planları uygulamışlardır.

Sonuç olarak; ergoterapinin birçok farklı yoğun bakım alanlarında yer alması gereken bir meslek olduğu görülmüştür. Buna karşın ergoterapistler yoğun bakımda kısıtlı alanlarda çalışmaktadırlar. Ergoterapistlerin YBÜ'de hastalara sağlayacağı faydalara yönelik daha fazla araştırmalar yapılmalı disiplinler arası çalışmalarda ergoterapistlere de yer verilmelidir.

Teşekkür: Yoğun bakımda ergoterapi uygulamaları konusunda bir derleme yazılması ihtiyacını ortaya koyan Dr. Öğretim Üyesi H. Atacan Tonak'a, yazıyı düzenleyen Uzm. Erg. Ebru Yıldız'a, literatürdeki kaynaklara ulaşmamda destek veren Beyza Göney, Mervenur Turan ve Mine Ntourali'ye teşekkür ederim.

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ÖZGÜN ARAŞTIRMA / *ORIGINAL RESEARCH*

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Yoğun Bakım Hastalarında Ventilator İlişkili Pnömoni Etkenlerini İzole Etmede Mini-bronkoalveolar Lavaj Tekniğinin Endotrakeal Aspirat ve Bronkoskopik Örneklerle Karşılaştırılması

Comparison of Mini-bronchoalveolar Lavage Technique with Endotracheal Aspirate and Bronchoscopic Specimens in Isolating Ventilator-associated Pneumonia Factors in Patients Under Intensive Care

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ÖZ *Amaç:* Çalışmamızda yoğun bakım ünitesinde (YBÜ) nozokomiyal pnömoni tanısıyla izlenen hastalarda mini-bronkoalveolar lavaj (mini-BAL) yöntemi ile klasik yöntemler olan endotrakeal aspirasyon (ETA) ve BAL yönteminin karşılaştırılması amaçlanmıştır.
Gereç ve Yöntem: Çalışmamız İstanbul Üniversitesi İstanbul Tıp Fakültesi Anesteziyoloji ve Reanimasyon Anabilim Dalı YBÜ'de Şubat 2014-Ocak 2015 tarihleri arasında ventilator ilişkili pnömoni (VİP) şüphesiyle takip edilen 30 hastada gerçekleştirildi.
Bulgular: Hastaların %40'ı (12 kişi) kadın, %60'ı (18 kişi) erkektir ve yaş ortalaması 54,23±21,37'dir. Ortalama mekanik ventilasyonda kalma süreleri ise 9,7±22,8 gün olarak hesaplanmıştır. Hastaların ortalama Basitleştirilmiş Akut Fizyoloji Puanı III skoru 36,06±8,46, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II skoru 21,36±4,90 ve Klinik Akciğer Enfeksiyon skoru ise 5,90±1,91 olarak hesaplanmıştır.
Sonuç: Mini-BAL yönteminin bronkoskopiye göre tutarlılığı %86,7, trakeal aspirata göre tutarlılığı %63,3 olarak tespit edilmiştir. ETA ile bronkoskopi yönteminin birbiri ile tutarlılığı %60 olarak hesaplanmıştır. Sonuç olarak YBÜ'de VİP şüphesi olan hastaların tanısında kullanılan yöntemlerin karşılaştırılmasında, mini-BAL yönteminin erken ve güvenilir sonuçlar verdiği tespit edimiştir.
Anahtar Kelimeler: Ventilatör ilişkili pnömoni, mini-bronkoalveolar lavaj, bronkoalveolar lavaj, endotrakeal aspirat

ABSTRACT *Objective:* Our study aimed to compare the mini-bronchoalveolar lavage (mini-BAL) method with the classical methods of endotracheal aspiration (ETA) and BAL in patients followed up in the intensive care unit (ICU) diagnosed with nosocomial pneumonia.
Materials and Methods: Our study comprised 30 patients who were followed up with a suspicion of ventilator-associated pneumonia (VAP) between February 2014 and January 2015 at İstanbul University, İstanbul Faculty of Medicine, Department of Anesthesiology and Reanimation, ICU.
Results: A total of 40% (12 people) of the patients were women, 60% (18 people) were men, and the mean age was 54.23±21.37 years. The mean duration of mechanical ventilation was 9.7±22.8 days. The mean Simplified Acute Physiology Score III of the patients was 36.06±8.46, the Acute Physiology and Chronic Health Evaluation-II score was 21.36±4.90, and the Clinical Pulmoner Infection score was 5.90±1.91. The consistency of the mini-BAL method, according to bronchoscopy, was 86.7%, and its consistency, compared with tracheal aspiration, was 63.3%. The consistency between the ETA and bronchoscopy method was 60%.
Conclusion: Therefore, in the comparison of the methods used in the diagnosis of patients with suspected VAP in the ICU, mini-BAL gave reliable results in the early period.
Keywords: Ventilator-associated pneumonia, mini-bronchoalveolar lavage, bronchoalveolar lavage, endotracheal aspiration

Giriş

Hastane ile ilişkili enfeksiyonlar arasında üriner sistem enfeksiyonlarından sonra ikinci sırada olan nozokomiyal pnömoni, yatış sırasında inkübasyon döneminde olmadığı bilinen, yatıştan 48 saat sonrasında veya hastaneden taburcu olduktan sonraki ilk 48 saat içinde gelişen pnömoniler için kullanılan bir tanımlamadır (1). Bunun yanı sıra ventilatör ilişkili pnömoni (VİP); entübasyon sırasında pnömonisi olmayan invazif mekanik ventilasyon desteği altındaki bireylerde, entübasyondan en erken 48 saat sonra gelişen nozokomiyal pnömonidir (1-3). Mekanik ventilatör bağımlı hastalarda pnömoni tanısı zordur ve hala "altın standart" tanı yöntemi yoktur (4). Mekanik ventilatöre bağımlı, yoğun bakım hastalarında fiberoptik bronkoskopi tekniği ile yapılan örnekleme nozokomiyal pnömoni teşhisinde referans teknik olarak bilinmektedir. Ancak bu teknik invazif olup akut solunum yetmezliği olan hastalarda hipoksemi, tansiyon pnömotoraks ve bronşiyal hemorajiye yol açtığını bildiren literatürler de bulunmaktadır (5). Biz bu çalışmada, yoğun bakım ünitesinde (YBÜ) yatan 30 hastada, nozokomiyal pnömoni tanısında yeni bir yöntem olan mini-bronkoalveolar lavaj (mini-BAL) yöntemi ile klasik yöntemler olan endotrakeal aspirasyon (ETA) ve BAL yöntemini karşılaştırmayı amaçladık.

Gereç ve Yöntem

Çalışmaya, İstanbul Üniversitesi İstanbul Tıp Fakültesi Etik Kurulu'ndan 16.08.2013 tarihinde 14 sayılı toplantı ile 1136 numaralı etik kurul onayı alınmıştır (karar no: 14). Çalışmamızda Şubat 2014-Ocak 2015 tarihleri arasında İstanbul Üniversitesi İstanbul Tıp Fakültesi Anesteziyoloji ve Reanimasyon Anabilim Dalı YBÜ'de VİP şüphesi olan 30 hastaya nozokomiyal pnömoni tanısında yeni bir yöntem olan mini-BAL yöntemi uygulanarak (Şekil 1), klasik yöntemler olan ETA ve BAL ile karşılaştırmak amaçlanmıştır.

Çalışmaya alınma kriterleri şu şekilde belirlenmiştir:

A. Hastalar 48 saatten daha uzun süre yoğun bakımda kalmış olmalı ve 24 saatten daha uzun süre endotrakeal yerleştirilmiş tüpü olmalıdır.

B. Bu hastalardan akciğer grafisinde yeni gelişen veya uzun süredir devam eden pulmoner infiltrasyonu olan ve aşağıdaki kriterlerden en az iki tanesini karşılaması gerekmektedir:

a. Ateş (>38 °C) veya hipotermi (<36,5 °C),

b. Lökositoz (>10.10^3/L) veya lökopeni (<4.10^3/L),

c. Pürülan trakeal sekresyon.

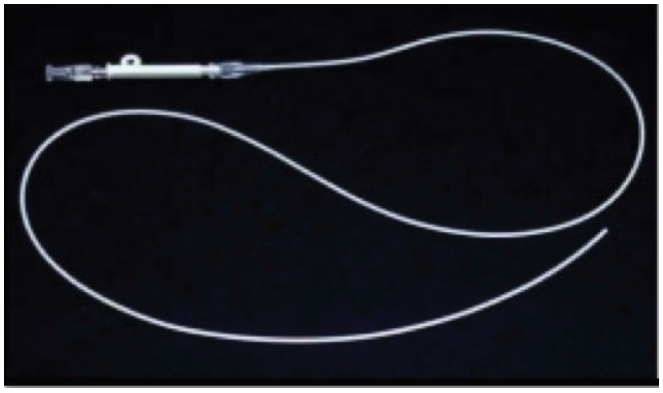
Ciddi hipoksemik hastalar (PaO_2/FiO_2<120), hemodinamik açıdan stabil olmayan hastalar, ciddi koagülasyon bozukluğu olan hastalar ve yoğun bakıma girişte akciğer enfeksiyonu olan hastalar çalışma dışında bırakılmıştır.

Çalışmaya alınan hastalardan ETA, mini-BAL ve BAL örnekleri aynı gün içinde 1 saat aralıklarla; önce ETA sonrasında sırasıyla mini-BAL ve BAL örnekleri alınmıştır. Örnekler enfeksiyon laboratuvarında Gram-boyama yapılmamış, direkt kültürlere ekilmiştir. ETA örneğinde >100.000 cfu/mL, BAL örneğinde >10.000 cfu/mL koloni sayısı anlamlı üreme olarak kabul edilmiştir.

Hastalar; demografik özellikler (yaş, cinsiyet), entübasyon/trakeotomi tarihi, mekanik ventilasyon süresi, önceki pulmoner enfeksiyonlar, örnekleme tarihi, örneklemeden önceki antibiyoterapi, giriş Basitleştirilmiş Akut Fizyoloji Puanı-III (SAPS III) skoru, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skoru, Klinik Akciğer Enfeksiyonu skoru (CPIS), mini-BAL ve bronkoskopi antibiyogram sonuçları ve trakeal kültür sonuçları açısından değerlendirildi.

İstatistiksel Analiz

İstatistiksel analizler SPSS (Statistical Package for Social Sciences, version 15, Inc, USA) programı kullanılarak yapıldı. Sürekli değişkenler ortalama ± standart sapma ve parantez içinde en düşük ile en yüksek değer olarak verildi. Kategorik değişkenler sıklık ve yüzdeler ile ifade edildi. Verilerin normal dağılıma uygunluğu Kolmogorov-Smirnov testi ile değerlendirildi. Gruplar arası farkı değerlendirmek için kategorik verilerde Pearson ki-kare ve Fisher'in kesin testi kullanıldı. Sayısal veriler için ise normal dağılıma uyan verilerde Student t-testi ve ANOVA testi, normal dağılım koşullarının sağlanmadığı durumlarda ise Mann-Whitney U



Şekil 1. Mini-BAL kateteri
Mini-BAL: Mini-bronkoalveolar lavaj

testi ve Kruskal-Wallis varyans analizi kullanıldı. İstatistiksel anlamlılık düzeyi olarak bütün testler için p<0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışmaya dahil edilen 30 hastanın demografik verileri Tablo 1'de özetlenmiştir, %40'ı (12 kişi) kadın, %60'ı (18 kişi) erkektir. Hastaların yaş ortalaması 54,23±21,37 yaş olup en küçük hasta yaşı 20, en büyük hasta yaşı ise 87'dir. Ortalama mekanik ventilasyonda kalma süreleri ise 9,7±22,8 gün olarak hesaplanmıştır. Hastaların ortalama SAPS III skoru 36,06±8,46, APACHE-II skoru 21,36±4,90 ve CPIS skoru ise 5,90±1,91 olarak hesaplanmıştır.

Hastaların mini-BAL yöntemi ile alınan örneklerindeki üreme durumu bronkoskopi ile karşılaştırıldığında; 26 hasta sonucunun tutarlı olduğu saptanmıştır. Mini-BAL yönteminin bronkoskopiye göre tutarlılığı %86,7 olarak tespit edilmiştir (Tablo 2). Ayrıca hastaların mini-BAL yöntemi ile alınan örneklerindeki üreme durumu trakeal aspirat ile karşılaştırıldığında; 19 hasta sonucunun tutarlı olduğu saptanmıştır. Mini-BAL yönteminin trakeal aspirata göre tutarlılığı %63,3 olarak tespit edilmiştir. ETA ile bronkoskopi ile alınan örnekler karşılaştırıldığında; 18 hastada sonuçların tutarlı olduğu saptanmış olup 3 yöntemin birbiriyle tutarlılığı %60 olarak hesaplanmıştır.

Tartışma

YBÜ'de yatan hastalarda mini-BAL tekniğinin bronkoskopi ile elde edilen sonuçlara göre duyarlılığını incelediğimiz bu çalışmada, mini-BAL tekniğinin %86,7 oranında bronkoskopik BAL sonuçları ile uyumlu olduğu gösterilmiştir.

Bronkoskopinin olmadığı merkezlerde VİP tanısında en yaygın olarak kullanılan yöntem ETA kantitatif kültürü olmakla beraber, bu yöntemin en önemli dezavantajı üst solunum yolları florası kontaminasyonudur. Salata ve ark.'nın (6) çalışmasında ETA kantitatif kültürünün özgüllüğü %29-59 arasında bulunmuştur. Marquette ve ark.'nın (7) çalışmasında pnömoni tanısında, akciğer dokusunun histolojik incelenmesi altın standart olarak kabul edilmekle birlikte, ETA, korumalı fırça numune tekniği (PSB), BAL yöntemleri ile alınan örneklerin kantitatif kültürü birbirleri ile kıyaslanmış ve yöntemler arasında benzer duyarlılık ve özgüllük saptanmıştır.

Mortalite açısından VİP'ye sebep olan bakterinin doğru tanımlanması, erken tanı konularak uygun tedaviye zamanında başlanması önemlidir. Brun-Buisson ve ark.'nın (8) çalışmasında mini-BAL'nin ve kantitatif kültürünün yapılması ve direkt Gram-boyamasının incelenmesi %80 hastada 2-24 saat içinde doğru tanı ve uygun tedavinin verilmesini sağlamıştır. Aynı çalışmada hastaların yaklaşık üçte ikisi antibiyotik almayan grup olarak belirlenmiş ve gereksiz antibiyotik kullanımının önüne geçilmiştir.

Neves ve ark. (9) yaptığı çalışmada kritik hastalarda mini-BAL ve ETA örnekleri ile pulmoner tüberküloz tanısının doğrulanması karşılaştırılmıştır. Mini-BAL, ETA ile karşılaştırıldığında pulmoner tüberküloz tanısı için benzer sonuçlar verdiği görülmüştür. Ayrıca, mini-BAL ile elde edilen solunum numunelerinde *M. tuberculosis*'in tespit edilebildiği ve pulmoner tüberküloz varsayımı olan kritik hastalarda ETA'ya kabul edilebilir bir alternatif olduğu gösterilmiştir. Ferreira-Coimbra ve ark. (10) VİP tanısında kullanılan tekniklerin de karşılaştırıldığı çalışmasında invaziv teknikler arasında mini-BAL ilk sırada, ardından BAL, teleskopik kateter ve transbronşiyal biyopsi yer almakta idi. Bu teknikler arasında mini-BAL en güvenli ve BAL daha riskli (transbronşiyal biyopsiden sonra, nadiren kullanılan) olarak saptanmıştır. Ayrıca mini-BAL uygulamasında daha az deneyime ihtiyaç olduğu belirtilmiştir. Bu durum, bazı yerlerde bronkoskopik BAL konusunda deneyimsiz ekibin olması veya deneyimli uygulayıcıların her zaman mevcut olmaması nedeniyle önemli olduğunu belirtmişlerdir.

Tablo 1. Hastaların demografik verileri

Hasta	Kadın	12
	Erkek	18
Yaş		54,23±21,37
Mekanik ventilator süresi (gün)		9,7±22,8
SAPS III skoru		36,06±8,46
APACHE-II skoru		21,36±4,90
CPIS skoru		5,90±1,91

SAPS III: Basitleştirilmiş Akut Fizyoloji Puanı-III, APACHE-II: Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II, CPIS: Klinik akciğer enfeksiyonu skoru

Tablo 2. Hastaların mini-BAL ve bronkoskopi üreme sonuçlarının tutarlılıklarının değerlendirilmesi

Mini-BAL üremeleri	Bronkoskopi üremeleri																														
Hasta no	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
1	+																													
2		+																												
3			+																											
4				+																										
5					+																									
6						+																								
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Mini-BAL: Mini-bronkoalveolar lavaj

Literatürdeki çalışmalarda, mini-BAL ve bronkoskopik fırça yöntemleriyle elde edilen materyal sonuçları arasında güçlü bir uyumun (%77-88) olduğu gözlenmiştir (11-13). Buna karşın, Khilnani ve ark. (12) ETA yönteminin, distal hava yolu örneği elde etmek için kullanılan yöntemler arasında, en başarısız yöntem olduğunu belirtmişlerdir. Bacakoğlu ve ark. (14) ETA ile mini-BAL arasındaki uyumu %67 olarak bildirmişler, Artuk ve ark. (15) ise ETA ile mini-BAL arasındaki uyumu %50 gibi düşük bir oranda tespit etmişlerdir. Bizim çalışmamızda da diğer çalışmalara benzer şekilde mini-BAL ile ETA arasındaki uyum %60 olarak saptanmıştır.

Nozokomiyal pnömoni riskini 2-3 kat artıran önemli risk faktörlerinden biri ileri yaştır. Bunun yanı sıra mekanik ventilatöre bağlı olunan her gün VİP gelişimi riskini %1-3 oranında artırmaktadır (16). Gedik ve ark.'nın (17) çalışmasında, VİP gelişen hastaların ortalama mekanik ventilasyona bağlı kalma süresi 20 gün, yaş ortalaması 56 yıl olarak saptanmıştır. Khilnani ve ark.'nın (12) yaptığı çalışmada ortalama mekanik ventilasyon süresi 34,88±32 gün, yaş ortalaması 55,6±16,17 yıl; Bacakoğlu ve ark.'nın (14) yaptığı diğer bir çalışmada ortalama mekanik ventilasyon süresi 7,4±6,3 gün yaş ortalaması 63,9±19 yıl olarak bildirilmiştir. Artuk ve ark.'nın (15) yaptığı çalışmada ise VİP hastalarının ortalama mekanik ventilasyon süresi 29,57±15,78 gün, yaş ortalaması 68,23±16,19 yıl olarak rapor edilmiştir. Ayrıca çok değişkenli lojistik regresyon analizi değerlendirilmesi sonucunda, mekanik ventilasyon uygulanan hastalarda mekanik ventilasyon uygulama süresi ($p<0,001$) ve hasta yaşı ($p<0,001$) VİP gelişimi açısından birer risk faktörü olarak saptanmış olup mekanik ventilasyon süresi ile yaş arasında anlamlı bir korelasyon bulunduğu rapor edilmiştir. Bu çalışmada ise hastaların yaş ortalaması 54,23±21,37 yaş olarak saptanmış olup ortalama mekanik ventilasyon süresi ise 9,7±22,8 gündür. Olguların ortalama değerleri genel olarak literatür ile uyumlu bulunmuştur**.**

VİP tanısında kullanılan CPIS skoru hesaplamasında değişkenlerin subjektif olması ve bunun sonucunda yanlış hesaplanması bu skorlamanın en büyük dezavantajıdır (18). CPIS'nin 6'nın üzerinde bulunması pnömoni olasılığını güçlendirmektedir. Yapılan bir çalışmada VİP tanısı koymada; CPIS ≥6 olarak hesaplanmasının duyarlılığı %93, özgüllüğü %100 olarak saptanmıştır. Ancak bazı araştırmacılar ise CPIS'nin, tedavinin yönlendirilmesi ve değerlendirilmesi aşamasında kullanılması gerektiğini belirtmektedirler. Khilnani ve ark. (12), VİP tanısı konan hastaların ortalama CPIS skorunu 6,76±1,67 puan; Bacakoğlu ve ark. (14) ise 7,2±2,1 puan olarak rapor etmişlerdir. Artuk ve ark. (15) ise VİP tanısı konan hastalarda CPIS skoru ortalamasını 6,8±1,15 puan olarak hesaplamışlardır. Bizim çalışmamızda ise CPIS skoru 5,90±1,91 puan olarak hesaplanmıştır.

Sonuç

YBÜ'de VİP şüphesi olan hastalarda nozokomiyal pnömoni tanısında kullanılan yöntemlerin karşılaştırılmasında mini-BAL'nin erken dönemde elde edilen güvenilir sonuçları ve bronkoskopiye göre tutarlılığının yüksek olması dikkat çekmektedir.

Etik

Etik Kurul Onayı: Çalışmaya, İstanbul Üniversitesi İstanbul Tıp Fakültesi Etik Kurulu'ndan 16.08.2013 tarihinde 14 sayılı toplantı ile 1136 numaralı etik kurul onayı alınmıştır (karar no: 14).

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Is There a Relationship Between Mortality Rates and Nutritional Factors in Critical Ill Patients with COVID-19?

COVİD-19'lu Kritik Hastalardaki Ölüm Oranları ile Beslenme Faktörleri Arasında Bir İlişki Var mıdır?

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ABSTRACT *Objective:* Our aim in this study was to examine whether critically ill patients with coronavirus disease-2019 (COVID-19) achieved the targeted calories (ATC) while being treated in the intensive care unit (ICU) and their relationship with the modified nitric score (mNUTRIC) and mortality.

Materials and Methods: The patients were categorized into two cohorts based on the attainment of the intended caloric intake during their stay in the ICU: the ATC group and the not achieved target calorie (NATC) group. A comparative analysis was conducted on the mNUTRIC scores, as well as the ICU and hospital mortality rates, between these two groups.

Results: The number of patients in the ATC group was 59 (63.4%) and the number of patients in the group that could NATC was 34 (36.6%). mNUTRIC scores on admission were 3 (2-4) in the ATC group and 5 (4-6) in the NATC group. In multivariate regression analysis, a mNUTRIC score of 5 and higher ($p<0.01$), hemodynamic instability ($p=0.02$) and male gender ($p=0.04$) were found to be significant as independent risk factors for NATC. ICU and hospital mortality was higher in the NATC group than in the ACT group ($p<0.01$, $p<0.03$ respectively).

Conclusion: Inability to reach the targeted calories and high mNUTRIC score might relate to mortality in critically ill COVID-19 patients treated in the ICU.

Keywords: Nutrition, targeted calory, intensive care, modified nutric score, mortality

ÖZ *Amaç:* Bu çalışmadaki amacımız, koronavirüs hastalığı-2019'lu (COVİD-19) kritik hastaların yoğun bakım ünitesinde (YBÜ) tedavi edilirken hedeflenen kaloriye (ATC) ulaşıp ulaşmadığını ve bunun modifiye nutrik skoru (mNUTRIC) ve mortalite ile ilişkisini incelemekti.

Gereç ve Yöntem: Hastalar YBÜ'de kaldıkları süre içerisinde hedeflenen kaloriye ulaşılıp ulaşılmadığına (ATC grubu) ve sağlanamamasına (NATC grubu) göre iki gruba ayrıldı. Hastaların mNUTRIC skorları, YBÜ ve hastane mortalite oranları her iki grup için karşılaştırıldı.

Bulgular: ATC grubundaki hasta sayısı 59 (%63,4), NATC gruptaki hasta sayısı ise 34 (%36,6) idi. Başvuru anında mNUTRIC puanları ATC grubunda 3 (2-4) ve NATC grubunda 5 (4-6) olarak bulundu. Çok değişkenli regresyon analizinde mNUTRIC puanı 5 ve üzeri ($p<0,01$), hemodinamik instabilite ($p=0,02$) ve erkek cinsiyet ($p=0,04$) NATC için bağımsız risk faktörleri olarak anlamlı bulundu. YBÜ ve hastane mortalitesi NATC grubunda ACT grubuna göre daha yüksekti (sırasıyla $p<0,01$, $p<0,03$).

Sonuç: YBÜ'de tedavi edilen kritik durumdaki COVİD-19 hastalarında hedeflenen kaloriye ulaşamama ve yüksek mNUTRIC puanı mortalite ile ilişkilendirilebilir.

Anahtar Kelimeler: Beslenme, hedeflenen kalori, yoğun bakım, modifiye nutrik skor, mortalite

Introduction

Respiratory failure represents a primary cause for admitting patients with coronavirus disease-2019 (COVID-19) to the intensive care unit (ICU) (1). Among COVID-19 patients receiving ICU care, the mortality rate for those treated with invasive mechanical ventilation ranges from 40% to 60% (2). The entry of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) into various cell types, including lymphocytes, monocytes, lung alveolar type 2 cells, esophageal epithelial cells, enterocytes, and colonocytes, occurs through the angiotensin-converting enzyme 2 receptor. This leads to cellular damage resulting from rapid viral replication, triggering cytokine release and inflammation (3). In severe cases, elevated levels of proinflammatory cytokines in the plasma induce a cytokine storm (4). The cytokine storm contributes to organ damage. However, it has been emphasized that the initiation of nutritional therapy should not be hindered as the primary focus in cytokine storm management (5).

Critically ill patients often experience energy intake and utilization dysfunction due to systemic inflammatory response and organ dysfunction. Additionally, COVID-19 patients requiring invasive mechanical ventilation tend to have prolonged ICU stays, averaging around 9 days (6). Consequently, these patients are highly susceptible to severe malnutrition and muscle mass loss (5). Furthermore, the involvement of SARS-CoV-2 in the gastrointestinal system (GIS) has a detrimental impact on nutrition delivery and, consequently, the nutritional status of COVID-19 patients. This factor may contribute to the overall clinical outcome (7). Limited information is available regarding the effects of nutritional therapy in ICU patients with COVID-19 (8). Therefore, our objective is to assess the nutritional risks of COVID-19 patients upon ICU admission, determine the achievement of appropriate nutritional goals during the ICU stay, and investigate the relationship between nutritional status and clinical outcomes.

Materials and Methods

This retrospective observational study was conducted in the ICU that reserved for COVID-19 patients, with the approval of the Non-Interventional Research Ethics Committee of Dokuz Eylül University (decision no: 2021/02-17, approval date: 18.01.2021).

Since our study was conducted as a retrospective file review and data analysis, patient consent was waived. Between May and September 2020, COVID-19 93 patients who were approve by the polymerase chain reaction test and admitted to the intensive care unit were included in the study. Those who were younger than 18 years of age, those with less than 24 hours of intensive care stay, and with insufficient medical knowledge and anamnesis were excluded from the study. Pregnant and lactating patients were also not included in the study. Demographic data, medical histories, laboratory parameters, ventilator support and mortality were retrospectively collected from the hospital records.

Within the initial 24 hours of ICU admission, the disease severity of each patient was determined utilizing the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) and Sequential Organ Failure Assessment (SOFA) scoring systems (9,10).

At the time of ICU admission, the nutritional risk of each patient was evaluated using the modified nitric score (mNUTRIC) score. This score, which excludes IL-6 values, incorporates the following five variables: age, APACHE-II score and SOFA score upon admission, the number of comorbidities present in the patient, and the duration of hospitalization before ICU admission (11).

It has been reported that a modified NUTRIC score of 5 and above indicates that the patient has a high nutritional risk (9).

Daily needed calories and achieved values of the patients' calories, types of nutritional support (oral, enteral or parenteral) were also recorded.

In this study, the patients were divided into two groups: group of achieved the target calories (ATC) and the group that did not achieved the target calories (NATC). In order to determine on which day the target calorie (TC) was achieved if it was achieved, the amount of calories that could be given to the patient on the 1^{st}, 2^{nd}, 3^{rd}, 4^{th}, 5^{th}, 7^{th}, 10^{th} and 14^{th} days were calculated from the hospital records.

The daily calorie intake of patients was planned as 14 kcal/kg/day for patients with a body mass index (BMI) above 30 kg/m^2 and 25 kcal/kg/day for patients with a BMI below 30 kg/m^2 which is as recommended by the American Society for Parenteral and Enteral Nutrition and European Society for Parenteral and Enteral Nutrition (ESPEN) (12,13). The day on which the planned calories were achieved was recorded as the day on which target calory as achieved.

As hemodynamic status is an important parameter for feeding, the date of hemodynamic stabilization and the start of nutritional support were recorded. According to ICU feeding protocol systolic blood pressure of 90 mmHg and a mean arterial pressure of 65 mmHg and above without vasopressor support or with dopamine <5 µg/kg/min or norepinephrine <0.5 µg/kg/min support was considered as hemodynamic stabilization (14). The day which the patients were hemodynamically stable and started feeding, determined and recorded. We started parenteral nutrition (TPN) therapy for patients who could not tolerate enteral nutrition (EN) therapy [stopping planned feeding, GI intolerance (vomiting, diarrhea, bleeding) or high inotropic support].

Statistical Analysis

All continuous variables were reported as mean ± standard deviation or as median (interquartile range), while categorical variables were presented as numbers and percentages (%). In our study, we collected two types of data: categorical and numerical. For numerical data, we performed t-tests and Mann-Whitney U tests, depending on the distribution of the data. For categorical data, we used the chi-square independence test to assess associations.

To identify the risk factors for the inability to achieve the TC intake, we conducted multivariate logistic regression analysis. A p-value of <0.05 was considered statistically significant. The statistical analysis was performed using IBM SPSS Statistics version 26.0.

Results

A total of 93 confirmed COVID-19 patients were included into the study. Of the patients, 65 (69.9%) were male and 28 (30.1%) were female. Among the patients included in the study, the mean age of the ATC group was 68 (61-76), while the mean age of the NATC group was 70 (59-70) (Table 1).

Of them 59 were in ATC group and 34 were in NATC group. The median age of the patients in the (ATC) group was 68 (61-74) years, and the median age of the patients in the (NATC) group was 70 (59-77) years (p=0.89). Among

Table 1. Clinical characteristics of patient population

	All patients (n=93)	ATC group (n=59)	NATC group (n=34)	p-value
Age (year)	68 (61-76)	68 (61-74)	70 (59-77)	0.89
Gender (male)	65 (69.9)	36 (61)	29 (85.3	0.01
APACHE-II score	18 (14-27)	18 (12-24)	22 (6-20)	0.03
SOFA score	8 (5.5-10.5)	6(4-8)	8 (6-10)	0.02
GCS score	14 (7.5-15)	14 (6-15)	14 (8.5-15)	0.66
BMI (kg/m^2)	27 (24-31)	27 (24-32)	28 (24-31)	0.94
Hypertension	59 (63.4%)	38 (64.4)	21 (61.8)	0.80
Diabetes mellitus	37 (39.8)	23 (39.0)	14 (41.2)	0.83
Coronary artery disease	31 (33.3)	20 (33.9)	11 (32.4)	0.88
Chronic obstructive pulmonary disease	18 (19.4)	14 (23.7)	4 (11.8)	0.16
Chronic renal failure	10 (10.8)	7 (11.9)	3 (8.8)	0.65
Congestive heart failure	14 (15.1)	10 (16.9)	4 (11.8)	0.50
Atrial fibrillation	14 (15.1)	7 (11.9)	7 (20.6)	0.26
Cirrhosis	5 (5.4)	2 (3.4)	3 (8.8)	0.26
Acute kidney failure	30 (32.3)	18 (30.5)	12 (35.3)	0.63
Cerebro-vascular event	8 (8.6)	5 (8.5)	3 (8.8)	0.95
Dementia	7 (7.5)	4 (6.8)	3 (8.8)	0.72
Parkinson's disease	2 (2.2)	1 (1.7)	1 (2.9)	0.69
Malignancy	10 (10.8)	7 (11.9)	3 (8.8)	0.65

All values are expressed as numbers (percentages) or median (interquartile range), APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma score, BMI: body mass index, ATC: achieved the targeted calories, NATC: not achieved target calorie. SOFA score and APACHE-II was calculated 24th hour intensive care unit admission

the patients, APACHE-II and SOFA scores were found to be significantly higher in the (NATC) group than (ATC) group [22 (6-20), p=0.03; 8 (6-20), p=0.02 respectively]. There was no significant difference between the BMI of (ATC) patients and (NATC) patients [28 (24-31); p=0.94] (Table 1).

There was no significant relationship between achieve TC and age [68 (61-74), p=0.89]. (Table 1).

The nutritional characteristics of all patients are presented in Table 2.

The majority of the patients (94.6%) received nutritional treatment with the EN method. TPN was started for only 5 critically ill COVID-19 patients. In the patient group in whom TPN was started, EN was tried to be continued at a trophic dose. All study patients received EN or TPN. The feeding tube route was used in all patients who underwent EN therapy.

The reasons that were observed for the interruption of feeding in the (NATC) group of the patients was as follows; stopping planned feeding (7, 20.6%) [due to surgical procedure (2, 5.9%); tracheostomy (5, 14.7%)], GIS intolerance (13, 38.2%) (vomiting, diarrhea, bleeding), high inotropic support (14, 41.2%). GIS intolerance and high inotropic support were found to be significantly higher in the (NATC) group [(13, 38.2%); (14, 41.2%) respectively p=0.03 and p<0.01] (Table 3).

The mNUTRIC scores on admission to the ICU were 3 (2-4) in the (ATC) group and 5 (4-6) in the (NATC) group (p<0.01). In addition, as stated in the ESPEN guideline, daily

Table 2. Nutiritional charactheristics of study groups

	ATC group (n=59)	NATC group (n=34)	p-value
Target calories*	1370 (300-1500)	1370 (300-1500)	
Mean values of calories on the 1st day (min-max)	1200 (800-1400)	760 (400-1050)	<0.01
Mean values of calories on the 2nd day (min-max)	1400 (1000-1500)	1000 (800-1225)	<0.01
Mean values of calories on the 3rd day (min-max)	1400 (1000-1500)	1200 (1000-1400)	<0.01
Mean values of calories on the 4th day (min-max)	1400 (1000-1500)	1200 (980-1440)	0.07
Mean values of calories on the 5th day (min-max)	1400 (1000-1500)	1200 (980-1440)	0.07
Mean values of calories g on the 7th day (min-max)	1400 (1000-1500)	1200 (1000-1440)	0.24
Mean values of calories on the 10th day (min-max)	1400 (1000-1455)	1200 (970-1400)	0.15
Mean values of calories on the 14th day (min-max)	1100 (1000-1360)	1300 (1000-1440)	0.32
Number of days to reach target calories	2 (2-3)	-	NA

*The target calorie amount calculated according to the ESPEN and ASPEN guidelines was found to be similar in both groups. ASPEN: American Society for Parenteral and Enteral Nutrition, ESPEN: European Society for Parenteral and Enteral Nutrition, ATC: achieved the targeted calories, NATC: not achieved target calorie, min-max: minimum-maximum

Table 3. mNUTRIC score and reasons for interruption of feeding

	ATC group (n=59)	NATC group (n=34)	p-value
mNUTRIC score	3 (2-4)	5 (4-6)	<0.01
Additional protein intake (Number of patients-percentage)	21 (35.6%)	1 (2.9%)	<0.01
Additional vitamin intake (Number of patients-percentage)	53 (89.6%)	26 (76.5%)	0.05
Nutrition shutdown: planned shutdown (Number of patients-percentage)	10 (16.9%)	7 (20.6%)	0.66
Suspension of feeding due to gastrointestinal intolerance (Number of patients-percentage)	11 (18.6%)	13 (38.2%)	0.03
Interruption of feeding due to hemodynamic instability (Number of patients-percentage)	9 (16.3%)	14 (41.2%)	<0.01

ATC: achieved the targeted calories, NATC: not achieved target calorie, mNUTRIC: modified nitric score

1.3 g/kg protein supplementation could be given to the ATC group, but not to the NATC group [(1, 2.9%); p<0.01)] (Table 3) (12).

When the laboratory results of the patients in the (NATC) group were analyzed, it was found that the serum albumin (ALB) levels on admission in the ICU the were statistically significantly lower [2.82 (2.35-3.21) g/dL, p=0.03] (Table 4).

Considering both the ICU mortality rates (88.2%) and hospital mortality rates (88.2%) of COVID-19 patients followed up as critically ill in the ICU, it was found to be significantly higher in the (NATC) group (p<0.01, p<0.03 respectively) (Table 5).

When the multivariate regression analysis of risk factors related to not achieve targeted calorie was performed,

Table 4. Laboratory findings on admission in the ICU

	All patients (n=59)	ATC group (n=34)	NATC group	p-value
Leukocyte 10^3/UI	11700 (9200-16000)	12800 (9700-16300)	9700 (8450-15050)	0.06
Lymphocyte 10^3/UI	500 (300-900)	500 (300-800)	550 (300-100)	0.60
Hemoglobin g/dL	12.4 (10.8-13.4)	12.6 (10.8-13.5)	12.1 (10.4-13.3)	0.64
C-reactive protein mg/L	146 (73-203)	141 (73-194)	161 (69-229)	0.40
Procalcitonin ng/mL	0.46 (0.11-2.19)	0.47 (011-1.53)	0.43 (0.14-3.54)	0.54
Ferritin ng/mL	476 (275-940)	461 (272-954)	620 (277-920)	0.88
Lactate dehydrogenase U/L	557 (386-728)	554 (403-684)	563 (320-761)	1.00
Alanine transaminase U/L	33 (22-64)	32 (23-65)	38 (21-60)	0.96
Aspartate aminotransferase U/L	48 (33-74)	47 (33-73)	50 (34-82)	0.51
Total bilirubin mg/dL	0.89 (0.63-1.10)	0.89 (0.62-1.11)	1.00 (0.65-1.22)	0.45
D-dimer ug/mL	1.73 (0.94-4.30)	1.50 (0.95-5.17)	1.90 (0.93-3.64)	0.67
Creatinine mg/dL	1.00 (0.76-1.80)	0.99 (0.76-1.76)	1.00 (0.79-1.85)	0.68
Albumin g/dL	3.07 (2.70-3.29)	3.07 (2.88-3.24)	2.82 (2.35-3.21)	0.03
Blood urea nitrogen mg/dL	33 (22-57)	32 (23-50)	35 (20-67)	0.65

ATC: Achieved the targeted calories, NATC: not achieved target calorie, ICU: intensive care unit

Table 5. Treatments and outcomes of study population

	All patients n=93	ATC (n=54)	NATC (n=34)	p-value
Renal replacement therapy	26 (28%)	18 (30.5)	8 (23.5)	0.47
Tocilizumab therapy	7 (7.5%)	6 (10.2)	1 (2.9)	0.20
Intravenous corticosteroids therapy	76 (81.7)	24 (70.6)	52 (88.1)	0.127
Pulse corticosteroid therapy*	34 (34.6)	25 (42.4)	9 (26.5)	0.04
Vasopressor need**	65 (69.9)	26 (44.1)	23 (66.7)	0.03
Those who received sedation	67 (72)	43 (72.9)	24 (70.6)	0.81
Oxygen mask	25 (26.9)	16 (27.1)	9 (26.5)	1.00
High-flow nasal cannula application	26 (28%)	17 (28.8)	9 (26.5)	1.00
Non-invasive mechanical ventilator therapy	14 (15.1%)	10 (16.9)	4 (11.8)	0.56
Invasive mechanical ventilation therapy	27 (29%)	15 (25.4)	12 (35.3)	0.34
Mechanical ventilation duration (days)	5 (2-11)	4 (1-10)	2 (1-5)	0.35
Hospitalization length of stay (days)	16 (9-22)	17 (10-23)	12 (6-21)	0.04
ICU length of stay (days)	9 (4-14)	9 (5-14)	8 (3-14)	0.24
Hospital mortality rate	70 (75.3)	40 (67.8)	30 (88.2)	0.03
ICU mortality rate	68 (73.1)	38 (64.4)	30 (88.2)	0.01

*Pulse corticosteroid >250 mg/day, **norepinephrine >30 µg/kg/min. ATC: achieved the targeted calories, NATC: not achieved target calorie, ICU: intensive care unit

mNUTRIC score of 5 and higher [odds ratio: 0.05 (0.01-0.17), 95% confidence interval; p<0.01), hemodynamic instability (p=0.02) and gender (p=0.04) were found to be significant as independent risk factors (Table 6).

Both ICU mortality rates (88.2%) and hospital mortality rates (88.2%) were higher in the NATC group (p=0.01).

Discussion

Among the 93 critically ill patients with COVID-19 treated in this study, it was found that in 59 (%) patients TC was achieved. mNUTRIC, APACHE-II and SOFA scores in the first 24 hours were found to be significantly higher in the (NATC) group. Also in (NATC) group there was male predominancy. In the group whose TC could not be achieved, both ICU and hospital mortality were high. In the group whose targeted calorie could not be achieved, mNUTRIC score of 5 and above, hemodynamic instability and male gender were found to be significant as independent risk factors. As seen in the ICU, patients with severe forms of COVID-19 are generally aged, they have serious comorbidities, and therefore they are at risk of malnutrition and sarcopenia (15). COVID-19 patients are faced with severe respiratory tract infections and increased energy expenditure due to increased respiratory work Infection, hypermetabolism, and physical inactivity cause rapid muscle loss (16).

It was found that the general condition of the patients was poor, the critical illness scores were high, and the mortality rates were high in the group whose targeted calories could not be reached. The mNUTRIC score was also found to be high in the group that did not reach sufficient calories. Using the APACHE-II score and SOFA scores when calculating the mNUTRIC score, the mNUTRIC score was high in patients with the poor general condition due to the nature of the job. It was thought that effective nutritional therapy could not be applied in this patient group due to the reasons listed.

According to a study conducted in China, 14% of COVID-19 cases were classified as severe and 5% as critically ill (17,18). In a meta-analysis investigating the mortality rate of COVID-19 patients in the ICU in China, the mortality rate was found to be 41.6% (19). In our study, the ICU mortality of COVID-19 patients was 68%. This can be explained by the fact that patients admitted to the ICU are very severe, which is consistent with their high APACHE-II, SOFA and mNUTRIC scores within the first 24 hours of admission.

Apart from its impact on the respiratory system and the development of acute respiratory distress syndrome (ARDS), the coronavirus can also lead to dysfunction in other organs, such as sepsis and myocardial damage (20). Patients admitted to the ICU may be at a higher nutritional risk due to factors like a high viral load or an exaggerated immune response (8). Additionally, some patients experience gastrointestinal symptoms, further exacerbating their nutritional risk (20). A meta-analysis of 60 studies involving 4,243 patients, although not limited to critically ill individuals, revealed the following percentages: loss of appetite in 26.8% of patients, nausea and vomiting in 10.2%, diarrhea in 12.5%, and abdominal pain or discomfort in 9.2% (21). The development of these symptoms suggests that the severity of the disease increases (21). It has been reported that nutritional support should be started early in patients whose severity increased because intubated patients could not use the oral route during mechanical ventilation (22). EN should be preferred to TPN because it is known to be associated with a lower incidence of infectious complications, fewer days of hospital stay, and reduced mortality rates as stated in previous meta-analyses (21). Although nasogastric tube application caused concern due to the risk of transmission to healthcare workers in the early stages of the pandemic, the priority of EN was not compromised in our clinic and EN was applied except for only 5 patients who could not tolerate EN. It has been reported that TPN support can be given

Table 6. Multivariate regression analysis of independent risk factors for not achieved target calories group (95% CI: 95%)

	OR (95% CI)	p-value
mNUTRIC score ≥5	0.05 (0.01-0.17)	<0.01
Hemodynamic instability	0.23 (0.06-0.82)	0.02
Gender	4.48 (1.08-18.46)	0.04
BMI	0.95 (0.85-1.06)	0.39
APACHE-II score	0.95 (0.88-1.01)	0.14

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CI: confidence interval, OR: odds ratio, BMI: body mass index, mNUTRIC: modified nitric score

to patients who cannot receive adequate calorie support through the enteral route (22). However, it is known that it is important to provide trophic doses of EN for the nutrition of the intestinal mucosa, even in cases where the required calorie needs of the patients cannot be met by the enteral route (10). Thus, bacterial translocation can be prevented by preventing atrophy of the intestinal mucosa and ensuring mucosal integrity (22,23). In our study group, trophic dose EN was tried in a limited number of patients with TPN, but it was not successful.

Additionally, vasopressor therapy may increase the risk of gastrointestinal intolerance in cases of hemodynamic instability characterized by hypovolemia, hypotension, hyperlactatemia and tissue hypoperfusion (24). In this study, the presence of GIS intolerance and high-dose inotropic use was found to be statistically significant in the patient group who could not reach the TC. In this patient group, the same approach was generally followed and additional risk factors were evaluated.

Therefore, a more comprehensive analysis of the clinical characteristics and nutritional status of critically ill COVID-19 patients admitted to the ICU is warranted. Researchers have emphasized the necessity of employing nutritional risk assessment scales specifically designed for adult patients with COVID-19 (25).

There is currently no universally accepted standard for determining nutritional risk or identifying malnutrition (24). Various tools and scoring systems have been developed to address this issue, including the Mini Nutritional Assessment-Short Form, Geriatric Nutrition Risk index, Nutritional Risk Screening 2002, Malnutrition Universal, as well as screening tools such as the Screening Tool, Nutritional Risk index, Short Nutrition Assessment Questionnaire, and Nutritional Risk in Critically Ill Patients. These tools and systems are practical and cost-effective (25). The utilization of the NUTRIC scoring system in ICU settings was initially proposed by Canadian researchers (26,27). Although the specific nutritional screening tool for critically ill patients with COVID-19 remains to be determined, the mNUTRIC score is a parameter that can be routinely employed in ICUs, including those dedicated to COVID-19 patients (11).

The mNUTRIC score is user-friendly, as the variables in this scoring system are objectively obtained from the routine data in the medical records of the patients and can be easily used in patients who cannot respond verbally (11). In addition, we thought that the mNUTRIC scoring system is more useful for determining the nutritional risk of patients, since IL-6 levels are not routinely checked in our hospital.

In critically ill COVID-19 patients, Li et al. (17) reported a high prevalence of nutritional risk in 61% of patients in a retrospective study with data from three ICUs in Wuhan, China. In another study conducted in Latin America, it was found that 66% of critically ill COVID-19 patients had a high nutritional risk according to mNUTRIC-score calculations during ICU admission (28). In our study, the group of patients whose mNUTRIC score was higher than 5 points when they were admitted to the ICU was 28%. This situation also indicates that patients with COVID-19 were at risk of malnutrition due to infection-related loss of apetite, shortness of breath, dysosmia, dysgeusia, stress, advanced age with fragility a various comorbidities, long hospital stay, isolation, and organizational problems limiting participation in meals in the period prior to their admission to the ICU (23).

Both ICU and hospital mortality rates were found higher in the NATC group. This can be explained by reasons such as increased susceptibility to infection, secondary infections, impaired immune response, higher incidence of ARDS, prolonged mechanical ventilation, acute myocardial damage, and shock (19). In addition, it is not surprising that the APACHE-II and SOFA scores, which indicate the severity of critical illness, are taken as a basis when calculating the mNUTRIC score, and the mortality rates are high in those with high nutritional risk (11).

In NATC group, the decrease in serum ALB level, which is one of the laboratory values obtained while being admitted to the ICU, was found to be statistically significant. ALB levels are the classic laboratory index in traditional nutritional assessment (29). Although not used as index of evaluation of nutritional status alone, it can provide insight into nutritional status or disease severity in clinical practice (30). Again, Wu et al. (30), found that patients who developed ARDS had lower levels of ALB, prealbumin, and lipoprotein cholesterol.

We could not use any anthropometric measurements for nutritional assessment in this study because these data were not available in our medical records. Secondly, 93 patients who met the inclusion criteria were included and studies with larger sample sizes may be useful in this regard. Finally, randomized and controlled studies are needed because of the limitations inherent in retrospective observational studies.

Conclusion

Providing appropriate nutritional support treatment for critically ill COVID-19 patients is crucial for meeting their energy requirements, mitigating the detrimental effects of metabolic disturbances on the disease course, reducing oxidative damage to cells, and regulating immune responses. Given the prolonged treatment duration for critical COVID-19 cases, nutritional support plays a vital role and necessitates increased attention.

Since there is currently no universally accepted standard for determining nutritional risk in critically ill COVID-19 patients, further advancements and research in developing disease-specific nutritional assessment tools are warranted. Therefore, the mNUTRIC score appears to be a suitable tool for assessing nutritional risk and predicting prognosis in critically ill COVID-19 patients.

Ethics

Ethics Committee Approval: This retrospective observational study was conducted in the ICU that reserved for COVID-19 patients, with the approval of the Non-Interventional Research Ethics Committee of Dokuz Eylül University (decision no: 2021/02-17, approval date: 18.01.2021).

Informed Consent: Since our study was conducted as a retrospective file review and data analysis, patient consent was waived.

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Authorship Contributions

Surgical and Medical Practices: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Concept: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Design: Ö.Ö., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Data Collection and Process: Ö.Ö., B.E., M.Ç.G., O.Ö.E.K., E.Y., A.N.G., Analysis or Interpretation: Ö.Ö., M.K., E.Y., A.N.G., Literature Search: Ö.Ö., B.E., E.Y., A.N.G., Writing: Ö.Ö., M.K., O.Ö.E.K., E.Y., A.N.G.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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The Association of Chest CT-based Measurements with Myocardial Injury in Critically Ill Patients with COVID-19

COVİD-19'lu Kritik Hastalarda Toraks BT Tabanlı Ölçümlerin Miyokard Hasarı ile İlişkisi

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ABSTRACT *Objective:* Myocardial injury incidence is high in critically ill patients with coronavirus disease-2019 (COVID-19) and mortality increases in COVID-19 patients with myocardial injury. Our objective was to determine the association between chest computed tomography (CT)-based measurements and myocardial injury in critically ill patients with COVID-19.
Materials and Methods: We conducted a single-center cohort study of patients admitted to the intensive care unit (ICU) with a diagnosis of COVID-19 who underwent chest CT. Myocardial injury was defined as high-sensitivity troponin I blood levels above the 99th percentile upper reference limit, independent of new abnormalities in electrocardiography and echocardiography. Demographic, clinical, laboratory results, and chest CT findings were collected at ICU admission.
Results: A total of 213 patients were included. Of the 213 patients, 69 (32.4%) were female, and 144 (67.6%) were male. Myocardial injury incidence was 61.0% (n=130). Acute Physiology and Chronic Health Evaluation-II score [odds ratio (OR): 1.07, 95% confidence interval (CI): 1.02-1.12, p=0.005], having a chest CT severity score ≥18 (OR: 2.85, 95% CI: 1.29-6.32, p=0.010), having any coronary artery calcification (CAC) (OR: 2.45, 95% CI: 1.09-5.52, p=0.030), and age (OR: 1.04, 95% CI: 1.01-1.08, p=0.041), as factors independently associated with an increased risk of myocardial injury.
Conclusion: The incidence of myocardial injury is high in critically ill COVID-19 patients. Chest CT severity score ≥18 and presence of CAC are practical and valuable tools readily available from existing chest CT to predict myocardial injury in critically ill patients with COVID-19.
Keywords: Chest CT severity score, coronary artery calcification, critical care, intensive care unit, myocardial injury, SARS-CoV-2

ÖZ *Amaç:* Koronavirüs hastalığı-2019 (COVİD-19) olan kritik hastalarda miyokardiyal yaralanma insidansı yüksektir ve miyokard yaralanması olan COVİD-19 hastalarında mortalite artar. Amacımız, COVİD-19'lu kritik hastalarda toraks bilgisayarlı tomografi (BT) tabanlı ölçümler ile miyokard hasarı arasındaki ilişkiyi belirlemekti.
Gereç ve Yöntem: Tek merkezli kohort çalışmamız toraks BT çekilen ve COVİD-19 tanısı ile yoğun bakım ünitesine kabul edilen hastalar üzerinde gerçekleştirildi. Miyokard hasarı, elektrokardiyografi ve ekokardiyografideki yeni anormalliklerden bağımsız olarak, high-sensitivity troponin I kan seviyesinin 99. persentil üst referans sınırının üzerinde olması olarak tanımlandı. Hastaların demografik, klinik, laboratuvar sonuçları ve toraks BT bulguları kaydedildi.
Bulgular: Toplam 213 hasta dahil edildi. İki yüz on üç hastanın 69'u (%32,4) kadın, 144'ü (%67,6) erkekti. Miyokardiyal yaralanma insidansı %61,0 (n=130) idi. Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II skoru [olasılık oranı (OO): 1,07, %95 güven aralığı (GA): 1,02-1,12, p=0,005], toraks BT şiddet skoru ≥18 (OO: 2,85, %95 GA: 1,29-6,32, p=0,010), herhangi bir koroner arter kalsifikasyonu varlığı (OO: 2,45, %95 GA: 1,09-5,52, p=0,030) ve yaş (OO: 1,04, %95 GA: 1,01-1,08, p=0,041), miyokardiyal yaralanma riskini bağımsız olarak artıran faktörlerdi.
Sonuç: Kritik hastalığı olan COVİD-19 hastalarında miyokard yaralanması insidansı yüksektir. Toraks BT şiddet puanı ≥18 ve koroner arter kalsifikasyonu varlığı, COVİD-19'lu kritik hastalarda miyokard hasarını tahmin etmek için halihazırda çekilmiş olan toraks BT üzerinden kolayca elde edilebilen pratik ve değerli parametrelerdir.
Anahtar Kelimeler: Toraks BT şiddet skoru, koroner arter kalsifikasyonu, yoğun bakım, yoğun bakım ünitesi, miyokard yaralanması, SARS-CoV-2

Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), can cause various cardiovascular disorders such as myocardial injury (1,2).

The etiology of COVID-19 associated myocardial injury, which is mostly defined by the elevation of troponin I level in the absence of acute coronary syndrome, has not yet been fully clarified. The trigger of acute coronary events, a direct viral effect, inflammatory damage of the heart, and development of exacerbation of heart failure are several putative mechanisms (3,4).

The incidence of COVID-19 associated acute myocardial injury ranges from 16.1% to 23.8% in hospitalized patients (5) and up to 53.2% in critically ill patients (6,7). Mortality increases in patients with myocardial injury with a diagnosis of COVID-19, independent of the presence of cardiovascular disease (8,9).

Non-contrast chest computed tomography (CT) provides significant benefits in diagnosing, managing, and monitoring the progression of the COVID-19 disease (10). Chest CT enables measurements of CT severity score, which is associated with inflammation, oxygen requirement, length of hospital stay, and mortality in COVID-19 patients (11-13). Chest CT can provide additional potential clinical significant parameters including ascending aortic (AA) diameter, cardiothoracic ratio (CTR), pulmonary artery (PA) diameter, and coronary artery calcification (CAC) (14-17). A recent study of hospitalized patients, including both stable and intensive care unit (ICU) patients, demonstrated that enlarged PA diameter was independently associated with myocardial injury (18). However, since many potential factors can cause myocardial injury, the association between myocardial injury and chest CT-based measurements should be analyzed in detail with other proven risk factors such as underlying cardiovascular disease (6-9), COVID-19-specific high inflammatory burden (6), and critical illness disease severity (6,7).

In this study, we aimed to determine the association between chest CT-based measurements and myocardial injury in critically ill patients with COVID-19.

Materials and Methods

Study Population

This retrospective cohort study was conducted in the adult ICU of our center after the approval of the Dokuz Eylül University Non-Invasive Research Ethics Committee (decision no: 2021/05-08, date: 15.02.2021) and the Turkish Ministry of Health. All adult patients (age ≥18 years) who were admitted to the ICU with the diagnosis of COVID-19 disease between March 2020 and January 2021 and had a chest CT image were included in the study. A reverse transcriptase-polymerase chain reaction test was used in respiratory samples to confirm SARS-CoV-2.

Factors affecting high-sensitivity (HS)-troponin levels, such as a history of the acute coronary syndrome, cardiopulmonary resuscitation, and pulmonary thromboembolism after the diagnosis of COVID-19, were determined as the exclusion criteria of the study. Patients with a history of coronary artery stenting were excluded for impaired quantitative CAC measurement.

Definitions and Measurements

Myocardial injury was defined as serum HS-troponin-I levels above the 99th percentile upper reference limit without any new and specific abnormality in echocardiography and electrocardiography (2). Patients were categorized into two groups according to the presence or absence of myocardial injury. In this study, only the patients' initial CT examinations at admission were evaluated. The highest value of serum HS-troponin-I levels was recorded in the first 24 hours of admission to the ICU.

Chest CT Technique and Image Interpretation

Non-contrast chest CT was performed in clinically suspected patients in line with the recommendations of our national COVID-19 guidelines. Images were obtained from A 64-channel multidetector CT scanner (Brilliance, Philips Medical Systems) reserved for only COVID-19 suspected patients. CT examinations were performed without an intravenous contrast medium. Chest CT imaging protocol was as follows: 120 kVp, 80 mA, slice thickness 1.5 mm, and high-spatial-frequency reconstruction algorithm (bone algorithm). 2 mm reconstruction interval and 1.5 mm slice thickness were used for coronal and sagittal image reconstruction.

Chest CT examinations were independently interpreted by radiologists with 15 and 4 years of experience and the final decision was reached by consensus. Radiologists were blinded to clinical characteristics and laboratory data of the patients.

All scans were reviewed for the assessment of pneumonia associated with COVID-19. A scoring system

that demonstrates a typical and indeterminate appearance for COVID-19 was used to estimate the pulmonary involvement of CT scans (11-13). Each of the five lung lobes was visually scored on a scale of 0 to 5. No involvement was scored as 0 points. Involvements were scored, 1 point for less than 5%; 2 points for 5-25%; 3 points for 26-49%; 4 points for 50-75%; and 5 points for more than 75%. The total CT score was obtained by summing the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement). Patients were categorized into mild (7 or less), moderate (8-17), and severe (18 or more) groups according to the total score. Atypical CT scans were not scored because the radiological findings were not compatible with COVID-19. CTR measurements (dividing the largest transverse cardiac diameter from outer-to-outer myocardium by the largest transverse thoracic diameter from inner to the inner chest wall, usually at the level of the diaphragmatic apex) were obtained from axial CT images. PA/AA ratio was calculated from the axial CT slice by dividing the diameter of PA measured at the level of the PA bifurcation by AA diameter measured at the level of the right PA. The average transverse/anteroposterior inferior vena cava (IVC) diameter ratio was measured by dividing the maximum transverse diameters of IVC by maximum anteroposterior diameters at the level of the right diaphragmatic crus (Figure 1, 2) (19). In this study, we also measured the maximum transverse diameter of the arcus aorta from axial CT images and the maximum transverse diameter of the trachea at the same slice. Abnormal twists and turns (tortuosity) of the aorta were also evaluated at coronal and sagittal CT images and were recorded. The presence of CAC was determined using a simple patient-based score (17) and defined as any area

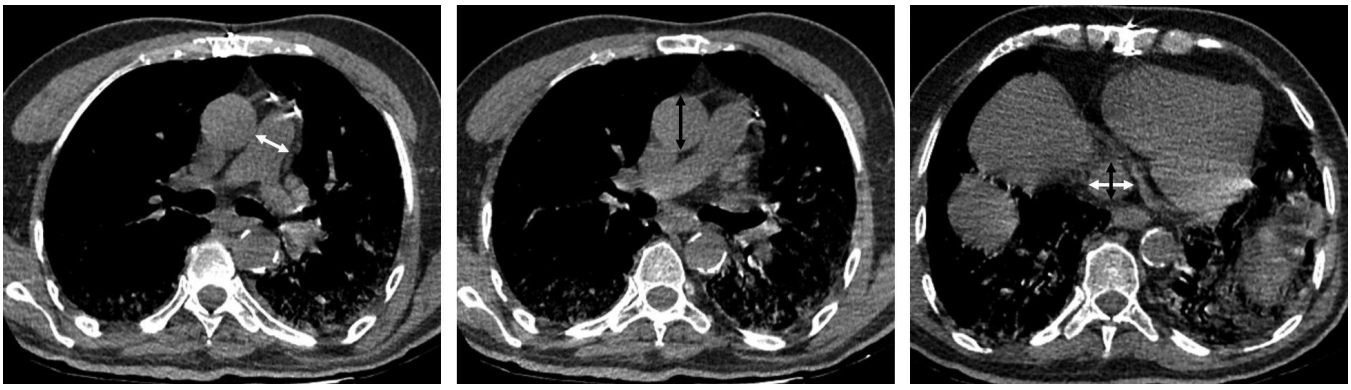

Figure 1. PA to A ratio was calculated from the axial CT slice by dividing the diameter of PA measured at the level of the PA bifurcation (white arrow) (A) by ascending aortic diameter measured at the level of right pulmonary artery (black arrow) (B). The average diameters of IVC were measured at the level of the right diaphragmatic crus by dividing the maximum transverse diameters of IVC (white arrow) by maximum anteroposterior diameters (black arrow) (C)
PA: Pulmonary artery, CT: computed tomography, IVC: inferior vena cava

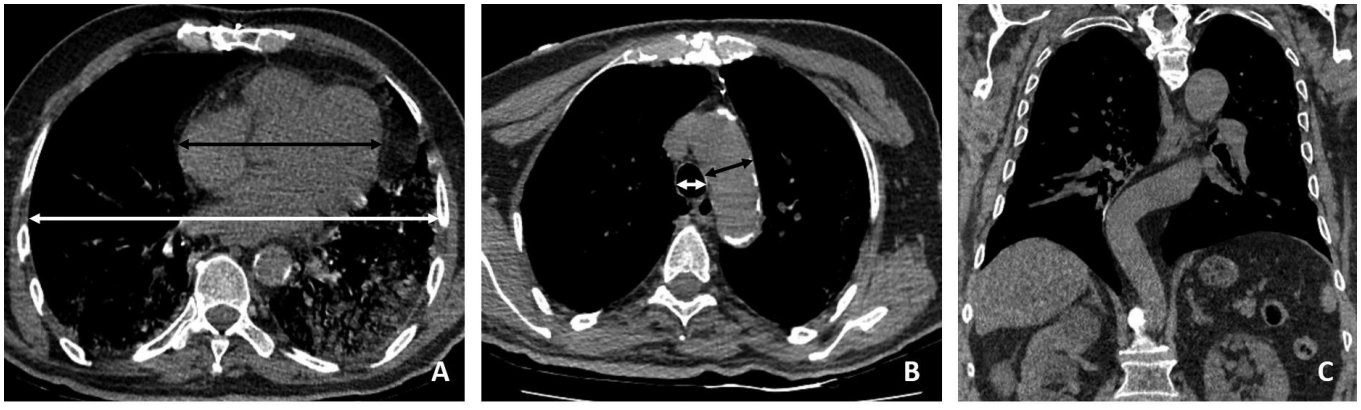

Figure 2. Cardiothoracic ratio was calculated from axial CT images by dividing the greatest transverse cardiac diameter from outer to outer myocardium (black arrow) by the greatest transverse thoracic diameter from inner to inner chest wall (white arrow), usually at the level of the diaphragmatic apex (A). Measurement of maximum transverse diameter of arcus aorta from axial CT images and the maximum transverse diameter of trachea at the same slice (B). Abnormal twists and turns (tortuosity) of the aorta wasvels evaluated at coronal and sagittal CT images (C)
CT: Computed tomography

≥1 mm^2 in the coronary artery tract with a density >130 Hounsfield units (20). All measurements were performed using mediastinal windows.

Variables

The demographic data, medical history, anthropometric measurements, Acute Physiology and Chronic Health Evaluation (APACHE)-II, Sequential Organ Failure Assessment (SOFA) scores, and Charlson Comorbidity index (CCI) were recorded. Blood pressure records were obtained from the first measurement of ICU admission. Major events during ICU stay [secondary bacterial infections, septic shock, acute kidney injury (AKI), renal replacement therapy, need for invasive mechanical ventilation (IMV)] were recorded. Mortality, length of stay in the ICU and hospital stay were recorded.

Outcomes

Our primary outcome was to assess the association of chest CT-based measurements with myocardial injury in ICU patients with COVID-19. The secondary outcome was to identify other clinical and biochemical risk factors for myocardial injury.

Statistical Analysis

All continuous variables were expressed as a median and interquartile range, and categorical variables were expressed as numbers and percentages. Continuous variables between groups were compared with the Mann-Whitney U test. Categorical variables were compared with chi-square or Fisher's Exact test. A multivariate logistic regression analysis model was performed to evaluate the independent risk factors for myocardial injury. To construct the model, a purposeful selection method was used to select a subset of the covariates considered clinically important, adjusting for confounding factors and statistical significance. For each independent risk factor, an adjusted odds ratio (OR) and a 95% confidence interval (CI) were reported. A two-tailed p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences Version 24, IBM Corp., Armonk, N.Y., USA).

Results

General Characteristics

A total of 213 eligible ICU patients, 69 (32.4%) female and 144 (67.6%) male, with a diagnosis of COVID-19 infection were included in the study. Of them, 130 had (61.0%) myocardial injury.

Patients with myocardial injury were significantly older [75.5 (67.8-83.0) vs. 66.0 (56.0-76.0) years; p<0.001; Table 1] and had a higher prevalence of comorbidities including hypertension (84.6% vs. 69.9%; p=0.015) and congestive heart failure (18.5% vs. 7.2%; p=0.026) than patients without myocardial injury. The median CCI score was higher in patients with myocardial injury than the patients without myocardial injury as well [6.0 (4.0-8.0) vs. 4.0 (2.0-5.0); p<0.001]. In patients with myocardial injury median APACHE-II score [24.0 (16.0-30.0) vs. 16.0 (11.0-23.0); p<0.001], and median SOFA score at admission to ICU [6.0 (5.0-8.0) vs. 4.0 (3.0-6.0); p<0.001] were higher than in patients without myocardial injury.

Laboratory Findings

In patients with myocardial injury, median D-dimer levels [1.80 (1.20-4.70) vs. 1.10 (0.60-2.30) µg/mL; p<0.001], and median B-type natriuretic peptide levels [165.0 (46.0-519.8) vs. 53.6 (27.0-118.0) pg/mL; p<0.001] were higher than in patients without myocardial injury. The median levels of blood urea nitrogen, creatinine, aspartate transaminase, C-reactive protein, and procalcitonin were higher in patients with myocardial injury than in patients without myocardial injury.

Major Events During ICU Stay

The need for the IMV was higher in patients with myocardial injury than patients without myocardial injury (90.0% vs. 61.4%; p<0.001). In patients with myocardial injury, vasopressor use (76.2% vs. 57.8%; p=0.006), AKI (73.8% vs. 50.6%; p=0.001), and secondary bacterial infections (63.1% vs. 48.2%; p=0.034) were more frequent than patients without myocardial injury. Both ICU mortality (80.8%, vs. 54.2%; p<0.001) and hospital mortality (83.8%, vs. 54.2%; p<0.001) were higher in patients with myocardial injury than in patients without myocardial injury.

CT Findings

In patients with myocardial injury median chest CT severity score was higher when compared with patients without myocardial injury [16.0 (12.0-20.0) vs. 13.5 (10.0-18.3); p=0.021; Table 2]. Patients with a chest CT severity score ≥18 were more common in the myocardial injury group than the no myocardial injury group (43.9% vs. 26.9%; p=0.021). CAC was detected in 153 (71.8%) patients. Patients with CAC were more common in the myocardial

injury group than the no myocardial injury group (81.5% vs. 56.6%; p<0.001). In patients with myocardial injury median CTR was higher when compared with patients without myocardial injury [0.54 (0.50-0.59) vs. 0.51 (0.47-0.54); p<0.001].

Risk Factors for Myocardial Injury

Multivariable analysis (Table 3) showed APACHE-II score (OR: 1.07, 95% CI: 1.02-1.12, p=0.005), having a chest CT severity score ≥18 (OR: 2.85, 95% CI: 1.29-6.32, p=0.010), having any CAC (OR: 2.45, 95% CI: 1.09-5.52, p=0.030), and age (OR: 1.04, 95% CI: 1.01-1.08, p=0.041), as factors independently associated with an increased risk of myocardial injury.

Discussion

This retrospective cohort study has some important results. First, myocardial injury incidence in critically ill COVID-19 patients is 61.0%. Second, APACHE-II score, chest CT severity score ≥18, presence of any CAC, and age are independently associated with myocardial injury in critically ill COVID-19 patients. Third, hospital mortality is higher in patients with myocardial injury than in patients without myocardial injury.

The incidence of acute myocardial injury is between 16.1-23.8% in hospitalized patients with COVID-19 (5), and up to 53.2% in critically ill patients with COVID-19 (7). In this study, the incidence of myocardial injury was relatively high, with a rate of 61.0%. As emphasized in previous studies, advanced age and underlying cardiovascular comorbidities are important risk factors for myocardial injury (6-9). Similarly, in our study, hypertension and congestive heart failure comorbidities were more common in patients with myocardial injury than the patients without myocardial injury. Additionally, advanced age was an independent risk factor for the risk of myocardial injury in our analysis. The high incidence of myocardial injury in our study may be due to the relatively advanced age of our population and the presence of multiple complicated comorbid diseases.

Previous studies evaluated the correlation between myocardial injury and disease severity scores, and they demonstrated that patients with myocardial injury had higher APACHE-II scores than patients without myocardial injury (6,7). Similarly, in our study, high APACHE-II scores were independently associated with myocardial injury. APACHE-II score is a predictive scoring system that measures disease severity to predict mortality in the ICU (21). However, since the APACHE-II score is not a disease-specific score, it may not predict the severity of the COVID-19 disease. Some studies used a chest CT score to estimate COVID-19 disease severity and outcomes (11-13). CT severity score was positively correlated with inflammatory biomarkers (11-13), oxygen requirement (11), disease severity (12,13), disease progression (13), and length of hospital stays (11) in patients with COVID-19. Likewise, short-term mortality was highly predicted with a CT score ≥18 (12). In this study, we evaluated the association between chest CT score and myocardial injury. We demonstrated that a CT score ≥18 is also independently associated with myocardial injury.

CAC is an important biomarker that represents atherosclerosis burden and the absence of calcification most likely indicates a low atherosclerotic plaque load (22). CAC is a strong predictor of cardiovascular events (especially coronary heart disease) and all-cause mortality in the general population (23,24). CAC has been studied in patients with COVID-19 as well. In a study of 209 hospitalized COVID-19 patients without pre-existing cardiovascular disease, the presence of any CAC on chest CT was significantly associated with the mechanical ventilation requirement (non-invasive or invasive) or death within 30 days of hospitalization (20). In another study of 180 COVID-19 patients who underwent non-contrast chest CT, patients with any CAC were more likely to need intubation and die than those who did not have CAC (25). In the present study, we demonstrated that the presence of any CAC is independently associated with myocardial injury.

Mortality in patients with myocardial injury is high, ranging between 37.4-59.6% in hospitalized patients (2,9,26), and 85.3% in ICU patients (6,7). Mortality increases in COVID-19 patients with myocardial injury regardless of the presence of cardiovascular disease (8,9). The myocardial injury was an independent risk factor for high mortality in a small study including 64 critically ill patients with COVID-19 (6). In our study, the hospital mortality rate was higher in patients with myocardial injury than the patients without myocardial injury.

This study has several limitations. First, cardiac complications related to myocardial injury were not evaluated. Second, the effect of cardiac movements and respiratory changes on the chest CT measurements was not evaluated.

Table 1. Demographic and clinical characteristics in patients with and without myocardial injury (univariate analysis)				
Characteristics	**All cases**	**Myocardial injury**	**No myocardial injury**	**p-value**
	(n=213)	**(n=130)**	**(n=83)**	
Age, years	71.0 (62.0-80.0)	75.5 (67.8-83.0)	66.0 (56.0-76.0)	<0.001
Gender				
Female	69 (32.4)	48 (36.9)	21 (25.3)	0.09
Male	144 (67.6)	82 (63.1)	62 (74.7)	
Smoking history	46 (21.6)	27 (20.8)	19 (22.9)	0.74
Body mass index, kg/m^2	26.7 (24.2-29.5)	26.4 (24.2-29.4)	27.3 (24.0-30.1)	0.19
Comorbidities				
Hypertension	168 (78.9)	110 (84.6)	58 (69.9)	0.015
Congestive heart failure	30 (14.1)	24 (18.5)	6 (7.2)	0.026
Chronic atrial fibrillation	10 (4.7)	10 (7.7)	1 (1.2)	0.054
Coronary artery disease	55 (25.8)	38 (29.2)	17 (20.5)	0.20
Neurological disease [1]	38 (17.8)	29 (22.3)	9 (10.8)	0.043
Chronic kidney disease	51 (23.9)	41 (31.5)	10 (12.0)	0.001
Dialysis dependent	6 (2.8)	5 (3.8)	1 (1.2)	0.41
Diabetes mellitus	91 (42.7)	53 (40.8)	38 (45.8)	0.48
Hyperlipidemia	45 (21.1)	27 (20.8)	18 (21.7)	0.87
COPD	25 (11.7)	13 (10.0)	12 (14.5)	0.38
Malignancy [2]	23 (10.8)	18 (13.8)	5 (6.0)	0.11
Chronic liver disease	1 (0.5)	1 (0.8)	0 (0.0)	N/A
Blood pressure measurement				
Systolic blood pressure	135 (110-151)	128 (110-150)	140 (110-159)	0.10
Mean arterial blood pressure	84 (71-100)	82 (70-99)	73 (87-100)	0.94
Prior medication history				
ACE-inhibitors or ARBs	97 (45.5)	60 (46.2)	37 (44.6)	0.89
Diuretics	82 (38.5)	52 (40.0)	30 (36.1)	0.67
Beta-blockers	75 (35.2)	44 (33.8)	31 (37.3)	0.66
Calcium channel blockers	50 (23.5)	29 (22.3)	21 (25.3)	0.62
Alfa-blockers	11 (5.2)	7 (5.4)	4 (4.8)	1.00
Anti-arrhythmic agents	6 (2.8)	5 (3.8)	1 (1.2)	0.41
Anti-hyperlipidemic agents	45 (21.1)	28 (21.5)	17 (20.5)	1.00
Insulin	45 (21.1)	27 (20.8)	18 (21.7)	0.87
1 oral antidiabetic agent	34 (16.0)	19 (14.6)	15 (18.1)	0.57
>1 oral antidiabetic agents	31 (14.6)	14 (10.8)	17 (20.5)	0.07
APACHE-II	22.0 (13.0-28.0)	24.0 (16.0-30.0)	16.0 (11.0-23.0)	<0.001
SOFA [3]	5.0 (4.0-7.0)	6.0 (5.0-8.0)	4.0 (3.0-6.0)	<0.001
CCI	5.0 (3.0-7.0)	6.0 (4.0-8.0)	4.0 (2.0-5.0)	<0.001
Laboratory data [4]				
HS-troponin I, ng/L	27.0 (9.6-142.5)	84.0 (30.7-465.2)	8.60 (6.0-11.4)	<0.001
D-dimer, µg/mL	1.50 (0.90-3.50)	1.80 (1.20-4.70)	1.10 (0.60-2.30)	<0.001
BNP (plasma), pg/mL	87.0 (38.2-290.5)	165.0 (46.0-519.8)	53.6 (27.0-118.0)	<0.001
BNP >100 pg/mL [5]	101 (47.4)	78 (60.0)	23 (27.7)	<0.001
BUN, mg/dL	31.6 (24.0-52.5)	40.5 (25.0-59.4)	29.0 (20.0-39.0)	<0.001
Creatinine, mg/dL	1.10 (0.81-1.78)	1.31 (0.89-1.98)	0.96 (0.74-1.20)	<0.001
AST, U/L	54.0 (37.0-90.0)	63.0 (40.0-102.8)	48.0 (34.0-75.0)	0.005
ALT, U/L	37.0 (24.0-62.5)	37.0 (23.0-61.5)	39.0 (27.0-63.0)	0.50

Table 1. continued

Characteristics	All cases	Myocardial injury	No myocardial injury	p-value
	(n=213)	(n=130)	(n=83)	
CRP, mg/L	156 (85-235)	172 (104-254)	137 (68-215)	0.014
Procalcitonin, ng/mL	0.34 (0.14-1.49)	0.54 (0.20-1.81)	0.17 (0.08-0.41)	<0.001
Glucose, mg/dL	139 (110-185)	143 (108-190)	135 (112-162)	0.22
Total bilirubin, mg/dL	0.83 (0.63-1.12)	0.88 (0.63-1.12)	0.78 (0.61-1.16)	0.35
LDH, U/L	546 (428-699)	554 (451-728)	521 (388-659)	0.10
Ferritin ng/mL	617 (363-1129)	615 (345-1156)	632 (374-1115)	0.99
WBC, $x10^3$/µL	11.3 (80.5-150.5)	12.6 (9.2-15.6)	10.1 (7.0-13.1)	0.002
Neutrophil, $x10^3$/µL	9.8 (6.8-13.8)	10.4 (7.5-14.4)	8.6 (5.6-11.6)	0.004
Lymphocyte, $x10^3$/µL	0.50 (0.30-0.90)	0.50 (0.40-10.25)	0.50 (0.30-0.80)	0.28
Lymphocyte percentages, %	5.5 (3.1-8.5)	5.1 (2.8-8.6)	5.7 (3.9-8.2)	0.55
Hemoglobin, g/dL	12.4 (10.8-13.8)	11.8 (10.2-13.5)	13.2 (12.0-14.3)	<0.001
Platelet, $x10^3$/µL	255 (171-335)	243 (170-332)	275 (177-354)	0.31
Arterial blood gas analysis[4]				
pH	7.41 (7.34-7.47)	7.39 (7.31-7.46)	7.44 (7.37-7.47)	0.006
HCO_3, mmol/L	22.0 (19.9-25.0)	22.0 (18.7-24.0)	24.0 (21.0-26.0)	0.001
PaO_2, mmHg	61.0 (52.0-70.7)	61.0 (51.8-70.1)	62.0 (52.0-74.0)	0.30
PaO_2/FiO_2	110 (93-132)	106 (88-127)	115 (98-148)	0.010
PaO_2/FiO_2 <150, n (%)	191 (89.7)	121 (93.1)	70 (84.3)	0.06
$PaCO_2$, mmHg	34.0 (29.0-43.0)	35.0 (29.0-44.0)	33.0 (30.0-38.0)	0.27
Lactate, mmol/L	2.00 (1.40-3.00)	2.05 (1.40-3.00)	2.00 (1.40-3.10)	0.98
Events/therapies during ICU stay				
IMV	168 (78.9)	117 (90.0)	51 (61.4)	<0.001
Vasopressor requirement[6]	147 (69.0)	99 (76.2)	48 (57.8)	0.006
Acute kidney injury	138 (64.8)	96 (73.8)	42 (50.6)	0.001
Renal replacement therapy	51 (23.9)	37 (28.5)	14 (16.9)	0.07
Secondary bacterial infections	122 (57.3)	82 (63.1)	40 (48.2)	0.034
New-onset atrial fibrillation	28 (13.1)	16 (12.3)	12 (14.5)	0.68
Treatment for COVID-19				
Favipiravir	203 (95.3)	121 (93.1)	82 (98.8)	0.09
LMWH	203 (95.3)	123 (94.6)	80 (96.4)	0.74
ASA	164 (77.0)	96 (73.8)	68 (81.9)	0.19
Dipyridamole	130 (61.0)	76 (58.5)	54 (65.1)	0.39
Corticosteroids	167 (78.4)	99 (76.2)	68 (81.9)	0.39
Pulse corticosteroid	87 (40.8)	53 (40.8)	34 (41.0)	1.00
Hydroxychloroquine	47 (22.1)	31 (23.8)	16 (19.3)	0.50
Tocilizumab	24 (11.3)	12 (9.2)	12 (14.5)	0.27
Azithromycin	7 (3.3)	5 (3.8)	2 (2.4)	0.71
Length of ICU stay, days	8.0 (4.0-14.0)	9.0 (4.0-15.0)	8.0 (5.0-14.0)	0.99
Length of hospital stay, days	14.0 (9.0-21.0)	13.0 (8.0-20.0)	16.0 (12.0-21.0)	0.012
ICU mortality	150 (70.4)	105 (80.8)	45 (54.2)	<0.001
Hospital mortality	154 (72.3)	109 (83.8)	45 (54.2)	<0.001

All values are expressed as numbers (percentages) or median (interquartile range), [1]history of cerebrovascular disease or dementia, [2]includes hematological and solid organ malignancies, [3]calculated on the day of ICU admission, [4]tested on the day of ICU admission, [5]laboratory upper limit of BNP (100 pg/mL), [6]use of any dose of vasopressor. APACHE-II: Acute Physiology and Chronic Health Evaluation-II, ALT: alanine transaminase, AST: aspartate transaminase, ASA: acetylsalicylic acid, BUN: blood urea nitrogen, BNP: brain natriuretic peptide, CCI: Charlson Comorbidity index, COPD: chronic obstructive pulmonary disease, CPR: cardiopulmonary resuscitation, CRP: C-reactive protein, FiO_2: fraction of inspired oxygen, HS troponin I: high-sensitivity troponin I, ICU: intensive care unit, IMV: invasive mechanical ventilation, LDH: lactate dehydrogenase, LMWH: low molecular weight heparin, N/A: not applicable, PaO_2: partial pressure of arterial oxygen, $PaCO_2$: partial pressure of arterial carbon dioxide, RT-PCR: reverse transcription-polymerase chain reaction, SOFA score: The Sequential Organ Failure Assessment score, WBC: white blood cell count

Table 2. Chest CT-based measurements in patients with and without myocardial injury (univariate analysis)				
Characteristics	**All cases**	**Myocardial injury**	**No myocardial injury**	**p-value**
	(n=213)	**(n=130)**	**(n=83)**	
Chest CT severity score[1]	15.0 (10.0-20.0)	16.0 (12.0-20.0)	13.5 (10.0-18.3)	0.021
Chest CT severity score of 18 or more (severe group), n (%)[1]	68 (36.8)	47 (43.9)	21 (26.9)	0.021
Patients with any coronary artery calcification, n (%)	153 (71.8)	106 (81.5)	47 (56.6)	<0.001
Cardiothoracic ratio	0.52 (0.48-0.57)	0.54 (0.50-0.59)	0.51 (0.47-0.54)	<0.001
Aortic tortuosity, n (%)	32 (15.0)	27 (20.8)	5 (6.0)	0.003
AA diameter, mm	36.5 (34.1-39.1)	36.6 (34.1-39.6)	36.3 (34.1-38.7)	0.64
Arcus aorta diameter, mm	29.8 (27.7-31.9)	30.0 (27.5-32.5)	29.7 (27.7-31.4)	0.34
PA diameter, mm	28.5 (25.5-31.7)	28.8 (25.4-32.6)	28.5 (25.5-31.2)	0.49
PA/AA diameter ratio	0.77 (0.69-0.86)	0.77 (0.69-0.87)	0.77 (0.70-0.84)	0.71
T/AP IVC diameter ratio	1.26 (1.11-1.44)	1.26 (1.09-1.46)	1.27 (1.13-1.43)	0.84
T/AP trachea diameter ratio	0.96 (0.85-1.07)	0.96 (0.85-1.06)	0.97 (0.86-1.09)	0.43

All values are expressed as numbers (percentages) or median (interquartile range). [1]Chest CT severity score was calculated on 185 patients.
AA: Ascending aorta, CT: computed tomography, IVC: inferior vena cava, PA: pulmonary artery, T/AP: transverse/anteroposterior

Table 3. Logistic regression analysis for risk factors of myocardial injury		
	OR (95% CI)	**p-value**
APACHE-II score	1.07 (1.02-1.12)	0.005
Chest CT severity score of 18 or more	2.85 (1.29-6.32)	0.010
Patients with any coronary artery calcification	2.45 (1.09-5.52)	0.030
Age	1.04 (1.01-1.08)	0.041
Gender	1.06 (0.48-2.36)	0.886
Hypertension	1.16 (0.46-2.98)	0.751
Congestive heart failure	1.21 (0.36-4.04)	0.757
Coronary artery disease	0.73 (0.29-1.81)	0.503
Cardiothoracic ratio	1.05 (0.98-1.11)	0.192

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CI: confidence interval, CT: computed tomography, OR: odds ratio

Conclusion

Myocardial injury incidence in critically ill COVID-19 patients is 61.0%. The APACHE-II score, chest CT severity score ≥18, presence of any CAC, and age were independently associated with myocardial injury in critically ill patients with COVID-19. The chest CT severity score and the presence of CAC can be easily obtained from existing chest CT and are valuable in predicting the development of myocardial injury in critically ill patients with COVID-19.

Ethics

Ethics Committee Approval: This retrospective cohort study was conducted in the adult intensive care unit of our center after the approval of the Dokuz Eylül University Non-Invasive Research Ethics Committee (decision no: 2021/05-08, date: 15.02.2021) and the Turkish Ministry of Health.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.E., M.K., M.N.Y., M.C.Ö., B.C., N.G., Be.E., Design: B.E., N.S.G., M.K., M.N.Y., E.Y., N.G., Be.E., Data Collection and Process: B.E., M.K., M.N.Y., M.C.Ö., M.D., Analysis or Interpretation: B.E., N.S.G., M.K., M.N.Y., M.C.Ö., B.C., N.G., Be.E., Literature Search: B.E., M.K., M.N.Y., M.C.Ö., E.Y., B.C., N.G., Be.E., Writing: B.E., M.K., M.N.Y., M.C.Ö., E.Y., N.G., Be.E.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Potential Drug-drug Interactions in Intensive Care Units in Turkey: A Point Prevalence Study

Türkiye'deki Yoğun Bakımlarda Potansiyel İlaç-ilaç Etkileşimlerinin Değerlendirilmesi: Nokta Prevalans Çalışması

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ABSTRACT *Objective:* Drug-drug interaction (DDI) is related with complications and diminished efficacy of medications throughout the treatment process. Intensive care units (ICU) involve patients who are at elevated risk of potential drug-drug interactions (pDDI).
Materials and Methods: Here, we identified potential DDIs in similar patient groups in ICUs in Turkey. Invitations were sent to 20 hospitals in Turkey for a multicenter point prevalence study. Patient orders were determined for potential DDI using the Lexi Interact Online Interaction Checker software. Of 236 patients whose data were collected, patients <18 years of age, those <5 drugs in their drug order, and those with incomplete data were excluded. The remaining 194 patients were included in the study.
Results: A total 684 pDDIs were detected, of which 92 (13.4%) were major, 531 (77.6%) were moderate, and 61 (9%) were minor interactions. There was at least one drug interaction in 159 (81.9%) patients. A notable disparity was observed in the quantity of drugs in the 159 patients with drug interactions and those in the 36 patients without drug interactions (p<0.001). A substantial correlation was detected between the quantity of medications and the incidence of interactions among patients experiencing drug interactions (p<0.001, r=0.707).
Conclusion: No significant correlation was found between the length of stay in ICU and the number of drugs or the number of drug interactions (p=0.216, r=0.092; p=0.284, r=-0.080, respectively). The increased risk of pDDI due to the use of multiple drugs was observed in ICU patients.
Keywords: Drug interactions, intensive care unit, adverse drug reactions

ÖZ *Amaç:* İlaç-ilaç etkileşimi (İİE), birden fazla ilacın birlikte kullanımıyla ortaya çıkan, advers ilaç reaksiyonlarından (AİR) olup, ilaçların tedavideki etkinliğinin azalması ve komplikasyonlarla ilişkilidir. Yoğun bakım ünitesi (YBÜ) hastalarında çoklu ilaç kullanımı potansiyel İİE açısından bu hastaları risk grubu haline getirmektedir. Çalışmamızda, ülkemizdeki farklı yoğun bakımlarında benzer hasta gruplarındaki potansiyel ilaç-ilaç etkileşimlerini (pİİE) belirlemek istedik.
Gereç ve Yöntem: Bu çalışma Türkiye'deki YBÜ'de yatan kritik hastalarda çok merkezli nokta prevalans çalışması olarak tasarlanmıştır. Hasta orderları Lexi interact online interaction checker program (https: //www.uptodate.com/drug-interactions) ile pİİE açısından analiz edildi.
Bulgular: İki yüz otuz altı hasta verisi içinden yaş <18 ve ilaç orderlarındaki ilaç sayı kriteri <5 veya verisi eksik doldurulan hastalar çalışma dışı bırakıldığında 194 hasta çalışmaya dahil edildi. Altı yüz seksen dört tane pİİE saptanmış olup bunların 92 (%13,4) tanesi majör, 531 (%77,6) tanesi moderate, 61 (%9) tanesi minör etkileşim idi. Yüz elli dokuz (%81,9) hastada en az bir tane ilaç etkileşimi mevcuttu. İlaç etkileşimi olan hastalar ile (159 hasta) olmayan 36 hastanın ilaç sayıları arasında anlamlı düzeyde fark mevcuttu (p<0,001). İlaç etkileşimi saptanan hasta grubunda ilaç sayıları ile etkileşim sayıları arasında yüksek düzeyde anlamlı korelasyon saptandı (p<0,001, r=0,707). İlaç sayısı ve ilaç etkileşim sayıları ile yoğun bakım yatış süresi arasında anlamlı düzeyde bir korelasyon saptanmamıştır (p=0,216 r=0,092; p=0,284 r=-0,080, sırasıyla).
Sonuç: Bu çalışma ile benzer YBÜ'lerdeki kritik hastalarda çoklu ilaç kullanımına bağlı pİİE görülme riskinin arttığı görülmüştür. Saptanan pİİE'lerin çoğunluğunu orta düzeyde etkileşimler oluşturmakla beraber bu etkileşimlerin önceden saptanması hasta güvenliğini artırıcı nitelikte olabilir.
Anahtar Kelimeler: İlaç etkileşimleri, yoğun bakım ünitesi, advers ilaç reaksiyonları

Introduction

Drug-drug interactions (DDI) are adverse drug reactions (ADR) that occur due to the combined use of more than one drug. This circumstance is associated with the occurrence of complications and a decline in the effectiveness of medications during treatment (1,2). The conditions that arise as a consequence of drug interactions, as opposed to ADRs, are referred to as potential drug-drug interactions (pDDI).

Intensive care unit (ICU) patients are commonly considered to belong to the high-risk category for pDDI due to the utilization of multiple medications and changes in drug metabolism (3-8). Evidence suggests that this circumstance elevates illness severity and amplifies healthcare expenses through the extension of ICU duration (9-11). Therefore, the identification of pDDIs and implementation of precautionary measures in intensive care patients hold significant importance.

Due to variation in the databases used to detect the pDDIs, several reports on the prevalence of different pDDIs are available. In addition, apart from the differences in the intensive care population studied here (such as surgical/medical intensive care or transplant patients), drug use habits and intensive care levels are other factors that cause variable pDDIs (10,12-14).

In the present study, we aimed to determine pDDIs in similar patient groups from different ICUs in Turkey. Furthermore, our objective was to identify the drug pairs that exhibited the highest frequency of interactions and subsequently elaborate on the significance of these interactions.

Materials and Methods

This study was carried out between January and February 2021 after receiving the approval of the Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital numbered 2011-KAEK-25 2019/04-10 (date: 10.04.2019) and the approval of the ethics committees of the participating hospitals responding to the invitation. This study was designed as a multicenter point prevalence study in critically ill patients under intensive care in Turkey. Twenty hospitals with multidisciplinary ICUs and intensive care sub-branch specialists were invited for the study. Due to the observational nature of the study, patient informed consent form was not obtained. A study chart was created, and it included the following information: patients' age, sex, comorbidities, diagnosis at intensive care hospitalization, Acute Physiology and Chronic Health Evaluation-II (APACHE-II), study day Sequential Organ Failure Assessment (SOFA) scores, ordered drugs and their numbers, drug doses and drug administration routes, and length of stay (LOS) in the ICU. This chart was sent to the physicians responsible for patient treatment in the general ICU of the relevant hospital by e-mail. On the day after the e-mail was sent, the charts containing the single day information were requested for each patient and were subsequently collected by e-mail every day and the data were computerized. The orders of patients in the chart were analyzed for pDDI using the Lexi Interact Online Interaction Checker software program (https://www.uptodate.com/drug-interactions). Nutritional support, electrolyte replacements, and vitamins were excluded from the analysis. The identified interactions were categorized based on their severity and risk rating. Severity was defined as major/moderate/minor interaction, and Risk Rating as X: avoid the combination, D: consider treatment change, C: monitor the treatment, and B: no change needed.

Statistical Analysis

Statistical analyses in this study were performed using the IBM SPSS statistics 20.0 (IBM Corp., Armonk, New York, USA) software package. For the evaluation of the data, in addition to descriptive statistical methods (median, interquartile range), the distribution of variables was checked using the Shapiro-Wilk test. Intergroup comparisons of non-normally distributed variables were made using the Mann-Whitney U test. Spearman correlation test was further used to identify the relations of variables with each other. The outcomes were examined utilizing a significance threshold of $p<0.05$.

Results

Requests for participation were sent to 20 hospitals and 10 positive responses were received. Data of a total of 236 patients were collected from these 10 hospitals. The patients who were <18 years of age, those with <5 drugs in their drug orders, or those whose data were filled incompletely were excluded from the study. The remaining 194 were included in the study. While 103 (53.1%) of the patients were male, their median age was determined to be 69.5 years (59-78) (Table 1).

The number of pDDIs detected in the patient orders were 684; of which 92 (13.4%) were major, 531 (77.6%) were moderate, and 61 (9%) were minor interactions (Figure 1). There was at least one drug interaction present in 159 (81.9%) patients. According to risk the rating, the number of patients under category X was determined to be 10 (1.5%); category D had 166 (24.3%), category C had 444 (64.9%), and category B had 64 (9.3%) patients.

There was a significant difference between the number of drugs in the 159 patients with drug interactions and those in the 36 patients without drug interactions (p<0.001). There was no difference between the age, APACHE-II, and SOFA scores of these two patient groups and their ICU hospitalization days (p=0.831, p=0.918, p=0.087, p=0.253, respectively) (Table 2).

Significantly positive correlation was found between the number of drugs and the number of interactions in the patient group with drug interactions (p<0.001, r=0.707).

In the patient group with drug interaction, there was no significant correlation between the number of drug interactions and the APACHE-II or SOFA scores (p=0.937, r=0.006; p=0.910, r=0.008, respectively); however, there was a weak correlation between the SOFA score and major drug interactions (p=0.024 r=0.167). A moderate level significant correlation was found between the number of interactions and the number of major drug interactions (p<0.001, r=0.574).

There was no statistically significant correlation identified between the duration of ICU stay and either the quantity of medications or the occurrence of drug interactions (p=0.216, r=0.092; p=0.284, r=-0.080, respectively). A weak correlation was found between the APACHE-II score and the LOS in the ICU (p=0.036, r=0.256).

Among drug interactions, acetylsalicylic acid-enoxaparin (44 times), enoxaparin-clopidogrel (20 times), furosemide-methylprednisolone (19 times), and furosemide-acetylsalicylic acid (19 times) pairs were observed most frequently (Table 3, 4).

Discussion

Our study showed that most of the critically ill patients (81.9%) were exposed to pDDI when their drug orders were reviewed on any day during their ICU hospitalization.

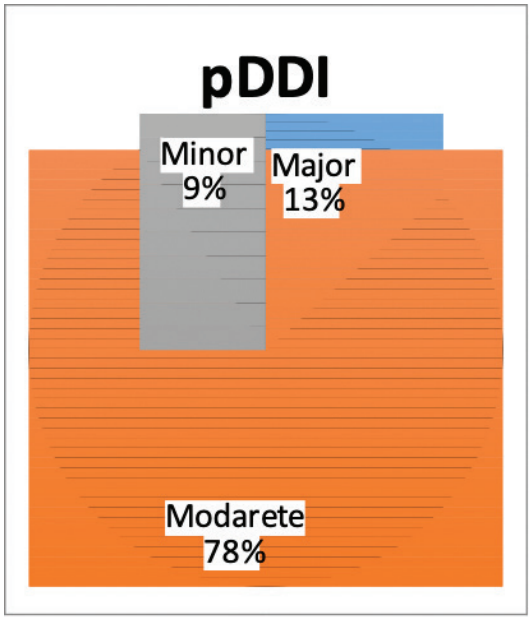

Figure 1. Distribution of detected pDDIs by severity category
pDDI: Potential drug-drug interactions

Table 1. Demographical data

	Median (Q1-Q3) n=194
Age (year)	69.5 (59-78.25)
Gender (male), n (%)	103 (53.1%)
APACHE-II	22 (14-28)
SOFA	5 (3-8)
Length of stay (days)	11 (5-22)
Number of drugs (n)	8 (7-10)
Number of intereaction (n)	2 (1-5)

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment

Table 2. Comparison of age, APACHE-II, SOFA score, intensive care hospitalization day and number of drugs in the order of patients with and without pDDI

	Patients without pDDI n=35	Patients with pDDI n=158	p-value
Age (year)	68 (55-78)	70 (59-79)	0.831
APACHE-II	22 (14-28)	21.5 (14-28)	0.918
SOFA	6.5 (4-9.5)	5 (3-8)	0.087
Hospitalization day	17 (5-24)	11 (5-21)	0.253
Number of drugs	6 (5-7)	9 (7-10.2)	<0.001

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, pDDI: potential drug-drug interactions. Mann-Whitney U test was used. A value of p<0.05 was considered significant

Table 3. The most common pDDI and risk rating categories

pDDI	Frequency	
	n	%
Contraindicated		
Quetiapine-ipratropium	5	50%
D		
Consider therapy modification		
Acetylsalicylic acid -enoxaparin	44	26.5%
Enoxaparin-clopidogrel	20	12%
Enoxaparin-piracetam	9	5.4%
Clopidogrel-omeprazole	8	4.8%
Fentanyl-midazolam	7	4.2%
C		
Monitor therapy		
Acetylsalicylic acid-furosemide	19	4.3%
Fentanyl-furosemide	15	3.4%
Acetylsalicylic acid-clopidogrel	13	2.9%
Clopidogrel-pantoprazole	13	2.9%
Furosemide-methylprednisolone	11	2.5%
Amlodipine-doxazosine	11	2.5%
B		
No action needed		
Pantoprazole-levothyroxine	10	15.6%
Atorvastatin-amlodipine	5	7.8%
Atorvastatin-clopidogrel	5	7.8%

pDDI: Potential drug-drug interactions

Although there was an increase in the number of drug interactions as the quantity of medications escalated, no statistically significant correlation was observed between the LOS in ICU and either the number of drugs or the number of drug interactions.

According to literature reports, the occurrence of pDDIs in intensive care patients exhibits significant variations. In their studies, Abarca et al. (15) and Vanham et al. (13) have indicated that the concordance among databases utilized for the detection of pDDIs was remarkably low. Acharya et al. (10) had also used the same Lexicomp Interaction Checker software program and reported similar pDDI prevalence. In the same study, similar rates of severity category and risk rating have been reported. The prevalence differences observed in the literature may be due to the data bank used or may arise from the different drug use habits of patient groups or their physicians. In order to mitigate this effect, similar ICUs were invited to our study and attempts were made to reduce such differences.

Numerous studies have provided evidence that the incidence of pDDIs escalates in correlation with the augmentation in the quantity of administered medications. (7,8,10,16). Similarly, in our study, we discovered a substantial level of correlation (r=0.707) between the two conditions. This high correlation reveals the necessity of checking the prescribed drug orders with respect to pDDIs.

When we consider the recommended risk rating for interacting drug pairs, we observe that the 'category C: monitor therapy' is the most common. In this category, a follow-up is recommended to monitor potential effects without making a change in the treatment. Such follow-up for effects was included in the daily routine follow-up of most critically ill patients (17). As an example, the effect furosemide-methylprednisolone interaction was evident from the hypokalemia-inducing effect of furosemide. In routine biochemistry or arterial blood gas analyses of intensive care patients, routine follow-up of the interaction with electrolyte monitoring and treatment can protect patients from the effects of pDDIs of such electrolytes.

Table 4. The interaction mechanisms of the most frequently interacting drug pairs		
Most frequent drug pairs	**Risk category**	**Mechanism of action**
Acetylsalicyclic acid/enoxaparin	Moderate (D)	Enhance the anticoagulant effect
Enoxaparin/clopidogrel	Moderate (D)	Enhance the anticoagulant effect
Acetylsalicyclic acid/furosemide	Moderate (C)	Enhance the anticoagulant effect
Fentanyl/furosemide	Moderate (C)	Opioids may diminish the effects of diüretics
Acetylsalicyclic acid/clopidogrel	Moderate (C)	Enhance the anticoagulant effect
Clopidogrel/pantaprozole	Major (C)	Pantoprazole may decrease serum concentrations of the active metabolite(s) of clopidogrel
Furodemide/methylprednisolone	Moderate (C)	Corticosteroids (systemic) may enhance the hypokalemic effect of loop diuretics
Amlodipine/doxazosin	Moderate (C)	Alpha1-blockers may enhance the hypotensive effect of calcium channel blockers
Enoxaparin/piracetam	Moderate (D)	Enhance the anticoagulant effect

Within our study, we established that the acetylsalicylic acid-enoxaparin drug pair exhibited the highest frequency of interactions. We believe that prolonged intensive care hospitalization after coronavirus disease-2019 has caused this situation. The most common drug pairs reported in the literature are also quite variable, probably due to difference in drug availability among countries, drug use habits, and different patient groups (4,12,15,18). For example, in their study with renal transplantation patients, Amkreutz et al. (12) have reported the most frequently interacting drug pair to be tacrolimus-prednisolone, which causes an immunosuppressive effect. Also, Rodrigues et al. (19) have reported the most frequently interacting drug pair is enoxaparin-dipyrone. However, dipyrone is not available in every country.

In contrast to the findings reported in the existing literature (9,10,20), our study did not reveal a positive association between the LOS in ICU and either the number of medications or the number of drug interactions. We anticipated such results due to the limitation of using working days as a measure for hospital stay, which may not accurately reflect the total length of ICU stay. Notably, no significant differences were observed in the APACHE-II score, SOFA score, and number of medications between the groups with and without drug interactions, and there were no disparities in the duration of hospitalization among these groups. These findings suggest that an increased number of pDDIs may not necessarily lead to a prolonged ICU stay, which contradicts previous literature findings (9,10,20). However, it is worth noting that a moderate correlation was found between the SOFA score and major drug interactions, indicating that the severity of the disease might contribute to a higher likelihood of prescribing multiple medications. This, in turn, increases the potential occurrence of pDDIs and the subsequent prolongation of hospital stay.

The most important limitation of our study is that pDDI-related ADR could not be examined. Moreover, considering hospitalization duration based on working days to derive the total LOS in the ICU constitutes another limitation of this study, as this duration did not reflect the actual total LOS in the ICU.

Conclusion

In this study, the risk of pDDI due to disease severity and simultaneous use of multiple drugs was observed to increase in patients in similar ICUs. Although the majority of pDDIs detected consist of moderate-level interactions, the early detection of these interactions may reduce pDDI risk in patients.

Ethics

Ethics Committee Approval: This study was carried out between January and February 2021 after receiving the approval of the Ethics Committee of Bursa Yüksek İhtisas Training and Research Hospital numbered 2011-KAEK-25 1029/04-10 (date: 10.04.2019) and the approval of the ethics committees of the participating hospitals responding to the invitation.

Informed Consent: Due to the observational nature of the study, patient informed consent form was not obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.G., M.Ş.D., İ.C., N.K.G., Concept: D.G., N.K.G., Design: D.G., M.Ş.D., İ.C., Data Collection and Process: D.G., M.Ş.D., Analysis or Interpretation: D.G., M.Ş.D., İ.C., N.K.G., Literature Search: D.G., M.Ş.D., Writing: D.G., M.Ş.D., İ.C.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Usefulness of APACHE-II, SOFA, ISARIC/WHO 4C Mortality Score and CO-RADS for Mortality Prediction of Critically Ill Coronavirus Disease-2019 Patients

APACHE-II, SOFA, ISARIC/WHO 4C Mortalite Skoru ve CO-RADS'nin Kritik Koronavirüs Hastalığı-2019 Hastalarının Mortalite Tahmininde Kullanımı

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ABSTRACT *Objective:* It was aimed to report the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow coma scale (GCS), 4C mortality score and the coronavirus disease-2019 (COVID-19) Reporting and Data System (CO-RADS) in predicting the outcome of critically ill COVID-19 patients.

Materials and Methods: Patients with laboratory-confirmed COVID-19 infection or clinical and radiological confirmed COVID-19 infection who were admitted to adult intensive care unit (ICU) were included. Clinical characteristics, outcomes, APACHE-II score, SOFA score, International Severe Acute Respiratory and Emerging Infections Consortium/World Health Organization 4C mortality score and CO-RADS classification were reported at admission.

Results: Two hundred seventy six patients were included in this study. The mean age was higher in non-survivor patients. The most common cause of hospitalization was respiratory failure (67%). The common co-morbidities were hypertension (51.8%), cardiac disease (43.4%) and diabetes (33.6%). Organ failure was present in 61.5% of the patients. The mean APACHE-II, SOFA, GCS and 4C mortality scores were higher in non-survivor patients. 4C mortality and SOFA scores showed higher predictive accuracy for mortality with an area under the curve 0.736 and 0.706, respectively. 4C mortality had sensitivity of 78.9% and specificity of 58.1% whereas of SOFA had a sensitivity of 78.9% and a specificity of 53.3%.

Conclusion: 4C mortality and SOFA scores could be a predictors of mortality in COVID-19 patients in the ICU.

Keywords: COVID-19, intensive care, CO-RADS classification, 4C mortality score, SOFA score, APACHE-II score

ÖZ *Amaç:* Kritik koronavirüs hastalığı-2019 (COVİD-19) hastalarının mortalite tahmininde Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skoru, Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skoru, Glasgow koma skalası (GCS), 4C mortalite skoru ve COVİD-19 Raporlama ve Veri Sistemi'nin (CO-RADS) araştırılması amaçlanmıştır.

Gereç ve Yöntem: Laboratuvarca doğrulanmış COVİD-19 enfeksiyonu veya klinik ve radyolojik olarak doğrulanmış COVİD-19 enfeksiyonu olan erişkin yoğun bakım ünitesine (YBÜ) kabul edilen hastalar dahil edildi. Klinik özellikler, sonuçlar, APACHE-II skoru, SOFA skoru, Uluslararası Şiddetli Akut Solunum ve Ortaya Çıkan Enfeksiyonlar Konsorsiyumu/Dünya Sağlık Örgütü *(International Severe Acute Respiratory and Emerging Infections Consortium/World Health Organization)* 4C mortalite skoru ve CO-RADS sınıflandırması yatış esnasında kaydedildi.

Bulgular: Bu çalışmaya 276 hasta dahil edildi. Ölen hastalarda yaş ortalaması daha yüksekti. En sık hastaneye yatış nedeni solunum yetmezliğiydi (%67). En sık eşlik eden hastalıklar hipertansiyon (%51,8), kalp hastalığı (%43,4) ve diyabet (%33,6) idi. Hastaların %61,5'inde organ yetmezliği mevcuttu. Ortalama APACHE-II, SOFA, GCS ve 4C mortalite skorları ölen hastalarda daha yüksekti. Mortalite için 4C mortalite ve SOFA skorları, sırasıyla eğri altındaki alan 0,736 ve 0,706 alan ile daha yüksek öngörü bulundu. 4C mortalite skoru %78,9 duyarlılık ve %58,1 özgüllüğe sahipken, SOFA'nın duyarlılığı %78,9 ve özgüllüğü %53,3 idi.

Sonuç: 4C mortalite ve SOFA skorları, YBÜ'deki COVİD-19 hastalarında mortalitenin tahmin ettirici bir göstergesi olabilir.

Anahtar Kelimeler: COVİD-19, yoğun bakım, CO-RADS sınıflandırması, 4C mortalite skoru, SOFA skoru, APACHE-II skoru

Introduction

The severe acute respiratory syndrome coronavirus disease-2019 (COVID-19) began in Wuhan, China, and has spread worldwide, infecting millions of people since than December 2019. The COVID-19 pandemic has caused an intense loss of human life worldwide and presents an extraordinary challenge to public health systems and the world economy.

Predicting the outcomes in intensive care patients is very important in terms of both guiding the treatment and preventing unnecessary treatments. Various laboratory tests, clinical findings or scoring systems are used to predict outcomes in intensive care patients. Research and large-scale vaccination campaigns are ongoing for effective treatment of COVID-19. Meanwhile, it is very important to predict in-hospital mortality during hospitalization for COVID-19.

The Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores was designed to calculate the severity of disease of intensive care unit (ICU) patients and to predict mortality. The APACHE-II score is calculated based on body temperature, heart and respiratory rate, mean arterial pressure, pH. Range of APACHE-II is 0 to 71. Increasing score is associated with an increasing risk of hospital death (1). The SOFA score was designed to assess the severity of organ dysfunction in critically ill septic patients. The original SOFA score was studied from a cohort of 1449 patients admitted to ICUs in sixteen countries (2). It was published that a high correlation between hospital mortality and the SOFA score in COVID-19 patients. They reported that SOFA score was a risk factor for death in COVID-19 patients (3). However the discriminant accuracy of the SOFA score for mortality prediction in patients with COVID-19 pneumonia requiring mechanical ventilation was poor (4).

In a review for prediction models for COVID-19 patients, they identified 107 prognostic models for patients with a diagnosis of COVID-19. The suggested use of these models was not visibly described. The most frequently used categories of prognostic factors (included at least 20 times for any outcome) included age, comorbidities, vital signs, image features, sex, lymphocyte count, and C-reactive protein (CRP) (5). It was recommended the models by Knight et al. (6) and Jehi et al. (7) are good candidates for validation studies in other data for prediction models. Knight et al. (6) published the International Severe Acute Respiratory and emerging Infections Consortium/World Health Organization (ISARIC/WHO) 4C mortality score for COVID-19. ISARIC/WHO 4C mortality score includes the biological and clinical variables, like breathing rate, peripheral oxygen saturation, age, sex, Glasgow coma scale (GCS), urea, CRP levels and number of comorbidities. The score ranges from zero to twenty-one points. A score of ≤3 had a 1% mortality risk compared with 62% mortality risk for those with a score of ≥15.

Chest computerized tomography (CT) scans are used as a valuable tool in the diagnostic process of COVID-19 viral pneumonia cases. Chest CT specificity (82.9% to 96%) and sensitivity (80% to 90%) were reported to be higher than real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing for COVID-19 diagnosis. This highlights the need to recognize and understand imaging findings of the lungs (8). COVID-19 Reporting and Data System (CO-RADS) is published in Mid-March of 2020 that grades the findings on how likely the diagnosis of COVID-19 is. It was evaluated using 105 randomly selected chest CT scans of patients admitted to the emergency department with clinical suspicion of COVID-19. CO-RADS system has seven categories. Categories zero and grade 1 to 6. Grade 1 to 6 means that from very low risk to proven infection with a positive RT-PCR assay. The system very well in estimating COVID-19 in patients with moderate to severe clinical disease (9).

The objective of this paper is to report APACHE-II score, SOFA score, the 4C mortality score and the CO-RADS classification in predicting outcome of COVID-19 in the ICU.

Materials and Methods

This is a single-center; retrospective cohort study that was analyzed anonymized data. After the Non-Invasive Clinical Researches Ethics Committee of the Pamukkale University this study was performed (no: 60116787-020-14366, date: 02.02.2021). Informed consent was waived because of the retrospective design of the study. Between September 1, 2020 and January 30, 2021 (the second wave of the COVID-19 pandemic), all adult patients (over than 18 years of the age) with RT-PCR assay confirmed COVID-19 infection or clinical and radiological confirmed COVID-19 infection were included.

Diagnosis of COVID-19 was accepted according to these findings: 1) Positive result of RT-PCR assay for COVID-19, 2), Typical COVID-19 lung CT scan abnormalities, 3)

COVID-19 clinical findings and symptoms and/or the recent contact and/or travel history with certain case of COVID-19, associated with CO-RADS 3, 4 chest CT scan. Laboratory confirmation for COVID-19 was defined as a positive result of RT-PCR test from a specimen collected on an endotracheal aspirate or nasopharyngeal swab. RT-PCR assays (COVID-19 RT-qPCR, Bio-Speedy) were performed according to the protocol approved by WHO in the General Office of Public Health Microbiology Reference Laboratory and laboratories in the specified areas (10). Patient's data was obtained from hospital information systems. Data was recorded on daily basis.

Data Collection

The demographics and characteristics, clinical findings, therapies and laboratory data were recorded. The demographics and characteristics were age, sex, smoking history, APACHE-II, GCS, SOFA, the 4C mortality score, laboratory data, clinical symptoms or signs, the recent exposure and travel history, comorbidities. The demographics and characteristics APACHE-II, GCS, SOFA, the 4C mortality score, clinical symptoms or signs, the recent exposure and travel history, comorbidities were recorded at admission.

Laboratory data consisted of complete blood count, alkaline phosphatase, alanine aminotransferases, aspartate aminotransferases (AST), lactate dehydrogenase, serum creatinine (Cr), serum potassium, phosphate, sodium, D-dimer, prothrombin time, international normalized ratio (INR), partial thromboplastin time, serum CRP, and serum procalcitonin. Invasive and noninvasive mechanical ventilation parameters were recorded. Arterial blood gas analysis were performed according to the patient's needs.

The ISARIC/WHO 4C mortality score was calculated on admission for each patient. This score includes eight parameters: age, sex, peripheral oxygen saturation, respiratory rate, number of comorbidities, level of consciousness (assessed using the GCS) and results of laboratory tests: serum urea and CRP (6). CT was performed at 1st day and as needed. All chest CT scans were performed without contrast agent and with a section thickness of 5 mm. The chest CT scans were reported according to CO-RADS. The CO-RADS scoring system has classification such as CO-RADS category 0 for technically insufficient imaging and CO-RADS category 6 for the confirmed disease through RT-PCR testing (9).

Outcome

Patients' length of mechanical ventilation in ICU and discharge status (non-survivor, survivor) was entered patent's data form. Patients were treated according to the guide was prepared by scientific committee of the Ministry of Health and available literature (11). Therapies of the patients were documented daily. Since there was not enough evidence at the beginning of the pandemic, we did not routinely use steroids in our patients. Microbial cultures from blood tracheal aspirate, and urine were taken at admission and in need of clinical situation.

Statistical Analysis

Statistical analyses were performed with SPSS for Windows 19 software. Continuous variable are shown as mean (standard deviation), median and minimum-maximum, categorical variables were reported as frequency with odds ratio and 95% confidence interval (CI). The conformity of data to normal distribution were evaluated with Shapiro-Wilk test. The comparisons between groups were evaluated with Mann-Whitney U test for continuous variables, chi-square test and Fisher's Exact chi-square test for categorical values. Receiver operating characteristic (ROC) curves of APACHE-II, SOFA, the 4C mortality score and CO-RADS were presented with area under curve (AUC), 95% CI, cut-off value, sensitivity, specificity. Statistical analyses were evaluated with 95% CI and $p<0.05$ was accepted as a significant difference.

Results

Two hundred seventy six patients included to this study. Total 276 patients were grouped into two groups, depending on the survival status. One hundred seventy one patients (61.9%) were included in the non-survivor group. The rest of 105 patients (38.1%) had included in the survivor group. Total female and male patient were 98 (36.6%) and 178 (64.4%) respectively. The mean age was 68.6 (13.3) years for all patients. In non-survivor patient group, the mean age were higher than in survivor patients ($p<0.001$) (Table 1, 2). One hundred eighty nine patients (68.4%) were admitted from emergency department. The most common cause of hospitalization was respiratory failure with a rate of 67%. The second most common cause was sepsis (33%). The reasons for hospitalization was statistically different between survivor and non-survivor patients. Sepsis is higher in non-survivor group than survivor group at admission ($p<0.001$).

Table 1. Demographics and clinical characteristics of the patients

Variable	Alive			Ex			All			p
	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	
Age	64.4±13.6	66	23-95	71.2±12.5	72	23-96	68.6±13.3	70	23-96	<0.001
BMI	29.7±3.4	30	22-42	29.5±3.6	29	20-46	29.6±3.5	29.3	20-46	0.566
Duration of symptom (day)	6.0±3.9	5	0-30	6.8±4.4	6	0-30	6.3±4.2	5	0-30	0.273
APACHE-II	17.8±8.6	15	5-42	21.6±9.8	21	5-44	20.2±9.5	18	5-44	0.001
SOFA	5.0±2.5	4	0-12	7.4±3.5	7	0-18	6.5±3.3	6	0-18	<0.001
GCS	14.0±2.6	15	3-15	10.4±5.3	13	3-15	11.7±4.8	15	3-15	<0.001
4C mortality	11.2±3.5	11	4-19	14.2±3.3	15	6-21	13.0±3.7	13	4-21	<0.001
CO-RADS	5.0±0.9	5	2-6	5.0±0.9	5	2-6	5.0±0.9	5	2-6	0.784
Fever	37.0±0.5	37	35.8-38.6	37.1±0.8	37	35.7-39.0	37.0±0.7	37	35.7-39.0	0.346
Heart rate (/min)	90.7±12.7	89	60-130	99.0±15.5	100	52-150	95.8±15.0	96	52-150	<0.001
Mean arterial pressure (mmHg)	81.1±9.1	80	66-120	77.7±12.7	75	50-122	79.0±11.5	78	50-122	0.003
FiO_2	50.9±7.8	50	40-80	63.1±10.1	60	40-90	58.5±11.0	60	40-90	<0.001
SPO_2	91.9±3.0	92	78-99	90.9±5.0	91	62-100	91.3±4.3	91	62-100	0.053
PEEP	6.0±1.1	6	5-10	7.8±1.9	8	5-14	7.1±1.9	7	5-14	<0.001
Tidal volume	388.6±46.2	390	320-450	418.3±43.9	420	300-600	416.0±44.6	410	300-600	0.032
Compliance mL cmH_2O	23.4±5.0	22	20-34.7	24.5±6.2	24	12-45	24.4±6.1	23.6	12-45	0.549
Driving pressure	15.5±4.7	14	10-25	15.6±4.4	14	9-24	15.6±4.4	14	9-25	0.637
PaO_2/FiO_2	143.2±50.5	134	75-381	125.2±51.4	112	45-353	132.0±51.7	122	45-381	<0.001
Max PEEP during ICU	6.8±1.6	7	5-12	10.3±2.5	10	5-16	8.9±2.7	8	5-16	<0.001
Min PEEP during ICU	5.2±0.5	5	5-8	7.1±1.6	7	5-13	6.4±1.6	6	5-13	<0.001
Max PaO_2/FiO_2	279.3±74.8	261.5	132-520	186.7±70.4	180	17-456	221.7±89.7	220	17-520	<0.001
Min PaO_2/FiO_2	136.8±43.4	127	65-319	100.8±34.3	95	43-213	114.4±41.8	108	43-319	<0.001
Max PaO_2	109.9±34.9	99	55-202	98.8±37.6	88	42-212	103.0±36.9	93	42-212	0.003
Min PaO_2	61.6±22.0	54	41-185	59.1±19.7	52	30-132	60.1±20.6	53	30-185	0.204
Invasive mechanical ventilation (day)	9.6±8.4	7.5	1-27	7.1±7.7	4	1-36	7.2±7.7	4	1-36	0.197
Noninvasive mechanical ventilation (day)	7.9±5.7	6	1-26	4.8±4.4	3	1-27	6.6±5.4	5	1-27	<0.001

BMI: Body mass index, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, ICU: intensive care unit, SD: standard deviation, min: minimum, max: maximum, PEEP: positive-end-expiratory respiration

Table 2. Data frequencies of the patients

Variable	Alive (n=105)	Ex (n=171)	p	OR	CI	Variable	Alive (n=105)	Ex (n=171)	p	OR	CI
Gender (F/M)	36/69	62/109	0.740	0.92	0.51-1.53	CT (-/+)	8/97	16/155	0.782[a]	0.80	0.33-1.94
Comorbidity (-/+)	27/78	20/151	0.004[a]	2.61	1.38-4.95	CT bilateral ground glass opacification (-/+)	17/77	44/127	0.207[a]	0.64	0.34-1.19
Hypertension (-/+)	58/47	75/96	0.066	1.58	0.97-2.58	CT pleural effusion (-/+)	80/14	119/52	0.008[a]	2.50	1.30-4.81
Diabetes mellitus (-/+)	66/39	114/57	0.519	0.85	0.51-1.41	CT nodul (-/+)	86/6	163/8	0.712[b]	0.70	0.24-2.09
Cardiac disease (-/+)	70/35	86/85	0.008	1.98	1.19-3.27	Therapies and interventions					
Pulmonary disease (-/+)	93/12	130/41	0.016	2.44	1.22-4.90	Recruitment (-/+)	103/2	146/25	0.001	8.82	2.04-38.050
Malignity (-/+)	93/12	138/33	0.121[a]	1.85	0.91-3.77	Prone position (-/+)	69/36	156/15	<0.001	0.18	0.10-0.36
Chronic renal failure (-/+)	94/11	145/26	0.349[a]	1.53	0.72-3.25	Renal replacement therapy (-/+)	104/1	158/13	0.031[a]	8.56	1.10-66.39
Immune deficiency (-/+)	104/1	166/5	0.524[b]	3.13	0.36-27.19	Plasma therapy (-/+)	99/6	158/13	0.721[a]	1.36	0.45-3.69
Symptom (-/+)	3/102	1/170	0.311[b]	5.00	0.51-48.70	Hidroxy chloroquine (-/+)	99/6	167/4	0.262[a]	0.40	0.11-1.44
Fever (-/+)	77/28	124/47	0.882	1.04	0.60-1.80	Antibiotic therapy (-/+)	5/100	6/165	0.825[b]	1.38	0.41-4.62
Dyspnea (-/+)	6/99	8/163	0.922[a]	1.24	0.42-3.66	Antiviral (-/+)	1/104	4/167	0.740[b]	0.40	0.04-3.64
Cough (-/+)	45/60	105/66	0.003	0.47	0.29-0.77	Vasopressor (-/+)	93/12	17/154	<0.001	70.21	32.1-153.5
Smoking (-/+)	74/31	127/44	0.492	0.83	0.48-1.42	Tocilizumab (-/+)	98/7	162/9	0.827[a]	0.78	0.28-2.16
Contact history (-/+)	80/25	136/35	0.513	0.82	0.46-1.48	Cytokine adsorption (-/+)	104/1	157/14	0.021[a]	9.27	1.20-71.59
						Aspirin (-/+)	0/105	2/169	0.383[b]	0.54*	0.06-5.21
Reason for admission (respiratory failure/sepsis)	84/21	101/70	<0.001	2.77	1.57-4.89	Low molecular weight heparin (-/+)	0/105	2/169	0.383[b]	0.54*	0.06-5.21
PCR at admission (-/+)	12/93	5/166	0.009[a]	4.28	1.46-12.53	Microbial culture (-/+)	74/31	116/55	0.646	1.13	0.67-1.92
Radiography (-/+)	27/78	42/129	0.830	1.06	0.61-1.86	Organ failure (-/+)	49/56	57/114	0.027	1.75	1.06-2.88
Radiography bilateral infiltrate (-/+)	29/76	44/127	0.730	1.10	0.64-1.91	Organ failure (-/single/ multiple)	49/52/4	57/55/59	<0.001	-	-
Radiography effusion (-/+)	92/13	125/46	0.007[a]	2.60	1.33-5.10	Invasive mechanical ventilation (-/+)	95/10	4/167	<0.001	396.6	121.1-1299.0
Radiography ground glass opacities (-/+)	30/75	47/124	0.845	1.06	0.62-1.81	Noninvasive mechanical ventilation (-/+)	3/102	74/97	<0.001	0.04	0.01-0.13

[a]Yates corrected chi-square, [b]Fisher's Exact chi-square. PCR: Polymerase chain reaction, F: female, M: male, OR: odds ratio, CI: confidence interval, CT: computed tomography

Table 3. Laboratory data of the patients

Variable	Alive			Ex			All			p
	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	
White blood cell (per mm^3)	10893.1±5811.0	9720	100-28900	13116.3±13903.8	11090	340-171000	12270.5±11551.8	10870	100-171000	0.110
Lymphocyte (per mm^3)	822.7±1356.4	530	78-10100	684.0±459.3	520	100-2800	737.0±912.7	520	78-10100	0.883
Platelet (per mm^3)	1061.4±8369.7	225	36-86000	230.2±167.3	216	15-1900	546.4±5164.6	218	15-86000	0.232
Neutrophil to lymphocyte ratio	16.3±11.4	13.2	1.5-67	17.3±12.8	15	1.2-82	16.9±12.3	14.2	1.2-82	0.679
INR	1.2±0.5	1.1	0.9-4.6	1.4±1.8	1.2	0.9-9.3	1.3±0.7	1.2	0.9-9.3	<0.001
D-dimer ng/mL	1991.9±5589.1	570	48-46000	3556.6±6716.2	1290	106-55046	2961.4±6346.5	915	48-55046	<0.001
Fibrinogen mg/dL	583.1±246.5	586	99-1567	541.0±248.6	528	97-2000	557.0±248.2	550	97-2000	0.166
Creatinine mg/dL	1.2±1.3	0.9	0.4-9.7	1.7±1.3	1.2	0.3-8.9	1.5±1.3	1.1	0.3-9.7	<0.001
Aspartate aminotransferase	54.3±155.9	33	8-1612	143.9±530.1	38	8-6145	109.8±429.9	35.5	8-6145	0.009
Alanine aminotransferase	38.4±34.5	30	241	103.7±329.9	24	2-2864	78.9±262.1	26	2-2864	0.376
Ferritin ug/L	794.2±549.1	676.5	54-2000	852.7±627.0	663	32-3162	830.3±598.1	668.5	32-3162	0.745
C-reactive protein	98.9±70.6	88	0.9-388	136.1±143.8	106	6.7-1654	121.9±122.4	99.5	0.9-1654	0.006
Procalcitonin	1.6±6.8	0.2	0.03-66	5.3±13.0	0.7	0.01-80	3.9±11.2	0.4	0.01-80	<0.001
Lactate ug/L	1.7±0.4	1.8	0.8-3.1	2.4±1.9	2	0.8-16	2.2±1.7	1.9	0.8-16	0.005
IL-6	58.5±76.4	32.5	3.4-397.8	256.3±701.1	63.5	12.1-3700	163.7±521.1	51.2	3.4-3700	0.001
Amylase	73.7±57.6	51	18-233	87.9±76.0	59	10-338	80.8±67.3	58.5	10-338	0.553
Lipase	41.8±42.5	28.3	10-232	79.0±134.8	42.5	4-726	60.1±100.4	32.6	4-726	0.259
Urea	56.8±32.4	49	13-159	93.3±60.2	75	19-353	79.4±54.3	62	13-353	<0.001

SD: Standard deviation, min: minimum, max: maximum, INR: international normalized ratio

Two hundred twenty nine patients have comorbidities. Comorbidities have higher in the non-survivor group than survivor group. The most common co-morbidities were hypertension (51.8%), cardiac disease (43.4%) and diabetes (33.6%). Compared to the survivor group, non-survivor group had a significantly higher proportion of cardiac disease and pulmonary disease; the differences were statistically significant ($p<0.05$). Dyspnea was the most common symptom. Ninety five percent of the patients have dyspnea. The other common symptoms were, coughing and fever. Coughing was significantly higher in non-survivor patients than survivor patients were ($p=0.003$) (Table 2).

Heart rate and FiO_2 was lower in survivor patients than non-survivor patients ($p<0.001$), whereas the mean arterial pressure, was higher in survivor patients ($p=0.003$). In terms of comparison laboratory biomarkers taken during admission between 2 groups, it was found INR, D-dimer, Cr, urea, CRP, AST, procalcitonin, lactate and IL-6 were significantly lower in the survivor group ($p<0.001$) (Table 3). Chest radiography was available in 207 patients at admission. Pleural effusion were seen significantly higher in non-survivor patients ($p=0.007$). Two hundred fifty two patient got CT scan at admission. Same as the radiography pleural effusion were shown significantly higher in non-survivor patients on CT scan ($p=0.008$) (Table 2).

Seventy percent of the patients were underwent invasive mechanical ventilation therapy. Invasive mechanical ventilation therapy was applied to the majority of patients who died whereas non-invasive mechanical ventilation therapy was applied to the majority of survivor patients. This difference was statistically significant (p<0.001) (Table 2). Positive-end-expiratory respiration and tidal volume values statistically were different between survivor and non-survivor groups. When we compared arterial blood gas analysis, it was found that non-survivor group had lower PaO_2 and PaO_2: FiO_2 ratio than the survivor group (p<0.001) (Table 1). Therapies and interventions were given in Table 2. Recruitment maneuver, prone position, renal replacement therapy, vasopressor usage and cytokine adsorption were higher in non-survivor patients and were statistically different from survivor patients (p<0.001). Organ failure was present in 61.5% of all patients. Multiple organ failure was more common in the non-survivor -group. The length of invasive and non-invasive mechanical ventilation were statistically significantly longer in survivor group (p<0.001) Table 2.

The mean APACHE-II, SOFA, GCS and the 4C mortality scores were higher in non-survivor patients than in survivor patients (p<0.001) (Table 2). The mean CO-RADS classification value was not different between groups. ROC curves were computed to assess the accuracy of scores and CO-RADS in predicting mortality. 4C mortality and SOFA scores showed higher predictive accuracy for mortality with an area AUC 0.736 and 0.706 respectively (p<0.001) (Figure 1) (Table 4). The 4C mortality cut-off value of 11.5 had a sensitivity of 78.9% and specificity of 58.1%. The cut-off value of SOFA was 4.5, which corresponded to a sensitivity of 78.9% and a specificity of 53.3%. CO-RADS have not good results for predicting mortality with 5.5 cut-off value in ICU patients (p=0.802).

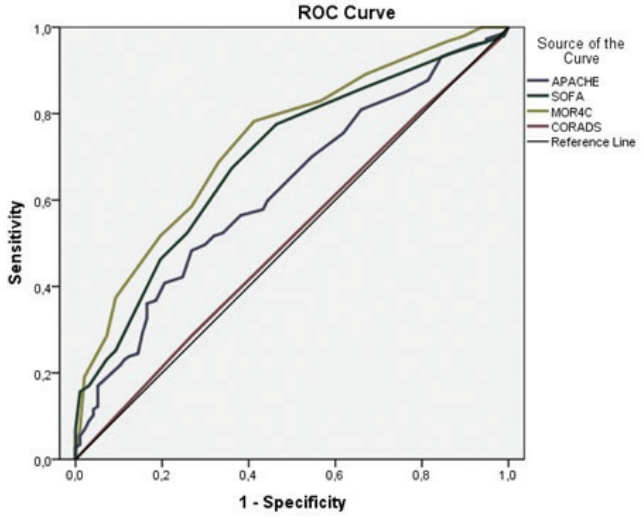

Figure 1. Four score ROC
ROC: Receiver operating characteristic, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, MOR4C: 4C mortality

Discussion

It was aimed to report APACHE-II score, SOFA score, the 4C mortality score and the CO-RADS classification in predicting outcome of COVID-19 in the ICU in this study. Mortality was 61.9% and was higher in older patients and septic patients.

Previous studies from China, Europe, and United States, have described different mortality rates among critically ill patients ranging from 53.8% to 60.4% (12-14). Studies from have reported that critically ill COVID-19 patients are generally older and have underlying medical conditions, such as hypertension and diabetes (12-14). Intensive Care National Audit & Research Centre have evaluated data for 12,420 admissions of 10,873 patents critically ill with confirmed COVID-19. They reported that mortality was 55.9% patients with confirmed COVID-19 and any advanced respiratory

Table 4. ROC analysis results by mortality

	Area under the curve (ROC)	95% CI	p	Cut-off	Sensitivity	Specificity
APACHE-II	0.616	0.549-0.684	0.001	≥19.5	53.2	65.7
SOFA	0.706	0.644-0.768	<0.001	≥4.5	78.9	53.3
GCS	0.688	0.626-0.750	<0.001	≤13.5	50.9	83.8
CO-RADS	0.509	0.435-0.583	0.802	≥5.5	28.6	26.8
4C mortality score	0.736	0.676-0.796	<0.001	≥11.5	78.9	58.1

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, ROC: receiver operating characteristic, CI: confidence interval

support (13). In our study, we found also that older patients and patients have comorbidities higher mortality than others.

COVID-19 mainly in severe cases in addition to lung involves different organs such as heart, liver, and kidney, as well as hematological and nervous system, and induce multi-organ failure (15). In our study, patients have high percentage of respiratory failure and sepsis.

Despite advances in patient care, distance measures, and population vaccination campaigns COVID-19 still causes a high rate of death, especially in elderly and comorbid patients. As of 21 October 2021 more than 250 million cases of COVID-19 have been stated with more than 4 million deaths globally since than December 2019 (16). Hospitals all over the world are confronted with an influx of patients with COVID-19. There is an urgent need for a practical risk identification which will allow which patients are at the highest risk of death. Clinicians should consider prioritizing some therapies for patients at highest risk of clinical progression because of the optimize resource allocation and to guide management. Prediction models for COVID-19 are quickly entering the COVID-19 literature to support therapeutic choice making at a time when needed.

Yang et al. (17) were reported that APACHE score and SOFA score were higher in died patients than in surviving patients. It was admitted fifty-two critically ill adult patients were with COVID-19 pneumonia in their study. Zou et al. (18) was aimed to investigate the APACHE score as a predictor for survival to facilitate decision-making for treatment in Wuhan. In predicting hospital mortality, APACHE-II score showed better discriminative ability (AUC, 0.966; 0.942-0.990, 95% CI) than SOFA score (AUC, 0.867; 0.808-0.926, 95% CI). APACHE-II demonstrated a sensitivity and specificity of 96% and 86%, respectively in ICU patients. Stephens et al. (19) wrote a letter to the editor for Zou's study (18) and stated that raising questions about the calibration of APACHE-II for COVID-19 patients. They noticed mortality higher than expected compared to relatively low APACHE-II scores. One hundred and sixteen COVID-19 patients admitted to the ICU were retrospectively analyzed in Vandenbrande et al. (20) study. They calculated APACHE-II, APACHE-IV scores and SOFA scores at admission. APACHE-IV had a higher value for AUC than APACHE-II (AUC, 0.67 vs. 0.63). APACHE-IV and APACHE-II have moderate discriminative power whereas the SOFA score had poor discriminative power (AUC: 0.53) in all patients. In another paper, it was used multivariable logistic regression methods to investigate the risk factors associated with in-hospital mortality. It was reported increasing odds of in-hospital mortality associated with higher SOFA score in 191 adult COVID-19 patients (21). In our study, we also reported that higher APACHE-II, SOFA, GCS and 4C mortality scores in non-survivor patients. APACHE-II and SOFA have AUC 0.616 and 0.706 respectively in our ICU paients. APACHE-II and SOFA have same sensitivity such as 78.9%. SOFA score have better AUC data than APACHE-II for predicting mortality in ICU COVID-19 patients.

The ISARIC/WHO 4C mortality score and the Jehi diagnostic model were reported as encouraging prediction models for COVID-19 (5). It was compared the ISARIC/WHO 4C mortality score to the CURB65, CRB65 and quick SOFA scores for to estimate 30-day mortality in patients with variety of respiratory infection in 606 patients. Fifty-three of 606 patients had COVID-19 infection. The ISARIC/WHO 4C mortality score had the highest AUC in COVID-19 patients for predicting mortality with value of 0.83 (22). Yildiz et al. (23) prospectively evaluated 4C mortality score, COVID-GRAM, NEWS2, CURB-65 and compare them for progress of critical disease and poor outcome in a COVID-19 patients. The ISARIC/WHO 4C mortality score, COVID-GRAM, CURB-65 and NLR on admission showed strong predictive accuracy for mortality with an AUC of 0.80, 0.74, 0.74 and 0.76 respectively. 4C mortality score had the highest value for mortality prediction in COVID-19 hospitalized patients. In this model, a total score was calculated. In our study, the highest predictive score was 4C mortality score in our critically ill patients.

Chest CT imaging shows a vital role in the diagnosis and evaluation of COVID-19 patients. The predictive value of high-resolution CT findings was reported in 181 mild-to-moderate and severe COVID-19 patients. It was shown that CT severity score might be a significant predictor of mortality in COVID-19 patients. The major chest CT finding is ground-glass opacity in both lungs, and multiple lobes in COVID-19 patients (24). The CO-RADS assessment scheme allows for the categorization of a chest CT scan. CO-RADS chest CT was greatly accurate for detecting COVID-19 pneumonia. The highest AUC (0.865) and accuracy (86.0%) was reported in the CO-RADS 4/5 group with a specificity of 112/132 (84.9%) and a sensitivity of 60/80 (88.2%) for diagnosing COVID-19 by RT-PCR test as the gold standard. Diagnostic value of CO-RADS on chest CT for the diagnosis of COVID-19 infection using the final clinical diagnosis as the standard of reference also have good result with AUC:

0.902 and accuracy (90.5%) in the CO-RADS 4/5 group (25). In our critically ill patients, CO-RADS was used for predicting of mortality in critically ill COVID-19 patients. CO-RADS was poor in predicting mortality in COVID-19 intensive care patients. In literature, there is no study that CO-RADS used COVID-19 for predicting mortality purposes.

If we were to comment on the mortality prediction of these five scorings used in our study, first, ROC curves studies may reach different values in different studies because of the difference in the patient population and the cut-off value chosen in the statistical method. In our study, CO-RADS did not give a significant result for predicting mortality. Although the most appropriate cut-off value is 5.5 and above, sensitivity and specificity values are quite low. The other four scores gave meaningful results and can be recommended for use mortality prediction. In our study, SOFA and 4C mortality score had the highest rates of accurate determination of mortality with 78.9%, but the probability of accurately determining survival in both was low.

This study has several limitations. It is a single center retrospective study and the study population was small. It was based on data mainly recorded hospital data base systems. Observer bias could be possible for CO-RADS evaluation.

Conclusion

SOFA and the 4C mortality score can be used to triage, guide decisions, and the clinical settings, to analyze early assessment of outcomes at admission. These scores may provide clinicians with a clue to discharge patients with low mortality scores or to manage early in patients whom need extra treatments. Future large studies should be aimed at developing and validating diagnostic and/or prognostic models for COVID-19 in ICU.

Ethics

Ethics Committee Approval: This is a single-center; retrospective cohort study that was analyzed anonymized data. After the Non-Invasive Clinical Researches Ethics Committee of the Pamukkale University this study was performed (no: 60116787-020-14366, date: 02.02.2021).

Informed Consent: Informed consent was waived because of the retrospective design of the study.

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Authorship Contributions

Surgical and Medical Practices: F.S., M.K., Mi.K., M.A., F.A., A.Ç., Concept: H.S., Design: H.S., Data Collection and Process: F.S., M.K., Mi.K., M.A., S.K., Analysis or Interpretation: H.S., F.A., Literature Search: H.S., F.S., M.K., Mi.K., M.A., Writing: H.S.

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ÖZGÜN ARAŞTIRMA / *ORIGINAL RESEARCH*

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Yoğun Bakım Hemşirelerinin Deliryum Hakkındaki Bilgi ve Yaklaşımlarının Değerlendirilmesi: Nitel Bir Çalışma

Evaluation of Intensive Care Nurses' Knowledge and Approaches About Delirium: A Qualitative Study

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ÖZ *Amaç:* Bu nitel çalışma, yoğun bakım hemşirelerinin deliryum hakkındaki bilgi ve yaklaşımlarını değerlendirmek amacıyla yapılmıştır.

Gereç ve Yöntem: Çalışmanın örneklemini dahiliye, cerrahi, nöroloji ve koroner yoğun bakımlarda çalışan 15 hemşire oluşturmuştur. Veriler, 15 Nisan-30 Haziran 2019 tarihlerinde yarı yapılandırılmış görüşme formu hazırlanarak Google Form aracılığıyla toplanmıştır. Verilerin analizinde içerik analizi yöntemi kullanılmıştır.

Bulgular: Araştırmaya katılan hemşirelerin yaş ortalaması 37,73±9,43 olup hepsi kadındır. Hemşirelerin %40'ı cerrahi, %26,7'si koroner, %20'si dahiliye ve %13,3'ü nöroloji yoğun bakımda çalışmaktadır. Meslekteki çalışma yılı ortalaması 17,27±10,40 ve yoğun bakımda çalışma yılı ortalaması 8,20±7,42'dir. Deliryumlu hastaya hepsi bakım vermiş ama sadece %33,3'ü deliryum hakkında eğitim almıştır. Yapılan içerik analizinden beş ana tema elde edilmiştir: Deliryumu tanımlama, deliryumu yönetme, bakımda yaşanan sorunlar, fiziksel ve ruhsal sorunlar yaşama ve bilgi ve beceri eksikliği.

Sonuç: Yoğun bakımdaki hemşirelerin deliryum konusunda bilgi gereksinimlerinin olduğu belirlenmiştir. Yoğun bakım hemşirelerine yönelik deliryum hakkında düzenli eğitimlerin planlanması önerilmiştir.

Anahtar Kelimeler: Yoğun bakım ünitesi, hemşire, deliryum, nitel çalışma

ABSTRACT *Objective:* This qualitative study was conducted to evaluate the knowledge and approaches of intensive care nurses to delirium.

Materials and Methods: The sample of the study consisted of 15 nurses working in the internal medicine, surgery, neurology and coronary intensive care units. Data were collected through Google Form by preparing a semi-structured interview form between April 15 and June 30, 2019. The content analysis method was used in the analysis of the data.

Results: The mean age of the nurses is 37.73±9.43, and all of them are women. Of them, 40% worked in surgery, 26.7% in coronary, 20% in internal medicine, and 13.3% in neurology intensive care. The average of working years in the profession is 17.27±10.40 and the average of working years in intensive care is 8.20±7.42. All of them provided care to the patients with delirium, but only 33.3% received training on delirium. Five main themes are obtained from the content analysis: defining delirium, managing delirium, problems in care, experiencing physical and mental problems, and lack of knowledge and skills.

Conclusion: It has been determined that nurses in intensive care need knowledge about delirium. It is recommended to plan regular training on delirium for intensive care nurses.

Keywords: Intensive care unit, nurse, delirium, qualitative study

Giriş

Deliryum, bilişsel değişim ve çevreye sınırlı dikkat ile karakterize edilen bir bilinç bozukluğudur. Hastaların uyku bozuklukları, bilişsel işlevlerde değişiklikler, kaygı, korku veya sinirlilik geliştirme olasılığı vardır. Hafıza, algı, çevreyi anlama gibi alanlar da bozulmaktadır (1). Deliryum sırasında serebral kan akımı etkilenmiş gibi görünmektedir ve bu bozukluk bir süre devam ederse nöral doku ölümünü de tetikleyebilmektedir (2). Deliryum olguları en çok yoğun bakım ünitelerinde görülmektedir. Yoğun bakım ünitesinde deliryum insidansı %11 ile %87 arasında değişmektedir. Deliryum riski özellikle yaşlı kişilerde, önceden bilişsel bozukluğu olanlarda, ölümcül hastalıkları olanlarda, büyük cerrahi geçiren hastalarda ve yoğun bakım ünitesine kabul edilenlerde yüksektir. Komorbiditeler, hastalık şiddeti, ilaçlar ve tütün bırakma, yoğun bakım koşulları ve çeşitli tedaviler, yoğun bakım ünitesinde deliryum için ortak risk faktörleridir (3).

Deliryumun erken dönemde tanılanıp tedavi edilmesi önemlidir çünkü pek çok olumsuz sonuca ve ölüme yol açabilmektedir. Yoğun bakımda yatan hastalarla yapılan bir çalışmada, deliryum gelişen ve gelişmeyen hastalar karşılaştırılmıştır. Deliryum gelişen hastaların daha hasta oldukları, mekanik ventilasyon ile hastanede kalış sürelerinin daha uzun olduğu, demansla uyumlu bilişsel fonksiyonlarının bozulduğu ve daha çok akut stres ve travma sonrası stres bozukluğu geliştiği saptanmıştır (4). Dahiliye yoğun bakımda yapılan diğer bir çalışmada, hastaların %19'unda deliryum geliştiği, mekanik ventilasyon süresinin ve yoğun bakımda yatış süresinin uzun olmasının deliryum ile ilişkili olduğu saptanmıştır (3). Yoğun bakımlarda yapılan bir başka çalışmada ise hastaların %44,4'ünde deliryum geliştiği ve fiziksel sınırlılıkların, ortam değişiklikleri gibi uygulamaların deliryum gelişiminde önemli faktörler olduğu bildirilmiştir (5).

Deliryumun erken tanınması, tıbbi hastalığın tedavisi, hastanın uyumu ve sendromun geri dönüşümsüz aşamaya gelmemesi ya da yaygın hasar bırakmaması açısından çok önemlidir. Deliryumla ilgili çok şey bilinmesine karşın, genel hastanelerde deliryum tanısı sık sık atlanmakta ve sağlık çalışanları bu konuda eğitime ihtiyaç duymaktadır. Bu konuda hastaya 24 saat kesintisiz bakım veren hemşirelerin konuya ilişkin bilgi düzeyleri önem taşımaktadır. Dahili ve cerrahi yoğun bakımlarda çalışan hemşirelerle yapılan bir çalışmada, hemşirelerin %70'i deliryum tanısı alan hastaların yönetilmesinin çok zor olduğunu ve özel eğitim alınması gerektiğini, %85'i deliryum konusunda eğitim almak istediklerini belirtmişlerdir (6). Yoğun bakım ünitelerinde çalışan hemşirelerle yapılan diğer bir çalışmada, hemşirelerin %67,6'sı deliryum tanımını bildiklerini ifade etmelerine karşın yalnızca %32,9'unun deliryum tanımını doğru yapabildikleri belirlenmiştir (7).

Bu çalışmada ilimizdeki yoğun bakım hemşirelerinde deliryum hakkında bilgi ve uygulamaların ne durumda olduğu araştırılmak istenmiştir. Daha önce yapılan çalışmalar incelenmiştir. Eğitimsel müdahalelerin yoğun bakım hemşirelerinin deliryum konusunda bilgilerini ve özgüvenlerini artırdığı ve deliryumlu hastaya yönelik tutumlarını geliştirdiği belirlenmiştir (8). Ayrıca hemşirelerin yoğun bakımda yatan hastaları deliryum açısından değerlendirme becerilerinin ve oranlarının arttığı saptanmıştır (9). Uygulanan deliryum değerlendirme ve önleme programı sağlık çalışanlarının bilgi düzeylerini artırmış, hastanın hastanede kalış süresini kısaltmış ve deliryum oranlarını azaltmıştır (10). Bu sonuçlar doğrultusunda, hemşirelerin deliryum konusunda bilgi düzeylerini değerlendirmenin ve geliştirmenin hastanın yaşam kalitesi açısından çok değerli olduğunu söyleyebiliriz. Bu nedenle bu çalışmada, yoğun bakımlarda çalışan hemşirelerin deliryum hakkındaki bilgi ve yaklaşımlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem

Araştırmanın Türü

Araştırma yoğun bakımlarda çalışan hemşirelerin deliryum hakkındaki bilgi ve yaklaşımlarını belirlemek amacıyla fenomenolojik tanımlayıcı nitel bir çalışma olarak yapılmıştır. Bu çalışma Consolidated Criteria for Qualitative Studies kontrol listesine göre rapor edilmiştir (11).

Araştırmanın Evreni ve Örneklemi

Araştırmanın evrenini, bir eğitim ve araştırma hastanesi 2. basamak yoğun bakımlarda çalışan 39 hemşire oluşturmuştur. Dahiliye yoğun bakımda 9, cerrahi yoğun bakımda 8, nöroloji yoğun bakımda 9 ve koroner yoğun bakımda 13 hemşire çalışmaktadır. Evrende ulaşılacak kişi sayısının az olması, hemşirelerin yoğun çalışma koşullarında çalışmaları ve boş zaman bulabilmelerinin zor olması gibi nedenlerle ve nitel yöntemlerle derinlemesine analiz yapılacağı için yeterli kişiye ulaşabilmek için herhangi bir örnekleme yönteme kullanılmamış olup bütün evrene ulaşılmaya çalışılmıştır. Araştırmaya katılmayı kabul eden ve dahil olma kriterlerine uyan 15 hemşire araştırmanın örneklemini oluşturmuştur.

Dahil Olma Kriterleri

Çalışmaya dahil olma kriterleri; 18-65 yaş aralığında olmak, 2. basamak yoğun bakımlardan birinde en az bir yıldır çalışıyor olmak, çalışmaya katılmaya gönüllü olduğuna dair yazılı onam vermek ve sorulan soruları eksiksiz yanıtlandırmaktır.

Veri Toplama Süreci

Veriler, 15 Nisan-30 Haziran 2019 tarihlerinde yarı yapılandırılmış görüşme formu hazırlanarak Google Form aracılığıyla toplanmıştır. Oluşturulan link eğitim hemşiresi tarafından WhatsApp gruplarında paylaşılmıştır. Formun ilk bölümüne, araştırmanın amacı ve süresi, isimlerin gizli tutulacağı, bilgilerin yalnızca araştırma amacıyla kullanılacağı konusunda bilgi verilmiş ve hemşirelerin çalışmaya gönüllü katıldıklarına dair bir soru eklenmiştir. Bu soruda "evet" seçeneğini işaretleyerek çalışmaya katılmayı kabul eden hemşirelerin yazılı onamları online olarak alınmıştır.

Araştırma ekibi hemşirelik alanında uzman ve uygulama deneyimi olan akademisyenlerden oluşmuştur. Araştırmacılardan biri, bir devlet üniversitesinde psikiyatri hemşireliği alanında doçent olarak çalışan kadın bir akademisyendir. Diğer iki araştırmacı ise bir devlet üniversitesinde hemşirelik esasları alanında doktor öğretim üyesi olarak çalışan kadın akademisyenlerdir. Araştırmacıların hepsi nitel araştırma yöntemleri konusunda eğitim almışlardır.

Veri Toplama Formları

Araştırmada verilerin toplanmasında; "Demografik Bilgi Formu" ve "Yarı Yapılandırılmış Görüşme Formu" kullanıldı.

Demografik Bilgi Formu: Hemşirenin yaşı, cinsiyeti, eğitim düzeyi, çalıştığı birim, meslekteki yılı, bulunduğu yoğun bakımdaki çalışma yılı, deliryum hakkında eğitim alıp almadığı ve deliryumlu bir hastaya bakım verip vermediği gibi bilgileri elde etmeye yönelik sorulardan oluşmaktadır (6-10).

Yarı Yapılandırılmış Görüşme Formu: İlgili literatür doğrultusunda hazırlanan form (12,13), hemşirenin deliryum hakkındaki bilgi ve yaklaşımlarını değerlendirebilmek için şu sorulardan oluşmaktadır:

1. Bakım verdiğiniz hastanızda hangi belirtileri gördüğünüzde hastanızda deliryum geliştiğini düşünürsünüz?

2. Deliryumlu bir hastaya bakım verdiğinizde, özellikle deliryuma özgü belirti ve bulgulara yönelik hastaya hangi girişimleri uygularsınız?

3. Deliryumlu bir hastaya bakım verirken hangi konularda sorunlar yaşıyorsunuz ya da zorlandığınızı hissediyorsunuz? Hangi belirtileri yönetmede zorlanıyorsunuz?

4. Bu sorunlarla mücadele ederken neler hissediyorsunuz? Neler düşünüyorsunuz?

5. Deliryumlu bir hastanın bakımını etkin bir biçimde yönetebilmek için sizce bir hemşire hangi konularda bilgi sahibi olmalıdır ve hangi becerilere sahip olmalıdır?

İstatistiksel Analiz

Katılımcılardan elde edilen veriler, Corbın ve Strauss (14) tarafından önerilen ve benzer özellikleri bulmak için verileri analiz eden, organize eden ve karşılaştıran sürekli karşılaştırmalı yöntem kullanılarak kopyalanmış ve analiz edilmiştir. Analizler teorik doygunluk noktasına, yani benzer içeriğin tekrar tekrar ortaya çıktığı ve yeni kategorilerin ortaya çıkmadığı noktaya kadar yapılmıştır (15). Açık kodlama sırasında, ana temalar ve alt temalar belirlenmiş ve araştırmacılar arasında tartışma ve fikir birliği oluşturularak aralarındaki ilişkiler belirlenmiştir. Araştırmada 4 tema ve 14 alt tema belirlenmiştir.

Verilerin Güvenilirliği

Her bir açıklamayı desteklemek ve verilerin güvenilirliğini sağlamak için alıntılar seçilmiştir (16). Güvenilirlik genellikle güvenilirlik, uygunluk, aktarılabilirlik ve özgünlük gibi terimler kullanılarak sunulur. Güvenilirliği sağlamak için araştırmaya katılan hemşirelerin doğru bir şekilde belirlenmesini ve tanımlanmalarını sağlıyoruz. Uygunluğu sağlamak için, iki araştırmacı arasındaki verilerin doğruluğu, uygunluğu veya anlamı hakkında uyumu değerlendiririz. Aktarılabilirlik, ekstrapolasyon potansiyelini ifade eder. Bulguların genelleştirilebileceği veya diğer ortamlara veya gruplara aktarılabileceği mantığına dayanır. Son kriter olan özgünlük, araştırmacıların adil ve sadık bir şekilde bir dizi gerçekliği ne ölçüde gösterdiğini ifade eder (17).

Araştırmanın Etik Boyutu

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Bulgular

Katılımcıların sosyodemografik özellikleri Tablo 1'de görülmektedir. Araştırmaya katılan hemşirelerin yaş ortalaması 37,73±9,43 [minimum (min) =23, maksimum (maks) =48] olup hepsi kadındır. Hemşirelerin 14'ü lisans ve 1'i

Tablo 1. Katılımcıların sosyodemografik özellikleri

Katılımcı	Yaş	Cinsiyet	Eğitim durumu	Çalıştığı birim	Meslekteki yılı	Yoğun bakımdaki yılı	Deliryum hakkında eğitim	Deliryumlu hastaya bakım
N1	40	Kadın	Lisans	Koroner YB	22	17	Hayır	Evet
N2	44	Kadın	Lisans	Koroner YB	26	26	Evet	Evet
N3	38	Kadın	Lisans	Koroner YB	20	18	Hayır	Evet
N4	48	Kadın	Lisans	Koroner YB	28	5	Hayır	Evet
N5	35	Kadın	Lisans	Nöroloji YB	14	6	Hayır	Evet
N6	41	Kadın	Lisans	Cerrahi YB	20	6	Hayır	Evet
N7	48	Kadın	Lisans	Dahiliye YB	27	13	Evet	Evet
N8	23	Kadın	Lise	Cerrahi YB	1	1	Hayır	Evet
N9	23	Kadın	Lisans	Cerrahi YB	1	1	Hayır	Evet
N10	41	Kadın	Lisans	Dahiliye YB	21	2	Hayır	Evet
N11	24	Kadın	Lisans	Nöroloji YB	2	1	Hayır	Evet
N12	46	Kadın	Lisans	Cerrahi YB	28	10	Evet	Evet
N13	44	Kadın	Lisans	Cerrahi YB	20	8	Evet	Evet
N14	46	Kadın	Lisans	Cerrahi YB	26	7	Evet	Evet
N15	25	Kadın	Lisans	Dahiliye YB	3	2	Hayır	Evet

YB: Yoğun bakım

lise mezunudur. Onların 6'sı cerrahi, 4'ü koroner, 3'ü dahiliye ve 2'si nöroloji yoğun bakımda çalışmaktadır. Meslekteki çalışma yılı ortalaması 17,27±10,40 (min =1, maks =28) ve yoğun bakımda çalışma yılı ortalaması 8,20±7,42'dir (min =1, maks =26). Deliryumlu hastaya hepsi bakım vermiş ama sadece beş kişi deliryum hakkında eğitim almıştır.

Yapılan içerik analizinde beş ana tema elde edilmiştir: Deliryumu tanımlama, deliryumu yönetme, bakımda yaşanan sorunlar, fiziksel ve ruhsal sorunlar yaşama ve bilgi ve beceri eksikliğidir (Tablo 2).

Tema 1: Deliryumu Tanımlama

Burada elde edilen alt temalar bilinçte bozulma, algılamada bozulma, duygulanımda bozulma, oryantasyonda bozulma ve davranışta bozulmadır. Hemşirelerin deliryumu tanımlamada zorlandıkları belirlenmiştir. Kimisi algılamada yaşanan sorunlar doğrultusunda ifade ederken kimisi bilinçte geçici bozulma şeklinde ifade etmiştir. Saldırganlık olarak tanımlayanlar olduğu gibi oryante olamama şeklinde de tanımlanmıştır.

"Geçici bilinç bulanıklığıdır." (N1)

"Hastanın psikolojik olarak olduğu ortama uyum sağlamayıp belirli tepkiler vermesidir. Örneğin; krize girmesi…" (N9)

"Hastanın anlamsız davranışarı ile beraber yaşadığı öfke nöbetleridir." (N12)

"Halüsinasyon görme, bilinç bulanıklığıdır." (N15)

Tema 2: Deliryumu Yönetme

Burada elde edilen alt temalar fizyolojik gereksinimlerini karşılama, güvenli bir ortam oluşturma, sosyal destek sağlama, psikososyal bakım verme ve ilaç tedavisini uygulamadır. Hemşireler kapsamlı bir şekilde deliryumlu hastanın yönetimini sağlamada yetersiz kalmışlardır. Kimisi fiziksel bakıma odaklanırken kimisi de psikososyal bakıma odaklanmıştır. Bir kısmı da sadece ilaç tedavisinden söz etmiştir.

"Konuşmaya, sakinleştirmeye çalışırım ama eğer baş edemiyorsam doktora haber veririm." (N5)

"Hasta ile iletişimde bulunarak hastanın güvende olduğunu hissetmesi için sakinleşmesini sağlarım. Empati kurarak girişimler uygulamaya çalışırım." (N10)

"Saturasyon düşüklüğü sebebiyle olduysa hemen oksijen desteği sağlarım. Yer ve zamanı hatırlatırım. Ajitasyonun giderilmesine yönelik sakinleştirmeye çalışırım." (N11)

"Doktora haber vererek hastayı kısıtlarım." (N15)

Tablo 2. Temalar, alt temalar ve hemşirelerin ifadeleri		
Temalar	**Alt temalar**	**Hemşirelerin ifadeleri**
Deliryumu tanımlama	Bilinçte bozulma Algılamada bozulma Duygulanımda bozulma Oryantasyonda bozulma Davranışta bozulma	"…. geçici bilinç bulanıklığı" (N1) "… halüsinasyon görmesi" (N15) "… anlamsız konuşması" (N13) "… zaman ve mekan uyumlarında bozulma olması" (N4) "… bir anda bağırıp çağırması ve etrafa saldırmaya başlaması" (N5)
Deliryumu yönetme	Fizyolojik gereksinimlerini karşılama Güvenli bir ortam oluşturma Sosyal destek sağlama Psikososyal bakım verme İlaç tedavisini uygulama	"Saturasyon düşüklüğü nedeniyle olduysa hemen oksijen desteği veririm." (N10) "Çevresinin farkında olmayan hastanın öncelikle güvenliğini sağlar, sakin ve sessiz bir ortam oluştururum." (N12) "Yakınını bir süre yanına alırım." (N3) "Konuşmaya, sakinleştirmeye çalışırım." (N4) "Anksiyolitik ilaca ihtiyacı olabileceği için doktora haber veririm." (N15)
Bakımda yaşanan sorunlar	Ajitasyonu yönetme İletişim kurma Hastanın güvenliğini sağlama Tedavi uyumunu sağlama	"Saldırgan tavırlara karşı zorlanıyorum." (N14) "Anlatılanları anlamama konusunda çok sıkıntı yaşıyorum." (N2) "Düşme riski ve kendine zarar verme riskini yönetmede zorlanıyorum." (N7) "Hasta serumunu çıkartabiliyor ve kendine zarar verebiliyor." (N9)
Fiziksel ve ruhsal sorunlar yaşama	Tükenmişlik Yorgunluk Stres Direnmek	"Meslekten bıktığımı hissediyorum." (N15) "Çok yorucu ve zor bir süreç." (N7) "Kendimi gergin hissediyorum." (N11) "Sabırlı olmaya, uyumla yaklaşmaya çalışıyorum." (N13)
Bilgi ve beceri eksikliği	Yardım edici iletişim becerileri Hastalık bilgisi Psikobiyolojik girişimler Duygu yönetimi	"Hastanın ne hissettiğini anlayabilmek isterdim." (N6) "Deliryum bir kişilik bozukluğu değildir. Hastalık hakkında bilgi almak isterdim." (N4) "Stresle başa çıkma, davranış yönetimi ve psikoteknikler konusunda eğitim almak isterdim." (N8) "Sabırlı olmayı, sinirlerime hakim olmayı ve sakin kalabilmeyi öğrenmek isterdim." (N10)

Tema 3: Bakımda Yaşanan Sorunlar

Hemşireler bakım verirken birtakım sorunlar yaşadıklarını ifade etmişlerdir. Bu doğrultuda elde edilen alt temalar ajitasyonu yönetme, iletişim kurma, hastanın güvenliğini sağlama ve tedavi uyumunu sağlamadır. Hemşireler hastanın saldırgan davranışını yönetmede, bilişsel yetileri bozulan hasta ile iletişim kurmada ve hastanın tedaviye uyumunu sağlamada zorlandıklarını bildirmişlerdir. Deliryumlu hastanın düşme riskini ve kendine zarar verme davranışını yönetmede de zorlanmışlardır.

"Tedavi ve bakım konusunda, saldırganlığı yönetmede ve anlatılanları anlamama konusunda hastayla çok sıkıntı yaşıyorum." (N2)

"Kısıtlamak zorunda kalırsak hastanın deliryumu derinleşiyor. Saldırgan tavırlar çoğu zaman etrafa zarar veriyor." (N4)

"İnvaziv girişimleri çıkartabiliyor ve kendine zarar verebiliyor." (N9)

"Öfke nöbetleri konusunda zorlanıyorum. Hasta hem kendisi hem de çevresi için tehlike arz edebiliyor." (N12)

Tema 4: Fiziksel ve Ruhsal Sorunlar Yaşama

Burada elde edilen alt temalar tükenmişlik, yorgunluk, stres ve direnmektir. Yoğun bakımda çalışan hemşireler deliryumlu hasta ile çalışırken mesleklerinden soğuduklarını ifade etmişlerdir. Deliryumlu hasta ile çalışmanın yorucu bir süreç olduğunu ve bu nedenle kendilerini gergin hissettiklerini bildirmişlerdir. Hemşirelerin bazıları ise hastaya karşı sabırlı olmaya çalıştıklarını ve ılımlı bir yaklaşım gösterdiklerini belirtmişlerdir.

"Ajite hastaya bakarken hem hastayı hem kendimi hem de diğer hastaları güvende hissetmiyorum. Kendimi çok yoğun bir stres altında hissediyorum. Güvenliğimden endişe duyuyorum." (N3)

"Çok yorucu ve zor bir süreç." (N7)

"Çok zorlandığımı hissediyorum ve nasıl bir çözüm bulmam gerektiğini bilmiyorum." (N8)

"Meslekten bıktığımı hissediyorum." (N15)

Tema 5: Bilgi ve Beceri Eksikliği

Burada elde edilen alt temalar ise yardım edici iletişim becerileri, hastalık bilgisi, psikobiyolojik girişimler ve duygu yönetimidir. Hemşireler, deliryumlu hastaya bakım verirken bilgi ve beceriye ihtiyaç duymuşlardır. Hemşireler hastalık konusunda daha fazla bilgi almak, hastanın duygularını tanımlama, hastanın stresini ve davranışını yönetme ile kendi duygularını yönetme konusunda becerilerini geliştirmek istediklerini bildirmişlerdir.

"Deliryum konusunda daha kapsamlı bir bilgiye ihtiyaç duyuyorum." (N2)

"Sakin, sabırlı olma, iyi bir iletişim becerisi ve iyi bir psikiyatri bilgisine sahip olma konusunda eğitime ihtiyaç olduğunu düşünüyorum." (N3)

"Empati kurmak, etkin iletişim kurmak, sabırlı ve şefkatli olmak gibi konularda bilgili ve beceriye ihtiyaç var." (N10)

"Hastanın sağlığını geliştirmek, iyileşmesini sağlamak ve hastalığın nüksetmesini önlemek için bilgi ve beceriye gereksinim duyulmaktadır." (N12)

Tartışma

Bu çalışmada, yoğun bakımda çalışan hemşirelerin deliryum tablosunu tanımlamada zorlandıkları belirlenmiştir. Tanımlar bilinçte bozulma, algılamada bozulma, duygulanımda bozulma, oryantasyonda bozulma ve davranışta bozulma olarak ayrı ayrı yapılmıştır. Bütüncül bir tanımlama yapılamamıştır. Oysaki deliryum, bilişsel değişim ve çevreye sınırlı dikkat ile karakterize edilen bir bilinç bozukluğudur. Hafıza, algı, çevreyi anlama gibi alanlar da bozulmaktadır. Bu çalışmada olduğu gibi konfüzyon, oryantasyon bozukluğu ve ajitasyon gibi temel deliryum semptomları hemşireler tarafından daha iyi tanımlanmaktadır (1). Benzer şekilde, yoğun bakım ünitelerinde çalışan hemşirelerle yapılan bir çalışmada, hemşirelerin çoğunluğu deliryum tanımını bildiklerini ifade etmelerine karşın yalnızca üçte birinin deliryum tanımını doğru yapabildikleri belirlenmiştir (7). Bir başka çalışmada, hemşirelerin deliryum hakkında sınırlı bilgiye sahip oldukları ve sadece %38'inin deliryumu doğru tanımlayabildikleri belirlenmiştir (18). Yapılan bir başka çalışmada ise deliryum hakkında eğitim almayan hemşirelerin deliryum hakkında daha düşük düzeyde bilgiye sahip oldukları ve son bir yıl içinde sadece bir hemşirenin (%1,6) deliryum ile ilgili eğitime/derslere katıldığını, %98,4'ünün ise deliryum hakkında herhangi bir eğitime/derse katılmadığını ortaya koymuştur (19). Bu sonuçlar doğrultusunda, yoğun bakımda çalışan hemşirelerin deliryum konusunda bir eğitime ihtiyaç duyduklarını söyleyebiliriz.

Bu çalışmada, hemşirelerin deliryumlu bir hastayı yönetmede ve hastanın yönetimini tanımlamada sorunlar yaşadıkları saptanmıştır. Elde edilen başlıklar fizyolojik gereksinimlerini karşılama, güvenli bir ortam oluşturma, sosyal destek sağlama, psikososyal bakım verme ve ilaç tedavisi olarak belirlense de çoğunluk bu girişimlerden bir tanesini söyleyebilmiştir. Yoğun bakımlarda çalışan hemşirelerle yapılan bir çalışmada, hemşirelerin %70'i deliryum tanısı alan hastaların yönetilmesinin çok zor olduğunu ve özel eğitim alınması gerektiğini ifade etmiştir (6). Bir başka çalışmada, hemşirelerin deliryumlu hastalara karşı negatif tutumları nedeniyle deliryum tablosunu yönetmede zorlandıkları bildirilmiştir (18). Avustralya'da yoğun bakımda çalışan hemşire ve doktorlarla yapılan bir çalışmada, girişimi hastanın sakin veya ajite olup olmamasına göre karar verdikleri, ajite hastaya ilaç tedavisi uyguladıkları ve sakin hastaya gereksiz ilaç tedavisinden kaçındıkları belirlenmiştir. Katılımcıların hepsi non-farmakolojik yöntemlerin iyi bir hemşirelik bakımı olduğunu bildirmişlerdir (20). Güvenli destekleyici bir ortam oluşturma, hastanın oryantasyonunu sağlama, vital bulgularını yakından takip etme, deliryuma neden olan etiyolojiyi tanımlama, laboratuvar bulgularını gözden geçirme, ağrıyı değerlendirme ve yönetme, uyku hijyenini sağlama, hastanın mobilizasyonunu sağlama, ailenin katılımını artırma ve ajitasyonu azaltmak için müzik dinleme gibi teknikler kullanmak non-farmakolojik yöntemlerdendir (21,22). Non-farmakolojik yöntemler deliryumun sıklığını ve süresini, hastanın hastanede kalış süresini ve mortalite oranlarını azaltmada önemli girişimlerdir (23). Bu bulgular, hemşirelerin deliryumlu hastayı yönetmede yetersiz olduklarını göstermektedir.

Bu çalışma, hemşireler deliryumlu hastaya bakım verirken ajitasyonu yönetme, iletişim kurma, hastanın güvenliğini sağlama ve tedavi uyumunu sağlama gibi alanlarda sorunlar yaşadıklarını saptamıştır. Benzer bir çalışmada, yoğun bakım ünitesinde çalışan hemşireler deliryumlu hastanın yönetiminin çok zor olduğunu, çevresel etkenlerin, sağlık personeli, hasta ve hasta yakınları arasındaki etkileşimin ve hemşirelerin tutumlarının bu süreci olumsuz etkileyebileceğini ifade etmişlerdir (23). Hemşireler ve doktorlarla yapılan bir çalışmada, onlar deliryumlu hastanın teşhisinde

ve yönetiminde yetersizlikler olduğunu bildirmişlerdir. Hemşireler, özellikle, sözel kısıtlama uygularken, uyku bozukluklarını yönetirken ve erken mobilizasyonu sağlarken zorluklarla karşılaştıklarını belirtmişlerdir (24).

Yoğun bakımda hastanın yönetimi hemşireler için önemli bir stres kaynağıdır. Çünkü hastalar etkin bir biçimde yönetilemediğinde hemşireler saldırı, şok ve korku gibi fiziksel ve ruhsal sorunlar yaşamaya başlamaktadır (25). Bu çalışmada da hemşireler tükenmişlik, yorgunluk, stres gibi sorunlar yaşadıklarını ifade etmişlerdir. Ayrıca hastaya karşı sabırlı olmaya çalışan ve ılımlı bir yaklaşım gösteren hemşireler bu duruma daha iyi direnç gösterdiğini ifade etmiştir. Benzer şekilde, deliryumlu hastaya bakım verirken hemşirelerin %64,5'inin özellikle zorlayıcı davranışları olan hasta karşısında endişe, korku, kaygı, stres, şok ve panik duyguları yaşadıkları belirlenmiştir. Bazıları da fiziksel olarak yıpranmış, bitkin ve yorgun hissettiklerini bildirmiştir (10). Bir başka çalışmada, hemşireler, deliryumlu hastayı dinleme ve takip etme gibi bakım stratejilerinin hemşirelerin zamanını tükettiğini bildirmiştir. Ayrıca, deliryumlu hastalara bakmak stres, kaygı ve zihinsel çatışmalar yaratmıştır (26). Bu sonuçlar, hemşirelerin fiziksel ve ruhsal anlamda sağlıklarını korumak ve sürdürmek için desteklenmeleri gerektiğini de ortaya koymuştur.

Son olarak, bu çalışmada hemşireler yardım edici iletişim becerileri, hastalık bilgisi, psikobiyolojik girişimler ve duygu yönetimi gibi konularda eğitim almak gerektiğini ifade etmişlerdir. Yapılan çalışmalarda, hemşireler deliryum konusunda eğitim almak istediklerini, hastayla iletişim kurmanın çok zor olduğunu ve hastayla iletişimi geliştirecek araçlardan yoksun olduklarını belirtmişlerdir (6,27). Hemşireler, deliryumun süreci ve seyri hakkında bilgisiz olduklarını, hastalarını anlamakta, hastalara ve gerçeklerine ulaşmakta güçlük çektiklerini ifade etmişlerdir. Bilgi ve eğitim eksikliğinin hasta ihtiyaçlarının karşılanmasında önemli bir engel olduğunu da eklemişlerdir (26). Diğer çalışmalarda ise yoğun bakımda çalışan hemşirelerin büyük çoğunluğunun deliryum değerlendirmesinde, standart bir değerlendirme aracı kullanmadığı da belirtilmiştir (28-30). Bu sonuçlar doğrultusunda, yoğun bakımda çalışan hemşirelerin bütüncül ve kapsamlı bir eğitime ihtiyaç duydukları söylenebilir.

Bu çalışmada nitel araştırma yöntemlerinden fenomenolojik yaklaşım kullanılmıştır. Nitel araştırma, araştırmacının belirli bir olgunun nasıl veya neden oluştuğuna ilişkin soruları yanıtlamaya çalıştığı bir sorgulama yöntemini ifade etmektedir (31). Fenomenolojik araştırma yöntemi ile az sayıda örneklem ile detaylı veri toplanabildiği ifade edilmekte ve örneklem sayısının nitel araştırmalar için önemli olmadığı belirtilmektedir. Bu yöntemde, araştırmacının bu konuda eğitim almış olması ve konuya hakim olması da çok önemlidir. Çünkü derinlemesine ve yoğun bir analiz ile kişilerin öznel yaşantıları ayrıntılı bir biçimde değerlendirilebilmektedir (32). Nitel araştırmalar, kronik hastalığı olan hastaların geçirdiği bazı süreçleri ve kronik hastalıkla yaşamanın ne anlama geldiğini ortaya çıkarmaktadır. Bakım alma ve bakım vermeyle ilgili süreçler hakkında yeni bilgiler edinilmektedir. Hemşirelere hastaların yaşanmış deneyimlerini anlamalarını sağlamaktadır. Bu anlayış iyi bir hemşirelik bakımı için gereklidir (33). Dolayısıyla kullanılan yöntem deliryum konusunda yoğun bakımda çalışan hemşirelerin deneyimlerini, bilgi ve becerilerini daha kapsamlı, yoğun ve derinlemesine analiz etmek için güzel bir fırsat sunmuştur. Sorunun daha iyi anlaşılmasını, hemşirelerin hem bilgi ve beceri konusunda eğitime hem de yaşadıkları psikolojik semptomlar nedeniyle psikolojik olarak desteklenmeye ihtiyaç duyduklarını göstermiştir.

Bu çalışmanın bazı sınırlılıkları bulunmaktadır. Araştırma bulguları sadece bu örneklem için genellenebilir. Bütün evrene genelleyebilmek için daha kapsamlı çalışmalar yapılmalıdır. Deliryum olgusu ile hemşirelerin deliryum hakkında bilgi ve becerilerinin, deneyimlerinin ve yaşadıkları sorunların daha iyi anlaşılabilmesi daha geniş örneklemlerde benzer çalışmalar yürütülmelidir.

Sonuç

Araştırmaya 15 yoğun bakım hemşiresi katılmıştır. Çoğunluğu deliryum hakkında eğitim almamıştır. Toplanan nitel verilerin analizi sonucunda, hemşirelerin deliryumu tanımlamada ve uygun girişimleri planlamada zorlandıkları, deliryumlu hastanın yönetiminde iletişim, ajitasyon, güvenlik ve tedaviye uyum konularında sıkıntılar yaşadıkları, hastaya bakım verirken çoğunluğun tükenmişlik ve stres gibi duygular yaşadıkları ve iletişim becerileri, hastalık bilgisi, psikobiyolojik girişimler ve duygu yönetimi gibi konularda eğitime gereksinim olduğu belirlenmiştir. Bu doğrultuda, yoğun bakımda çalışan hemşirelere deliryumun tanılanması ve yönetimi konusunda eğitim verilmelidir. Fiziksel ve ruhsal sorunlar yaşayan hemşireler belirlenerek danışmanlık almaları konusunda desteklenmelidir. Bu anlamda, eğitim eksikliğinin giderilmesi, stres yönetimi, gevşeme egzersizleri ve bilinçli farkındalık temelli girişimlerin uygulanması yararlı

olabilir. Ayrıca ajite hastaya yaklaşım, non-farmakolojik tedavi yöntemleri, zor hastayla iletişim gibi konularda da eğitim verilmesi hemşireleri ve hemşirelik bakımını güçlendirecektir. Hastaların yaşam kalitesini yükseltmek ve morbidite ile mortalite oranlarını düşürmek adına hemşirelerin deliryum konusundaki bilgi ve beceri düzeylerinin tanımlanması önemlidir. Bu nedenle bu konunun daha geniş örneklemlerde çalışılması yararlı olacaktır.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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The Impact of the COVID-19 Pandemic on Tracheostomy Applications in the COVID and Non-COVID Intensive Care Units: A Single-center Experience

COVİD-19 Pandemisinin COVİD ve COVİD Dışı Yoğun Bakımlarda Trakeostomi Uygulamalarına Etkisi: Tek Merkez Deneyimi

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ABSTRACT *Objective:* In the early stages of the pandemic, there were reservations about early tracheostomy due to the high risk of infection transmission. We reported the clinical characteristics and outcomes of patients who underwent an elective tracheostomy during the pandemic.
Materials and Methods: The data from patients who underwent the elective tracheostomy between March 20, 2020, and January 01, 2021, were evaluated retrospectively. Medical records were analyzed for age, gender, comorbidities, complications, and outcomes. The duration from intubation to tracheostomy and the length of intensive care unit (ICU) and hospital stay were calculated. The data of coronavirus disease-2019 (COVID-19) patients (group I) and non-COVID-19 patients (group II) were compared. Additionally, early tracheostomy (≤14 days) and late tracheostomy (>14 days) groups were compared in terms of clinical outcomes.
Results: A total of 144 patients, 70 of whom were diagnosed with COVID-19, were included. Tracheostomy was performed on the median 19th day in both groups (p=0.85). Percutaneous tracheostomy (68.6%) was performed more frequently in COVID-19 patients. The time of tracheostomy application had no positive effect on mortality in either groups. Bleeding occurred less frequently in group I.
Conclusion: Percutaneous tracheostomy was performed more frequently in COVID-19 patients. Percutaneous tracheostomy is feasible to be conducted by the ICU team at the bedside with few complications.
Keywords: Intensive care unit, tracheostomy, invasive mechanical ventilation, COVID-19

ÖZ *Amaç:* Koronavirüs hastalığı-2019 (COVİD-19) hastalarında, yüksek ölüm oranlarına ilişkin raporlar ve enfeksiyon bulaşmasıyla ilgili endişeler nedeniyle trakeostomi uygulanması konusunda pandeminin erken dönemlerinde tereddütler mevcuttu. Çalışmamızda, pandemi döneminde elektif trakeostomi uygulanan hastaların klinik özelliklerini ve sonuçlarını sunmayı amaçladık.
Gereç ve Yöntem: 20 Mart 2020-01 Ocak 2021 tarihleri arasında elektif trakeostomi uygulanan hastaların verileri geriye dönük olarak değerlendirildi. Tıbbi kayıtlar yaş, cinsiyet, komorbiditeler, komplikasyonlar ve sonuçlar açısından analiz edildi. Entübasyondan trakeostomiye kadar geçen süre, yoğun bakım ünitesinde (YBÜ) ve hastanede kalış süreleri hesaplandı. COVİD-19 (grup I) ve COVİD-19 tanılı olmayan (grup II) hastaların verileri karşılaştırıldı. Ayrıca, erken trakeostomi (≤14 gün) ve geç trakeostomi (>14 gün) grupları klinik sonuçlar açısından karşılaştırıldı.
Bulgular: Çalışmaya 70'i COVİD-19 tanılı toplam 144 hasta dahil edildi. Her iki grupta da ortanca 19. günde trakeostomi açılmıştı (p=0,85). COVİD-19 hastalarında perkütan trakeostomi (%68,6) daha sıktı. Her iki grupta da trakeostomi uygulama süresinin mortalite üzerine olumlu etkisi tespit edilmedi. Kanama grup I'de daha az meydana gelmişti.
Sonuç: COVİD-19 hastalarında perkütan trakeostomi daha sık ve daha erken uygulanmıştı. Perkütan trakeostomi, YBÜ ekibi tarafından yatak başı düşük komplikasyon riski ile uygulanabilir.
Anahtar Kelimeler: Yoğun bakım ünitesi, trakeostomi, invaziv mekanik ventilasyon, COVİD-19

Introduction

During the coronavirus disease-2019 (COVID-19) pandemic, the increasing number of patients caused difficulty on the intensive care unit (ICU) processes (1). COVID-19 can induce severe respiratory problems that require invasive mechanical ventilation (IMV) hence tracheostomy opening due to prolonged IMV (2).

Tracheostomy is one of the commonly performed procedures during prolonged IMV in critically ill patients. Traditionally, tracheostomy is performed to ease weaning from ventilator support, clearance of secretions, improve patient comfort and mobility (3). Additionally, some studies have reported that early tracheostomy shortens the duration of ICU stay (4). However, it's important to note that tracheostomy carries potential complications, including bleeding, stoma infection, pneumothorax or pneumomediastinum, and even mortality (5-7). Therefore, when deciding whether to perform a tracheostomy, a careful evaluation of the risks and benefits must be conducted (2). Initially, there was reluctance to perform tracheostomies in COVID-19 patients due to high mortality rates and concerns about the transmission of infection (5,6-8). To address the uncertainties, multiple consensus reports have been published specifically addressing tracheostomy in COVID-19 patients (4,6-9). There is insufficient data to make an evidence-based recommendation regarding the timing of tracheostomy in COVID-19 patients (5-7). Besides, the optimal tracheostomy technique (surgical versus percutaneous) in the COVID-19 patients is unclear (5,6). A high level of consensus has been achieved in guidelines on safety standards such as the use of personal protective equipment (PPE) (hair cover, N95 mask, surgical mask, face shield, gown and gloves) and an apneic approach during tracheostomy (10-12). Despite many of the guidelines on tracheostomy practice, there is limited experience and data on tracheostomy performance (5,6,13,14).

Due to the rapid increase in the number of patients with pneumonia who required intensive care treatment during the pandemic in Turkey, existing intensive care beds and even some operating rooms have been converted to ICUs for the treatment of COVID-19 patients. In addition, while anesthesiologists and intensive care specialists were mostly responsible for COVID-19 ICUs, other physicians were assigned to non-COVID-19 ICUs. All these non-routine practices are also likely to cause differences in standard intensive care procedures.

This study had two aims: to compare the clinical features and outcomes of patients with and without COVID-19 who underwent elective tracheostomy; and to evaluate whether the COVID-19 pandemic changed the approach of intensive care specialists to the practice of tracheostomy, which is frequently applied in ICU.

Materials and Methods

Study Design and Patients

This study was approved by the University of Health Sciences Turkey, Bursa City Hospital Clinical Research Ethics Committee (decision no: 2021-1/17, date: 06.01.2021). This retrospective, observational study was conducted in COVID-19 and non-COVID-19 ICUs. The data from patients treated between March 20, 2020, to January 01, 2021, were evaluated. Adult patients (>18 years) who underwent elective tracheostomy were included. The diagnosis of COVID-19 followed the interim guidance provided by the World Health Organization (15).

Data Collection

The demographic and clinical data were obtained from the electronic medical records. Medical records were analyzed for age, gender, comorbidities, laboratory tests, Acute Physiology and Chronic Health Evaluation (APACHE)-II scores, complications due to tracheostomy, and outcomes. The following information was recorded and analyzed: the duration in days from the start of IMV to tracheostomy, from tracheostomy to successful weaning, from tracheostomy to discharge from the ICU, the length of stay (LOS) in the ICU, and the length of hospital stay. Additionally, data regarding the tracheostomy technique (surgical or percutaneous) and potential transmission to healthcare workers were also documented.

Outcomes

The primary outcome was the 28-day survival (from the date of ICU admission). We also determined the 60-day mortality. The secondary outcome measures were tracheostomy technique, ICU stay, discharge from ICU, tracheostomy decannulation rate, and complications.

Exploratory Analyses

We divided the patients who underwent elective tracheostomy into two groups: patients diagnosed with COVID-19 (group I) and those who were not diagnosed with COVID-19 (group II). These groups were compared in terms of demographic, clinical, and outcome data.

Additionally, both groups were divided into two subgroups according to the timing of tracheostomy. There was no difference between the groups in terms of age, gender, APACHE-II values and indication. The study population was divided into two groups: the early tracheostomy group, consisting of patients who underwent tracheostomy within the first 14 days of initiating IMV, and the late tracheostomy group, comprising patients who underwent tracheostomy after 14 days of IMV. Laboratory data at the time of admission to ICU for patients with a diagnosis of COVID-19 were compared for the early and late tracheostomy groups.

Tracheostomy Technique and Procedure

The decision regarding the performance of tracheostomy was made by the intensive care specialist who was responsible for the patients' care. Furthermore, percutaneous tracheostomies were carried out by the intensive care specialist at the bedside. Our ICU is in the form of single rooms, and the number of personnel inside was limited to three during the procedure. Percutaneous tracheostomy was performed using Griggs percutaneous technique, known as the guidewire dilating forceps technique (16). All surgical tracheostomies were performed by an otolaryngologist and because of viral load and risk to the healthcare team, it was decided to perform a tracheostomy for all patients, specifically after at least 21 days of ventilation and at least one negative reverse transcription-polymerase chain reaction (RT-PCR) test. There was a minimum of five personnel in the negative pressure operating room during the procedure. The surgical technique was performed with a horizontal incision between the 2nd and 3rd rings of the trachea (16). All patients were completely paralyzed by a muscle relaxant. In both techniques, all personnel wore full PPE, and all patients received volume/pressure-controlled ventilation of the lungs with a fraction of inspired oxygen (FiO_2) of 100% during the procedure. The ventilator was paused while the tracheostomy cannula was inserted.

Statistical Analysis

The data were analyzed with the statistical software IBM SPSS Statistics for Windows version 20.0 (IBM Corp., Armonk, New York, USA). The descriptive statistics were presented as number (n), percentage (%), mean ± standard deviation, median, and interquartile range values. The normal distribution of the data of the numerical variables was evaluated using the Shapiro-Wilk normality test. Comparisons between groups were performed using Student's t-test for variables with normal distribution and Mann-Whitney U test for variables not showing normal distribution. The relationship between categorical data was evaluated using chi-square test statistics. A p-value of <0.05 was considered statistically significant.

Results

During the study period, a total of 144 patients, 70 of whom were diagnosed with COVID-19, were included in our study. The mean age of patients diagnosed with COVID-19 (group I) was 68.4 years; 71.4% were male. In group II, the mean age of patients was 67.8 years, and 56.8% were male. Although the groups did not differ significantly by gender and age, the APACHE-II score was significantly higher in group I (p=0.019). Hypertension (44.3%) was the most common comorbidity in group I, while it was cerebrovascular disease (54.1%) in group II. There was no significant difference between the two groups regarding the ICU LOS and duration from tracheostomy to ICU discharge. However, the hospital LOS was significantly shorter in group I (Table 1, 2).

The indication for tracheostomy in all patients was prolonged IMV. The cause of prolonged IMV in group I was pulmonary dysfunction, while it was neuromuscular dysfunction in group II. The median timing of tracheostomy was 19 days after intubation in both groups (range: 1-44 and 1-69 days, respectively). While percutaneous tracheostomy (68.6%) was performed more frequently in group I, surgical tracheostomy (71.6%) was performed more frequently in group II (p<0.001). Early and late tracheostomy rates were similar in the two groups. Early tracheostomy was performed in 17 patients in both groups (p=0.85). The most frequent perioperative complication was bleeding in group II patients as opposed to group I (1.4 vs. 9.5%; p=0.06) (Table 2).

Both groups were divided into two subgroups according to the timing of tracheostomy. There was no difference between the groups in terms of age, gender, APACHE-II values and indication (Table 3). Diabetes mellitus and hypertension were higher in group I. The median duration from intubation to tracheostomy was significantly shorter

Table 1. Baseline characteristics of patients			
	Group I (n=70)	**Group II (n=77)**	**p-value**
Age, years, mean ± SD	68.4±12.8	67.8±13.7	0.88
Gender, male-n (%)	50 (71.4)	42 (56.8)	0.06
APACHE-II score, median (IQR)	23 (11)	20 (9)	0.019
Chronic medical illness*- n (%)			
Hypertension	31 (44.3)	32 (43.2)	0.9
COPD	7 (10)	5 (6.5)	0.48
Cerebrovascular disease	16 (22.9)	40 (54.1)	<0.001
Diabetes	27 (38.6)	14 (18.9)	0.009
Coronary heart disease	11 (15.7)	18 (24.3)	0.19
Asthma	4 (5.7)	0	0.053
Length of ICU stay, median (IQR) days	38 (23)	42 (28)	0.39
Length of hospital stay, median (IQR) days	38 (20)	44 (27)	0.04
Mortality-n (%)			
28th day	13 (18.6)	8 (10.8)	0.23
60th day	42 (60)	32 (43.2)	0.04

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, COPD: chronic obstructive pulmonary disease, ICU: intensive care unit, SD: standard deviation, IQR: interquartile range, *one patient had more than one chronic disease

Table 2. Tracheostomy procedural and technical considerations			
	Group I (n=70)	**Group II (n=74)**	**p-value**
Indications for tracheostomy, n (%)			
Prolonged IMV, n (%)			
Pulmonary dysfunction	52 (74.3)	15 (20.3)	<0.001
Neuromusculer dysfunction	17 (24.3)	56 (75.7)	<0.001
Airway obstruction-n (%)			
Laryngomalacia	1 (1.4)	3 (4.1)	-
Duration from intubation to tracheostomy, days, median (IQR)	19 (9)	19 (13)	0.85
Duration from tracheostomy to ICU discharge, days, median (IQR)	18 (18)	19 (24)	0.73
Tracheostomy technique, n (%)			
Percutaneous	48 (68.6)	21 (28.4)	<0.001
Open	22 (31.4)	53 (71.6)	<0.001
Tracheostomy time-n (%)			
Early (≤14 days)	17 (24.3)	17 (23)	0.85
Late (>14 days)	53 (75.7)	57 (77)	0.85
Complications-n (%)			
Tracheostoma bleeding	1 (1.4)	7 (9.5)	0.06
Tracheostomy tube malposition	1 (1.4)	0	0.3
Pneumothorax	1 (1.4)	0	0.3
Tracheostoma infection	0	1 (1.4)	0.3

IMV: Invasive mechanical ventilation, ICU: intensive care unit, IQR: interquartile range

in the early group (for both of them p<0.001). In group I, percutaneous tracheostomy was performed more frequently in the early tracheostomy patients (88.2%, p=0.07). It was observed that early tracheostomy in COVID-19 patients was associated with shorter durations of ICU and hospital stays (p=0.008 for both). There was no difference between the 28th or 60th-day mortality in the groups who underwent early and late tracheostomy patients (Table 3).

Two patients in group I and five patients in group II were decannulated. The discharge data of the patients from the ICU are presented in Table 4.

Table 3. Baseline characteristics and outcomes of patients receiving early and late tracheostomies

	Group I (n=70)			Group II (n=74)		
	Early (n=17) (≤14 days)	Late (n=53) (>14 days)	p-value	Early (n=17) (≤14 days)	Late (n=57) (>14 days)	p-value
Age, years-mean ± SD	66.7±12.2	68.9±13.1	0.47	65.8±18.3	68.4±12.1	0.87
Gender, male-n (%)	12 (70.6)	38 (71.7)	1.00	9 (52.9)	23 (40.4)	0.41
APACHE-II score, median (IQR)	22 (12)	23 (10)	0.52	18 (12)	21 (10)	0.30
Chronic medical illness*, n (%)						
Hypertension	8 (47.1)	23 (43.4)	1.00	7 (41.2)	25 (43.9)	1.00
COPD	2 (11.8)	5 (9.4)	1.00	0	5 (8.8)	0.33
Cerebrovascular disease	2 (11.8)	14 (26.4)	0.32	10 (58.8)	32 (52.6)	0.78
Diabetes	10 (58.8)	17 (32.1)	0.08	3 (17.6)	11 (19.3)	1.00
Coronary heart disease	3 (17.6)	8 (15.1)	1.00	4 (23.5)	14 (24.6)	1.00
Asthma	2 (11.8)	2 (3.8)	0.24	0	0	-
Duration from intubation to tracheostomy, days, median (IQR)	11 (4)	21 (7)	<0.001	10 (6)	24 (12)	<0.001
Duration from tracheostomy to ICU discharge, days, median (IQR)	17 (14)	18 (21)	0.73	17 (17)	19 (26)	0.71
Indications for tracheostomy, n (%)			0.20			0.008
Pulmonary dysfunction	11 (64.7)	41 (77.4)		4 (23.5)	11 (19.3)	
Neuromusculer dysfunction	5 (29.4)	12 (22.6)		10 (58.8)	46 (80.7)	
Laryngomalacia	1 (5.9)	0		3 (17.6)		
Tracheostomy technique, n (%)			0.07			0.22
Percutaneous	15 (88.2)	33 (62.3)		7 (41.2)	17 (24.1)	
Open	2 (11.8)	20 (37.7)		10 (58.8)	43 (75.4)	
Length of ICU stay, days, median (IQR)	28 (15)	42 (20)	0.008	34 (31)	43 (28)	1.00
Length of hospital stay, days, median (IQR)	31 (13)	42 (20)	0.008	45 (30)	51 (27)	0.67
28th day mortality, n (%)	6 (35.3)	7 (13.2)	0.06	1 (5.9)	7 (12.3)	0.67
60th day mortality, n (%)	12 (70.6)	30 (56.6)	0.39	6 (35.3)	26 (45.6)	0.58

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, IQR: interquartile range, ICU: intensive care unit, COPD: chronic obstructive pulmonary disease, SD: standard deviation, *one patient had more than one chronic disease

Table 4. Outcome of patients discharged alive

	Group I (n=17)	Group II (n=25)
Decannulated, n (%)	2 (11.8)	5 (20)
Oxygen via tracheostomy, n (%)	1 (5.9)	10 (40)
Completely ventilator dependent, n (%)	14 (82.3)	10 (40)

Discussion

The COVID-19 pandemic caused an unprecedented increase in the number of critically ill patients. Hospitals are overwhelmed, and medical professionals had to make difficult decisions regarding the care of these patients. The reported transmission of infection and high mortality in COVID-19 patients have raised important questions that need to be addressed for making informed decisions regarding tracheostomy. There is no clear timing for tracheostomy in COVID-19 patients. In addition, it is unknown whether percutaneous or surgical tracheostomy is superior to each other or if it is different in terms of the risk of transmission (13,14,16,17).

Different from other studies, we evaluated tracheostomy applications in critically ill patients with COVID-19 and without COVID-19 (5,13,14). The most common indication for tracheostomy in non-COVID-19 patients was neuromuscular dysfunction, while pulmonary dysfunction in COVID-19 patients. Tracheostomy was performed on the median 19th day in both groups. Considering that the tracheostomy was performed mostly due to neuromuscular dysfunction in the non-COVID-19 patients, the average time from intubation to tracheostomy would be expected to be shorter. We think that this situation is caused by the fact that physicians other than the ICU specialist and anesthesiologist were responsible for non-COVID ICUs during the pandemic and that tracheostomy was performed at least on the 21st day after intubation with one negative RT-PCR test result. Insufficient data on the clinical course, the risk of viral transmission in the early stages of the pandemic, and the presence of asymptomatic carriers were also influential in this decision taken by otolaryngologists. Routine negative RT-PCR test before the procedure was not decided by the ICU team in the COVID ICU. Delaying tracheostomy to achieve negative tests is likely to prolong endotracheal ventilation and thus alter the potential benefits of tracheostomy while increasing the risk of complications related to endotracheal intubation. Critical patients can test positive for PCR for several weeks after the onset of symptoms, but it remains uncertain whether a positive PCR test indicates the presence of infectiousness (18,19).

Although the effects of tracheostomy are mostly revealed by retrospective observational studies, the data on the timing in patients with COVID-19 are even more limited (14,20-22). Glibbery et al. (22) demonstrated a significant positive correlation between the duration from intubation to tracheostomy and variables such as the duration of IMV, time from intubation to decannulation, and time from intubation to ICU discharge. In a multicenter study including 153 patients, it was shown that early tracheostomy application (<15 days) was associated with shorter ICU stay, although no difference was found in terms of mortality (23). Especially during the pandemic, shortening the duration of intensive care and hospital stay is critical for managing the patient population that complicates the hospital operation. Although the ICU stay was short in the early tracheostomy group in our study, mortality was very high in this group.

Tracheostomy is a procedure that can be performed with surgical or percutaneous techniques. With the increasing experience over the years, the number of patients who have undergone percutaneous tracheostomy has increased. However, the pandemic has led to debates on the efficacy and safety of percutaneous and surgical tracheostomy techniques (24-26). Bassi et al. (27) reported that if the suggested precautions are strictly followed, percutaneous tracheostomy could be performed with minimal aerosol spread as well as surgical tracheostomy. In a multicenter prospective observational study that included 1890 COVID-19 patients, Martin-Villares et al. (28) reported that most of the procedures were performed at the bedside in ICU and used the surgical technique. It was reported that there were no cases of COVID-19 related to the procedures among healthcare workers in the study. In our study, the majority of tracheostomy procedures in COVID-19 patients were conducted by intensivist using the percutaneous technique at the patient's bedside. The utilization of bedside percutaneous tracheostomy has effectively minimized the need for transporting ventilated patients and the associated risks of repeated disconnection and reconnection of ventilator circuits during transportation. In addition, the number of personnel could be kept more limited with the percutaneous tracheostomy compared to the surgical tracheostomy (three versus a minimum of five staff, respectively). Unlike the period before the pandemic, in both percutaneous and open techniques, ventilation was stopped from the time of opening the trachea to placing the tracheostomy tube and inflating the cuff, and the whole team used the appropriate PPE. Although we did not have a strict protocol on the timing or method for tracheostomy, we had a standard approach, and all precautions were consistently taken to minimize risks to clinicians. No transmissions to healthcare workers occurred during any procedure.

The most frequently reported complication associated with a tracheostomy procedure is minor bleeding (28). The most common complication in our study was also bleeding. Surgical tracheostomy was performed in five of the eight patients who developed bleeding (one patient in group I, four patients in group II). None of the patients required blood transfusion or surgical procedures related to tracheostomy bleeding. It has been reported that the use of a smaller incision and blunt dissection are associated with less bleeding in percutaneous tracheostomy. Also, the stoma fits tightly around the tracheostomy tube and is effective in reducing bleeding with its compression effect (24-26).

This study is one of the first and largest series to describe early outcomes of COVID-19 patients undergoing tracheostomy in Turkey. In addition, according to our research, it is the first study in the literature to compare tracheostomy applications in COVID-19 and non-COVID-19 patients during the pandemic period. However, our study has several limitations. This is a retrospective cohort study with a relatively small number of patients and short-term mortality. Therefore, the power to detect mortality differences may be inadequate. The analysis of long-term outcomes, long-term disability, and chronic care were also lacking. Comparing patients according to the diagnosis of COVID-19 is one of the strengths of our study.

Conclusion

The impact of tracheostomy procedures on the clinical outcomes of COVID-19 patients remains uncertain, and there is currently no definitive indication regarding the timing of tracheostomy in these patients. There is a need for studies that will guide the timing of tracheostomy and the effect of tracheostomy techniques on morbidity and mortality in critically ill, mechanically ventilated COVID-19 patients.

This study shows that percutaneous tracheostomy can be performed by the ICU physician at the bedside with few complications. Since percutaneous tracheostomy can be applied safely at the bedside, it seems more advantageous than surgical tracheostomy, as there is no need for patient transport, and the number of personnel can be kept more limited during the procedure. However, the timing and type of tracheostomy did not affect survival.

Ethics

Ethics Committee Approval: Ethics approval was received from the University of Health Sciences Turkey, Bursa City Hospital Clinical Research Ethics Committee on January 6, 2021, with the decision number 2021-1/17.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.Ç., S.T., P.K.K., G.T., Concept: G.Ç., P.K.K., E.U., N.K.G., Design: G.Ç., S.T., G.T., N.K.G., Data Collection and Process: S.T., P.K.K., G.T., E.U., Analysis or Interpretation: G.Ç., P.K.K., N.K.G., Literature Search: S.T., G.T., E.U., Writing: G.Ç., N.K.G.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Root Cause Analysis and Prevalence of Pressure Injuries a Neurointensive Care Unit

Basınç Yaralarının Sıklığı ve Kök Neden Analizi: Nöroloji Yoğun Bakım Örneği

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ABSTRACT *Objective:* This study determined the prevalence and causes of the pressure injuries (PIs) in patients hospitalized our neurology intensive care unit (NICU).
Materials and Methods: Planned as a cross-sectional, descriptive design, this study was conducted in training and research hospital NICU. The population of the study consisted of 338 patients. We retrospectively collected data from the hospital information management system that included the study period from January 1, 2020 to December 31, 2020.
Results: Most 338 patients (54.4%) were male, the mean age of the patients was 68.44±15.5. Most patients were found to have comorbidities that may have contributed to the development of the PIs. The prevalence of the PI first appeared to be 15.4%, but since the PIs of 11 patients were found to have developed before admission to the NICU, yet with no stage progression, the prevalence of the PI was finally specified as 12.1% (n=41).
Conclusion: It is of great importance to note that since the patients in the NICUs are at high risk of the PIs, close follow-up is accordingly necessary in terms of the PIs until discharge, it is necessary that nurses be informed as regard current guidelines to ensure offering appropriate nursing care.
Keywords: Intensive care unit, nursing care, pressure injury, root cause analysis

ÖZ *Amaç:* Bu çalışmada hastanemiz nöroloji yoğun bakım ünitesinde (NYBÜ) yatan hastalarda basınç yarası (BY) sıklığı ve nedenlerinin belirlenmesi amaçlandı.
Gereç ve Yöntem: Kesitsel ve tanımlayıcı olarak planlanan bu çalışma bir eğitim ve araştırma hastanesi NYBÜ'de gerçekleştirildi. Araştırmanın evrenini 338 hasta oluşturmuş olup, 1 Ocak 2020 ile 31 Aralık 2020 arasındaki çalışma dönemini içeren veriler hastane bilgi yönetim sisteminden elde edildi.
Bulgular: Üç yüz otuz sekiz hastanın çoğunluğu (%54,4) erkek olup, hastaların yaş ortalaması 68,44±15,5 idi. Hastaların çoğunluğunun BY gelişimine katkıda bulunabilecek komorbiditeye bulunmaktaydı. BY prevalansı ilk başta %15,4 idi, ancak 11 hastanın BY'nin NYBÜ'ye kabul edilmeden önce geliştiği ve herhangi bir evre ilerlemesi olmadığı tespit edildiğinden, BY nihai prevalansı %12,1 olarak belirlendi (n=41).
Sonuç: NYBÜ'deki hastalar BY açısından yüksek risk altında olduğu için, hastaların BY açısından taburcu olana kadar yakın takip gerekliliği unutulmamalı, hemşirelerin uygun hemşirelik bakımının sunulabilmesi için güncel kılavuzlar hakkında bilgilendirilmesi gerekmektedir.
Anahtar Kelimeler: Yoğun bakım ünitesi, hemşirelik bakımı, basınç yarası, kök neden analizi

Introduction

Pressure injury (PI) is a localized damage over a visible bony prominence or in the skin and/or underlying soft tissue, in relation to the use of medical or other devices (1,2). PI refer to a very costly complication that triggers substantial problems in patient care and an important indicator for patient safety and health care quality (2,3). The PI classification is used to describe the extent of tissue loss and the physical appearance of the injury as a result of pressure and/or shear. The National Pressure Injury Advisory Panel and the European Pressure Ulcer Advisory Panel have added two further classifications to the PI framework that range from stage I to IV depending on the depth of the lesion (4-6). These classifications are known as unstageable

and suspected deep tissue injury. Since intensive care units (ICUs) are complicated health care facilities that provide treatment for critically ill and unstable patients who have undergone numerous medical interventions, those who are hospitalized there are especially at risk of acquiring PIs (7,8). ICU nurses need to be mindful of PI formation and treatment for this reason. Mobility/activity, perfusion, skin condition, skin moisture, age, hematological parameters, diet, body temperature, and sensory perception are some of its main risk factors (9). The risk of developing a PI is typically higher in individuals who are sedentary, older adults, have low serum albumin and body mass index, have had surgery, or have received ICU treatment (5). Other factors such as diabetes, smoking, peripheral vascular disease and hypoproteinemia are also likely to contribute to the formation of such ulcers (2,10). Research has shown that one of the most common factors that lead to prolonged hospitalization of the patients after surgery is the PIs with a rate of 3.4-66% (2). It has been reported that the incidence of pressure injuries varies between 1.9% and 35%, with the prevalence ranging between 11.1% and 31% (11). In a similar sense, the incidence of pressure injuries in the ICUs has been reported to be 4.7-15%, a rate reaching up to 56% (12,13).

In the event of a PI, a root cause analysis (RCA) should be performed to explore the underlying causes of the problem, without focusing only on the apparent cause (14). RCA is a systematic process used to identify the source of the problem, address problems or non-conformity (15). In Turkey, there are standards expressing the necessity of performing RCA as included in Health Quality Standards and Health Accreditation Standards (16,17). The purpose of a RCA is to identify, discuss and question the practices and habits of any given institution. Instead of dealing with "what happened" and "how it happened", it is aimed to find an answer to the question of why it happened, as well as to reveal the factors that caused it, and prevent the reoccurrence of any undesirable experience (18-20).

Neurological diseases with a progressive course those are among chronic diseases as well, differ from other diseases due to the burden they bring to caregivers and society (21). Cerebrovascular diseases (CVDs), which ranks first among the causes of mortality in the world (22) and is the most common among neurological diseases. CVDs are in the second place among the causes of morbidity in Turkey (23). While intensive care need appears in the acute period of neurological diseases; the need for intensive care can increase in the later stages of motor neuron diseases (24). With the establishment of neurological ICUs, it has been observed that many patients, who were thought to be difficult to cope with, were brought back to life with quality health care delivery (21). We focused to determine the characteristics of the patients hospitalized in neurology intensive care units (NICUs), and performed RCA to find out the causes those leading to formation of pressure injuries.

Materials and Methods

Planned as a cross-sectional and descriptive design, this study was carried out in a Hospital, NICU. The NICU has 10 beds and has been registered as a tertiary ICU. Patient data were obtained from the hospital information management system (HIMS). The evolution of study consisted of 52 patients, a sample of 338 patients. We collected data retrospectively from the HIMS which including the study period from 1 October 2020 to 31 December 2020.

The data of age, gender, diagnosis, hospitalized days, Acute Physiology and Health Evaluation-II (APACHE-II) scores, Nutritional Screening Tool-2002 (NRS2002) scores, Braden risk scores, comorbidity, nutrition, haemoglobin levels, albumin levels, discharging condition of patients was obtained.

Braden risk assessment scale: Developed by Braden and Bergstrom, the Braden scale is frequently used in the PI assessment, and its validity and reliability in Turkey was confirmed in 1997. The scale had six subscales, including friction, shear, wetness, activity, mobility, nutrition, and sensory perception (25). The risk level is classified as being either high risk (12 points or less), medium risk (13 points to 14 points), or low risk (15 points to 16 points, with 15 points to 18 points for those over 75) (25-29).

APACHE-II: For critically ill patients, scoring systems can assist forecast how long they will stay in the hospital and their outcome. The measure for determining the severity of acute diseases that is most well-known and frequently used is the APACHE-II score. There are three primary parts to this scoring system: Age points, chronic health points, and acute physiology points (30,31).

NRS2002: NRS2002 is system for screening of nutritional risks developed by Kondrup et al. (32) in 2002 with the support of Danish Society of Parenteral and Enteral Nutrition. It is a method that is scored on three factors: age (0-1 point), disease severity (0-3 point), and inadequate nutritional

status (0-3 point). Extra one score is added for aged 70+ patients. The patients those have ≥3 scores is determined under nutritional risk. The Turkish validity and reliability of the system was determined by Bolayır 2014 (32,33).

Study was approved by the Clinical Research Ethics Committee of the University Health Sciences Turkey, Antalya Training and Research Hospital (decision no: 14/4, date: 16.09.2021). Because of it is a retrospective study, data usage permission was obtained from the ethics committee and the hospital management.

Statistical Analysis

Continuous data were presented with mean ± standard deviation or median (interquartile range: 25-75th percentile). Categorical variables were presented with frequency (n) and percentage (%), and analysed with Pearson chi-square and Fisher's Exact test. The normality assumptions were controlled by the Shapiro-Wilk test. Independent t-test and Mann-Whitney U test were used for comparing the numerical data between two groups, as appropriate. One-Way ANOVA was used for comparing the parametric variables among Braden risk groups and Tukey HSD test was used as a post-hoc test for significant cases. Comparison of non-parametric variables among Braden risk groups was performed using Kruskal-Wallis test and Bonferroni-Dunn test was used as a post-hoc test for significant cases. Statistical analysis was made using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). Two-sided p-value less than 0.05 was considered statistically significant.

Results

A total of 338 patients were hospitalized in the NICU in 2020. The majority of 338 patients (54.4%) were male, and the mean age of all patients was 68.44±15.5 with the mean hospital stay of 4 days. Of all the patients, 59.8% of them were hospitalized with the diagnosis of CVD, while 21.3% of them with the diagnosis of hemiplegia. The majority of the patients (74%) were found to have comorbidities [diabetes mellitus (DM), hypertension (HT) or both] that may have contributed to the development of pressure injuries. The mean score in Braden risk assessment scale was 14, and 36.4% of the patients were in the high-risk group. When the prevalence of the PIs was examined, 52 (15.4%) patients appeared to have the PI, but 11 of them were found to have developed it outside the hospital before hospitalization in the NICU, though with no stage progression. The frequency of the PIs in the NICU was found as 12.1% (n=41). The average length of stay (23 days) of the patients with the PIs was longer than those without. A statistical significance was found between the two groups (p<0.001). In 80.8% of the patients who developed the PIs, the albumin level seemed quite low, with a mean value of 2.92±0.58, indicating statistical significance when compared with the patients who did not develop any PIs (p<0.001). Furthermore, 88.5% of the patients who developed pressure injuries had low hemoglobin levels, with a mean value of 10.74±2.18, signifying statistical significance when compared with those who did not (p<0.001). All patients who developed the PIs were in the high-risk group in terms of their NRS2002 scores, being statistically significant between the two groups (p<0.001). Of all the patients, 50.3% were discharged, but 46.2% died. Statistical significance was found between the two groups (p=0.011) (Table 1).

Having examined pressure injuries according to their stages, it appeared that 91.7% of the patients who developed a PI in the sacrum region were at stage 2, 77.8% of which developed in the hospital, yet with no statistical significance. It is apparent that 63.9% of the patients with the PIs developed them 10 days after hospitalization, and there was a statistically significant difference between the stage of the PI and the length of hospital stay (p=0.002) (Table 2).

The mean age of the patients in the high-risk group was 72.15, and 54.5% of them were female, according to the Braden risk assessment scale score. Age and gender differences among the risk groups were statistically significant (p<0.001, p=0.017). We determined that patients in the high-risk group in terms of Braden risk assessment scale score had a longer hospital stay, lower albumin and hemoglobin levels, indicating statistical significance. We also found that the vast majority of the patients (82.1%) in the high-risk group according to the Braden risk assessment scale score were likewise in the risk group as to the NRS2002 score due to their high scores, indicating statistical significance. The patients in the high-risk group had higher APACHE-II scores with a statistically significant difference (p=0.001). No statistically significant difference was found between the Braden risk assessment scale score and the diagnosis of hospitalization. Though not statistically significant, comorbidities such as HT and DM were found in the majority of patients with the PIs (Table 3).

Table 1. Patient characteristics				
Variables	**No PIs (n=286)**	**PIs (n=52)**	**All patients (n=338)**	**p**
Age (years), mean ± SD	67.87±15.57	71.58±14.91	68.44±15.5	0.113
Gender, n (%)				
Female	127 (44.4)	27 (51.9)	154 (45.6)	0.317
Male	159 (55.6)	25 (48.1)	184 (54.4)	
Diagnosis, n (%)				
DM with neurological complications	2 (0.7)	0 (0)	2 (0.6)	0.517
Middle cerebral artery syndrome and cerebrovascular disease	6 (2.1)	2 (3.8)	8 (2.4)	
Cerebrovascular disease	172 (60.1)	30 (57.7)	202 (59.8)	
Hemiplegia	62 (21.7)	10 (19.2)	72 (21.3)	
Parkinson's disease	1 (0.3)	1 (1.9)	2 (0.6)	
Epilepsy	5 (1.7)	2 (3.8)	7 (2.1)	
Other	38 (13.3)	7 (13.5)	45 (13.3)	
Length of hospital stay (days), median (IQR)	3.5 (1-9)	23 (6-43)	4 (2-12)	<0.001
Comorbidity, n (%)				
HT	80 (28)	15 (28.8)	95 (28.1)	0.897
DM	35 (12.2)	6 (11.5)	41 (12.1)	0.887
Heart disease	51 (17.8)	8 (15.4)	59 (17.5)	0.669
Neurological disease	21 (7.3)	7 (13.5)	28 (8.3)	0.168
Other	19 (6.6)	8 (15.4)	27 (8)	0.048
Albumin, mean ± SD	3.58±0.58	2.92±0.58	3.48±0.63	<0.001
Albumin category, n (%)				
Normal	189 (66.1)	10 (19.2)	199 (58.9)	<0.001
Low	97 (33.9)	42 (80.8)	139 (41.1)	
Hemoglobin, mean ± SD	12.1±2.17	10.74±2.18	11.89±2.23	<0.001
Hemoglobin category, n (%)				
Normal	79 (27.6)	6 (11.5)	85 (25.1)	0.014
Low	207 (72.4)	46 (88.5)	253 (74.9)	
APACHE-II score, median (IQR)	13.5 (8-20)	16 (10.5-20.5)	14 (8-20)	0.048
NRS2002 score, median (IQR)	2 (2-3)	3 (3-4)	3 (2-4)	<0.001
NRS2002 score category, n (%)				
Normal	152 (53.1)	0 (0)	152 (45)	<0.001
High	134 (46.9)	52 (100)	186 (55)	
Braden score, median (IQR)	14 (12-16)	11 (7-12)	14 (12-15)	<0.001
Braden score category, n (%)				
No risk	19 (6.6)	0 (0)	19 (5.6)	<0.001
Low risk	100 (35)	0 (0)	100 (29.6)	
Moderate risk	94 (32.9)	2 (3.8)	96 (28.4)	
High risk	73 (25.5)	50 (96.2)	123 (36.4)	
Result				
Referred	5 (1.7)[a]	0 (0)[a]	5 (1.5)	0.011
Discharged	152 (53.1)[a]	18 (34.6)[b]	170 (50.3)	
Left the hospital on his/her own will	1 (0.3)[a]	0 (0)[a]	1 (0.3)	
Partially recovered	63 (22)[a]	10 (19.2)[a]	73 (21.6)	
Ex	65 (22.7)[a]	24 (46.2)[b]	89 (26.3)	

Independent t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test. Same letters in a row denote the lack of statistically significant difference. NRS2002: Nutrional Risk Screening, APACHE-II: Acute Physiology and Health Evaluation-II, DM: diabetes mellitus, HT: hypertension, SD: standard deviation, PI: pressure injury, IQR: interquartile range, Ex: exitus

Table 2. Features of patient with pressure injuries according to the stage				
Variables	**Stage 1**	**Stage 2**	**Stage 3**	**p**
Location, n (%)				
Sacrum	11 (91.7)	33 (91.7)	3 (75)	0.402
Heels	1 (8.3)	6 (16.7)	2 (50)	0.205
Back	0 (0)	3 (8.3)	0 (0)	0.658
Legs	1 (8.3)	3 (8.3)	1 (25)	0.402
Place of developing the PIs, n (%)				
Home	5 (41.7)	8 (22.2)	0 (0)	0.198
Hospital	7 (58.3)	28 (77.8)	4 (100)	
Which day? n (%)				
<10 days	7 (58.3)[a]	6 (16.7)[b]	2 (50)[a,b]	0.002
>10 days	1 (8.3)[a]	23 (63.9)[b]	2 (50)[b]	
Pre-existing condition	4 (33.3)[a]	7 (19.4)[a]	0 (0)[a]	

PI: pressure injury. Fisher's Exact test. Same letters in a row denote the lack of statistically significant difference.
*Some patients had more than one pressure injury

Table 4 presents the detailed information regarding 52 patients (27 women, 25 men) with the PIs, most of whom were found to be in stage II, with the majority (90.4%) having developed it in the sacrum region, and 75% of them were found to develop it during their stay in the hospital. We determined that 50 patients who developed the PIs were in the high-risk group according to the Braden risk score, that all patients had a high-risk score of NRS2002 and received enteral nutrition, and that most of the PIs developed in the sacrum region, though they were found in more than one region. Based on the evaluation of the PI RCA, sufficient data could not be found in only 8 patients, whereas in others, RCA results revealed advanced age, nutritional deficiency, prolonged hospital stay, low albumin and hemoglobin levels, and comorbidities as the root causes resulting in the PIs. It appeared that 27 of the 52 patients who developed the PIs had at least one comorbidity and more than half of them had two. Stage progression was detected in only 2 of the patients with the PI developing outside the hospital (Table 4). In the light of such data, it is clear that the factors belonging to the patients are predominant in the analysis of the root cause in the formation of the PIs. In our study, advanced age, any kind of disease that may cause limitation of movement, comorbidities, nutritional deficiency and prolonged stay appeared to be influential factors in the development of the PIs (Table 4).

Discussion

Although there are conflicting statistics available about the incidence of PIs, the pace of their development appears to be higher in ICUs as compared to other healthcare units (34-38).

Prevelance and Feature Risk of PIs

In this study, the prevalence of the PIs was found to be 12.1%. Research conducted on the PI incidence and prevalence has shown that the rate of the PIs in the NICU 10.9% (38) and 15% hospital-wide NICU (36). These variations may have been caused by a variety of variables, such as the size of the hospital where the study was done, whether it was a public or private university hospital, the type of ICU, whether the researcher was an employee of the organization, the exclusion of the PIs in stage I from the study, and the variation in the ability of ICU nurses to assess and be aware of PIs. This study's significance comes from the fact that it was carried out in the NICU, where elderly patients with chronic illnesses who typically have limited mobility were present, and from the fact that the RCA of the patients' components and other factors were presented simultaneously.

Although the sacrum, trochanter, and heels are listed as the areas where PIs are frequently observed (29), it has been shown in a number of studies that it most frequently occurs in the sacrum (29,37,39-41). Similar to this, we discovered

that the sacrum region was where PIs most frequently developed, which is consistent with the literature. The PIs in the sacrum region in the ICU patients may be caused by the increase in pressure applied to the sacral region, with the heads of the patients elevated to prevent aspiration pneumonia and ventilator-associated pneumonia (41). With frequent positioning, pressure and cutting time can be reduced. For example, if both the head and foot end of the bed are raised 30 degrees when the semi-fowler position is given, the lowest contact pressure occurs at this angle

Table 3. Patient characteristics according to the Braden score

Variables	No risk-low risk (n=119)	Moderate risk (n=96)	High risk (n=123)	p
Age (years), mean ± SD	63.45±16.78[a]	69.85±14.19[b]	72.15±13.97[b]	<0.001
Gender, n (%)				
Female	43 (36.1)[a]	44 (45.8)[a.b]	67 (54.5)[b]	0.017
Male	76 (63.9)[a]	52 (54.2)[a.b]	56 (45.5)[b]	
Diagnosis, n (%)				
DM with neurological complications	0 (0)	1 (1)	1 (0.8)	0.482
Middle cerebral artery syndrome + cerebrovascular disease	3 (2.5)	1 (1)	4 (3.3)	
Cerebrovascular disease	62 (52.1)	60 (62.5)	80 (65)	
Hemiplegia	27 (22.7)	22 (22.9)	23 (18.7)	
Parkinson's disease	1 (0.8)	0 (0)	1 (0.8)	
Epilepsy	4 (3.4)	1 (1)	2 (1.6)	
Other	22 (18.5)	11 (11.5)	12 (9.8)	
Hospital stay (days), median (IQR)	2 (1-5)[a]	4.5 (2-13.5)[b]	7 (3-28)[c]	<0.001
Comorbidity, n (%)				
HT	29 (24.4)	25 (26)	41 (33.3)	0.261
DM	14 (11.8)	12 (12.5)	15 (12.2)	0.986
Coronary disease	18 (15.1)	21 (21.9)	20 (16.3)	0.392
Neurological disorders	10 (8.4)	8 (8.3)	10 (8.1)	0.997
Other	10 (8.4)	7 (7.3)	10 (8.1)	0.954
Albumin, mean ± SD	3.64±0.53[a]	3.54±0.66[a]	3.27±0.63[b]	<0.001
Albumin category, n (%)				
Normal	84 (70.6)[a]	62 (64.6)[a]	53 (43.1)[b]	<0.001
Low	35 (29.4)[a]	34 (35.4)[a]	70 (56.9)[b]	
Hemoglobin, mean ± SD	12.33±2.12[a]	11.77±2.16[a.b]	11.57±2.33[b]	0.022
Hemoglobin category, n (%)				
Normal	36 (30.3)	22 (22.9)	27 (22)	0.277
Low	83 (69.7)	74 (77.1)	96 (78)	
APACHE-II score, median (IQR)	12 (6-19)[a]	12 (8-18)[a]	16 (10-22)[b]	0.001
NRS2002 score, median (IQR)	2 (2-3)[a]	2 (2-3)[a]	3 (3-4)[b]	<0.001
NRS2002 score category, n (%)				
Normal	78 (65.5)[a]	52 (54.2)[a]	22 (17.9)[b]	<0.001
High	41 (34.5)[a]	44 (45.8)[a]	101 (82.1)[b]	

One-way ANOVA, Kruskal-Wallis test, Pearson chi-square test, Fisher's Exact test. Same letters in a row denote the lack of statistically significant difference.
NRS2002: Nutritional Risk Screening, APACHE-II: Acute Physiology and Health Evaluation-II, DM: diabetes mellitus, HT: hypertension, SD: standard deviation, IQR: interquartile range

(42). Due to such reasons, it is necessary to monitor and protect the parts under pressure to avoid any PI formation by changing positions at certain intervals. In the ICU where the study was conducted, all patients were recorded by changing their positions every 2 hours.

There are many factors that can lead to the PI formation, such as moisture status of the skin, age, nutrition, inactivity, anaemia, albumin level, and comorbidities (2,5,35).

It was determined that PIs developed in a shorter time in patients who could not get enough calories and protein than those who did (43).

The PI risk is higher in patients over the age of 65, and risk factors increase in those over the age of 51, indicating that the risk of developing the PIs increases with age (42). Research shows that the mean age of the patients in the previous studies was 64.9 (38), 63 (44) and 72.5 years (40). The mean age of the patients who developed the PIs was 71.6 in our study.

PIs Causes

According to the pertinent literature evaluation, patients with low albumin levels (3.5 g/dL) are more likely to develop PIs. In another study, the mean serum albumin values of patients who developed the PIs were reported as 3.41±0.58 gr/dL (45,46). Haematological and biochemical parameters should be closely monitored in ICU patients, and it should be kept in mind that the PIs may develop, especially in patients with low hemoglobin and albumin levels, and necessary precautions must be taken.

It has been stated that the comorbidity accompanying the neurological diagnosis affects the formation of the PIs, in addition to other factors (47). In our study, although no significant correlation was found between comorbid chronic diseases such as HT, DM, heart disease, and the PI formation, such disorders turned out to be more common in the majority of patients with the PIs. In our study, despite the fact that we found the APACHE-II score of the group with the PIs as higher than that of the group that did not, a statistical significance was found at the border (p=0.048).

A popular method for determining the risk of pressure injuries is the Braden scale. According to the meta-analysis study, the Braden scale demonstrated a modest level of predictive power (48). The Braden risk assessment scale score found as 11.0±2.64 is regarded in the high-risk group (49). In our study, the Braden risk assessment score of the patients who developed the PIs was likewise found to be 11. It should be noted that it is very important to monitor the patients in the risk group in terms of Braden risk score, and especially those hospitalized in the ICU should be closely monitored by the ICU nurses in order not to overlook stage I, in particular.

It is known that the PIs five times prolong the hospital stay of patients. Research shows that the length of hospitalization in PI patients has been reported as 25.14±9.87 days (50), 20.2±18.3 (38). The average length of hospital stays of the patients who developed the PIs was 23 days in our study.

A study in the literature focusing on thirty-two cases of PIs in order to perform root cause analyses, reported malnutrition as the most important cause (51). In our study, patient-related factors such as age, comorbidities, nutritional status, and length of hospital stay were by far the most important causes. Nonetheless, apart from the given reasons, it should be noted that there may be a lack of sufficient medical materials or personnel, or a defect in the PI evaluation method. Figure 1 presents the reasons for the PIs in the form of a fishbone diagram based on our study data.

In the ICU, where we performed this study on the prevention of the PIs, the following measures are taken: all patients are recorded by changing their lying positions every 2 hours, and they are given daily body hygiene, air mattresses are used, the bed linens are changed daily, ensuring that they stay tight, Braden risk scores are evaluated at each shift change once any PIs are detected, skin care is provided (such as keeping the skin dry), barrier cream is used, position pads in different sizes are used to reduce pressure, necessary treatment (enteral/parenteral) is initiated in cooperation with the nutrition team based on the results of the evaluation regarding the patients' nutritional care, and the dressings are routinely changed as part of nursing interventions. The study has stressed that PI rates can be greatly decreased from 13.86% to 10.41% by employing basic precautionary measures (52). When a patient is being discharged from the ICU, it is crucial for the ICU nurse to instruct the patient and/or the patient's family members and caregivers on how to avoid and treat PIs (26). It is necessary that patients be evaluated at their admission to the hospital, and that continuity of care be ensured by planning and monitoring the care to be given in the ongoing process (25).

Table 4. Details of patients with pressure injuries

Patient no	Age	Sex	HSD	Albumin	Hemoglobin	Nutrition risk	Braden risk	Comorbidity	PI stage	PI location	Where PI Develops	PI development	Root cause found?	Was it avoidable?	Nutrition
1	44	F	1	L	L	Yes	High	None/ unknown	Stage II	Sacrum	Home	Available/No phase progress	Sequence of events	No, patient had this PI on admission	Enteral
2	65	M	1	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Home	Available/No phase progress	Sequence of events	No, patient had this PI on admission	Enteral
3	53	M	6	N	L	Yes	Moderate	None/ unknown	Stage I	Leg + Heel	Hospital	Within 10 days	Sequence of events	Yes	Enteral
4	54	M	44	N	N	Yes	High	DM	Stage II	Sacrum	Home	Available/Yes phase progress	Yes	No, patient had this PI on admission	Enteral
5	81	F	41	N	L	Yes	High	HT, CAD	Stage II	Sacrum + Back	Hospital	After 10 days	Yes	Yes	Enteral
6	69	M	40	L	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
7	76	M	12	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Home	Available/Yes phase progress	Yes	No, patient had this PI on admission	Enteral
8	84	M	16	N	L	Yes	High	None/ unknown	Stage III	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
9	73	F	11	N	L	Yes	High	None/ unknown	Stage II	Sacrum + Heel	Hospital	After 10 days	Yes	Yes	Enteral
10	86	F	11	L	L	Yes	High	None/ unknown	Stage II	Leg + Heel	Hospital	After 10 days	Yes	Yes	Enteral
11	61	M	2	N	L	Yes	High	None/ unknown	Stage II	Sacrum + Heel	Home	Available/No phase progress	Sequence of events	No, patient had this PI on admission	Enteral
12	48	F	4	N	L	Yes	High	None/ unknown	Stage I	Sacrum	Home	Available/No phase progress	Sequence of events	No, patient had this PI on admission	Enteral
13	77	M	42	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
14	60	M	41	N	L	Yes	High	DM	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
15	91	M	2	N	L	Yes	High	BPH	Stage I	Sacrum	Home	Available/No phase progress	Yes	No, patient had this PI on admission	Enteral

Table 4. Details of patients with pressure injuries

Patient no	Age	Sex	HSD	Albumin	Hemoglobin	Nutrition Risk	Braden risk	Comorbidity	PI stage	PI location	Where PI Develops	PI development	Root cause found?	Was it avoidable?	Nutrition
16	79	F	10	L	L	Yes	High	Malignancy	Stage II	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
17	80	M	21	N	L	Yes	High	None/ unknown	Stage II	Sacrum + Heel	Hospital	After 10 days	Yes	Yes	Enteral
18	93	F	13	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
19	64	F	64	N	L	Yes	High	Epilepsy	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
20	80	F	25	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
21	71	F	75	N	L	Yes	High	HT	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
22	88	F	2	L	L	Yes	High	HT	Stage II	Sacrum	Home	Available/No phase progress	Yes	No, patient had this PI on admission	Enteral
23	52	M	44	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
24	64	F	4	N	L	Yes	High	HT, DM	Stage II	Sacrum	Hospital	Within 10 days	Sequence of events	Yes	Enteral
25	87	F	9	N	N	Yes	High	Parkinson's, dementia	Stage I	Sacrum + Back	Hospital	Within 10 days	Yes	Yes	Enteral
26	95	F	1	L	L	Yes	High	None/ unknown	Stage II	Sacrum	Home	Available/No phase progress	Yes	No, patient had this PI on admission	Enteral
27	56	F	3	N	L	Yes	Moderate	DM, asthma	Stage I	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
28	74	M	3	L	N	Yes	High	Asthma, CVD	Stage I	Sacrum	Home	Available /No phase progress	Yes	No, patient had this PI on admission	Enteral
29	64	F	52	L	L	Yes	High	None/ unknown	Stage III	Leg + Heel	Hospital	After 10 days	Yes	Yes	Enteral
30	76	F	70	N	N	Yes	High	None/ unknown	Stage I	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
31	88	F	25	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
32	84	F	41	N	L	Yes	High	HT, DM, CVD, CHF	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
33	31	M	6	N	L	Yes	High	None/ unknown	Stage I	Sacrum	Home	Available /No phase progress	Sequence of events	No, patient had this PI on admission	Enteral

Table 4. Details of patients with pressure injuries

Patient no	Age	Sex	HSD	Albumin	Hemoglobin	Nutrition Risk	Braden risk	Comorbidity	PI stage	PI location	Where PI Develops	PI development	Root cause found?	Was it avoidable?	Nutrition
34	85	M	10	N	L	Yes	High	CVD, HT	Stage II	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
35	56	M	30	L	L	Yes	High	HT	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
36	85	F	45	N	L	Yes	High	None/ unknown	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
37	46	M	39	L	L	Yes	High	None/ unknown	Stage III	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
38	80	M	69	L	L	Yes	High	BPH	Stage II	Sacrum + Hell	Hospital	After 10 days	Yes	Yes	Enteral
39	79	F	9	L	L	Yes	High	HT, CVD, CAD	Stage I	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
40	91	F	30	N	L	Yes	High	HT	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
41	86	F	6	N	L	Yes	High	HT, bypass	Stage I	Sacrum	Home	Available/No phase progress	Yes	No, patient had this PI on admission	Enteral
42	65	M	7	L	L	Yes	High	None/ unknown	Stage III	Sacrum	Hospital	Within 10 days	Sequence of events	Yes	Enteral
43	81	F	1	L	L	Yes	High	None/ unknown	Stage II	Leg + Heel	Home	Available/No phase progress	Yes	No, patient had this PI on admission	Enteral
44	72	M	13	N	L	Yes	High	DM, CAD, HF	Stage I	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral
45	45	M	183	N	L	Yes	High	None/ unknown	Stage II	Leg + Heel	Hospital	After 10 days	Yes	Yes	Enteral
46	81	F	41	L	L	Yes	High	HT, CAD, CHF	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
47	54	M	165	N	N	Yes	High	Asthma, CAD, HT	Stage II	Sacrum + Back	Hospital	After 10 days	Yes	Yes	Enteral
48	83	M	83	N	N	Yes	High	HT	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
49	64	M	63	L	L	Yes	High	HT, CAD, COPD	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
50	74	M	28	N	L	Yes	High	CHF, HT, COPD	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
51	83	F	31	L	L	Yes	High	HT, Alzheimer	Stage II	Sacrum	Hospital	After 10 days	Yes	Yes	Enteral
52	64	F	96	N	L	Yes	High	HT	Stage I	Sacrum	Hospital	Within 10 days	Yes	Yes	Enteral

PI: Pressure injury, HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, CHF: chronic heart failure, HF: heart failure, CVD: cardiovascular disease, BPH: benign prostate hyperplasia, M: male, F: female, HSD: hospital stay days, L: low, N: normal

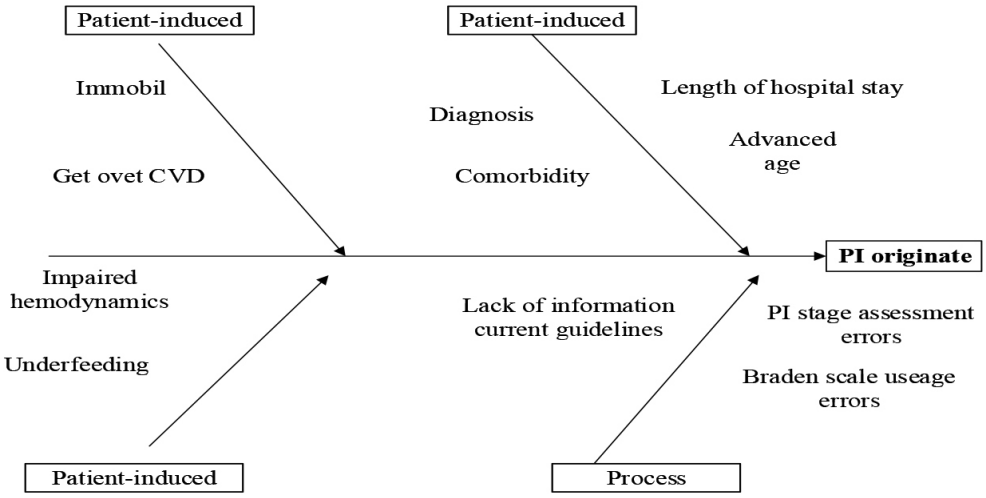

Figure 1. Root cause analysis of pressure injuries
PI: Pressure injury, CVD: cerebrovascular disease

As the study was conducted only a tertiary training and research hospital in a single NICU makes it difficult to generalize the results. On the other hand, it is considered important that it is one of the largest public hospitals in the service universe in the province of Antalya, where the study was conducted. Another limitation is that the study data only covers a one-year period.

Conclusion

We observed that the patients in the NICU were in the high-risk group in terms of PI development. Immobilization, age, length of stay and nutritional status during their stay in the ICU are risk factors for the PI formation. It should be highlighted that PIs in hospitalized patients are only being evaluated as a first step in the prevention of PI formation.

In conclusion, since the patients with mechanical ventilator support (in terms of a PI caused by a medical device), as well as those who are unconscious, those with oedematous skin, those fed by enteral nutrition, those getting 12 points or less from Braden pressure sore risk assessment scale, those with infection, and those with low levels of albumin and hemoglobin are at high risk for the PI development, it is necessary that the patients -especially those hospitalized in the ICUs- are periodically evaluated considering the risk factors and that appropriate nursing interventions are provided to prevent any PI development. In this context, the evaluation of patients in terms of PI risk is important in both way the the quality of care and the patient safety. There is a need for more comprehensive multi-center studies that reveal other causes of PIs (such as health personnel-related, material-related) with a holistic approach.

In future studies, there is a need for comprehensive and long-term data covering multi-centre intensive care and clinics, in which the opinions of intensive care nurses are taken, and not only patient-related causes, but also health professionals and equipment-related reasons (like socio-economic, home care and nutritional problems) of PIs.

Ethics

Ethics Committee Approval: This study was aproved by the Clinical Research Ethics Committee of the University Health Sciences Turkey, Antalya Training and Research Hospital (decision no: 14/4, date: 16.09.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.E., C.Ö., Concept: H.E., C.Ö., Design: H.E., C.Ö., Data Collection and Process: H.E., C.Ö., Analysis or Interpretation: H.E., C.Ö., Literature Search: H.E., C.Ö., Writing: H.E., C.Ö.

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CASE REPORT / *OLGU SUNUMU*

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A Fatal Case of COVID-19 with Diffuse Leukocytoclastic Vasculitis of Both Hips, Breasts, Feet, and Back

Kalça, Göğüs, Ayak ve Sırtta Diffüz Lökositoklastik Vasküliti Olan Ölümcül Bir COVİD-19 Olgusu

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Presented in: Information about the first hospitalization of this case was presented at the congress of International Congress of Future Medical Pioneers 2021 with the name "A COVID-19 case complicated by ecchymosis and cyanosis".

ABSTRACT A 47-year-old female patient with no known disease other than rheumatoid arthritis in remission was admitted to the hospital with complaints of bruising on her feet, breasts, hips, and back. It was determined that her severe acute respiratory syndrome coronavirus-2 polymerase chain reaction test was positive 7 days ago and she received favipiravir treatment for 5 days. In the physical examination, ecchymotic lesions were detected in her both feet, breasts, trochanteric regions, and posterior thoracic regions, which were symmetrical and did not change color with pressure in varying sizes. There were diffuse bilateral ground glass and consolidation areas in the computed tomography of the lungs. Because of the histopathological examination of the biopsy taken from the skin lesions, the patient was diagnosed with leukocytoclastic vasculitis. In the lower extremity venous Doppler ultrasonography examination, there was complete occlusion due to thrombus in the subacute period in the right vena saphena parva. During the subsequent intensive care follow-up period, necrotic lesions progressed to amputation in the right foot, debridement in the left foot, and trochanteric regions, and bilateral mastectomy. Our patient required multidisciplinary management involving many specialties during her long-term stay in the intensive care unit. Here, we present a case of coronavirus disease-2019 leading to severe and diffuse leukocytoclastic vasculitis resulting in amputation.
Keywords: Coagulopathy, leukocytoclastic vasculitis, COVID-19, amputation

ÖZ Remisyon evresinde romatoid artrit dışında bilinen bir hastalığı olmayan 47 yaşında kadın hasta ayaklarında, göğüslerinde, kalçalarında ve sırtında morarma şikayetleri ile hastaneye başvurdu. Yedi gün önce şiddetli akut solunum sendromu koronavirüs-2 polimeraz zincir reaksiyonu testinin pozitif çıktığı ve beş gün favipiravir tedavisi aldığı öğrenildi. Fizik muayenesinde; her iki ayak ve memelerde, torakanterik bölgede ve sırtta simetrik ve basmakla renk değiştirmeyen değişen büyüklüklerde ekimotik lezyonlar görüldü. Akciğer bilgisayarlı tomografisinde diffüz bilateral buzlu cam ve konsolidasyon alanları mevcuttu. Deri lezyonlarından alınan biyopsinin histopatolojik incelemesi sonucunda hastaya lökositoklastik vaskülit tanısı kondu. Alt ekstremite venöz Doppler ultrasonografi incelemesinde sağ vena safena parvada subakut dönemde trombüs nedeniyle tam tıkanma mevcuttu. Takip eden yoğun bakım sürecinde; nekrotik lezyonlar sağ ayakta amputasyona, sol ayakta ve sırtta debridmana ve bilateral mastektomiye kadar ilerledi. Hastamız yoğun bakım ünitesinde kaldığı uzun süre boyunca birçok uzmanlığı içeren multidisipliner bir yönetime ihtiyaç duymuştur. Burada amputasyonla sonuçlanan şiddetli ve yaygın lökositoklastik vaskülite yol açan bir koronavirüs hastalığı-2019 olgusu sunuyoruz.
Anahtar Kelimeler: Koagülopati, lökositoklastik vaskülit, COVİD-19, amputasyon

Introduction

Since its identification in December 2019, coronavirus disease-2019 (COVID-19) has affected millions of people worldwide. Although COVID-19 is primarily viewed as a respiratory disease, it should be considered as a systemic disease that affects multiple neurological, cardiovascular, gastrointestinal, hematopoietic and immune systems (1). This case report presents a case with multisystemic involvement due to COVID-19 and skin involvement.

Case Report

A 47-year-old female patient, who had no other known disease other than rheumatoid arthritis (RA) in remission and did not use any medication other than colchicine and adalimumab, admitted to the hospital with complaints of bruising on her feet, both breasts, hips and back. In her medical history, it was found out that her severe acute respiratory syndrome coronavirus-2 polymerase chain reaction test was positive 7 days ago and she received favipiravir treatment for 5 days. Her bruising started on the 3rd day of the favipiravir treatment. As a result of the physical examination, ecchymotic lesions were detected in her both feet, breasts, trochanteric regions, and posterior thoracic region, which were symmetrical and did not change color with pressure in varying sizes (Figure 1a, b). The evaluation of vital findings were as follows: Body temperature 36.2 °C, pulse 96/min, blood pressure arterial 116/68 mmHg, respiratory rate 22/min, and partial oxygen saturation was 96% at 5 lt/min oxygen support with a reservoir mask. Her initial and subsequent laboratory findings of the patient are given in the table (Table 1). There were diffuse bilateral ground glass and consolidation areas in the computed tomography

Figure 1. Ecchymoses in the patient (**a.** Bilateral ecchymoses in both feet; **b.** Ecchymoses in the thoracentesis region and breast)

Table 1. Some laboratory findings of the patient since hospitalization

Day	Admission to the hospital	1	2	3	5	10	15	20	30	50	70
D-dimer mg/L (0-0.5)	>35.2	>35.2	15.4	5.4	5.6	3.4	2.52	2.79	2.6	1.93	13.7
WBC 10^9/L (4.5-10.5)	24.8	23.2	28.9	20.9	18.6	15.2	14.6	25.4	11.9	22.8	4.8
Neu 10^9/L (2-6.9)	18.3	19.6	24.7	18.7	14.1	13.6	11.6	16.1	9.2	20.2	0.3
Lym 10^9/L (06-3.4)	1.6	1.7	1.4	0.7	0.5	0.4	0.4	2	1.7	1.4	1.7
Plt 10^9/L (142-424)	195	198	275	237	283	158	124	279	162	213	28
PT sec (10-14)	12.5	12.8	12.4	13.4	12.1	12.8	13.1	12.9	11.1	11.1	69.9
aPTT sec (18-36)	27.3	27.1	27.6	27.7	24.3	28.1	26.3	26.6	23.3	18	124.7
INR (0.8-1.2)	1.18	1.13	1.09	1.18	0.98	1.1	1.08	0.99	0.76	0.97	6.8
Fibrinogen mg/dL (180-350)	365	342	288	322	296	317	308	369	376	133	54
CRP mg/L (0-5)	162	155	103	190	170	106	83.4	18.6		15	357.6
Procal. mg/L (0-0.046)	0.71	-	-	0.28	0.82	0.75	0.53	0.64	1.83	0.75	27.5
Ferritin µg/L (13-150)	698	692	586	395	439	443	717	623	572	602	>2000

WBC: White blood cell, Neu: neutrophil, Lym: lymphocyte, Plt: platelet, PT: prothrombin time, aPTT: activated partial thromboplastin time, CRP: C-reactive protein, procal.: procalcitonin, INR: international normalized ratio

(CT) of the lungs (Figure 2). There was a toxic granulation and a left shift in peripheral smear. In the lower extremity venous Doppler ultrasonography examination, there was complete occlusion due to thrombus in the subacute period in the right vena saphena parva. In the lower extremity arterial system Doppler ultrasonography, we found no evidence of arterial thrombosis.

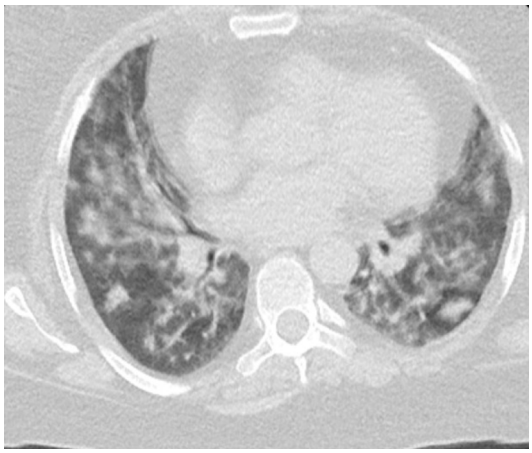

Figure 2. Thoracic CT image of the patient. Common ground glass and consolidation areas consistent with COVID-19 pneumonia
CT: Computed tomography, COVID-19: coronavirus disease-2019

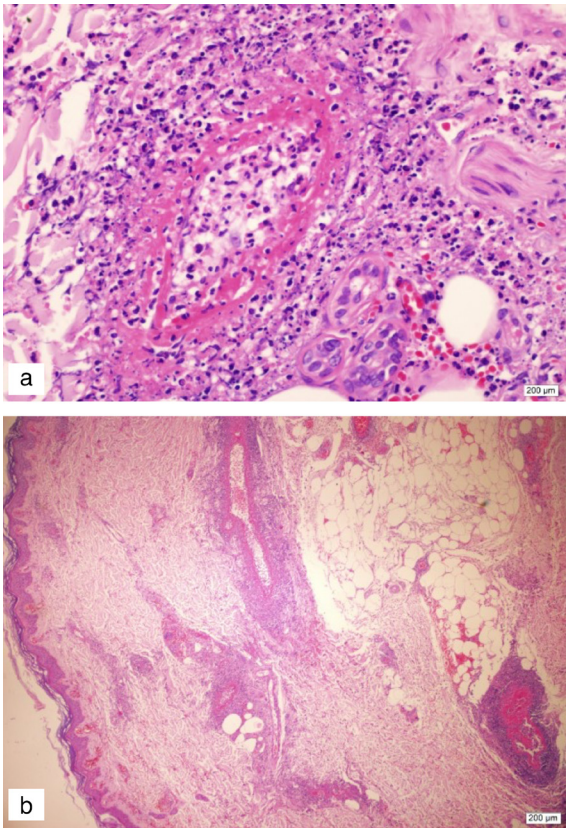

Figure 3. Histopathological image of the biopsy material. **a.** Fibrinoid necrosis of the relatively large vessel wall and surrounding leukocytoclastic are observed (H&E, x400). **b.** Subepidermal separation is observed in the epidermis secondary to diffuse vasculitis (H&E, x200)

According to peripheral smear and laboratory findings of blood, urine, and sputum cultures of the patient, empirical piperacillin-tazobactam (3x4.5 g), methylprednisolone (250 mg/day) and enoxaparin (1x0.6 mL) treatment were initiated, considering COVID-19-related pneumonia due to findings in lung CT. Due to high D-dimer and possible arterial microthrombosis, 0.5 ng/kg/min iloprost infusion was added to the treatment and the infusion was continued for six days. In addition, when it was reported that there was no growth in the cultures taken, de-escalation to ceftriaxone was performed. Both cytoplasmic type and myeloperoxidase type anti-neutrophil cytoplasmic antibody (p and c-ANCA) tests were negative. On the 3rd day of her hospitalization, a biopsy was taken from the dorsum of the right foot for pathological examination with the preliminary diagnosis of small vessel vasculitis. Histopathological examination was reported as leukocytoclastic vasculitis (Figure 3). Then, the dose of the methylprednisolone was increased to 1 g/day which was administered for 3 days and decreased gradually on the follow-up period. On the 12th day of her hospitalization, the patient had signs of hypoxia despite high-flow oxygen therapy and non-invasive ventilation support. After intubation invasive mechanical ventilation and sedation were started. On the 26th day of the intensive care follow-up, meropenem, vancomycin and colistin treatment was started according to the antibiogram results for *Klebsiella pneumoniae* in the tracheal aspirate culture and *Enterococcus faecalis* in the blood culture. On the 30th day of her admission to the intensive care unit, due to the development of significant necrosis of the lesions (Figure 4), amputation of the right foot below the knee, debridement of the left foot (Figure 5), and bilateral mastectomy were performed under general anesthesia. In addition, surgical tracheostomy was performed on the 18th day of intubation. Pathological examination of the mastectomy material was also reported as leukocytoclastic vasculitis. The patient, who could not wean from mechanical ventilator support during the intensive care follow-up, died on the 71st day of hospitalization due to sepsis associated multiorgan failure.

Informed consent was obtained from the patient.

Discussion

COVID-19 continues to be investigated in all its aspects since the day it was first identified. In this disease, coagulation abnormalities and skin findings can be observed alone or in combination with many systemic involvements. This is a very rare case due to the systemic manifestations such as severe pneumonia, coagulopathy, and leukocytoclastic vasculitis associated with COVID-19 being seen together.

Coagulopathy is one of the critical complications in COVID-19 and effects the mortality and morbidity of patients (1). Inflammatory response and vascular endothelial damage resulting from COVID-19 trigger the coagulation cascade

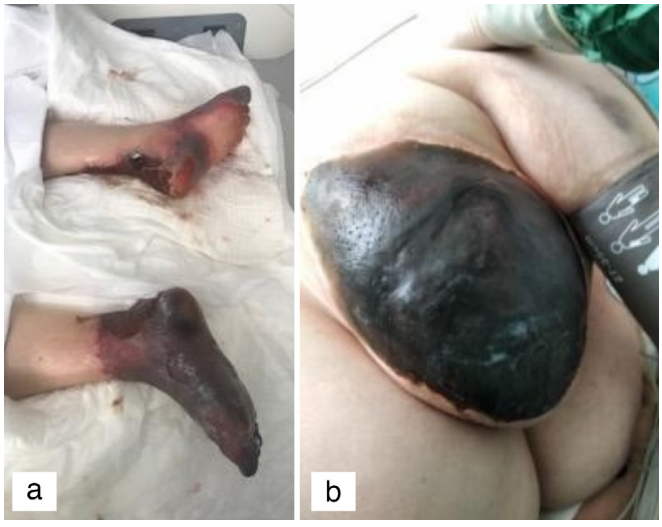

Figure 4. Necrotic lesions developed in the patient (**a.** both feet; **b.** right breast)

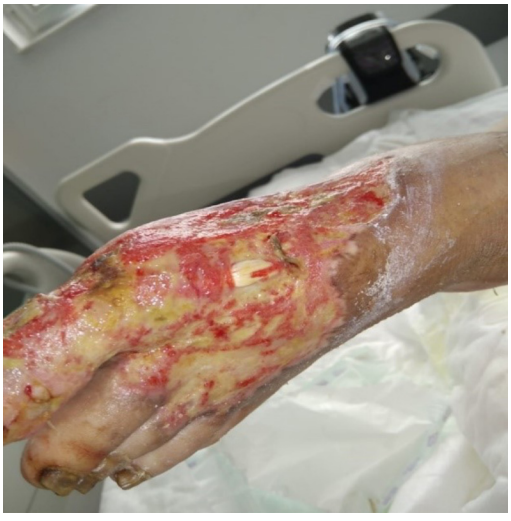

Figure 5. Debridement in the right foot

(2). The best laboratory test for the diagnosis of COVID-19 related hemostatic abnormalities is considered to be D-dimer (3). While circulating D-dimer levels are low in healthy individuals, high levels are found to be associated with increased coagulation and fibrinolytic activity (1). D-dimer is routinely used clinically for the diagnosis of diffuse intravascular coagulation (DIC), deep venous thrombosis, and pulmonary thromboembolism (4). D-dimer elevation has also been reported in COVID-19 patients and it is one of the most common laboratory findings in COVID-19 patients requiring hospitalization (1,5). An increase in D-dimer may indicate activation of the coagulation system due to infection/sepsis, cytokine storm or organ failure (6). High D-dimer levels are indicated as a reliable parameter in predicting mortality (1). In the case of COVID-19, although laboratory findings are similar, including a marked increase in D-dimer and, in some cases, mild thrombocytopenia, other coagulation parameters differ from DIC. In particular, high fibrinogen and high factor-VIII activity observed in the course of the disease indicate that coagulation pathologies do not occur and DIC does not develop in most patients (7). In our case, disseminated intravascular coagulation was not considered according to peripheral smear findings and DIC scoring results (8). In our case, D-dimer values were quite high, as observed in the literature. In addition to leukocytoclastic vasculitis detected in skin lesions, deep vein thrombosis was also present.

Leukocytoclastic vasculitis is a common histopathological term to describe small vessel vasculitis. Basic features of cutaneous leukocytoclastic vasculitis are palpable purpura, lower extremity localization, and small vessel involvement (9). About half of the cases are idiopathic. In cases with secondary development, infections and drugs are among the most common triggering factors. However, it may develop secondary to autoimmune diseases, chronic infections, and malignancies. Skin manifestations of leukocytoclastic vasculitis appear approximately 1-3 weeks after the triggering event. Lesions may present as purpura, erythematous macules, hemorrhagic bullae, or other clinical findings secondary to ischemia, such as ulcers (10). Lesions on the lower extremities and buttocks are usually symmetrical and not associated with trauma (11). A biopsy should be taken from the lesion area to confirm the diagnosis in cases with suspected vasculitis. Basic histological features in biopsy are evidence of tissue damage such as polymorphonuclear leukocyte infiltration, fibrinoid necrosis, extravasated red blood cells, and damaged

endothelial cells in and around the vessel wall (12). Our case had leukocytoclastic vasculitis, which developed during COVID-19 infection and was histopathologically proven in both skin biopsy and debridement samples. There are some case reports of leukocytoclastic vasculitis associated with COVID-19 in the literature. In a similar case report including findings of a 41-year-old male patient published by Alattar et al. (13), histopathological examination of the biopsies of skin lesions and skin debridements obtained from more than one region were compatible with leukocytoclastic vasculitis and left toe amputation was required. Like our case, Iraji et al. (14) described a case of cutaneous leukocytoclastic vasculitis in a 49-year-old male patient which started simultaneously with COVID-19-associated pneumonia and presented with purpuric skin rashes in the lower extremities. Gouveia et al. (15) reported the presence of leukocytoclastic vasculitis in a 27-year-old male patient with COVID-19 in the biopsies they obtained from purpuric lesions and hemorrhagic vesiculobullous lesions, which are more common in the lower extremity skin and less common in the back and upper extremities. Another feature of this case was microthrombi in small vessels revealed in histopathology. Camprodon Gómez et al. (16) published a case of leukocytoclastic vasculitis that developed in the 1st month of infection and presented with palpable purpura in a 29-year-old male patient who had COVID-19 and recovered completely. Similarly, Mayor-Ibarguren et al. (17) published a paper including leukocytoclastic vasculitis occurred during recovery from COVID-19 in an 83-year-old female patient. In a case-control study published by Kutlu et al. (18), it was reported that leukocytoclastic vasculitis accounted for 1.8% of all skin lesions in patients with COVID-19.

It is thought that approximately 20-30% of all vasculitis cases are due to drug use (19). Leukocytoclastic vasculitis has been suggested to have an association with many drugs, most notably beta-lactam antibiotics. If drug-induced vasculitis is considered as a diagnosis, new drugs and their associated comorbidities should be investigated. For most patients, symptoms or signs should be expected to develop usually 7-10 days after exposure due to the time for the formation of antigen-antibody complexes. Symptoms can be expected to regress upon discontinuation of the drug. In our case, favipiravir treatment was started for the treatment of COVID-19 three days before the onset of clinical symptoms, and it can be considered as a suspicious agent in terms of triggering the development of leukocytic vasculitis. However, favipiravir has a low side-effect profile, and to the best of our knowledge there is no report in the literature including vasculitis related to the use of favipiravir. In addition, vasculitis developed on the 3rd day of favipiravir treatment in our case. We believe that this period is not sufficient enough to trigger the vasculitic immune mechanism.

Autoimmune diseases are also important diseases to be considered in the etiology of leukocytoclastic vasculitis (20). Our case was a patient with a long-term diagnosis of RA who was in remission under adalimumab treatment. The development of a small vessel vasculitis associated with RA under the anti-tumor necrosis factor antagonist adalimumab treatment seems to be less likely in the presence of a risk factor such as COVID-19.

The data in the literature contains reports supporting that some cutaneous involvements may occur at the onset, during, and even after COVID-19. Some of these cutaneous involvements may be associated with leukocytoclastic vasculitis. Our case is crucial because it reveals a rare condition such as leukocytoclastic vasculitis, in addition to COVID-19-associated pneumonia and coagulopathy. Since there is no publication, it seems difficult to decide whether the use of favipiravir is a trigger for the development of leukocytoclastic vasculitis.

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Authorship Contributions

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CASE REPORT / *OLGU SUNUMU*

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Bacteremia and Pneumoniae Caused by *Kocuria Kristinae*: A Rare Case

Kocuria Kristinae'nin Sebep Olduğu Bakteriyemi ve Pnömoni: Nadir Bir Olgu

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ABSTRACT *Kocuria kristinae*, previously known as *Micrococcus kristinae*, are common in nature but are included in the normal skin flora, mucous membrane, and oropharynx in humans and are generally not pathogenic. Kocuria species are facultative anaerobic, catalase positive, and coagulase negative cocci. It can cause peritonitis associated with peritoneal dialysis, catheter-related urinary tract infections, acute cholecystitis, infective endocarditis, meningitis, brain abscess, and pneumonia in patients with chronic disease and immunocompromised patients. This article presents a case of pneumonia and bacteremia due to *Kocuria kristinae*, reported for the first time in Turkey, in a 72-year-old female patient with a history of comorbid diseases and tracheostomy.
Keywords: *Kocuria kristinae*, pneumonia, bacteremia, intensive care unit

ÖZ Önceleri *Micrococcus kristinae* olarak bilinen *Kocuria kristinae*, doğada yaygın bulunmakla beraber insanlarda deri, müköz membran ve orofarenksin normal flora elemanları arasındadır ve genellikle patojen değildir. Kocuria türleri fakültatif anaerop, katalaz pozitif, koagülaz negatif koklardır. Kronik hastalığı olan, bağışıklık sistemi baskılanmış hastalarda periton diyalizi ile ilişkili peritonit, kateter ilişkili üriner sistem enfeksiyonları, akut kolesistit, enfektif endokardit, menenjit, beyin apsesi ve pnömoniye sebep olabilmektedir. Bu makalede, 72 yaşında komorbit hastalıkları ve trakeostomi öyküsü olan kadın hastada Türkiye'den ilk defa bildirilen *Kocuria kristinae*'ya bağlı pnömoni ve bakteriyemi olgusu sunulmuştur.
Anahtar Kelimeler: *Kocuria kristinae*, pnömoni, bakteriyemi, yoğun bakım ünitesi

Introduction

Kocuria species are facultatively anaerobic, catalase-positive, coagulase-negative cocci, which are considered sensitive to most antimicrobials (1). Although Kocuria species are common in nature, they are among the standard flora elements of the skin, mucous membrane, and oropharynx in humans and are generally not pathogenic. Cases of peritonitis associated with peritoneal dialysis, catheter-related urinary tract infections, acute cholecystitis, infective endocarditis, meningitis, brain abscess, and rarely pneumonia have been reported in patients with chronic disease and whose immune system is suppressed (2-8).

This study presents the first case of pneumonia and bacteremia due to *Kocuria kristinae* in Turkey, which was treated in the intensive care unit (ICU).

Case Report

A 72-year-old, body mass index: 42.9 kg/m^2 obese female patient with chronic obstructive pulmonary disease (COPD), heart failure, and hyperthyroidism was admitted to the emergency department with complaints of respiratory failure, tachypnea, fever, and cough lasting for several days. It was learned that the patient was followed in the ICU for three months due to respiratory distress due to COPD and

heart failure two months ago. A percutaneous tracheostomy was performed during the ICU follow-ups. The tracheostomy of the patient, who was followed up at home for two months with a home ventilator, was closed one month ago.

In her physical examination, the patient was confused. She had subfebrile fever (37.9) and bilateral crepitant rales on lung auscultation. Heart rate was 100-105 min^{-1}, blood pressure was 85/60 mmHg, respiratory rate was 22 min^{-1}, SPO_2 in pulse oximetry was 75-80% in room air and 88-90% under oxygen. The laboratory examination showed white blood cell: $11x10^3$ μL^{-1}, C-reactive protein: 130 mg L^{-1}, and procalcitonin 0.29 μL^{-1}. No abnormality was detected except a small number of erythrocytes in the urinalysis.

When a radiological examination was performed, no pathology was observed in the cranial tomography of the patient. Chest tomography showed cardiomegaly, bronchopneumonia infiltrates, and atelectatic areas. The patient, who was diagnosed with pneumonia, was admitted to the ICU as extubated. Peripheral blood cultures, urine culture, and tracheal aspirate culture (TAC) were taken from both arms, and empirical antibiotic therapy of meropenem 1 g 2x1 and amikacin 500 mg 3x1 was started.

Non-invasive mechanical ventilation was started on the patient. The patient was unconscious, peripheral oxygen saturation decreased, hypotension was observed, and the patient was intubated. Low-dose vasopressor support was started. The patient was extubated on the third day of intubation. *K. kristinae* was isolated in both blood cultures of the patient, who was reintubated due to severe respiratory failure and tachypnea. No growth was observed in the urine culture and TAC. A culture antibiogram showed it was resistant to ampicillin/sulbactam and meropenem but sensitive to tigecycline. Thereupon, meropenem was stopped, and after loading tigecycline 100 mg, maintenance treatment was started with 50 mg 2x1.

On the fifth day of intubation, the patient was extubated, whose hemodynamic stabilization was achieved, and his breathing was relieved. The patient, who was followed up and treated in the ICU for 13 days, was discharged from the inpatient service.

Verbal and written consent was obtained from the patient and her relatives for the case report.

Discussion

K. kristinae, previously known as *Micrococcus kristinae*, was first described in 1974. It is a natural member of many mammals' skin and mucosal flora and functions as an opportunistic pathogen. Although the disease caused by this organism is sporadic, it has been reported more frequently since the end of the 20th century. Five of the 18 known species of the genus Kocuria spp. have been reported to be pathogenic *(K. kristinae, K. rhizophila, K. rosea, K. varians*, and *K. marina*) (9). A systematic meta-analysis reported that *K. kristinae* was the causative agent of central venous catheter-related bacteremia in 17 cases, infective endocarditis in four cases, acute peritonitis in three cases, and abdominal abscess, acute cholecystitis, and urinary tract infection in one case (10). When the literature is reviewed, although cases of infective bacteremia, endocarditis, and meningitis caused by Kocuria species have been reported from Turkey, no pneumonia cases have been reported (5,11).

Kim et al. (12) reported a case of empyema caused by *K. kristinae* in a 57-year-old man with diabetes mellitus. It was reported that the patient was started on ceftriaxone, levofloxacin, and clindamycin antibiotics. When his fever did not decrease, he was switched to a piperacillin-tazobactam antibiotic, and the patient recovered after three weeks of treatment (12).

As far as we can reach in the literature, two cases of pneumonia caused by *K. kristinae* and *K. rosea* have been reported (7,8). Bernshteyn et al. (7) reported a case of bacteremia and pneumonia due to *K. kristinae* in a 62-year-old man with heart failure, hypertension, diabetes mellitus, and hypothyroidism. Piperacillin-tazobactam and azithromycin treatment was started for pneumonia in the patient who developed acute hypoxic respiratory failure and was intubated. After an unsuccessful extubation attempt in the patient after four days of treatment, *K. kristinae* was isolated in both blood cultures. It was stated that after switching to linezolid treatment, the patient's clinical condition improved within two weeks, and he was discharged.

Páez et al. (8) also reported a case of bacteremia and community-acquired pneumonia due to *K. rosea* in a 71-year-old male patient with a history of diabetes mellitus, COPD, and previous cerebrovascular accident. The patient, who had a productive cough and severe respiratory distress for three days, was intubated and taken to the ICU under vasopressor support. It was stated that piperacillin-tazobactam and clarithromycin antibiotic therapy was started on the patient, and *K. rosea* was grown in the bronchoalveolar lavage culture. It has been reported that the patient was discharged with hemodynamic stabilization after five days of treatment.

It has been reported that the Kocuria species causes infections in patients with comorbid diseases or weakened immune systems (1-12). In our case, COPD, heart failure, hyperthyroidism, and morbid obesity stand out as risk factors. In addition, we think that the recent follow-up of the patient in the ICU for three months, opening and closing a percutaneous tracheostomy, facilitated this agent, a member of the normal skin flora, to become a cause of bacteremia and pneumonia. Empirical antibiotic therapy was started for the patient, whose follow-up and treatment were started in the ICU, but no clinical response was obtained. According to the culture antibiogram results, the patient whose pneumonia regressed with tigecycline was discharged.

Kocuria species can be mistakenly interpreted as coagulase-negative *staphylococci* in microbiology laboratories (7). It has been reported that it cannot be differentiated when evaluated with manual methods due to their similarities. It is important to use automated systems such as VITEK-2 that help with accurate identification (7,9). Szczerba (13) stated that Kocuria species are sensitive to doxycycline, ceftriaxone, cefuroxime, amikacin, and amoxicillin-clavulanic acid, while they are resistant to ampicillin and erythromycin.

In our case, species-level identification was made with the VITEK-2 (bioMerieux, France) method to isolate the agent. The patient was empirically treated with meropenem and amikacin antibiotics. As a result of the culture antibiogram, the agent was found to be resistant to meropenem and ampicillin/sulbactam, and tigecycline treatment was started.

In conclusion, *K. kristinae* and other sub-strains are among the standard flora elements of the mucous membranes and oropharynx. They may rarely lead to life-threatening conditions such as pneumonia. Although it may be difficult to distinguish by manual methods due to its similarities to coagulase-negative *staphylococci*, it is more frequently defined and reported with automated systems today. It should be kept in mind that although it is generally sensitive to antibiotics, it cannot respond to empirical treatment. It is essential to regulate the treatment according to the culture antibiogram result.

Ethics

Informed Consent: Verbal and written consent was obtained from the patient and her relatives for the case report.

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Authorship Contributions

Concept: K.A., A.S.Ş., Design: K.A., A.S.Ş., Data Collection and/or Processing: K.A., Analysis and/or Interpretation: K.A., A.S.Ş., Literature Search: K.A., Writing: K.A.

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Lütfi Telci

Yorum "Asit-baz Bozukluklarına Stewart Yaklaşımı: Güçlü İyon Farkı Yoğun Bakım Mortalitesini Etkiler mi?"

Comment on "Stewart's Approach for Acid-base Disorders: Does the Strong Ion Difference and Effects Have an Impact on Intensive Care Unit Mortality?"

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Keywords: Acid-base, SID, lactate, intensive care, mortality

Sayın Editör;

Derginizin 2023/1 sayısında "Stewart's Approach for Acid-base Disorders: Does the Strong Ion Difference and Effects Have an Impact on Intensive Care Unit Mortality?" başlıkla yayınlanmış olan yazıya ilişkin olan karşı çıkışımı duyurmak istiyorum (1).

Yoğun bakıma alınmış hastaların kan gazı değerlerini izlemek, değerlendirmek ve gerek görüldüğü anda gerekeni yapmak, yoğun bakım uzmanının görevidir. Klinik ve laboratuvar değerlerini birlikte yorumlayarak prognostik tahminlerde bulunur. Yalnızca laboratuvar değerlerini göz önüne alarak prognostik yorum yapmak kanımca doğru değildir. Laboratuvar değerlerinin "ölüm oranını" ne kadar artırıp azalttığını merak edip, istatistiksel arayışa gitmek ve sonuçları anlamlı çıkınca, prognozu öne çıkaran yorum yapmaya karşı çıkıyorum. Asidoz, alkaloz, baz açığı (*base excess*), laktat … gibi laboratuvar değerlerinin mortaliteye etki ettiği bilgisi çok uzun zaman önce terk edilmiştir. Stewart'ın Asit-Baz fizyolojisine kattığı yeni parametrelerin, diğer parametrelere göre bir ayrıcalığı yoktur. Stewart yaklaşımı asit-baz fizyolojisine ve doğal olarak klinik uygulamalarımıza çok yararlı derinlikler katmıştır. Bu bilgilerden kesinlikle yararlanalım ve daha etkin klinik uygulamalarımızı sürdürelim. Prognostik yorum yapmayı, kapsamlı değerlendirmelerimize bağlı kalarak yapalım.

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Furkan Tontu

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Keywords: Acid-base balance, prognose, mortality, strong ion difference, lactate

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Asit-baz dengesinin analizinde hangi yaklaşımın daha doğru olduğu yıllardır süregelen bir tartışmadır. Bununla birlikte, geleneksel yaklaşımların nedensel mekanizmaları açığa çıkarmakta yetersiz kaldığı da bilinmektedir (1). Stewart yaklaşımı ise asit-baz bozukluğunu kolaylıkla tiplendirebilmektedir. Stewart yaklaşımının yorumlanması; Henderson-Hasselbalch ve baz açığı (base excess, BE) yaklaşımlarından daha karmaşıktır. Laboratuvardan valide edilmiş verilerle elektronik ortamda parametrelerin hesaplanmasında bir bilgisayar yazılımına ihtiyaç duyulabilmektedir (2). Günümüzde, yoğun bakım ünitelerinde (YBÜ) klinik karar destek sistemlerinin kullanımının yaygınlaşması Stewart yönteminin yatak başında daha kolay uygulanabilir hale gelmesini sağlamıştır (3). Yazar editöre mektubunda, laboratuvar değerlerinin ve formüllerle üretilen parametrelerin mortalite ve prognoz üzerindeki etkilerinin araştırılmasının gereksiz olduğunu belirtmiştir. Oysaki, yatak başında kullanım sıklığı artan bu parametrelerin prognostik önemlerinin olup olmadığının klinisyenlerce merak edilip araştırılması bilimsel sürecin yadsınamaz bir parçasıdır. Bizim çalışmamızın sonuçlarına göre, laktat dışı güçlü iyon farkı (*non-lactate strong ion difference*, SID_{nl}) YBÜ mortalitesi ile ilişkili bulunurken; pH, standart BE (SBE) ve laktat gibi parametrelerin mortalite ile ilişkisi gösterilememiştir (4). Elbetteki bizim çalışmamızdan elde edilen sonuçlar, bir parametrenin diğerinden prognostik açıdan her koşulda daha üstün olduğu veya tek başına hastanın tedavisini yönlendirmesi gerektiği anlamına gelmemektedir. Bu parametreler, klinisyen tarafından hastanın klinik seyri izlenirken kullanılan terapotik yöntemlere yardımcı elemanlardır. Çalışmamızda vurgulanmak istenen esas nokta; Stewart yaklaşımı kullanılarak elektronik klinik karar destek sistemlerinin yardımıyla elde edilen parametrelerin, yatak başı kan gazı değerlendirmelerine katkısının ve tanıya

giden yoldaki rehberliğinin göz ardı edilmemesi gerektiğidir. Ayrıca yazar, asidoz, alkaloz, BE ve laktat gibi parametrelerin mortalite üzerindeki etkilerinin incelenmesinin çok uzun zaman önce terk edildiğini belirtmekte fakat burada da referans göstermemektedir. Literatürde pH, SBE, SID, SID_{nl} ve laktat gibi parametrelerin mortalite ve prognoz üzerinde etkilerini inceleyen birçok güncel çalışma bulunmaktadır (5-14). Son olarak, yazara katkılarından dolayı teşekkür eder, Stewart yaklaşımının tartışılarak gündeme gelmesinden duyduğum mutluluğu belirtmek isterim.

Saygılarımla

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