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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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# YAZARLARA BİLGİ

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].

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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.

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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.

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## ÖZGÜN ARAŞTIRMALAR / ORIGINAL RESEARCHES



## OLGU SUNUMLARI / CASE REPORTS

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**Fatemeh Hoomani Majdabadi,**
**Mehdi Harorani**

# Investigating the Impact of Airway Management Training on the Moral Distress and Compassion Fatigue of Nurses Working in Intensive Care Units

## Havayolu Yönetimi Eğitiminin Yoğun Bakım Ünitelerinde Çalışan Hemşirelerin Ahlaki Sıkıntı ve Şefkat Yorgunluğuna Etkisinin Araştırılması

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**ABSTRACT** *Objective:* Nurses in the intensive care unit (ICU) experienced high prevalence of compassion fatigue and moral distress that can reduce job satisfaction and impact the quality of care due to specific conditions of patients, thus identifying the factors affecting the compassion fatigue and moral distress is very important. This study aimed to investigate the impact of airway management training on the quality of care delivery and moral distress and compassion fatigue in nurses.

*Materials and Methods:* This study was conducted on 50 nurses working in the ICU. Data collection tools included Moral Distress Scale and Multidimensional Fatigue Inventory, along with an airway care checklist prepared according to nursing standards. Before the intervention, participants completed the questionnaires and their function of airway care was investigated through the checklist. Nurses were trained face to face. After training, assessors evaluated the nurses by observing the quality of airway care through the standard checklist. Then, moral distress and fatigue questionnaires were filled again, and results before and after training were analysed.

*Results:* The rate of moral distress and fatigue among nurses has significantly reduced before and after training ($p<0.001$). In addition, the quality of airway management increased from 70% to 86% ($p<0.001$).

*Conclusion:* Airway management training can decrease the nurses' moral distress and compassion fatigue and improve the quality of airway care. The ability of nurses working in the ICU including knowledge and practice increased leading to improved quality of care and reduced moral distress and compassion fatigue. Therefore, periodic training workshops in airway management can be very effective.

**Keywords:** Airway management, compassion fatigue, education in practice, intensive care units, moral distress, respiratory care

**ÖZ** *Amaç:* Yoğun bakım ünitesinde (YBÜ) çalışan hemşireler, iş doyumunu azaltabilecek ve hastaların özel durumları nedeniyle bakım kalitesini etkileyebilecek şekilde, yaygın olarak şefkat yorgunluğu ve ahlaki sıkıntı yaşamaktadırlar. Bu nedenle şefkat yorgunluğunu ve ahlaki sıkıntıyı etkileyen faktörlerin belirlenmesi çok önemlidir. Bu çalışma, hemşirelerde havayolu yönetimi eğitiminin bakım kalitesi ile ahlaki sıkıntı ve şefkat yorgunluğuna etkisini araştırmayı amaçlamaktadır.

*Gereç ve Yöntem:* Bu çalışma YBÜ'de çalışan 50 hemşire üzerinde yapılmıştır. Veri toplama araçları olarak Ahlaki Sıkıntı Ölçeği ve Çok Boyutlu Yorgunluk Envanteri ile birlikte hemşirelik standartlarına göre hazırlanmış bir havayolu bakım kontrol listesi kullanıldı. Müdahaleden önce, katılımcılar anketleri doldurdular ve hava yolu bakımının işlevleri kontrol listesi aracılığıyla araştırıldı. Hemşireler yüz yüze eğitim aldılar. Eğitimden sonra değerlendiriciler, standart kontrol listesi aracılığıyla havayolu bakımının kalitesini gözlemleyerek hemşireleri değerlendirdiler. Daha sonra ahlaki sıkıntı ve yorgunluk anketleri tekrar doldurularak sonuçlar eğitim öncesi ve sonrası analiz edildi.

*Bulgular:* Hemşireler arasında ahlaki sıkıntı ve yorgunluk oranı eğitim öncesi ve sonrası önemli ölçüde azaldı ($p<0,001$). Ek olarak, havayolu yönetiminin kalitesi %70'den %86'ya yükseldi ($p<0,001$).

*Sonuç:* Havayolu yönetimi eğitimi hemşirelerin ahlaki sıkıntısını ve şefkat yorgunluğunu azaltabilir ve havayolu bakımının kalitesini iyileştirebilir. YBÜ'de çalışan hemşirelerin bilgi ve pratiğe dair yeteneği, bakım kalitesinin artmasına ve ahlaki sıkıntı ve şefkat yorgunluğunun azalmasına yol açtı. Bu nedenle havayolu yönetimi konusunda periyodik eğitim çalıştayları çok etkili olabilir.

**Anahtar Kelimeler:** Havayolu yönetimi, şefkat yorgunluğu, uygulamalı eğitim, yoğun bakım üniteleri, ahlaki sıkıntı, solunum bakımı

## 1. Introduction

Nurses play an important role in managing intensive care units (ICUs) (1) and taking care of patient's receiving ventilation is regarded as one of their responsibilities. In addition, artificial airway is an invasive procedure. Airway management will increases patient's chance of survival although it can be distressful and difficult for caregivers (2). The failure for performing necessary cares by artificial airways among the patients may lead to a lot of damages (3,4). However, considering the accurate care and its standards result in reducing hospitalization time, costs, risks, complications, and distress along with improving the quality of patient and his family's lives is very important (5,6).

Many studies reported that nurses working in ICUs face numerous psychological and physical distresses, which can influence the quality of their care (7). ICU staff can suffer moral distress and compassion fatigue due to high mortality rate, painful conditions of patients, and technology and advanced tools (8-10). It has been estimated that 80% of ICU nurses are experiencing moral distress (11). Shorideh indicated a high level of moral distress in ICU nurses (12) which can lead to adverse consequences such as loss of belonging, lack of confidence, hopeless, anger, as well as the feeling of inability to take care of patients (13,14).

In general, moral distress in nurses occurs when a specific moral action is needed or in a specific situation, where he should choose a treatment guideline based on his personal moral bias. In addition, internal or external limits which interference the performance of caring programs cause moral distress (15). Moral distress prevalence is very high in ICU because of crisis situations they face which lead to decision making and therapeutic actions (10). For example one of the most cause of nurses experienced distress as a consequence of inadequate care provided by other nurses and physicians the other cause was pain management and its relation to extubation (16).

In another study, 81% of ICU nurses described themselves powerless and ineffective. In addition, they may fail to make decisions for their patients because of moral conflicts (10). Since moral distress is often associated with compassion fatigue, it will cause emotional exhaustion, job exhaustion, position loss, or even profession leaving if the nurses fail to overcome this feeling (17,18).

According to the culture and specific value in Iran, organizational constraints, unnecessary measures, wrong treatment, medical and medicinal errors, as well as responsibility, competence and incorrect resources can cause moral distress in ICU (12). Since nurses are the greatest group in health care team, their training is considered as a priority. Enough knowledge and skill in nursing field result in developing the quality of patient care and feeling self-satisfying (19,20). As a result, the present study aimed to evaluate the impact of training the airway management on the rate of moral distress and compassion fatigue of nurses in ICUs in a medical and educational center.

## 2. Materials and Methods

### 2.1. Design

This study was approved by the Research Council and the Ethics Committee of our University of Medical Sciences (ethics committee reference number: IR.ARAKMU.REC.1395.417) and received a license from the National Center for Clinical Trials Control at IRCT2017062513110N3. Then, the data were collected after the permission of the hospital authorities, the satisfaction of the nurses, and an explanation of the nature and objectives of the research. The questionnaires were completed anonymously and the subjects were allowed to leave during the study. This semi-experimental study was conducted from February to July 2018.

### 2.2. Subjects and Recruitment

In this study, due to the limited statistical population, the sampling method was census. All nurses working in ICUs of an educational hospital in Arak city, Iran, were invited to participate in the study. Finally, the number of samples was 50 nurses who met the inclusion criteria and agreed to participate in the study. The inclusion criteria were having Bachelor of Science in Nursing or higher degree, working in ICU at least for a year, and inclining to participate in the study.

### 2.3. Training Course

The intervention type was face-to-face training about standard care of artificial airway, which took a 30-60-minute session. The training covered a description of standard controlling and suctioning the airway, oropharynx, tracheostomy, and tracheal tube, along with an educating pamphlet of verbal summary about the subject. The questionnaires and related checklist were completed before and after the intervention.

### 2.4. Data Collection

The data were collected by using demographic data questionnaire, Corley Moral Distress scale, and Multidimensional Fatigue inventory.

#### 2.4.1. Corley Moral Distress Scale

Moral distress questionnaire was used to measure the frequency and intensity of moral distress among the subjects in 24 questions based on the five-point Likert scale. Moral distress in this questionnaire describes the times facing distressful factors which is scored 0 for "I've never confronted" to 4 for "I've been much confronted". Further, the intensity of moral distress defines the rate of tension one felt while meeting distressful situations and varies from "does not make me distressed" (score 0) to "makes me distressed a lot" (score 4). The scores of each dimension starts from zero to 96 and higher score indicates more frequency or intensity of moral distress. This questionnaire has been used in several studies in Iran in 2012 by Joolaee by considering the specific conditions of the system of providing services in Iran. Its validity was determined by the content method and its reliability was confirmed by the internal consistency method ($\alpha$=0.86) (21).

In the current study, the internal consistency of the questionnaire was completed by 10 samples was measured using SPSS software as well as the Cronbach's alpha coefficient, and the reliability coefficient was obtained to be 0.853

#### 2.4.2. Multidimensional Fatigue Inventory

Fatigue inventory included 20 questions and examined 5 different dimensions including general fatigue, physical exhaustion, mental fatigue, decreased activity and motivation. Based on the Likert scale, it was ranged from "Yes, it is completely correct" (score 1) to "No, it is totally wrong" (score 5). Altogether, scores between 21 and 47 are mild, 74-48 moderate and 100-75 severe fatigue. Validity and reliability of this questionnaire were investigated by various studies such as Najafi (22,23).

#### 2.4.3. Operation Checklist

The checklist of nurses' performance in quality of airway care was obtained from reliable resources, American Nurses Association guidelines and nursing techniques and has been approved by nursing professors of the university. Intra-class correlations method was used to determine the reliability. To this aim, two observers evaluated the performance of 10 nurses according to the checklist simultaneously. Then, the correlation coefficient was calculated 95.8%. The checklist consists of 41 items about the standards of artificial airway care based on a three-point Likert scale including systematic actions score (1), non-systematic actions (0.5), and non-taken actions (0). The range of the scores was between 0-41 and higher scores represented higher operation based on percentage. The checklist completed by direct observation of nurses' operation in 3 working shifts. The individual operating score was gained through observation in three times.

### 2.5. Statistical Analysis

According to the objectives of the study, descriptive statistics (frequency, frequency percentage, mean and standard deviation) and analytical statistics (paired sample t-test, Kolmogorov-Smirnov test, Pearson correlation test) were used to analyze the collected data based on the significance level of 5% and confidence level of 80% by using SPSS software version 20.

## 3. Results

In this study, 50 nurses working in ICUs with average age of 33.14±5/54 were investigated. Among the subjects, 48 (96%) were women and 2 men. In addition, 17 people (34%) had one-year experience in ICUs (Table 1).

**Table 1. Frequency distribution of research units based on demographic characteristics**

| Variable | | n=50 no (%) |
|---|---|---|
| Gender | Female | 48 (96) |
| | Male | 2 (4) |
| Marriage | Single | 11 (22) |
| | Married | 39 (78) |
| Degree | BS | 46 (92) |
| | MS | 4 (8) |
| Experience of nursing (years) | 1-5 | 14 (28) |
| | 6-10 | 15 (30) |
| | 11-15 | 15 (30) |
| | 15-20 | 5 (10) |
| | 21-25 | 1 (2) |
| Experience of working in ICU (years) | 1-3 | 25 (50) |
| | 4-6 | 11 (32) |
| | 7-9 | 6 (12) |
| | 10-12 | 3 (6) |

ICU: Intensive care unit, BS: Bachelor of Science in Nursing, MS: Master's Degree in Nursing

As examining the nurses' quality of airway care before and after the intervention program, 70% of the subjects were able to provide an appropriate care before the training while it increased to 86% after the training.

After intervention intensity and frequency of moral distress, fatigue decreased, as well as the quality of airway care increased after the training. Further, the result of paired sample t-test indicated a significant difference between the scores before and after training ($p<0.05$).

The result of Kolmogorov-Smirnov test indicated the normal distribution of the data. Pearson correlation test was used for examining the correlation coefficient between intensity and frequency of moral distress and fatigue. As shown in Table 2, a direct correlation was observed between the rate of fatigue and frequency of moral distress ($r= 0.661$, $p<0.050$), the intensity of moral distress and rate of fatigue ($r=0.666$, $p<0.05$), the quality of airway care and intensity of moral distress ($r=-0.343$, $p<0.05$), and the quality of airway care and frequency of moral distress ($r=-0.323$, $p<0.001$), as well as the quality of airway care and rate of fatigue ($r=-0.381$, $p<0.05$) (Table 2).

## 4. Discussion

The present study aimed to investigate the relationship between the airway care quality and the moral distress and compassion fatigue in nurses working in ICU. The result indicated that training the airway management and enhancing the quality of care in intensive care patients could reduce the moral distress and compassion fatigue among the practitioners working in these units. The results in line with McAndrew's study, which investigated the moral distress in the nurses who were helpless in carrying out some nursing care (24). In another study, it was claimed that training and empowering nurses, working in the ICUs has a direct relationship with reducing their moral distress (25). In addition, the moral distress decreases when professional competence increases (26). Further, Saechao revealed that training the nurses, along with participating in webinar can reduce their moral distress and fatigue (27).

In addition to enhancing self-efficacy, airway management training will improve safety in taking care of patients (28,29). In a qualitative study, the concern about the extent and quality of care of patients, as well as lack of proper communication between personnel and lack of autonomy in the care of patients was cited as the factors causing moral distress in the ICU (30). By considering the result of this study, more ability to manage the airway reduces the moral distress.

Further, the results of the present study indicated significant relationship between moral distress and fatigue, which is consistent with the Mohammadi at al.'s (31) study. Furthermore, some studies indicated that nurses' fatigue can be reduced by their training (32,33).

In addition, a significant relationship was observed between the clinical experience and the quality of airway care in the present study, which is in line with Whyte et al.'s (34) study, which indicated that experienced nurses have better knowledge in the care of patients. Further, Cason et al. (35) reported that work experience in the ICU could be effective in the optimal performance of the personnel, which is consistent with the results of the present study this means that further training of nurses will increase their mastery of airway management. However, compared

**Table 2. Results of correlation coefficients among the variables**

| | Quality of airway care | | Frequency of moral distress | | Intensity of moral distress | | Fatigue | |
|---|---|---|---|---|---|---|---|---|
| | p | r | p | r | p | r | p | r |
| Quality of airway care | - | - | <0.001 | -0.323 | <0.001 | -0.343 | <0.001 | -0.381 |
| Frequency of moral distress | <0.001 | -0.323 | - | - | - | - | <0.001 | 0.661 |
| Intensity of moral distress | <0.001 | -0.343 | - | - | - | - | <0.001 | 0.666 |
| Fatigue | <0.001 | -0.381 | <0.001 | 0.661 | <0.001 | 0.666 | - | - |
| Degree | <0.009 | 0.261 | 0.346 | -0.095 | 0.932 | -0.009 | 0.250 | -0.116 |
| Experience of nursing | 0.014 | 0.246 | 0.036 | -0.210 | 0.006 | -0.275 | 0.170 | -0.138 |
| Experience of working in ICU | 0.004 | 0.282 | 0.024 | -0.226 | <0.001 | -0.364 | 0.003 | -0.290 |
| Age | 0.009 | 0.260 | 0.058 | -0.190 | 0.003 | -0.296 | 0.151 | -0.145 |

ICU: Intensive care unit

to the study conducted by physicians, it was revealed that physicians with more experience offer less care quality (36). This contradicting result may be related to the differences in disciplines.

The present study found that more training and knowledge of nurses in intensive care leads to less moral distress and fatigue, which is congruent with the result of another study which proved that the clinical experience tends to improve nurses' performance in acute situations (37). A study shows that experienced nurses in pediatric oncology unit have better coping responses than rookie nurses (38). So consider to the result of present study it may be possible to offset the nurses' inexperience by increasing their education.

## 5. Conclusion

Based on the results, training the management of airway to nurses working in ICUs can reduce moral distress and fatigue and improve the quality of their care.

### Ethics

**Ethics Committee Approval:** This study was approved by the Research Council and the Ethics Committee of Islamic Republic of Iran Arak University of Medical Sciences (ethics committee reference number: IR.ARAKMU.REC.1395.417) and received a license from the National Center for Clinical Trials Control at IRCT2017062513110N3.

**Informed Consent:** Then, the data were collected after the permission of the hospital authorities, the satisfaction of the nurses, and an explanation of the nature and objectives of the research.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: M.G., B.M., A.J., F.H.M., M.H., Concept: M.G., B.M., A.J., F.H.M., M.H., Design: M.G., B.M., A.J., F.H.M., M.H., Data Collection and Process: M.G., A.J., M.H., Analysis or Interpretation: B.M., A.J., M.H., Literature Search: M.G., A.J., M.H., Writing: M.G., B.M., F.H.M., M.H.

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ÖZGÜN ARAŞTIRMA / *ORIGINAL RESEARCH*

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# Yoğun Bakım Ünitesinde Eldiven Kullanımı

## Glove Usage in the Intensive Care Unit

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**ÖZ** *Amaç:* Eldiven kullanımı, sağlık çalışanlarının kendilerini korumalarının yanı sıra ellerine bulaşan biyolojik vücut sıvılarını hastaya veya hastadan diğer hastaya bulaştırma riskini azaltmak için önerilmektedir. Eldivenlerin gereksiz ve yanlış kullanımı çapraz bulaş riskini arttırabilir. Bu çalışmada daha önce eldiven giyme gözlemi yapılmayan bir yoğun bakım ünitesinde, eldivenlerin doğru ve gerekli kullanımının değerlendirilmesi amaçlandı.

*Gereç ve Yöntem:* Bu çalışma prospektif, kesitsel, gözlemsel bir çalışmadır. Çalışma, bir üniversite hastanesinin 3. düzey genel yoğun bakım ünitesinde yapıldı. Yoğun bakım ünitesinde çalışan hekim, hemşire, hasta bakıcıların eldiven kullanım eylemleri gözlem yöntemi ile belirlendi. Doğru eldiven kullanımında "5 gerekli durum" gözlendi. Gerekli olmayan durumlarda eldiven giyilmesi "gereksiz eldiven kullanımı" olarak değerlendirildi. Gözlemler, yoğun bakım ünitesi sorumlu hemşiresi, enfeksiyon kontrol hemşiresi tarafından yapıldı.

*Bulgular:* Eldiven kullanımında toplam 395 gözlem yapıldı. Doğru eldiven kullanımı oranı %67,8, yanlış eldiven kullanım oranı %32,2 idi. Kan ve/veya vücut sıvıları ile temas olasılığı durumunda %86,1 (n=101) olarak en yüksek oranda eldiven doğru kullanıldı. Aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişimi hiç (n=68) yapılmadı. Gereksiz eldiven kullanımı ise, %85,1 (n=74) oranında gözlemlendi. Eldiven kullanımının mesleklere göre dağılımı istatistiksel olarak anlamlı iken (ki-kare: 44,15, p<0,001), cinsiyete göre anlamlı değildi (ki-kare: 2,13, p<0,144 ).

*Sonuç:* Eldiven kullanımının sistematik olarak gözlemlenmesi, doğru ve gerekli eldiven kullanımının değerlendirilmesini sağlamıştır. Sağlık çalışanlarının, eldiven kullanma konusundaki davranış nedenlerini belirleyen, doğru eldiven kullanımını iyileştiren, gereksiz eldiven kullanımını önleyen çalışmalar yapılmalıdır.

**Anahtar Kelimeler:** Eldiven kullanma, doğru eldiven kullanma, gerekli eldiven kullanma, yoğun bakım ünitesi

**ABSTRACT** *Objective:* Glove usage is recommended for healthcare professionals to protect themselves and reduce the risk of transmission of biological body fluids that get in contact with their hands from one patient to another. Unnecessary and incorrect usage of gloves increases the risk of cross contamination. This study aimed to evaluate the correct and necessary glove usage in the intensive care unit (ICU) where wearing gloves is not observed.

*Materials and Methods:* This is a prospective, cross-sectional and observational study. The study was made in a third level general ICU of a university hospital. Glove usage practice of physicians, nurses and caregivers working in the ICU were determined by observation method. The "5 necessary moments" was observed in the appropriate glove usage. Wearing of gloves when unnecessary was evaluated as "unnecessary glove usage". Observations were made by the ICU nurse and the infection control nurse.

*Results:* A total of 395 observations were made on glove usage. The rate of appropriate glove usage is 67.8%, and misused gloves are 32.2%. The highest rate of correct glove usage was 86.1% (n=101), which was observed in the event of blood and/or body fluid contact. In the same patient, dirty procedures/changing gloves between different regions (n=68) were not performed. Unnecessary glove usage was observed at a rate of 85.1% (n=74). The distribution of glove usage by profession was statistically significant (chi-square: 44.15, p<0.001); however, it was not significant according to gender (chi-square: 2.13, p<0.144).

*Conclusion:* Systematic observation of glove usage provided an appropriate evaluation, thus studies about necessary glove usage should be carried out to determine the reasons for healthcare professionals' behaviour in using gloves to improve correct glove usage and prevent its unnecessary usage.

**Keywords:** Glove usage, correct glove usage, necessary glove usage, intensive care unit

## Giriş

Sağlık çalışanlarının kendilerini korumaları, ellerine bulaşan biyolojik vücut sıvılarını hastaya veya hastadan diğer hastaya bulaştırma risklerini azaltmak için eldiven kullanmaları önerilmektedir (1,2). Eldivenlerin rutin kullanımı, ilk olarak edinilmiş bağışıklık yetmezliği sendromu (*acquired immune deficiency syndrome* - AIDS) salgınına yanıt olarak önerilmiş ve Hastalık Kontrol Önleme Merkezi tarafından 1980'lerin sonlarında "evrensel önlemler" şeklinde adlandırılarak kullanıma girmiştir (2-4). Rutin eldiven kullanımı daha sonraları temasla ilişkili olarak artan kontaminasyon risklerini de bertaraf edebilmek üzere yaygınlaştırılmış ve vücut sıvılarına temas gerektiren ilgili tüm uygulamalarda standart önlemler arasında eldiven kullanımına da yer verilmiştir (2,4).

Kan, idrar, mukus, sekresyon gibi vücut sıvıları, vücut çıkartıları ve gözle görülür şekilde vücut sıvıları ile kirlenen maddelere dokunma sırasında eldiven kullanılmalıdır. Kan ve benzeri; vücut sıvılarına veya kontamine olmuş yüzeylere maruz kalma potansiyeli yok ise eldiven kullanılmamalıdır (5,6).

Eldiven kullanımı, sağlık çalışanını korumak, hastadan hastaya bulaşı önlemek adına oldukça etkili bir önlem olmakla birlikte el kontaminasyonuna karşı tam koruma sağlamamaktadır. Mikroorganizmalar eldivenlerin küçük kusurlarından kaynaklı veya eldivenlerin çıkarılması sırasında ellerin kirlenmesi ile sağlık çalışanlarının ellerine bulaşabilmektedir. Eldivenin çıkarılmasından sonra yapılan el hijyeni, el dekontaminasyonunu sağlayan temel unsurdur (5-9). Dünya Sağlık Örgütü (DSÖ) verilerine göre, hastaları kolonize eden mikroorganizmaların %30'u, hasta teması sırasında eldiven giyen sağlık çalışanlarından bulaşır (5,6). Eldivenlerin zamanında çıkarılmaması veya değiştirilmemesi, işlemler arasında ve rutin hasta bakımı sırasında eldiven çıkarma oranlarının düşük olması, bir hastadan diğer hastaya geçiş sırasında veya aynı hasta üzerinde farklı bölgeler arasında değiştirilmemesi gibi yanlış kullanımları tehlikelidir. Eldiven kullanımına ilişkin kılavuzlar, bir hastadan diğer hastaya geçiş sırasında eldiven değiştirmenin ve eldiven çıkarılmasının ardından el hijyeninin sağlanmasının önemini vurgulamaktadır (5,8,10).

Loveday ve ark'nın (8) çalışmasında eldivenlerin yanlış kullanımının çapraz bulaşa neden olduğu bulunmuştur. Wilson ve ark'nın (10) çalışmasında eldivenlerin yanlış kullanıldığı gösterilmiştir. Fuller ve ark'nın (11) çalışmasında, eldivenlerin yanlış ve gerekli olmayan işlemlerde kullanıldığı gözlemlenmiştir. Yoğun bakım ünitelerinde hastaların durumundan dolayı enfeksiyon kapma riski yüksek olduğu için mikroorganizmaların elle bulaşması önemlidir (9). Daha önce eldiven giyme gözlemi yapılmayan bir yoğun bakım ünitesinde, eldivenlerin doğru ve gerekli kullanımını değerlendirmesi amaçlandı.

## Gereç ve Yöntem

Bu çalışma, prospektif, kesitsel, gözlemsel tipte bir çalışmadır. Çalışma, bir üniversite hastanesi anesteziyoloji anabilim dalı 3. düzey, 12 yataklı yoğun bakım ünitesinde yapıldı. Yoğun bakım ünitesi, uygun eldiven giyme önerilerine uyulmasını gerektirdiği için seçildi. Çalışan hekim, hemşire, hasta bakıcıların, eldiven doğru ve gereksiz kullanımı gözlem yöntemi ile belirlendi. DSÖ'nün tavsiye ettiği eldiven kullanım durumlarına göre; veri toplama aracında toplam 7 parametreden oluşan "doğru eldiven kullanım" formu kullanıldı. Veri toplama formunda, eldiven kullanım durumları olarak 5 eylem belirlendi. Bu eylemler;

- Kan ve/veya vücut sıvıları ile temas olasılığı,
- Bütünlüğü bozulmuş deri veya mukoza ile temas durumu,
- Kontamine olmuş eşya ve çevre yüzeyleriyle temas durumu,
- Temas izolasyonu uygulanan hasta ve çevresine dokunmadan önce,
- Aynı hastada farklı işlemler/farklı bölgeler arasında eldiven değişimidir.

Bu eylemler dışında eldiven kullanılması "gereksiz eldiven kullanımı" olarak kayıt edildi. Gereksiz eldiven kullanımında cihazların (hasta takip monitörleri, ventilatör, infüzyon pumpları) alarmlarının susturulması, hasta ile ilgili kayıtların tutulması, telefon kullanılması, ilaçların yerleştirilmesi gibi işlemler sayıldı. Bu parametrelerin uygulanma durumu gözlemlenerek, doğru/yanlış eldiven kullanımı ve gerekli/gereksiz eldiven kullanımı belirlendi. Sağlık personelinin elinde kesik, çizik ve çatlaklar olması durumunda eldiven giyme gözlemi, hiçbir sağlık çalışanının elinde kesik, çizik ve çatlak olduğu belirlenemediği için bu parametre gözlemden çıkarıldı.

Gözlemler, araştırmaya dahil edilen sağlık çalışanının haberi olmadan yapıldı. Bu nedenle çalışmaya katılanlardan onam alınmadı. Ocak-Şubat 2020 döneminde, toplam 48 sağlık çalışanının (8 hekim, 28 hemşire, 12 hasta bakıcı)

eldiven giyme eylemleri gözlemlendi. Gözlemlerimiz, ülkemizde COVID-19 olgusu görüldüğünde sonlandırıldı. Veriler, yoğun bakım sorumlu hemşiresi ve enfeksiyon kontrol hemşiresi tarafından, hafta içi 08.00-16.00 saatleri arasında, gözlemcilerin rastgele saatlerde yoğun bakım ünitesinde bulundukları zamanlarda toplandı. Gözlemciler, sağlık çalışanlarının gözlem formundaki "eldiven giyme eylemlerini" gözlemledi. Verilerde, sağlık çalışanının meslek ve cinsiyet bilgileri kayıt edildi. Sağlık çalışanının eldiven kullanımı ile ilgili eylemleri veri olarak toplandı.

Araştırma için İstanbul Üniversitesi-Cerrahpaşa, Cerrahpaşa Tıp Fakültesi Klinik Araştırmalar Etik Kurulu'ndan izin alındı (karar no: A-07, tarih: 07.04.2020). Çalışma yapılan yoğun bakım ünitesi yöneticilerinden onam alındı.

### İstatistiksel Analiz

Çalışmada, eldiven kullanma eylemleri sıklık, yüzdelik verileri ile değişkenler arasında ilişki aramak için ki-kare testi kullanıldı.

Çalışmaya dahil etme ölçütleri: Yoğun bakım ünitesinde 08-16 vardiyasında çalışan tüm hekim, hemşire, hasta bakıcılar araştırmaya dahil edildi.

Çalışmadan dışlanma ölçütleri: Yoğun bakım ünitesinde çalışan diğer meslek çalışanları, gece vardiyasında çalışan asistan doktorlar araştırma dışında tutuldu.

## Bulgular

### Tanımlayıcı Bulgular

Sağlık çalışanlarının endikasyonlara göre doğru-yanlış eldiven kullanımına ilişkin bulgular Tablo 1'de gösterildi. Elde edilen verilere göre; kan ve/veya vücut sıvıları ile temas olasılığında doğru eldiven kullanım oranı %86,1'dir (n=87). Aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişimi gerekliliği gözleminde (n=68) katılımcıların hiç değişim yapmadığı gözlemlendi (Tablo 1).

Gereksiz eldiven kullanımına ilişkin bulgular Tablo 2'de gösterildi. Katılımcıların gereksiz eldiven kullanım oranı ise %85,1'dir (n=74) (Tablo 2).

Katılımcıların doğru-yanlış eldiven kullanımına ilişkin bulgular cinsiyete göre değerlendirildiğinde kadınlarda doğru eldiven kullanım oranı %71,9 (n=167), erkeklerde %64,9 (n=228) olarak tespit edildi. Meslek gruplarına göre yapılan değerlendirmede ise doğru eldiven kullanım oranının en yüksek olduğu meslek grubunun hasta bakıcılar %77,9 (n=95), doğru eldiven kullanımının en düşük olduğu meslek grubunun hekimler olduğu tespit edildi %41,9 (n=105). Katılımcıların cinsiyet ve meslek grubuna göre eldiven kullanım oranları Tablo 3'te gösterildi. Doğru eldiven kullanımı açısından cinsiyet ve meslekler arasında ilişki arayıcı analiz sonucunda cinsiyetler arasında istatistiksel olarak anlamlı fark tespit edilmedi, meslek grupları arasında istatistiksel olarak anlamlı fark olduğu tespit edildi ($p<0,001$) (Tablo 3).

Eldiven kullanım endikasyonlarında mesleklere göre doğru eldiven kullanımının yer aldığı Tablo 4 incelendiğinde; kan ve/veya vücut sıvıları ile temas olasılığı, bütünlüğü bozulmuş deri veya mukoza ile temas durumunda, temas izolasyonu uygulanan hasta ve çevresine dokunmadan önce endikasyonlarına göre meslek gruplarına göre eldiven kullanımının istatistiksel olarak ileri düzeyde anlamlı bulundu ($p<0,0001$). Kontamine olmuş eşya ve çevre yüzeyleriyle temas durumunda meslek gruplarına göre eldiven kullanımı istatistiksel olarak anlamlı bulundu ($p>0,05$). Aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişiminin sağlanması uygulamasında bir sabit olduğu için istatistiksel olarak hesaplanmadı (Tablo 4).

Gereksiz eldiven kullanımının cinsiyet ve meslek gruplarına göre Tablo 5 incelendiğinde, cinsiyete ve meslek gruplarına göre istatistiksel olarak anlamlı olmadığı bulundu ($p>0,05$) (Tablo 5).

**Tablo 1. Eldiven kullanımının durumlara göre dağılımı (n=395)**

| Durumlar | Doğru | | Yanlış | | Toplam | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Kan ve/veya vücut sıvıları ile temas olasılığı durumunda | 87 | 86,1 | 14 | 13,9 | 101 | 100 |
| Bütünlüğü bozulmuş deri veya mukoza ile temas durumu | 58 | 84,1 | 11 | 15,9 | 69 | 100 |
| Kontamine olmuş eşya ve çevre yüzeyleriyle temas durumu | 59 | 83,1 | 12 | 16,9 | 71 | 100 |
| Temas izolasyonu uygulanan hasta ve çevresine dokunmadan önce | 64 | 74,4 | 22 | 25,6 | 88 | 100 |
| Aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişiminin sağlanması | 0 | 0 | 68 | 100 | 68 | 100 |
| Toplam | 268 | 67,8 | 127 | 32,2 | 395 | 100 |

## Tartışma

Bu çalışma, eldiven giyme durumunu tespit eden sınırlı sayıda çalışmadan biridir. Gözlemlerimiz eldivenlerin doğru ve yanlış kullanımının yanı sıra gereksiz kullanım oranını da ortaya koymuştur. Çalışmamızda doğru eldiven kullanım oranı %67,8 olarak tespit edilmiştir. Loveday ve ark. (8) tarafından yoğun bakım ünitesinde yaptıkları çalışmada, doğru eldiven kullanım oranı %35,4 olduğu, Wilson ve ark.'nın (10) çalışmasında %45,7 oranında eldivenin doğru kullanıldığı, Chau ve ark.'nın (4) çalışmasında eldiven kullanım genel uyumu %72,4, Flores ve Pevalin'in (2) çalışmasında ise eldiven kullanım genel uyumu %92 oranındadır. Sonuçlardaki bu farklılıklar, çalışmaların ayrı ülkelerde ve birbirinden farklı birimlerde yapılmasından, sağlık çalışanlarının eldiven giyme bilgi düzeylerinin birbirinden ayrı olmasından kaynaklanmış olabilir. Çalışmamızda eldivenin doğru kullanımı, istenen düzeyin altında değerlendirilir. Bu sonucun nedenleri, eldiven kullanımı ile ilgili çalışan eğitimlerinin düzenli yapılmaması, sağlık çalışanlarının yanlış eldiven kullanımının, çapraz bulaşa neden olacağını bilmemeleri veya inanmamalarından ötürü olabilir.

Eldivenlerin, sağlık çalışanlarının kan ve diğer vücut sıvılarıyla temas etme riskini azaltmak, sağlık çalışanından hastaya veya hastadan diğer hastaya bulaşma riskini azaltmak için kullanılması önerilir. DSÖ; evrensel önlemler kapsamında tıbbi eldivenlerin, sağlık çalışanlarının elinde kan ve diğer vücut sıvılarıyla kirlenme riskini azaltmak için kullanılmasını önerir (5). AIDS salgınına yanıt olarak eldiven kullanımını, Hastalık Kontrol Önleme Merkezi 1980'lerin sonlarında önerir (3). Çalışmamızda kan ve/veya vücut sıvıları ile temas olasılığında doğru eldiven kullanım oranı %86,1 olarak tespit edildi. Loveday ve ark. (8) tarafından yapılan çalışmada, kan ve/veya vücut sıvıları ile yüksek riskte bir bulaş olasılığı durumunda çalışanların eldiven kullanımı uygun iken, orta riskte bulaş olasılığı durumunda eldiven kullanım oranının %16, düşük riskte bulaş olasılığı riskinde ise eldiven kullanım oranının %1'e kadar düştüğü, aynı zamanda eldiven kullanımının, tiksinti ve korku duygusundan ötürü olduğu bu nedenle kullanıldığı belirtilmiştir. Wilson ve ark. (10) tarafından yapılan çalışmada %20,1 kan ve vücut sıvılarıyla bulaş durumu oluşmuş ve %44,1 oranında eldiven uygun kullanıldığı belirtilmiştir. Chau ve ark.'nın (4) çalışmasında gözlenen eldiven kullanım durumlarının %71,4'ünde kan, vücut sıvıları, boşaltım, sağlam olmayan deri veya mukoza zarlarına maruz bırakan prosedürler sırasında katılımcılar eldiven giymişlerdir. Çalışma sonuçlarına göre, sağlık çalışanları kendilerine kan ve vücut sıvıları ile bulaş riski yüksek olduğunda, bu bulaştan doğan kendilerinin hastalık kapma korkusundan, bulaştan doğan tiksinti hissinden dolayı eldiven giydikleri söylenebilir.

Evrensel önlemler, çapraz kontaminasyonu önlemek için aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişiminin sağlanmasını önerir (1,4,12). Eldivenler aynı hastadaki kirli işlemler/farklı bölgeler arasında

**Tablo 2. Gereksiz eldiven kullanımı (n=74)**

| Gereksiz eldiven giyme | Doğru | | Yanlış | | Toplam | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| | 11 | 14,9 | 63 | 85,1 | 74 | 100 |

**Tablo 3. Eldiven kullanımının cinsiyet ve mesleklere göre dağılımı (n=395)**

| Cinsiyet | Doğru | | Yanlış | | Toplam | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Kadın | 120 | 71,9 | 47 | 28,1 | 167 | 100 |
| Erkek | 148 | 64,9 | 80 | 35,1 | 228 | 100 |
| Toplam | 268 | 67,8 | 127 | 32,2 | 395 | 100 |
| Ki-kare: 2,13, p<0,144 istatistiksel olarak anlamlı değil | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | n | % | n | % | n | % |
| Hemşire | 150 | 76,9 | 45 | 23,1 | 195 | 100 |
| Hekim | 44 | 41,9 | 61 | 58,1 | 105 | 100 |
| Hasta bakıcı | 74 | 77,9 | 21 | 22,1 | 95 | 100 |
| Toplam | 268 | 67,8 | 127 | 32,2 | 395 | 100 |
| Ki-kare: 44,15, p<0,001 istatistiksel olarak anlamlı | | | | | | |

| **Tablo 4. Eldiven kullanım durumlarının mesleklere göre dağılımı (n=395)** | | | | | | |
|---|---|---|---|---|---|---|
| **Kan ve/veya vücut sıvıları ile temas olasılığı endikasyonu** | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | **n** | **%** | **n** | **%** | **n** | **%** |
| Hemşire | 51 | 98,1 | 1 | 1,9 | 52 | 100 |
| Hekim | 15 | 53,6 | 13 | 46,4 | 28 | 100 |
| Hasta bakıcı | 21 | 100 | 0 | 0 | 21 | 100 |
| Toplam | 87 | 86,1 | 14 | 13,9 | 101 | 100 |
| Ki-kare: 34,45, p<0,0001 istatistiksel olarak anlamlı | | | | | | |
| **Bütünlüğü bozulmuş deri veya mukoza ile temas durumu endikasyonu** | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | **n** | **%** | **n** | **%** | **n** | **%** |
| Hemşire | 31 | 96,9 | 1 | 3,1 | 32 | 100 |
| Hekim | 9 | 47,4 | 10 | 52,6 | 19 | 100 |
| Hasta bakıcı | 18 | 100 | 0 | 0 | 18 | 100 |
| Toplam | 58 | 84,1 | 11 | 15,9 | 69 | 100 |
| Ki-kare: 26,42, p<0,0001 istatistiksel olarak anlamlı | | | | | | |
| **Kontamine olmuş eşya ve çevre yüzeyleriyle temas durumu endikasyonu** | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | **n** | **%** | **n** | **%** | **n** | **%** |
| Hemşire | 29 | 90,6 | 3 | 9,4 | 32 | 100 |
| Hekim | 12 | 63,2 | 7 | 36,8 | 19 | 100 |
| Hasta bakıcı | 18 | 90,0 | 2 | 10,0 | 20 | 100 |
| Toplam | 59 | 83,1 | 12 | 16,9 | 71 | 100 |
| Ki-kare: 7,34, p<0,025 istatistiksel olarak anlamlı | | | | | | |
| **Eldiven kullanım durumlarının mesleklere göre eldiven kullanımı (n=395)**<br>**Temas izolasyonu uygulanan hasta ve çevresine dokunmadan önce** | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | **n** | **%** | **n** | **%** | **n** | **%** |
| Hemşire | 39 | 79,6 | 10 | 20,4 | 49 | 100 |
| Hekim | 8 | 40,0 | 12 | 60,0 | 20 | 100 |
| Hasta bakıcı | 17 | 100 | 0 | 0 | 17 | 100 |
| Toplam | 64 | 74,4 | 22 | 25,5 | 86 | 100 |
| Ki-kare: 18,97, p<0,0001 istatistiksel olarak anlamlı | | | | | | |
| **Aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişiminin sağlanması** | | | | | | |
| **Meslek** | **Doğru** | | **Yanlış** | | **Toplam** | |
| | **n** | **%** | **n** | **%** | **n** | **%** |
| Hemşire | 0 | 0 | 30 | 100 | 30 | 100 |
| Hekim | 0 | 0 | 19 | 100 | 19 | 100 |
| Hasta bakıcı | 0 | 0 | 19 | 100 | 19 | 100 |
| Toplam | 0 | 0 | 68 | 100 | 68 | 100 |

| Tablo 5. Gereksiz eldiven kullanımının cinsiyet ve mesleklere göre eldiven kullanımı (n=74) | | | | | | |
|---|---|---|---|---|---|---|
| Cinsiyet | Doğru | | Yanlış | | Toplam | |
| | n | % | n | % | n | % |
| Kadın | 3 | 10 | 27 | 90,0 | 30 | 100 |
| Erkek | 8 | 18,2 | 36 | 81,8 | 44 | 100 |
| Toplam | 11 | 14,9 | 63 | 85,1 | 74 | 100 |
| p=0,508 istatistiksel olarak anlamlı değil | | | | | | |
| Meslek | Doğru | | Yanlış | | Toplam | |
| | n | % | n | % | n | % |
| Hemşire | 4 | 11,4 | 31 | 88,6 | 35 | 100 |
| Hekim | 2 | 10,0 | 18 | 90,0 | 20 | 100 |
| Hasta bakıcı | 5 | 26,3 | 14 | 73,7 | 19 | 100 |
| Toplam | 11 | 14,9 | 63 | 85,1 | 74 | 100 |
| Ki-kare: 2,66, p=0,263 istatistiksel olarak anlamlı değil | | | | | | |

değiştirilmemesi çapraz bulaşma riskini artırır. Yoğun bakım ünitelerinde hastane enfeksiyonlarının yüksek olduğu ve çapraz bulaş ile bu oranın arttığı bilinmektedir. Çalışmamızda, aynı hastada kirli işlemler/farklı bölgeler arasında eldiven değişimi hiç yapılmamıştır. Kim ve ark.'nın (13) (2003) Amerika'daki yoğun bakım ünitelerinde yürüttüğü gözlemsel çalışmada, sağlık çalışanlarının sadece %7,9'u, aynı hastanın birden fazla vücut bölgesine/salgılarına temas durumunda bir kez eldiven değişimi yapmışlardır. Çalışmamızda aynı hastadaki kirli işlemler ve/veya farklı bölgeler arasında eldivenin hiç değiştirilmemesi, sağlık çalışanlarının, bu durumun çapraz bulaşa neden olabileceği konusundaki bilgi eksikliği, bulaşa neden olabileceğine inanmamalarından dolayı olabilir.

Çalışmamızda bulunan diğer bir veri eldivenlerin gereksiz kullanımıdır. Çalışmamızda gereksiz eldiven kullanımı %85,1 oranında gözlemlendi. Flores ve Pevalin'in (2) çalışmasında, eldivenlerin gereksiz kullanım oranı %42, Tel'in (14) çalışmasında hemşirelerin gereksiz eldiven kullanımı %89 olarak belirtilmiştir. Gereksiz eldiven kullanım oranının yüksek olması, sağlık çalışanlarının temiz işlemler olarak tanımlanan işlemleri, kirli işlemler olarak tanımlamaları bu durumdan dolayı kendilerini bulaştan korumak için eldiven giydikleri söylenebilir.

Çalışmamızda, doğru eldiven kullanım oranının %77,9 ile en yüksek olduğu meslek grubunun hasta bakıcılar, %41,9 oranıyla en düşük olduğu meslek grubunun hekimler, hemşirelerin ise %76,9 oranında doğru eldiven kullandığı tespit edildi. Çalışmamızda kan ve vücut sıvıları ile bulaş riski durumunda, hasta bakıcıların her işlemde, hekimlerin %53,6 oranında, hemşirelerin ise %98,1 oranında eldiven giydiği bulundu. Benzer şekilde Loveday ve ark.'nın (8) yaptığı çalışmada da doğru eldiven kullanım oranı %80 oranıyla en yüksek olduğu meslek grubunun hasta bakıcılar, %23,8 oranıyla en düşük olduğu meslek grubunun ise hekimler olduğu belirlenmiştir. Hasta bakıcıların gerçekleştirdiği işlemlerin %60'ında kan ve kan ürünleri ile temas etme risklerinin yüksek olduğu belirtilmiştir. Bu nedenle eldiven kullanımına özen gösterdikleri düşünülebilir. Buna karşın hekimler kendilerine bulaş riskini düşük olarak değerlendirdikleri veya hızlı davranmak zorunda kaldıkları için eldiven kullanma oranları düşük kalmış olabilir.

Çalışmamızdaki sınırlılık, eldiven kullanımının tek başına ve sadece bir birimde gözlenmesidir.

## Sonuç

Eldiven kullanımının sistematik olarak gözlemlenmesi, doğru ve gerekli eldiven kullanımının değerlendirilmesini sağlamıştır. Sağlık çalışanlarının, eldiven kullanım bilgi durumu, eldiven giyme ve/veya giymeme ile ilgili davranış nedenlerini belirleyen, doğru eldiven kullanımını iyileştiren, gereksiz eldiven kullanımını önleyen çalışmalar yapılmalıdır. Enfeksiyon kontrol komiteleri, sağlık çalışanlarına eldivenlerin gereksiz ve yanlış kullanımlarıyla ilişkili oluşabilecek tehlikeler hakkında bilgilendirmeleri artırmalıdır. Gereksiz eldiven kullanımı, sağlık hizmetlerinde maliyetleri artıran parametreler arasında değerlendirmeli, maliyeti azaltan tedbirler içinde yer almalıdır.

Çalışmalarda el hijyeni ile eldiven kullanımı birlikte gözlemlenmelidir. Çapraz bulaşı gösteren çalışmalar ile el hijyeni ve eldiven kullanımının önemi ortaya çıkarılmalıdır.

**Teşekkür:** Çalışmamızı yürüttüğümüz yoğun bakım ünitesi sağlık çalışanlarına teşekkür ederiz.

## Etik

**Etik Kurul Onayı:** Araştırma için İstanbul Üniversitesi-Cerrahpaşa, Cerrahpaşa Tıp Fakültesi Klinik Araştırmalar Etik Kurulu'ndan izin alındı (karar no: A-07, tarih: 07.04.2020).

**Hasta Onamı:** Gözlemler, araştırmaya dahil edilen sağlık çalışanının haberi olmadan yapıldı. Bu nedenle çalışmaya katılanlardan onam alınmadı. Çalışma yapılan yoğun bakım ünitesi yöneticilerinden onam alındı.

**Hakem Değerlendirmesi:** Editörler kurulu dışında olan kişiler tarafından değerlendirilmiştir.

## Yazarlık Katkıları

Cerrahi ve Medikal Uygulama: N.A., S.Y., Konsept: N.A., S.Y., Dizayn: N.A., Veri Toplama veya İşleme: N.A., S.Y., Analiz veya Yorumlama: N.A., Literatür Arama: N.A., Yazan: N.A.

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**ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA***

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# Predictors of in-hospital Mortality After Rapid Response System Activation in a Newly Established Tertiary Hospital

## Yeni Kurulan Üçüncü Basamak Bir Hastanede Hızlı Müdahale Sistem Aktivasyonu Sonrası Hastane İçi Mortalite Prediktörleri

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**ABSTRACT** *Objective:* Rapid response systems (RRSs), which aim to prevent cardiac arrests and unexpected deaths, have been implemented across hospitals worldwide. Most studies on RRS shave evaluated the effects of its implementation on in-hospital mortality. In this study, we evaluated the predictive factors of in-hospital mortality for patients who were subjects of RRS activation in a newly established major hospital in Turkey.

*Materials and Methods:* Data on RRS activations were reviewed from paper charts and electronic medical records between March 2019 and February 2020. The demographic characteristics of patients, time of and reasons for RRS activation, initial cardiac rhythm, heart rate, mean arterial pressure, pulse oximetry-measured blood oxygen saturation ($SpO_2$), time of arrival of the rapid response team, red cell distribution width, platelet distribution width obtained from the first blood gas analysis and haemogram test results as well as glucose, sodium, potassium, pH, lactate, neutrophils and lymphocyte levelswere recorded. Univariate and multivariate logistic regression analyses were conducted to determine the independent predictors of in-hospital mortality.

*Results:* A total of 531 patients were included in the analysis. Of these, 189 (35.6%) died during hospital admission. Compared with survivors, non-survivors were older (median age, 64 vs. 52 years) and more likely to be male (65.6% vs. 34.4%); be admitted for cardiovascular, pulmonary and oncologic diseases and trigger RRS at nightand weekends than during the day. Activation of RRS by respiratory and haemodynamic triggers as well as during nighttime and weekend hours oncologic reasons for hospital admission, low $SpO_2$ levels, high neutrophil-to-lymphocyte ratio (NLR), potassium levels and lactate levels were predictive of in-hospital mortality.

*Conclusion:* This study found some weaknesses in the current RRS of the hospital. Hospital staffs working overnight and on weekends should be trained and empowered. $SpO_2$, potassium and lactate levels as well as NLR are predictors of in-hospital mortality and can guide triage decision making, which is usually a challenging and stressful task.

**Keywords:** Rapid response team, code blue, medical emergency team, predictor, mortality

**ÖZ** *Amaç:* Amacı kardiyak arrest ve beklenmeyen ölümleri engellemek olan hızlı müdahale sistemleri (RRS) dünya hastanelerinde genellikle kullanılmaktadır. İlgili çalışmaların çoğunda RRS kullanımının hastane mortalitesine etkileri araştırılmıştır. Bu çalışmada Türkiye'deki yeni kurulan majör bir hastanede, RRS aktivasyonu yapılan hastalardaki hastane içi mortalite için prediktif faktörleri değerlendirdik.

*Gereç ve Yöntem:* Mart 2019 ve Şubat 2020 arasındaki RRS aktivasyonları, basılı ve medikal elektronik kayıtlardan incelendi. Hastaların demografik özellikleri, RRS aktivasyon zamanı, aktivasyon nedeni, ilk kardiyak ritim, kalp hızı, ortalama arteriyel basınç, pulse oksimetre ile ölçülen kan oksijen satürasyonu, hızlı müdahale ekibinin varış süresi, ilk kan gazı ve hemogram analizindeki glukoz, sodyum, potasyum, pH, laktat, nötrofil, lenfosit, kırmızı hücre dağılım genişliği, platelet dağılım genişliği kaydedildi. Bağımsız hastane içi mortalite prediktörlerini belirlemek için univariate ve multivariate lojistik regresyon analizleri yapıldı.

*Bulgular:* Toplamda 531 hasta analize dahil edildi. Bunlardan 189'u (%35,6) hastane yatışı sırasında öldü. Ölenler yaşayanlarla kıyaslandığında daha yaşlı (medyan yaş 64 ve 52 yıl), daha çok erkek (%65,6 ve 34,4) ve daha fazla kardiyovasküler, solunumsal ve onkolojik nedenlerle yatışı yapılmış hastalardı. Ayrıca gündüz saatleriyle karşılaştırıldığında RRS'nin daha çok gece saatleri ve hafta sonunda aktive edildiği hastalardan oluşmaktaydı. RRS'nin solunumsal ve hemodinamik nedenlerle, gece ve hafta sonu, onkolojik nedenlerle yatışı yapılan hastalarda aktivasyonu, düşük $SpO_2$ düzeyleri, yüksek nötrofil-lenfosit oranı (NLR), potasyum ve laktat düzeyleri hastane içi mortalite prediktörleriydi.
*Sonuç:* Bulgularımız hastanemiz RRS sisteminde bazı zayıflıklar olduğunu göstermiştir. Hafta sonu ve gece personeli eğitilmeli ve güçlendirilmelidir. Ayrıca $SpO_2$, potasyum, laktat ve NLR düzeyleri hastane içi mortalite prediktörleri olarak genellikle zor ve stresli olan triyaj kararlarını yönlendirebilir.
**Anahtar Kelimeler:** Hızlı müdahale ekibi, mavi kod, tıbbi acil ekibi, prediktör, mortalite

## Introduction

Rapid response systems (RRS) have been widely implemented across world hospitals since the introduction of this concept in the 1990s (1,2). These systems include an afferent arm which is based on identifying non-intensive care unit (ICU) patients with clinical deterioration, especially those who are at an earlier stage (3). Rapid response teams (RRT) constitute the efferent arm of the RRS and mainly triage patients to intensive care units. These systems aim to prevent cardiac arrests and unexpected deaths (4).

Most of the studies about RRS aim to evaluate the utility of these systems and have focused on the comparison of patient outcomes before and after the implementation (5-7). Predictors of in-hospital mortality for patients who are subjects of a RRS activation are less studied. In this study we aimed to determine the predictors of in-hospital mortality for these patients and thereby improve the organization of the RRS.

## Materials and Methods

This was a retrospective study conducted in a tertiary education and research hospital. The study protocol was reviewed and approved by the Ankara City Hospital Ethics Committee (IRB number: 72300690-799, date: 29.07.2019). Personal informed consent was not required.

### RRT Description

Ankara City Hospital is a new tertiary education and research hospital with 3,810 beds in the capital of Turkey. It has been designed as a conglomerate of seven blocks; a main connecting block and six blocks serving as branch hospitals connected with the central block. The hospital has been functioning since February 2019 and a new RRS which is active at wards and other hospital areas except emergency and intensive care departments has been established since its opening. Each branch hospital has its own RRT. The team consists of a resident physician and two nurses from 8 am to 5 pm on week days, whereas it consists of a physician assistant and a nurseat nighttime and on weekends. Activation of the team can occur by any hospital staff member via a pager system. The criteria for RRT activation include the following: acute and persistent declining oxygen saturation ($SpO_2$) <90%, acute and persistent changes in heart rate <40 or >120 bpm, mean arterial pressure (MAP) <65 mmHg and respiratory rate <8 and >28/min, acute mental status changes, unexplained agitation more than 10 minutes and staff concern for any other reason.

### Patients

The records of RRT activations in two branch hospitals were reviewed from paper charts and electronic medical records between March 2019 and February 2020 (12 months). These two branch hospitals include 1,029 beds and care for adult patients with cardiovascular, pulmonary, oncologic, haematologic, gastroenterelogic, renal and urologic problems. Calls with missing or incomplete data were excluded.

### Patient Variables

Demographic characteristics of patients, time of RRT activation, reasons for activation, initial cardiac rhythm, heart rate, MAP, pulse oximetry measured blood $SpO_2$, arrival time of the RRT, parameters obtained from first blood gas (glucose, Na, K, pH, lactate) analysis and hemogram test (neutrophil, lymphocyte, red cell distribution width, platelet distribution width) were recorded. Blood samples were collected immediately after the first intervention as a routine procedure of our hospital. The study outcome was in-hospital mortality.

### Statistical Analysis

All statistical analysis was performed using SPSS Statistics 18 (IBM corp., Inc., Chicago, IL, USA). Differences between patients who survived to discharge and those who did not were evaluated using chi-square or Fisher's Exact tests for categorical variables and Student's t-test or

Mann-Whitney U test for continuous variables. Continuous variables were presented as mean ± standard deviation or median (minimum-maximum) and categorical data were summarized as percentages. Univariate logistic regression analyses were performed to examine the association between each predictor and in-hospital mortality separately. We also conducted a backward stepwise multivariate logistic regression to determine the independent predictors of mortality. A criterion of $p<0.05$ for entry was imposed in this procedure. We have introduced in the multivariate logistic regression analysis variables that are plausibly important based on theory even if the p-value was <0.05 in the univariate analysis (8). Model fit was assessed with the Hosmer-Lemeshow goodness-of-fit test. Odds ratios (ORs) for continuous variables were described using standardized ORs, which were associated with a one standard deviation change in the variable.

## Results

Between March 1, 2019 and February 1, 2020, the RRT was activated 543 times resulting in an average of 45 activations per month. The most common reason for activation of the RRT was haemodynamic deterioration, followed by mental status changes. Respiratory deterioration was present in 17.3% of the activations. Twelve calls were excluded because of missing data. A final total of 531 patients who were the subjects of RRT activations were included in the analysis. Of these, 189 (35.6%) died during hospital admission. Patient and RRT event characteristics in patients who survived versus those who did not are shown in Table 1. Nonsurvivors were older (median age 64 years vs. 52 years), were more likely to be male (65.6% vs. 34.4%), were more likely to be admitted for cardiovascular, pulmonary and oncologic diseases and were more likely to trigger RRS activation during nighttime and weekend hours (NWH) than daytime hours (DH). Other reasons for hospital admission included a heterogeneous group of patients who were admitted for benign urologic and gastroenterologic reasons, the family members of patients and hospital staff. Vital signs were more likely to be abnormal in nonsurvivors with higher rates of bradycardia (heart rate <40 bpm; 62.4% vs. 19.3%), hypotension (MAP <65 mmHg; 78.8% vs. 46.5%), and hypoxia ($SpO_2$ <90%; 83.6% vs. 33.6%). Survivors had lower rates of comorbidities (42.1% vs. 66.7%). Arrival time of the RRS was not different between survivors and nonsurvivors. The levels of potassium, lactate and neutrophil-to-lymphocyte ratio (NLR), red cell distribution width (RDW) and platelet distribution width (PDW) were significantly lower in survivors, while lymphocyte count was significantly higher in this group.

### Predictors of in-hospital Mortality

Univariate logistic regression analysis demonstrated that activation of RRS by respiratory and haemodynamic triggers and during NWH, male sex, older age, cardiovascular, pulmonary and oncologic diseases as the main reason for hospital admission, respiratoryand multiple comorbidities, heart rate, bradycardia (<40 bpm) MAP, hypotension (MAP <65 mmHg), $SpO_2$, hypoxia ($SpO_2$ ≤90%), asystole and pulseless electrical activity (PEA) as initial rhythm, higher potassium, lactate, NLR, RDW levels andlower lymphocyte countwere significantly associated with mortality (Table 2).

Activation time and triggers of RRS, sex, age, reasons for hospital admission (cardiovascular, pulmonary and oncologic diseases), comorbidities (respiratory and multiple comorbidities), heart rate, MAP, $SpO_2$, initial rhythms, potassium, lactate, NLR, RDW levels, lymphocyte count were included in the multivariate analysis. The final step of multivariate analysis retained activation time and triggers of RRS, reasons for hospital admission, $SpO_2$, comorbidities, PEA as initial rhthyhm and potassium, lactate, NLR levels. Activation of RRS by respiratory and haemodynamic triggers and during NWH, oncologic diseases for hospital admission, low $SpO_2$ levels, high NLR, potassium and lactate levels remained significant as predictors of mortality (Table 2).

## Discussion

In this study we retrospectively evaluated the predictors of in-hospital mortality in patients who were the subjects of a RRS activation by using the paper and electronic records of patients. Our study demonstrates that independent predictors of in-hospital mortality were: 1) activation of RRS during NWH (factor associated with RRS); 2) respiratory and haemodynamic deterioration as RRS trigger, oncologic reasons for hospital admission, low $SpO_2$ values(factors associated with clinical variables of the patients); and 3) NLR, potassium and lactate levels (factors associated with the first blood test of the patient).

RRTs are specialised teams that aims to immediately respond non-ICU patients experiencing clinical deterioration. They are the efferent arms of RRS, whereas the afferent

| Table 1. Comparison between survivors and non-survivors | | | | |
|---|---|---|---|---|
| | Demographics, clinical presentation and labaratory findings of patients | | | |
| | Total (n=531) | Survivors (n=342) | Non-survivors (n=189) | p |
| **Activation time of RRS** | | | | |
| Daytime hours | 268 (50.5) | 224 (65.5) | 44 (23.2) | **<0.001** |
| Nighttime and weekend hours | 263 (49.5) | 118 (34.5) | 145 (76.8) | |
| Trigger for RRS activation | | | | |
| Mental status changes | 142 (26.7%) | 137 (40.1) | 5 (2.6) | **<0.001** |
| Unexplained agitation | 34 (6.4%) | 34 (9.9) | 0 (0.0) | **<0.001** |
| Staff concern | 109 (20.5%) | 105 (30.7) | 4 (2.1) | **<0.001** |
| Respiratory deterioration | 92 (17.3%) | 34 (9.9) | 58 (30.7) | **<0.001** |
| Haemodynamic deterioration | 154 (29.0%) | 32 (9.4) | 122 (64.6) | **<0.001** |
| **Sex** | | | | |
| Male | 304 (57.3) | 180 (52.6) | 124 (65.6) | **0.004** |
| Female | 227 (42.7) | 162 (47.4) | 65 (34.4) | |
| Age (years) | 56.7±17.7 (60;18-91) | 52.3±18.4 (53;18-91) | 64.7±13.0 (66;21-91) | **<0.001** |
| **Reason for hospital admission** | | | | |
| Cardiovascular | 123 (23.2) | 70 (20.5) | 53 (28.0) | **0.048** |
| Pulmonary | 51 (9.6) | 25 (7.3) | 26 (13.8) | **0.016** |
| Oncologic | 162 (30.5) | 75 (21.9) | 87 (46.0) | **<0.001** |
| Hematologic | 14 (2.6) | 12 (3.5) | 2 (1.1) | 0.092 |
| Renal | 42 (7.9) | 35 (10.2) | 7 (3.7) | **0.008** |
| Other | 139 (26.2) | 125 (36.5) | 14 (7.4) | **<0.001** |
| Pulse (bpm) | 58±47 (71;0-218) | 71±1 (78;0-218) | 34±48 (0;0-162) | **<0.001** |
| >120 | 40 (7.5) | 26 (7.6) | 14 (7.4) | 0.935 |
| <40 | 345 (65.0) | 66 (19.3) | 118 (62.4) | **<0.001** |
| MAP (mmHg) | 42±43 (47;0-147) | 52±44 (69;0-147) | 24±36 (0;0-133) | |
| <65 | 223 (42.0) | 159 (46.5) | 149 (78.8) | **<0.001** |
| ≥65 | 308 (58.0) | 183 (53.5) | 40 (21.2) | **<0.001** |
| $SpO_2$ (%) | 56±45 (88;0-100) | 70±41 (95;0-100) | 29±40 (0;0-100) | |
| ≥90 | 258 (48.6) | 227 (66.4) | 31 (16.4) | **<0.001** |
| <90 | 273 (51.4) | 115 (33.6) | 158 (83.6) | **<0.001** |
| **Comorbities** | | | | |
| None | 261 (49.2) | 198 (57.9) | 63 (33.3) | **<0.001** |
| Respiratory | 21 (4) | 8 (2.3) | 13 (6.9) | **0.010** |
| Cardiac | 64 (12.1) | 38 (11.1) | 26 (13.8) | 0.371 |
| Neurologic | 11 (2.1) | 8 (2.3) | 3 (1.6) | 0.561 |
| Malignancy | 16 (3.0) | 8 (2.3) | 8 (4.2) | 0.222 |
| Diabetes mellitus | 20 (3.8) | 15 (4.4) | 5 (2.6) | 0.314 |
| Renal | 15 (2.8) | 11 (3.2) | 4 (2.1) | 0.465 |
| Multiple | 123 (23.2) | 56 (16.4) | 67 (35.4) | **<0.001** |
| Time to arrival of RRT (min) | 1.3±0.8 (1;0.2-8) | 1.2±0.8 (1;0.2-8) | 1.5±0.8 (1;0.2-6) | 0.304 |

| | | | | |
|---|---|---|---|---|
| **Initial rhythm** | | | | |
| NSR | 253 (47.7) | 207 (60.5) | 46 (24.3) | **<0.001** |
| Asystole | 146 (27.5) | 49 (14.3) | 97 (51.3) | **<0.001** |
| Bradicardia | 31 (5.8) | 15 (4.4) | 16 (8.5) | 0.055 |
| PEA | 80 (15.1) | 20 (5.8) | 60 (31.7) | **0.032** |
| VT/VF | 5 (0.9) | 3 (0.9) | 2 (1.1) | 0.837 |
| Unknown | 16 (3.0) | 8 (2.3) | 8 (4.2) | 0.222 |
| **Blood gas parameters** | | | | |
| Glucose | 110±78 (94;29-390) | 105±69 (94;29-390) | 121±93 (96;29-390) | 0.410 |
| Na | 134±8 (135;102-163) | 134±8 (137;102-155) | 134±8 (133;102-163) | 0.561 |
| K | 4.1±1.1 (4.0;2.6-9.0) | 3.7±1.0 (3.9;2.6-8.7) | 4.7±1.1 (5.0;2.6-9.0) | **<0.001** |
| pH | 7.09±0.19 (7.0;6.8-7.6) | 7.09±0.19 (7.0;6.8-7.55) | 7.09±0.19 (7.0;6.78-7.55) | 0.866 |
| Lactate | 5.7±3.12 (7.0;0.8-21) | 5.1±2.3 (6.0;0.8-14) | 6.7±4.0 (6.4;0.8-21) | **<0.001** |
| **Hemogram parameters** | | | | |
| Neutrophil | 6.3±7.4 (3.5;1.0-82.2) | 5.7±6.1 (3.6;1-82.2) | 7.7±9.2 (3.0;1-66.6) | 0.410 |
| Lymphocyte | 1.5±1.9 (1.0;0.1-24.8) | 1.7±2.1 (1.3;0.1-24.8) | 1.2±1.5 (1.0;0.1-12.3) | **<0.001** |
| NLR | 11.9±22.9 (3.7;0.8-225.0) | 8.5±16.3 (3.2;0.2-130) | 18.1±30.6 (6.2;0.6-225) | **<0.001** |
| RDW | 15.8±2.6 (15.3;5.4-26.0) | 15.4±2.5 (14.6;5.4-23.8) | 16.5±2.6 (16.4;5.4-26.0) | **<0.001** |
| PDW | 55.9±12.7 (57.0;18.0-84.0) | 55.0±12.1 (56.4;18.0-84.0) | 57.6±13.5 (57.6;18.9-84.0) | **0.004** |

Values are shown as number (percentage) or mean ± standard deviation (median; minimum-maximum). Significant values marked in bold. RRS: Rapid response system, MAP: mean arterial pressure, $SpO_2$: pulse oximetry derived oxygen saturation, RRT: rapid response team, NSR: normal sinus rhythm, PEA: pulseless electrical activity, VT: ventricular tachycardia, VF: ventricular fibrillation, NLR: neutrophil-to-lymphocyte ratio, RDW: red cell distribution width, PDW: platelet distribution width

arm is based upon hospital staff who determines the patient with acute physiological derangement and triggers the RRS activation. The composition of RRTs is tailored to some factors like aim of the team and resources of the hospital (4). The amount and level of experience of staff who are available in both arms of the RRS at NWH may differ from those available at DH (9). These working periods include fewer and less-experienced physicians coupled with reduced patient/nursing ratios on both the wards as well as the RRT. As a result; delays in RRT activations and mismanagement of deteriorating patient may occur more frequently at NWH. In our study RRT activation during NWH was an independent predictor of mortality. Our findings are consistent with a national registry study in the United States and a smaller study in Canada that reported increased mortality with overnight RRT activations (9,10). Our study differs from these reports by comparing DH and NWH. Nighttime and weekend hours resemble each other in some key aspects including fewer andless-experienced staff members. The problem in our hospital may arise from the limited staff resource of this newly established hospital and use of paper based observation charts in wards. The afferent and efferent arms of RRS can be improved by strengthening the staff in size and competence at NWH and moving from paper based observation charts to electronic medical records (11).

Other predictors of mortality were respiratory and haemodynamic deterioration as RRS trigger, oncologic reasons for hospital admission, low pulse oximetry values, high potassium and lactate levels after RRS activation. This finding is not surprising considering that most of these factors, including respiratory and haemodynamic triggers, low pulse oximetry values and high lactate levels are associated with impairment of tissue oxygenation. Shappell et al. (12) also reported that patients who died more likely to have a respiratory or cardiovascular triggers for RRS activation in their study. Hyperkalemia decreases the resting membrane potential of the myocardium, thereby myocardial cell conduction velocity decreases and rate of repolarization increases (13). McMahon et al. (14) demonstrated that potassium level is robustly associated with mortality risk even at moderate increases above normal. This is the most possible explanation for potassium-mortality association.

Cancer and its treatment usually lead to diminished physiological reserve (15). Almost one third of our study

| Table 2. Univariate and multivariate analysis of risk factors for mortality after RRS activation | | | | |
|---|---|---|---|---|
| | Univariate analysis of mortality | | Multivariate logistic regression analysis of mortality | |
| | OR (95% CI) | p | OR (95% CI) | p |
| **Activation time of RRS** | | | | |
| - Daytime hours<br>- Nighttime and weekend hours | 6.25 (4.17-9.37) | **<0.001** | 2.91 (1.52-5.88) | **0.002** |
| **Trigger for RRS** | | | | |
| - Respiratory deterioration | 4.01 (2.5-6.4) | **<0.001** | 31.12 (11.88-81.51) | **<0.001** |
| - Haemodynamic deterioration | 17.64 (11.0-28.2) | **<0.001** | 43.02 (17.65-104.83) | **<0.001** |
| **Sex** | | | | |
| - Male<br>- Female | 0.58 (0.40-0.84) | **0.004** | - | - |
| Age (years) | 1.04 (1.03-1.06) | **<0.001** | - | - |
| **Reason for hospital admission** | | | | |
| - Cardiovascular | 1.51 (1.003-2.28) | **0.040** | 2.08 (0.79-5.52) | 0.140 |
| - Respiratory | 2.02 (1.13-3.61) | **0.016** | 2.67 (0.84-8.54) | 0.098 |
| - Oncologic | 3.03 (2.06-4.45) | **<0.001** | 6.29 (2.34-16.9) | **<0.001** |
| Pulse (bpm) | 0.98 (0.98-0.99) | **<0.001** | | |
| <40 | 0.14 (0.09-0.21) | **<0.001** | | |
| **MAP (mmHg)** | | | | |
| <65 | 0.98 (0.98-0.98) | **<0.001** | | |
| ≥65 | 0.23 (0.15-0.35) | **<0.001** | | |
| **$SpO_2$ (%)** | | | | |
| ≥90 | 0.98 (0.96-0.98) | **<0.001** | 0.99 (0.98-0.10) | **0.002** |
| <90 | 10.00 (6.44-15.70) | **<0.001** | | |
| **Comorbities** | | | | |
| Respiratory | 3.08 (1.25-7.58) | **0.01** | 4.49 (0.92-21.85) | 0.063 |
| Multiple | 2.8 (1.85-4.2) | **<0.001** | 1.96 (0.97-4.02) | 0.060 |
| **Initial rhythm** | | | | |
| - Asystole | 6.3 (4.1-9.5) | **<0.001** | 0.46 (0.18-1.17) | 0.102 |
| - PEA | 0.6 (0.3-1.0) | **<0.001** | | |
| **Blood gas parameters** | | | | |
| - K | 2.46 (2.01-3.02) | **<0.001** | 1.95 (1.42-2.67) | **<0.001** |
| - Lactate | 1.19 (1.11-1.27) | **<0.001** | 1.33 (1.18-1.50) | **<0.001** |
| **Hemogram parameters** | | | | |
| - Lymphocyte | 0.83 (0.71-0.97) | **0.020** | 1.02 (1.00-1.03) | 0.440 |
| - NLR | 1.02 (1.01-1.03) | **<0.001** | | |
| - RDW | 1.17 (1.09-1.26) | **<0.001** | | |
| - PDW | 1.01 (1.01-1.03) | **0.02** | | |

Values are shown as number (percentage) or mean ± standard deviation (median; minimum-maximum). Significant values marked in bold. RRS: Rapid response system, OR: odds ratio, CI: confidence interval, MAP: mean arterial pressure, $SpO_2$: pulse oximetry derived oxygen saturation, RRT: rapid response team, PEA: pulseless electrical activity, NLR: neutrophil-to-lymphocyte ratio, RDW: red cell distribution width, PDW: platelet distribution width

population was cancer patients and 53.7% of these patients did not survive after RRS activation. This result is in line with previous two studies suggesting that cancer patients have worse outcomes following in-hospital cardiac arrest and hematologic oncology patients for whom the RRS was activated have high rates of subsequent ICU admission and mortality.

Interestingly, our results indicate that a MAP did not predict mortality whereas pulse oximetry did. Although MAP is commonly used as a surrogate of organ perfusion (16); it provides a reasonable estimate of the adequacy of organ perfusion as long as venous pressure and vascular resistance remains constant (17,18). Therefore a target of keeping MAP ≥65 mmHg should be individualized based on comorbidities (16). Besides this; it is known that peripheral circulation is the first to reflect a disturbance of the microcirculation and pulse oximeters generally have been shown to be accurate incritically ill patients (19,20). Ebmeier et al. (21) reported that there was no overall statistically significant bias in paired $SpO_2$/$SaO_2$ measurements in critically ill patients. Therefore we think that macrohemodynamic parameters like MAP and heart rate (as a determinant of cardiac output) may be less predictive of mortality than $SpO_2$ which provides a measure of microvascular oxygenation, especially if they are evaluated with cut off points.

To our knowledge, this is the first study to demonstrate the predictive value of NLR in patients receiving RRS activation. NLR is a helpful biomarker associated with the severity and prognosis of many conditions including cardiovascular diseases, certain types of cancers and sepsis (22). It is inexpensive, easily accessible and can be used for assessing the systemic inflammatory state as well as physiological stress (23).

It is obvious that ICU resources are scarce and costly. Therefore triage decisions during RRT activations should also give priority for patients with greater benefit (24). Patients who are less likely to survive or likely to have morbidity if not admitted to the ICU should be preffered (25). Furthermore some patients can benefit from "comfort care only" orders which should be discussed with patients and/or families. Our results provide more evidence for appropriate and quick triage decisions since most of the factors we found to predict mortality can be simply assessed at bedside using patients' charts and blood gas analysis. On the other hand; NLR is calculated from a complete blood count test and can be obtained in a short period of time. We think that it can be used for appropriateness of triage decisions as well as avoiding futile interventions at the end of life.

There are several limitations of this study. First, this was a retrospective observational study and has the limitations inherent in this study design. Second the sample size was relatively small compared to other published studies (12,26,27). On the other hand, we analyzed some predictive factors of mortality in the first hour after RRS activation, which may be the most important but not the only ones. Other factors that affect prognosis, but may appear in the following hours and days, were not analyzed.

## Conclusion

In conclusion, we found that the most important mortality risk factors in patients for whom the RRS was activated were presence of respiratory or haemodynamic triggers, activation of RRS during NWH, oncologic reasons for hospital admission, low $SpO_2$ values, high NLR, potassium and lactate levels. Since our findings demonstrate some weakness in the current RRS of our hospital; overnight staff, both in RRT and hospital wards, should be trained and empowered. Besides this; $SpO_2$, potassium and lactate levels can guide triage decisions which is usually a challenging and stressful duty. We also found NLR as a predictive of mortality that may help to reevaluate the appropriateness of these decisions.

### Ethics

**Ethics Committee Approval:** The study protocol was reviewed and approved by the Ankara City Hospital Ethics Committee (IRB number: 72300690-799, date: 29.07.2019).

**Informed Consent:** Personal informed consent was not required.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: B.T., Ç.B.D., İ.M., D.A., Concept: B.T., Design: B.T., Data Collection and Process: B.T., M.C., Ç.B.D., Analysis or Interpretation: B.T., İ.M., Literature Search: B.T., M.C., Writing: B.T.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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# Sepsis and Fibroblast Growth Factor 21: A New Acute Phase Reactant?

## Sepsis ve Fibroblast Büyüme Faktörü 21: Yeni Bir Akut Faz Reaktanı mı?

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**ABSTRACT** *Objective:* This study aimed to compare the levels of fibroblast growth factor 21 (FGF 21) in patients with acute metabolic decompensation, sepsis and non-infectious inflammatory status using infection parameters and scoring systems.
*Materials and Methods:* This cross-sectional study included 46 patients with sepsis and 29 patients with non-infectious inflammatory conditions in the case group. A total of 39 healthy volunteers were included in the control group. C-reactive protein, procalcitonin (PCT), sedimentation and FGF 21 levels were measured in all patients. Acute physiology and chronic health evaluation II and sequential organ failure assessment scores were also calculated.
*Results:* FGF 21 levels in the patients in the case group were significantly higher than those in the patients in the control group ($p<0.001$). A weak positive correlation was found between the FGF 21 and PCT levels ($r=0.292$, $p=0.011$). It was estimated that FGF 21 levels of 492.4 pg/mL and higher could predict the diagnosis of sepsis and non-infectious inflammatory status with 82.4% sensitivity and 80% specificity.
*Conclusion:* FGF 21 can be considered an acute phase reactant in cases of infection, rising like PCT but not increasing in every acute condition.
**Keywords:** Fibroblast growth factor 21, sepsis, mortality

**ÖZ** *Amaç:* Bu çalışmada akut metabolik dekompanzasyon olan sepsisli ve non-enfeksiyöz enflamatuvar durumlu hastaların fibroblast büyüme faktörü 21 (FGF 21) düzeylerini, enfeksiyon parametreleri ve skorlama sistemleri ile karşılaştırmak amaçlandı.
*Gereç ve Yöntem:* Kesitsel olarak dizayn edilen çalışmada olgu grubuna 46 sepsis tanısı olan hasta ile 29 non-enfeksiyöz enflamatuvar durum tanısı olan hasta ve kontrol grubuna da 39 sağlıklı gönüllü dahil edildi. Tüm hastaların C-reaktif protein, prokalsitonin (PCT), sedimentasyon ve FGF 21 düzey ölçümleri yapıldı. Akut fizyoloji ve kronik sağlık değerlendirmesi-II, sequential organ failure assessment skorlamaları hesaplandı.
*Bulgular:* Sepsis ve non-enfeksiyöz enflamatuvar durum gruplarındaki FGF 21 düzeyleri, kontrol grubuna göre anlamlı olarak daha yüksek bulundu ($p<0,001$). FGF 21 düzeyi ile sadece PCT düzeyi arasında zayıf pozitif bir korelasyon olduğu görüldü ($r=0,292$ $p=0,011$). FGF 21 ölçümlerinin 492,4 pg/mL ve üzerinde olmasının %82,4 sensitivite ve %80 spesifisite ile sepsis ve non-enfeksiyöz enflamatuvar durum tanılarını öngörebildiği gösterildi.
*Sonuç:* Sonuç olarak, FGF 21, enfeksiyöz tablolarda PCT gibi yükselmesi, ancak her akut tabloda artmaması nedeni ile akut faz reaktanı olarak kabul edilmesinden dolayı şüpheli bir parametre olarak değerlendirilebilir.
**Anahtar Kelimeler:** Fibroblast büyüme faktörü 21, sepsis, mortalite

## Introduction

Sepsis is a systemic inflammatory response to infection, with high clinical mortality and increased incidence and clinical severity over the years (1). Sepsis is the most important cause of mortality in intensive care units (ICUs) and the mortality rate can reach up to 50% (2,3). The most effective method for reducing mortality is to initiate rapid treatment. Due to the diversity of clinical findings and different clinical courses in sepsis, delays are frequently encountered in diagnosis, and there is an increasing need for markers that provide early intervention and predict rapid clinical instability and also predict mortality (4,5). Therefore, new sensitive and specific markers are needed in this regard. In addition, the exact role of biomarkers in the treatment of septic patients has not been identified and this issue needs clarification (2,5,6).

For the follow-up of sepsis and infection in the clinic, indicators such as sedimentation, C-reactive protein (CRP), and procalcitonin (PCT) are used (7-9). In addition to these indicators, for intensive care patients, scoring systems have been developed for determining the severity of the disease, managing the treatment, grouping patients for clinical studies, and comparing the effectiveness of ICUs within themselves or between each other. These systems include the Acute Physiology and Chronic Health Evaluation-II (APACHE-II), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology score II, Mortality Probability Model II, Therapeutic Intervention Scoring System 28, Logistic Organ Dysfunction System, and Multiple Organ Dysfunction score, among others (10,11). APACHE-II and SOFA are the most frequently used of these scoring systems (12,13).

Fibroblast growth factors (FGFs) are a large family of polypeptide growth factors that act as homeostatic factors in tissue repair and angiogenesis in the adult organism and maintain cell proliferation, migration, and differentiation during embryonic development (14,15). Recently, it has been demonstrated that some members of the FGF family have important roles in determining and regulating the functions of some hormonal tissues and organs as well as modulating various metabolic processes. One of the most studied members of this family is FGF 21. There are many findings in the literature showing that FGF 21 is increased in chronic metabolic conditions such as polycystic ovarian syndrome, non-alcoholic steatohepatitis (NASH), diabetes mellitus (DM), and chronic kidney failure (16-20). Studies showing that FGF 21 is also increased in cases such as acute metabolic conditions such as sepsis and non-infectious inflammatory status have been published recently. However, these studies are generally based on animal experiments and there are limited numbers of human studies among them (21-23).

Our aim in this study was to compare the FGF 21 levels of patients with acute metabolic decompensation, sepsis, and non-infectious inflammatory status with infection parameters and scoring systems and to determine a threshold value so that high levels of FGF can be used in the diagnosis of these diseases and to determine severity.

## Materials and Methods

Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Keçiören Training and Research Hospital (decision no: 2012-KAEK-15/1061, date: 27.01.2016). Informed consents were taken from all participants. Seventy-five patients those aged 18 and over (n=75) hospitalized in the ICU of University of Health Sciences Turkey, Keçiören Training and Research Hospital for a period of six months (January 2017-June 2017) who diagnosed with sepsis and/or non-infectious inflammatory conditions were included in this study which was designed as a prospective observational study. Sepsis was defined according to the current criteria (For clinical operationalization, organ dysfunction can be represented by a 2 points or more increase in the SOFA score, which is associated with an in-hospital mortality greater than 10%) (1). Patients who had no suspected or documented infection but had two or more of the criteria of fever (>38 °C), hypothermia (<36 °C), leukocytosis (>12,000 $mm^3$), leukopenia (<4000 $mm^3$), tachycardia (>90 beats/minute), or tachypnea (>20 breaths/minute) were assigned to group 2 (24). The exclusion criteria for group 1 and group 2 were pregnancy, puerperium, refusal of the study by the patient or his/her conservator, and those with suspicion in the diagnosis of sepsis or non-infectious inflammatory conditions. Thirty-nine volunteers who had no acute signs or symptoms of infection and had applied to our hospital for any reason, without chronic metabolic diagnoses such as DM, hypertension, coronary artery disease, or cerebrovascular disease and without hematological or solid organ malignancies or any known inflammatory diseases (ulcerative colitis, etc.), and not diagnosed with any disease were assigned to the control group (group 3) (n=39).

Demographic and biochemical (liver and kidney functions, complete blood count, CRP, PCT) data of group 1 and group 2 patients within 24 hours of admission to the hospital were obtained from their records. The calculation SOFA and APACHE-II scores of all patients were recorded and serums obtained from fasting blood samples in the morning were stored at -80 °C for all participants to measure FGF 21 levels within first 24 hours. After the patient groups were formed, FGF 21 levels were measured from stored blood samples by sandwich assay ELISA [BioVendor Research and Diagnostic Products (antibody-coated 96-well plate human FGF 21)]. Samples were diluted one-to-one with 75 mL of saline. Testing proceeded with biotin and streptavidin. Absorbance measurements at 450 nm were performed on an ELx800 microplate reading device (BioTek Instruments, Inc.). For the measurement of FGF 21 levels according to the FGF 21 ELISA kit's instructions, serum samples were diluted 1:2 by buffer dilution before analysis. The standard curve range for the analysis is 30-1,920 pg/mL. Sensitivity was 7 pg/mL, and intraassay and interassay ranges were 3-4.1% and 3.6-3.9%, respectively.

### Statistical Analysis

SPSS 15.0 (SPSS Inc.) was used for the analysis. The distribution of the data was assessed using a one-sample Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean and standard deviation, skewed-distributed continuous variables were expressed as median (minimum-maximum), and categorical variables were expressed as number and percentage. Categorical variables were compared with the chi-square test. Non-normally distributed data were compared with the Mann-Whitney U test. Correlation analyses between continuous variables that did not fit the normal distribution were analyzed with the Spearman test. The power of FGF 21 measurements to predict sepsis and non-infectious inflammatory conditions diagnosis was evaluated by receiver operating characteristics (ROC) analysis. The results were evaluated in a confidence interval of 95% and at a significance level of $p<0.05$.

## Results

There were 34 females in the patient group (19 in group 1, 15 in group 2) and 19 females in the control group in our study. Group 1, group 2, and group 3 had similar characteristics in terms of gender and age distribution (Table 1).

FGF 21 levels in group 1 and group 2 were significantly higher than in group 3 ($p<0.001$) (Figure 1). There was no significant difference between group 1 and group 2 in terms of FGF 21 level, CRP level, PCT level, APACHE-II score, APACHE-II mortality, or SOFA score (Table 2).

As a result of the correlation analysis between FGF 21 levels and APACHE-II, SOFA, PCT, and CRP values, there was a positive correlation only between FGF 21 levels and PCT levels ($r=0.292$, $p=0.011$, $r^2=0.085$). According to the ROC analysis, FGF 21 level was found to significantly predict sepsis and non-infectious inflammatory conditions (area under the curve: 0.884, 95% confidence interval: 0.824-0.944, $p<0.001$). FGF 21 measurements of 492.4 pg/mL and above could predict sepsis and non-infectious inflammatory conditions with 82.4% sensitivity and 80% specificity (Figure 2).

## Discussion

According to the results of our study, FGF 21 level has been shown to significantly predict sepsis and non-infectious inflammatory conditions. FGF 21 measurements of 492.4 pg/mL and above could predict sepsis and non-infectious inflammatory conditions with 82.4% sensitivity and 80% specificity. In addition, a weak correlation was found between FGF 21 level and inflammatory markers and PCT level.

In addition to inflammatory markers, a number of scoring systems have been frequently used in ICUs in recent years in the follow-up of sepsis and non-infectious inflammatory status due to rapid clinical instability. However, there is still a need for new parameters to help make decisions faster. For this purpose, studies investigating a large number of parameters are common in the literature (3,5,6,9). One of

**Table 1. Basic demographic data and FGF 21 levels of sepsis, non-infectious inflammatory status, and control groups**

| | Group 1 (sepsis) (n=46) | Group 2 (non-infectious inflammatory status) (n=29) | Group 3 (control) (n=39) | p-value |
|---|---|---|---|---|
| Age (years) | 76 (47-92) | 72 (18-87) | 67 (53-82) | 0.001 |
| Gender (%) | 19 (41.3%) females | 15 (51.7%) females | 19 (48.7%) females | 0.639 |
| FGF 21 (pg/mL) | 1970 (66-2402) | 1696 (222-2255) | 330 (65-1028) | 0.001 |

FGF 21: Fibroblast growth factor 21

these parameters is FGF 21. One reason why FGF 21 is investigated is that it has an important role in determining and regulating the functions of some hormonal tissues and organs, as well as controlling processes such as various glucose, fat, and ketone metabolisms (15). On the other hand, unlike other members of the FGF family, FGF 21 has no heparin binding sites, so it shows its effects systemically in a hormone-like manner and thus can be easily detected in the blood (21).

A study published by Gariani et al. (21) in 2013 is methodologically similar to our study but was conducted with fewer participants. They compared sepsis and systemic inflammatory response syndrome (SIRS) groups with healthy controls. According to the sepsis classification updated in 2016, the definition of SIRS is no longer used (1). However, group 2 in our study, comprising patients with non-infectious inflammatory status, can be considered as acceptably similar to the SIRS group in the study of Gariani et al. (21) As a result of their study, similar to our study, FGF 21 levels were found higher in patients with sepsis and SIRS compared to healthy controls. Unlike our results, FGF 21 levels were found higher in the sepsis group than the SIRS group and FGF 21 level was found to be positively correlated with APACHE-II score, while no correlation was found with PCT level (21). We found a significant difference in FGF 21 levels between the case and control groups, but there was no difference between groups in terms of gender and age. Unlike the study of Gariani et al. (21), the fact that the level of FGF 21 was significantly higher in group 2 in our study may be due to our study having a larger number of participants. In a study published in 2018, the level of FGF 21 was shown to have sensitivity of 81.3% and specificity of 89.8% to predict 28-day mortality (23). The recently published study of Li et al. (4)

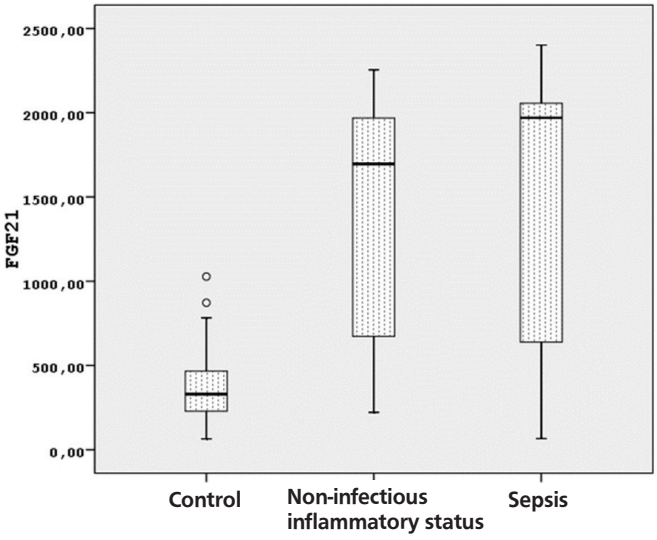


**Figure 1.** Distribution of FGF 21 (pg/mL) levels by groups
FGF 21: Fibroblast growth factor 21

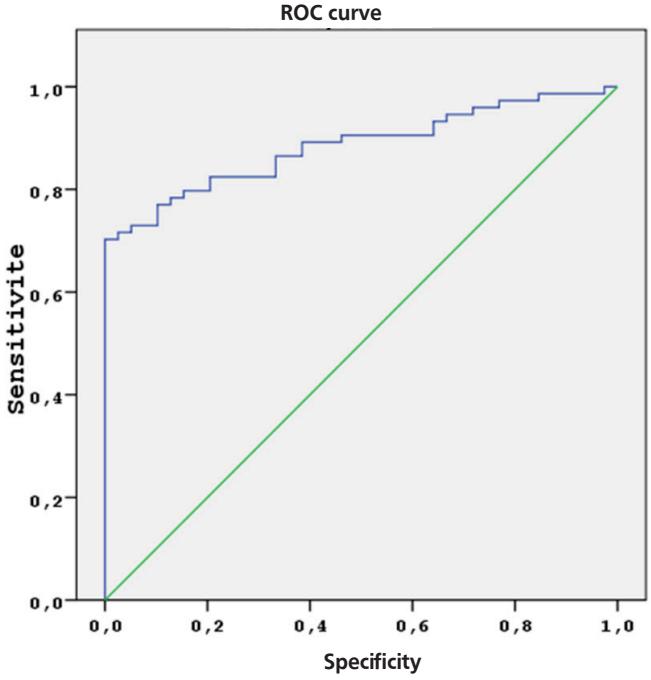


**Figure 2.** ROC curve of FGF 21 for prediction of patients' mortality
FGF 21: Fibroblast growth factor 21, ROC: receiver operating characteristics

**Table 2. Inflammatory markers, APACHE-II scores, APACHE-II mortality, and SOFA scores in sepsis and non-infectious inflammatory status groups**

| | Group 1 (sepsis) | Group 2 (non-infectious inflammatory status) | p-value |
|---|---|---|---|
| CRP (mg/dL) | 14.65 (1.26-32) | 15.54 (1.13-35) | 0.654 |
| PCT (ng/mL) | 4.56 (0.10-100) | 4.47 (0.14-100) | 0.794 |
| APACHE II score | 28 (9-51) | 24 (11-39) | 0.107 |
| APACHE II mortality | 63.9 (9.9-98.1) | 53.3 (12.9-89.8) | 0.113 |
| SOFA | 9 (2-18) | 6 (1-15) | 0.140 |

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CRP: C-reactive protein, PCT: procalcitonin, SOFA: Sequential Organ Failure Assessment

supports our study results; in their work, SOFA score and serum FGF 21 concentration were shown to be important markers of 28-day mortality in patients with sepsis.

We found a positive correlation between FGF 21 level and PCT level (r=0.292, p=0.011). PCT is a more specific marker in cases of infection than CRP and sedimentation levels (5,25). Due to the presence of infection in most of our patient population, there was a relationship between PCT and FGF 21, while no relationship could be detected between CRP and sedimentation. With a larger number of participants, we think that a relationship between CRP and sedimentation levels could be found, which are less specific in infection than PCT and FGF 21 levels.

Wang and Chen (26) suggested that PCT, compared to CRP, showed a more significant correlation with APACHE-II and SOFA scores, and that PCT was a better indicator in the evaluation of prognosis and severity in patients with sepsis. Based on this assumption, we compared APACHE-II and SOFA scores and the levels of markers in our study. We could not find a relationship between those scores and FGF 21 levels. Gariani et al. (21) showed a poor correlation between FGF 21 level and APACHE-II score. In a study published in 2018, there was a positive correlation between FGF 21 level and APACHE-II and SOFA scores. The APACHE-II scoring system gives more meaningful results in patients with postoperative and/or cranial pathology (23). When we compare the APACHE-II and SOFA scores with the FGF 21 levels, we see that the patient population in our study was hospitalized for internal medicine reasons, which may be why we did not find a correlation.

In animal studies, it has been suggested that FGF 21 injections can be considered as a possible pharmacological treatment in diseases such as DM, obesity, and NASH (27,28). FGF 21 was shown to be an acute phase protein that protects against the toxic effects of lipopolysaccharides and sepsis in a study on rats (22). Recently, FGF 21 was also found to provide anti-inflammatory effects by inhibiting some signals in macrophages (29). As a result of our research, FGF 21 elevation may be an anti-inflammatory response to sepsis and SIRS in humans. We believe that our study has prepared a basis for pharmacological treatment based on FGF 21 that can be applied in humans in the future.

Our study has some limitations. First of all, the relatively limited sample prevents generalizing our study results. Second, low levels of free triiodothyronine (fT3) and free thyroxine (fT4) (euthyroid patient syndrome) are associated with disease severity and mortality in ICU patients, but we did not use thyroid function evaluations of the patient population in our study for analysis and we consider this a limitation (4,13). As other limiting factors, we did not evaluate the levels of tumor necrosis factor alpha, interleukin-6, or other inflammatory markers, and we did not use scoring systems other than the SOFA and APACHE-II scores. In addition, due to the small sample size, confounding factors known to increase FGF 21 levels such as DM or NASH could not be excluded.

## Conclusion

In conclusion, FGF 21 can be considered as a suspicious acute phase reactant in cases of infection, as it is ascending similarly to PCT, but is not increased in every acute condition.

### Ethics

**Ethics Committee Approval:** Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Keçiören Training and Research Hospital (decision no: 2012-KAEK-15/1061, date: 27.01.2016).

**Informed Consent:** Informed consents were taken from all participants.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Concept: D.T.E., E.B., Design: T.A., E.B., Data Collection and Process: S.D., Analysis or Interpretation: D.T.E., T.A., Literature Search: S.D., A.O.K., Writing: S.D., A.O.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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İkbal Çavdar

# The Impact of Care Bundle Approach in Preventing Central Line-associated Bloodstream Infections in Surgical Intensive Care Units

## Cerrahi Yoğun Bakımlarda Santral Kateter İlişkili Kan Dolaşımı Enfeksiyonunu Önlemede Bakım Paketi Yaklaşımının Etkisi

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*This study was planned and conducted as a master's dissertation.*

**ABSTRACT** *Objective:* Healthcare-associated infections (HAI), which pose a significant risk to patient safety, are one of the most frequent complications that inpatients encounter. The growing concern about HAI urged the development of evidence-based guidelines for prevention. This study aimed to determine the impact of care bundle approach in preventing central line-associated bloodstream infections (CLABSI) in surgical intensive care units.
*Materials and Methods:* This semiexperimental controlled study included 163 subjects (83 patients and 80 controls) who were admitted to surgical intensive care units between September 2017 and October 2018, had a central venous catheter (CVC), and met the inclusion criteria. For CVC care, care bundle recommended by the US Centers for Disease Control and Prevention was applied to the study group.
*Results:* In 23.3% of patients, signs and symptoms of hospital infections were observed. Moreover, 25.2% of catheter tip cultures were positive, and the most frequently isolated microorganism was *Staphylococcus epidermidis* (58.5%). Patients were evaluated according to the diagnostic criteria for CLABSI. Further, CLABSI was not observed in the intervention group but was diagnosed in 10% (n=8) of the patients in the control group.
*Conclusion:* Care bundle approach is effective in preventing CLABSI.
**Keywords:** Central venous catheters, intensive care units, infections, patient care bundle

**ÖZ** *Amaç:* Hasta güvenliği için önemli bir tehdit olan sağlık hizmeti ilişkili enfeksiyon oranları hastaneye yatan hastaların en sık karşı karşıya kaldığı komplikasyonlardan biridir. Sağlık hizmetlerinde sağlık hizmeti ilişkili enfeksiyonlar için artan kaygı, kanıta dayalı rehberlerin geliştirilmesinde uyarıcı etken olmuştur. Bu çalışma cerrahi yoğun bakım ünitelerinde santral venöz kateter (SVK) ilişkili kan dolaşımı enfeksiyonlarının önlenmesinde bakım paketi yaklaşımının etkisini belirlemek amacıyla gerçekleştirildi.
*Gereç ve Yöntem:* Yarı deneysel kontrol gruplu bir çalışma olarak planlanan araştırma, Eylül 2017 ve Ekim 2018 tarihleri arasında cerrahi yoğun bakım ünitelerinde yatan, SVK'si bulunan ve örneklem özelliklerini karşılayan 163 hasta (83 deney, 80 kontrol) ile gerçekleştirildi. Deney grubuna SVK bakımında Hastalık Kontrol ve Önleme Merkezi tarafından önerilen bakım paketi uygulandı.
*Bulgular:* Hastaların %23,3'ünde hastane enfeksiyonu belirti ve bulguları gözlendiği, kateter ucu kültürlerinin %25,2'sinde üreme olduğu, en fazla üreyen mikroorganizmanın *Staphylococcus epidermidis* (%58,5) olduğu, %4,9'unda SVK ilişkili kan dolaşımı enfeksiyonu geliştiği, enfeksiyon gelişen hastaların tamamının bakım paketi uygulanmayan hastalar olduğu belirlendi.
*Sonuç:* Bakım paketi yaklaşımının SVK ilişkili kan dolaşımı enfeksiyonunu önlemede etkili olduğu bulundu.
**Anahtar Kelimeler:** Santral venöz kateter, yoğun bakım ünitesi, enfeksiyon, hasta bakım paketi

## Introduction

According to the old definition, "Healthcare-Associated Infections (HAI)" is defined as nosocomial infections, infections that do not have an infection at the time of application to the health institution or are not in the incubation period, and that occur on the third day of admission to the hospital and after. HAI, which possess a great threat for patient safety, is one of the most frequent complications that inpatients encounter. There are many invasive instruments used to treat patients and help them recover in modern healthcare. Central venous catheterization is a method used for many reasons such as drug and fluid therapy, invasive hemodynamic monitoring, parenteral nutrition, administration of blood and blood products, continuous renal replacement therapy, plasmapheresis or failure to provide peripheral vascular access. Central venous catheters (CVC) is the most important risk factor for the development of catheter-related bloodstream infections. Approximately 90% of central line-associated bloodstream infections (CLABSI) are due to CVCs. (1-3).

The US Centers for Disease Control and Prevention (CDC) reported that there are 80,000 CLABSIs diagnosed in intensive care units (ICUs) (4). Ista et al. (5) recent meta-analysis involving 2,216 adult ICUs, the median incidence of CLABSI decreased significantly from 5.7 to 2.0 per 1,000 CL-days after the bundle implementation. According to the National Nosocomial Infections Surveillance Network report by the Turkish Ministry of Health in 2013, the rate of CLABSIs vary between 1.9 to 7.1 per 1,000 catheter days depending on the type of ICU (6).

The increasing concern over HAI has been a triggering factor for developing evidence-based guidelines for prevention. The quality, equality, and efficiency of patient care is expected to increase as healthcare professionals follow these guidelines (7). Care bundle approach is a set of scientifically proven practices that when performed step-by-step, collectively, and completely rather than individually have been shown to improve patient outcomes (2).

The first application of care bundle approach is the prevention of CLABSI. Studies aimed to prevent catheter infections that implemented care bundle approach focused on training healthcare professionals, using maximum barrier measures when inserting catheters and removing the catheter as soon as possible. Also, easy and rapid access to equipment used during these practices, daily evaluation of catheter requirement and catheter use and maintenance care according to guidelines were ensured. CLABSI is a health problem that results from CVC application, individual characteristics of patients and many elements of healthcare process causing undesirables consequences. Health institutions should aim to create institutional evidence-based protocols for CVC application and care that rely on efficient and feasible recommendations from recent guidelines, support individual education with detailed theoretical approach and reflect them onto daily practices (8).

This study aims to determine the impact of care bundle approach in preventing CLABSI in patients admitted to surgical ICUs of a university hospital.

## Materials and Methods

### Study Design

This study was designed as a semi-experimental controlled study.

### Time and Place of the Study

This studys' data were collected from January to October 2018 in neurosurgery ICU, cardiovascular surgery ICU, general surgery ICU and anesthesiology and reanimation ICUs of a 600-bed university hospital in Istanbul, Turkey.

### Ethics Approval

Permission from the Haydarpaşa Numune Training and Research Hospital Ethics Committee (decision no: HNEAH-KAEK 2017/KK/143, date: 25.12.2017) and the institution were obtained prior to the start of the study. Patients and/or their first-degree relatives were informed about the study and written informed consents were obtained. The study was performed in accordance with the Declaration of Helsinki.

### Universe and Sample Selection

The universe of the study was made of 2,700 patients who were admitted to surgical ICUs between 2016 and 2017. The sample of the study consisted of 163 subjects, 83 patients and 80 controls, who were selected among subjects older than 18 years, admitted to surgical ICUs 2018, had a CVC using power analysis version 3.1.7 with 95% confidence interval, 5% margin of error, 0.5 effect size and 80% power (9). Patients who had an active infection when admitted to ICU and patients without a CVC were excluded. The question whether care bundle for CLABSIs is effective in preventing CLABSIs was investigated.

### Data Collecting Tools

In this study, three forms that were developed by the researcher and revised according to the opinions of 10 specialists, Patient Information Form, Central Venous Catheter Care and Follow-up Form and Nosocomial Infection Surveillance Information Form, were used for data collection.

Patient Information Form: This form included questions about the patient's age, sex, diagnosis, chronic diseases, risk factors, duration of hospital stay, and duration of ICU stay.

Central Venous Catheter Care and Follow-up Form: It consisted of information about the type of catheter inserted, date of insertion, date of dressing changes, materials used and reason for dressing changes, duration of catheter, and catheter observation.

Nosocomial Infection Surveillance Information Form: This form included signs and symptoms of infections, cultures obtained from the patient and their results, presence of any other infection, and antibiotics used and their duration.

Acute Physiology and Chronic Health Evaluation-II (APACHE-II): This scoring system, which is a disease severity scoring tool used in ICUs, was used for acute physiology and chronic health evaluation. It consists of three parts: Chronic health evaluation, age, and physiology. The score of these three parts along with the surgical intervention status predicts hospital mortality.

### Conducting the Study

All patients included in the study were listed from weekly lists of surgery plans. The minimum number of patients was estimated to be 163 in power analysis but 85 subjects in each group (total 170) were included, predicting there may be data losses. During data collection, 7 subjects had to be excluded due to death or transfer to another hospital and therefore the study was completed with 83 patients and 80 control subjects. Included in the care bundle;

1. Hand hygiene,
2. Maximum barrier precautions,
3. Skin antisepsis with chlorhexidine,
4. Selection of the most appropriate catheter insertion site, avoidance of the femoral vein,
5. Daily assessment of CVC requirement and removal of unnecessary lines components were fully applied to the intervention group. Checklist for preventing CLABSI as recommended by CDC defined under these 5 main components was also used (Figure 1).

All subjects in the intervention and control groups were followed for HAI. Subjects included in the study were closely monitored by Infection Control Committee (ICC) and the researcher nurse. Subjects in the intervention and control groups were daily monitored for white blood cell, tachycardia, and fever after 24 hours in the ICU. CVC observation data of subjects in both groups was evaluated daily with the data collecting form developed by the researcher. The control group received routine CVC care using sterile gauze, povidone iodine and elastic fixation tape. When the central line was removed, the catheter tip was sent to culture. Equipment present in the hospital and routine tests were used in both groups (Figure 2).

### Statistical Analysis

SPSS version 21.0 (IBM SPSS Inc, Armonk, NY) software was used for statistical analyses of data obtained in the study. Sociodemographic characteristics, chronic diseases, cancer and smoking status of subjects were defined using descriptive statistics (number, percentage), mean and standard deviation. Mann-Whitney U test and Pearson chi-squared tests were used to determine the differences between the intervention and control groups. Results were assessed in 95% confidence interval and $p<0.05$ significance.

## Results

Mean age of patients in the intervention group was 57.96±17.17 years. Out of these patients, 54.6% were male, 91.6% did not smoke, 68.7% had a history of chronic illness and 34.9% had a history of cancer. Mean duration of stay in the ICU was 6.38±10.24 days and mean APACHE score was 10.34±8.28. On the other hand, mean age of subjects in the control group was 64.06±14.92 years. Out of these subjects, 58.8% were male, 91.3% did not smoke, 63.8% had a history of chronic illness and 33.8% had a history of cancer. Mean duration of stay in the ICU was 11.91±18.60 days and mean APACHE score was 13.87±7.85.

Age ≥65 years, smoking and cancer history were considered as intensive care risk factors. Among the intervention group, 61.4% of subjects had a risk factor, while 72.5% of subjects in the control group had an intensive care risk factor.

There was a significant difference between the intervention and control groups in terms of mean age, duration of ICU stay and APACHE-II score ($p<0.05$), while

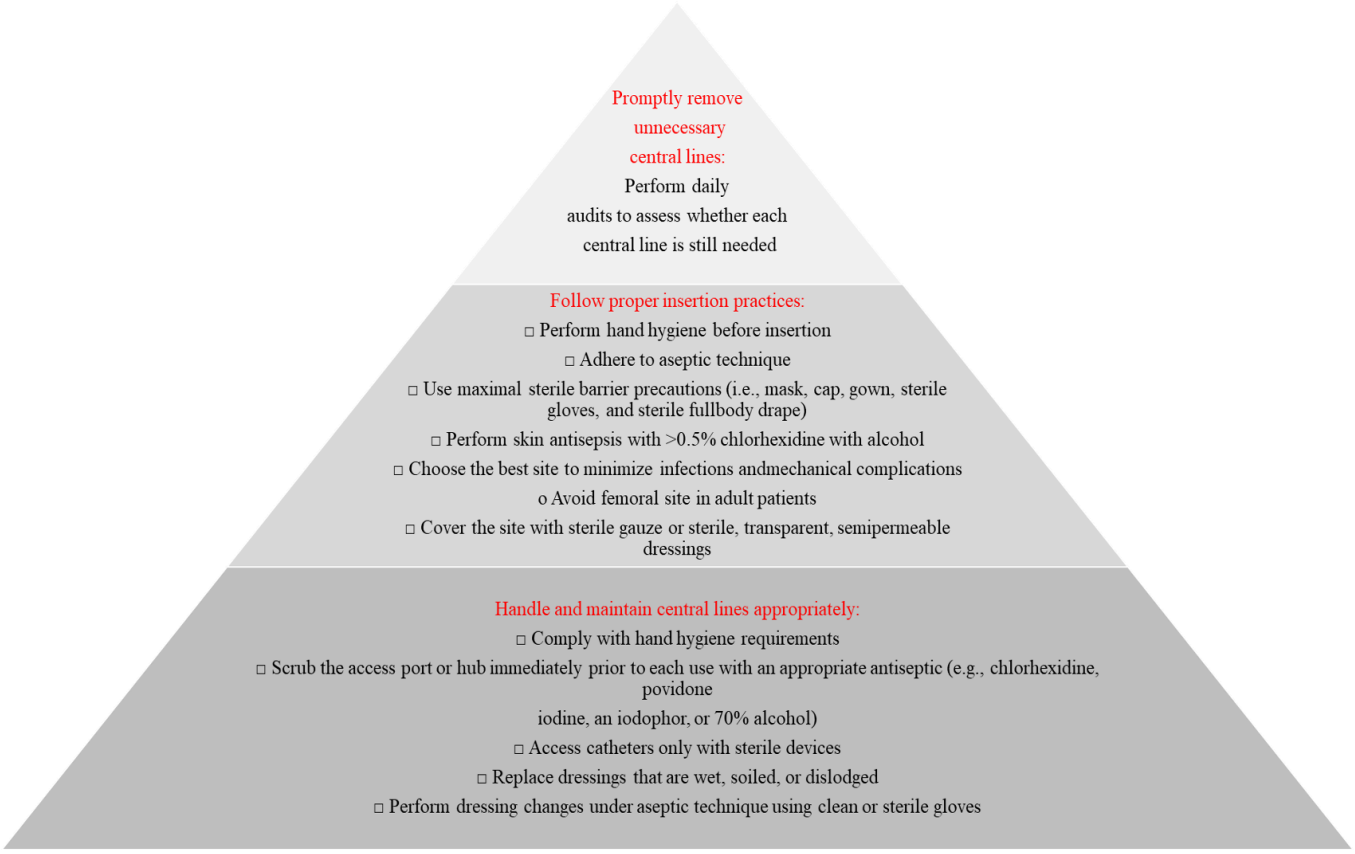


**Figure 1.** Contents of care bundle

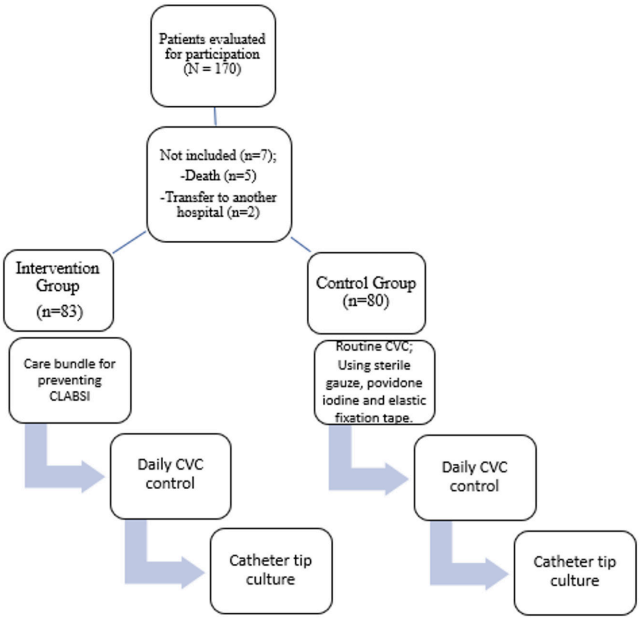


**Figure 2.** Patients' randomization flowchart
CVC: Central venous catheter, CLABSI: central line-associated bloodstream infections

the duration of hospital stay did not show a statistically significant difference between two groups (p=0.105) (Table 1).

The central line was inserted through the right jugular vein (RJV) in 77.1% and the left subclavian vein in 19.3% of patients in the intervention group. For the control group, RJV was preferred in 75% and left subclavian vein was preferred in 15% (Table 2).

All subjects included in the study was closely monitored for signs and symptoms of HAIs by the ICC and the researcher. Nine patients in the intervention group (10.8%) exhibited signs and symptoms of infection. Among those, all nine had fever (>38.5 °C), 44.4% had leukocytosis and 55.6% had tachycardia (>120 bpm). The remaining 89.2% had no signs or symptoms of infection. In the control group, 36.2% exhibited signs and symptoms of infection, which were leukocytosis, fever, and tachycardia (93.1%, 96.6% and 44.8%, respectively). The remaining 51 control subjects (63.8%) did not develop any related signs of symptoms. The difference in signs and symptoms of infection between the intervention and control groups was statistically significant (p<0.05) (Table 3).

| Table 1. Comparison of descriptive and medical characteristics of patients who received and did not receive care bundle | | | | | |
|---|---|---|---|---|---|
| | | Intervention group n=83 | Control group n=80 | | |
| | | n (%) | n (%) | $x^2$ | p-value |
| Gender | Female | 36 (43.4%) | 33 (41.3%) | 0.075 | 0.874 |
| | Male | 47 (54.6%) | 47 (58.8%) | | |
| History of smoke | Yes | 7 (8.4%) | 7 (8.8%) | 0.05 | 0.943 |
| | No | 76 (91.6%) | 73 (91.3%) | | |
| History of chronic illness | Yes | 57 (68.7%) | 51 (63.8%) | 0.442 | 0.506 |
| | No | 26 (31.3%) | 29 (36.3%) | | |
| History of cancer | Yes | 29 (34.9%) | 27 (33.8%) | 0.026 | 0.873 |
| | No | 54 (65.1%) | 53 (66.3%) | | |
| Risk factors | Yes | 51 (61.4%) | 58 (72.5%) | 2.247 | 0.134 |
| | No | 32 (38.6%) | 22 (22.5%) | | |
| | | Mean ± SD | Mean ± SD | $Z_{MWU}$ | p-value |
| Age | | 57.96±17.17 | 64.06±14.92 | -2.333 | 0.020 |
| Stay in the hospital | | 13.03±10.53 | 18.9±20.85 | -1.619 | 0.105 |
| Stay in the ICU | | 6.38±10.24 | 11.91±18.60 | -2.450 | 0.014 |
| APACHE-II score | | 10.34±8.28 | 13.87±7.85 | -3.906 | 0.000 |

$x^2$: Chi-square test, SD: standard deviation, ICU: intensive care unit, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, $Z_{MWU}$: Mann-Whitney U test; p<0.05

| Table 2. Distribution of CVC sites | | |
|---|---|---|
| | Intervention group | Control group |
| | n (%) | n (%) |
| Right jugular vein | 64 (77.1%) | 60 (75%) |
| Right subclavian vein | 16 (19.3%) | 12 (15%) |
| Left subclavian vein | 2 (2.4%) | 1 (1.3%) |
| Right femoral vein | 1 (1.2%) | 3 (3.8%) |
| Left jugular vein | - | 3 (3.8%) |
| Left femoral vein | - | 1 (1.3%) |

CVC: Central venous catheter

| Table 3. Comparison of infection signs in patients who received and did not receive care bundle | | | |
|---|---|---|---|
| Symptom of infection* | n (%) | $x^2$ | p-value |
| Intervention group | | 14.708 | 0.000 |
| Signs (yes) | 9 (10.8%) | | |
| Leukocytosis | 4 (44.4%) | | |
| Fever | 9 (100%) | | |
| Tachycardia | 5 (55.6%) | | |
| Signs (no) | 74 (89.2%) | | |
| Control group | | | |
| Signs (yes) | 29 (36.2%) | | |
| Leukocytosis | 27 (93.1%) | | |
| Fever | 28 (96.6) | | |
| Tachycardia | 13 (44.8%) | | |
| Signs (no) | 51 (63.8%) | | |

*More than one symptoms, $x^2$: chi-square test; p<0.05

The catheter tip cultures obtained from subjects included in the study were positive in 8.4% of the intervention group and in 40.5% of the control group. The most frequently isolated microorganism was *Staphylococcus epidermidis* (4 vs. 20) and the difference was statistically significant.

All central lines of patients included in the study were observed for redness, swelling and discharge by the researcher and the findings were recorded to the Central Venous Catheter Care and Follow-up Form developed by the researcher. Signs of local inflammation in the catheter entry site were observed in 7.2% of patients in the intervention group. All 6 patients had redness, 16.6% had swelling and none had discharge. On the other hand, 41.3% of patients in the control group exhibited signs of local inflammation in the catheter entry site. All of those had redness, 21.2% had discharge and 6.0% had swelling. The difference between the intervention and control groups in terms of redness and discharge in the catheter entry site was statistically significant (p<0.05) (Table 4).

**Table 4. Comparison of CVC observations of patients who received and did not receive care bundle**

| | Intervention group | Control group | | |
|---|---|---|---|---|
| | n (%) | n (%) | $x^2$ | p-value |
| Symptom of infection* | 6 (7.2%) | 33 (41.3%) | 25.904 | 0.000 |
| Redness | 6 (100%) | 33 (100%) | 25.904 | 0.000 |
| Discharge | 0 (0%) | 7 (21.2%) | 7588 | 0.000 |
| Swelling | 1 (16.6) | 2 (6%) | 0.378 | 0.530 |

*More than one symptoms, CVC: Central venous catheter, $x^2$: chi-square test; $p<0.05$

All subjects included in the study were evaluated according to the diagnostic criteria of CLABSI. No patients in the intervention group had CLABSI while 10% of the patients in the control group were diagnosed with CLABSI.

## Discussion

HAIs are observed more often in ICUs due to patient-healthcare worker relationship, common use of mechanic ventilators and invasive equipment, common use of broad-spectrum antibiotics and more frequent colonization of resistant microorganisms. The incidence of HAI in the world varies between 7% and 10%. An estimated 1.4 million people worldwide are thought to have nosocomial infections every day. It is reported that nosocomial infections develop in 5% to 10% of hospitalized patients in a year in the USA, while this rate is between 6-9% in Europe, and this rate varies between 1-3% and 16% in Turkey. Although 5-10% of hospitalized patients are primarily treated in the ICU, 20-25% of all HAIs are seen in ICUs. Patients hospitalized in the ICU are at higher risk of developing infection compared to patients treated in other units, due to the severity of their condition and exposure to highly invasive procedures. It is stated that 53.6% of HAIs seen in ICUs result in death, and considering this rate, the prevention and control of HCAIs is of great importance (10-12).

Although the care bundle is a new concept, its strongest feature is that it includes evidence-based care interventions. The fact that science is behind it and the method of intervention requires continuity gives it national and international standards. It is generally recommended that the number of maintenance-related items (maintenance intervention) in the bundle be between 3 and 5. It is stated that each intervention should be the most accepted (the most effective care for the patient) intervention in its field. The care bundle is often confused with checklists. A checklist is a mix of useful practices or processes (important and useful, but not evidence-based changes), while a bundle is a mix of imperative processes (proven by randomized controlled experiments) (13). It can also be used with the 5 basic component checklists included in the care bundle. Organizations such as the Institute for Healthcare Improvement and The Joint Commission have created lists of CLABSI prevention interventions. In the study, the CDC checklist, which includes the subtitles of the main components in the care bundle and has been proven by studies in the literature, was used.

The use of care bundle for placement and maintenance of CVCs is an important strategy for CLABSI prevention. Care bundle consist of structured evidence-based practices that aim to improve the care process and patient outcomes when followed collectively and reliably. Care bundle have proven effective in reducing CLABSIs in ICU patients (14).

As the longer duration of hospital and ICU stay increases the need for a CVC, it also increases the risk of CLABSI (15-17). On the other hand, Bohart et al. (18) reported no significant association between the duration of ICU stay and CLABSI risk. In the current study, we found that the risk of CLABSI was higher in patients with longer ICU stay. However, the mean duration of hospital stay had no statistically significant difference.

The studies about the association of age and HAIs have reported conflicting results. While some authors state then age is associated with infection (19,20), there is other report that found no association between age and risk of HAI (21). In our study, the mean age of the intervention and control groups were significantly different.

APACHE-II, which predicts disease severity by incorporating changes in physiological measurements, is the most common scoring system used in ICUs. It consists of three parts: chronic health evaluation, age and acute physiology score. The total score of these three parts along with whether the patient is planned to undergo a surgical intervention predicts hospital mortality. In our study, the difference between the mean APACHE-II scores was statistically significant, which was consistent with Pawar et al. (22) but contradictory to Hsin et al. (23).

The preferred anatomical site of CVC insertion is determined by the applying physician. The care bundle states that when selecting the site of CVC use of femoral vein

should be avoided when possible and emergency femoral vein interventions should be switched to a more appropriate site when the patient is hemodynamically stable (2). It was thought that the location of the catheter also affected the development of infection, and the infection rate would be higher due to the risk of urinary and fecal contamination, especially in the femoral vein, but it was reported that there was no difference in infection between the femoral vein and the subclavian vein in studies (24). In our study, most of the central lines of patients in the intervention group were inserted through the RJV. Femoral vein was used in only one patient in the intervention group and the site of CVC was changed as soon as possible in this patient. RJV was also the most preferred entry site in the control group. RJV was a commonly preferred route in the study hospital due to its easy access and availability of rapid intervention in the risk of complications. Aygun et al. (25) also did not find a significant relationship between the location of the catheter and the risk of infection.

Preperation the area where the catheter will be inserted is another matter to be considered. Chlorhexidine, povidine iodine and 70% alcohol are antiseptic products used. In recent years, due to the strong binding of chlorhexidine to skin proteins and its antimicrobial effect on the skin for 48 hours, it is recommended to perform skin antisepsis with 2% chlorhexidine gluconate among the components of the care bundle. In this study, 10% povidine iodine was used in the control group. Although transparent polyurethane or chlorhexidine-impregnated closure covers are among the preferred methods for the prevention of CLABSI in ICU, it is also known that the use of these products does not reduce the infection rate (26,27). Hatler et al. (28) compared transparent polyurethane and chlorhexidine-impregnated closure dressings, and no significant difference was reported in terms of the risk of infection development. In this study, all the catheters were inserted with aseptic technique, they were maintained with the same care and the entry points were checked. The dressings applied to the control group with sterile gauze were changed daily. Transparent dressings impregnated with chlorhexidine were used in the experimental group, and catheter care was performed weekly as long as the integrity of the dressing was not impaired.

Certain studies, however, report that there is no significant difference between the intervention and control groups in terms of signs of local inflammation (29-31). In our study, signs and symptoms of local inflammation were significantly lower in the intervention group ($p<0.05$). Among the control group, patients with signs and symptoms of local inflammation were found to have a higher risk of developing CLABSI. Our significant findings indicate that all stages of care bundle should be performed step-by-step.

In the current study various microorganisms causing CLABSI were isolated. Of these microorganisms, 50% were Gram-positive while the other 50% were Gram-negative. Gram-positive (Coagulase-negative *staphylococci*, *Staphylococcus aureus*) are the most frequently detected microbiological agents in CLABSI's. It is known that *staphylococci* are protected from antibiotics by wrapping the catheter thanks to their biofilm feature made of exopolysaccharides. Gram-negative agents and fungi are also common infectious agents (25). Lin et al. (19) showed that the most commonly isolated pathogens were Gram-negative bacteria with 38%, Gram-positive bacteria with 34.7%, Candida spp. with 24.0%, and anerobic bacteria with 4.7%. İnan et al. (32) reported that 47.6% of microorganisms causing CLABSIs were Gram-negative bacteria, 44.8% Gram-positive, 6.1% Candida spp. and 1.5% other pathogens. Yoshida et al. (33) reported that Gram-negative bacteria were the most common pathogens with 61.8%, among which *Pseudomonas aeruginosa* was seen at a rate of 28.2%. Jaggi et al. (34) reported that 25% *Klebsiella* and 16% *Pseudomonas aeruginosa* 15% Candida are the pathogens causing CLABSI in their study. In our study, the most common microorganism causing CLABSI was *Staphylococcus epidermidis* with 37.5%.

## Conclusion

Care bundle approach is found to be effective in preventing CLABSI. Interdisciplinary interactions should not be disregarded when implementing care bundle approach. It is important that nurses should take an active role in universalizing the care bundle and making sure each step is performed. Care bundle approach should be integrated into nursing care and nurses should be effective in its implementation. Applying the care bundle for preventing CLABSIs for all patients with a central line will increase the quality of care, patient satisfaction, improve nurses' job satisfaction and have a positive impact on economy.

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### Ethics

**Ethics Committee Approval:** Permission from the Haydarpaşa Numune Training and Research Hospital Ethics Committee (decision no: HNEAH-KAEK 2017/KK/143, date: 25.12.2017) and the institution were obtained prior to the start of the study.

**Informed Consent:** Patients and/or their first-degree relatives were informed about the study and written informed consents were obtained.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: E.P., İ.Ç., Concept: E.P., İ.Ç., Design: E.P., İ.Ç., Data Collection and Process: E.P., İ.Ç., Analysis or Interpretation: E.P., İ.Ç., Literature Search: E.P., İ.Ç., Writing: E.P., İ.Ç.

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ÖZGÜN ARAŞTIRMA / *ORIGINAL RESEARCH*

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# Pandemi Sürecinde Non-COVİD-19 Yoğun Bakım Ünitesinde Mortalite

## Mortality in Non-COVID-19 Intensive Care Unit During the Pandemic

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**ÖZ** *Amaç:* Koronavirüs hastalığı-2019 (COVİD-19) pandemisi tüm sağlık hizmetlerini olumsuz etkilemektedir. Bu çalışmada pandemi döneminde merkezimizde, yoğun bakım ünitelerinin önemli kalite göstergesi olan yoğun bakım mortalite oranının nasıl etkilendiğini araştırdık.
*Gereç ve Yöntem:* Bu retrospektif tek merkezli çalışmada, dahili cerrahi non-COVİD-19 hastaların kabul edildiği 20 yataklı yoğun bakım ünitesinde mortalite oranları, pandemi öncesi ve sonrası 6 aylık zaman periyotlarında karşılaştırıldı.
*Bulgular:* Pandemi döneminde yoğun bakım ünitemizde takip edilen hastalarda mortalite oranı artmıştır. Mortalite ile yoğun bakım ünitesine kabul endikasyonu (cerrahi nedenle kabul sonrası, medikal nedenle kabul sonrası, travma sonrası) ve yoğun bakım ünitesine kabul yeri (acil servis, farklı hastane) arasında anlamlı bir ilişki olduğu görülmüştür ($p<0,05$).
*Sonuç:* Rutin sağlık hizmetlerindeki aksamalar, pandemi döneminde COVİD-19 enfeksiyonu taşımayan hastalarda önemli sağlık sorunlarını beraberinde getirecektir.
**Anahtar Kelimeler:** COVİD-19 pandemisi, mortalite, yoğun bakım ünitesi

**ABSTRACT** *Objective:* The coronavirus disease-2019 (COVID-19) pandemic has had a negative impact on all healthcare services. We investigated how the intensive care mortality rate, an important quality indicator of intensive care units, was affected during the pandemic at our center.
*Materials and Methods:* In a retrospective single-center internal surgery setting with a 20-bed intensive care unit, patients without COVID-19 were admitted. The mortality rates over a 6-month time period pre- and postpandemic were compared.
*Results:* During the pandemic, the mortality rate at our intensive care unit has increased. We also observed that there was a significant relationship between mortality and the indication for admission to the intensive care unit (postsurgical admission, postadmission for medical reasons, and post-traumatic) and the place of admission to the intensive care unit (emergency department, different hospital) ($p<0.05$).
*Conclusion:* During the pandemic period, disruptions in routine health services can cause significant health problems in patients who do not have COVID-19 infection.
**Keywords:** COVID-19 pandemic, mortality, intensive care unit

## Giriş

3 Haziran 2021 tarihine kadar, koronavirüs hastalığı-2019 (COVİD-19) salgını nedeniyle dünya çapında, 170.812.850 doğrulanmış olgu ve 3.557.586 ölüm, meydana geldi (1). Asya, Avrupa ve Kuzey Amerika'daki merkezlerden 10.150 COVİD-19 (+) hastayı içeren 24 gözlemsel çalışma sonucuna göre yoğun bakım ünitesinde tedavi edilen hastaların mortalite oranı %41,6 olarak belirlendi (2). COVİD-19 pandemisi özellikle başlangıç aşamasında yüksek oranda yoğun bakım hizmeti ihtiyacı, tıbbi ürünlerde arz talep dengesizliği ve virüsün ölümcül etkileri nedeniyle tüm hayatı ve sağlık hizmetlerini sekteye uğrattı (3,4). Dünya genelinde yoğun bakım yataklarının ve ekipmanının optimal kullanılabilmesi amacıyla triyaj prosedürlerindeki etik belirsizlikler tüm sağlık sistemini zorladı. Yoğun bakım yataklarının büyük bölümü COVİD-19 enfekte hastalar için organize edilmeye çalışıldı. Birçok ülke yeni yoğun bakım üniteleri oluşturarak artan talebi karşılamaya çalıştı. COVİD-19 pandemisi ile mücadele devam ederken, COVİD-19 enfeksiyonu taşımayan hastaların takip edildiği yoğun bakım üniteleri, zaten kısıtlı olan imkanların daha da azalmasına rağmen hizmet vermeye devam etti.

Kısa sürede artan yüksek ve komplike hasta hacmi, hastane kaynaklarını normal koşullarda bile zorlarken, pandemi döneminde süreç yönetimi baş edilemez hale geldi.

Arz ve talep arasındaki uyumsuzluktan kaynaklanan sorunların, çeşitli çalışmalarda özellikle acil servislerde artmış mortalite ile ilişkili olduğu gösterilmiştir (5,6). Çalışmamızda pandemi döneminde dahili-cerrahi hastaların takip edildiği yoğun bakım ünitemizde COVİD-19 ile enfekte ya da taşıyıcı olmadığı bilinen hastaların mortalite oranlarını ve etkileyen faktörleri, pandemi öncesi dönem ile karşılaştırmayı planladık.

## Gereç ve Yöntem

Çalışma, Ondokuz Mayıs Üniversitesi Klinik Araştırmalar Etik Kurul onayı (karar no: 2020/616, tarih: 21.10.2020) alındıktan sonra retrospektif olarak planlandı. Dahili ve cerrahi yoğun bakım hastalarının kabul edildiği 20 yatak kapasiteli yoğun bakım ünitesinde bir yıl süre ile (COVİD-19 öncesi ve sonrası 6 aylık zaman dilimlerinde) takip edilen ve eksitus kabul edilmiş hastalar çalışmaya dahil edildi. On sekiz yaş altı, terminal dönem malignitesi bulunan hastalar çalışma dışı bırakılmıştır.

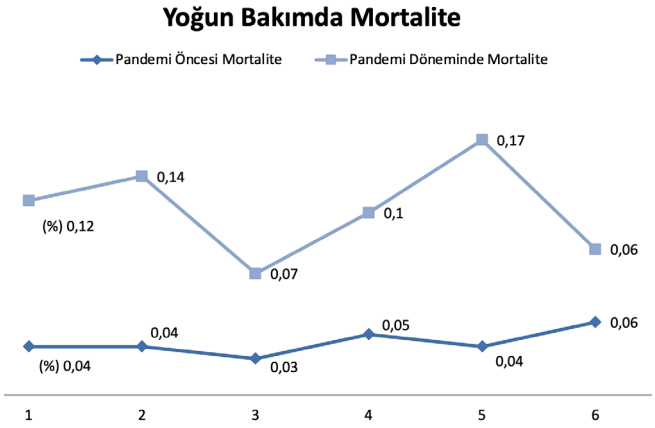
Hastaların demografik verileri (yaş, cinsiyet, vücut kitle indeksi, kronik hastalıkları), yoğun bakımlarda hastaların akut sağlık sorunları ve kronik sağlık durumları üzerinden mortalite öngörme skoru (APACHE-II), hastaların yoğun bakım kabulleri sırasındaki ve günlük organ yetmezliği değerlendirme skoru (SOFA) skorları, yoğun bakım yatış endikasyonu [cerrahi (acil, elektif), medikal (septik şok, post-resüstasyon, klinik kötüleşme)], yoğun bakım öncesi takip eden servis, yoğun bakım sürecinde hastalara hizmet veren personel sayıları, personel mesai süreleri, yoğun bakımda kalış süreleri, mortalite nedeni, mortalite zamanı COVİD-19 öncesi ve sonrası dönem olarak karşılaştırıldı.

### İstatistiksel Analiz

Veriler IBM SPSS Statistics 21.0 software programı yardımıyla incelendi. Grup içi karşılaştırmalar için Friedman ve Wilcoxon testleri, gruplar arası karşılaştırmalarda ise sayısal parametreler için Mann-Whitney U testi, kategorik parametreler için ise ki-kare testi kullanıldı. Yoğun bakım mortalite sonuçları risk faktörlerini belirlemek için lojistik regresyon modelleri kullanılarak $p<0,05$ anlamlı kabul edildi.

## Bulgular

Yoğun bakım ünitemizde COVİD-19 pandemi ve öncesi dönemdeki mortalite oranlarını değerlendirdiğimiz bir yıllık süre içinde toplam 1.730 hasta yoğun bakım ünitemize kabul edilmiş ve eks olan 208 hastanın, 196'sı çalışmaya dahil edilmiştir. Çalışmaya dahil edilen hastaların 129'u (%65,8) pandemi döneminde, 67'si (%34,2) pandemi öncesi dönemde kaybedilmiştir. Pandemi öncesi yoğun bakım mortalite oranımız %5,3 iken pandemi sonrası mortalite oranımız %12,9'a yükselmiştir (Şekil 1; $p<0,01$). Hastaların demografik verileri, ek sistemik hastalıkları ve klinik özellikleri Tablo 1'de özetlenmiştir. Pandemi öncesi yoğun bakım ünitemize %92,4 oranında cerrahi sonrası hasta




**Şekil 1.** Pandemi öncesi ve sonrası 6 aylık ölüm oranları (%) ($p<0,01$)

| Tablo 1. Hastaların demografik verileri, ek sistemik hastalıkları, klinik özellikleri | | | |
|---|---|---|---|
| | **COVİD-19 pandemi öncesi mortalite n=67** | **COVİD-19 pandemi döneminde mortalite n=129** | **p-değeri** |
| Yaş, yıl ortalama ± SS | 62,5±19,3 | 65,1±16,4 | 0,213 |
| Cinsiyet (K/E) % | 55,2/44,8 | 32,6/67,4 | 0,036 |
| **Sistemik hastalık** | | | |
| Diabetes mellitus % | 22,4 | 20,9 | 0,672 |
| Hipertansiyon % | 50,7 | 54,3 | 0,355 |
| Malignensi % | 13,4 | 17,8 | 0,938 |
| KOAH % | 6 | 12,4 | 0,165 |
| Koroner arter hastalığı % | 14,9 | 20,2 | 0,248 |
| Siroz % | 3 | 3,9 | 0,733 |
| Kronik böbrek yetmezliği % | 6 | 15,5 | 0,563 |
| Serebro vasküler hastalık % | 6 | 9,3 | 0,521 |
| Kalp yetmezliği % | 4,5 | 12,4 | 0,307 |
| APACHE-II skoru ortalama ± SS | 27,9±7,1 | 32,5±7,4 | 0,013 |
| SOFA skoru ± SS | 13,07±3,6 | 15,9±4,4 | 0,001 |
| Renal replasman tedavisi % | 19,4 | 42,6 | 0,001 |
| **Hasta türleri** | | | |
| Cerrahi % | 55,2 | 25,6 | 0,001 |
| Medikal % | 34,3 | 68,2 | 0,023 |
| Travma % | 10,4 | 6,2 | 0,01 |
| **YBÜ öncesi kabul yeri** | | | |
| Acil servis % | 25,4 | 27,1 | 0,001 |
| Ameliyathane % | 47,8 | 26,4 | 0,068 |
| Hastane servis odası % | 20,9 | 45,7 | 0,206 |
| Farklı hastane % | 6 | 0,8 | 0,015 |

SS: Standart sapma, KOAH: kronik obstrüktif akciğer hastalığı, APACHE: akut sağlık sorunları ve kronik sağlık durumları üzerinden mortalite öngörme skoru, SOFA: günlük organ yetmezliği değerlendirme skoru, YBÜ: yoğun bakım ünitesi, COVİD-19: koronavirüs hastalığı-2019

kabul edilirken, pandemi döneminde cerrahi sonrası hasta kabulü oranı %82,6'ya gerilemiştir. Pandemi döneminde acil cerrahi sonrası yoğun bakım kabulü, pandemi öncesi döneme göre artmıştır (%32,6/%19,8). Pandemi döneminde eksitus kabul edilen hastalarda, cerrahi sonrası kabul oranı azalmış, ancak acil cerrahi sonrası kabul edilen hasta sayısı ve hastalarda mortalite oranı istatistiksel olarak artmıştır [pandemi öncesi, sonrası acil cerrahi mortalite ilişkisi (%21,6/30,3) p<0,01]. Pandemi öncesi medikal nedenler ile yoğun bakıma kabul oranı %7,6 iken pandemi döneminde oran %17,4'e yükselmiştir. Medikal nedenle yoğun bakıma kabul edilen hastalarda mortalite oranı istatistiksel olarak artmıştır. Medikal nedenli yoğun bakım kabulü ve mortalite ilişkisi sırasıyla pandemi öncesi/sonrası; sepsis: %43,5/19,3 p=0,01, post resüsitasyon bakım: %17,4/21,6 p=0,023, klinik kötüleşme: %39,1/59,1 p=0,786 olarak tespit edilmiştir. Pandemi öncesi eksitus kabul edilen hastaların yoğun bakım kalış süresi ortalama [± standart sapma (SS)]: 7,6 (±11,02) gün; pandemi döneminde ise ortalama (±SS): 9.5 (±14,1) gün olduğu görülmüştür. Her iki zaman diliminde eksitus kabul edilen hastaların yoğun bakım süreleri benzerdir (p=0,532). Çalışma süresi içinde gelişen mortalite nedenleri ve gruplar arasındaki ilişki Tablo 2'de özetlenmiştir.

Yoğun bakım ünitemizde 13 doktor, 14 yardımcı sağlık personeli, 33 hemşire tam zamanlı görev yapmaktadır. Pandemi döneminde yoğun bakım ünitemizde 12 hemşire, 3 yardımcı sağlık personeli, 3 doktor COVİD-19 virüsü ile enfekte olmuş; yoğun çalışma temposu içindeki hemşire

| Tablo 2. Gruplar arası ölüm nedenleri | | | |
|---|---|---|---|
| | COVİD-19 pandemi öncesi mortalite n=67 | COVİD-19 pandemi döneminde mortalite n=129 | p-değeri |
| Septik şok % | 37,3 | 35,7 | 0,562 |
| Solunum yetmezliği % | 16,4 | 20,9 | 0,768 |
| Multipl travma % | 10,4 | 5,4 | 0,673 |
| Kalp yetmezliği % | 35,8 | 38 | 0,226 |
| COVİD-19: koronavirüs hastalığı-2019 | | | |

arkadaşlarımız süreçten önemli şekilde etkilenmiştir. Hemşirelerimizin yaklaşık 1/3'ü en az 10 günlük periyodlarda tedavi ve izolasyon amacıyla görevlerinde çalışamamıştır. Personel açığı diğer servislerde çalışan yoğun bakım deneyimi az olan hemşire arkadaşlarımızla tamamlanmıştır. Pandemi öncesi 6 aylık zaman sürecinde yoğun bakım ünitemize yeni başlayan hemşire sayısı aylık ortalama (±SS): 1,16±0,98; pandemi döneminde 3,0±0,89 olduğu ve mortalite oranı ile yoğun bakım ünitesine yeni görevlendirilen hemşire sayısı arasında istatistiksel olarak anlamlı ilişki olduğu (p=0,026) görüldü. Pandemi öncesi ortalama 4,38 hastaya bir hemşire, pandemi döneminde ise 4,21 hastaya bir hemşire ile hizmet verilmeye çalışıldığı ve iki dönemde hastalara hizmet veren hemşire sayılarının benzer olduğu tespit edilmiştir.

## Tartışma

Pandemi döneminde tek merkez 20 yataklı dahili-cerrahi yoğun bakım hastalarının takip edildiği COVİD-19 ile enfekte ya da taşıyıcı olmadığı bilinen hastaların mortalite oranlarını değerlendirdiğimiz çalışmamızda, pandemi döneminde, öncesi döneme oranla mortalite oranımızın istatistiksel olarak arttığını tespit ettik.

2020 yılında Çakır ve ark.'nın (7) 757 hastayı dahil ettikleri çalışmada yoğun bakım mortalite oranı %34,7, ülkemizdeki erişkin hastalarda yapılan diğer yoğun bakım çalışmalarında ise mortalitenin %20,5-60,4 arasında değiştiği bulunmuştur. Polonya'da yapılan çalışmada yoğun bakım mortalite oranı %41-44, diğer Avrupa ülkelerinde %6,7-17,8, Amerika Birleşik Devletleri'nde %11,3, Avustralya ve Yeni Zelanda'da %7 olduğu belirtilmiştir (8-12). Çalışma sürecinde yoğun bakım ünitemizde toplam mortalite oranı %11,3 olarak bulunmuştur. Mortalite oranımız literatür ile uyumlu ancak ülkemizde yoğun bakım mortalite çalışmalarına göre düşüktür. Bu durum anestezi sonrası bakım bölümü (PACU) olarak da hizmet veren yoğun bakım ünitemize yatış endikasyonları ile bağlantılı olabilir. Çalışmaya kabul edilen pre-COVİD dönem eksitus kabul edilmiş hastaların APACHE-II skoru ortalama 22,9, pandemi döneminde ise 32,5; SOFA skorları ise sırasıyla ortalama 9, 15,9 olduğu ve yoğun bakıma kabul sırasında pandemi döneminde daha yüksek APACHE-II ve SOFA skorları, mortalite açısından genel durumu daha kötü hastaların yoğun bakım ünitemize kabul edildiklerini göstermiştir.

Tüm dünyada elektif cerrahiler pandemi önlemleri kapsamında ertelenmiştir. Birleşik Krallık'ta pandemi öncesi elektif cerrahi bekleyen hasta sayısı 4 milyon iken, pandemi döneminde sayı 10 milyon insanı geçmiş, Amerika Birleşik Devletleri'nde yayınlanan bir rapora göre 2022 ortasına kadar sadece eklem ve omurga ameliyatı bekleyen hasta sayısı 1 milyondan fazla olacağı öngörülmüştür (13). Ülkemizde de pandemi döneminde elektif cerrahiler ertelenmiştir. Bu durum PACU olarak da hizmet veren yoğun bakım ünitemizde hasta profilinin değişimine neden olmuş, pandemi döneminde artmış mortalite ve azalmış elektif cerrahiler arasında anlamlı ilişki olduğu görülmüştür.

Yapılan çalışmalar pandemi döneminde acil servis başvurularında azalma olduğunu göstermektedir (14-17). Sokağa çıkma kısıtlamaları, COVİD-19'a maruz kalma korkusu, hastaların uygun sağlık hizmetine erişememesi ya da geç erişmesine neden olabilir. COVİD-19 salgını sırasında miyokard enfarktüsü ve inme nedeniyle dahi hastaneye başvurularda düşüşler olduğu bildirilmiştir (18,19). Kronik kompanse hastalıkların pandemi dönemi ilişkili geç acil servis başvurusu sonucu dekompanse hale gelmesi pandemi döneminde mortalite oranlarını artırması beklenmektedir (20,21). Merkezimizde pandemi dönemindeki acil servisten yoğun bakım ünitesine kabul edilen hasta sayısının arttığı ve bunun artan mortalite ile ilişkili olduğu görülmüştür. Subgrup analizlerinde acil servisten kabul edilen yoğun bakımda eksitus kabul edilmiş hastaların demografik verileri, ek sistemik hastalıkları, APACHE-II skorları her iki dönemde benzer ancak pandemi döneminde SOFA skorlarının anlamlı şekilde yüksek olduğu görülmüştür (p=0,018).

Sen-Crowe ve ark. (22) yaptığı çalışmada pandemi döneminde sokağa çıkma kısıtlamaları nedeniyle özellikle trafik kazalarında azalma olduğu ve sonuçta travma sonrası ölümlerin azaldığı bildirilmiştir. Çalışmamızda da pandemi döneminde travma sonrası yoğun bakıma kabul edilen azalmış hasta sayısı ile travma sonrası mortalite oranın istatistiksel olarak ilişkili bulunmuştur.

Artan mortalite ile ilişkili bir başka önemli bulgumuzda pandemi döneminde, COVİD-19 bulaşı nedeniyle meydana gelen personel açığının daha az deneyimli personel geçici görevlendirmeleriyle tamamlanmaya çalışılmasıdır. Yapılan çalışmalar özellikle yoğun bakım ünitelerinde artmış hemşire deneyiminin azalmış mortalite ile ilgili olduğunu göstermektedir. Aynı zamanda geçici görevlendirmelerle fiziksel ortam adaptasyon sorunları da çalışma performansını olumsuz etkileyebilmektedir (23-25).

## Sonuç

Pandemi ve pandemi ilişkili zorluklar ile mücadele devam etmektedir. Tüm dünya salgını kontrol altına alarak COVİD-19 enfeksiyonunu ve ilişkili mortaliteyi önlemeye odaklanmıştır. Ancak rutin sağlık hizmetlerindeki aksamalar önemli sorunları beraberinde getirecektir. Bunlardan bir tanesi de beklenmeyen ölüm oranlarındaki artış miktarıdır. COVİD-19 enfeksiyonu taşımayan yoğun bakım hastalarında mortalite oranını değerlendirdiğimiz çalışmamızda, hasta profilindeki değişim, yoğun bakım ünitesi COVİD-19 enfeksiyonu nedeniyle oluşan personel açığının daha az deneyimli sağlık çalışanları ile kapatılmaya çalışılması ile mortalite oranının ilişkili olduğu ve pandemi döneminde yoğun bakım mortalite oranımızın arttığı bulunmuştur.

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**ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA***

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# Dysphagia in the Intensive Care Units in Turkey: A Cross-sectional Survey Study

## Türkiye'de Yoğun Bakım Ünitelerinde Disfaji: Kesitsel Bir Anket Çalışması

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**ABSTRACT** *Objective:* This study aimed to investigate the current dysphagia practices and their defined awareness in the intensive care units (ICUs) in Turkey.
*Materials and Methods:* The study was part of an international, multi-center survey, called Dysphagia in Intensive Care Evaluation. The survey included questions related to the descriptive information and questions under three subgroups, including current practice, awareness, and perceived best practice, and was sent to ICU department managers via Google forms for them to answer on behalf of their ICU.
*Results:* A total of 39 responses were received, which revealed no standard protocol in all ICUs that indicates which patients should be screened for dysphagia. Cough reflex testing and water swallow tests were the most common methods to confirm dysphagia. Oral hygiene, postural adjustments, modifications, and delay feeding and retry the next day were reported as the most common preventions for aspiration, and repetitive swallowing exercises/maneuvers, muscle strengthening exercises, and respiratory exercises were most common for dysphagia treatment. The awareness-related survey items revealed a mean score of >5 on a 7-level Likert scale.
*Conclusion:* Dysphagia practice in the ICUs in Turkey needs improvement, with established standardized management protocol.
**Keywords:** Intensive care, deglutition, dysphagia, deglutition disorders

**ÖZ** *Amaç:* Bu çalışma, Türkiye'deki yoğun bakım ünitelerinde (YBÜ) mevcut disfaji uygulamalarını araştırmış ve disfajiye ilişkin farkındalığı tanımlamıştır.
*Gereç ve Yöntem:* Çalışma, Yoğun Bakım Değerlendirmesinde Disfaji (YBDD) adı verilen uluslararası, çok merkezli bir anket çalışmasının bir parçasıdır. Anket, açıklayıcı bilgilerle ilgili soruları ve mevcut uygulama, farkındalık ve algılanan en iyi uygulamayı içeren üç alt grup altındaki soruları içermektedir. Anket, yoğun bakım departmanı yöneticilerine YBÜ'ler adına yanıtlamaları için Google formları aracılığıyla gönderildi.
*Bulgular:* Toplam 39 yanıt alındı. YBÜ'lerin hiçbirinde, hangi hastaların disfaji için taranması gerektiğini belirten standart bir protokol yoktu. Öksürük refleksi testi ve su yutma testi, disfajiyi doğrulamak için kullanılan en yaygın yöntemlerdendi. Ağız hijyeni, postür ayarlamaları, modifikasyonlar ve beslemeyi geciktirme ve ertesi gün yeniden deneme aspirasyon için en yaygın kullanılan önlemler olarak rapor edildi ve tekrarlayan yutma egzersizleri/manevraları, kas güçlendirme egzersizleri ve solunum egzersizleri disfajiyi tedavi etmek için en yaygın kullanılan müdahalelerdi. Farkındalıkla ilgili anket maddelerinden alınan ortalama puan 7 seviyeli Likert ölçeğinde 5'in üzerindeydi.
*Sonuç:* Türkiye'de YBÜ'lerde disfaji uygulamasının iyileştirilmesi ve standart bir yönetim protokolü oluşturulması gerekmektedir.
**Anahtar Kelimeler:** Yoğun bakım, yutma, yutma güçlüğü, yutma bozuklukları

## Introduction

Dysphagia is a condition that includes the ability to eat and drink, and affects body functions (1). It ranges from conditions that mostly affect oral area including food retention in the mouth to difficulty in food delivery to life-threatening situations such as penetration and aspiration (2). Assessments related to dysphagia include biomechanical parameters, integrity and movements of anatomical structures, bolus transport, penetration and aspiration of foods into airway (3,4). In dysphagia treatment, medical, surgical, rehabilitatitive and behavioral approaches are used to to teach compensation mechanisms and improve swallowing physiology (4,5).

Dysphagia occurs with symptoms including coughing during swallowing, wheezing, sputum, weight loss, and recurrent pneumonia (1). It may also affect both patient's and caregiver's quality of life. Therefore, identifying and defining swallowing disorders in the early period enables the patient to be included in the swallowing rehabilitation program in the early period and to shorten the recovery period (6-8). The early identification increases the quality of life of both patients and their families, and contributes to the reduction of health-care expenses (9). Thus, it is very important to increase the awareness of clinicians about dysphagia and to identify the presence of dysphagia in the early period.

Dysphagia can be seen between 3 to 62% in critically ill patients on the intensice care units (ICUs) (10). The potential causes were reported as direct trauma caused by endotracheal and tracheostomy tubes, decreased muscular strength and laryngeal sensory function, gastroesophageal reflux, and incoordination of breathing and swallowing (11). Its clinical consequences including dysphagia complications (i.e., pneumonia, reintubation), longer hospitalization, increased healtcare costs, increased mortality are also crucial (12,13). Therefore, early identification of dysphagia in ICU patients become more important, and swallowing function should be evaluated in a timely manner in ICUs. At this point, clinicians in ICUs must have sufficient knowledge and awareness regarding dysphagia, and standardized screening protocols should be established. Despite this need, there is no standardized guidelines for ICU patients related to the management of dysphagia. To establish standardized guidelines, studies investigating national and international practices are necessary to define the needs and best practices. Therefore, this study was aimed to determine the current dysphagia practices, and define awareness regarding dysphagia in ICUs in Turkey.

## Materials and Methods

The study was conducted at a university hospital. The Ethics Commission of the Hacettepe University approved the study protocol (approval number: 35853172/431-318, date: 16.01.2018).

This study was conducted as a part of an international, multi-center survey study which is called Dysphagia in Intensive Care Evaluation (DICE). As Turkey local study coordinators, we received the developed survey based on available literature for forward backward translation process. The forward-backward translation process was followed to translate the survey English into Turkish language. The forward translation was performed by two bilingual Turkish physical therapists. Two Turkish translations were analyzed, and turned into a single survey with a consensus. The Turkish version was then translated into English by a native English-speaking language expert who also speaks Turkish for backward translation. The backward version was compared to the original survey in a meeting, and the Turkish version was completed. The backward translation was presented to the main study coordinators for their confirmation.

The survey was sent to ICU department managers via Google forms. Participants were asked to answer the survey on behalf of their ICU. An informed consent was obtained from the participants by clicking the start button of the Google forms. If there are non-responders, a follow-up inquiry was sent two weeks interval.

The survey had questions related to descriptive information, and questions under three subgroups including current practice, awareness, and perceived best practice. The descriptive information related to the hospital and ICU was questioned. In the current practice section, screening procedures, evaluation methods, methods used to prevent aspiration/aspiration pneumonia, interventions to treat dysphagia were questioned. In awareness section, the participants were asked the relationships between and ICU, duration of intubation, ICU length of stay, hospital length of stay, physical functioning, nursing home, risk of ICU-readmission. In the perceived best practice, the need for standard protocol for screening, screening before discharge and screening for post-extubation dysphagia.

### Statistical Analysis

The statistical analysis was conducted by using the IBM-SPSS for Windows version 20. Descriptive statistics were calculated as a number/percent for qualitative data, and

mean, standard deviation, minimum and maximum values for quantitative data.

## Results

The Turkish translation of the survey did not have any linguistic problem, and the final version was presented to the DICE study coordinators, and every item was identical to the original version.

A total of 39 responses was received. Most responding centers were university hospitals (n=32, 82.1%). The descriptive information related to the hospital and ICU is presented in Table 1.

### Current Practice

Most ICUs (n=15, 38.5%) did not screen patients for dysphagia after extubation who were intubated for >48 hours, and only 7 ICUs (17.9%) screened them more than >75% of the time. Almost half of ICUs (n=14, 35.9%) did not screen tracheotomized patients for dysphagia routinely, and the other half (35.9%) screened them more than >50% of the time. None of the ICUs reported a standard protocol that indicates which patients should be screened for dysphagia. The most frequently screened patients for dysphagia after extubation were patients demonstrating signs of dysphagia (n=21, 53.8%), patients with known pre-existing neurological disorders (n=13, 33.3%), patients with tracheostomy (n=11, 28.2%) and patients with recurrent pneumonia in the ICU (n=10, 25.6%).

The most common methods used to confirm the presence of dysphagia were cough reflex testing (n=17, 43.6%) and water swallow test (n=16, 41.0%) for >50% of assessments. Details regarding dysphagia evaluation are shown in Table 2.

The most common preventions for aspiration or aspiration pneumonia were oral hygiene, postural adjustments, using occupational-therapy tools, dietary texture modifications, and delay feeding and retry the next day. The most common interventions to treat dysphagia were repetitive swallowing exercises/maneuvers, muscle strengthening exercises without swallowing (e.g. shaker exercise), and respiratory exercises (e.g. expiratory muscle strength training). Details regarding dysphagia treatment are presented in Table 2.

### Awareness

Three (7.7%) ICUs reported that dysphagia occurs in >50% of patients intubated for >48 hours, 18 (46.2%) ICUs reported that dysphagia occurs in >50% of patients intubated for >7 days, and 14 (35.9%) reported that dysphagia occurs in >50% of patients who received a tracheostomy. Table 3 indicates the details regarding dysphagia awareness.

### Perceived Best Practice

The mean score for the need for standard protocol or algorithm for screening for post-extubation oropharyngeal dysphagia, the need for routine screening of all patients admitted >48 hours in the ICU for oropharyngeal dysphagia

**Table 1. The descriptive information related to the hospital and ICUs in Turkey**

| Hospital | n | % |
|---|---|---|
| University hospital | 32 | 82.1 |
| Educational hospital | 4 | 10.2 |
| Governmental hospital | 3 | 7.7 |
| **Professions in ICU to discuss the survey** | | |
| Intensivist | 35 | 89.7 |
| Physical therapist | 10 | 25.6 |
| Nurse | 10 | 25.6 |
| Otolaryngologist | 5 | 12.8 |
| Physiatrist/rehabilitation physician | 4 | 10.3 |
| Speech language pathologist | 4 | 10.3 |
| Dietitian | 3 | 7.7 |
| Neurologist | 3 | 7.7 |
| Internal medicine specialist | 1 | 2.6 |
| Anesthetist | 1 | 2.6 |
| **Number of beds in the hospital** | | |
| <200 | 5 | 12.8 |
| 200-499 | 10 | 25.6 |
| 500-799 | 7 | 17.9 |
| ≥800 | 17 | 43.6 |
| **Number of bed capacity in their ICU** | | |
| <5 | 1 | 2.6 |
| 5-9 | 6 | 15.4 |
| 10-14 | 13 | 33.3 |
| 15-19 | 8 | 20.5 |
| 20-49 | 7 | 17.9 |
| ≥50 | 4 | 10.3 |
| **Patient categories treated in their ICU** | | |
| Mixed | 30 | 76.9 |
| Medical only | 8 | 20.5 |
| Trauma only | 1 | 2.6 |

ICU: Intensive care unit

before discharge, and the need for routine screening of all patients requiring >48 hours of intubation for post-extubation oropharyngeal dysphagia were 5±3.46 (minimum =1, maximum =7).

## Discussion

ICU related dysphagia is an important issue due its clinical consequences. Therefore, dysphagia awareness in ICUs should be increased, and standardized management guidelines should be developed. Due to this need, recently several studies were conducted to define ICU related dysphagia from different perspectives, and the necessity of studies regarding current practices has been demonstrated (14-17). There is no evidence related to dysphagia awareness and practices in Turkish ICUs. Thus, we conducted this study which is a part of international cross-sectional study to determine the current dysphagia practices, and define awareness regarding dysphagia in ICUs in Turkey.

**Table 2. Dysphagia management in ICUs**

| **Timing of dysphagia screening after extubation** | **n** | **%** |
|---|---|---|
| Never | 15 | 38.5 |
| Same day of extubation | 7 | 17.9 |
| 24-48 hours after extubation | 14 | 35.9 |
| 3-7 days after extubation | 2 | 5.1 |
| 1-2 weeks after extubation | 1 | 2.6 |
| **Professions to assess dysphagia in ICU** | | |
| Intensivist | 31 | 79.5 |
| Nurse | 25 | 64.1 |
| Physical therapist | 7 | 17.9 |
| Otolaryngologist | 6 | 15.4 |
| Speech language pathologist | 4 | 10.3 |
| Physiatrist/rehabilitation physician | 4 | 10.3 |
| Neurologist | 3 | 7.7 |
| Internal medicine specialist | 1 | 2.6 |
| **Professions to treat dysphagia in ICU** | | |
| Nurse | 14 | 48.7 |
| Physical therapist | 11 | 28.2 |
| Intensivist | 9 | 23.1 |
| Speech language pathologist | 3 | 7.7. |
| Otolaryngologist | 2 | 5.1 |
| **Timing of PEG tube insertion** | | |
| When dysphagia is present <7 days | 2 | 5.1 |
| When dysphagia is present 8-14 days | 3 | 7.7 |
| When dysphagia is present 14-21 days | 5 | 12.8 |
| When dysphagia is present >21 days | 8 | 20.5 |
| Not performed routinely, only on an individual basis | 20 | 51.3 |
| Never insert PEG for post-ext./tracheostomy dysphagia | 1 | 2.6 |

ICU: Intensive care unit, PEG: percutaneous endoscopic gastrostomy, post ext.: post-extubation

In current practice of ICUs, screening, evaluation methods, and interventions were questioned. The most striking result was that none of the ICUs had a standard protocol that indicates which patients should be screened for dysphagia. In addition, most ICUs did not screen patients for dysphagia after extubation who were intubated for >48 hours, or almost half of them did not screen tracheotomized patients for dysphagia routinely. In support of these results, the most frequently screened patients were patients demonstrating signs of dysphagia. However, screening should be done in the population at risk, and it was known that baseline neurologic disease, duration of invasive mechanical ventilation, extubation, having a tracheostomy tube were reported as risk factors for dysphagia in ICU settings (11,18,19). But, the current study results show that there is a gap in terms of dysphagia screening procedures in ICUs in Turkey which is bigger than other countries conducted similar studies (15-17). Therefore, a standard dysphagia screening protocol needs to be developed for who will be evaluated, when and how in Turkish ICU services.

Cough reflex testing and water swallow test was the most mentioned methods to confirm the presence of dysphagia in ICUs in Turkey. Water swallow test was also reported as a routinely used screening method in ICUs in literature (15-17,20,21). Besides its frequent use, it should be noted that the accuracy of this screening protocol is low compared instrumental swallowing evaluation methods (22). Oral hygiene, postural adjustments, using occupational-therapy tools, dietary texture modifications, and delay feeding and retry the next day were reported to be used to prevent aspiration or aspiration pneumonia. In addition, swallowing exercises/maneuvers, muscle strengthening exercises without swallowing and respiratory exercises were the most mentioned methods to treat dysphagia in ICU. According to these results, it was understood that ICUs have attempts to prevent aspiration and treat dysphagia, and the methods used were generally similar to practices in other countries (15-17,23).

| Table 3. Awareness regarding dysphagia in ICUs | | |
|---|---|---|
| **Prevalence on dysphagia for patients intubated for >48 hours** | **n** | **%** |
| 0 | 1 | 2.6 |
| <25% | 16 | 41.0 |
| 25-50% | 19 | 48.7 |
| 51-75% | 2 | 5.1 |
| >75% | 1 | 2.6 |
| **Prevalence on dysphagia for patients intubated for >7 days** | | |
| <25% | 9 | 23.1 |
| 25-50% | 12 | 30.8 |
| 51-75% | 14 | 35.9 |
| >75% | 4 | 10.3 |
| **Prevalence on dysphagia for patients who received a tracheostomy** | | |
| <25% | 9 | 23.1 |
| 25-50% | 16 | 41.0 |
| 51-75% | 9 | 23.1 |
| >75% | 5 | 12.8 |
| **Survey items related to awareness** | **Mean (SD)** | **Min-max** |
| Oropharyngeal dysphagia is prevalent in ICUs. | 5.07 (1.75) | 1-7 |
| Oropharyngeal dysphagia is associated with duration of intubation. | 5.17 (1.63) | 1-7 |
| Oropharyngeal dysphagia prolongs ICU length of stay. | 6.17 (1.57) | 1-7 |
| Oropharyngeal dysphagia prolongs hospital length of stay. | 5.58 (2.16) | 1-7 |
| Oropharyngeal dysphagia contributes to delay in return to independent physical functioning after critical illness. | 6.05 (1.53) | 1-7 |
| Oropharyngeal dysphagia increases the need for care at long-term facilities or nursing homes after critical illness. | 6.02 (1.49) | 1-7 |
| Patients with oropharyngeal dysphagia have an increased risk of ICU-readmission. | 5.41 (1.94) | 1-7 |
| ICU: Intensive care unit, SD: standard deviation, min-max: minimum-maximum | | |

Intubation and having tracheostomy tube could be considered as risk factors for dysphagia in ICU according to our results. The frequency of dysphagia was found to be increase as the intubation time increases. Dysphagia following intubation for >48 hours mostly ranges between 25% to 50%, and the prevalence increases between 25% to 75% in case of intubation for >7 days. Our study results are compatible with the current literature that dysphagia is common after endotracheal intubation (24), and prolonged intubation causes highest dysphagia frequencies (10). In addition, dysphagia is frequently seen in patients with tracheostomy in ICU settings (25). Therefore, it could be suggested that dysphagia should be considered in patients with endotracheal intubation and tracheostomy tube, and dysphagia screening should be performed to define swallowing related problems in early period and plan appropriate management programs. ESPEN guideline on clinical nutrition in ICUs also recommends swallowing evaluation in these patients to prevent complications related to oral feeding (26).

Dysphagia awareness among ICUs in Turkey was found to be generally well above the average. Complementary to dysphagia awareness in ICUs, and despite their clinical practice, it was reported that there is a need for standard protocol for dysphagia screening and routine screening of all patients admitted >48 hours in the ICU before discharge, and all patients requiring >48 hours of intubation. This is a promising finding of this study, and thereby standardized protocol for dysphagia management from screening to treatment and rehabilitation should be established.

## Conclusion

In conclusion, the current study demonstrates the current status, awareness and perceived best practices regarding dysphagia in ICUs in Turkey. The current dysphagia practice

in ICUs needs to be improved, but hopefully the awareness regarding dysphagia is quite high and participants are also aware of the need to improve their practice. Therefore, ICUs in Turkey need to be trained in terms of dysphagia, and a standardized management protocol should be established.

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## Ethics

**Ethical Commite Approval:** The Ethics Commission of the Hacettepe University approved the study protocol (approval number: 35853172/431-318, date: 16.01.2018).

**Informed Consent:** An informed consent was obtained from the participants by clicking the start button of the Google forms.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: S.S.A., N.D., Design: S.S.A., N.D., Data Collection and Process: S.S.A., N.D., Analysis or Interpretation: S.S.A., N.D., Literature Search: S.S.A., Writing: S.S.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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CASE REPORT / *OLGU SUNUMU*

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# The Cardiogenic Shock with Antihypertensive Drugs Intoxication in a Child

## Antihipertansif İlaç Zehirlenmesi Olan Bir Çocuktaki Kardiyojenik Şok

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**ABSTRACT** Combination antihypertensive treatments are usually used in everyday life, which has a life-threatening risk of using an overdose accidentally or suicidally. The effects of calcium channel blockers on the cardiovascular system are negative chronotropic, myocardial depression, decreasing atrioventricular signals, and vasodilatation. Beta blocker drugs are affected to beta receptors of catecholamines with competitively inhibition. Hypotension and bradycardia are the most common cardiac manifestations, and the others are arrhythmias, pulmonary edema, depression of the central nervous system. A previously healthy 4-year-old boy used accidentally 240 mg verapamil/4 mg trandolapril two pieces and 5 mg nebivolol one, at the time of admission his clinical condition was in cardiogenic shock. We successfully treated him with insulin-euglycemia/glucagon treatment, calcium, and lipid infusion therapy, plasmapheresis, and continuous venovenous hemodiafiltration without any sequels. The intoxication of calcium channel blockers and beta blocker drugs are rare but severe cases because of life-threatening.
**Keywords:** Antihypertensive treatments, calcium channel blocker, beta blocker, cardiogenic shock, intoxication

**ÖZ** Günlük yaşamda genellikle kombine antihipertansif ilaçlar kullanılmaktadır ve kazara veya intihar amaçlı olarak aşırı dozda kullanılması hayati tehlike taşıyabilir. Kalsiyum kanal blokerinin kardiyovasküler sistemler üzerindeki etkileri negatif kronotropi, miyokardiyal depresyon, atriyoventriküler sinyallerde azalma ve vazodilatasyondur. Beta bloker ilaçlar ise katekolaminlerin beta reseptörlerine yarışmalı inhibisyonu ile etki ederler. Hipotansiyon ve bradikardi en sık görülen kardiyak belirtiler olup aritmiler, pulmoner ödem ve merkezi sinir sisteminin depresyonu da görülür. Daha önce sağlıklı olan 4 yaşındaki bir erkek çocuk, kazara iki adet 240 mg verapamil/4 mg trandolapril ve bir adet 5 mg nebivolol kullanmıştı. Başvuru anında hastanın klinik durumu kardiyojenik şok idi. İnsülin-öglisemi/glukagon tedavisi, kalsiyum ve lipit infüzyon tedavisi, plazmaferez ve sürekli venovenöz hemodiyafiltrasyon tedavileri ile başarılı bir şekilde herhangi bir sekel gelişmeden hasta tedavi edildi. Kalsiyum kanal blokeri ve beta bloker ilaç intoksikasyonu nadir fakat hayatı tehdit edici olması nedeniyle ciddi olgulardır.
**Anahtar Kelimeler:** Antihipertansif tedavi, kalsiyum kanal blokeri, beta bloker, kardiyojenik şok, zehirlenme

## Introduction

The combination antihypertensive treatments are usually used in everyday life for being easy (1,2). However, these drugs have a life-threatening risk for using an overdose. Intoxication is rare and can be caused serious problems. Severe hypotension, cardiac failure, multiple organ failure, arrhythmias can be developed, and then the patient may be die (3). In this case report, we presented a 4-year-old boy who used combined antihypertensive drugs accidentally. These two drugs contained combined verapamil/trandolapril and nebivolol. When the patient was admitted to the hospital, he had a severe cardiogenic shock. We successfully treated him with insulin-euglycemia/glucagon treatment, calcium (Ca), and lipid infusion therapy, plasmapheresis, and continuous venovenous hemodiafiltration (CVVHDF) without any sequels.

## Case Report

A previously healthy 4-year-old boy was admitted to the pediatric emergency department for suddenly developed weakness and conscious. After questions about his medical history, it has learned that he used accidentally 240 mg verapamil/4 mg trandolapril two pieces and 5 mg nebivolol one, they were antihypertensive drugs of his grandfather.

At the time of admission, his heart rate was 62/min, respiratory rate 18/min, blood pressure 53/22 (39) mmHg. Glasgow coma scale (GCS) was 12, he was conscious. His body temperatures were 36.5 °C, oxygen saturation 100% in room air, capillary refill time was normal. The physical examination revealed, there was no obvious physical examination finding other than weakness. Arterial blood gas examination, pH:7.20 $pCO_2$: 57 mmHg $HCO_3$: 18 mmol/L lactate: 4.8 mmol/L was consistent with metabolic acidosis. Additional blood test results were as follows: his complete blood count white blood cell was $32.210\times10^3/mm^3$, his haemoglobin was 10.4 g/dL, total platelet count was $306\times10^3/mm^3$; serum urea/creatinine was 44/0.8 mg/dL, serum sodium/potassium was 139/3.9 mEq/L, aspartate transaminase/alanine aminotransferase was 19/26 U/L, glucose was 160 mg/dL, ınternational normalized ratio: 1, prothrombin time: 12.8 seconds (sec), activated plasma thromboplastin time: 25.7 sec, troponin-T: 6.6 pg/mL.

The patient was admitted to pediatric intensive care unit (PICU) for close monitoring and treatment. Rapid intravenous (IV) fluid boluses (20 cc/kg IV bolus three times) were given and inotropic agents were initiated for severe hypotension. Gastric lavage and activated charcoal treatment were not applied because of six hours before being admitted to the hospital he used 27 mg/kg verapamil, 0.45 mg/kg trandolapril, and 0.28 mg/kg nebivolol.

His GCS was below 8 and then intubated to protect his airway and required mechanical ventilation. Although inotropic drugs (noradrenaline 1 mcg/kg/min, adrenalin 1 mcg/kg/min and dopamin 20 mcg/kg/min) and hydrocortisone 4 mg/kg/day IV were given, his blood pressure was 47/12 (29) mmHg. Therefore insülin/glucagon, lipid and Ca infusion treatment was initiated. IV fluid was given 2,000 $cc/m^2$ and insulin infusion 0.5 U/kg/h, glucagon 1 mg/dosage twice times, lipid 0.25 mL/kg/min and 10% Ca gluconate infusion 0.1 cc/kg/h were initiated. In the 6$^{th}$ hour of being transferred to PICU, his resistance hypotension was continued, then developed oligo/anuria and renal failure. Supporting to decrease blood drug levels, we began high volume (1.5 times plasma volume) plasmapheresis centrifugally with femoral venovenous hemodialysis catheter and then CVVHDF extracorporeal treatment at the time of the 8$^{th}$ hour of being transferred to PICU. Only hemodiafiltration treatment was begun at the beginning, after that by following closely his blood pressure ultrafiltration (UF) was done and slowly increased. The aim volume of UF was determined to 1-2 cc/kg/h negative balance.

After these extracorporeal treatments, his blood pressure increased hour by hour, consequently, his inotropic doses were decreased gradually. The urine output of the patient increased due to the improvement of renal perfusion, accordingly, we stopped CVVHDF at the 30$^{th}$ hour of treatment. In the 32$^{th}$ hour of admitted to PICU, his insulin/glucagon, lipid and Ca infusion treatment was terminated, he extubated. In the 50$^{th}$ hour of admitted to PICU, he transferred to the general ward without any sequels. The patient informed consent form was obtained from his parents.

## Discussion

The intoxication of Ca channel blocker (CCB) and beta-blocker (BB) drugs are rare but severe cases because of life-threatening. The reason of drug intoxication deaths was reported to CCB 40% and BB 65% in America (4). The effects of CCB on cardiovascular systems are negative chronotropic, myocardial depression, decreasing atrioventricular signals, and vasodilatation. In addition to that the effects of CCB drugs in pancreas are dysfunctional

beta cell, and hyperinsulinemia and hyperglycemia. BB drugs are effected to beta receptors of catecholamines with competetively inhibition. Clinical findings in poisoning with these drugs are dependent on the receptor selectivity, lipit solubility, partial agonist effect and dose. Hypotension and bradycardia are the most common cardiac manifestations, and others are arrhythmias, pulmonary edema, depression of the central nervous system (5).

The combination drug which contains 240 mg verapamil hydrochloride and 4 mg trandolapril is generally using for antihypertensive treatment in adults in Turkey. Also, nebivolol 5 mg is a BB drug to protect from arrhythmias and hypertension. The toxic dose of verapamil, trandolapril and nebivolol has not been known yet in childhood. The case of verapamil/trandolapril combination drug's intoxication is reported on a 3.5 year-old is an remarkable. Seven hours after ingestion, the patient was detected hypotension and bradycardia then implanted pacemaker, was reported (6).

Supportive care is important which contains airway, breathing, and circulation firstly. CCB and BB poisonings have the same principles of treatment mainly. Gastrointestinal decontamination can be applied if suitable for ingestion time. In the treatment of hypotension and cardiovascular collapse fluid, inotropic, vasopressor and chronotropic agents are used. If these treatments are insufficient, glucagon, insulin-euglysemia, Ca and lipid infusion treatment should be applied. Mortality is decreased when insulin-euglycemia treatment is added in addition to adrenaline or glucagon (7). In our case, although inotropic drugs were given, there was no adequate response. Therefore insulin/glucagon, lipid and Ca infusion treatment was initiated. In cardiogenic shock, insulin 0.5-1 U/kg loading dose followed by 0.5-2 U/kg/hour infusion therapy is recommended (7).

Lipid infusion is recommended as salvage therapy, especially in severe poisoning with lipophilic anesthetic drugs. It was reported that a 13-year-old girl was responded to lipid treatment after suicidal use of drugs containing carvedilol and verapamil (8). The lipid infusion dose is either 1.5 mL/kg bolus or 0.25-0.5 mL/kg/min of 20% lipid emulsion infusion. We were initiated lipid 0.25 mL/kg/min and 10% Ca gluconate infusion 0.1 cc/kg/h. After all these treatments were initiated, he has been observed close monitored for vital signs and the changing of biochemical parameters. Three hours later his blood pressure was begun to increase. Associated with increased renal perfusion his diuresis was begun and accordingly, his edema was decreased.

In CCB and BB overdose, extracorporeal treatment strategy has limited usefulness because of drugs' lipid-soluble (4,9). These drugs verapamil (90%), trandolapril (80%) and nebivolol (98%) which our patient ingested accidentally bound to plasma proteins highly (2,4). In plasmapheresis treatments are 100-150% of plasma volume (1-1.5 times plasma volume) rate of change. When plasmapheresis is applied at this rate, 50-70% of pathological proteins are removed in a single session. In severe cases like intoxication with 2-3 plasma exchange rates can be treated (10). In our case, we thought that the plasmapheresis could have an active role, because of drugs that cause intoxication are highly protein bound. In addition, our patient is 4 years old and could not give a history because of unconsciousness. His family was socioculturally poor, so no clear communication could be established. Therefore, it could not be clarified whether he also took other drugs. Although the efficacy is known to be low, it can be applied in selected cases. In our local tertiary hospital limited opportunities and having no extracorporeal membrane oxygenation support, for decreasing blood drug levels, we began plasmapheresis and CVVHDF treatment at the time of the 8$^{th}$ hour of being transferred to PICU. Thanks to all the treatments we were able to provide, our patient was transferred to the service without sequelae.

The intoxication of CCB and BB drugs are rare but severe cases because of life-threatening. Especially in children these drugs are ingested accidentally. In clinically, hypotension and bradycardia are the most common cardiac manifestations. Developing subsequently sustained hypotension and cardiac failure are related to mortality. If treatments are not started early and managed well, it causes to hypotension-induced multiple organ failure syndrome and the patient may be die.

### Ethics

**Informed Consent:** The patient informed consent form was obtained from his parents.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: H.F.A., F.E., D.B., İ.A., Concept: H.F.A., Design: H.F.A., Data Collection and/or Processing: F.E., D.B., İ.A., Analysis and/or Interpretation: F.E., Literature Search: D.B., İ.A., Writing: H.F.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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CASE REPORT / *OLGU SUNUMU*

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**Mehtap Pehlivanlar Küçük**

# Effectiveness of Early Combined Rehabilitation in COVID-19 Related ARDS Patients After the Successfull Application of Extracorporeal Membrane Oxygenation: Two Case Reports

## COVİD-19 ile İlişkili ARDS Hastalarında Ekstrakorporeal Membran Oksijenasyonun Başarıyla Uygulaması Sonrası Erken Kombine Rehabilitasyonun Etkinliği: İki Olgu Raporu

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**ABSTRACT** Many cardiac, pulmonary, and psychiatric complications occur due to long-term bed rest, infection, and critical illness neuropathy/myopathy in extra-corporeal membrane oxygenation (ECMO) applied coronavirus disease-2019 (COVID-19) inpatients in intensive care units. Physiotherapy plays an important role in restoring physical functions in the subacute phase following ECMO decannulation. After being discharged, and with combined rehabilitation, these patients experience a faster recovery and their quality of life increases. In this article, the effects of the combined physiotherapy program, which was applied to two patients with COVID-19 who received ECMO treatment and were discharged from the intensive care unit, is discussed. Early application of the combined rehabilitation program after discharge resulted in a positive outcome.
**Keywords:** COVID-19, early rehabilitation, extra-corporeal membrane oxygenation

**ÖZ** Yoğun bakım ünitelerinde yatan ve ekstra-korporeal membran oksijenasyonu (ECMO) uygulanan koronavirüs hastalığı-2019 (COVİD-19) hastalarında uzun süreli yatak istirahati, enfeksiyon ve kritik hastalık nöropatisi/miyopatisi nedeniyle birçok kardiyak, pulmoner ve psikiyatrik komplikasyon ortaya çıkmaktadır. Fizyoterapi, ECMO dekanülasyonunu takiben subakut fazda fiziksel fonksiyonların eski haline getirilmesinde önemli bir rol oynamaktadır. Taburcu olduktan sonra, bu hastalar kombine rehabilitasyon ile daha hızlı iyileşmekte ve yaşam kaliteleri artmaktadır. Bu yazıda, ECMO tedavisi gören ve yoğun bakım ünitesinden taburcu olan COVİD-19'lu iki hastaya uygulanan kombine fizyoterapi programının etkileri tartışılmaktadır. Kombine rehabilitasyon programının taburcu olduktan sonra erken uygulanması olumlu sonuçlanmıştır.
**Anahtar Kelimeler:** COVİD-19, erken rehabilitasyon, ekstrakorporeal membran oksijenasyonu

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## Introduction

ECMO is an invasive supportive therapy used to treat cardiac, respiratory, or combined cardiorespiratory failure when conventional treatment options fail. Veno-venous extra-corporeal membrane oxygenation (VV-ECMO) was used effectively to treat severe respiratory failure during the influenza A (H1N1) epidemic in 2009 (1,2). The Extracorporeal Life Support Organisation recommends the use of VV-ECMO in the treatment of selected coronavirus disease-2019 (COVID-19) cases resistant to standard medical and mechanical ventilation strategies (3). Many cardiac, pulmonary, and psychiatric complications occur due to long-term bed rest, infection, and critical illness neuropathy/myopathy in COVID-19 patients who cease to use ECMO in the intensive care unit (ICU). Dyspnea, tachycardia, peripheral and respiratory muscle strength losses, loss of functional performance and decreased health-related quality of life are the most common ones (4). Physiotherapy plays an important role in restoring physical function in the subacute phase following ECMO decannulation (5,6). In the rehabilitation of post-COVID patients, respiratory muscle strength training (7,8), lower/upper extremity muscle strength training (resistive), balance and gait training, thoracic mobilization (9) and thoracic muscle stretching (8-10), neuromuscular electrical stimulation (NMES) (8,10) is applied. The intensity, volume, progression and type of exercise should be personalized based on the physical condition and tolerance during the application of the exercise program. We could not find any publication in literature that shared the effects of early post-discharge combined physiotherapy in patients treated with ECMO due to COVID-19. In this study, the effect of the application of the combined physiotherapy program to two patients who received ECMO treatment in the ICU due to COVID-19 and who were discharged, is discussed.

Before and after the treatment, vital signs (heart rate, blood pressure, oxygen saturation and respiratory frequency), dyspnea according to modified Medical Research Council (MRC) were evaluated. Peripheral muscle strength was evaluated with the MRC scale. The scale is rated through a score between 0-60 points. MRC score less than 48 points suggests intensive care-related weakness (11). Respiratory muscle strength was measured using a portable electronic mouth pressure monitor (Micro RPM, Micro Medical Ltd, Kent, UK). Inspiratory muscle strength was measured at residual volume after a maximal expiration (7). The Barthel index was used for functional level. This index is rated between 0 and 100 points. It is classified as mild, moderate, advanced, fully dependent and independent. As the scores decrease, the level of dependency increases (12). Quality of life was assessed with the Short Form-36 quality of life questionnaire which is involved physical functioning, social functioning, physical role limitations, mental role limitations, mental health, energy/vitality, bodily pain, general health perceptions and it consists of 36 items that measure eight sub-dimensions. Subscales rate health between 0-100, and the higher the score, the better the quality of life (13). The Modified Borg scale was used to rate dyspnea in rehabilitation (9). Informed consent of the patients was obtained for the case reports.

## Case Reports

### Case 1

A 32-year-old, 35-week pregnant patient was taken to the emergency C/S on the 1st day of diagnosis, after she was tested positive for severe acute respiratory syndrome-coronavirus-2 polymerase chain reaction (PCR) and her Non stress test deteriorated. On the 4th day of her hospitalization, due to depeening of the desaturation of the patient, she was taken to the ICU where pulse methylprednisolone (250 mg/day) and tocilizumab in the dose of 800 mg treatments were administered for 3 days, and she received stem cell therapies 2 times with an interval of 3 days. On the 10th day of her hospitalization, the patient was intubated due to clinical progression and was referred to the 3rd step ICU of the university hospital. The curarized patient was followed in A/C mode and in the prone position for 16 hours a day for 3 days with an application of lung protective mechanical ventilation strategies. When the target oxygenation could not be achieved on the 4th day, she was taken to VV-ECMO support. Empirical broad-spectrum antibiotics, fluid resuscitation, noradrenaline and terlipressin were administered, considering the local flora in the patient who went into septic shock in the follow-up. The patient was extubated on the 10th day of mechanical ventilation and followed up with a high-flow nasal cannula. On the 14th day of the follow-up, the patient was ECMO decannulated. The patient, who was followed up with a reservoir mask, was transferred to the service on the 18th day of the follow-up. She was discharged home after a total of 32 days of hospitalization. After being discharged home, the rehabilitation program was started. No nutritional monitoring was performed at home after discharge. And also

after discaherge nutritional recommendations were made according to ESPEN recommendations (14). The detailed results of the pre-rehabilitation evaluations are shown in Table 1 and Table 2.

In the evaluations, the patient was able to stand up with a support of two people, but could not stand without support. At the end of the 10 m assisted walking, the heart rate was 175 beats/min, and shortness of breath occurred with a severity of 9 according to the modified Borg scale. At the end of the evaluation, it was concluded that the patient had inspiratory muscle weakness, cardiac responses, dyspnea, and decreased peripheral musclestrength which prevented exercise. A combined physiotherapy program was applied to the patient for one hour a day for 8 weeks at home. Combined physiotherapy program includes;

1) Respiratory muscle training: Two times a day, 7 days of the week, 15 minutes with Treshold IMT Inspiratory muscle training was performed at 40% of maximum inspiratory pressure (Pimax), combined with pursed lip breathing and thoracic expansion exercises.

2) Resistive muscle strength training: Training was given at 30-80% of a maximum repetition using free weights and dumbbells. Upper extremity was exercised bilaterally and lower extremity unilaterally. Upper extremity (biceps, triceps, deltoid and rhomboids), lower extremity (hip flexion, hip abduction, knee extension, ankle dorsiflexion) were exercised. Each exercise was coordinated with 10 repetitions and breaths. Rest periods between exercises were kept long.

3) Walking: Five-15 minutes with Borg scale 3-5 intensity, in the following days 0.5 kg weights were attached to each ankles.

4) Balance training: It included standing with eyes open/closed, standing on one leg, trunk rotation.

Exercises were performed with heart rate and oxygen saturation monitoring (10), performed with a scale of 3-5 according to the modified Borg scale. Our patient was a mother who had recently given birth. She could not breast feed due to medications. She wanted to take care of her baby as soon as possible. For that, it was important to develop balance, walkingand arm strength in a short time. It was aimed to increase the patient's participation in daily activities, so she was encouraged to take some responsibilities in the kitchen. She was allowed to undertake baby caring activities (changing diapers, sleeping, feeding with a bottle) that she could do while sitting, and she was given the opportunity to develop the relationship with her baby. At the end of

**Table 1. The detailed results of the 8 and 4 weeks of pre and post-rehabilitation evaluations of case 1 and 2 respectively**

| | Case 1 (8 weeks) | | Case 2 (4 weeks) | |
|---|---|---|---|---|
| | Pre-rehabilitation | Post-rehabilitation | Pre-rehabilitation | Post-rehabilitation |
| Heart rate | 156 beats/min | 90 beats/min | 85 beats/min | 78 beats/min |
| Blood pressure | 1117/84 | 115/75 | 120/80 | 118/80 |
| $SaO_2$ | 94 | 99 | 90 | 96 |
| Respiratory rate | 21 breaths/min | 16 breaths/min | 28 breaths/min | 19 breaths/min |
| mMRC | 3 | 0 | 5 | 1 |
| MRC (0-60) | 42 | 58 | 53 | 60 |
| Pimax | 62 $cmH_20$ | 125 $cmH_2O$ | 68 $cmH_20$ | 132 $cmH_2O$ |
| Pimax % | 71.80 | 144.75 | 64 | 124.23 |
| Barthel index | 50 | 100 | 35 | 90 |
| SF-36 physical functioning | 0 | 80 | 0 | 80 |
| SF-36 physical role limitations | 0 | 50 | 0 | 25 |
| SF-36 emotional role limitations | 0 | 66.66 | 0 | 100 |
| SF-36 energy/vitality | 25 | 75 | 10 | 85 |
| SF-36 mental health | 48 | 72 | 16 | 72 |
| SF-36 social functioning | 0 | 100 | 0 | 75 |
| SF-36 bodily pain | 0 | 80 | 0 | 90 |
| SF-36 general health perceptions | 0 | 55 | 20 | 65 |

mMRC: Modified Medical Research Council, MRC: Medical Research Council, Pimax: maximal inspiratory pressure, $SaO_2$: oxygen saturation, SF-36: Short Form-36

**Table 2. The results of the pre and post-rehabilitation MRC scores**

| | Case 1 | | Case 2 | |
|---|---|---|---|---|
| | 1st week right/left | 8th week right/left | 1st week right/left | 4th week right/left |
| Shoulder abduction | 3/3 | 5/4 | 5/4 | 5/5 |
| Elbow flexion | 4/4 | 5/5 | 5/5 | 5/5 |
| Wrist extension | 4/3 | 5/5 | 5/4 | 5/5 |
| Hip flexion | 4/3 | 5/4 | 4/4 | 5/5 |
| Knee extension | 4/4 | 5/5 | 5/4 | 5/5 |
| Ankle dorsiflexion | 3/3 | 5/5 | 4/4 | 5/5 |

MRC: Medical Research Council

the combined rehabilitation program, the rate of exertional dyspnea decreased. Resting heart rate decreased, reaching the limits of normal heart rate (85 beats/min). The patient's respiratory muscle strength and peripheral muscle strength increased. By the end, her functional level improved and her quality of life increased. The bilateral diffuse pulmonary infiltration of the patient during her hospitalization in the ICU and her images with marked regression after combined physiotherapy program are shown in Figure 1A and 1B respectively. The detailed results of the post-rehabilitation evaluation are shown in Table 1 and Table 2.

### Case 2

A 63-year-old male patient applied to a health institution due to increased dyspnea while receiving oral methylprednisolone and long-term oxygen therapy at home due to a previous COVID-19 infection. The blood test's results were as; white blood cell: 22.51x$10^3$/μL, ferritin: 98.1 μg/L, C-reactive protein: 324.9 mg/L and procalcitonin: 0.52 μg/L and the patient needed High Flow. Thorax tomography showed interlobular septal thickenings, traction bronchiectasis, diffuse ground glass opasities and crazy paving appearance. Trimethoprim and sulfamethoxazole treatment was started empirically for potential Pneumocystis carinii pneumonia. He was intubated on the fourth day with progressive desaturation, and was taken to VV-ECMO due to her hypoxemic course. Subsequently, bronchoalveolar lavage was performed and PCP-PCR was positive. On the fourth day of ECMO application, oxygen demand and bilateral infiltrations on chest X-ray decreased, and she was followed by awake ECMO protocol. On the 7th day of ECMO, when the partial oxygen pressure did not decrease and hypercapnia did not develop in the 24-hour follow-up, he was decannulated with the support of sweep gas flow: 1 L/min and $FiO_2$: 21%. He was discharged with a nasal cannula on the 10th day of follow-up and a combined rehabilitation program was started at home on the second day. No nutritional monitoring was performed at home after discharge. And also after discaherge nutritional recommendations were made according to

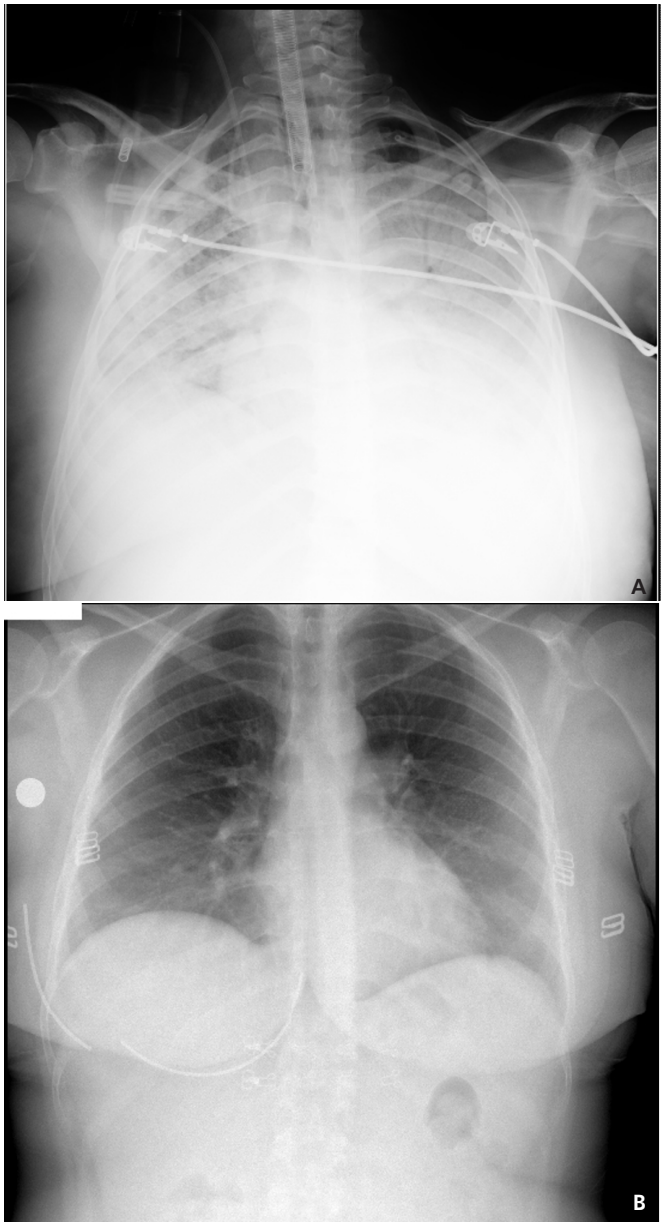


**Figure 1.** A. Image of case 1 during her hospitalization in the intensive care unit. B. Image of case 1 after combined physiotherapy program

ESPEN recommendations (14). The detailed results of the pre-rehabilitation evaluation are shown in Table 1 and Table 2.

In the pre-rehabilitation evaluation, the patient did not have cough and sputum complaints. The patient was able to stand up with a support of two people, but could not stand alone. Resting dyspnea was 5 on the Modified Borg scale. Decreased peripheral muscle strength and shortness of breath prevented exertion. After considering the results of the evaluation, a combined rehabilitation program was planned for the patient. In addition, NMES for rapid recovery of muscle strength and autogenic relaxation training for dyspnea control were added to the program. This program was applied to the patient for one hour a day for 4 weeks at home. Combined physiotherapy program;

1) Respiratory muscle training: Two times a day, 7 days of the week, 15 minutes with Treshold IMT Inspiratory muscle training was performed at 40% of Pimax, combined with pursed lip breathing and thoracic expansion exercises. Thoracal mobilization: This included stretching and autogenic relaxation of the m. latissimus dorsi, m. pectoralis major/minor, m.serratus anterior and m. trapezius muscles.

2) Resistive muscle strength training: Training was given at 30-80% of a maximum repetition using free weights and dumb-bells. The upper extremity was operated bilaterally and the lower extremity unilaterally. Upper extremity (m. biceps, m. triceps, m. deltoid and m. rhomboids), lower extremity (hip flexion, hip abduction, knee extension, ankle dorsi flexion) were exercised. Each exercise was coordinated with 10 repetitions and breaths. Rest periods between exercises were kept long.

3) Walking: In the second week, out-of-bed movements were started, 5-15 minutes, Borg scale 3-5 intensity, in the following days 0.5 kg weights were attached to each ankles. The last 3 sessions of stair climbing exercise were performed.

4) Balance training: It included standing with eyes open/closed, standing on one leg, trunk rotation.

5) NMES: NMES was applied to the m. tibialis anterior, and m. quadriceps femoris muscles at 50 Hz, 350-400 ms for 20 minutes.

Exercises were performed with heart rate and oxygen saturation monitoring (10). They were performed according to the modified Borg scale with a severity of 3-5. The patient was the coach of a football team and he wanted to go training as soon as possible. Dependence on oxygen concentrator and low effort-related functional performance decreased his exercise motivation. We performed some exercises using soccer balls like holding balls that thrown at different angles or raising the ball in the air. At the end of the combined treatment, peripheral muscle strength increased, respiratory muscle strength developed, and accordingly, dyspnea that developed with exertion decreased. The patient was able to climb stairs and walk unassisted without the need for nasal oxygen intake. Correlative to this, the patient's functional level improved and his quality of life increased. The bilateral diffuse pulmonary infiltration of the patient during his hospitalization in the ICU and his images with marked regression after combined physiotherapy program are shown in Figure 2A and 2B respectively. The detailed results of the post-rehabilitation evaluation are shown in Table 1 and Table 2. At the end of the 4$^{th}$ week, the patient was able to oversee the training of the football team.

## Discussion

Long-term mechanical ventilation, ECMO therapy and high-dose corticosteroids affect patients' recovery after discharge. Patients' pulmonary function may be singificantly reduced due to alveolar damage in the early post-weaning phase (5). Peripheral and respiratory muscle atrophies due to prolonged bed rest reduce the quality of life in patients (15,16). Nutritional support, especially protein intake, is very important for muscle strength during acute illness. Nutritional goals were determined for each patient during their intensive care hospitalization, takinging to account the ESPEN guideline recommendations (14). According to early enteral nutrition and disease phases (acute phase-early period, acute phase late period or late phase), nutritional and protein targets have been tried to be achieved (14). There was no statistically significant effect of interventional nutrition on muscle mass or muscle strength and walking speed. However, according to AWGS 2019, the combination of nutrition and exercise therapy can improve muscle strength and function (17). In the early period after extubation, patients have muscle weakness and loss of motor function, and the combination of exercise and nutrition in this period gives better results in order to achieve recovery (18).

Therefore, it is important to start physiotherapy early in the hospital and after discharge (5,19,20). There is little evidence of early rehabilitation after ECMO decannulation for COVID-19 patients.In a case series, a rehabilitation, including extremity movements, sitting, in-bed cycling, respiratory

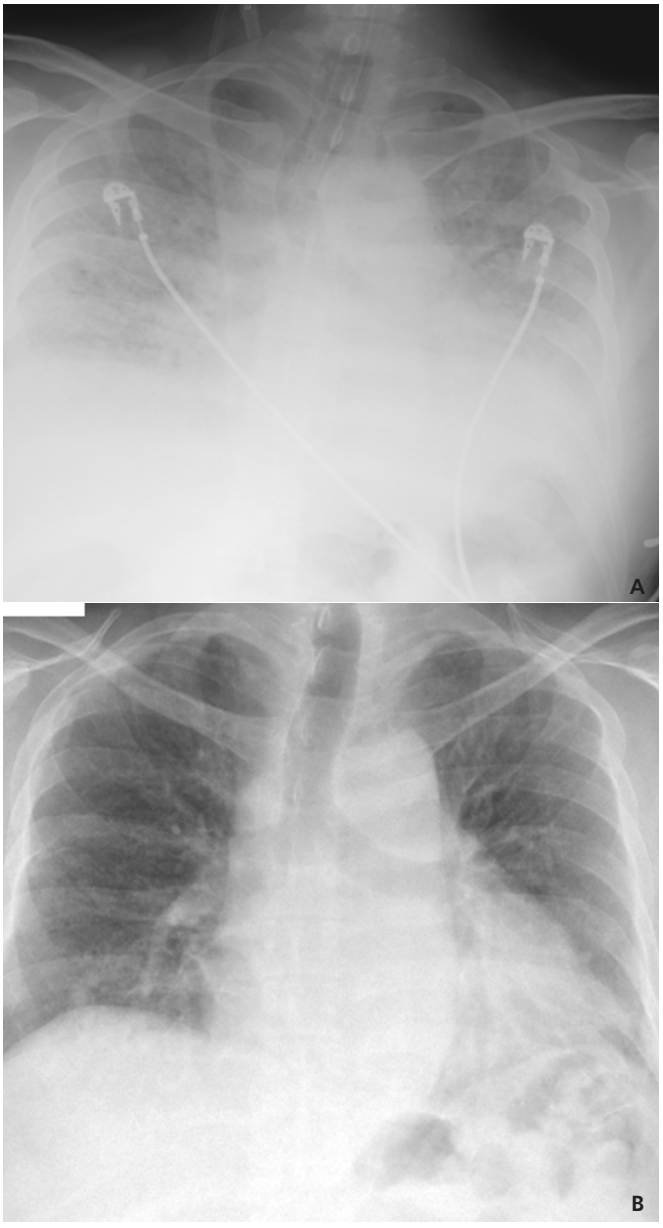


**Figure 2.** A. Image of case 2 during his hospitalization in the intensive care unit. B. Image of case 2 after combined physiotherapy program

muscle training and muscle strength training, was applied after ECMO decannulation in patients who underwent lung transplantation due to COVID-19-related pulmonary fibrosis (6). It has been stated that rehabilitation plays a very important role in the subacute phase by restoring physical function after ECMO decannulation (5,6). The effects of multi-component therapeutic exercises on dyspnea, functional performance and quality of life in COVID-19 patients after weaning and discharge from ICU have been shown (9). Strengthening, balance and respiratory muscle training should be included in patient follow-up programs. Physiotherapists should individualize their treatment programs and aim to monitor side effects and symptoms (21). Rehabilitation programs should be prepared with a holistic perspective to manage post-COVID-19 symptoms. At the same time, rehabilitation should be planned according to the patients' comorbidities, current functional and cognitive status (21). Although the needs of the patients we mentioned in our study were similar, their responses to exercise during treatment were different. Case 1 completed the exercises with a higher heart rate response, while the second case finished the exercises with a higher dyspnea score and low oxygen saturation. For this reason, the recovery time after each set was determined by taking these personalized answers into consideration. Early combined physiotherapy application improved the functional capacities, respiratory muscle strength and peripheral muscle strength of the patients in a short time, thus improving the walking capacity and accordingly the life quality.

Our study shows the positive effects of early combined physiotherapy after decannulation in patients receiving high-level invasive support such as mechanical ventilation and ECMO due to COVID-19 infection. After ECMO decannulation in COVID-19 patients, the early combined rehabilitation program enabled patients to recover in a short time and to participate in daily activities.

## Ethics

**Informed Consent:** Informed consent of the patients was obtained for the case reports.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: N.E., A.O.K., M.Ö.A., M.P.K., Concept: N.E., M.P.K., Design: N.E., M.P.K., Data Collection and/or Processing: N.E., A.O.K., M.P.K., Analysis and/or Interpretation: N.E., A.O.K., M.P.K., Literature Search: N.E., Writing: N.E., M.Ö.A., M.P.K.

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