TÜRK YOĞUN BAKIM DERGİSİ

TURKISH JOURNAL OF INTENSIVE CARE

TYBD
Türk Yoğun Bakım Derneği
Turkish Society of Intensive Care

E-ISSN: 2602-2974

CİLT / VOLUME 22
SAYI / ISSUE 3
EYLÜL / SEPTEMBER 2024

REVIEW / DERLEME

Intensive Care Fellowship Training in the United States of America
Amerika Birleşik Devletleri'nde Yoğun Bakım Eğitimi
Mary Rose Gaylor, Reade E. Tillman
154

ORIGINAL RESEARCHES / ÖZGÜN ARAŞTIRMALAR

Factors Affecting Survival of Pregnant Women with COVID-19 and Our First Extracorporeal Membrane Oxygenation Results
COVID-19 ile Enfekte Gebelerin Sağkalımını Etkileyen Faktörler ve İlk Ekstrakorporeal Membran Oksijenasyonu Sonuçlarımız
Selda Tekin, Esra Adıyeke, Elif Erdoğan Öngel, Nurten Bakan
161

Radiation Safety Practices and Improvement of Knowledge Level in Intensive Care Unit Working Conditions: An Experimental Study on Nurses
Yoğun Bakım Ünitesi Çalışma Koşullarında Radyasyon Güvenliği Uygulamaları ve Bilgi Düzeyinin Geliştirilmesi: Hemşireler Üzerinde Deneysel Bir Çalışma
Habip Balsak, Ayşe Beşer
170

Investigation of Opinions of Nurses Working in Surgical Intensive Care Units about the Participation of Family Members in the Care of Patients during the Dying Process: A Cross-sectional Design
Cerrahi Yoğun Bakım Ünitelerinde Çalışan Hemşirelerin Ölüm Sürecindeki Hastaların Bakımına Aile Üyelerinin Katılmaları Konusunda Görüşlerinin İncelenmesi: Kesitsel Bir Çalışma
Aynur Koyuncu, Yasemin Eren, Ayla Yava
180

Does Tube Resistance Compensation Change Metabolic Parameters When Added to Pressure Support Mode During Weaning?
Weaning Sürecinde Basınç Destekli Ventilasyon Moduna Tüp Direnci Kompanzasyonu Eklenmesi Metabolik Parametreleri Değiştirir mi?
İclal Doruk, Kubilay Demirağ, Mehmet Uyar
190

Efficacy of Tocilizumab in Critically Ill COVID-19 Patients Followed in the Intensive Care Unit
Yoğun Bakım Ünitesinde Takip Edilen Kritik COVID-19 Hastalarında Tocilizumab Tedavisinin Etkinliği
Reşit Saruhan, Osman Uzundere
197

Are *Myroides* spp. Isolated From Urinary Catheter Cultures of Patients in Intensive Care Units an Infection or Colonization? Analysis of 36 Cases
Yoğun Bakım Ünitesi Hastalarının Üriner Kateter Kültürlerinden İzole Edilen Myroides spp. İzolatları Enfeksiyon mu Yoksa Kolonizasyon mu? 36 Olgunun Analizi
Yücel Duman, Döndü Çelik, Emine Nalan Parmaksız, Yasemin Ersoy, Ayşe Belin Özer
207

Comparison of USCOM and PiCCO Cardiac Output Measurements in Intensive Care Unit
Yoğun Bakım Ünitesinde USCOM ve PiCCO ile Kalp Debisi Ölçümlerinin Karşılaştırılması
Özlem Çakın, Orbay Harmandar, Hakan Parlak, Melike Cengiz, Murat Yılmaz, Atilla Ramazanoğlu
212

Reasons for Intensive Care Unit Admission and Prognosis After Surgery for Gynaecologic Malignancies
Jinekolojik Malignite Cerrahisi Sonrası Yoğun Bakım Ünitesine Başvuru Nedenleri ve Prognoz
Aysun Alcı, Nilgün Kavrut Öztürk, Gülsüm Ekin Sarı, Mustafa Gökkaya, Necim Yalçın, Işın Üreyen,Tayfun Toptaş
218

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OF INTENSIVE CARE

CİLT / VOLUME 22
SAYI / ISSUE 3
EYLÜL / SEPTEMBER 2024

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Turkish Society of Intensive Care

TÜRK
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URL: http://www.yogunbakimderg.com

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34093 İstanbul, Türkiye
Telefon/Phone: +90 530 177 30 97 / +90 539 307 32 03
E-posta/E-mail: info@galenos.com.tr/yayin@galenos.com.tr
Web: www.galenos.com.tr
Yayıncı Sertifika No/Publisher Certificate Number: 14521

Online Yayınlanma Tarihi/Online Publication Date: Eylül 2024/September 2024
E-ISSN: 2602-2974

Üç ayda bir yayımlanan süreli yayındır.
International scientific journal published quarterly.

TURKISH JOURNAL OF INTENSIVE CARE

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TÜRK YOĞUN BAKIM DERGİSİ

Derginin "Amaç ve Kapsam", "Yazarlara Bilgi" ve "Yayın Etiği" konularında bilgi almak için lütfen web sayfasına **(https://www.turkishjic.org/)** başvurun.

Derginin editöryal ve yayın süreçleri ile etik kuralları ICMJE, WAME, CSE, COPE, EASE ve NISO gibi uluslararası kuruluşların kurallarına uygun olarak şekillenmektedir. Dergimiz, "şeffaf olma ilkeleri ve akademik yayıncılıkta en iyi uygulamalar ilkeleri" ile uyum içindedir.

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

Dergi elektronik olarak yayınlanmaktadır.

İmtiyaz Sahibi: Türk Yoğun Bakım Derneği Adına Tuğhan UTKU

Baş Editör: Perihan ERGİN ÖZCAN

Please refer to the journal's webpage **(https://www.turkishjic.org/)** for "Aims and Scope", "Instructions to Authors" and "Ethical Policy".

The editorial and publication process of the Turkish Journal of Intensive Care are shaped in accordance with the guidelines of ICMJE, WAME, CSE, COPE, EASE, and NISO. The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

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

The journal is published electronically.

Owner: Tuğhan UTKU on Behalf of Turkish Society of Intensive Care

Responsible Manager: Perihan ERGİN ÖZCAN

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İÇİNDEKİLER/CONTENTS

REVIEW / DERLEME

Intensive Care Fellowship Training in the United States of America
Amerika Birleşik Devletleri'nde Yoğun Bakım Eğitimi
Mary Rose Gaylor, Reade E. Tillman **154**

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Factors Affecting Survival of Pregnant Women with COVID-19 and Our First Extracorporeal Membrane Oxygenation Results
COVID-19 ile Enfekte Gebelerin Sağkalımını Etkileyen Faktörler ve İlk Ekstrakorporeal Membran Oksijenasyonu Sonuçlarımız
Selda Tekin, Esra Adıyeke, Elif Erdoğan Öngel, Nurten Bakan **161**

Radiation Safety Practices and Improvement of Knowledge Level in Intensive Care Unit Working Conditions: An Experimental Study on Nurses
Yoğun Bakım Ünitesi Çalışma Koşullarında Radyasyon Güvenliği Uygulamaları ve Bilgi Düzeyinin Geliştirilmesi: Hemşireler Üzerinde Deneysel Bir Çalışma
Habip Balsak, Ayşe Beşer **170**

Investigation of Opinions of Nurses Working in Surgical Intensive Care Units about the Participation of Family Members in the Care of Patients during the Dying Process: A Cross-sectional Design
Cerrahi Yoğun Bakım Ünitelerinde Çalışan Hemşirelerin Ölüm Sürecindeki Hastaların Bakımına Aile Üyelerinin Katılmaları Konusunda Görüşlerinin İncelenmesi: Kesitsel Bir Çalışma
Aynur Koyuncu, Yasemin Eren, Ayla Yava **180**

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Weaning Sürecinde Basınç Destekli Ventilasyon Moduna Tüp Direnci Kompanzasyonu Eklenmesi Metabolik Parametreleri Değiştirir mi?
İclal Doruk, Kubilay Demirağ, Mehmet Uyar **190**

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Yoğun Bakım Ünitesinde Takip Edilen Kritik COVID-19 Hastalarında Tocilizumab Tedavisinin Etkinliği
Reşit Saruhan, Osman Uzundere **197**

Are *Myroides* spp. Isolated From Urinary Catheter Cultures of Patients in Intensive Care Units an Infection or Colonization? Analysis of 36 Cases
Yoğun Bakım Ünitesi Hastalarının Üriner Kateter Kültürlerinden İzole Edilen Myroides spp. İzolatları Enfeksiyon mu Yoksa Kolonizasyon mu? 36 Olgunun Analizi
Yücel Duman, Döndü Çelik, Emine Nalan Parmaksız, Yasemin Ersoy, Ayşe Belin Özer **207**

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Özlem Çakın, Orbay Harmandar, Hakan Parlak, Melike Cengiz, Murat Yılmaz, Atilla Ramazanoğlu **212**

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Jinekolojik Malignite Cerrahisi Sonrası Yoğun Bakım Ünitesine Başvuru Nedenleri ve Prognoz
Aysun Alcı, Nilgün Kavrut Öztürk, Gülsüm Ekin Sarı, Mustafa Gökkaya, Necim Yalçın, Işın Üreyen,Tayfun Toptaş **218**

Turk J Intensive Care 2024;22:154-60
DOI: 10.4274/tybd.galenos.2024.65002

REVIEW / *DERLEME*

Mary Rose Gaylor,
Reade E. Tillman

Intensive Care Fellowship Training in the United States of America

Amerika Birleşik Devletleri'nde Yoğun Bakım Eğitimi

Received/Geliş Tarihi : 14.08.2024
Accepted/Kabul Tarihi : 21.08.2024

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ABSTRACT This article provides a general overview of the pathway to become an intensivist in the United States of America (USA). It begins with a detailed description of the current structure of critical care training in the USA and the application process to fellowship training programs. There is then a presentation of the general structure of critical care units within the USA and how intensive care unit physicians fit into it. The article concludes with a discussion of how American critical care fits globally within international critical care societies.
Keywords: Critical care, fellowship, intensivist, ICU, training, education

ÖZ Bu makale Amerika Birleşik Devletleri'nde (ABD) yoğun bakım uzmanı olmanın yolu hakkında bilgi vermektedir. ABD'deki yoğun bakım eğitiminin mevcut yapısının ve eğitim programlarına başvuru sürecinin ayrıntılı bir açıklamasıyla başlamaktadır. Daha sonra ABD'deki yoğun bakım ünitelerinin genel yapısına ve yoğun bakım ünitesi doktorlarının bu yapıya nasıl uyum sağladığına dair bir sunum içermektedir. Makale, Amerikan yoğun bakımının uluslararası yoğun bakım toplulukları içerisinde küresel olarak nasıl yer aldığının tartışılmasıyla son bulmaktadır.
Anahtar Kelimeler: Yoğun bakım, burs, yoğun bakım uzmanı, YBÜ, eğitim

Introduction

Aging of the general population is a problem confronting medical systems across the world, posing an impending need for increased critical care services. In the United States of America (USA), estimates suggest that there will be a worsening shortage of critical care providers within the next 10 years (1,2). Given that intensive care units (ICUs) with in-house intensivists are associated with lower mortality and reduced hospital and ICU length of stay (3), there is continued demand for increased critical care training programs to provide this needed supply of intensivists. In the Unites States, intensivist training spans many different healthcare specialties and could grow to include more as the demand for intensive care increases. The traditional route to becoming an intensivist in the USA was via specialty training in internal medicine, surgery, or anesthesiology followed by a fellowship of 1 to 3 years duration. Pathways to a career in intensive care have expanded to include other specialties such as neurology and emergency medicine (EM) (Figure 1) and may diversify further to accommodate increased demand.

The following article provides a general overview of the pathway to becoming an intensivist in the USA. It begins with a detailed description of the current structure of critical care training in the USA and the application process to fellowship training programs. It then discusses overall fellowship popularity and the general structure of critical care units within the USA and concludes with a discussion of how American critical care fits globally within international critical care societies.

Intensivist Training Pathways in the United States of America

For most USA medical trainees, specialty training begins after obtaining a 4-year medical degree in either allopathic (Doctor of Medicine) or osteopathic (Doctor of Osteopathic Medicine) medicine. A newly graduated physician must then enter residency that is accredited by the Accreditation Council for Graduate Medical Education (ACGME), an independent organization that sets the professional standards for post-graduate physician training programs and monitors compliance with these standards (4).

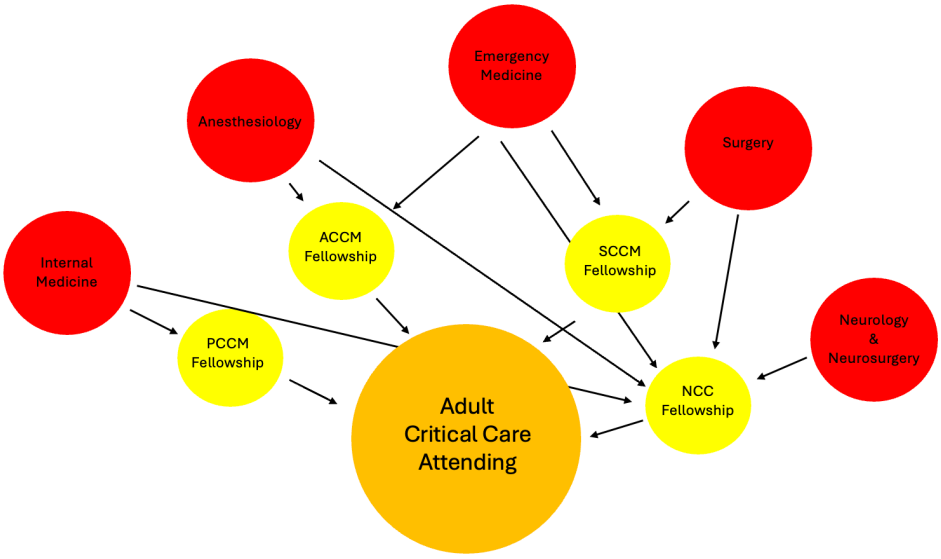

Figure 1. Integration of specialties in adult critical care
SCCM: Society of Critical Care Medicine, ACCM: Anesthesiology & Critical Care Medicine

Currently, the medical specialties that have an ACGME-accredited critical care fellowship are anesthesiology, internal medicine, general surgery, and neurology. Pediatrics has ACGME-accredited training programs in pediatric critical care and neonatal-perinatal medicine, which are critical care subspecialties outside of the scope of this article. Entry to an ACGME fellowship program requires completion of a residency program that is either accredited by the ACGME, or approved by the American Osteopathic Association, ACGME-International, Royal College of Physicians and Surgeons of Canada, or College of Family Physicians of Canada (5-7).

Regardless of the initial specialty of entry, the ACGME has general requirements that apply equally to critical care fellowships across all specialty fields. Each program must set competency-based goals and objectives and progressively increase responsibility throughout the duration of fellowship. Rather than specifying a particular curriculum that must be identical in all fellowships, the ACGME provides a list of "competencies" in which it expects all fellows to be able to practice by graduation (5-7), which are summarized in Table 1. Each subspecialty then individualizes these competencies further, as described below:

Pulmonary Critical Care

Pulmonary and critical care medicine is a three-year fellowship for graduates of internal medicine residency that trains fellows in the dual specialties of pulmonary medicine and critical care. The curriculum includes the core competencies (see Table 1) plus an extensive list of pulmonary pathologies and procedures. For example, these fellows must be well-versed in pulmonary vascular diseases, malignancies of the lung, and pulmonary manifestations of systemic diseases such as collagen vascular diseases (6). The curriculum also specifies that fellows must have procedural competence in ventilator management, bronchoscopy requiring biopsy, and pulmonary function testing as these are pertinent to the practice of pulmonology (6). Pulmonary critical care fellows are also required to have exposure to the management of surgical critical care patients, specifically the "hemodynamic and ventilatory support" (6) of perioperative patients.

Anesthesiology Critical Care

For graduates of anesthesiology residency, critical care fellowship is a one-year program. While anesthesiology residents in the USA have significant exposure to critically ill patients both in the operating room and during their rotations in the ICU, they are not eligible to take critical care boards unless a fellowship is completed. Anesthesiology critical care fellowship requires mastery of the core competencies for critical illness of each organ system (see Table 1) but less extensive procedural mastery of the pulmonary system, as anesthesia intensivists are not expected to carry out pulmonologist procedures such as bronchoscopy with biopsy. Some areas in which the

Table 1. Summary of ACGME core competencies shared among the different critical care fellowships	
Competency	**Additional details**
Acute lung injury	ARDS, inhalational and traumatic injury
Acute metabolic disturbances	Overdoses, Intoxication
Anaphylaxis, Allergic reactions	
Cardiovascular diseases	
Circulatory failure	Cardiorespiratory resuscitation
Coagulation, blood disorders	
Nosocomial/iatrogenic ICU problems	
Pulmonary disease	
End-of-life and palliative care	
Immunosuppressed ICU conditions	
Nutritional and endocrine effects of critical illness	
Peri-operative critical illness	
Psychosocial and emotional effects of critical illness	For both patients and families
Renal disorders of the ICU	Electrolyte and acid-base disturbance, acute renal failure
Sepsis	
Shock syndromes, multi-organ failure	
ACGME: Accreditation Council for Graduate Medical Education, ARDS: acute respiratory distress syndrome, ICU: intensive care unit	

anesthesiology curriculum requires more focused expertise are in the areas of complex airway management (to include video laryngoscopy and fiberoptic approaches), as well as competency in management of the obstetric, burn and trauma patients (7).

Surgical Critical Care

Like anesthesiologists, surgeons have the option of a one-year fellowship to be certified as intensivists, with a similar ACGME curriculum. In addition to the core competencies, the curriculum for surgeons focuses primarily on pathologies that would be found in a surgical ICU (SICU), including trauma, burn, and obstetrics. This curriculum goes so far as to specify a required amount of time that trainees must spend specifically in a SICU, and that "experiences in non-SICUs, such as medical…must not exceed 2 months (5)."

Neurosciences Critical Care

Neurocritical care has a separate fellowship focused on patients with critical illness resulting from neurologic disease, trauma, or neurosurgery (8). This fellowship on its own is 24 months in duration but may be completed in 12 months if the trainee has already completed one of the above-mentioned critical care fellowships, or if the trainee has completed residency in neurosurgery (8). As the pulmonary critical care fellowship places additional emphasis on training in pulmonary conditions, the neurocritical care fellowship places additional emphasis on care of the neurologic patient with such skills as intracranial pressure monitoring, interpretation of EEG and evoked potentials, and cerebrospinal fluid analysis (8).

Emergency Critical Care

EM physicians also contribute to the critical care work force and most recently reinvented the training path to become an intensivist. There is no ACGME-accredited critical care fellowship specifically for EM graduates, so these physicians must complete one of the above-mentioned fellowships. The only fellowship for which they are ineligible is pulmonary critical care, as they have not completed internal medicine training and therefore cannot work as pulmonologists. As there is no dedicated fellowship for emergency physicians, there is also no dedicated board exam and so upon completion of fellowship, EM physicians must sit for the board exam corresponding to their fellowship of choice (9).

Specialty ICUs Without ACGME-accredited Training

Many USA hospitals, especially academic institutions, have highly specific ICUs that fall outside the realm of specialties presented above, such as cardiac, cardiovascular surgical, and burn ICUs. While there are not specific

fellowships tailored to every type of ICU, these units generally hire providers from clinically relevant fields. For example, the cardiac surgery ICU may hire anesthesiologists who have done fellowships both in critical care and cardiac anesthesiology. Additionally, the unit may hire cardiac surgeons who have completed ICU fellowship, forming a staff group of physicians with diverse backgrounds and skill sets.

Application Process

Application to fellowship in the US is much like application to residency: potential fellows must go through a match process. Most programs utilize the Electronic Residency Application Service hosted by the American Association of Medical Colleges (AAMC), and applicants must compile an extensive application including board exam scores, recommendation letters, and a personal statement. The AAMC has a detailed listing of all participating institutions and their specific application requirements on its fellowship application webpage (10).

Certification Process

Board certification in critical care medicine is required to work in the ICU, and each specialty pathway has its own distinct certification process. For example, board certification is offered by the American Board of Internal Medicine (ABIM) for pulmonary critical care physicians (11), the American Board of Anesthesiology for critical care anesthesiologists (12) and the American Board of Surgery (ABS) for critical care trained surgeons (13). Neurocritical care certification is offered through the ABS, the American Board of Psychiatry and Neurology (ABPN) (14) and the American Board of Neurological Surgery (ABNS) (15). Finally, EM physicians may take any of the above-mentioned board exams, as over the past two decades the American Board of Emergency Medicine has joined forces with these other board organizations to allow emergency physicians to sit for the critical care board exam. The ABIM was the first to allow EM physicians to sit for its critical care board in 2011, with all other specialties following suit, most recently with the ABPN allowing certification for EM physicians in 2021 (9).

Board examinations are generally offered annually, with most physicians opting to complete this step in the first 1-2 years after fellowship. There may be a time limitation, like the ABS post-fellowship eligibility period of seven years (13). Certain boards, such as the ABS and ABIM, may accept some candidates with international training if particular criteria are met; others, such as the ABPN, do not.

Demographics of Intensive Care Units Across the USA

The American Hospital Association lists over 5000 hospitals that have at least one intensive care bed and reports an average ICU size of 10-12 beds (16). ICU size is likely to change correspondingly with hospital size, and tertiary care tertiary care academic centers with 300-500+ beds are likely to have at least 2-3 distinct ICUs subspecialized to their primary patient populations. This could include the medical ICU, SICU, cardiac care unit, cardiovascular SICU, neurological critical care unit, pediatric ICU, neonatal ICU, and burn ICU, among others (17-19).

Given the over 112,000 ICU beds across the USA with 4.5 million ICU admissions annually, the demand for intensivists remains high. While in the past, critically ill patients may have been cared for by a generalist like an internist or surgeon, many studies over the past few decades show improved outcomes when ICU patients are cared for by a physician with critical care training (17,18). These outcomes include decreased mortality, increased survival, decreased ICU length of stay, and decreased hospital length of stay (20). However, ongoing staffing shortages, especially after the COVID-19 pandemic, reduce supply for 24-hour intensivist coverage, threatening care for some of the hospital's most vulnerable patients.

This staffing strain is most heavily concentrated in rural and low-income areas, as academic centers in larger metropolitan areas are more likely to have a consistent influx of recently graduated critical care physicians. Some hospitals have adopted creative strategies for addressing this such as employing telehealth intensivists as consultants for the primary medical or surgical team. These tele-intensivists join critical care rounds over video and provide virtual consultation to non-ICU trained physicians. The COVID-19 pandemic popularized the use of telehealth services to extend resources beyond geographic constraints; however, technology limitations remain a challenge in lower-resource settings, especially areas with unstable internet connectivity.

Advanced Practice Providers in Intensive Care

One strategy to address the ICU physician shortage is the utilization of advanced practice providers (APPs) or "midlevel providers" with critical care training. In the USA, APPs are healthcare professionals who have undergone

additional advanced training and work in collaboration with or under the supervision of a physician. While APPs work in many hospital settings (for example, nurse anesthetists in the operating room and nurse midwives on labor and delivery), there only two categories of APPs who work in the ICU: acute care nurse practitioners (ACNPs) and physician assistants (PAs) (21). Both ACNPs and PAs must obtain a graduate degree (either masters or doctorate) that includes both didactic course work and clinical rotations as well as apprentice-like experience in the ICU (22,23). Both PAs and NPs are credentialed to perform technical skills, like central lines and intubations, as well as clinical skills, like ventilator management (23).

Since the time required to train PAs and NPs to work in the ICU, approximately 2-5 years, is shorter than that to train an intensive care physician, leveraging a multidisciplinary workforce can help expand the reach of the current intensivist physicians (21) and address the ongoing and increasing demand for intensive care providers.

Job Prospects

The diversification of and increase in fellowship spots has created an intensive care workforce of physicians from various backgrounds and with different career goals (21). These physicians may choose to practice in community settings or academic hospitals, or even both. They may choose to work in one sub-specialized ICU, like the cardiac SICU, or a mixed medical-SICU. Contracts may only include ICU time, or split time with another specialty, such as operative time for surgeons or clinic time for pulmonologists. According to a 2023 survey, about half of intensivists spend more than 75% of their clinical time in the ICU, with others spending more or less, some significantly less (24). Some intensivist jobs may even include telehealth consulting for hospitals that can't staff full-time ICU physicians (25). Call structure may include 24-hour coverage with either in-hospital or home call; alternatively, two intensivists can split the coverage into 12-hour shifts to allow for shorter work hours.

An intensivist may work with a team including APPs, physician trainees, or a combination of the two. Community hospitals are likely to have intensivists working solo or with APPs, while academic centers will likely have the intensivist supervising residents and/or fellows. In both models, the trainee physicians or APPs are primarily responsible for placing orders, writing notes and are often the first line of contact for questions from nurses or other members of the care team, with the intensivist acting in more of a supervisory or consulting role. Physicians pursuing critical care training should be prepared to work on a truly multidisciplinary team with APPs, residents, and/or both, especially as the landscape of critical care medicine evolves and the need for increased staffing continues.

Graduates of International Medical Schools

In general, most physicians who apply for critical care medicine fellowship in the USA have completed an ACGME-accredited residency, as described above. However, non-USA medical graduates may be considered if they have completed a core residency outside the continental USA and demonstrated clinical excellence and exceptional qualifications including research, scholarship and/or leadership. Verification of credentials is done through the Educational Commission for Foreign Medical Graduates (5-8). It is worth noting that board certification in critical care medicine may require additional documentation or approval for those who have not completed an ACGME-accredited residency.

Critical Care Societies, Global Impact, Government Involvement

Given the diverse backgrounds of ICU physicians, multiple professional scientific societies exist to promote community in critical care. Nationally, the Critical Care Society Collaborative (CCSC) is a coalition of four societies: American Association of Critical-Care Nurses, American Thoracic Society, American College of Chest Physicians (CHEST), and Society of Critical Care Medicine (SCCM). Each has a distinct member population and lens for approaching critical care medicine. The coalition, CCSC, functions to harmonize and unify the societies; together, they work with the USA government, the Centers for Disease Control and USA Department of Health and Human Services on healthcare policy, improving patient care, optimizing high-value care, and addressing workforce issues (26).

Two USA critical care societies, SCCM and Neurocritical Care Society, belong to the World Federation of Intensive and Critical Care (27). There is a robust global intensive care community, including the Asian Society for Neuroanesthesia and Critical Care, the Pan-American and Iberian Federation of Critical Medicine and Intensive Therapy (FEPIMCTI), the Critical Care Society of Southern Africa and the European Society of Intensive Care Medicine which offers dual membership to national intensive care in more than 60 countries across the world (28). Beyond offering

international collaboration on research, innovation and clinical advancement, there is also a sense of solidarity, shared resources, and educational opportunities.

Conclusion

As the population of the USA ages and develops more complex healthcare needs, the demand for intensive care physicians is quickly outpacing the supply. The training pipeline to become an intensivist spans at least 9-11 years, including medical school, an ACGME-accredited residency program or a valid alternative, and a critical care fellowship with respective board certification. While a variety of specialties can lead to a career in critical care medicine, each pathway comes with a slightly different lens, patient population, and practice structure. Innovative responses to the demand for intensivists include tele-health consulting and the inclusion of APPs to help extend the reach of each fully trained intensivist. There are opportunities for non-USA trained physicians to pursue critical care fellowship training and board certification in the USA, with specifications outlined by the ACGME and specialty-distinct certifying bodies. Although there are several different and historically separate intensive care societies in the USA, there is a growing movement to align these societies together for improved cohesion, collaboration, and cooperation with each other and the international community to promote global initiatives to improve the care of critically ill patients worldwide.

Acknowledgement: Acknowledgement to Ozan Akca, MD, FCCM for reviewing and editing this submission.

Ethics

Authorship Contributions

Concept: M.R.G., Design: M.R.G., Literature Search: M.R.G., R.E.T., Writing: M.R.G., R.E.T.

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

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

References

1. Lois M. The shortage of critical care physicians: Is there a solution? J Crit Care. 2014;29:1121-2.
2. Angus DC, Kelley MA, Schmitz RJ, White A, Popovich J Jr; Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS). Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: can we meet the requirements of an aging population? JAMA. 2000;284:2762-70.
3. Provonost PJ, Angus DC, Dorman T, Robinson KA, Dremsizov TT, Young TL. Physician staffing patterns and clinical outcomes in critically III patients: A systematic review. JAMA. 2002;288:2151-62.
4. ACGME overview. Accreditation Council for Graduate Medical Education Web site. Available from: URL: https://www.acgme.org/about/overview/. Updated 2024. Accessed 27 June, 2024.
5. ACGME program requirements for graduate medical education in surgical critical care. Available from: URL: https://www.acgme.org/globalassets/pfassets/programrequirements/442_surgicalcriticalcare_2023.pdf. Updated 2022. Accessed 1 July, 2024.
6. ACGME program requirements for graduate medical education in pulmonary disease and critical care medicine. Available from: URL: https://www.acgme.org/globalassets/pfassets/programrequirements/2024-prs/156_pulmonarydiseasecriticalcaremedicine_2024.pdf. Updated 2022. Accessed 1 July, 2024.
7. ACGME program requirements for graduate medical education in anesthesiology critical care medicine. Available from: URL: https://www.acgme.org/globalassets/pfassets/programrequirements/045_anesthesiologycriticalcare_2023.pdf. Updated 2022. Accessed 1 July, 2024.
8. ACGME program requirements for graduate medical education in neurocritical care. Available from: URL: https://www.acgme.org/globalassets/pfassets/programrequirements/550_neurocriticalcare_2023.pdf. Updated 2021. Accessed 1 July, 2024.
9. Strickler SS, Choi DJ, Singer DJ, Oropello JM. Emergency physicians in critical care: Where are we now? J Am Coll Emerg Physicians Open. 2020;1:1062-70.
10. Applying to fellowships with the ERAS system. AAMC Web site. Available from: URL: https://students-residents.aamc.org/applying-fellowships-eras/applying-fellowships-eras-system. Accessed 5 August, 2024.
11. American board of internal medicine: Critical care medicine certification exam. Available from: URL: https://www.abim.org/certification/exam-information/critical-care-medicine/schedule-exam. Accessed 5 August, 2024.
12. American board of anesthesiology: Critical care medicine exam. Available from: URL: https://www.theaba.org/subspecialty-exam-type/critical-care-medicine-exam/. Accessed 5 August, 2024.
13. American board of surgery: Surgical critical care. Available from: URL: https://www.absurgery.org/get-certified/surgical-critical-care/. Accessed 5 August, 2024.
14. American board of psychiatry and neurology: Neurocritical care. Available from: URL: https://abpn.org/become-certified/taking-a-subspecialty-exam/neurocritical-care/. Accessed 5 August, 2024.
15. American board of neurological surgery: Recognition of focused practice: Neurocritical care. Available from: URL: https://abns.org/rfp-neurocritical-care/. Accessed 5 August, 2024.
16. AHA hospital statistics. 2024 Edition Web site. Available from: URL: https://www.aha.org/statistics/fast-facts-us-hospitals. Updated 2024. Accessed 23 July, 2024.
17. Groeger JS, Guntupalli KK, Strosberg M, Halpern N, Raphaely RC, Cerra F, et al. Descriptive analysis of critical care units in the united states: Patient characteristics and intensive care unit utilization. Crit Care Med. 1993;21:279-91.
18. Halpern NA, Goldman DA, Tan KS, Pastores SM. Trends in critical care beds and use among population groups and medicare and medicaid beneficiaries in the united states: 2000-2010. Crit Care Med. 2016;44:1490-9.
19. Halpern NA, Pastores SM. Critical care medicine beds, use, occupancy, and costs in the united states: A methodological review. Crit Care Med. 2015;43:2452-9.
20. Burchardi H, Moerer O. Twenty-four hour presence of physicians in the ICU. Crit Care. 2001;5:131-7.
21. Thompson SL, LeTourneau JL. SCCM critical care workforce update 2023. 2024. https://sccm.org/Home
22. Kreeftenberg HG, Pouwels S, Bindels AJGH, de Bie A, van der Voort PHJ. Impact of the Advanced Practice Provider in Adult Critical Care: A Systematic Review and Meta-Analysis. Crit Care Med. 2019;47:722-30.
23. Hoffman LA, Guttendorf J. Preparation and evolving role of the acute care nurse practitioner. Chest. 2017;152:1339-45.
24. Barshied CB, Russell C. Satisfaction, stress, and turnover: Comparing U.S. intensivist physicians before and during the severe acute respiratory syndrome coronavirus 2 pandemic. Crit Care Explor. 2023;5:e0883.
25. Abraham J, Kandasamy M, Fritz B, Konzen L, White J, Drewry A, et al. Expanding critical care delivery beyond the intensive care unit: Determining the design and implementation needs for a tele-critical care consultation service. Appl Clin Inform. 2024;15:178-91.
26. Critical care societies collaborative. SCCM Web site. Available from: URL: https://sccm.org/About-SCCM/Critical-Care-Societies-Collaborative. Accessed July 23, 2024.
27. World federation of intensive and critical care: Societies. World Federation of Intensive and Critical Care Web site. Available from: URL: https://www.wficc.com/societies. Updated 2024. Accessed July 23, 2024.
28. European society of intensive care medicine: National societies. Available from: URL: https://www.esicm.org/the-esicm/national-societies/. Accessed 5 August, 2024.

Turk J Intensive Care 2024;22:161-9
DOI: 10.4274/tybd.galenos.2023.41275

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Factors Affecting Survival of Pregnant Women with COVID-19 and Our First Extracorporeal Membrane Oxygenation Results

COVID-19 ile Enfekte Gebelerin Sağkalımını Etkileyen Faktörler ve İlk Ekstrakorporeal Membran Oksijenasyonu Sonuçlarımız

Received/Geliş Tarihi : 18.10.2022
Accepted/Kabul Tarihi : 15.05.2023

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ABSTRACT *Objective:* The purposes of our study were to determine the relationship between coronavirus disease (COVID) pneumonia and mortality and immunization status of patients and to present our first extracorporeal membrane oxygenation (ECMO) experiences by retrospectively evaluating pregnant women.
Materials and Methods: The research was conducted by screening the files of 37 pregnant/postpartum COVID-2019 cases monitored and treated in the intensive care unit between March 1, 2020 and December 1, 2021. The patients' ages, systemic comorbidities, vaccination details, and clinical and laboratory features were recorded and analyzed. The patients were divided into two groups as survivors (group 1; n=17) and exitus ones (group 2; n=20); and the results were compared statistically.
Results: Of 37 patients, 17 (45.9%) survived (group 1) and 20 (54.1%) died (group 2) with a median of 31 gestational weeks and 9 days length of stay in the ICU. ICU admission time [which day of polymerase chain reaction (PCR)+] and cesarean time (which day of PCR+) were 8 days. Nine (24%) patients received ECMO and mechanical ventilation, with 6 (66.6%) exitus and 3 (33.3%) survivors who were discharged from the hospital without sequelae. Of 37 pregnant/postpartum patients, 36 were unvaccinated.
Conclusion: Vaccination should be given priority in pregnant women, and ECMO may be effective in the recovery of oxygenation in pregnant COVID-19 patients.
Keywords: COVID-19, ECMO, pregnancy, vaccines, ICU

ÖZ *Amaç:* Çalışmamızın amacı, gebeleri retrospektif olarak değerlendirerek koronavirüs hastalığı (COVID) pnömonisi ile mortalite, hastaların bağışıklama durumları arasındaki ilişkiyi ortaya koymak ve ilk ekstrakorporeal membran oksijenasyonu (ECMO) deneyimlerimizi sunmaktır.
Gereç ve Yöntem: Araştırma, 1 Mart 2020 ile 1 Aralık 2021 tarihleri arasında yoğun bakım ünitesinde takip ve tedavi edilen toplam 37 gebe/postpartum COVID-2019 olgusunun dosyaları taranarak gerçekleştirildi. Hastaların yaşları, sistemik komorbiditeleri, aşı detayları, klinik ve laboratuvar özellikleri kaydedildi ve analiz edildi. Hastalar sağkalanlar (grup 1; n=17) ve eksitus olanlar (grup 2; n=20) olarak 2 gruba ayrıldı ve sonuçlar istatistiksel olarak karşılaştırıldı.
Bulgular: Çalışmamızda 37 hastanın 17'si (%45,9) hayatta kaldı (grup 1) ve 20'si (%54,1) öldü (grup 2). Medyan gebelik haftası 31 hafta olup, yoğun bakım yatış süresi 9 gündü. Yoğun bakım ünitesine yatış günü [polimeraz zincir reaksiyonu (PZR) pozitifliğinin (+) kaçıncı günü] ve sezeryan süresi [polimeraz zincir reaksiyonu (PZR) pozitifliğinin (+) kaçıncı günü] ortalama 8. gündü. Dokuz (%24) hasta ECMO ve mekanik ventilasyon desteğinde takip edildi, bu hastaların 6'sı (%66,6) eksitus oldu. Üç (%33,3) sağ kalan hasta sekelsiz taburcu edildi. Otuz yedi gebe/postpartum hastanın 36'sı aşısızdı.
Sonuç: Gebelerde aşı ile bağışıklamaya öncelik verilmelidir, ECMO COVID-19(+) gebe hastalarda oksijenlenmenin düzenlenmesinde etkili olabilir.
Anahtar Kelimeler: COVID-19, ECMO, gebelik, aşı, YBÜ

Introduction

The respiratory tract infections observed in the pregnant women may be severer due to the physiological, anatomical, and immunological changes in this group (1). Several studies have shown that the mortality and morbidity of pregnant patients infected with viral agents such as influenza, Middle East respiratory syndrome and severe acute respiratory syndrome caused by H_1N_1 are higher than their peers (2,3).

Although the guide issued by the World Health Organization in March 2020 states that the incidence of novel coronavirus disease-2019 (COVID-19) is relatively low among pregnant women, recent studies have reported serious hypoxia requiring mechanical ventilation (MV), increased mortality and morbidity in the pneumonia cases (4-6). We planned this study considering that descriptive studies, (that include high numbers of patients), to be conducted in this field would decrease maternal and fetal losses, and ensure planning stronger strategies in monitoring and treatment.

In our hospital, which is one of the first pandemic hospitals, 1,302 polymerase chain reaction (PCR) positive COVID-19 cases were monitored from March 1, 2020 to December 1, 2021. Of these pregnant women, 37 were monitored in intensive care unit (ICU). In the present study, we aimed to investigate the relationship between COVID-19 pneumonia and mortality, immunization status of patients and to present our first extracorporeal membrane oxygenation (ECMO) experiences in pregnant women.

Materials and Methods

This single-center, retrospective study was conducted at the University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Anesthesiology and Reanimation ICU of a tertiary care center between March 1st, 2020 and December 1st, 2021. The files of pregnant/postpartum COVID-19 cases who were treated in the ICU due to COVID-19 pneumonia were reviewed. The patients, who had unproven positive status of PCR analysis, under 18 years of age, referred to an external center due to the lack of ICU beds in our institution, or still being treated in our hospital during the collection of data were excluded. The vaccination details of the included patients were acquired through the electronic data system of the Republic of Turkey, Ministry of Health. During the study period, a total of 1,302 PCR-positive COVID-19 cases were admitted to our hospital. Of these pregnant women, 37 who were monitored in the ICU setting were included. The study was approved by the University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-invasive Clinical Research Ethics Committee (no: 2022-260, date: 12.01.2022) and conducted in accordance with the principles of the Declaration of Helsinki.

Through the electronic data system of our hospital, data including age, systemic comorbidities, on which day of COVID-19 positive status they were admitted to ICU, and if they had ceserean section (C/S), on which day of PCR-positive status they had it, the reason for C/S, the anesthesia method used in C/S, the immunomodulatory drugs, antibiotics, antiviral drugs, anticoagulants used, the dose and length of corticosteroid administration, blood/trachea/urine culture results, laboratory analyses at the time of ICU admission such as white blood cell (WBC) count, C-reactive protein (CRP), procalcitonin, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase (LDH), creatinine, ferritin, fibrinogen, D-dimer, hemoglobin, hematocrit, platelet count, international normalized ratio (INR), eosinophil count and triglyceride, radiological imaging results, need for oxygen (O_2) support, MV requirement, ECMO requirement, length of ICU stay were recorded and analyzed.

The patients were divided into two groups as survivors (group 1) and non-survivors (group 2); and the results were compared statistically.

In the ICU admission, the standard third-level ICU admission criteria [dyspnea and respiratory distress, respiratory rate over 30, partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) <300, oxygen saturation (SpO_2<90%) or PaO_2<70 mmHg, despite the oxygen therapy of 5 L/min, hypotension, development of acute organ failure, high lactate levels, confusion] were employed. Depending on the patients' clinical status, the conventional oxygen therapies [mask, reservoir, high-flow nasal oxygen (HFNO) and continuous positive airway pressure (CPAP)] and MV were applied. For the patients in whom sufficient oxygenation could not be achieved through MV despite the maximum support, ECMO initiated.

If PaO_2<60 mmHg and/or PaO_2/FiO_2<100 with conventional therapies, HFNO and CPAP were applied. If PaO_2<60 mmHg and/or PaO_2/FiO_2<100 with HFNO and CPAP, invasive MV was applied. For the endotracheally intubated patients in whom sufficient oxygenation could not be achieved through MV less than 7 days, and if they

met one of the following criteria; 1) PaO_2/FiO_2<50 for >3 hours, 2) PaO_2/FiO_2<80 for >6 hours, 3) pH <7.25 with partial carbondioxide pressure (pCO_2)≥60 mmHg, respiratory rate increased to 35 breaths min^{-1}, and plateau pressure ≤32 mmHg despite the maximum ventilator support (FiO_2≥0.80, a tidal volume of 6 mL kg^{-1} of predicted body weight, and a positive end-expiratory pressure ≥10 cm H_2O), ECMO was initiated.

If PaO_2<60 mmHg and/or PaO_2/FiO_2<100 general anestesia was applied in the C/S as anesthesia method.

Statistical Analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation, median (minimum-maximum) or number and frequency, where applicable. The normality distribution of the variables was checked using the Kolmogorov-Smirnov and Shapiro-Wilk. The Student t-test was used to compare normally distributed variables, while the Mann-Whitney U test was used to compare non-normally distributed variables. The Fisher Exact chi-square test, Fisher-Freeman-Halton exact chi-square test, and Continuity (Yates) correction were used to compare the qualitative data. A p-value of <0.05 was considered statistically significant.

Results

During the study, totally 37 COVID positive pregnant women, who were older than 18 years old, were evaluated.

The gestational weeks were ranging from 18 weeks to 38 weeks with an average of 30.08±5.03 and a median of 31 weeks. While the average length of stay (LOS) in the service before the transfer to ICU was 4.43±2.62 days with a median of 4 days, 2 patients were admitted directly to the ICU due to maternal hypoxia after emergency application to the hospital. The ICU LOS was ranging from 1 to 70 days with an average of 14.48±14.07 and a median of 9 days. The total LOS in hospital was ranging from 3 to 72 days with an average of 22.27±14.90 and a median of 18 days. Of the pregnant women in the study, 20 (54.1%) became ex.

Of 37 pregnant/postpartum patients, 36 were unvaccinated. One patient received a single dose of messenger ribonucleic acid vaccine 14 days before getting infected. Demographic and clinical characteristics of the patients are shown in Table 1.

Three of six patients in whom C/S was not applied died. The gestational week of the patients who died was below 21 weeks (18, 20, 20 weeks). In the surviving group, the pregnancy of three patients (20, 26, and 33 weeks) continued healthily, and they were discharged from the ICU uneventfully.

According to mortality, there was no statistically significant difference in terms of average ages, gestational weeks, LOS in hospital before the ICU transfer, the day of ICU admission after PCR + result, rates of observing asthma, hypothyroidism, and varicose, C/S etiology and anesthesia methods (spinal/general), and the rates of secondary infections as confirmed by blood culture and trachea culture (p>0.05).

The rate of use of azithromycin in group 1 was statistically significantly higher than group 2 (23.5% vs. 0%, respectively) (p=0.036). The rate of use of cefuroxime axetil in group 2 was statistically significantly higher than group 1 (35% vs. 5.9%, respectively) (p=0.048). There was no statistically significant difference in the rates of the use of other drugs between the two groups (p>0.05).

There was no statistically significant difference between 2 groups in terms of the doses of use of methyl prednisolone (p>0.05). The duration of methyl prednisolone administration in group 1 was ranging from 3 to 10 days with an average of 5.27±1.68 and a median of 5 days. The duration of methylprednisolone administration in group 2 was ranging from 3 to 10 days with an average of 6.39±2.87 and a median of 5 days. There was no statistically significant difference between the durations of methylprednisolone administration by mortality as well (p=0.470) (Table 2).

The rate of MV support in group 2 was statistically significantly higher than group 1 (100% vs. 35.3%, respectively) (p=0.001 and p<0.05) (Table 3). The mean duration of MV support was 7.65±13.8 days in group 1 and 11.05±9.28 in group 2, indicating a statistically significant difference between the groups (p=0.016 and p<0.05).

There was no statistically significant difference between the groups in terms of ECMO rates (p>0.05) (Table 3). The duration of ECMO in group 1 was ranging from 26 to 50 days with an average of 37.0±12.12 and a median of 35 days. The duration of ECMO in group 2 was ranging from 1 to 27 days with an average of 17.83±10.15 and a median of 23 days. When two groups were compared, the duration of ECMO in group 1 was statistically significantly longer than group 2 (p=0.038; p<0.05) (Table 3).

There was no statistically significant difference between the groups in terms of the rates of use of HFNO and CPAP in the ICU (p>0.05).

The computed tomography (CT) involvement was above 50% in 85% of the patients in group 2 while this ratio was 29.4% in group 1, indicating a significant difference between two groups (p<0.001) (Table 3).

According to the laboratory analysis results at the time of ICU admission, the ferritin levels (p=0.007), INR levels (p=0.034), and platelet counts (p=0.019) were statistically significantly higher in group 2. There was no statistically significant difference in the other biochemical parameters between the groups according to mortality (p>0.05) (Table 4).

There was no statistically significant difference between group 1 and group 2 in terms of ICU LOS and total LOS in hospital (p>0.05) (Table 5).

Discussion

In the present study, we investigated the relationship between COVID-19 pneumonia and mortality and reported our first ECMO experiences in pregnant women during the pandemic. Of the cases, 45.9% (n=17) survived, while 31.03% of the patients required MV support (MV, MV + ECMO). Despite conventional oxygen therapy, these patients needed to be transferred to ICU due to hypoxia and dyspnea. Totally 26 patients were monitored with MV. Thoracic CT of non-survivors showed bilateral widespread ground-glass opacities, and all of these patients were monitored under the MV support. The ECMO (24%) was needed in nine patients who could not reach the target SpO_2 despite maximum MV support. Of these patients, six (66.6%) died and three (33.3%) were discharged without any sequelae. Of 37 pregnant/postpartum patients monitored in the ICU, 36 were unvaccinated. One patient had taken a single dose of mRNA vaccine 14 days before becoming COVID PCR positivity;

Table 1. Demographic and clinical characteristics of patients

		Group 1 (n=17)	Group 2 (n=20)	Total (n=37)	[1]p-value
		Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
Age		28.53±4.78 (28)	31.3±5.73 (32.5)	30.03±5.43 (30)	0.138
Gestational week		31.65±4.65 (32)	28.75±5.08 (28)	30.08±5.04 (31)	0.067
Length of stay in the service (before ICU)		3.82±2.9 (3)	4.95±2.31 (5)	4.43±2.62 (4)	0.097
ICU admission time (which day of PCR+)		8.94±2.08 (9)	8.35±2.11 (8)	8.62±2.09 (8)	0.476
C/S time (which day of PCR+)		8.57±1.99 (8.5)	8.71±3.14 (9)	8.65±2.64 (9)	0.984
		n (%)	n (%)	n (%)	
Comorbid diseases	Asthma	2 (11.8%)	1 (5%)	3 (8.1%)	[2]0.584
	Diabetes	0 (0%)	0 (0%)	0 (0%)	-
	Hypertension	0 (0%)	0 (0%)	0 (0%)	-
	Hypothyroidism	3 (17.6%)	1 (5%)	4 (10.8%)	[2]0.315
	Varicose	1 (5.9%)	0 (0%)	1 (2.7%)	[2]0.459
C/S etiology	Not done	3 (17.6%)	3 (15%)	6 (16.2%)	[3]1.000
	Maternal hypoxia	12 (70.6%)	14 (70%)	26 (70.3%)	
	Preeclampsia	2 (11.8%)	3 (15%)	5 (13.5%)	
C/S anesthesia type	Not done	3 (17.6%)	3 (15%)	6 (16.2%)	[3]0.090
	Spinal	13 (76.5%)	10 (50%)	23 (62.2%)	
	General	1 (5.9%)	7 (35%)	8 (21.6%)	
Culture result	Blood culture	6 (35.3%)	10 (50%)	16 (43.2%)	[4]0.571
	Urinary culture	0 (0%)	0 (0%)	0 (0%)	-
	Trachea culture	2 (11.8%)	3 (15%)	5 (13.5%)	[2]1.000

[1]Mann-Whitney U test, [2]Fisher's Exact test, [3]Fisher-Freeman-Halton Exact test, [4]Continuity (Yates) correction, ICU: intensive care unit, C/S: caesarean section, SD: standard deviation

Table 2. Evaluation of drugs used according to patient groups					
		Group 1 (Surviving; n=17)	Group 2 (Exitus; n=20)	Total	
		n (%)	n (%)	n (%)	p-value
Drugs	Azithromycin	4 (23.5%)	0 (0%)	4 (10.8%)	[1]0.036*
	Linezolid	1 (5.9%)	0 (0%)	1 (2.7%)	[1]0.459
	Meropenem	7 (41.2%)	10 (50%)	17 (45.9%)	[2]0.837
	Vancomycin	2 (11.8%)	8 (40%)	10 (27%)	[1]0.073
	Piperacillin/tazobactam	4 (23.5%)	10 (50%)	14 (37.8%)	[2]0.189
	Colistimethate sodium	2 (11.8%)	4 (20%)	6 (16.2%)	[1]0.667
	Cefuroxime axetil	1 (5.9%)	7 (35%)	8 (21.6%)	[1]0.048*
	Clarithromycin	1 (5.9%)	4 (20%)	5 (13.5%)	[1]0.348
	Hydroxychloroquine	2 (11.8%)	1 (5%)	3 (8.1%)	[1]0.584
	Lopinavir/ritonavir	8 (47.1%)	9 (45%)	17 (45.9%)	[2]1.000
	Favipiravir	10 (58.8%)	13 (65%)	23 (62.2%)	[2]0.963
	IVIG	0 (0%)	1 (5%)	1 (2.7%)	[1]1.000
	Plasmapheresis	1 (5.9%)	4 (20%)	5 (13.5%)	[1]0.348
	Tocilizumab	3 (17.6%)	3 (15%)	6 (16.2%)	[1]1.000
	Immune plasma	0 (0%)	1 (5%)	1 (2.7%)	[1]1.000
Anticoagulant	Service	17 (100%)	20 (100%)	37 (100%)	-
	ICU	17 (100%)	20 (100%)	37 (100%)	-
Methylprednisolone	Not administered	6 (35.3%)	2 (10%)	8 (21.6%)	[3]0.220
	40 mg	2 (11.8%)	1 (5%)	3 (8.1%)	
	250 mg	8 (47.1%)	15 (75%)	23 (62.2%)	
	1000 mg	1 (5.9%)	2 (10%)	3 (8.1%)	

[1]Fisher's Exact test, [2]Continuity (Yates) correction, [3]Fisher-Freeman-Halton Exact test, *p<0.05, ICU: intensive care unit, IVIG: intravenous immunoglobuline

Table 3. Evaluation of oxygen therapies and CT results according to patient groups					
		Group 1 (n=17)	Group 2 (n=20)	Total	p
		n (%)	n (%)	n (%)	
MV		6 (35.3%)	20 (100%)	26 (70.3%)	[1]0.001*
ECMO + MV		3 (17.6%)	6 (30%)	9 (24.3%)	[2]0.462
ICU COT	Nasal	9 (52.9%)	0 (0%)	9 (24.3%)	[2]0.000*
	Reservoir	10 (58.8%)	0 (0%)	10 (27%)	[2]0.000*
	HFNO	7 (41.2%)	9 (45%)	16 (43.2%)	[1]1.000
	CPAP	5 (29.4%)	9 (45%)	14 (37.8%)	[1]0.526
Pulmonary involvement on CT	Not taken	3 (17.6%)	3 (15%)	6 (16.2%)	
	Below 50%	9 (52.9%)	0 (0%)	9 (24.3%)	
	Above 50%	5 (29.4%)	17 (85%)	22 (59.5%)	[3]0.000*

[1]Continuity (Yates) correction, [2]Fisher's Exact test, [3]Fisher-Freeman-Halton Exact test, *p<0.05.
ECMO: Extracorporeal membrane oxygenation, MV: mechanical ventilation, ICU: intensive care unit, COT: conventional oxygen therapy, HFNO: high flow nasal oxygen, CPAP: continuous positive airway pressure, CT: computed tomography

Table 4. Biochemical parameters according to patient groups				
	Group 1 (n=17)	Group 2 (n=20)	Total	p-value
	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
WBC (4.00-10.00 10^3/uL)	11.76±4.59 (11.42)	15.52±8.58 (12.99)	13.79±7.2 (12)	0.315
CRP (0-5 mg/L)	60.72±61.88 (32.63)	89.83±57.34 (96.5)	76.46±60.44 (72.48)	0.053
Procalcitonin (<0.05 mcgr/L)	0.38±0.36 (0.2)	1.15±2.5 (0.26)	0.79±1.87 (0.23)	0.116
Ferritin (13-150 mcgr/L)	141.68±122.63 (104.7)	256.02±152.73 (238.3)	203.48±149.44 (166.4)	0.007*
D-dimer (0-0.55 mg/L)	5.59±8.28 (3.43)	6.9±9.13 (4.04)	6.3±8.66 (3.65)	0.583
Fibrinogen (200-400 mg/dL)	534.06±112.26 (543)	517.6±213.54 (479.5)	525.16±172.44 (499)	0.253
INR (0.75-1.27)	0.97±0.1 (0.95)	1.08±0.17 (1.07)	1.03±0.15 (0.98)	0.034*
LDH (135-214 U/L)	453±124.47 (460)	541.45±217.81 (462)	500.81±184.18 (460)	0.368
Creatinine (0.5-0.9 mg/dL)	0.49±0.19 (0.46)	0.51±0.28 (0.46)	0.5±0.24 (0.46)	0.915
AST (6-40 U/L)	72.82±97.78 (42)	65.86±81.04 (45)	69.06±87.91 (42)	0.964
ALT (6-33 U/L)	83.32±141.67 (24)	66.29±144.29 (22.5)	74.11±141.36 (23)	0.807
EOS (0.02-0.5 10^3/uL)	0.05±0.06 (0)	0.12±0.21 (0)	0.09±0.16 (0)	0.472
Hemoglobin (12-16 gr/dL)	10.46±1.24 (10.6)	10.16±1.1 (9.9)	10.3±1.16 (10.1)	+0.426
Hematocrit (40-54%)	32.03±2.99 (32)	31.39±3.27 (30.7)	31.68±3.12 (31.3)	+0.542
Platelet (100-400 10^3/uL)	231.65±99.26 (210)	315.55±106.67 (292.5)	277±110.37 (253)	+0.019*

Mann-Whitney U test, +Student t-test, *p<0.05
CRP: C-reactive protein, WBC: white blood cell, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, INR: international normalized ratio, EOS: eosinophil, SD: standard deviation

Table 5. Length of ICU stay and total length of hospital stay according to patient groups				
	Group 1 (n=17)	Group 2 (n=20)	Total	p-value
	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
ICU length of stay	16±18.4 (9)	13.2±9.3 (10.5)	14.49±14.07 (9)	0.647
Total length of stay in hospital	27.65±18.54 (20)	17.7±9.14 (17.5)	22.27±14.9 (18)	0.099

Mann-Whitney U test, ICU: intensive care unit, SD: standard deviation

she was in the week 21 of her pregnancy, and she died due to multiple organ dysfunction.

Earlier studies conducted on pregnant COVID-19 patients in the United States showed that the pregnant women with COVID-19 and the patients who were not pregnant had similar disease characteristics, with a milder disease severity (7). In other words, COVID-19 was not a risk factor for pregnancy. Another study conducted in the United Kingdom including 91,412 female patients between the ages of 15 and 44 years and of whom 8,207 were pregnant reported that the pregnant women needed hospitalization, ICU, and MV support more (8). However, the aforementioned study excluded non-survivors. Another cohort study conducted by Tekbali et al. (9) in pregnant women within the first four weeks of the pandemic also found that although the hospitalization rate increased, this increase was relatively low compared to the overall population.

On the other hand, studies conducted in the ongoing process have shown that the COVID-19 is associated with increased maternal mortality and morbidity in pregnant women. Mortality in infected pregnant women has been shown to be correlated with ethnicity, gestational week, comorbidity, the need for oxygen at the time of hospital admission, and the need for ICU and MV support. The ICU admission time of the hospitalized pregnant COVID-19 patients varies from 7 to 10 days (10-12). Similarly, in our study, the average time to ICU admission was 8 days.

All pregnant women monitored in the study of Hessami et al. (13) were in the third trimester. Obesity, diabetes mellitus, hypertension, and asthma were the most frequently

observed comorbidities. The maternal age was higher in the deceased cases (13). Another study examining 20 maternal deaths between the ages of 20 and 43 years showed that 11 patients had comorbidities accompanying severe pneumonia. Asthma was the most frequently observed comorbidity (14). In our study, eight patients had comorbidities, although there was no difference between two groups. None of our patients had diabetes and/or hypertension. One patient with asthma history died, while two other patients survived. Three patients, who had hypothyroidism, survived while one other patient died. In the non-survivor group, the mean maternal age was 31.3±5.73 (32.5) years, and the gestational age was 28.75±5.08 (28) weeks. Although there was no statistically significant difference in our study, the maternal age was higher among the non-survivors.

The study conducted by Juan et al. (15), in which they examined the maternal deaths caused by the COVID-19, reported that severe pulmonary damage had been detected in all patients in consequence of CT evaluation, and that the ground glass opacity was the most specific finding. In our study, all of 31 patients who were examined with CT had pulmonary findings, and all of the non-survivors had widespread bilateral infiltration and ground glass opacity (above 50%). However, although they had over 50% CT involvement, five pregnant patients (22%) survived.

Although there is a limited number of data regarding the ECMO application in PCR-confirmed COVID-19 pregnant patients, there are case reports with satisfactory results (16-18). In our study, we applied venous-venous ECMO therapy to nine patients in whom sufficient oxygenation could not be achieved despite the maximum MV support. Eight cases were supported with ECMO after emergency C/S due to maternal hypoxia. The survival rate was 33.3%. In only one of these cases (gestational age: 26 weeks), pregnancy continued; this patient, whose pregnancy continued healthily, was discharged without any sequelae in the room air after discharging her from the ECMO unit. In her follow-up, a healthy and normal infant was born at the 36th week of pregnancy. The mean ECMO duration was longer among survivors, and this duration was shorter in six patients who died, and these patients were lost due to multiple organ dysfunction syndrome caused by prolonged hypoxia and insufficient tissue perfusion. Taken together, we believe that the ECMO support is beneficial in eligible cases to prevent pulmonary damage caused by the COVID-19 and prolonged hypoxia in the lung tissue recovery period.

In our study, the emergency C/S was applied to 70.3% of the patients in the ICU settings due to maternal hypoxia and to 13.5% due to preeclampsia. Three of the six patients to whom C/S was not died. The gestational week of non-surviving patients was below 21 weeks (18, 20, and 20 weeks). All of them had over 50% pulmonary involvement on CT and were under MV support due to maternal hypoxia. In the surviving group, the pregnancy of three patients (20, 26, and 33 weeks) continued healthily; lung involvement on CT was below 50%, and the patients receiving conventional oxygen therapy were discharged from the ICU. The results of the INTERCOVID study comparing 706 COVID-19 positive pregnant women with 1,424 non-infected pregnant patients also indicate that the premature C/S, maternal morbidity and mortality risks in the infected pregnant women have increased due to eclampsia/preeclampsia, fetal distress, or maternal hypoxia (10).

In our study, there were 23 patients, who gave birth to their children under the spinal anesthesia method. During the operation no changes were made about respiratuar support or anesthesia method. But after the surgery 16 of these patients needed MV support due to maternal hypoxia, and 11 of these patients were lost. Based on these findings, we consider that it is necessary to evaluate the clinical condition, arterial blood gas analysis, and oxygenation of the patient while selecting the most appropriate anesthesia method.

In the COVID-19 pneumonia characterized by tachypnea, hypoxaemia, widespread pulmonary infiltration, and diffuse lung damage, acute respiratory distress syndrome (ARDS) is the most frequently observed cause of death (19). The RECOVERY trial recommended the administration of the low-dose dexamethasone for the patients whose oxygen needs were high or for patients under MV support (20). There are also reports suggesting the use of methylprednisolone that has a higher implantation to the lung tissue in ARDS treatment (21,22). In our study, there was no relationship between the use of methylprednisolone and mortality. On the other hand, the corticosteroids may cause increase in the maternal infections due to immunosuppression (23). We consider that the use of corticosteroid may have played a role in the existence of the bacterial secondary infections confirmed with the blood and trachea cultures in the single intensive care rooms of our hospital that was transformed into a pandemic hospital in March 2020 despite the tight control of the Infection Control Committee and the maximum hand

hygiene and isolation measures. Therefore, we consider that a careful cost-benefit analysis in the patient selection and a close follow-up of the patients using corticosteroid against the bacterial secondary infections would be beneficial.

In the clinical follow-up of COVID-19 cases, the laboratory findings are also critical and, thus, INR, D-dimer, fibrinogen, procalcitonin, CRP, WBC, platelet count, and ferritin must be monitored. In our study, the elevated levels of ferritin, INR, and platelet counts were found to be correlated with mortality. However, although these values were higher among non-survivors, the INR and platelet counts were with in normal limits. Overall, we detected low levels of anemia and eosinophil count, as well as high D-dimer, fibrinogen, LDH, WBC, procalcitonin, and CRP levels. Our results are consistent with previous findings in the literature (24,25).

Several studies have reported that vaccination decreases ICU admission and mortality in the course of the COVID-19 infection. It was not different for the pregnant patients, either (26,27). None of the patients who were in the ICU and included in our study was immunized (one patient was vaccinated incompletely, while 36 patients were not vaccinated at all). As there is still no definitive treatment method and antiviral medication for the pregnant patients infected with COVID-19, we consider that immunization by vaccination must be given the top priority in this patient group that may have high mortality rates, as well.

Nonetheless, there are some limitations to this study. Since our study was designed retrospectively, it did not include information on the variant analysis of the infected patients. At the beginning of the pandemic, the clinical results of the pregnant patients were not different when compared to the non-pregnant patients in the same age group. Meanwhile, the dominant variant was the alpha variant. We consider that the later reports of mortality may have been caused by the change in the dominant viral variants. Conducting a variant analysis in the future studies may be a guide in predicting the course of the disease.

As the case number increases, new prognostic factors would be identified in relation to mortality.

Conclusion

In conclusion, advanced age, gestational week, vaccination status, ICU LOS, pulmonary involvement on CT (over 50%), and MV requirement can affect the mortality status of pregnant women infected with COVID-19. In addition, MV combined with ECMO is an effective rescue therapy for pregnant women with COVID-19 pneumonia in the ICU setting. However, anesthesia method for delivery should be selected individually. Further large-scale, prospective studies are warranted to confirm these findings and to gain a better understanding of COVID-19 pneumonia in pregnant women.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-invasive Clinical Research Ethics Committee (no: 2022-260, date: 12.01.2022) and conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: S.T., Concept: S.T., Design: S.T., E.A., N.B., Data Collection and Process: S.T., E.E.Ö., Analysis or Interpretation: S.T., E.A., N.B., Literature Search: S.T., Writing: S.T.

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

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

References

1. Goodnight WH, Soper DE. Pneumonia in pregnancy. Crit Care Med. 2005;33:S390-7.
2. Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. BMC Infect Dis. 2016;16:105.
3. Landt S, Sina F, Kimmig R, Schmidt M. H1N1 - Risikofaktor Schwangerschaft [H1N1--pregnancy as risk factor]. Z Geburtshilfe Neonatol. 2010;214:48-51.
4. World Health Organization (WHO). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Available from: URL: https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19). Accessed April 1, 2020.
5. Eman A, Balaban O, Kocayiğit H, Süner KÖ, Cırdı Y, Erdem AF. Maternal and Neonatal Outcomes of Critically Ill Pregnant and Puerperal Patients Diagnosed with COVID-19 Disease: Retrospective Comparative Study. J Korean Med Sci. 2021;36:e309.
6. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320.
7. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM. 2020;2:100118.
8. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:769-75.
9. Tekbali A, Grünebaum A, Saraya A, McCullough L, Bornstein E, Chervenak FA. Pregnant vs nonpregnant severe acute respiratory syndrome coronavirus 2 and coronavirus disease 2019 hospital admissions: the first 4 weeks in New York. Am J Obstet Gynecol. 2020;223:126-7.
10. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr. 2021;175:817-26.
11. Mark EG, McAleese S, Golden WC, Gilmore MM, Sick-Samuels A, Curless MS, et al. Coronavirus Disease 2019 in Pregnancy and Outcomes Among Pregnant Women and Neonates: A Literature Review. Pediatr Infect Dis J. 2021;40:473-8.
12. Siqueira TS, de Souza EKG, Martins-Filho PR, Silva JRS, Gurgel RQ, Cuevas LE, et al. Clinical characteristics and risk factors for maternal deaths due to COVID-19 in Brazil: a nationwide population-based cohort study. J Travel Med. 2022;29:taab199.
13. Hessami K, Homayoon N, Hashemi A, Vafaei H, Kasraeian M, Asadi N. COVID-19 and maternal, fetal and neonatal mortality: a systematic review. J Matern Fetal Neonatal Med. 2022;35:2936-41.
14. Takemoto MLS, Menezes MO, Andreucci CB, Knobel R, Sousa LAR, Katz L, et al. Maternal mortality and COVID-19. J Matern Fetal Neonatal Med. 2022;35:2355-61.
15. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. Ultrasound Obstet Gynecol. 2020;56:15-27.
16. Douglass KM, Strobel KM, Richley M, Mok T, de St Maurice A, Fajardo V, et al. Maternal-Neonatal Dyad Outcomes of Maternal COVID-19 Requiring Extracorporeal Membrane Support: A Case Series. Am J Perinatol. 2021;38:82-7.
17. Barrantes JH, Ortoleva J, O'Neil ER, Suarez EE, Beth Larson S, Rali AS, et al. Successful Treatment of Pregnant and Postpartum Women With Severe COVID-19 Associated Acute Respiratory Distress Syndrome With Extracorporeal Membrane Oxygenation. ASAIO J. 2021;67:132-6.
18. Bauer ME, Chiware R, Pancaro C. Neuraxial Procedures in COVID-19-Positive Parturients: A Review of Current Reports. Anesth Analg. 2020;131:e22-4.
19. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382:1708-20.
20. University of Oxford. The Recovery trial. https://www.recoverytrial.net/. Accessed March4, 2021.
21. Meduri GU, Bridges L, Shih MC, Marik PE, Siemieniuk RAC, Kocak M. Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. Intensive Care Med. 2016;42:829-40.
22. Magala Ssekandi A, Sserwanja Q, Olal E, Kawuki J, Bashir Adam M. Corticosteroids Use in Pregnant Women with COVID-19: Recommendations from Available Evidence. J Multidiscip Healthc. 2021;14:659-63.
23. Mariotti V, Marconi AM, Pardi G. Undesired effects of steroids during pregnancy. J Matern Fetal Neonatal Med. 2004;16 Suppl 2:5-7.
24. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18:844-7.
25. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020;18:1324-9.
26. Bookstein Peretz S, Regev N, Novick L, Nachshol M, Goffer E, Ben-David A, et al. Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine. Ultrasound Obstet Gynecol. 2021;58:450-6.
27. Rasmussen SA, Jamieson DJ. COVID-19 and Pregnancy. Infect Dis Clin North Am. 2022;36:423-33.

Turk J Intensive Care 2024;22:170-9
DOI: 10.4274/tybd.galenos.2023.04909

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Radiation Safety Practices and Improvement of Knowledge Level in Intensive Care Unit Working Conditions: An Experimental Study on Nurses

Yoğun Bakım Ünitesi Çalışma Koşullarında Radyasyon Güvenliği Uygulamaları ve Bilgi Düzeyinin Geliştirilmesi: Hemşireler Üzerinde Deneysel Bir Çalışma

Received/Geliş Tarihi : 09.07.2023
Accepted/Kabul Tarihi : 17.08.2023

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ABSTRACT *Objective:* The aim of this study is to evaluate the effectiveness of radiation safety training developed for nurses working in intensive care units (ICUs).
Materials and Methods: This study was carried out on a total of 144 nurses working in the neonatal and pediatric ICUs of two different hospitals. The radiation safety training developed for the nurses of the ICU for the nurses in the training group (n=62) was given face-to-face in 7 sessions in groups of 8-10 people. The data were collected through the descriptive information form and the radiation safety information form, as well as the observations made by the researcher.
Results: As a result of the observations, the development of protective behaviors against ionized radiation of the nurses in the training group increased significantly both compared to the control group and pre-training case ($p<0.05$). It was determined that score averages of radiation safety knowledge levels of intensive care nurses in training group increased significantly. In the last observations, it was determined that there was a significant decrease in the use of some personal protective equipment by the nurses in the training group ($p<0.05$). Over time, a limited decrease was observed in the radiation safety knowledge levels of the nurses in the training group.
Conclusion: It has been concluded that the radiation safety training applied within the scope of the research is an effective method in ensuring the radiation safety of the nurses working in the ICUs. Correct safety practices of employees in ICU units are expected to have a positive impact on patient and employee safety.
Keywords: Nursing, radiation, intensive care unit, training, protection

ÖZ *Amaç:* Bu çalışmanın amacı, yoğun bakım ünitelerinde (YBÜ) çalışan hemşirelere yönelik geliştirilen radyasyon güvenliği eğitiminin etkinliğini değerlendirmektir.
Gereç ve Yöntem: Bu çalışma iki farklı hastanenin yenidoğan ve çocuk YBÜ'lerinde çalışan toplam 144 hemşire üzerinde gerçekleştirilmiştir. Eğitim grubundaki hemşirelere (n=62) yoğun bakım hemşireleri için geliştirilen radyasyon güvenliği eğitimi 8-10 kişilik gruplar halinde 7 oturumda yüz yüze verildi. Veriler tanımlayıcı bilgi formu ve radyasyon güvenliği bilgi formu ile araştırmacı tarafından yapılan gözlemler aracılığıyla toplanmıştır.
Bulgular: Gözlemler sonucunda eğitim grubundaki hemşirelerin iyonize radyasyona karşı koruyucu davranış geliştirmeleri hem kontrol grubuna hem de eğitim öncesi duruma göre anlamlı olarak artmıştır ($p<0,05$). Eğitim grubundaki yoğun bakım hemşirelerinin radyasyon güvenliği bilgi düzeylerinin puan ortalamalarının önemli düzeyde belirlendi. Son gözlemlerde eğitim grubundaki hemşirelerin bazı kişisel koruyucu ekipman kullanımlarında anlamlı azalma olduğu belirlendi ($p<0,05$). Eğitim grubundaki hemşirelerin radyasyon güvenliği bilgi düzeylerinde zaman içinde sınırlı bir düşüş gözlendi.
Sonuç: Araştırma kapsamında uygulanan radyasyon güvenliği eğitiminin YBÜ'lerinde çalışan hemşirelerin radyasyon güvenliğinin sağlanmasında etkili bir yöntem olduğu sonucuna varılmıştır. YBÜ'ler de çalışanların doğru radyasyon güvenlik uygulamalarına sahip olmalarının çalışan sağlığı ve hasta güvenliğine olumlu katkı sunması beklenmektedir.
Anahtar Kelimeler: Hemşirelik, radyasyon, yoğun bakım ünitesi, eğitim, korunma

Introduction

Today, it is known that the greatest amount of artificial ionize radiation (IR) exposure is caused by medical irradiation source (1). For this reason, many protection measures have been developed in order to protect the patients and health workers from risks and dangers stemming from IR exposure (2,3). Although annual permissible dose limits are determined for workers of medical irradiation, genetic disorders and carcinogenesis can emerge in people in low dose IR exposure for a long time (4). There are studies about the fact that many harmful effects such as breast cancer (5) and cataract formation in the eye (6) etc. are seen in health workers, who were exposed to low dose IR for a long time compared to normal population (2,7).

There are many studies showing that though IR has negative effects on the health of workers, health workers have insufficient information, attitudes and behaviors in protection from radiation (8,9). In a study conducted on cardiologists, it is established that cardiologists had insufficient information about protection from radiation (10) and the health workers of urology service did not sufficiently use personal protection equipment (PPE) (lead apron, goggles) during scopy investigation (11).

The nurses undertake responsibilities in many areas with IR such as intensive care units (ICUs), operating theaters etc. During care process, IR exposure due to their profession can be a significant occupational health problem for nurses because they are the health workers closest to the patients. When the studies are investigated, it is seen that the nurses have insufficient knowledge level about radiation safety compared to the other health workers (12,13). In some studies conducted specifically for nurses, it has been reported that the nurses working in the nuclear medical department do not know the basic principles of protection from radiation (14); and that the oncology nurses have not developed expected positive behaviors after radiation safety education has been performed (15).

Since the patients of ICU are not mobilized, X-ray shooting processes are carried out with mobile X-ray devices, which causes the ICU health workers to be exposed to IR. In their study carried out to measure the radiation that the doctors and nurses working in ICUs were exposed to, Xie et al. (16) stated that the doctors and nurses were exposed to radiation at a rate of 0.99 and 0.88 milisievert (msv), respectively; and this exposure showed a positive correlation with the working hours and the size of the service. When the insufficient knowledge level about radiation safety with the nurses are considered, it can be understood that this case is an important issue affecting the safety of ICU nurses and patients.

In X-ray radiographies conducted in ICU, it is in the responsibility of the nurse that the nurse accompany the patient and the taking care of the patient should not be interrupted. One study reported that some accidental extubations occurred when nurses tried to remove the patient from the machine during radiography (17). Likewise, it is possible that many tools such as ureteral catheter, central venous catheter and nasogastric catheter mounted on the patients for invasive attempts may be accidentially removed. Therefore, even during radiography, the nurses cannot go away from the environment because of patient's safety; and they can be exposed to IR more. In the literature, although there are trainings on radiation safety for nurses, there is not any standard application of this (18). With this study, after considering the working conditions of the nurses of ICUs, it is aimed to evaluate the effect of radiation safety training on the knowledge, attitude and behaviors of nurses. In accordance with this aim, the questions of the investigation are determined as follows:

1. Has radiation safety training applied to ICU nurses been effective on their radiation protection behaviors?

2. Has radiation safety education applied to ICU nurses been effective on their radiation protection knowledge and attitudes?

Materials and Methods

Trial Design

This study has been designed in quasi experimental and implemented. During the experimental design with the control group, one follow-up was performed before the intervention, and two follow-ups were performed after it. Radiation protection behaviors and knowledge levels were evaluated at one-month intervals after the intervention. Following all follow-ups, questionnaires, and observations were conducted before interventions were implemented.

Participant

The population of the study consists of nurses working in pediatrics and newborn ICUs of two hospitals which have similar properties. Within the context of the study, the training group and the control group were made up

with nurses of two different independent hospitals in order that the training can be evaluated impartially; hence, it was established that the health workers would not be affected from each other. The criteria to be included in the study are working as nurses in the pediatrics and neonatal ICUs of hospitals and being willing to participate in the study. On the other hand, the exclusion criteria of the study were determined as leaving the hospital during the process while the research was in progress (go on a leave, change the clinic etc.) and not accepting to participate in the study. The participants were appointed in 2 equal groups as training (75) and control group (75). During the process of the study, due to the leaving of some participants, the study was ended with total participants of 144 as 62 people in each the training and control groups (Figure 1).

Control group: The control group were not provided with radiation safety training prepared within the context of this study. The informative posters related with radiation safety were hung visible places of workplaces.

Training group: In the study, radiation safety training program developed specific to the ICU nurses were applied as a means of intervention to ICU nurses working in the hospital specified as training group. In the preparation of these training materials, International Radiological Protection Commission (ICRP) reports and updated literature were taken as bases (3,7,14,16,18-22). The aim of the training program is to teach ICU nurses to apply the basic standards of radiation protection by providing them with patient safety yet without hindering their services. The trainings made face to face were applied in practical terms with groups consisting 8-10 persons. In total six sessions, the intervention of the nurses in the training group was completed. The content and learning outputs of training are shown in Table 1.

Outcome Measures

Within the context of the study, the data were collected through face-to-face survey and questionnaire. Before starting the study, pretests were applied; after the homogeneity of the training and control groups was examined, intervention phase was started. The data in the study were collected by using introductory information form, radiation safety information level form and observation form.

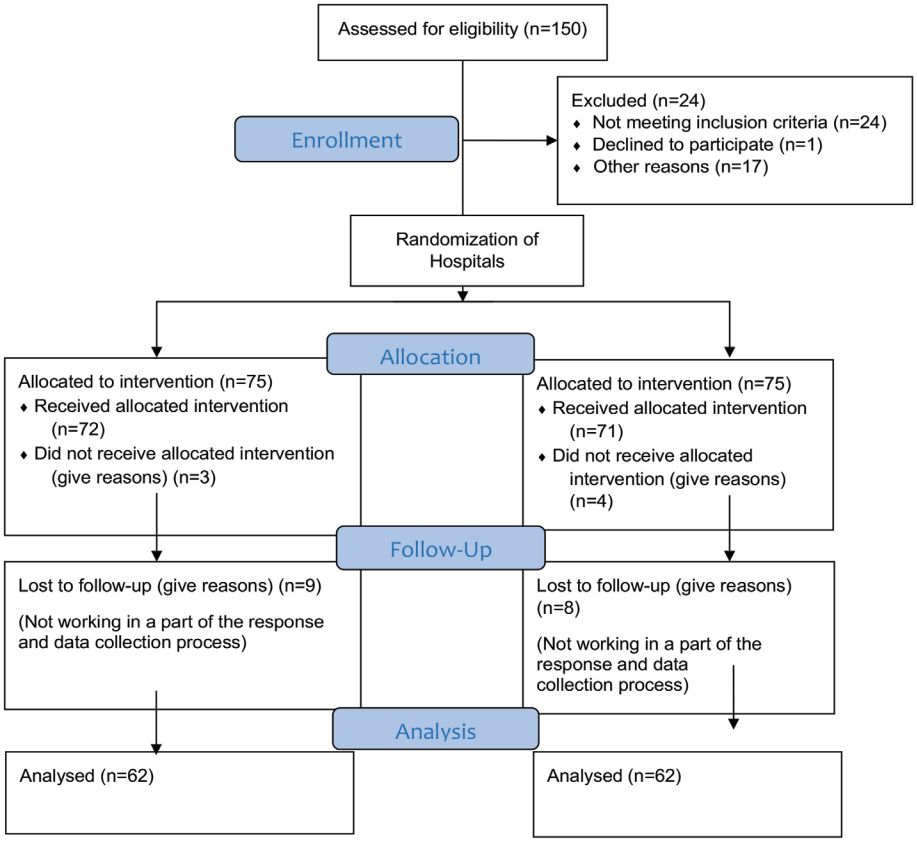

Figure 1. Consort flow diagram

Table 1. Radiation safety training program

Section	Content	Learning outcomes
Preparation and introducing	General information about issue	Making the importance of radiation safety understood and raising awareness.
Radiation safety	Definition of radiation, its sources, its biological effects, its dose unit s and the sensitivity of tissues to radiation	Knowing the difference between ionized and non-ionized radiation. Knowing the effects of radiation.
Radiated areas in hospitals	Controlled and supervised radiation areas	Knowing which areas of hospital need protection from radiation.
Basic principles to protect from radiation	Time, distance, barrier	Actions needed to be taken in radiated areas.
Protection from radiation in ICUs	Dose restriction in ICUs application of basic standards to protect from radiation in ICUs using personal protection equipment	Protection from radiation in working conditions of ICUs and providing the safety of the patients.
Questions and guidance	Institutions to obtain information on the subject.	

ICU: Intensive care unit

Introductory information form: Introductory information form consists of total 14 questions related with the working conditions of ICUs such as working years, number of shifts per month, besides sociodemographic data about the participants such as age, gender, civil status, and education level.

Radiation safety information level form: The researchers prepared it to assess nurses' radiation safety knowledge. The form was prepared based on the ICRP (22) and International Atomic Energy Agency (23) reports as well as current literature (8-16). It consists of three sections as information level about radiosensitive organs and tissues (sensitive-KL), knowledge level about the biological effects of IR (effect-KL), and knowledge level about radiological examinations having IR (examination-KL).

I. Sensitivity-KL: It is the score type obtained through truly knowing whether the organs and tissues (thyroid, blood tissue etc.) of different parts of human body are sensitive to radiation or not. The smallest score and the highest score are taken as zero and eight, respectively.

II. Effect-KL: It is the score type obtained through truly knowing the biological effects (cancer, infertility etc.) possible to occur with regard to long time low IR dose exposure. The smallest score and the highest score are taken as zero and six, respectively.

III. Examination-KL: It is the score type obtained through knowing the radiological examinations, used in different parts of the hospital, and in which IR is used and not used (MR, X-ray etc.). The smallest score and the highest score are taken as zero and twelve, respectively.

Observation form: In creating the observation form, updated literature (17-20) and guidance (22,23) were taken as bases; and the behaviors necessary to be conducted to protect from radiation in ICUs were investigated in five items. The specialists whose opinions were applied are of academician and radiology specialist doctor working at a university and at the radiation safety committee of a research hospital, respectively. Each item was scored in 5 Likert scale by the specialists and they were analyzed with the help of W analysis. At the end of the analysis, it was concluded that the scoring of each specialist were found not to be different from each other statistically (Kendall W =0.167; p=0.255); and there was a harmony between them. The observation items:

- Going away from the environment during irradiation,
- Using lead screen,
- Wearing lead apron during radiation,
- Using additional protectors during radiation (thyroid protector, goggles etc.),
- After radiological examination, ventilating the environment one stays.

Determination and Application of Observation Numbers

Defined protective behaviors were marked as "done" and "did not do" on the observation form. Daily records were attained by the researcher through observing the records of present cameras of the hospital.

The epi info Statcalc package program was used to determine the number of follow-ups. The number of monthly radiological examinations was recorded as 1,152. For this reason, it was concluded that at least 33 follow-ups were required for each group with a 5% margin of error in a two-group study design with a confidence interval of 80% before the training. In order to prevent duplicate observation of participants and to increase the confidence interval, all nurses included in the study were observed once in each follow-up. As a result, a total of 144 nurses included in the study were observed once in each follow-up.

Sample Size

G-Power 3.1.9.2 program was used in the study in order to determine the size of sample. In line with the reference, results obtained with literature scanning carried out before the study, while the effect size was 0.8 and alpha: 0.05, the sample to be taken for each group was obtained as 47 people and 94 people in total. Considering such cases as going on a leave during the study, withdrawing from the study and nurses changing their departments, all participants in training and control groups were included in the study. The data collected at the end of the study were obtained as alpha, 0.05 and total sample size, 124, while effect size, 0.99, as a result of post-hoc analysis.

Statistical Analysis

The data obtained as a result of the study were analyzed in the IBM SPSS 22 package program (Statistical Package for the Social Sciences). Frequency, percent arithmetic mean, minimum-maximum values and median were used from descriptive statistical methods. The paired simple t-test was used to evaluate the quantitative dependent variables showing normal distribution in the training and control groups. Chi-square test was used to evaluate categorical variables between groups. The McNeamer test was used to determine how the training and control groups changed during the intervention process. It was considered significant since the materiality value (p-value) was below 0.05.

Ethical Approval

Before starting the study, the necessary permission was obtained from Koç University Social Sciences Research Ethic Committee with decision number 2017.102.IRB3.055 (date: 22.06.2017). To conduct the study, the necessary permissions were obtained from the institutions to which ICUs are connected. The participants were informed in written and orally and their consent confirmations were obtained. The radiation safety training applied to the training group was later applied to control group as well.

Results

Sociodemographic and working features of the nurses: It was determined that the age average of the groups accepted in the study were training, 28.22±4.86 and control, 29.01±4.39; and that no statistically significant difference was found in age (p=0.345), gender (p=0.389), civil status (p=0.072) and education levels (p=0.931), total job experience (p=0.358) and their working types (p=0.075) and working years (p=0.358) in ICUs (Table 2).

In the pre-tests, no statistically significant difference was found in the behaviors of training and control groups in moving away from the environment (p=0.427), using protective shield (p=0.500), wearing lead apron (p=0.120), using additional protective (p=0.500) and ambient ventilation (p=0.320) that were observed (Table 3). The most frequent behavior observed in the nurses during radiological examination was moving away from the place where medical examination is done (training: 58.1%, control: 61.3%). Using protective shield (training: 11.3%, control: 12.9%) and using lead apron (training: 14.5%, control: 6.5%) and using additional protectors (training: 3.2%, control: 4.8%) and ambient ventilation (training: 6.5%, control: 4.8%) behaviors were found to be rarely applied radiation protection behaviors.

Pre-training radiation safety knowledge scores; sensitive-KL (training: 2.72±1.10; control: 2.80±1.08), effect-KL (training: 4.25±1.62; control: 4.46±1.71) scores were found to be at similar levels (Figure 2).

It was determined that the socio-demographic, working, radiation protection behavior and knowledge levels of the groups had similar characteristics (Table 2, 3, Figure 2).

Evaluation of radiation protection behaviors and knowledge scores of groups: The behavior of moving away the environment after the intervention was significantly higher in the control group than in the training group in the second and third follow-ups (p=0.000; p=0.012). On the contrary, it was observed that there was a significant difference in favor of the training group in other radiation protection behaviors such as using a radiation shield, wearing a lead apron, using additional protective equipment, and ambient ventilation (p=0.000).

It is seen that the score averages of radiation knowledge level (sensitivity-KL, examination-KL, effect-KL) have been given correct answers at similar levels in both groups, which is shown in Figure 2.

Evaluation of training group radiation protection behaviors and knowledge scores: In the evaluation of the radiation protection behaviors observed in each follow-up in the training group, no statistically significant change was observed in the protection behavior moving away from the environment (Table 4). There were 27 nurses who showed moving away behavior in the first and second follow-ups, 23 nurses in the first and third follow-ups, and 31 nurses in the first and third follow-ups (Table 4). Statistically significant increases were observed in the other four protective behaviors compared

Table 2. Sociodemographic characteristics of nurses

Introductory features		Training group	Control group	Examination values
Age	$\bar{x}$ ± SD (year)	28.22±4.86	29.01±4.39	t=-0.949 p=0.345
Working duration in ICU	$\bar{x}$ ± SD (year)	5.17±4.50	6.51±3.77	t=-1.795 p=0.075
Total working years	$\bar{x}$ ± SD (year)	3.41±3.01	3.96±3.57	t=-0.923 p=0.358
Gender	Female, n (%)	33 (53.2%)	36 (58.1%)	x^2=0.213 p=0389
	Male, n (%)	29 (46.8%)	26 (41.9%)	
Civil status	Married, n (%)	32 (51.6%)	41 (66.1%)	x^2=2.698 p=0.072
	Single, n (%)	30 (48.4%)	21 (33.9%)	
Education status	High school graduate, n (%)	9 (14.6%)	10 (16.1%)	x^2=0.444 p=0.931
	University graduate, n (%)	53 (85.6%)	52 (83.9%)	
Having shifts	Yes, n (%)	55 (88.7%)	60 (96.8%)	x^2=2.995 p=0.082
	No, n (%)	7 (11.3%)	2 (3.2%)	

χ^2: Chi-square test, t*: independent simple t-test, p: significant value, ICU: intensive care unit, $\bar{x}$ ± SD: mean ± standard deviation

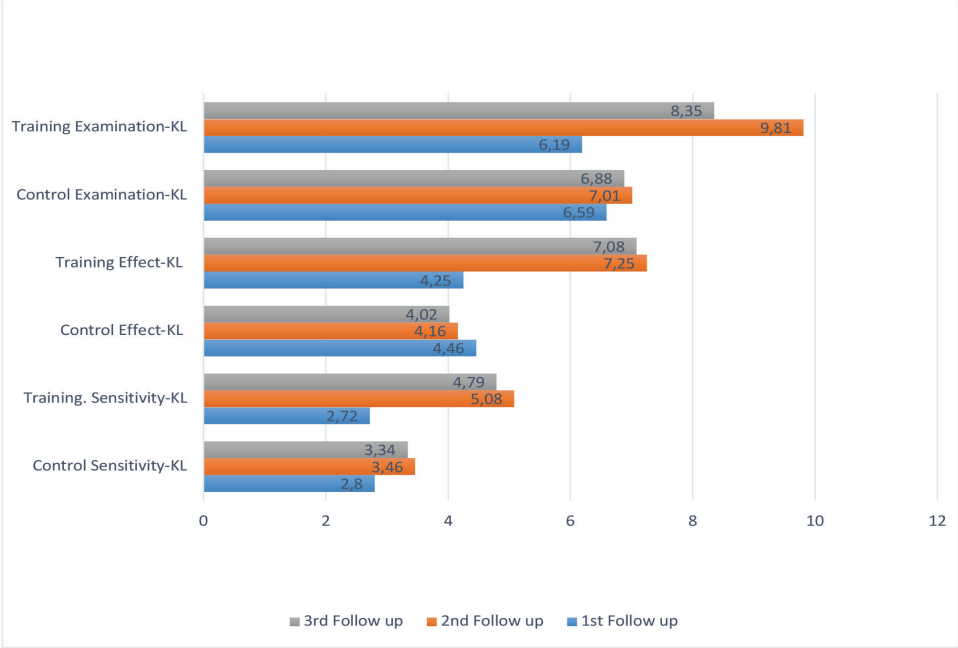

Figure 2. Evaluation of knowledge score averages in training and control groups

to the pre-intervention status (p=0.000). In the ICU, there were 51 people, who did not use protective shields during the radiological examination before the intervention, but there were 47 people, who applied it in the second and third follow-up after the intervention. Similarly, of 51 nurses, who did not use lead aprons, 43 nurses started using lead

Table 3. Investigation of radiation protection behaviors and radiation knowledge scores of training and control groups

Radiationprotection behaviors	Groups	1st Follow-up		2nd Follow-up		3rd Follow-up	
		Yes (n/%)	No (n/%)	Yes (n/%)	No (n/%)	Yes (n/%)	No (n/%)
Moving away the environment	Training	36/58.1%	26/41.9%	43/69.4%	19/30.6%	41/66.1%	21/33.9%
	Control	38/61.3%	24/38.7%	60/96.8%	2/3.2%	53/85.5%	9/14.5%
Examination values		x²*=0.134 p=0.427		x²*=14.676 p=0.000		x²*=6.332 p=0.012	
Using shield	Training	7/11.3%	55/88.7%	57/91.9%	5/8.1%	53/85.5%	9/14.5%
	Control	8/12.9%	54/87.1%	33/53.2%	29/46.8%	29/46.8%	33/53.2%
Examination values		x²*=0.076 p=0.500		x²*=21.437 p=0.000		x²*=20.739 p=0.000	
Wearing lead apron	Training	9/14.5%	53/83.5%	59/95.2%	3/4.8%	51/82.3%	11/17.7%
	Control	4/6.5%	58/93.5%	11/17.7%	51/82.3%	10/16.1%	52/83.9%
Examination values		x²*=2.148 p=0.120		x²*=72.465 p=0.000		x²*=54.240 p=0.000	
Using additional protectives	Training	2/3.2%	60/96.8%	54/87.1%	8/12.6%	46/74.2%	16/25.8%
	Control	3/4.8%	59/95.2%	11/17.7%	51/82.3%	7/11.2%	55/88.7%
Examination values		x²*=0.208 p=0.500		x²*=59.785 p=0.000		x²*=50.121 p=0.000	
Ventilating the environment	Training	4/6.5%	58/93.5%	57/91.9%	5/8.1%	47/75.8%	15/24.2%
	Control	3/4.8%	59/95.2%	13/21.0%	49/79.0%	11/17.7%	51/82.3%
Examination values		x²*=0.151 p=0.320		x²*=63.509 p=0.000		x²*=63.509 p=0.000	

x²: Chi-square test, p: significant value

Table 4. Examination of the training group's radiation protection behaviors and knowledge scores

Observed behaviors		1st & 2nd Follow-up		1st & 3rd Follow-up		2nd & 3rd Follow-up	
		Yes	No	Yes	No	Yes	No
Moving away the environment	Yes	27	9	23	13	31	12
	No	16	10	18	8	10	9
Examination values		x²*=0.412 p=0.230		x²*=0.516 p=0.472		x²*=0.674 p=0.832	
Using protective shield	Yes	6	1	6	1	52	5
	No	51	4	47	8	1	4
Examination values		x²*=46.173 p=0.000		x²*=42.188 p=0.000		x²*=0.245 p=0.219	
Using lead apron	Yes	8	1	8	1	51	8
	No	51	2	43	10	0	3
Examination values		x²*=44.290 p=0.0000		x²*=46.173 p=0.000		x²*=38.205 p=0.000	
Using additional protectives	Yes	1	1	1	1	46	8
	No	53	7	45	15	0	8
Examination values		x²*=4.429 p=0.000		x²*=48.167 p=0.000		x²*=40.196 p=0.000	
Ventilating the environment	Yes	3	0	3	0	47	10
	No	54	5	44	15	0	5
Examination values		x²*=4.429 p=0.000		x²*=52.019 p=0.000		x²*=42.023 p=0.000	

x²*: McNeamer test, p: significant value

aprons at the last follow-up after the intervention. There were 53 nurses, who did not use an additional PPE before the intervention, they used it at the first follow-up after the intervention, and 45 nurses used it at the last follow-up. Fifty four nurses, who did not ventilate the environment after the radiological examination, started to ventilate the environment in the first follow-up (Table 4). In the second and third follow ups made with a one month interval after the training, no statistically significant change was observed in the behavior of moving away from the environment and using protective shields (p=0.832; p=0.219). However, at the last follow-up (3rd follow-up), it was determined that there were significant decreases in wearing lead apron, additional PPE use and ambient ventilation protection behaviors. It was observed that after the intervention, 8 people using lead aprons, 8 people using additional PPE, and 10 people who ventilated the environment after radiological examination in the first follow-up did not apply these protective behaviors in the last follow-up (Table 4).

As shown in the graph, the radiation knowledge level score averages show remarkable rises, while these rises in control group are limited. As a matter of fact, remarkable score rises are observed in the training group at the first sight. Although some slight decreases are observed in sensitivity-KL, effect-KL scores in the last observation, this is more obvious in examination-KL score average (Figure 2).

Discussion

In order to prevent the effects of long-term low-dose IR exposure, radiation safety training developed specifically for ICU nurses was applied within the scope of the study. For this purpose, in the pre-tests (1st follow-up) in the experimental design conducted in two different hospitals, it was observed that the study groups had insufficient knowledge and behavior in radiation protection (Table 3, 4). When the protective behaviors of the training group during the radiological examination in the pre-training ICUs were examined, it was determined that the most protective behavior of the nurses was going away from the environment and they were insufficient in the use of PPE (Table 3). After the training, while no significant variation was observed in the doing away protection behavior in the training group, a significant increase was found in other protective behaviors (Table 4). Going away from the beam source is one of the basic principles of radiation protection and the square of the distance to the beam source is inversely proportional to the amount of radiation received (23). In this case, sufficient distance from the beam source will be effective in protection. However, it is not always possible to implement this situation in ICU working conditions. Divatia and Bhowmick (17), in their study in ICUs, reported that when nurses go out of the ICU during imaging, patients connected to the mechanical ventilation device may leave the device, and this will cause complications such as mortality that may develop due to hypoxia and an increase in the length of stay in the hospital. In addition, another problem is how far going away from the beam source will provide protection. When the sources are examined, values between two and six meters are given at the point of how far going away from the beam source should be (24,25). An important reason for this situation is that the position of the person changes relative to the beam source and the variability of the applied radiation dose. In ICUs, going away from the beam source may cause various accidents and complications in the patient, and it is not always a safe method of protection by itself, due to the ambiguity about how far away the person should be. In the second and third observations after the training, it was determined that while the going away and protection behavior was significantly higher in the control group (Table 4), there was a significant increase in other protective behaviors in the training group compared to the control group (Table 3). This situation shows that after the training, the use of PPE gained importance in the protective behaviors of the training group rather than going away from the environment.

In the last follow-up (3rd follow-up) in the training group after the radiation safety-training program was implemented, a significant decrease was observed in the protective behavior of additional protective, lead apron and ambient ventilation (Table 4). Although the radiation safety training given to the training group significantly increased the use of PPE, it is clear that there was a partial decrease in the use of PPE over time. In the literature, many reasons such as not adopting protective behaviors, personal beliefs and sensitivities are shown as the reasons for the decrease in the protective behaviors of health workers about occupational health and safety over time (26-28). In addition, the availability of PPE is an important factor affecting its use 15. When examined in terms of radiation protection, Flôr and Gelbcke (29), in their study on nurses working in the cardiac catheterization unit, found that the nurses did not use the PPE equipment used in radiation protection because they found it heavy and uncomfortable. In another study conducted on nurses in neonatal ICUs, it was stated that the use of PPE was closely related to employee-related

risks (30). Except for this, it is thought that this causes a decrease in the risk perception of time-dependent nurses and a decrease in the use of PPE over time, due to the fact that the use of PPE is disturbing and heavy. The knowledge levels of intensive care nurses on radiation protection were examined in three sections where basic radiation safety issues were questioned. In the evaluation made in the study groups before the training, it was observed that their knowledge about IR was quite limited (Table 3,4). Looking at the studies in the literature, there are studies showing that healthcare professionals from different professions such as doctors, dentists, and radiology technicians do not have sufficient knowledge about radiation safety (12,31,32). In a study on intensive care nurses, it was stated that 62.7% of the nurses had little knowledge about radiation safety, and the remaining 37.3% had moderate knowledge (33). In all these studies, different levels of information deficiencies have been identified due to different measurement tools. However, there are also studies reporting that nurses are more inadequate than some healthcare professionals such as doctors and radiology technicians (12,13,34). Since the level of knowledge about radiation protection is positively correlated with radiation protection behaviors (11), obtaining the right information is also an important requirement for developing correct behavior about radiation safety.

After the radiation safety training, it was determined that the level of knowledge about radiation safety among the nurses increased in the measurements made both in the training group and compared to the control group (Figure 2). In similar studies conducted, it is shown that radiation safety training provides increased knowledge at different levels (15,19). For this reason, it is an expected result consistent with literature that there is an increase in IR knowledge level in training group. However, in the last measurement, it is seen that there is a limited decrease in the knowledge level, which is more obvious in examination-KL knowledge average (Figure 1). In the third observation, there is a parallel situation in the decrease of protection behaviours and knowledge level of ICU nurses (Table 3,4). In their study, Morishima et al. (20) stated that the level of radiation protection knowledge of cardiology nurses decreased over time. In line with these data, which we have reached a similar conclusion with the literature, it has been concluded that it is an important necessity to conduct trainings periodically in order to perpetuate the increasing level of knowledge.

If the last follow-up was carried out three or six months after radiation safety training, this would have given more information about the persistence of radiation protection behaviors. However, the last follow-up could be made only one month after the second follow-up due to the frequent occurrence of situations such as leave for holiday and the nurses' change of service. In the study, since there was no measurement tool with reliability and validity in Turkish to measure the radiation knowledge level of ICU nurses, the evaluation of the radiation knowledge level was made using descriptive statistical methods and visuals.

Conclusion

The findings obtained within the scope of the study show that the radiation safety training developed for ICU nurses is an effective tool in ensuring radiation safety. However, in order to prevent the correct protection behaviors and decrease in knowledge level depending on time, the trainings should be organized periodically.

*This study was produced from the data of the Doctoral Thesis published in Koç University Health Sciences Institute Nursing Department (Thesis No: 568819).

Ethics

Ethics Committee Approval: Before starting the study, the necessary permission was obtained from Koç University Social Sciences Research Ethic Committee with decision number 2017.102.IRB3.055 (date: 22.06.2017).

Informed Consent: The participants were informed in written and orally and their consent confirmations were obtained.

Authorship Contributions

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

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

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

References

1. World Health Organization. Communicating radiation risks in paediatric imaging: Information to support health care discussions about benefit and risk. World Health Organization; 2016. p. 11-2. Available from:URL: https://www.who.int/publications/i/item/978924151034
2. Tang FR, Loganovsky K. Low dose or low dose rate ionizing radiation-induced health effect in the human. J Environ Radioact. 2018;192:32-47.
3. Vano E, Sanchez RM, Fernandez JM. Strategies to optimise occupational radiation protection in interventional cardiology using simultaneous registration of patient and staff doses. J Radiol Prot. 2018;38:1077-88.
4. Chang DS, Lasley FD, Das IJ, Mendonca MS, Dynlacht JR. Stochastic, Deterministic, and Heritable Effects (and Some Radiation Protection Basics). Basic Radiotherapy Physics and Biology. 2021:337-48.
5. Preston DL., Kitahara CM, Freedman DM, Sigurdson AJ, Simon SL, Little MP, et al. Breast cancer risk and protracted low-to-moderate dose occupational radiation exposure in the US Radiologic Technologists Cohort, 1983-2008. Br J Cancer. 2016;115:1105-12.
6. Azizova TV, Bragin EV, Hamada N, Bannikova MV. Risk of Cataract Incidence in a Cohort of Mayak PA Workers following Chronic Occupational Radiation Exposure. PLoS One. 2016;11:e0164357.
7. Baselet B, Rombouts C, Benotmane AM, Baatout S, Aerts A. Cardiovascular diseases related to ionizing radiation: The risk of low-dose exposure (Review). Int J Mol Med. 2016;38:1623-41.
8. Shabani F, Hasanzadeh H, Emadi A, Mirmohammadkhani M, Bitarafan-AR, Abedelahi A, et al. Radiation Protection Knowledge, Attitude, and Practice (KAP) in Interventional Radiology. Oman Med J. 2018;33:141-7.
9. Ditkofsky N, Shekhani HN, Cloutier M, Chen ZN, Zhang C, Hanna TN. Ionizing Radiation Knowledge Among Emergency Department Providers. J Am Coll Radiol. 2016;13:1044-9.
10. Carpeggiani C, Kraft G, Caramella D, Semelka R, Picano E. Radioprotection (un)awareness in cardiologists, and how to improve it. Int J Cardiovasc Imaging. 2012;28:1369-74.
11. Jindal T. The Knowledge of Radiation and the Attitude Towards Radio-Protection among Urology Residents in India. J Clin Diagn Res. 2015;9:JC08-11.
12. Balsak H, Güneş G, Ulutaşdemir N. Knowledge, Attitude and Behavior of Radiology Professionals about the Harmful Effects of Radiation Which is Used for Diagnosis. 2016;2:31-51.
13. Jacob K, Vivian G, Steel JR. X-ray dose training: are we exposed to enough? Clin Radiol. 2004;59:928-34.
14. Alotaibi M, Saeed R. Radiology nurses' awareness of radiation. Elsevier. 2006;25:7-12.
15. Dauer LT, Kelvin JF, Horan CL, st. Germain J. Evaluating the effectiveness of a radiation safety training intervention for oncology nurses: A pretest - intervention - posttest study. BMC Med Educ. 2006;6:32.
16. Xie Z, Liao X, Kang Y, Zhang J, Jia L. Radiation Exposure to Staff in Intensive Care Unit with Portable CT Scanner. Biomed Res Int. 2016;2016:5656480.
17. Divatia JV, Bhowmick K. Complications of endotracheal intubation and other airway management procedures. Indian J Anaesth. 2005;49:308-18.
18. Ohno K, Kaori T. Effective education in radiation safety for nurses. Radiat Prot Dosimetry. 2011;147:343-5.
19. Kim O, Kim MS, Jang HJ, Lee H, Kang Y, Pang Y, et al. Radiation safety education and compliance with safety procedures-The Korea Nurses' Health Study. J Clin Nurs. 2018;27:2650-60.
20. Morishima Y, Chida K, Katahira Y, Seto H, Chiba H, Tabayashi K. Need for radiation safety education for interventional cardiology staff, especially nurses. Acta Cardiol. 2016;71:151-5.
21. Needham G, Grimshaw J. Guidelines for healthcare professionals who prescribe imaging investigations involving ionising radiation. European Commission, 2008. p.383-98. Available from: URL: https://www.sergas.es/docs/profesional/boapraticaclinica/rp118.pdf
22. Valentin J. The 2007 recommendations of the International Commission on Radiological Protection. Ann ICRP. 2007. p.103. Available from: URL: https://icrp.org/docs/ICRP_Publication_103-Annals_of_the_ICRP_37(2-4)-Free_extract.pdf
23. Bennett GF. International basic safety standards for protection against ionizing radiation of and for the safety of radiation sources. Journal of Hazardous Materials. 1996;45:282.
24. McGovern PM, Vesley D, Kochevar L, Gershon RRM, Rhame FS, Anderson E. Factors affecting universal precautions compliance. J Bus Psychol. 2000;15:149-61.
25. Menzel HG, Harrison J. Effective dose: a radiation protection quantity. Ann ICRP. 2012;41:117-23.
26. Friis RH. Occupational Health and Safety for the 21st Century. Burlington: Jones & Bartlett Publishers; 2014.
27. Kang J, O'Donnell JM, Colaianne B, Bircher N, Ren D, Smith KJ. Use of personal protective equipment among health care personnel: results of clinical observations and simulations. Am J Infect Control. 2017;45:17-23.
28. Levin PF. Test of the Fishbein and Ajzen models as predictors of health care workers' glove use. ResNurs Health. 1999;22:295-307.
29. Flôr R de C, Gelbcke FL. Radiation protection and the attitude of nursing staff in a cardiac catherization laboratory. Texto & Contexto-Enfermagem. 2013;22:416-22.
30. Tanrıverdi H, Akova O, Latifoğlu NT. Yenidoğan Yoğun Bakım Ünitelerinde İş Kazaları Riskleri Ve Nedenlerine Yönelik Bir Araştırma. Business & Management Studies: An International Journal. 2015;3:234-60.
31. Ayatollahi J, Ayatollahi F, Ardekani AM. Occupational hazards to dental staff. Dent Res J (Isfahan). 2012;9:2.
32. Ünal ES, Geliş K, Baykan P. Investigation of awareness levels about the radiation safety of personnel working in the imaging units of the hospitals in Agri, Turkey. J Radiat Res Appl Sci. 2018;11:111-5.
33. Azimi H, Majd Teimouri Z, Mousavi S, Kazem Nezhad Leyli E, Jafaraghaee F. Individual protection adopted by ICU nurses against radiation and its related factors. J Holist Nurs. 2018;28:18-25.
34. Huda W. Radiation doses and risks in chest computed tomography examinations. Proc Am Thorac Soc. 2007;4:316-20.

Turk J Intensive Care 2024;22:180-9
DOI: 10.4274/tybd.galenos.2023.48344

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Investigation of Opinions of Nurses Working in Surgical Intensive Care Units about the Participation of Family Members in the Care of Patients during the Dying Process: A Cross-sectional Design

Cerrahi Yoğun Bakım Ünitelerinde Çalışan Hemşirelerin Ölüm Sürecindeki Hastaların Bakımına Aile Üyelerinin Katılmaları Konusunda Görüşlerinin İncelenmesi: Kesitsel Bir Çalışma

Received/Geliş Tarihi : 19.01.2023
Accepted/Kabul Tarihi : 21.08.2023

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ABSTRACT *Objective:* This study was conducted to determine the opinions of nurses working in surgical intensive care units (S-ICU) about the participation of family members (FM) in the care of patients during the dying process.
Materials and Methods: Ethical approval was obtained before starting the research. The study was conducted in descriptive type with 81 nurses working in the S-ICU of a training and research hospital between 15 March and 15 April 2022. The data were collected through the descriptive information form and the nurse's opinion determination form created by the researcher. STROBE checklist was used in reporting the research. A $p<0.05$ value was accepted for statistical significance.
Results: The mean age of the nurses participating in the study was 32.39±5.87 years, and the duration of working experience in S-ICUs was 5.69±5.76 years. The rate of nurses wanting the FM of patients in the dying process to participate in the patient care in the intensive care unit is 26%, the rate of not wanting is 57%, and the rate of undecided is 17%. 72.8% of the nurses think that the participation of FM in care is beneficial for the patients, while 27.2% think that it is harmful. It was determined that nurses with working experience had a higher support rate in cases where FMs participated in the care of patients in the dying process ($p=0.010$) ($p<0.05$).
Conclusion: Although nurses working in S-ICUs think that the participation of FM in the care of patients in the dying process will be beneficial for patients, the rate of support is low.
Keywords: Patient in the dying process, end of life care, good death, nursing, surgical intensive care

ÖZ *Amaç:* Bu çalışma cerrahi yoğun bakım ünitesinde (C-YBÜ) çalışan hemşirelerin, ölüm sürecindeki hastaların bakımına aile üyelerinin (AÜ) katılması konusundaki görüşlerini belirlemek amacıyla yapıldı.
Gereç ve Yöntem: Araştırmaya başlamadan önce etik onay alındı. Araştırma 15 Mart ve 15 Nisan 2022 tarihleri arasında bir eğitim ve araştırma hastanesinin C-YBÜ'de çalışan 81 hemşire ile tanımlayıcı türde yapıldı. Veriler araştırmacı tarafından oluşturulan, tanıtıcı bilgiler formu ve hemşire görüşleri belirleme formu aracılığı ile toplandı. Araştırmanın raporlanmasında STROBE kontrol listesi kullanıldı. İstatistiksel anlamlılık için $p<0,05$ değeri kabul edildi.
Bulgular: Çalışmaya katılan hemşirelerin yaş ortalaması 32,39±5,87, C-YBÜ'lerde çalışma deneyimi 5,69±5,76 yıldır. Ölüm sürecindeki hastaların AÜ'lerin yoğun bakımda bakıma katılmasını isteme oranı %26, istememe oranı %57, kararsızların oranı %17'dir. Hemşirelerin %72,8'i AÜ'lerin bakıma katılmasının hastalar için yararlı, %27,2'si ise zararlı olduğu görüşüne sahiptir. Ölüm sürecindeki hastaların bakımına AÜ'lerin katıldığı durumlarda çalışma deneyimine sahip hemşirelerin, destekleme oranı daha yüksek olduğu belirlendi ($p=0,010$) ($p<0,05$).
Sonuç: C-YBÜ'lerde çalışan hemşirelerin ölüm sürecindeki hastaların bakımına AÜ'lerin katılımının hastalar için yararlı olacağını düşünmelerine rağmen destekleme oranı düşüktür.
Anahtar Kelimeler: Ölüm sürecindeki hasta, yaşam sonu bakımı, iyi ölüm, hemşirelik, cerrahi yoğun bakım

Introduction

Death is a common phenomenon when providing comprehensive care to critically ill patients in surgical intensive care units (S-ICU) (1). Presence of family at the time of death (PFTD); is to maintain physical and psychosocial support by a representative, determined by the patient's family members (FM), while standing at a point that the patient can see (2,3). This practice takes its source from family-centered care theory. Family-centered care is a concept of care that prioritizes the preferences of patients and FMs. A representative from the family takes over the autonomy of the unconscious patient. The premise of this theory is that FMs are participants rather than spectators (2). However, in a limited number of studies, it has been shown that FMs can be with patients in ICUs, touch and talk to patients, participate in their care after death, and help health professionals (4-6). Despite the increase in the recovery possibilities of patients in S-ICUs, patients in the dying process spend their last days and hours in an isolation and separate from their FM (7,8). Patients often die before having the opportunity to say goodbye to their FMs (9).

Today, while the evidence for the benefits of PFTD application is increasing (10,11), there are also reports of its problems (10-14). In a study, it was determined that FMs want to participate in the PFTD application, but experience significant stress, fear, anxiety and depression during the death decision (10). In another study, it was determined that about half of FMs (48%) did not agree with the health professionals about the withdrawal of life support (11). Various studies have defined some obstacles and limitations about the implementation of PFTD (12-15). These limitations include; unrealistic demanding attitudes of FMs, conflict between FMs, presence of cultural and spiritual needs of FMs that healthcare professionals are unfamiliar with, exclusion of FMs in the decision-making process, racial and religious discrimination, and lack of awareness of health professionals (12,14).

PFTD practice is an unrealized goal for family-centered care, and its routine application is still controversial (3,16). A recent systematic review showed that healthcare professionals do not routinely practice PFTD (3). Most frequently reported causes include the thought that this practice may be distressing, destructive and traumatic for families, performance anxiety, fear of reaction, being sued, fear of exposure to violence of team members and architectural barriers (17).

FMs of patients are not allowed to participate in the patient care during dying process in surgical ICUs except for 10-15 minutes visits for once a day, and therefore uninterrupted family support cannot be provided. In addition, FMs cannot also participate in care after death. Although nurses' opinions are one of the determinants of PFTD practice, no study was found in the literature that examines the opinion of nurses. It was evaluated that the opinions of the nurses about the PFTD practice could contribute to the identification of the obstacles and to the elimination of the lack of knowledge. In this way, care can be planned in line with the preferences of the patient and their families, and the goal of family-centered care can be achieved. The aim of this study is to determine the opinions of nurses working in S-ICUs about the participation of FM in the care of patients during the dying process.

Materials and Methods

The research is a prospective, descriptive and cross-sectional study conducted with nurses working in S-ICUs of a training and research hospital between 15 March and 15 April 2022.

Setting and Sample

The universe of the study consisted of 108 nurses working in the S-ICU of a training and research hospital. The sample size of the study was calculated with the G*Power 3.1.9.7 program. Cohen's (d) standard effect size 18 was used with the one-way hypothesis. Assuming effect size: 0.3, α error 0.05, β error 0.20, power: 80%; it was calculated that the minimum number of participants to be included in the sample should be (n=71). Fifteen nurses who did not volunteer to participate in the study, 12 nurses who were on leave at the time of the study, and 7 nurses who filled in the data collection form incompletely were excluded from the study. The research was completed with 81 nurses. In the study, 75% of the universe was reached.

Nurses, who are working in the S-ICUs of a training and research hospital and volunteered to participate in the study were included. The data of nurses who volunteered to participate in the study but wanted to leave at any stage afterward were not included in the study.

Data Collection Tools and Methods

Data collection forms were created by the researcher (3,7,16-20). in accordance with the purpose of the research as a result of examining the literature. It consists of two parts, the descriptive information form and the nurse opinion determination form. In order to determine the validity of the nurse opinion determination form, expert opinion was

obtained from 1 intensive care specialist, 2 academician nurses, and 2 clinician nurses. Experts were asked to evaluate the clarity of each statement in the data collection form and its suitability with the aims and objectives of the research (1: not appropriate, 2: somewhat appropriate, 3: quite appropriate, 4: very appropriate). The content validity index (CVI) of the data collection forms was calculated as 1 according to the opinions of the experts. Since CVI: 1 was >0.80, data collection forms were considered suitable for this study (21). A pre-application was made with ten nurses to evaluate the appropriateness of the data collection forms.

In the first part of the data collection form, there are questions about the age, gender, education level, experience in nursing, duration of experience in the S-ICU, status of encountering a patient who has died before, status of losing a relative before, status of conflicting with a patient's family member before, status of being previously sued by a family member of nurses working of nurses working at a S-ICU. The second part of the data collection form consists of 34 structured questions to determine the opinions of nurses working in S-ICUs about the participation of FMs in post-mortem care practices. Eighteen of these questions are about determining the reason for wanting the family member to participate in the care of the patient in the dying process, and 16 of them are questions about the reason for not wanting the family member to participate in the care of the patient during the dying process.

A pilot study was conducted with 10 nurses to test the comprehensibility of the data collection forms before data collection. Since there was no need for correction in the data collection forms, the data obtained as a result of the pilot study were also included in the study. Before data collection, nurses working in S-ICUs were informed about the aims and objectives of the study. If nurses were volunteered to participate in the study, a voluntary information form was signed. Nurses who volunteered to participate in the study were asked to answer the questionnaire. It took 10-15 minutes for the nurses to answer the questions in the first and second parts of the data collection form.

Statistical Analysis

Statistical analysis of the data was performed in SPSS 20.0 Windows package program. In descriptive statistics, number (n) and percent (%) values were used to represent categorical variables, and mean ± standard deviation was used to represent numerical values. The dependent variable of the study is the opinions of nurses working in S-ICUs about the participation of FMs in post-mortem care. The independent variables are age, gender, education level, professional experience, and experience in the S-ICU. The opinions of nurses working in S-ICUs about the participation of FMs in the post-mortem care were statistically compared with independent variables. Pearson chi-square test was used for comparisons of categorical variables. A $p<0.05$ value was accepted for statistical significance.

Ethical and Research Approvals

Before starting the study, approval was Hasan Kalyoncu University Health Sciences Non-Interventional Research Ethics Committee (decision no: 2022/019, decision date: 28.02.2022). After informing the nurses about the study, their written consent was obtained for being volunteer to participate in the study (22). All phases of the study were carried out in accordance with the Declaration of Helsinki of the World Medical Association (23). In the training and research hospital where the study was conducted, FMs are allowed to visit patients once a day in S-ICUs and the visit time is limited to 10-15 minutes. FMs of patients, whose condition is critical and who are in the terminal period, are not allowed to participate in post-mortem care in S-ICUs. S-ICUs have a room to inform FMs routinely and to report death.

Results

Participant Characteristics

The mean age of the nurses participating in the study was 32.39±5.87, 56.8% of them were female, and 88.9% of them were undergraduate graduates. The mean professional experience of nurses was 10.40±6.44 years and the S-ICU experience was 5.69±5.76 years. 51.9% of the nurses work in the anesthesia ICU, and 69.1% of them received training on the care of the patient in the dying process. 27.2% of the nurses witnessed the death of a relative, 55.6% of them wanted to participate in the care of a relative in the dying process. 27.2% of the nurses have working experience in cases where FMs participate in the care of patients in the dying process. It was determined that 23.5% of the nurses had a different opinion with the FMs about the care of the patient. It was determined that 8.6% of the nurses were sued and 4.9% were subjected to violence by the FMs (Table 1).

Table 1. Distribution of descriptive characteristics of nurses working in surgical intensive care units (n=81)		
Characteristics	**n**	**%**
Age (mean ± SD: 32.39±5.87, youngest: 24-oldest: 48)		
≥30	35	43.2
31-40	36	44.4
≤41	10	12.3
Gender		
Female	46	56.8
Male	35	43.2
Educational status		
Health vocational high school	4	4.9
Graduate	72	88.9
Postgraduate	5	6.2
Experience in nursing (years) (mean ± SD: 10.40±6.44, minimum: 1-maximum: 27)		
≥5	13	16.0
6-10	39	48.2
≤11	29	35.8
Surgical intensive care experience (years) (mean ± SD: 5.69±5.76, minimum: 1-maximum: 25)		
≥5	54	66.7
6-10	17	21.0
≤11	10	12.3
Intensive care unit		
Surgical	16	19.8
Cardiovascular surgery	23	28.4
Anesthesia	42	51.9
Status of receiving education about patient care in the dying process		
Yes	56	69.1
No	25	30.9
Witnessing the death of a first-degree relative		
Yes	22	27.2
No	59	72.8
Request to participate in the care of the relatives in the dying process		
Yes	45	55.6
No	36	44.4
Work experience in case of family members participating in the care of the patient in dying process		
Yes	22	27.2
No	59	72.8
The situation of different opinions with family members on the care of the patient in the dying process		
Yes	19	23.5
No	62	76.5
Case of being sued by family members of patients in the dying process		
Yes	7	8.6
No	74	91.4
The situation of violence by family members of patients in the dying process		
Yes	4	4.9
No	77	95.1
SD: Standard deviation		

Opinions of Nurses

Nurses participating in the study answered the "Should FMs be involved in the care of dying patients in S-ICUs?" question as follows: 57% yes, 26% no, and 17% undecided (Figure 1).

72% of nurses working in S-ICUs included in the study think that PFTD is beneficial for patients. Most frequently reported causes are as follows, FMs will help patients feel safe by reducing their fears (71.6%), FMs will provide psychosocial support to patients (64.2%), FMs will facilitate communication with the patient and enable rapid resolution of problems (49.4%). In addition, 44.4% of the nurses stated that FMs would provide urgently necessary drugs, blood and supplies for the patients, 28.3% of the nurses stated that FMs would provide faster access to information about the patient. It was also determined that 27.2% of the nurses think that the presence of FMs at S-ICU will ensure that patients receive care in line with their cultural, religious preferences and beliefs, and 23.5% are of the opinion that patients have a fundamental right to be with their FMs (Table 2).

24.7% of the nurses working in S-ICUs included in the study think that PFTD is beneficial for FMs. Most frequently reported causes are as follows, FM see that the necessary intervention has been made for the patients (44.4%), FM find the opportunity to say goodbye (write off each other's debts) with patients (23.5%), and helps FM come to terms with death more quickly (23.5%). In addition, 19.8% of the nurses think that the grieving process will be alleviated by FMs, and 17.3% of nurses think that participation is a fundamental right for FMs (Table 2).

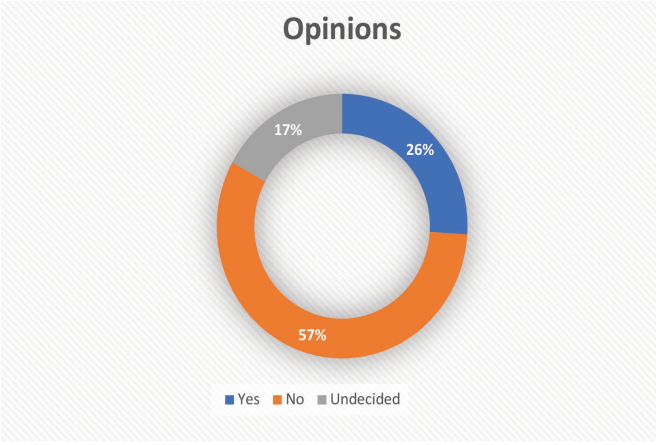

Figure 1. Opinions of nurses working in surgical intensive care units about the presence of family members in the intensive care unit of patients during the dying process (n=81)

18.5% of nurses working in S-ICUs included in the study think that PFTD is beneficial for healthcare professionals. 23.5% of the nurses think that it will make it easier to get approval for invasive procedures. It was determined that 17.3% of them were of the opinion that it would facilitate clinical decisions, and 16.0% thought that it would facilitate care and ease the workload of health professionals (Table 2).

33.3% of nurses working in S-ICUs included in the study think that PFTD is harmful for patients. Most frequently reported causes are as follows, the operation of the devices and equipment on the patients may be impaired (54.3%), may cause patients to become infected (54.3%). In addition, 53.1% of the nurses are of the opinion that it causes the patients to feel emotional, their stress and anxiety will increase, 50.6% of the nurses think that the treatment processes of the patients may be disrupted, and 49.4% of the nurses think that the vital signs of the patients may change (tachycardia, hypertension) (Table 3).

42% of nurses working in S-ICUs included in the study think that PFTD is harmful for FMs. 55.6% of the nurses think that this will be a traumatic process for FMs and will have long-term effects. 54.3% of the nurses think that the psychological health of FM (anxiety, depression, etc.) may deteriorate, and 51.9% of the nurses think that the physical health of FMs (high blood pressure, fainting, etc.) may deteriorate (Table 3).

56.7% of nurses working in S-ICUs included in the study think that PFTD is harmful for health professionals. Most frequently reported causes are as follows, FM may apply violence to nurses (54.3%), FM can complicate the work of nurses (54.3%), FM may react to nurses (54.3%). While 53.1% of nurses think that dealing with FMs will increase the workload of nurses, 51.9% of nurses think that FMs can sue nurses (Table 3).

When the opinions of nurses working in S-ICUs about PFTD were compared in terms of descriptive characteristics such as age, gender, education level, experience in nursing, experience in surgical intensive care, the difference was not statistically significant ($p>0.05$).

When the opinions of nurses working in S-ICUs about PFTD were compared in terms of the S-ICU, the difference was statistically significant ($p=0.014$) ($p<0.05$). On the

Table 2. Reasons for nurses working in surgical intensive care units to request PFTD (n=81)

Reasons for requesting PFTD	Yes n (%)	No n (%)	Undecided n (%)
Beneficial for patients	**59 (72.8)**	**2 (2.5)**	**20 (24.7)**
It reduces the fears of patients and makes them feel safe.	58 (71.6)	3 (3.7)	20 (24.7)
Provides physical and psychosocial support to patients.	52 (64.2)	5 (6.2)	24 (29.6)
It enables problems to be solved quickly by facilitating communication with the patient.	40 (49.4)	2 (2.5)	39 (48.1)
Provides the urgently needed medicine, blood, material for the patient.	36 (44.4)	7 (8.6)	38 (46.9)
Provides faster access to previous important information about the patient.	23 (28.4)	3 (3.7)	55 (67.9)
It ensures that patients receive care in line with their cultural, religious preferences and beliefs.	22 (27.2)	3 (3.7)	56 (69.1)
It is a fundamental right for patients.	19 (23.5)	4 (5.0)	58 (71.5)
Beneficial for family members	**20 (24.7)**	**2 (2.5)**	**59 (72.8)**
Family members see that the necessary intervention has been made for the patients.	36 (44.4)	3 (3.7)	42 (51.9)
Family members find the opportunity to say goodbye (write off each other's debts) with patients.	19 (23.5)	2 (2.5)	60 (74.1)
Helps family members come to terms with death more quickly.	19 (23.5)	5 (6.2)	57 (70.4)
Alleviates the grieving process of family members.	16 (19.8)	5 (6.2)	60 (74.1)
It is a fundamental right for family members.	14 (17.3)	7 (8.6)	60 (74.1)
Beneficial for health professionals	**15 (18.5)**	**5 (6.2)**	**61 (75.3)**
Makes it easier for healthcare professionals to obtain consent for invasive procedures.	19 (23.5)	2 (2.5)	60 (74.1)
Facilitates clinical decision making for healthcare professionals.	14 (17.3)	7 (8.6)	60 (74.1)
Relieves the workload of healthcare professionals, facilitates care.	13 (16.0)	8 (9.9)	60(74.1)

PFTD: Presence of family at the time of death

Table 3. Reasons for nurses working in surgical intensive care units not requesting PFTD (n=81)			
Reasons for not requesting PFTD	**Yes n (%)**	**No n (%)**	**Undecided n (%)**
Harmful for patients	**27 (33.3)**	**19 (23.5)**	**35 (43.2)**
The operation of the devices and equipment on the patients may be impaired.	44 (54.3)	2 (2.5)	35 (43.2)
May cause patients to become infected.	44 (54.3)	2 (2.5)	35 (43.2)
Causes patients to be emotional, increases their stress and anxiety.	43 (53.1)	3 (3.7)	35 (43.2)
It may disrupt the treatment processes of patients.	41 (50.6)	5 (6.2)	35 (43.2)
Patients' vital signs may change (tachycardia, hypertension).	40 (49.4)	6 (7.4)	35 (43.2)
Harmful for family members	**34 (42.0)**	**12 (14.8)**	**35 (43.2)**
It is a traumatic process for family members, has long-term effects.	45 (55.6)	1 (1.2)	35 (43.2)
It can impair the psychological health of family members (anxiety, depression, etc.).	44 (54.3)	2 (2.5)	35 (43.2)
It can impair the physical health of family members (high blood pressure, fainting, etc.).	42 (51.9)	4 (4.9)	35 (43.2)
Harmful for health professionals	**46 (56.7)**	**1 (1.2)**	**34 (42.1)**
Family members may apply violence to nurses.	44 (54.3)	2 (2.5)	35 (43.2)
Family members can complicate the work of nurses.	44 (54.3)	2 (2.5)	35 (43.2)
Family members may react to nurses.	44 (54.3)	2 (2.5)	35 (43.2)
Taking care of family members increases the workload of nurses.	43 (53.1)	3 (3.7)	35 (43.2)
Family members can sue nurses.	42 (51.9)	4 (4.9)	35 (43.2)
PFTD: Presence of family at the time of death			

other hand, when the opinions of nurses working in S-ICUs about PFTD were compared in terms of status of receiving education on patient care during the dying process, witnessing the death of a first-degree relative, willingness to participate in the care of the relative during the dying process, the difference was not statistically significant ($p>0.05$). When the opinions of nurses working in S-ICUs about PFTD were compared in terms of the work experience where FM are involved in the care of a dying patient, the difference was found to be statistically significant ($p=0.010$) ($p<0.05$). When the opinions of nurses working in S-ICUs about PFTD were compared in terms of the situation of having different opinions with FM about the care of the patient in the dying process, the situation of being sued, the situation of being exposed to violence; the difference was not statistically significant ($p>0.05$) (Table 4).

Discussion

The most important finding of the study, in which the views of nurses working in the S-ICU about the involvement of FMs in the care of patients in the dying process were examined, is the low rate of nurses supporting the participation of families in care. Only 26% of the nurses approve the PFTD practice. The reason for the very low rate of approval of PFTD by nurses in the study may be the thought of being subjected to verbal and physical violence by FMs of patients. It also suggested that nurses may lack knowledge about patient and family-centered care. Today, while there is a lot of evidence about the benefits of PFTD practice (6,11,24), there are also reports about its problems (10,11,24,25). Numerous studies have identified some barriers and limitations to the application of PFTD (12-15). These limitations include; unrealistic demanding attitudes of FMs, conflict between FMs, presence of cultural and spiritual needs of FMs that healthcare professionals are unfamiliar with, exclusion of FMs in the decision-making process, racial and religious discrimination, and lack of awareness of health professionals (12,14). In-service training programs should be organized to increase the awareness of nurses and clinical practice guides should be created.

Although the rate of nurses supporting the PFTD application was very low in the study, 72.8% of the nurses think that the participation of FM in care is beneficial for the patients, while 27.2% think that it is harmful. The most important reasons for thinking that PFTD is beneficial are

Table 4. Comparison of nurses working in surgical intensive care units on PFTD by descriptive characteristics (n=81)				
Characteristics	**Should participate n (%)**	**Should not participate n (%)**	**Undecided n (%)**	**Test*/p**
Age (mean ± SD: 32.39±5.87, youngest: 24-oldest: 48)				
≥30	8 (9.9)	22 (27.2)	5 (6.2)	X^2=3.304 p=0.508
31-40	12 (14.8)	17 (21.0)	7 (8.6)	
≤41	1 (1.2)	7 (8.6)	2 (2.5)	
Gender				
Female	11 (13.6)	26 (32.1)	9 (11.1)	X^2=0.488 p=0.783
Male	10 (12.3)	20 (24.7)	5 (6.2)	
Educational status				
Health vocational high school	2 (2.5)	2 (2.5)	0 (0.0)	X^2=1.765 p=0.779
Graduate	18 (22.2)	41 (50.6)	13 (16.0)	
Postgraduate	1 (1.2)	3 (3.7)	1 (1.2)	
Experience in nursing (years) (mean ± SD: 10.40±6.44, minimum: 1-maximum: 27)				
≥5	3 (3.7)	7 (8.6)	3 (3.7)	X^2=3.401 p=0.493
6-10	13 (16.0)	19 (23.5)	7 (8.6)	
≤11	5 (6.2)	20 (24.7)	4 (4.9)	
Surgical intensive care experience (years) (mean ± SD: 5.69±5.76, minimum: 1 - maximum: 25)				
≥5	16 (19.8)	29 (35.8)	9 (11.1)	X^2=1.768 p=0.778
6-10	4 (4.9)	10 (12.3)	3 (3.7)	
≤11	1 (1.2)	7 (8.6)	2 (2.5)	
Intensive care unit				
Surgical	1 (1.2)	8 (9.9)	7 (8.6)	**X^2=12.516 p=0.014**
Cardiovascular surgery	9 (11.1)	12 (14.8)	2 (2.5)	
Anesthesia	11 (13.6)	26 (32.1)	5 (6.2)	
Status of receiving education about patient care in the dying process				
Yes	14 (17.3)	33 (40.07)	9 (11.1)	X^2=0.360 p=0.835
No	7 (8.6)	13 (16.0)	5 (6.2)	
Witnessing the death of a first-degree relative				
Yes	5 (6.2)	12 (14.8)	5 (6.2)	X^2=0.664 p=0.718
No	16 (19.8)	34 (42.0)	9 (11.1)	
Request to participate in the care of the relatives in the dying process				
Yes	15 (18.5)	23 (28.4)	7 (8.6)	X^2=2.893 p=0.235
No	6 (7.4)	23 (28.4)	7 (8.6)	
Work experience in case of family members participating in the care of the patient in dying process				
Yes	10 (12.3)	7 (8.6)	2 (2.5)	**X^2=9.224 p=0.010**
No	11 (13.6)	39 (48.1)	12 (14.8)	
The situation of different opinions with family members on the care of the patient in the dying process				
Yes	6 (7.4)	13 (16.0)	3 (3.7)	X^2=0.282 p=0.869
No	15 (18.5)	33 (40.7)	11 (13.6)	
Case of being sued by family members of patients in the dying process				
Yes	3 (3.7)	3 (3.7)	1 (1.2)	X^2=1.149 p=0.563
No	18 (22.2)	43 (53.1)	13 (16)	
The situation of violence by family members of patients in the dying process				
Yes	0 (0)	4 (4.9)	0 (0)	X^2=0.664 p=0.718
No	21 (25.9)	42 (51.5)	14 (17.3)	

*Test: Pearson chi-square, SD: standard deviation

as follows: It reduces the fears of the patients, makes them feel safe (71.6%), provides physical and psychosocial support to the patients (64.2%), facilitates communication with the patient and ensures that the problems are solved quickly (49.4%). In the literature, it has been reported that patients in the dying process experience fear, uneasiness and security anxiety (3,24). In the study of Leske et al. (24), it was emphasized that it is important for patients in the dying process to feel safe and know that they are not surrounded only by people they do not know. In the study, most frequently reported reasons for being harmful are as follows, the operation of the devices and equipment on the patients may be impaired (54.3%), may cause patients to become infected (54.3%). In addition, 53.1% of the nurses are of the opinion that it causes the patients to feel emotional, their stress and anxiety will increase. When the existing literature on this subject is examined, contrary to this view, it is seen that PFTD practice is beneficial for patients. There are reports that patients are relieved by feeling the presence of their FM even if they are unconscious (24,25).

In the study, 24.7% and 42% of the nurses thought that the PFTD application is beneficial, and harmful for FMs, respectively. This finding of the study made us think that nurses put the patient in the center while working to solve various problems of the patient and put the benefits of FMs in the second plan. Nurses should be informed about patient and family-centered care, and the importance of PFTD in terms of FMs should be emphasized. In the study, the most frequently reported reasons by nurses that PFTD is beneficial for FMs are as follows; FMs see that the necessary intervention has been made for the patients (44.4%), FMs find the opportunity to say goodbye to the patients (23.5%), enable FMs to accept death more quickly (23.5%). This finding of the study is similar to the existing literature. Evidence for PFTD practice reports that FMs play crucial roles for relatives and suggest some benefits for families as well (26-28). When FMs are with patients, they can be sure that everything is done for their loved ones and protect their rights (8), they can improve the quality of communication between patients and healthcare professionals (8,28), they can contribute to solving problems so that patients can live as well as possible until death (29). In this way, the comfort of the patients in their last days can be increased and the quality of life can be kept at the highest level (27-29). FMs, who stay with the patient in the last moments, can continue to have memories with the patient, find the opportunity to say goodbye, and accept the information about the death of their loved ones faster (8). One study described how FMs tell a child they love him/her and let him/her die (5,8). This situation can prevent the pathological grief that threatens the health of FMs and alleviate the grieving process (8). In the study, the most frequently reported reasons by nurses that PFTD is harmful for FMs are as follows: It is a traumatic process for FMs and has long-term effects (55.6%), it can impair their psychological health (anxiety, depression) (54.3%), and it can impair their physical health (blood pressure, fainting) (51.9%). While the majority of FMs who are next to their relatives during the death process adapt well to the loss of their relative, 6-8% of them experience an intense and pathological mourning period with high psychological complications (9). The preferences of the patients and FMs should be kept in mind when making the PFTD decision. Precautions should also be taken against the possibility that FMs may be affected physically and psychologically.

In the study, 18.5% of the nurses think that PFTD application is beneficial for health professionals, and 56.7% of them think that it is harmful. The most common reasons reported by nurses that PFTD is beneficial for healthcare professionals are as follows: It facilitates the consent of health professionals for invasive procedures (23.5%), facilitates the clinical decision-making of health professionals (17.3%), eases the workload of health professionals and facilitates care (16%). Although a larger proportion of nurses think it is harmful, there is evidence in the literature about the benefits of PFTD. When the current literature about this subject is examined; it has been shown in a limited number of studies that FMs can contact patients, communicate with patients, participate in post-mortem care in case of death, and help health professionals (4,5,22). In the literature, it is also revealed that PFTD application has some benefits for health professionals. In a report published by the American Association of Intensive Care Nurses in 2016, it is reported that PFTD application facilitates medical decision making and increases the quality of care (30).

The most common reasons for nurses to think that PFTD practice is harmful to health professionals are as follows: Nurses may be exposed to violence by FMs (54.3%), FMs may complicate the work of nurses (54.3%), FMs may react to nurses (53.1%), FMs may sue nurses (51.9%). When the existing literature on this subject is examined, it has been shown that nurses are exposed to violence in their working

environments and can be sued (22,31-33). In a study of Pol et al. (31), it has been reported that ICU nurses are at risk for work-related violence. In a survey study conducted by Zhang et al. (32) with 4125 nurses in 28 hospitals; it was determined that 25.77%, 63.65% and 2.6% of the nurses were exposed to physical violence, to non-physical (verbal) violence, and to sexual harassment, respectively. It has been reported that 11.72% of the nurses have health problems due to this work-related violence (32). It has been reported in the study of Yavuz et al. (20), that FMs who witness the resuscitation of a relative may misunderstand the procedures, which increases the risks of violence and litigation against healthcare professionals. In a meta-analysis study by Aljohani et al. (33), It has been determined that 52% of violence against health professionals is perpetrated by FMs. Precautions should be taken for the safety of ICU nurses. Before admitting FMs to the ICU, FMs should be informed about the ICU environment, the characteristics of the patient and the rules they must follow.

The low rate of support for PFTD practice among anesthesia ICU workers in the study may be due to the fact that they frequently encountered patients in the dying process and were in dilemma about the benefits of PFTD. In the study, in cases where FMs participate in the care of patients in the dying process, nurses with working experience have a high rate of supporting PFTD. It was evaluated that concerns of nurses about PFTD could be reduced by sharing experience. Written procedures and practice guidelines are needed for the participation of FMs in ICUs.

The limitation of the study is that the study was conducted in a single center with a limited sample size. Therefore, the study findings cannot be generalized to the population. Being the first study on this subject makes the research findings valuable.

Conclusion

The rate of nurses working in S-ICUs to support the participation of FM in the care of patients in the dying process is low. Working experience increases the support rate of nurses in cases where FM participate in the care of patients in the dying process. It is thought that it would be beneficial to provide in-service training and to identify and remove preventable obstacles to eliminate the lack of knowledge on this subject while examining the opinions of nurses on the practice of family presence in the dying process, since it may contribute to achieving the goal of family-centered care in line with the preferences of the patient and FM.

Acknowledgements: We would like to thank to all nurses for their replying our questionnaire.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Non-Interventional Research Ethics Committee of Hasan Kalyoncu University Health Sciences (decision no: 2022/019, decision date: 28.02.2022).

Informed Consent: After informing the nurses about the study, their written consent was obtained for being volunteer to participate in the study.

Authorship Contributions

Surgical and Medical Practices: A.K., Y.E., A.Y., Concept: A.K., Y.E., A.Y., Design: A.K., Y.E., A.Y., Data Collection and Process: A.K., Y.E., A.Y., Analysis or Interpretation: A.K., Y.E., A.Y., Literature Search: A.K., Y.E., A.Y., Writing: A.K., Y.E., A.Y.

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

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

References

1. White DB, Ernecoff N, Billings JA, Arnold R. Is dying in an ICU a sign of poor quality end-of-life care? Am J Crit Care. 2013;22:263-6.
2. Goldfarb MJ, Bibas L, Bartlett V, Jones H, Khan N. Outcomes of Patient- and Family-Centered Care Interventions in the ICU: A Systematic Review and Meta-Analysis. Crit Care Med. 2017;45:1751-61.
3. Toronto CE, LaRocco SA. Family perception of and experience with family presence during cardiopulmonary resuscitation: An integrative review. J Clin Nurs. 2019;28:32-46.
4. Considine J, Eastwood K, Webster H, Smyth M, Nation K, Greif R, et al. Family presence during adult resuscitation from cardiac arrest: A systematic review. Resuscitation. 2022;180:11-23.
5. Barreto MDS, Peruzzo HE, Garcia-Vivar C, Marcon SS. Family presence during cardiopulmonary resuscitation and invasive procedures: a meta-synthesis. Rev Esc Enferm USP. 2019;53:e03435.
6. Bradley C. Family Presence and Support During Resuscitation. Crit Care Nurs Clin North Am. 2021;33:333-42.
7. Meier EA, Gallegos JV, Thomas LP, Depp CA, Irwin SA, Jeste DV. Defining a Good Death (Successful Dying): Literature Review and a Call for Research and Public Dialogue. Am J Geriatr Psychiatry. 2016;24:261-71.
8. Tenzek KE, Depner R. Still Searching: A Meta-Synthesis of a Good Death from the Bereaved Family Member Perspective. Behav Sci (Basel). 2017;7:25.
9. Krikorian A, Maldonado C, Pastrana T. Patient's Perspectives on the Notion of a Good Death: A Systematic Review of the Literature. J Pain Symptom Manage. 2020;59:152-64.
10. Bandini JI. Beyond the hour of death: Family experiences of grief and bereavement following an end-of-life hospitalization in the intensive care unit. Health (London). 2022;26:267-83.
11. Breen CM, Abernethy AP, Abbott KH, Tulsky JA. Conflict associated with decisions to limit life-sustaining treatment in intensive care units. J Gen Intern Med. 2001;16:283-9.
12. Fang ML, Sixsmith J, Sinclair S, Horst G. A knowledge synthesis of culturally-and spiritually-sensitive end-of-life care: findings from a scoping review. BMC Geriatr. 2016;16:107.
13. Erzincanlı S, Kasar KS. Hemşirelerin yaşam sonu bakıma yönelik tutum ve davranışlarının klinik karar vermeye etkisi. Turk J Intensive Care. 2021;00710.
14. Kirchhoff KT, Beckstrand RL. Critical care nurses' perceptions of obstacles and helpful behaviors in providing end-of-life care to dying patients. Am J Crit Care. 2000;9:96-105.
15. Eskigülek Y, KAV S. Palyatif Bakım Hastaları ve Hemşirelerinin Gözünden İtibarlı Bakım. THDD. 2020;1:1-18.
16. Park M, Giap TT, Lee M, Jeong H, Jeong M, Go Y. Patient- and family-centered care interventions for improving the quality of health care: A review of systematic reviews. Int J Nurs Stud. 2018;87:69-83.
17. Porter JE, Cooper SJ, Sellick K. Family presence during resuscitation (FPDR): Perceived benefits, barriers and enablers to implementation and practice. Int Emerg Nurs. 2014;22:69-74.
18. Cohen J. Statistical Power Analysis for the Behavioral Sciences. New York: Lawrence Erlbaum Associates; 1988.
19. Breen LJ, Aoun SM, O'Connor M, Howting D, Halkett GKB. Family Caregivers' Preparations for Death: A Qualitative Analysis. J Pain Symptom Manage. 2018;55:1473-9.
20. Yavuz M, Totur Dikmen B, Altınbaş Y, Aslan Başlı A. Opinions for Family Presence During Cardiopulmonary Resuscitation in Turkey: A Literature Review. Journal of Medical and Surgical Intensive Care Medicine. 2013;:13-7.
21. Davis LL, Grant JS. Guidelines for using psychometric consultants in nursing studies. Res Nurs Health. 1993;16:151-5.
22. Emanuel EJ, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. J Infect Dis. 2004;189:930-7.
23. World Medical Association. Declaration of Helsinki 2008. Available from: URL: http://www.wma.net/e/ethicsunit/helsinki.htm. Accessed December 21, 2022.
24. Leske JS, McAndrew NS, Brasel KJ, Feetham S. Family Presence During Resuscitation After Trauma. J Trauma Nurs. 2017;24:85-96.
25. Maxton FJ. Parental presence during resuscitation in the PICU: the parents' experience. Sharing and surviving the resuscitation: a phenomenological study. J Clin Nurs. 2008;17:3168-76.
26. Rainsford S, MacLeod RD, Glasgow NJ, Phillips CB, Wiles RB, Wilson DM. Rural end-of-life care from the experiences and perspectives of patients and family caregivers: A systematic literature review. Palliat Med. 2017;31:895-912.
27. Stajduhar KI, Funk L, Outcalt L. Family caregiver learning–how family caregivers learn to provide care at the end of life: a qualitative secondary analysis of four datasets. Palliat Med. 2013;27:657-64.
28. Chi NC, Demiris G. Family Caregivers' Pain Management in End-of-Life Care: A Systematic Review. Am J Hosp Palliat Care. 2017;34:470-85.
29. Olgun Ş, Yavuz Van Giersbergen M. Evidence-based approaches: Nursing care of adults in the last days of life. Ege Üniversitesi Hemşirelik Fakültesi Dergisi. 2018;34:179-91.
30. Family presence: visitation in the adult ICU. Crit Care Nurse. 2012;32:76-8.
31. Pol A, Carter M, Bouchoucha S. Violence and aggression in the intensive care unit: What is the impact of Australian National Emergency Access Target? Aust Crit Care. 2019;32:502-8.
32. Zhang L, Wang A, Xie X, Zhou Y, Li J, Yang L, et al. Workplace violence against nurses: A cross-sectional study. Int J Nurs Stud. 2017;72:8-14.
33. Aljohani B, Burkholder J, Tran QK, Chen C, Beisenova K, Pourmand A. Workplace violence in the emergency department: a systematic review and meta-analysis. Public Health. 2021;196:186-97.

Turk J Intensive Care 2024;22:190-6
DOI: 10.4274/tybd.galenos.2023.28190

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Does Tube Resistance Compensation Change Metabolic Parameters When Added to Pressure Support Mode During Weaning?

Weaning Sürecinde Basınç Destekli Ventilasyon Moduna Tüp Direnci Kompanzasyonu Eklenmesi Metabolik Parametreleri Değiştirir mi?

Received/Geliş Tarihi : 02.06.2023
Accepted/Kabul Tarihi : 28.08.2023

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ABSTRACT *Objective:* We postulated that adding tube resistance compensation (TRC) to pressure support ventilation (PSV) would have beneficial effects on metabolic parameters in patients scheduled for weaning. Here, the PSV and PSV + TRC were compared by measuring oxygen consumption (VO_2), energy expenditure (EE), and carbon dioxide production (VCO_2).
Materials and Methods: This was a prospective, randomised, crossover study. Seventy-eight adult patients were randomised to receive either PSV or PSV + TRC. Group 1 consisted of patients that started with PSV initially and then switched to PSV + TRC, whereas group 2 first received PSV + TRC and then switched to PSV. After 30 minutes (min) of monitoring and stabilization, an indirect calorimeter was connected and metabolic parameters measurement was taken every 5 min for 30 minutes, and the last measurement values were recorded at the 30th min. The patient was then switched to the second treatment mode, and the procedure was repeated.
Results: TRC + PSV ventilation had no clinical effects on metabolic parameters compared with PSV (EE, 1746 vs. 1763, respectively; VO_2, 255 vs. 260, respectively; VCO_2, 206 vs. 208, respectively; all p>0.05).
Conclusion: Adding TRC to PSV did not cause any changes in gas exchange, haemodynamic variables, or metabolic parameters in patients for weaning.
Keywords: Indirect calorimetry, pressure support ventilation, tube resistance compensation, work of breathing

ÖZ *Amaç:* Çalışmamızda weaning planlanan hastalarda basınç destekli ventilasyon moduna (PSV) tüp direnci kompanzasyonu (TRC) eklenmesinin metabolik parametreler üzerinde etkilerinin araştırılması amaçlanmıştır. PSV ve PSV + TRC modları, oksijen tüketimi (VO_2), enerji tüketimi (ET) ve karbondioksit üretimi (VCO_2) ölçülerek karşılaştırıldı.
Gereç ve Yöntem: Çalışmamız prospektif, randomize, crossover bir çalışmadır. Yetmiş sekiz yetişkin hasta başlangıç ventilasyon modları PSV veya PSV + TRC modu olmak üzere randomize edildi. Grup 1 PSV modu ile ventilasyona başlanan daha sonra PSV + TRC modunda ventilasyona devam edilen hastalardan, grup 2 ise önce PSV + TRC modu ile ventile edilen daha sonra PSV modu ile ventilasyona devam edilen hastalardan oluştu. Otuz dakikalık (dk) monitorizasyon ve stabilizasyonun ardından indirekt kalorimetre bağlanarak 30 dk boyunca 5 dk bir metabolik parametre ölçümü yapıldı ve son ölçüm değerleri 30. dk'de kaydedildi. Hasta daha sonra ikinci tedavi moduna geçildi ve işlem tekrarlandı.
Bulgular: PSV + TRC modu ile ventilasyonun, PSV modu ile karşılaştırıldığında metabolik parametreler üzerinde hiçbir klinik etkisi olmamıştır (sırasıyla ET; 1746, 1763, VO_2; 255, 260, VCO_2; 206, 208; tümü p>0,05).
Sonuç: PSV moduna TRC eklenmesi, weaning hastalarında gaz değişimi, hemodinamik değişkenler veya metabolik parametrelerde herhangi bir değişikliğe neden olmadı.
Anahtar Kelimeler: İndirekt kalorimetre, basınç destekli ventilasyon, tüp direnç kompanzasyonu, solunum işi

Introduction

Weaning is introduced to decrease the duration of mechanical ventilation and should be initiated as early as possible following elimination of the reasons for acute respiratory failure (1). One of the most important causes of weaning failure is imbalance between respiratory muscle capacity and respiratory workload against the resistance caused by the artificial airway (2). The rate of successful extubation can be increased by decreasing the work of breathing caused by the intubation tube [additional work of breathing (WOBadd)] (3).

Several ventilation modes may be used during weaning, one of the most common of which is pressure support ventilation (PSV) (4). Although the PSV mode has been reported to decrease the work of breathing by reducing resistance due to the artificial airway at pressure support (PS) levels appropriate for the respiratory requirements in the patient (5), this mode has some limitations. Work of breathing caused by the artificial airway is due to the diameter and length of the endotracheal tube, as well as the effort of the patient (6). WOBadd increases as minute (min) ventilation demand increases (6). The flow pattern is variable during each breath and WOB cannot be compensated by constant PS (7). Therefore, PSV mode leads to discomfort in patients because it cannot continuously adjust to changes in the resistance caused by changes in the inspiratory flow of the patient and, thus, provides a suboptimal decrease in the work of breathing (8).

Tube resistance compensation (TRC) [also known as automatic tube compensation (ATC)] has been developed to address this problem and to improve the weaning process (9). This method compensates for the pressure changes due to flow during inspiration and expiration through the continuously calculated tracheal pressure (7). In ventilators with the TRC feature, the pressure changes due to flow through the endotracheal tube is automatically compensated and the WOBadd is reduced (9).

A few studies recognised the reduction in work of breathing as a reduction in oxygen consumption and demonstrated that indirect calorimetry is a suitable bedside method to measure these parameters (10,11). In addition, many studies have evaluated the effects of mechanical ventilation modes on the metabolic parameters by measuring oxygen consumption (VO_2), energy expenditure (EE), and carbon dioxide production (VCO_2) using indirect calorimetry (12-14).

In the present study, we thought that adding TRC to PSV mode would have beneficial effects on metabolic parameters (VO_2, VCO_2, EE) in patients scheduled for weaning. Here we hypothesized that adding TRC to PSV mode would reduce VO_2 and reduce VCO_2 and EE. Therefore, in our study, PSV and PSV + TRC modes were compared by measuring VO_2, VCO_2 and EE by indirect calorimetry.

Materials and Methods

This prospective, randomised, crossover study was conducted in a mixed intensive care unit of a university hospital after receiving approval from the Ege University Clinical Research Ethics Committee (decision no: 14-9.2/6, date: 07.11.2014). The study population consisted of 78 adult patients after obtaining written informed consent from their relatives. According to the protocol of our clinic, patients with hemodynamic and respiratory stable, inspiratory PS below 10 cmH_20, positive end-expiratory pressure: 5-8 cmH_2O and fraction of inspired oxygen (FiO_2) level 40% and below, core body temperature <38 °C were considered to be ready for weaning. Patients who met the weaning criteria, had mechanical ventilation for more than 24 hours, had hemodynamic and respiratory stability, had hemoglobin >8 g/dL and core body temperature <38 °C were included in the study.

Patients with a respiratory rate (RR) >35 min-1, asynchrony with the ventilator, core body temperature >38 °C, SpO_2<90%, PaO_2<60 mmHg, $PaCO_2$>50 mmHg, or haemodynamic instability were excluded from the study.

The patients were randomised to receive either PSV or PSV with TRC (PSV + TRC) (Hamilton Raphael or Hamilton-G5; Hamilton, Rhazuns, Switzerland). Group 1 consisted of patients started with PSV mode initially followed by switching to PSV + TRC, whereas group 2 initially received PSV + TRC and were then switched to PSV. After a 30 min stabilisation period and normalisation of blood gas values, measurements were made using an indirect calorimetry device (Metabolic Monitor; Datex Ohmeda, Helsinki, Finland). VO_2, VCO_2, and EE were recorded after 30 min. The patient was then switched to the other mode and the same procedure was repeated.

Group 1 patients were followed with PSV mode for 30 min and after stabilization was achieved, they were connected to the indirect calorimeter and metabolic parameters were measured every 5 min for 30 min, and

the last 30th min measurement values were recorded. Then, PSV + TRC mode was started. After 30 min of monitoring and stabilization, an indirect calorimeter was connected and metabolic parameters measurement was taken every 5 min for 30 min, and the last measurement values were recorded at the 30th min.

Group 2 patients were followed with PSV + TRC mode for 30 min and after stabilization was achieved, they were connected to the indirect calorimeter and metabolic parameters measurements were taken every 5 min for 30 min, and the measurement values were recorded at 30 min. Then, PSV mode was started. After 30 min of monitoring and stabilization, an indirect calorimeter was connected and metabolic parameters measurement was taken every 5 min for 30 min, and the last metabolic parameters measurement values were recorded at the 30th min.

During the entire study period, RR, heart rate (HR), mean arterial pressure (MAP), oxygen saturation (SPO_2), tidal volume (Vt), peak airway pressure (Ppeak), and PS level were recorded every 10 min, and pH, partial arterial oxygen pressure (PaO_2), partial arterial carbon dioxide pressure ($PaCO_2$), and base excess and bicarbonate (HCO_3) levels were measured and recorded at 30 min intervals following the baseline measurements.

No interventions, such as tracheal aspiration, positioning, or wound dressing, were performed over the course of the study period. If any intervention was required, the measurement was terminated, and the procedure was repeated from the beginning when the patient was in a suitable condition.

Statistical Analysis

The data were evaluated by the Biostatistics and Medical Information Department of University Hospital. Demographic and clinical data were evaluated using the chi-square test. Metabolic, haemodynamic, respiratory parameters, and blood gas analysis results were compared using the paired t-test. In all analyses, $p<0.05$ was taken to indicate statistical significance.

Results

Seventy eight patients were selected for the study. The mean age, the mean acute physiology and chronic health evaluation-II score were 54.8±21.6 years and 20.7±6.5.

The demographic and clinical data of the patients are listed in Table 1.

Table 1. Demographic and clinical data of the patients

Variables	Values
Male, n (%)	49 (62.8%)
Female, n (%)	29 (37.2%)
Age (years) (mean ± SD)	54.8±21.6
APACHE-II score (mean ± SD)	20.7±6.5
Ideal body weight (kg) (mean ± SD)	64.4±9.07
Size of endotracheal tube, n (%)	7 (2, 2.69%) 7.5 (24, 30.8%) 8 (51, 65.4%) 9 (1, 1.3%)
PaO_2/FiO_2 (mmHg)	312.4±81.62

SD: Standard deviation, APACHE-II: acute physiology and chronic health evaluation-II

Table 2. Reasons for mechanical ventilation

Reasons for mechanical ventilation	Values
Postoperative, n (%)	20 (25, 6%)
Trauma, n (%)	16 (20, 5%)
Cardiovascular, n (%)	6 (7, 7%)
Gastrointestinal, n (%)	4 (5, 1%)
Respiratory, n (%)	5 (6, 4%)
Anoxic coma, n (%)	2 (2, 6%)
Hematological, n (%)	1 (1, 3%)
Neurological, n (%)	13 (16, 7%)
Others, n (%)	11 (14, 7%)

The most common reason for mechanical ventilator support was postoperative respiratory failure (Table 2).

There were no statistically significant differences in metabolic parameters (VO_2, VCO_2, and EE) between PSV and PSV + TRC periods in either group 1 or 2 ($p>0.05$) (Figure 1).

There were no statistically significant differences in metabolic parameters (VO_2, VCO_2, and EE) between PSV and PSV + TRC periods in group 1 ($p>0.05$) (Figure 2).

There were no statistically significant differences in metabolic parameters (VO_2, VCO_2, and EE) between PSV and PSV + TRC periods in group 2 ($p>0.05$) (Figure 3).

There were no significant differences in metabolic parameters, HR, MAP, Ppeak, Vt, RR, SPO_2 or blood gas values between the PSV and PSV + TRC periods ($p>0.05$) (Table 3).

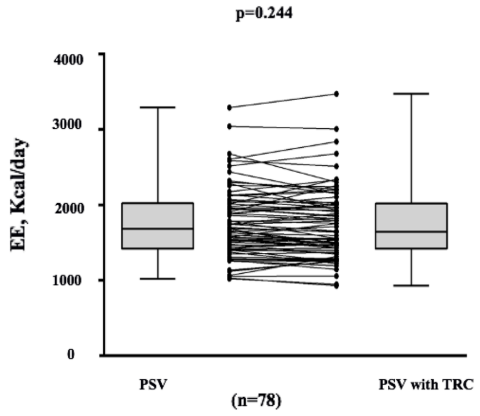

Figure 1a. There were no statistically significant energy expenditure (EE) between PSV and PSV + TRC periods in either group 1 or 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

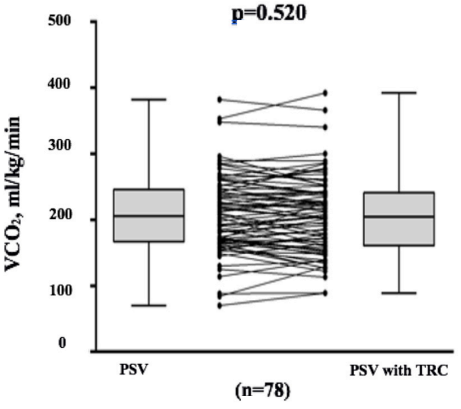

Figure 1b. There were no statistically significant carbon dioxide production (VCO_2) between PSV and PSV + TRC periods in either group 1 or 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

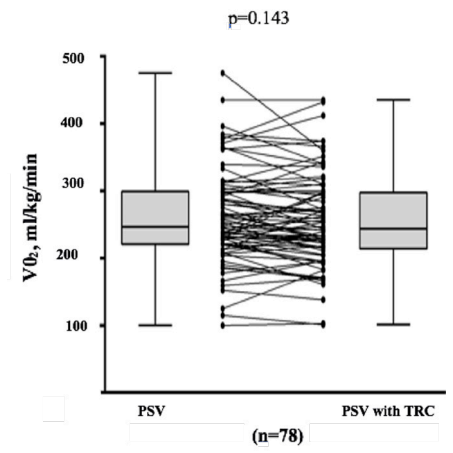

Figure 1c. There were no statistically significant oxygen consumption (VO_2) between PSV and PSV + TRC periods in either group 1 or 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

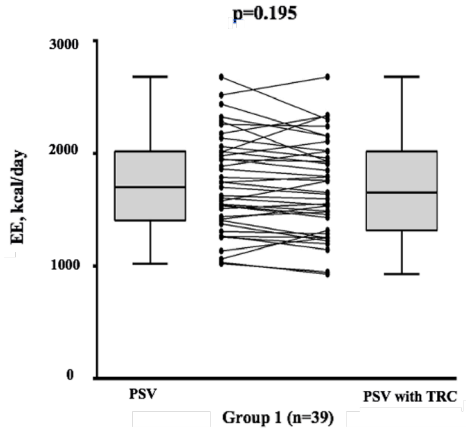

Figure 2a. There were no statistically significant differences energy expenditure (EE) between PSV and PSV + TRC periods in group 1 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

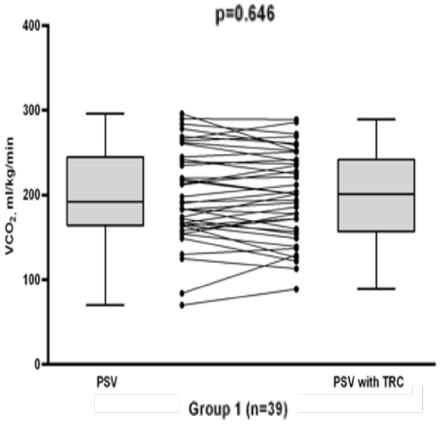

Figure 2b. There were no statistically significant differences carbon dioxide production (VCO_2) between PSV and PSV + TRC periods in group 1 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

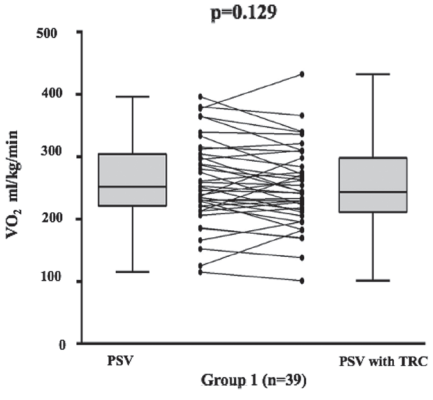

Figure 2c. There were no statistically significant differences oxygen consumption (VO_2) between PSV and PSV + TRC periods in group 1 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

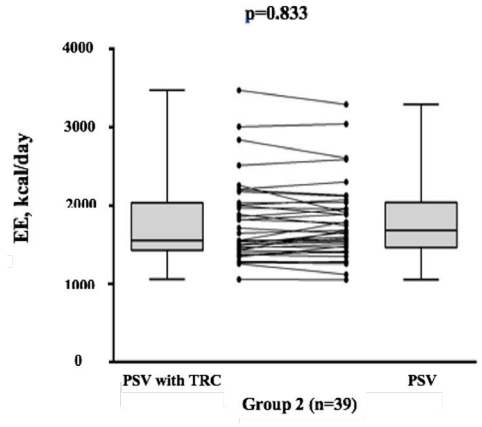

Figure 3a. There were no statistically significant energy expenditure (EE) between PSV and PSV + TRC periods in group 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

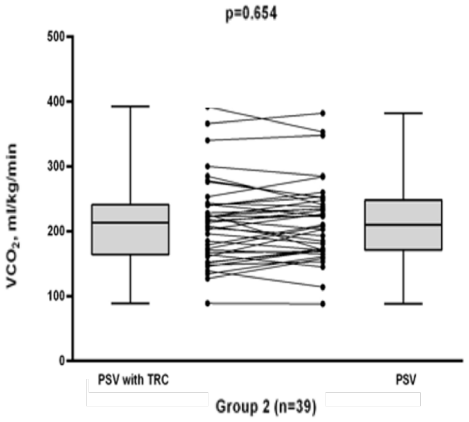

Figure 3b. There were no statistically significant differences carbon dioxide production (VCO_2) between PSV and PSV + TRC periods in group 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

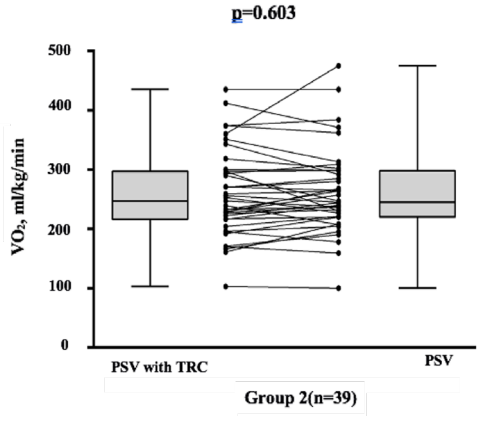

Figure 3c. There were no statistically significant oxygen consumption (VO_2) between PSV and PSV + TRC periods in group 2 (p>0.05)
PSV: Pressure support ventilation, TRC: tube resistance compensation

Table 3. Parameters measured during the PSV and PSV with TRC period

Variables	PSV (n=78)	PSV with TRC (n=78)	p-value
EE, (kcal/day) mean ± SD	1763.9±464.9	1746.3±476.9	0.24
VO_2, (mL/kg/min) mean ± SD	260.4±69.9	255.1±68.8	0.14
VCO_2, (mL/kg/min) mean ± SD	208±58.4	206.4±59.1	0.52
Vt, (mL) mean ± SD	437.5±101.6	437.1±103.9	0.87
RR, (breaths/min) mean ± SD	21.2±4.35	21.3±4.49	0.32
MAP, (mmHg) mean ± SD	79.1±10.3	78.9±10.7	0.55
HR, (beats/min) mean ± SD	90.5±18.3	90.4±18.08	0.76
SPO_2, (%) mean ± SD	96.6±1.5	96.7±1.57	0.26
Peak pressure, (cmH_2O) mean ± SD	16.6±3.59	16.7±3.5	0.48
pH, mean ± SD	7.47±0.04	7.47±0.04	0.85
PO_2, (mmHg) mean ± SD	93.4±23.7	93.1±23.8	0.76
PCO_2, (mmHg) mean ± SD	36.8±5.3	36.9±5.1	0.16
HCO_3, (mmol/L) mean ± SD	26.4±3.3	26.7±3.4	0.05
BE, (mmol/L) mean ± SD	3.4±4.2	3.3±4.2	0.22
FiO_2 (%) mean ± SD	37.6±3.3	37.5±3.4	0.15
VE (L/min) mean ± SD	8.7±1.3	8.6±1.5	0.76
PEEP (cmH_2O) mean ± SD	5.8±1.2	5.6±1.3	0.45

VO_2: Oxygen consumption, EE: energy expenditure, VCO_2: carbon dioxide production, HR: heart rate, MAP: mean arterial pressure, SPO_2: peripheral oxygen saturation, Vt: tidal volume, FiO_2: fraction of inspired oxygen, VE: minute ventilation, PEEP: positive end expiratory pressure, RR: respiratory rate, PaO_2: partial arterial oxygen pressure, $PaCO_2$: partial arterial carbondioxide pressure, SD: standard deviation, PSV: pressure support ventilation, TRC: tube resistance compensation

Discussion

In the present study, adding TRC to the PSV mode did not change the metabolic parameters in patients during the study period. Fabry et al. (9) investigated WOB imposed by the endotracheal tube (WOBadd) in the ATC and PSV mode with different PS in two populations of patients during

intubated spontaneous respiration. Imposed WOB was compensated with ATC and PSV settings of 10-15 cmH_2O in the postoperative patients without pulmonary injury (min ventilation 7.6±1.7 L/min), whereas PSV of 5 cmH_2O did not compensate for WOB. In severely ill patients with increased respiratory demand (min ventilation, 16.8±3.0 L/min), WOBadd increased significantly and none of the PSV levels could compensate for the WOB. It was noted that imposed WOB (WOBadd) could be compensated only by ATC. The patients included in the present study had min ventilation <10 L/min. Adding TRC to PSV did not significantly reduce these metabolic parameters. Therefore, we assumed that the effect of TRC on WOBadd was negligible in patients requiring low min ventilation.

Oczenski et al. (15) compared the effects of PSV, continuous positive airway pressure (CPAP), and CPAP with ATC on the oxygen consumption and respiratory pattern by measuring VO_2 with indirect calorimetry in 21 post-cardiac operation patients with normal ventilatory demand without pulmonary disease. There were no significant differences among the groups in oxygen consumption, respiratory pattern (Vt, RR), blood gas values, or haemodynamic parameters. They concluded that the clinical effect of the presumed benefits of ATC was low in patients with no increased ventilatory demand.

Lagoa et al. (12) randomised 40 mechanically ventilated intensive care patients into two groups in a prospective, randomised, crossover study. One group was ventilated in ATC with CPAP mode first and then only in CPAP mode, while the other group was ventilated in CPAP first and then in CPAP with ATC mode. Metabolic parameters were then measured by indirect calorimetry for 30 min. The researchers noted that there were no significant differences in the VO_2, EE, or VCO_2 values of the patients measured during the period with and without ATC.

In the present study, we compared the effects of TRC mode on metabolic parameters by measuring VO_2, VCO_2, and EE values by indirect calorimetry and found that TRC had no statistically significant effects on these parameters. The duration of measurement by indirect calorimetry was 30 min in the present study. We believe that our sample size was sufficient compared to other studies. In addition, although our primary aim was not to investigate the effects of TRC on haemodynamic and respiratory parameters, we did not find significant differences in these parameters between the periods with and without TRC.

We did not evaluate WOB directly or use the pressure-time product related to oxygen consumption by the respiratory muscles. Instead, we evaluated WOB indirectly by calorimetry to estimate oxygen consumption of the body as a whole.

In addition, the limitation of our study is that power analysis was not performed to determine the number of the study population.

Conclusion

In conclusion, adding TRC to the PSV mode did not cause any changes in metabolic parameters in patients scheduled for weaning.

Ethics

Ethics Committee Approval: This prospective, randomised, crossover study was conducted in a mixed intensive care unit of a university hospital after receiving approval from the Ege University Clinical Research Ethics Committee (decision no: 14-9.2/6, date: 07.11.2014).

Informed Consent: The study population consisted of 78 adult patients after obtaining written informed consent from their relatives.

Authorship Contributions

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

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

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

References

1. Tarogaard M, Freundlich M, Rasmussen BS. Respiratoraftrapning er en vigtig del af selve respiratorbehandlingen [Weaning from mechanical ventilation is an important part of the ventilation process]. Ugeskr Laeger. 2015;177:952-5.
2. MacIntyre NR. Respiratory mechanics in the patient who is weaning from the ventilator. Respir Care. 2005;50:275-86.
3. Cohen JD, Shapiro M, Grozovski E, Lev S, Fisher H, Singer P. Extubation outcome following a spontaneous breathing trial with automatic tube compensation versus continuous positive airway pressure. Crit Care Med. 2006;34:682-6.
4. Butler R, Keenan SP, Inman KJ, Sibbald WJ, Block G. Is there a preferred technique for weaning the difficult-to-wean patient? A systematic review of the literature. Crit Care Med. 1999;27:2331-6.
5. Brochard L, Rua F, Lorino H, Lemaire F, Harf A. Inspiratory pressure support compensates for the additional work of breathing caused by the endotracheal tube. Anesthesiology. 1991;75:739-45.
6. Shapiro M, Wilson RK, Casar G, Bloom K, Teague RB. Work of breathing through different sized endotracheal tubes. Crit Care Med. 1986;14:1028-31.
7. Fabry B, Guttmann J, Eberhard L, Wolff G. Automatic compensation of endotracheal tube resistance in spontaneously breathing patients. Technol Health Care. 1994;1:281-91.
8. Guttmann J, Bernhard H, Mols G, Benzing A, Hofmann P, Haberthür C, et al. Respiratory comfort of automatic tube compensation and inspiratory pressure support in conscious humans. Intensive Care Med. 1997;23:1119-24.
9. Fabry B, Haberthür C, Zappe D, Guttmann J, Kuhlen R, Stocker R. Breathing pattern and additional work of breathing in spontaneously breathing patients with different ventilatory demands during inspiratory pressure support and automatic tube compensation. Intensive Care Med. 1997;23:545-52.
10. Lewis WD, Chwals W, Benotti PN, Lakshman K, O'Donnell C, Blackburn GL, et al. Bedside assessment of the work of breathing. Crit Care Med. 1988;16:117-22.
11. Viale JP, Annat GJ, Bouffard YM, Delafosse BX, Bertrand OM, Motin JP. Oxygen cost of breathing in postoperative patients. Pressure support ventilation vs continuous positive airway pressure. Chest. 1988;93:506-9.
12. Lago AF, Goncalves EC, Silva EC, Menegueti MG, Nicolini EA, Auxiliadora-Martins M, et al. Comparison of Energy Expenditure and Oxygen Consumption of Spontaneous Breathing Trial Conducted With and Without Automatic Tube Compensation. J Clin Med Res. 2015;7:700-5.
13. Clapis FC, Auxiliadora-Martins M, Japur CC, Martins-Filho OA, Evora PR, Basile-Filho A. Mechanical ventilation mode (volume × pressure) does not change the variables obtained by indirect calorimetry in critically ill patients. J Crit Care. 2010;25:659.
14. Uyar M, Demirag K, Olgun E, Cankayali I, Moral AR. Comparison of oxygen cost of breathing between pressure-support ventilation and airway pressure release ventilation. Anaesth Intensive Care. 2005;33:218-22.
15. Oczenski W, Kepka A, Krenn H, Fitzgerald RD, Schwarz S, Hörmann C. Automatic tube compensation in patients after cardiac surgery: effects on oxygen consumption and breathing pattern. Crit Care Med. 2002;30:1467-71.

Turk J Intensive Care 2024;22:197-206
DOI: 10.4274/tybd.galenos.2023.28199

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Efficacy of Tocilizumab in Critically Ill COVID-19 Patients Followed in the Intensive Care Unit

Yoğun Bakım Ünitesinde Takip Edilen Kritik COVID-19 Hastalarında Tocilizumab Tedavisinin Etkinliği

Received/Geliş Tarihi : 19.10.2022
Accepted/Kabul Tarihi : 07.09.2023

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ABSTRACT *Objective:* In this retrospective and cross-sectional study, it was aimed to evaluate the efficacy of tocilizumab (TCZ) treatment in critical coronavirus disease-2019 (COVID-19) patients who were hospitalized in the intensive care unit (ICU) and developed cytokine storm.
Materials and Methods: The study included 219 critically ill COVID-19 patients followed in the ICU and treated with TCZ. All patients received 2 doses of 400 mg/day TCZ treatment during their stay in the ICU. Clinical conditions, laboratory data, inotrope requirement and chest radiographs before and after TCZ treatment were compared. Mortality rates at the 7th day, 28th day and total mortality rates of the patients were recorded.
Results: It was observed that there was a significant decrease in C-reactive protein (CRP) values over time after TCZ treatment. There was a significant increase in leukocyte, lymphocyte, lactate, urea, creatinine, aspartate transaminase, D-dimer, lactate dehydrogenase and procalcitonin values. The 7-day mortality of the patients was 21%, the 28-day mortality was 64.8%, and the total mortality rate was 65.3%.
Conclusion: It was determined that after TCZ treatment, only CRP levels, which are among the inflammatory parameters, decreased significantly in patients, and the mortality rates were still high with the increase in the values of kidney and liver function tests of the patients.
Keywords: Coronavirus disease-2019, intensive care unit, mortality rate, tocilizumab

ÖZ *Amaç:* Retrospektif ve kesitsel olarak planlanan bu çalışmada yoğun bakım ünitesinde (YBÜ) yatan ve sitokin fırtınası gelişen kritik koronavirüs hastalığı-2019 (COVID-19) hastalarında uygulanan tocilizumab (TCZ) tedavisinin etkinliğini değerlendirmeye çalıştık.
Gereç ve Yöntem: Çalışmaya, YBÜ'de takip edilen ve TCZ tedavisi uygulanmış olan 219 kritik COVID-19 hastası dahil edildi. Tüm hastalara, YBÜ'de yattığı süre içinde 400 mg/gün 2 doz TCZ tedavisi verildi. TCZ tedavisinden önceki ve sonraki klinik durumları, laboratuvar verileri, inotrop ihtiyacı ve akciğer grafileri karşılaştırıldı. Hastalara ait 7. gün, 28. gün ve total mortalite oranları kaydedildi.
Bulgular: TCZ tedavisinden sonra zamanla C-reaktif protein (CRP) değerlerinde anlamlı azalma olduğu görüldü. Lökosit, lenfosit, laktat, üre, kreatin, aspartat transferaz, D-dimer, laktat dehidrogenaz ve prokalsitonin değerlerinde ise anlamlı artış olduğu saptandı. Hastalara ait 7. günlük mortalite %21, 28 günlük mortalite %64,8 ve total mortalite oranı %65,3 olarak saptandı.
Sonuç: TCZ tedavisi sonrası hastalarda inflamatuar parametrelerden sadece CRP düzeylerinde anlamlı azalma olduğu, hastaların böbrek ve karaciğer fonksiyon testlerinde artış ile birlikte mortalite oranlarının hala yüksek seyrettiği saptanmıştır.
Anahtar Kelimeler: Koronavirüs hastalığı-2019, yoğun bakım ünitesi, mortalite oranı, tocilizumab

Introduction

Coronavirus disease-2019 (COVID-19) which began in Wuhan, China in December 2019 as a 2019 global pandemic and has since spread rapidly around the world (1). It was named COVID-19 on February 11, 2020 (2). COVID-19, which spread rapidly through person-to-person transmission and became a worldwide public health problem, affected 603,711,760 people and caused the death of 6,484,136 individuals as of September 7, 2022 (3-5). Pneumonia, which rapidly worsens and causes respiratory failure, developed in most of the patients (6). Especially elderly and immunocompromised individuals have higher mortality and morbidity rates (7).

The fact that there is still no effective treatment for COVID-19, the need for effective treatments, especially for critically ill patients treated in intensive care units (ICUs), is of great importance and studies on these treatments are continuing rapidly by scientists all over the world.

As the clinical course of COVID-19 progresses, patients begin a hyperinflammatory phase with dysregulation of adaptive immune responses. A cytokine storm then develops, accompanied by elevated plasma proinflammatory cytokine levels, including interleukin (IL) 2, 6, 7, 10 and granulocytes. Cytokine storm results in a prothrombotic environment, cardiomyopathy and ultimately multi-organ failure (8,9).

In the treatment of cytokine storm, immunomodulatory treatments such as IL-1 inhibitors (anakinra), IL-6 inhibitors [tocilizumab (TCZ)], corticosteroids (methylprednisolone) and intravenous immunoglobulin (IVIG) are applied (10). TCZ, a monoclonal antibody against the membrane-bound IL-6 receptor that inhibits the binding of soluble IL-6 and subsequent signal transduction, has been proposed as a therapeutic candidate to inhibit cytokine storm (11). In an observational study involving 544 patients with COVID-19, TCZ treatment was associated with a reduced need for subsequent invasive mechanical ventilation or a reduced risk of death (12). In another observational study, it was determined that TCZ treatment was thought to have association with a decrease in mortality among intubated COVID-19 patients (13).

In line with this information and recommendations, TCZ treatment, which is one of the immunomodulatory treatment methods, was used at the onset of clinical worsening in critically ill COVID-19 patients hospitalized in the ICU in our clinic. In this study, it was aimed to evaluate the effectiveness of TCZ treatment in critical COVID-19 patients by evaluating the effects of treatment on clinical, laboratory, lungs and mortality in critical COVID-19 patients who were treated with TCZ.

Materials and Methods

This study was carried out in University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research Hospital between 01.04.2020-30.11.2021. Ministry of Health Scientific Research Platform permission (20.10.2021), hospital management permission (25.10.2021), and University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee approval (dated 26.11.2021 and numbered 936) were obtained. The study was designed as a retrospective cross-sectional and was conducted in accordance with the 2013 criteria of the Declaration of Helsinki.

Patients who were diagnosed with COVID-19, whose nasopharyngeal samples were positive for at least one polymerase chain reaction test, were followed up and treated in the ICU, were older than 18 years old, and received 2 doses of 400 mg/day TCZ during their stay in the ICU were included in the study. COVID-19 patients who were younger than 18 years of age, followed in the wards and did not receive TCZ treatment or were not given two doses, were excluded from the study. In addition, patients whose data could not be reached in the hospital system and patient file records, and patients who died while undergoing TCZ treatment were also excluded from the study. In line with these criteria, 235 patients who started TCZ treatment within the specified date range were included in the study. However, three patients died before the completion of TCZ treatment, and 13 patients were excluded from the study since sufficient data could not be reached in their file records. During the ICU follow-up process, the non-mortal patients were included in group 1, while the mortal patients were included in group 2 and evaluated.

After the patients were admitted to the ICU, their clinical status was evaluated with acute physiology and chronic health evaluation II (APACHE-II) and Glasgow coma score (GCS). According to the clinical condition of the patients, appropriate medical treatment, respiratory and oxygen support were provided by infectious diseases, chest diseases and anesthesiology and reanimation specialists. The data of the patients were collected by examining the hospital information system and patient file records. Demographic

data of patients such as age and gender, comorbidity history, APACHE-II and GCS scores at admission to ICU, vital signs, arterial blood gases (pH, pCO_2, pO_2, lactate), hemogram parameters [leukocyte, neutrophil, lymphocyte, platelet (PLT) count], biochemical parameters [urea/creatine, aspartate transaminase (AST), sodium, potassium, D-dimer, C-reactive protein (CRP), creatine kinase (CK), lactate dehydrogenase (LDH)], procalcitonin (PCT) and ferritin levels, the changes in the chest X-ray, and the necessity of inotropic support were recorded.

The clinical conditions, laboratory data, inotrope requirement and chest X-rays were compared during the 1-week period, the day before TCZ treatment (day 1), the day after two-day TCZ treatment (day 4), and the fourth day after treatment (day 7). While evaluating the clinical situation, the patient's need for oxygen support, the change in respiratory distress compared to the previous evaluation, and regression in existing complaints or observation of new findings were considered. The change in the chest X-ray was evaluated by an experienced specialist doctor who has been working in the ICU since the pandemic process began. It was recorded whether the patients developed death during the follow-up period in the ICU.

Statistical Analysis

SPSS 20.0 for Windows software was used for statistical analysis. Numerical data were expressed as minimum-maximum and mean ± standard deviation, while categorical data were expressed as numbers and percentages. Shapiro-Wilk test was used to determine whether the numerical data fit the normality distribution. In the comparison of more than two groups, the data matching the normality distribution were evaluated with the ANOVA test in repetitive samples, while the Friedman test was used to compare the data that did not fit the normality distribution. In paired analyses, the data matching the normality distribution were evaluated with the t-test in dependent samples, and the data not complying with the normality distribution were evaluated with the Wilcoxon test. In all comparisons, $p<0.05$ was considered as significant.

Results

Two hundred and nineteen patients who were treated with TCZ and hospitalized in the COVID-19 ICU were included in this study. The mean age of the patients was 60.70±14.13, and 34.2% were female and 65.8% were male. While the mean APACHE-II score of the patients was 16.47±8.52, the mean GCS was 14.46±1.34. The demographic, comorbidity status, GCS and APACHE-II score data of the patients and the comparison of the data of the deceased-living patients are shown in Table 1. When group I and group II patients were compared in terms of comorbidity, it was observed that patients with a mortal course had more comorbidities, diabetes mellitus (DM) and hypertension (HT) than non-mortal patients (p-values: <0.001; 0.001; 0.003). There was no statistically significant difference between the two groups in terms of other clinical features and comorbidities (p>0.05).

The changes in vital signs and laboratory values over time in patients treated with TCZ are given in Table 2. The change of vital signs over time in patients treated with TCZ is given in Figure 1. The variation of the values of infection markers over time in patients treated with TCZ is given in Figure 2. Considering this change, it was observed that mean arterial pressure (MAP) and CRP values decreased significantly over time (p-values: <0.001; <0.001, respectively). Leukocytes, lymphocytes, lactate, urea, creatinine, AST, D-dimer, LDH and PCT values increased significantly over time (p<0.005). However, although there was a significant decrease in heart rate and CK values immediately after the treatment, an increase was observed in the later period (p-values: 0.015; 0.017, respectively). However, while a significant increase was observed in peripheral oxygen saturation (SpO_2), PLT and ferritin values after treatment, a decrease was observed with time (p-values: <0.001; <0.001; <0.001). Although there was an increase in neutrophil values over time, this difference was not statistically significant (p>0.05).

Information about the pre-treatment data of patients who received TCZ treatment, with and without mortality are given in Table 3. When these data were examined, laboratory values such as leukocytes, neutrophils, urea, D-dimer, LDH, lactate and PCT were higher in patients with a mortal course, while lymphocyte and AST values were found to be significantly lower (p<0.005). However, there was no statistically significant difference in terms of MAP, heart rate, PLT, creatine, CRP, CK, ferritin and inotrope requirements between patients who were and did not die before TCZ treatment (p>0.05).

Information on the post-TCZ treatment data of mortal and non-mortal patients is given in Table 4. After TCZ treatment, MAP was found to be significantly lower (p<0.001), while heart rate was higher (p<0.001) in mortal patients, and accordingly, the need for inotropes was significantly higher

Table 1. Comparison of demographic and clinical data of mortal and non-mortal patients receiving tocilizumab treatment				
Characteristics	**All patients (n=219) Mean ± SD**	**Survivors (n=76) Mean ± SD**	**Non-survivors (n=143) Mean ± SD**	**p-value**
Age	60.70±14.13	57.9±15.1	62.15±13.36	0.092
APACHE-II	16.47±8.52	15.34±7.12	17.07±9.15	0.221
Glasgow coma score	14.46±1.34	14.61±1.19	14.38±1.14	0.077
	n (%)	n (%)	n (%)	
Gender				
Female	75 (34.2)	27 (35.5)	49 (64.5)	0.771
Male	144 (65.8)	48 (33.6)	95 (66.4)	
Comorbidity				
Yes	143 (65.3)	34 (44.7)	109 (76.2)	**<0.001**
No	76 (34.7)	42 (55.3)	34 (23.8)	
Diabetes				
Yes	83 (37.9)	17 (22.4)	66 (46.2)	**0.001**
No	136 (62.1)	59 (77.6)	77 (53.8)	
Hypertension				
Yes	93 (42.5)	22 (28.9)	71 (49.7)	**0.003**
No	126 (57.5)	54 (71.1)	72 (50.3)	
Coronary artery disease				
Yes	37 (16.9)	9 (11.8)	28 (19.6)	0.146
No	182 (83.1)	67 (88.2)	115 (80.4)	
Chronic kidney disease				
Yes	7 (3.2)	0 (0)	7 (4.9)	0.099
No	212 (96.8)	76 (100)	136 (95.1)	
COPD				
Yes	18 (8.2)	7 (9.2)	11 (7.7)	0.697
No	201 (91.8)	69 (90.8)	132 (91.8)	

APACHE-II: Acute physiology and chronic health evaluation II, COPD: chronic obstructive pulmonary disease, SD: standard deviation

(p<0.001). When the laboratory values after treatment were examined, it was determined that leukocyte, neutrophil, lactate, urea, creatine, D-dimer, CRP, CK, LDH, PCT and ferritin values were significantly higher in mortal patients (p<0.05). Lymphocyte and PLT values were significantly higher in non-mortal patients (p-values: <0.001; <0.001, respectively). Again, when compared with pre-treatment radiological imaging, it was observed that progression (67.1%) in mortal patients and regression (67.1%) in non-mortal patients were prominent in chest radiographs (p-values: <0.001; <0.001, respectively).

When the effects of TCZ treatment on mortality were examined, it was found that 7-day mortality was 21%, 28-day mortality was 64.8%, and total mortality was 65.3%. Total mortality was significantly higher in patients with comorbidities (p<0.001). Especially in patients with DM (p=0.001) and HT (p=0.003), mortality was found to be significantly higher. There was no significant difference in terms of chronic obstructive pulmonary disease (p>0.05). Considering the 7-day mortality, PCT values were found to be statistically significantly higher in patients with a mortal course than in non-mortal patients (p=0.016). In the evaluation of 28-day mortality, comorbidity rates were significantly higher in patients with a mortal course compared to non-mortal patients (p<0.001), while a significantly lower lymphocyte count was found (p=0.006). Leukocyte, PCT and D-dimer values were significantly higher in mortal patients (p-values: 0.019; 0.003; <0.001, respectively).

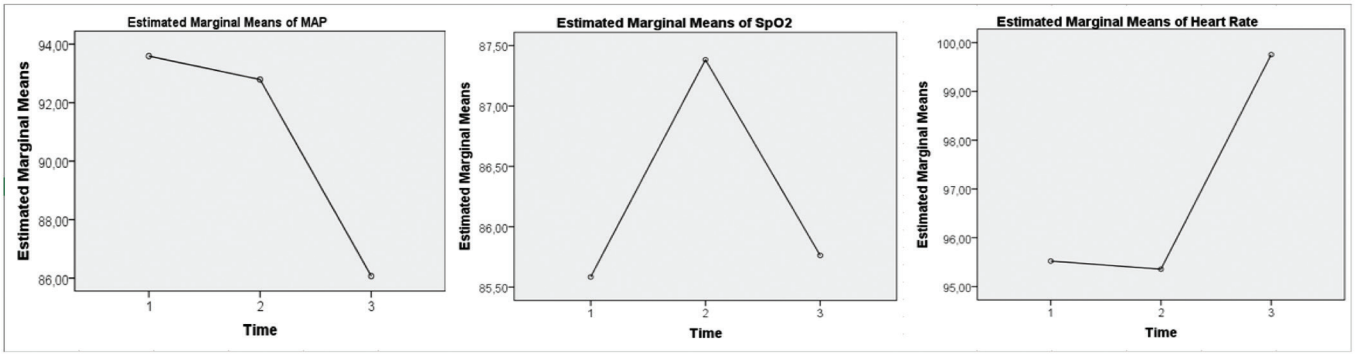

Figure 1. The effect of tocilizumab treatment on vital signs

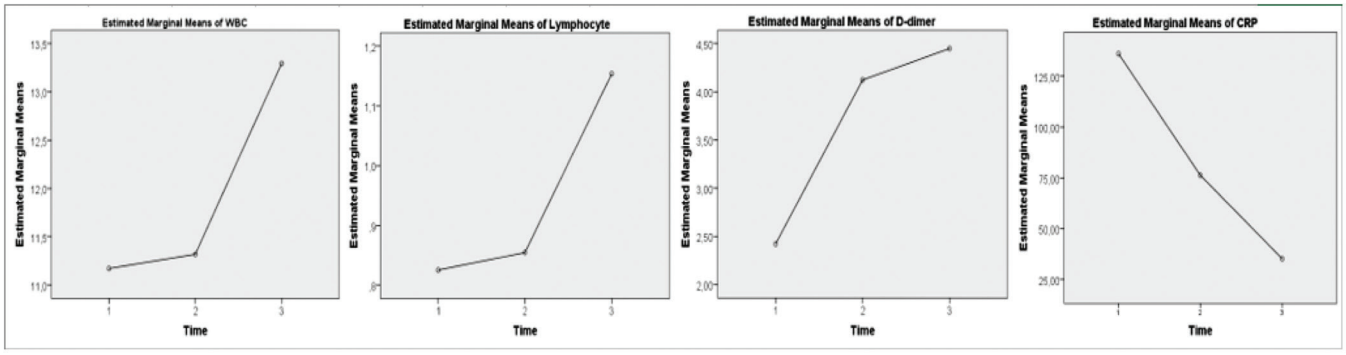

Figure 2. The effect of tocilizumab treatment on infection markers

Table 2. The effect of tocilizumab treatment on vital signs and laboratory values				
Characteristics	**Day 1 (mean ± SD)**	**Day 4 (mean ± SD)**	**Day 7 (mean ± SD)**	**p-value**
MAP (mmHg)	93.59±13.63	92.78±13.97	86.06±15.51	<0.001
Heart rate	95.52±18.04	95.36±18.50	99.75±21.21	0.015
SpO_2	85.58±7.29	87.38±8.06	85.76±11.18	<0.001
Leukocytes (x10^3/uL)	11.17±4.90	11.31±6.22	13.29±7.19	0.005
Neutrophil (x10^3/uL)	9.89±4.73	9.97±5.86	11.51±6.79	0.124
Lymphocyte (x10^3/uL)	0.82±0.54	0.85±0.80	1.15±1.00	<0.001
Platelet (x10^3/uL)	255.57±105.22	281.55±124.40	266.97±145.92	<0.001
Lactate (mmol/L)	2.34±1.49	2.35±1.58	3.25±4.08	0.037
Urea (mg/dL)	49.64±31.84	62.02±45.30	83.60±61.61	<0.001
Creatine (mg/dL)	0.98±0.58	1.07±0.84	1.44±1.36	<0.001
AST (U/L)	60.71±115.36	130.20±485.30	287.03±826.97	0.034
D-dimer (Ug/ml)	2.42±3.33	4.12±3.71	4.44±3.74	<0.001
C-reactvie protein (mg/L)	136.02±70.78	76.25±66.60	35.22±55.81	<0.001
Creatine kinase (IU/L)	242.29±417.58	231.98±505.17	298.33±609.24	0.017
Lactate dehydrogenase (U/L)	615.30±258.01	819.27±748.17	1080.71±1724.66	<0.001
Procalcitonin (ng/mL)	1.04±6.87	1.48±9.13	1.50±7.31	<0.001
Ferritin (µg/L)	1096.55±627.35	1146.68±622.91	1124.03±643.50	<0.001
MAP: Mean arterial pressure, AST: aspartate transaminase, SD: standard deviation				

Table 3. Comparison of pre-treatment data of mortal and non-mortal patients receiving tocilizumab treatment				
Characteristics	**All patients (n=219) Mean ± SD**	**Survivors (n=76) Mean ± SD**	**Non-survivors (n=143) Mean ± SD**	**p-value**
MAP (mmHg)	93.59±13.63	91.27±9.48	94.82±15.28	0.071
Heart rate	96.14±17.53	93.05±13.95	97.78±19.08	0.062
Leukocytes ($x10^3$/uL)	11.17±4.90	10.08±4.58	11.74±4.97	**0.015**
Neutrophil ($x10^3$/uL)	9.89±4.73	8.70±4.37	10.53±4.80	**0.006**
Lymphocyte ($x10^3$/uL)	0.82±0.54	0.92±0.49	0.77±0.57	**0.007**
Platelet ($x10^3$/uL)	255.57±105.22	256.50±103.25	255.08±106.61	0.892
Lactate (mmol/L)	2.34±1.49	2.26±1.99	2.39±1.16	**0.044**
Urea (mg/dL)	48.64±31.84	41.34±31.30	54.05±31.35	**<0.001**
Creatine (mg/dL)	0.98±0.58	0.92±0.42	1.02±0.64	0.567
AST (U/L)	60.71±115.36	61.13±41.48	60.48±139.72	**0.01**
D-dimer (Ug/mL)	2.42±3.33	1.36±2.56	2.98±3.56	**<0.001**
C-reactive protein (mg/L)	136.02±70.78	137.30±61.35	135.34±75.51	0.504
Creatine kinase (IU/L)	242.29±417.58	290.85±577.23	216.49±299.64	0.357
Lactate dehydrogenase (U/L)	615.30±258.01	527.49±189.70	661.97±277.26	**<0.001**
Procalcitonin (ng/mL)	1.04±6.87	0.43±0.91	1.36±8.48	**0.003**
Ferritin (µg/L)	1096.55±627.35	1049.51±617.17	1121.55±633.42	0.375
	n (%)	**n (%)**	**n (%)**	
Inotrope				
Yes	11 (5)	1 (1.3)	10 (7)	0.102
No	208 (95)	75 (98.7)	133 (93)	
MAP: Mean arterial pressure, AST: aspartate transaminase, SD: standard deviation				

Discussion

Cytokine storm seen during COVID-19 disease has been associated with mortality (14). It has been stated that the IL-6 receptor antibody TCZ, approved by the Food and Drug Administration, could provide clinical benefit for eligible COVID-19 patients with high inflammatory biomarkers (15). In this study, we found that after TCZ treatment, MAP and CRP values decreased and there was an increase in leukocyte, lymphocyte, lactate, urea, creatine, AST, D-dimer, LDH and PCT values. In addition, although there was a decrease in heart rate and CK values immediately after the treatment, there was an increase in the later period, and an increase was observed in SpO_2, PLT and ferritin values after the treatment, while a decrease was observed over time.

In our study, when mortal and non-mortal patients followed in the ICU and receiving TCZ treatment were compared, it was found that patients who developed mortality had more comorbidities, and that DM and HT were more common in patients with a mortal course. Considering the studies examining the relationship between comorbidity and COVID-19, de Cáceres et al. (16) reported that HT is an important risk factor in the development of mortality in their study in which they evaluated 75 patients who developed cytokine storm and were given TCZ. Zhou et al. (17), on the other hand, evaluated 191 patients and reported that the presence of comorbidity was higher in mortal patients, and additional diseases such as DM, HT and coronary artery disease were observed more frequently in mortal patients. In their study evaluating the effectiveness of TCZ, Kaya and Kavak (18) emphasized the relationship between DM and HT history and mortality. Unlike these results, Keske et al. (19) in their study with 43 patients, they found no difference in the presence of DM and HT in mortal and non-mortal patients. We think that the different results between studies are due to the difference in the patient populations included in the studies. Some studies included only ward patients, while others included ICU patients.

Table 4. Comparison of post-treatment data of mortal and non-mortal patients receiving tocilizumab treatment				
Characteristics	**All patients (n=219) Mean ± SD**	**Survivors (n=76) Mean ± SD**	**Non-survivors (n=143) Mean ± SD**	**p-value**
MAP (mmHg)	86.06±15.51	92.70±11.19	82.54±16.34	**<0.001**
Heart rate	99.75±21.21	87.57±14.36	106.23±21.45	**<0.001**
Leukocytes (x10^3/uL)	13.29±7.19	10.62±6.61	14.71±7.11	**<0.001**
Neutrophil (x10^3/uL)	11.51±6.79	8.54±6.30	13.09±6.52	**<0.001**
Lymphocyte (x10^3/uL)	1.15±1.00	1.37±0.74	1.03±1.10	**<0.001**
Platelet (x10^3/uL)	266.97±145.92	367.87±130.70	213.34±123.79	**<0.001**
Lactate (mmol/L)	3.25±4.08	2.15±0.87	3.84±4.91	**<0.001**
Urea (mg/dL)	83.60±61.61	46.59±33.81	103.27±64.04	**<0.001**
Creatine (mg/dL)	1.44±1.36	0.78±0.31	1.80±1.56	**<0.001**
AST (U/L)	287.03±826.97	54.79±42.15	410.45±1002.37	0.06
D-dimer (Ug/mL)	4.44±3.74	1.90±2.37	5.79±3.64	**<0.001**
C-reactive protein (mg/L)	35.22±55.81	12.59±17.14	47.25±64.86	**<0.001**
Creatine kinase (IU/L)	298.33±609.24	96.28±133.88	405.72±725.88	**<0.001**
Lactate dehydrogenase (U/L)	1080.72±1724.66	531.47±268.87	1372.63±2069.04	**<0.001**
Procalcitonin (ng/mL)	1.50±7.31	0.10±0.24	2.25±8.97	**<0.001**
Ferritin (µg/L)	1124.03±643.50	818.05±486.98	1286.65±658.58	**<0.001**
	n (%)	**n (%)**	**n (%)**	
Chest X-ray				
No change	44 (20.1)	20 (26.3)	24 (16.8)	**<0.001**
Progress	101 (46.1)	5 (6.6)	96 (67.1)	
Regress	74 (33.8)	51 (67.1)	23 (16.1)	
Inotrope				**<0.001**
Yes	57 (26)	2 (2.6)	55 (38.5)	
No	162 (74)	74 (97.4)	88 (61.5)	

MAP: Mean arterial pressure, AST: aspartate transaminase, SD: standard deviation

Klopfenstein et al. (20) reported in a study in which they compared two patient groups given standard treatment and standard treatment + TCZ treatment in the service, that there was no significant difference between the two groups in terms of mortality, but higher mortality rates were observed in the standard treatment group compared to the TCZ group (20). de Cáceres et al. (16) evaluated 75 patients who received TCZ treatment and reported that patients who received two or more doses of TCZ had higher mortality rates than those who received a single dose (13.5% vs. 47.4%). In the same study, they observed that the only comorbidity significantly associated with ICU admission was obesity, 85% of obese patients needed mechanical ventilation and 62% died (16). Morena et al. (21) found a 30-day mortality rate of 27% in their study with 45 COVID-19 patients followed in the service. Biran et al. (22) found the mortality rate to be 49% in patients hospitalized in the ICU and treated with TCZ in their multicenter and retrospective study. In their study with 52 patients hospitalized in the ICU, Yang et al. (23) observed that the 28-day mortality rate for critical cases increased up to 60.5%, like our study. Tiryaki et al. (24) found the mortality rate to be 78.1% in their study of 114 critical ICU patients who were treated with IVIG. We think that the lower mortality rates in some different studies compared to our study may be since the patient group in our study was critically ill in the ICU, and the emergence of more mortal COVID-19 variants considering the periods in which the studies were conducted.

In our study, it was observed that MAP and CRP values decreased and leukocyte, lymphocyte, lactate, urea,

creatine, AST, D-dimer, LDH and PCT values increased over time in patients treated with TCZ. In their study with 75 patients who were given TCZ treatment, de Cáceres et al. (16) observed a significant decrease in CRP values and a significant increase in lymphocyte count on the 5th day after TCZ treatment, similar to our study. However, they did not report a significant change in D-dimer and ferritin values (16). Biran et al. (22), in their study with 630 patients, found a decrease in CRP levels 3, 7 and 14 days after TCZ application, similar to our study. They found that there was no significant change in D-dimer, ferritin, or LDH values on the 3rd and 7th days after treatment in patients receiving TCZ. In addition, they reported a non-significant decrease in the oxygen percentage (FiO_2) of inspired air on the 1st day after treatment (22). Different reports have defined a correlation between ferritin, D-dimer, and LDH concentrations and the severity of COVID-19 (25,26).

Keske et al. (19), in their study with 43 patients who underwent TCZ treatment, found a significant decrease in CRP values after TCZ application, similar to our study. However, unlike our study, they reported that D-dimer and PCT values were significantly lower. They also reported an increase in lymphocyte percentage, a sharp decrease in CRP values, and a decrease in ferritin and D-dimer values after TCZ administration (19). Similar to our study, Kaya and Kavak (18) found a significant decrease in CRP values and an increase in lymphocyte counts after TCZ treatment in both non-mortal and mortal patients. They reported a significant decrease in serum ferritin levels in non-mortal patients and a significant increase in mortal patients (18). Hirao et al. (27), on the other hand, found that the median concentrations of CRP, PCT and fibrinogen decreased significantly in their study with 28 patients treated with TCZ. They also reported that the median lymphocyte and PLT counts increased significantly after treatment with TCZ (27). In their study with 21 patients who underwent TCZ, Xu et al. (28) found a significant improvement in SpO_2 values and a decrease in oxygen uptake within 5 days after TCZ treatment. They observed that the lymphocyte percentage returned to normal in 10 patients (52.6%), and CRP values decreased significantly in 84.2% of the patients on the 5th day after treatment. They reported an increase in SpO_2 and lymphocyte counts, a decrease in leukocyte and CRP values, and a decrease in PCT over time after TCZ treatment (28). Wang et al. (6), in their study with 138 COVID-19 patients, considered the decrease in lymphocyte percentage to be an important indicator for the diagnosis and assessment of severity in COVID-19 patients.

de Cáceres et al. (16) found a decrease in lymphocyte count in most of the patients (91.8%) in the analysis before TCZ application. They found an increase in CRP, D-dimer and ferritin. They reported that there is a significant correlation between mortality and ICU admission in patients with D-dimer baseline values >1.5 µg/mL (16). In their study with 544 patients with severe pneumonia, Guaraldi et al. (12) reported that patients with high CRP and IL-6 concentrations had higher LDH and worse inflammatory profiles. In the study by Keske et al. (19), IL-6, ferritin, CRP and D-dimer values in mortal cases were not statistically significant compared to non-mortal cases. Kaya and Kavak (18), in their study with 308 patients who were given TCZ treatment, found that D-dimer values were significantly higher in mortal patients than in non-mortal patients both before and after TCZ treatment. Therefore, a decrease in ferritin and CRP levels and an increase in lymphocyte count can be considered as indicators of response to TCZ. In our study, we found that lymphocyte counts were significantly lower in patients who were mortal before TCZ treatment compared to non-mortal patients. We observed that laboratory values such as leukocytes, neutrophils, urea, D-dimer, LDH, lactate and PCT were significantly higher. These findings, which we determined, were found to be compatible with the data in many studies in the literature.

In the study performed by Xu et al. (28), all patients had abnormal thorax computed tomography (CT) findings at presentation in radiological imaging, and CT scans found that the lesions were completely resolved in 19 (90.5%) patients and partial improvement in the others after TCZ treatment. In the study by Hirao et al. (27), they found a significant improvement in the changes in the lungs in repetitive chest X-ray or CT examinations after TCZ treatment. When we examined the repeated chest radiographs in our study, it was observed that there was no regression in 74 patients (33.8%), progression in 101 patients (46.1%), and no change in 44 patients (20.1%) after TCZ treatment.

Conclusion

It is thought that TCZ may have effective results in the treatment of COVID-19 disease, which still has no approved effective treatment, especially with the initiation of cytokine storm in the early period due to the high mortality risk.

Decrease in ferritin and CRP levels and increase in lymphocyte count can be considered as indicators of response to TCZ. Critically ill patients treated in the ICU still have high mortality rates despite receiving two or more doses. Our study is single-center and retrospective, and there is a need for larger and multicenter studies on the subject.

Ethics

Ethics Committee Approval: Ministry of Health Scientific Research Platform permission (20.10.2021), hospital management permission (25.10.2021), and University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee approval (dated 26.11.2021 and numbered 936) were obtained.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: R.S., O.U., Concept: R.S., O.U., Design: R.S., O.U., Data Collection and Process: R.S., Analysis or Interpretation: O.U., Literature Search: R.S., Writing: R.S., O.U.

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

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

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382:727-33.
2. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. Available from: URL: https://www.who.int/director-general/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020. Accessed February 11, 2020.
3. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395:514-23.
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13.
5. World Health Organization [Internet]. WHO Coronavirus (COVID-19) Dashboard. Available from: URL: https://covid19.who.int. Accessed September 7, 2022.
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang B, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323:1061-9.
7. Hu B, Zeng LP, Yang XL, Ge XY, Zhang W, Li B, et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog. 2017;13:e1006698.
8. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. Semin Immunopathol. 2017;39:529-39.
9. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
10. Alijotas-Reig J, Esteve-Valverde E, Belizna C, Selva-O'Callaghan A, Pardos-Gea J, Quintana A, et al. Immunomodulatory therapy for the management of severe COVID-19. Beyond the anti-viral therapy: A comprehensive review. Autoimmun Rev. 2020;19:102569.
11. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8:420-2.
12. Guaraldi G, Meschiari M, Cozzi-Lepri A, Milic J, Tonelli R, Menozzi M, et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. Lancet Rheumatol. 2020;2:e474-84.
13. Somers EC, Eschenauer GA, Troost JP, Golob JL, Gandhi TN, Wang L, et al. Tocilizumab for Treatment of Mechanically Ventilated Patients With COVID-19. Clin Infect Dis. 2021;73:e445-54.
14. Vu CA, DeRonde KJ, Vega AD, Maxam M, Holt G, Natori Y, et al. Effects of Tocilizumab in COVID-19 patients: a cohort study. BMC Infect Dis. 2020;20:964.
15. Le RQ, Li L, Yuan W, Shord SS, Nie L, Habtemariam BA, et al. FDA Approval Summary: Tocilizumab for Treatment of Chimeric Antigen Receptor T Cell-Induced Severe or Life-Threatening Cytokine Release Syndrome. Oncologist. 2018;23:943-7.
16. de Cáceres C, Martínez R, Bachiller P, Marín L, García JM. The effect of tocilizumab on cytokine release syndrome in COVID-19 patients. Pharmacol Rep. 2020;72:1529-37.
17. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-62.
18. Kaya S, Kavak S. Efficacy of Tocilizumab in COVID-19: Single-Center Experience. Biomed Res Int. 2021;2021:1934685.
19. Keske Ş, Tekin S, Sait B, İrkören P, Kapmaz M, Çimen C, et al. Appropriate use of tocilizumab in COVID-19 infection. Int J Infect Dis. 2020;99:338-43.
20. Klopfenstein T, Zayet S, Lohse A, Balblanc JC, Badie J, Royer PY, et al. Tocilizumab therapy reduced intensive care unit admissions and/or mortality in COVID-19 patients. Med Mal Infect. 2020;50:397-400.
21. Morena V, Milazzo L, Oreni L, Bestetti G, Fossali T, Bassoli C, et al. Off-label use of tocilizumab for the treatment of SARS-CoV-2 pneumonia in Milan, Italy. Eur J Intern Med. 2020;76:36-42.
22. Biran N, Ip A, Ahn J, Go RC, Wang S, Mathura S, et al. Tocilizumab among patients with COVID-19 in the intensive care unit: a multicentre observational study. Lancet Rheumatol. 2020;2:e603-12.
23. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8:475-81.
24. Tiryaki C, Uzundere O, Erdal Erbatur M, Kaçar CK. Factors affecting the mortality of patients in critical condition with coronavirus disease 2019 in the ıntensive care. Turkiye Klinikleri J Anest Reanim. 2021;19:124-32.
25. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19 - A systematic review. Life Sci. 2020;254:117788.
26. Cavalli G, De Luca G, Campochiaro C, Della-Torre E, Ripa M, Canetti D, et al. Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study. Lancet Rheumatol. 2020;2:e325-31.
27. Hirao M, Hashimoto J, Tsuboi H, Nampei A, Nakahara H, Yoshio N, et al. Laboratory and febrile features after joint surgery in patients with rheumatoid arthritis treated with tocilizumab. Ann Rheum Dis. 2009;68:654-7.
28. Xu X, Han M, Li T, Sun W, Wang D, Fu B, et al. Effective treatment of severe COVID-19 patients with tocilizumab. Proc Natl Acad Sci U S A. 2020;117:10970-5.

Turk J Intensive Care 2024;22:207-11
DOI: 10.4274/tybd.galenos.2023.64497

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Are *Myroides* spp. Isolated From Urinary Catheter Cultures of Patients in Intensive Care Units an Infection or Colonization? Analysis of 36 Cases

Yoğun Bakım Ünitesi Hastalarının Üriner Kateter Kültürlerinden İzole Edilen *Myroides* spp. İzolatları Enfeksiyon mu Yoksa Kolonizasyon mu? 36 Olgunun Analizi

Received/Geliş Tarihi : 20.01.2023
Accepted/Kabul Tarihi : 12.09.2023

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ABSTRACT *Objective: Myroides* species are mostly low-grade opportunistic pathogens and infect immunocompromised patients. Reports of *Myroides* spp. increased from clinical samples due to unique developments in molecular microbiology. However, clinical importance of this microorganism in intensive care units' patients is debated. We aimed to determine whether *Myroides* spp. strains isolated from urinary catheter cultures of patients in intensive care units are led to an infection or colonization by examining the risk factors of the patients between January 2018 and December 2022.

Materials and Methods: In a university hospital, the patients who *Myroides* spp. isolated from urine cultures in intensive care units between January 2018 and December 2022 were included in the study. The method and reasons of taking urine samples, the presence of a urinary catheter, blood cultures samples in terms of urinary sepsis, the antimicrobial susceptibility of the isolates, and hospital stay were evaluated retrospectively. Also, control culture samples were taken after 24 and 72 hours by changing the urinary catheters of these patients.

Results: Thirty-six patients were enrolled to the study. Urine cultures were taken for investigate the source of infection in 23 patients, and nine for control urinary culture and in three patients for macroscopic urine blurred and in one patient to detect colonization before urinary surgery. There was not any blood culture positivity found. All *Myroides* spp. isolated patients had urinary catheter. Average length of hospital stay was determined as 41.3 days (7-355). A total 34 of the 36 isolated *Myroides* spp. were pan-drug resistant. Antibacterial treatment was not initiated in any of the patients. Urinary catheters change after first isolation of *Myroides* spp. was recommended in all patients. After the patients' urinary catheters were changed, *Myroides* spp. were not grown in the control culture samples taken 24 and 72 hours after.

Conclusion: As a result of our study, *Myroides* spp. were isolated especially in patients with long hospital stays and urinary catheters. It was determined that the patients were controlled without treatment, only with urinary catheter replacement. We believe that this agent should be evaluated as having a very high rate of urinary colonization, and the urinary catheter should be changed first, urinary symptoms should be followed up, and unnecessary antimicrobial use should be avoided.
Keywords: *Myroides* species, urinary tract infections, colonization

ÖZ *Amaç: Myroides* türleri çoğunlukla düşük dereceli fırsatçı patojenlerdir ve bağışıklık sistemi baskılanmış hastaları enfekte eder. Moleküler mikrobiyoloji alanındaki benzersiz gelişmeler nedeniyle klinik örneklerden *Myroides* spp. identifikasyonu artmıştır. Ancak yoğun bakım hastalarında bu mikroorganizmanın klinik önemi tartışılmaktadır. Çalışmamızda, Ocak-2018 Aralık 2022 tarihleri arasında yoğun bakım ünitelerinde yatan hastaların üriner kateter kültürlerinden izole edilen *Myroides* spp. suşlarının enfeksiyona mı yoksa kolonizasyona mı yol açtığını, hastaların risk faktörlerini inceleyerek belirlemeyi amaçladık.

Gereç ve Yöntem: Bir üniversite hastanesinde Ocak 2018-Aralık 2022 tarihleri arasında yoğun bakım ünitelerinde idrar kültürlerinden *Myroides* spp. izole edilen hastalar çalışmaya dahil edildi. İdrar örneklerinin alınma yöntemi ve nedenleri, üriner kateter varlığı, üriner-sepsis açısından kan

kültürü örnekleri, izolatların antimikrobiyal duyarlılıkları ve hastanede kalış süreleri retrospektif olarak değerlendirildi. Ayrıca bu hastaların üriner kateterleri değiştirilerek 24 ve 72 saat sonra kontrol kültür örnekleri alındı.
Bulgular: Çalışmaya otuz altı hasta dahil edildi. Yirmi üç hastada enfeksiyon kaynağını araştırmak için, dokuz hastada kontrol idrar kültürü için, üç hastada makroskopik idrar bulanıklığı nedeniyle ve bir hastada cerrahi öncesi kolonizasyon tespiti için idrar kültürü alındı. Herhangi bir kan kültüründe pozitiflik saptanmadı. Tüm *Myroides* spp. izole hastalarda üriner kateter vardı. Ortalama hastanede kalış süresi 41,3 gün (7-355) olarak belirlendi. İzole edilen 36 *Myroides* spp. suşundan 34'ü çoklu ilaca dirençli idi. Hiçbir hastaya antibakteriyel tedavi başlanmadı. Tüm hastalara *Myroides* spp.'nin ilk izolasyonundan sonra üriner kateter değişimi önerildi. Hastaların üriner kateterleri değiştirildikten 24 ve 72 saat sonra alınan kontrol kültür örneklerinde *Myroides* spp. üremedi.
Sonuç: Çalışmamız sonucunda, *Myroides* spp. özellikle hastanede uzun süre yatan ve üriner kateteri olan hastalarda izole edilmiştir. Hastalara antimikrobiyal tedavi verilmeden sadece üriner kateter değişimi ile kontrol altına alındığı belirlendi. Bu mikroorganizmanın üriner kolonizasyon oranı çok yüksek olarak değerlendirilmesi ve öncelikle üriner kateterin değiştirilmesi, üriner semptomların takibi ve gereksiz antimikrobiyal kullanımından kaçınılması gerektiği kanaatindeyiz.
Anahtar Kelimeler: *Myroides* türleri, idrar yolu enfeksiyonu, kolonizasyon

Introduction

In recent years, in line with the unique developments in molecular microbiology, many bacteria that were previously isolated from clinical samples but could not be typed have begun to be typed. Therefore, the incidence of *Myroides* species reports has increased in clinical samples, especially urine culture samples taken from patients with urinary catheters (1).

Myroides species are yellow-pigmented, non-fermentative, Gram-negative bacilli and previously classified as *Flavobacterium* species. Also, *Myroides* spp. is widely found in environmental sources, especially in soil and water, but it is also isolated from seafood, and meat processing plants. Although *Myroides* spp. are ubiquitous in marine and soil environments, they have been associated with very few documented infections in humans since their first identification in the 1920s (2). *Myroides* spp. are reported to rarely cause infection in immunocompromised patients (3,4). Although this microorganism is considered a pathogen with low infection potential, it has been reported to be associated with various life-threatening infections such as meningitis, pneumonia, septicemia, urinary tract, and soft tissue infections in recent years. *Myroides* spp. are mostly low-grade opportunistic pathogens and infect immunocompromised patients such as those with kidney failure, liver cirrhosis, lung disease, cancer, and prolonged stays in intensive care units (4,5).

Myroides species were rarely isolated from a variety of clinical samples of human infections, such as urine, wounds, and blood. In the literature, the most common infections, depending on *Myroides* spp. are reported as urinary tract infections (UTIs). Urinary catheter use is an important risk factor for these infections. However, although infections caused by *Myroides* spp. are rare, they are resistant to multiple antibiotics, such as carbapenems, beta-lactams, and have variable sensitivity to aminoglycosides, quinolones, and sulfamethoxazole (6).

In this context, it was observed in our hospital that the reporting of multi-drug resistant *Myroides* spp. isolates increased. In this study, we aimed to determine whether *Myroides* spp. strains isolated from urinary catheter cultures of patients in intensive care units led to infection or colonization by examining the risk factors of the patients between January 2018 and December 2022.

Materials and Methods

Hospital Setting

The study was conducted in a tertiary university hospital with a capacity of 1370 beds and 352 intensive care beds. Thirty-six patients who were hospitalized in intensive care units between January 2018 and December 2022 and whose *Myroides* spp. were isolated from their clinical samples were included in the study. An informed consent form for the patients was provided. All clinical samples were urine culture samples. Repeated samples from the same patient were excluded from the study. The study was managed following the principles of the Declaration of Helsinki. Ethics committee approval was obtained from the İnönü University Scientific Research and Publication Ethics Committee (decision no: 2021/1240, date: 05.01.2021).

The method and reason for taking urine samples, the presence of a catheter in the patients, blood culture samples in terms of urinary sepsis, the antimicrobial susceptibility of the isolated *Myroides* spp., and hospital stay were evaluated. Also, control culture samples were taken after 24 and 72 hours by exchanging the urinary catheters of these patients.

Identification and Antimicrobial Susceptibility

Urine culture samples were taken from patients' catheters in accordance with aseptic techniques. The samples were sent to the microbiology laboratory to be processed within 30 minutes in sterile containers. Urine samples were quantitatively inoculated on 5% sheep blood agar and eosin methylene blue agar medium in the laboratory. After 18-24 hours' incubation at 37 °C, identification of the isolates that were grown as 1-2 mm round, smooth yellow pigmented, fruit-scented oxidase and catalase positive, Gram-negative bacilli was made by Matrix-Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) (BioMérieux, France). The antimicrobial susceptibility of the isolates to ciprofloxacin, levofloxacin, amoxicillin-clavulanic acid, cefepime, ceftazidime, cefotaxime, imipenem, meropenem, gentamicin, amikacin, piperacillin/tazobactam, and trimethoprim/sulfamethoxazole was determined by the disk diffusion method on Mueller-Hinton agar medium, and colistin susceptibility was determined by the broth micro-dilution method. Results were interpreted according to The European Committee on Antimicrobial Susceptibility Testing guideline recommendations (7). Blood culture samples sent to our laboratory were incubated for 5 days in the BACT/ALERT 3D (BioMérieux, France) fully automated blood culture system.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows, version 17.0 (IBM-SPSS Inc, Armonk, NY).

Results

Myroides spp. was isolated in 36 of the urine culture samples sent from intensive care units to our laboratory over a period of five years. The mean age of the patients was 59±19.9 years (10-84 years), and 22 (61.1%) were male patients. Patients were hospitalized in ICU due to trauma, intracranial events, myocardial infarction, acute renal failure. There was no comorbidity in 11 patients, the other patients had renal or urogenital problems, pulmonary and cardiac problems, intracranial events, and malignancy. All *Myroides* spp. isolated patients had urinary catheters. Thirty four isolates were resistant to the studied antimicrobials, ciprofloxacin, levofloxacin, amoxicillin-clavulanic acid, cefepime, ceftazidime, cefotaxime, imipenem, meropenem, gentamicin, amikacin, piperacillin/tazobactam, trimethoprim/sulfamethoxazole, and colistin. One isolate was susceptible to cefepime, ceftazidime, cefotaxime, gentamicin, amikacin, trimethoprim/sulfamethoxazole, and two isolates were susceptible to colistin. Based on these results, we concluded that the isolates were pan-drug resistant, except for two strains. It was found that urine cultures were taken during the investigation of the infection focus in 23 of the patients to determine whether the urinary agent was controlled in nine patients, in three patients because of turbidity in the urine color, and in one patient to detect colonization before urinary surgery. None of the patients had urinary symptoms. Before *Myroides* spp. was isolated, six patients were not receiving any antibiotic treatment, eight patients were using piperacillin/tazobactam, 19 patients were using meropenem, and three patients were using ciprofloxacin. However, spesific antibacterial treatment was not initiated in any of the patients against *Myroides* spp.

Urinary catheter changes were recommended for all patients. After the patients' urinary catheters were changed, *Myroides* spp. isolates were grown in only four of the control culture samples taken 24 hours later. There was no growth in the control culture samples taken 24 and 72 hours after exchanging the urinary catheters of the other thirty-two patients. Urinary catheters of the patients who had growth at the 24th hour was exchanged again, and there was no growth in the samples taken at the 24th and 72nd hours.

In blood cultures, *Myroides* spp. were not isolated. The average length of hospital stay was determined to be 41.3 days (7-355).

Discussion

Currently, the spectrum of healthcare associated, and community-acquired infections caused by new opportunistic pathogens is constantly increasing. This increase in the number of newly described microorganisms is due to the introduction of MALDI-TOF into clinical microbiology laboratories and the use of molecular identification methods such as 16S rRNA sequencing (1). Due to these technological advances, *Myroides* spp. are much more isolated in urine culture samples.

Myroides spp. is an aerobic, non-fermentative, immobile Gram-negative bacillus, usually found in water and soil. Due to the presence of flexirubin, they are bacteria with a yellow pigment and a characteristic fruity smell like strawberries (4). They do not belong to the normal human flora. However,

since they are rare pathogens in humans, they are considered low-grade opportunistic pathogens. Opportunistic infections have been reported mostly in immunocompromised patients (3,4). Also, despite their low pathogenicity potential, *Myroides* spp. isolates are multidrug resistant. They can also form biofilms and have a polysaccharide capsule that makes their surface hydrophobic (4,6).

It has been reported in the literature that *Myroides* spp. can cause the most common UTIs and rarely soft tissue, bone, pneumonia, and sepsis (8). *Myroides* spp. was first reported as an infection agent by Holmes et al. (9) after it was identified from urine cultures. Ktari et al. (10) reported seven UTIs cases due to *Myroides* spp. in patients who underwent endo-urological operations and had urinary stones. Licker et al. (11) reported four hospital acquired UTIs due to *Myroides odoratimimus* isolated from the urine specimens of immunocompromised patients. The patients had urinary catheters, and all isolates were resistant to antibiotics. In the report of Yağci et al. (12), in our country, it has been shown that patients with UTIs due to *Myroides* spp. are catheterized or have urinary tract neoplasia or stones. Kutlu et al. (13) reported an outbreak of UTIs in intensive care units. They isolated six strains of *M. odoratimimus* from the urine samples. They said that all the patients were immunocompromised, underwent urinary catheterization, and none of the patients had urinary neoplasm, surgery, or calculi. Additionally, they identified the isolates as *M. odoratimimus* by 16S rRNA-based sequencing and determined that the isolates were resistant to antibiotics.

Antimicrobial treatment of infections due to *Myroides* spp. isolates is difficult due to their production of metallo-betalactamase. Therefore, many strains are resistant to beta-lactams and carbapenems. They may show variable sensitivity to aminoglycosides, quinolones, and trimethoprim/sulfamethoxazole (6,8). A total of 34 of the isolated strains in our study were resistant to beta-lactams, carbapenems, aminoglycosides, quinolones, and trimethoprim/sulfamethoxazole. One isolate was susceptible to beta-lactams, aminoglycosides, and trimethoprim/sulfamethoxazole two isolates were susceptible to colistin. Kara et al. (14) reported that eleven *Myroides* spp. isolates they identified were resistant to all groups except tigecycline. Death has been reported in two cases due to *Myroides* spp. multi-drug resistance (15,16).

As a result of our study, *Myroides* spp. was isolated from urine culture samples taken from the urinary catheters of thirty-six intensive care patients. No growth was detected in the control cultures taken after 72 hours of exchanging the urinary catheters of the patients. The most important risk factors for *Myroides* spp. in these patients seems to be the length of hospital stay and the presence of a urinary catheter. The average length of hospital stay for the patients were determined to be 41.3 days. However, isolated *Myroides* spp. was not considered an infection agent, and antimicrobial treatment was not applied to any of the patients.

The limitation of the study was that clonal relationship between the isolates and the source of *Myroides* spp. spread was not determined.

Conclusion

Myroides spp. were isolated, especially in patients with long hospital stays and urinary catheters. It was determined that the patients were controlled without treatment, only with urinary catheter replacement. We believe that this agent should be evaluated as having a very high rate of urinary colonization, and the urinary catheter should be changed first, urinary symptoms should be followed up, and unnecessary antimicrobial use should be avoided.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the İnönü University Scientific Research and Publication Ethics Committee (decision no: 2021/1240, date: 05.01.2021).

Informed Consent: An informed consent form for the patients was provided.

Authorship Contributions

Surgical and Medical Practices: D.Ç., Y.E., A.B.Ö., Concept: Y.D., Y.E., A.B.Ö., Design: Y.D., E.N.P., Data Collection or Processing: D.Ç., Analysis or Interpretation: Y.D., E.N.P., Y.E., Literature Search: D.Ç., Y.E., A.B.Ö., Writing: Y.D., Final Approval: Y.D., Y.E., D.Ç., N.P., A.B.Ö.

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

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

References

1. Schröttner P, Rudolph WW, Eing BR, Bertram S, Gunzer F. Comparison of VITEK2, MALDI-TOF MS, and 16S rDNA sequencing for identification of Myroides odoratus and Myroides odoratimimus. Diagn Microbiol Infect Dis. 2014;79:155-9.
2. Zumla A. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Lancet Infect Dis. 2010;10:303-4.
3. Vancanneyt M, Segers P, Torck U, Hoste B, Bernardet JF, Vandamme P, et al. Reclassification of Flavobacterium odoratum (Stutzer 1929) strains to a new genus, Myroides, as Myroides odoratus comb. Nov. and Myroides odoratimimus sp. nov. Int J Syst Bacteriol. 1996;46:926-32.
4. Benedetti P, Rassu M, Pavan G, Sefton A, Pellizzer G. Septic shock, pneumonia, and soft tissue infection due to Myroides odoratimimus: report of a case and review of Myroides infections. Infection. 2011;39:161-5.
5. Elantamilan D, Lyngdoh VW, Choudhury B, Khyriem AB, Rajbongshi J. Septicaemia caused by Myroides spp. - A case report. JMM Case Reports. 2015;5:1-4.
6. Hu SH, Yuan SX, Qu H, Jiang T, Zhou YJ, Wang MX, et al. Antibiotic resistance mechanisms of Myroides sp. J Zhejiang Univ Sci B. 2016;17:188-99.
7. EUCAST (2021). Available from: URL: https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_14.0_Breakpoint_Tables.pdf.
8. Willems P, Muller J, Verhaegen J, Saegeman V, Desmet S. How to treat a fulminant erysipelas and sepsis caused by Myroides odoratimimus: case report and literature review. Acta Clin Belg. 2017;72:331-5.
9. Holmes B, Snell JJ, Lapage SP. Flavobacterium odoratum: a species resistant to a wide range of antimicrobial agents. J Clin Pathol. 1979;32:73-7.
10. Ktari S, Mnif B, Koubaa M, Mahjoubi F, Ben Jemaa M, Mhiri MN, Hammami A. Nosocomial outbreak of Myroides odoratimimus urinary tract infection in a Tunisian hospital. J Hosp Infect. 2012;80:77-81.
11. Licker M, Sorescu T, Rus M, Cirlea N, Horhat F, Jurescu C, et al. Extensively drug-resistant Myroides odoratimimus - a case series of urinary tract infections in immunocompromised patients. Infect Drug Resist. 2018;11:743-9.
12. Yağci A, Cerikcioğlu N, Kaufmann M E, Malnick H, Söyletir G, Babacan F, et al. Molecular typing of Myroides odoratimimus (Flavobacterium odoratum) urinary tract infections in a Turkish hospital. Eur J Clin Microbiol Infect Dis. 2000;19:731-2.
13. Kutlu HH, Avcı M, Dal T, Arı O, Durmaz R. A Healthcare-Associated Outbreak of Urinary Tract Infections Due to Myroides odoratimimus. Jpn J Infect Dis. 2020;73:421-6.
14. Kara I, Kalem F, Unaldı O, Arslan U. Myroides Sp, a Rare Opportunistic Infective Agent, at a Hospital in Turkey. Southeast Asian Journal of Tropical Medicine and Public Health. 2019;50:248-57.
15. Crum-Cianflone NF, Matson RW, Ballon-Landa G. Fatal case of necrotizing fasciitis due to Myroides odoratus. Infection. 2014;42:931-5.
16. Prateek S, Gupta P, Mittal G, Singh AK. Fatal Case of Pericardial Effusion Due to Myroides Odoratus: A Rare Case Report. J Clin Diagn Res. 2015;9:DD01-2.

Turk J Intensive Care 2024;22:212-7
DOI: 10.4274/tybd.galenos.2024.63644

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Comparison of USCOM and PiCCO Cardiac Output Measurements in Intensive Care Unit

Yoğun Bakım Ünitesinde USCOM ve PiCCO ile Kalp Debisi Ölçümlerinin Karşılaştırılması

Received/Geliş Tarihi : 12.10.2023
Accepted/Kabul Tarihi : 19.01.2024

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ABSTRACT *Objective:* In the management of haemodynamically unstable patients, cardiac output (CO) measurement provides clinicians with important data on organ tissue perfusion. This measurement can be performed by pulse-induced contour cardiac output (PiCCO) using thermodilution method, which is a less invasive method, and ultrasonic cardiac output monitoring (USCOM), which is completely non-invasive. The aim of this study was to investigate the clinical relevance of CO and cardiac index measurements obtained by USCOM in patient's with sepsis and septic shock by comparing them with the PiCCO technique, which has been used as a reference measurement method in recent years.
Materials and Methods: In this prospective study, 36 patient's with sepsis and septic shock ventilated with 8-10 mL/kg tidal volume without respiratory effort were included. Patient's with arrhythmia, known heart failure or pulmonary embolism were excluded.
Results: After averaging the PiCCO and USCOM measurements performed by different clinicians, the heart rate was found to be 3.23 L/min/m^2 with PiCCO and 2.24 L/min/m^2 with USCOM. When the two results were compared, the difference was statistically significant (p=0.01). Stroke volume variation was 15.80% with PiCCO and 52.89% with USCOM. When the two results were compared, the difference was statistically significant (p=0.01).
Conclusion: There was no agreement between USCOM and PiCCO measurements in sepsis patient's. In our opinion, more studies are needed for USCOM reliability.
Keywords: PiCCO, USCOM, cardiac output

ÖZ *Amaç:* Hemodinamik olarak stabil olmayan hastaların yönetiminde, kardiyak output (CO) ölçümü klinisyenlere organ doku perfüzyonu hakkında önemli veriler sağlar. Bu ölçüm daha az invaziv bir yöntem olan termodilüsyon yöntemi kullanılarak PiCCO (pulse-induced contour cardiac output) ve tamamen non-invaziv olan ultrasonik kardiyak output monitörizasyonu (USCOM) ile yapılabilmektedir. Bu çalışmanın amacı, sepsis ve septik şok hastalarında USCOM ile elde edilen CO ve kardiyak indeks ölçümlerinin, son yıllarda referans ölçüm yöntemi olarak kullanılan PiCCO tekniği ile karşılaştırılarak klinik anlamlılığının araştırılmasıdır.
Gereç ve Yöntem: Bu prospektif çalışmaya, solunum eforu olmadan 8-10 mL/kg tidal volüm ile ventile edilen 36 sepsis ve septik şok hastası dahil edildi. Aritmisi, bilinen kalp yetmezliği veya pulmoner embolisi olan hastalar çalışma dışı bırakıldı.
Bulgular: Farklı klinisyenler tarafından yapılan PiCCO ve USCOM ölçümlerinin ortalaması alındıktan sonra, kalp atım hızı PiCCO ile 3,23 L/dk/m^2 ve USCOM ile 2,24 L/dk/m^2 olarak bulundu. İki sonuç karşılaştırıldığında aradaki fark istatistiksel olarak anlamlı bulunmuştur (p=0,01). İnme hacmi değişimi PiCCO ile %15,80 ve USCOM ile %52,89 idi. İki sonuç karşılaştırıldığında aradaki fark istatistiksel olarak anlamlıydı (p=0,01).
Sonuç: Sepsis hastalarında USCOM ve PiCCO ölçümleri arasında uyum yoktu. USCOM güvenilirliği için daha fazla çalışmaya ihtiyaç olduğunu düşünüyoruz.
Anahtar Kelimeler: PiCCO, USCOM, kardiyak output

Introduction

In order to make the most accurate decision in the management of hemodynamically unstable patients, the use of many physiological parameters at the same time will minimize the margin of error. In addition to parameters such as blood pressure (BP), heart rate (HR), central venous pressure (CVP) and blood lactate level, cardiac output (CO) measurement provides clinicians with important data about organ tissue perfusion in patients followed and treated in the intensive care unit.

Although the use of a pulmonary artery catheter (PAC) for CO measurement is considered the gold standard, its use is gradually decreasing due to some risks. Instead of this invasive technique, measurement of CO with devices such as pulse-induced contour cardiac output (PiCCO), which uses the thermodilution method and is less invasive, is coming to the fore. Ultrasonic cardiac output monitoring (USCOM) is a device that performs CO measurement completely non-invasively by the continuous-wave Doppler method and provides rapid and economical cardiac measurements. The aim of this study was to investigate the clinical relevance of USCOM in patients with sepsis and septic shock by comparing the cardiac index (CI) measurements obtained by USCOM with the PiCCO technique, which is the most commonly used measurement method in recent years.

Materials and Methods

Ethics Committee Approval

This study was conducted in the Anaesthesiology and Reanimation Intensive Care Unit of Akdeniz University Faculty of Medicine Hospital. Approval from the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee was obtained before the commencement of the study (decision no: 299, decision date: 18.06.2014). The study was conducted in accordance with the principles stated in the Declaration of Helsinki. Patients and their relatives were informed and their consent was obtained for this prospective study.

Patients

In this prospective study, 37 patients with sepsis and septic shock hospitalized in the Department of Anaesthesiology and Reanimation, Intensive Care Unit of Akdeniz University Faculty of Medicine Hospital were included. One patient was excluded from the study because the PiCCO measurement could not be performed due to a technical error. All patients were followed up on mechanical ventilators. None of the patients had arrhythmia, valvular heart disease or previously known heart failure. We excluded patients diagnosed with pulmonary embolism from the study.

Method

The ultrasonic heart monitor (USCOM Pty Ltd., Coffs Harbour, NSW, Australia) is a non-invasive bedside measurement device. The USCOM records the blood Doppler flow curve through the aortic or pulmonary valve and calculates the CO by multiplying the stroke volume (SV) and HR. The USCOM software uses an algorithm based on the patient's height to determine the aortic valve area. Here, SV is the product of the velocity time integral (VTI) and the cross-sectional area (CSA) of the selected valve. An algorithmic result is obtained from the height and gender data previously recorded for each patient (1,2).

CO : SV x HR

In the measurements, a Doppler flow curve with a maximum blood flow characterized by a well-defined waveform is recorded and displayed on the monitor as a time velocity curve. After recording patient data (height, sex), the optimum flow profile is frozen. CO is calculated based on SV and HR (calculated with the device software using the SV time rate curve and measured valve CSA values) (3). Initially, the operator placed the ultrasound probe at the suprasternal angle (aortic valve view) and manipulated it to obtain the best waveform and audible signal. In the study, the USCOM was used to measure the CI in the direction of the aortic valve axis from the jugular notch three times and the mean of these measurements was taken as the basis.

PiCCO Pulsion Medical Systems, Feldkirchen, Germany is a way to check blood flow that combines both steady and changing blood flow information with pulse contour analysis and transcardiopulmonary thermodilution (3,4). It is a less invasive hemodynamic monitor that does not require pulmonary artery catheterization, requires only a central venous catheter and femoral artery catheter, and measures continuous CO (5). The principle of operation is based on transpulmonary thermodilution and pulse contour technology. The PiCCO catheter injects a known amount of cold liquid at a known temperature through a central catheter. The device measures the change in blood temperature near the tip of

the PiCCO catheter in the artery after injection. The device displays and calculates the curve of the resulting temperature change. As the injected fluid passes through the heart and lungs, the device can also determine parameters such as preload and extra vascular lung fluid. The PiCCO device was the first pulse contour device used for CO measurement in clinical practice. PiCCO provides information about patient preload and systemic vascular resistance, guiding intensive care specialists in planning fluid and inotropic therapy (6).

The study conducted measurements within the first 24 hours after admitting patients to intensive care. For patients measured with PiCCO, we took three measurements from the central catheter (vena jugularis interna or subclavian vein) and simultaneously took three measurements from the jugular notch with USCOM. We then calculated the average of these measurements as the basis. To eliminate observer-based variability and the risk of bias, all USCOM measurements were performed by a single investigator and PiCCO measurements were performed by a separate investigator.

This study was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee with decision no. 299, dated June 18, 2014. Patients' consent was not obtained due to the prospective design of the research.

Statistical Analysis

In the statistical analysis of data, descriptive statistics were presented with frequency, percentage, mean and standard deviation values. Paired t-test and Wilcoxon signed-rank were used to analyze the difference between the measurement values of the two groups. Bland-Altman analysis confirmed the difference in measurements using the Jamovi program. We applied correlation analysis to determine the relationship between measurement methods and patient scores. In the study, p-values below 0.05 were considered statistically significant. We conducted the analyses using the SPSS 22.0 package program.

Results

Thirty-six patients hospitalized in intensive care and diagnosed with sepsis and septic shock were included in our study. PiCCO device was installed for hemodynamic monitoring of the patients and hemodynamic parameters were evaluated simultaneously with USCOM methods. Table 1 presents the demographic characteristics of the patients.

The distribution of patients administered noradrenalin, dobutamine, dopamine and adrenalin during follow-up is given in Table 2. The results obtained by comparing the CO, CI, SV and SV index (SVI) measurements of the patients in the study according to PiCCO and USCOM devices are given in Table 3 below.

According to the results obtained, it was determined that CO, CI, SV and SVI measurements gave different results according to PICCO and USCOM devices. The CO measurement values obtained in the PICCO device were higher than those measured in USCOM device and the difference was statistically significant.

Table 1. Demographic data	
Gender (n, %)	
Female	10 (27.8)
Male	26 (72.2)
APACHE-II (min-max)	18.86 (5-35)
Age (years, SD)	59.2±18.5
Weight (kg)	76.1±8.5
MAP (mmHg)	79.9±16.6
Sepsis (n, %)	7 (19.4%)
Pneumosepsis	4 (57.1%)
Meningitis	1 (14.3%)
Diabetic foot infection	1 (14.3%)
Abdominal sepsis	1 (14.3%)
Septic shock	29 (80.6%)
Pneumosepsis	16 (55.3%)
Abdominal sepsis	8 (27.6%)
Urosepsis	1 (3.4%)
Diabetic foot infection	2 (6.9%)
Catheter-related sepsis	1 (3.4%)
Necrotizing soft tissue infection	1 (3.4%)

Gender is expressed as number of people and percentage (%), APACHE-II value is expressed as minimum and maximum. Age, weight expressed as mean (standard deviation). MAP: Middle arterial pressure, APACHE-II: acute physiology and chronic health evaluation-II, min-max: minimum-maximum, SD: standard deviation

Table 2. Doses of vasopressors and inotropes used		
Drug	**n (%)**	**Mean drug dose (mcg/kg/min)**
Noradrenaline	23 (63.9%)	0.5
Dobutamine	5 (13.9%)	5.1
Dopamine	1 (2.8%)	6.6
Adrenaline	1 (2.8%)	0.1

Table 3. Comparison of measurements according to PiCCO and USCOM methods (n=36)

Measurement	Method	Mean ± SD	p-value
CO	PiCCO USCOM	5.9±2.2 4.3±1.7	0.01
CI	PiCCO USCOM	3.2±1.1 2.2±0.8	0.01
SV	PiCCO USCOM	64.1±23.8 43.6±15.9	0.01
SVI	PiCCO USCOM	35.1±12.5 22.8±8.1	0.01

PiCCO: Pulse-induced contour cardiac output, USCOM: ultrasonic cardiac output monitoring, CO: cardiac output (L/min), CI: cardiac index (L/min/m^2), SV: stroke volume (mL/beat), SVI: stroke index (mL/beat/m^2)

Discussion

Hemodynamic monitoring plays an indispensable role in intensive care and patient management, but it is important to remember that no monitoring tool can improve patient outcomes on its own (7). The fact that the changes in the CI determined by USCOM correspond very well with the changes measured by PiCCO is of great practical importance, especially in clinical use (8).

We aimed to compare the CI measurements obtained by USCOM with the PiCCO technique, which has been used as a reference measurement method in recent years, to investigate the clinical suitability of USCOM in patients with sepsis and septic shock. According to the data obtained, it was observed that CI measurements gave different results according to PiCCO and USCOM devices, (PiCCO 3.23 L/min/m^2, USCOM 2.24 L/min/m^2). This difference was statistically significant ($p<0.05$). Horster et al. (9) evaluated seventy sepsis patients in their study and found that the results obtained with the USCOM technique were significantly similar to those obtained with PiCCO. A similar comparison was made in a meta-analysis including six studies and there was a consistent and significant relationship between USCOM measurements and PiCCO measurements (10). The poor agreement between USCOM and PiCCO measurements in our study may be due to a number of factors. Although all measurements were made by a single user in our study, we think that instantaneous changes in patient dynamics, the environment factor, and the fact that the appropriate angle for doopler measurement of the patient varies for each patient and cannot be standardized are the reasons for the incompatibility. The quality of CO measurement depends on operator as well as patient factors. Tan et al. (11) reported that 25% of the examinations performed with the patient in the supine position failed to produce a satisfactory Doopler profile, but a change to a left lateral tilt of 15° to 30° provided a satisfactory profile. Phillips et al. (12) found a deviation of 0.6 L/min/m^2 and a mean error percentage of 56% in measurements made with the USCOM technique and the results were discordant. This result showed that USCOM measurements tended to significantly underestimate CI compared with PiCCO measurements. Failure to obtain measurements in 16% of interventions raises questions about the applicability of the USCOM device. There are also studies in the literature comparing CO measurements by USCOM technique and PAC. Jain et al. (13) obtained correlated results with PAC in USCOM measurements in their study. Phillips et al. (14) found poor accuracy and sensitivity between the two methods. Vandenbogaerde et al. (15) found that 22% of the patient population did not have an acceptable aortic flow signal, and they concluded that the transoesophageal approach was more reliable. In addition, mechanical ventilation may cause difficulties in measuring CO with a US-based device. The accuracy of USCOM depends on obtaining appropriate VTI and heart valve area measurements. Appropriate CCA measurement requires a good flow signal. An inappropriate beam alignment in relation to the direction of blood flow may lead to a suboptimal Doppler signal, which may lead to an underestimation of the CO value. The inaccuracy of CO determination, even for Doppler profiles that fulfill the acceptability criteria, shows that factors other than operator-dependent ones also contribute significantly to poor results. Continuous wave Doppler devices have been studied since the early 1980s. The main problems encountered are the inability to obtain acceptable flow signals with a transthoracic approach and the difficulty in measuring the CSA of the flow. Further evaluation of the USCOM device in low and high CO conditions is required (11). This study has several limitations. The study was single-centre and had a limited number of patients.

Hemodynamic monitoring techniques should be able to identify failure and guide personalized hemodynamic treatments when combined with clinical examinations to assess perfusion adequacy. All monitoring will not improve outcomes unless it is combined with appropriate and effective treatment. Hemodynamic monitoring can be invasive or non-invasive. In recent years, we see that

non-invasive monitoring techniques have increased in intensive care units, while invasive methods such as PAC have decreased (16). We would like to remind you that no matter what method is used, it is necessary to consider each patient individually. We summarize the management of intensive care hemodynamics in Figure 1.

The main goal after shock recognition is to guarantee life-sustaining tissue perfusion levels. BP measurement, skin mottling, and capillary refill time inform the progress of resuscitation (17). Utilizing lactate levels for triage is beneficial due to their good predictive value. Repeatedly measuring lactate levels is useful because they tend to decrease in recovered patients and frequently remain elevated, sometimes even rising in cases where septic shock is not properly managed. Lowering lactate levels during resuscitation has been linked to a decrease in hospital mortality (18). Quick echocardiographic analysis can help with hemodynamic assessment (19). Assessing blood lactate levels can help identify tissue perfusion impairments. It may also be helpful to know the difference in carbon dioxide partial pressure (pCO_2) between central venous blood and arterial blood ($Pv\text{-}aCO_2$) and central venous oxygen saturation ($ScvO_2$) when putting in a central venous catheter (20). CVP

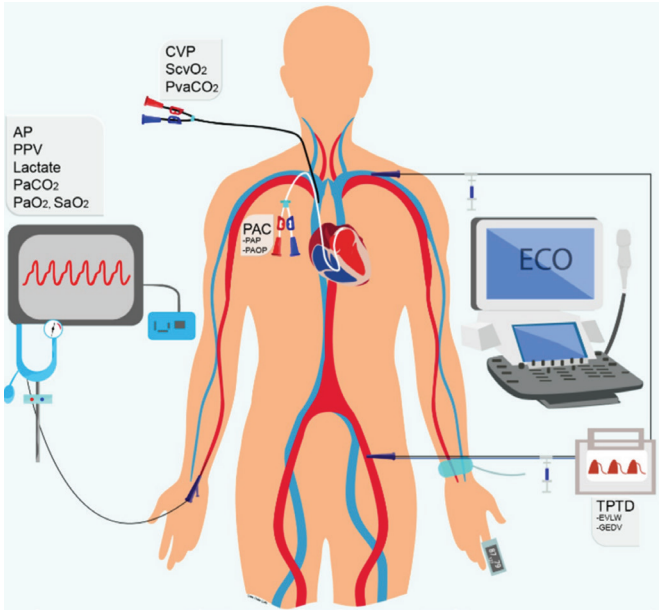

Figure 1. Hemodynamic monitoring in intensive care

PAC: Pulmonary artery catheter, PAP: pulmonary artery pressure, PAOP: pulmonary artery occlusion pressure, TPTD: transpulmonary thermodilution, EVLW: Extravascular lung water, CVP: central venous pressure, PPV: pulse pressure variation, GEDV: global end-diastolic volume, ECO: effective cardiac output

is a complex variable that reflects right ventricular preload and function and is affected by intrathoracic pressure (21). It should be measured in shock even if it is not a reliable indicator of how the patient will react to fluids. Nevertheless, it offers valuable insights about the patient's fluid state and right ventricular reserve (22). In monitoring, more complex patients (based on comorbidities, associated organ dysfunction, or poor evolution) will benefit from the use of transpulmonary thermodilution (TPTD) or eventually a PAC combined with echocardiography when necessary (23). TPTD is used to estimate calibrated measurements of CO, fluid response, static volumetric preload indices, cardiac function indices, extravascular lung water, and vascular permeability. This comprehensive hemodynamic assessment is particularly useful in fluid management as it provides a dynamic assessment of fluid response and an assessment of the risks associated with volume administration (22).

Conclusion

Although USCOM is not a substitute for invasive methods such as PiCCO, its use in patient management under appropriate conditions is debatable. The USCOM device is easy to use and safe as it utilizes ultrasound technology, allowing for repeated measurements to track changes over time. It avoids the complications of pulmonary artery catheterization or central and arterial catheterization procedures in PiCCO or transoesophageal echocardiography. Awake patients can also tolerate it. Apart from all these, USCOM is limited to the measurement of CO because it is unfortunately inadequate to determine variables such as pressure measurements (pulse pressure variation, SV variation, systemic vascular resistance index) or $ScvO_2$.

The poor agreement and failure rate in obtaining an acceptable Doppler profile suggest that this device currently has little clinical utility in intensive care. Further studies are necessary to establish its reliability.

Consequently, the choice of monitoring technique should be based on the patient's condition, local experience and availability, and the expected response to treatment. A phased approach is recommended for the patient in septic shock, evaluated individually.

Ethics

Ethics Committee Approval: This study was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee with decision no. 299, dated June 18, 2014.

Informed Consent: Patients' consent was not obtained due to the prospective design of the research.

Authorship Contributions

Surgical and Medical practice: Ö.Ç., Concept: A.R., O.H., Design: M.C., Data Collection and Process: H.P., Analysis or Interpretation: Ö.Ç, O.H., Literature Search: M.Y., Writing: Ö.Ç.

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

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

References

1. Beltramo F, Menteer J, Razavi A, Khemani RG, Szmuszkovicz J, Newth CJ, et al. Validation of an Ultrasound Cardiac Output Monitor as a Bedside Tool for Pediatric Patients. Pediatr Cardiol. 2016;37:177-83.
2. Nidorf SM, Picard MH, Triulzi MO, Thomas JD, Newell J, King ME, et al. New perspectives in the assessment of cardiac chamber dimensions during development and adulthood. J Am Coll Cardiol. 1992;19:983-8.
3. Hofkens PJ, Verrijcken A, Merveille K, Neirynck S, Van Regenmortel N, De Laet I, et al. Common pitfalls and tips and tricks to get the most out of your transpulmonary thermodilution device: results of a survey and state-of-the-art review. Anaesthesiol Intensive Ther. 2015;47:89-116.
4. Oren-Grinberg A. The PiCCO Monitor. Int Anesthesiol Clin. 2010;48:57-85.
5. Tibby S. Transpulmonary thermodilution: finally, a gold standard for pediatric cardiac output measurement. Pediatr Crit Care Med. 2008;9:341-2.
6. Monnet X, Persichini R, Ktari M, Jozwiak M, Richard C, Teboul JL. Precision of the transpulmonary thermodilution measurements. Crit Care. 2011;15:R204.
7. Pinsky MR, Payen D. Functional hemodynamic monitoring. Crit Care. 2005;9:566-72.
8. Stemmler HJ, Weigert O, Grüner N, Tschop K, Lange V, Parhofer KG. Nicht-invasives hämodynamisches Monitoring bei Intensivpatienten. Intensivmed. 2007;44:366-71.
9. Horster S, Stemmler HJ, Strecker N, Brettner F, Hausmann A, Cnossen J, et al. Cardiac Output Measurements in Septic Patients: Comparing the Accuracy of USCOM to PiCCO. Crit Care Res Pract. 2012;2012:270631.
10. Chong SW, Peyton PJ. A meta-analysis of the accuracy and precision of the ultrasonic cardiac output monitor (USCOM). Anaesthesia. 2012;67:1266-71.
11. Tan HL, Pinder M, Parsons R, Roberts B, van Heerden PV. Clinical evaluation of USCOM ultrasonic cardiac output monitor in cardiac surgical patients in intensive care unit. Br J Anaesth. 2005;94:287-91.
12. Phillips RA, Smith BE, Madigan VM, Boyle M, Steel L, Flynn GM, et al. Assessment of the clinical utility of an ultrasonic monitor of cardiac output (the USCOM) and agreement with thermodilution measurement. Crit Care Resusc. 2010;12:209-13.
13. Jain S, Allins A, Salim A, Vafa A, Wilson MT, Margulies DR. Noninvasive Doppler ultrasonography for assessing cardiac function: can it replace the Swan-Ganz catheter? Am J Surg. 2008;196:961-7.
14. Phillips RA, Hood SG, Jacobson BM, West MJ, Wan L, May CN. Pulmonary Artery Catheter (PAC) Accuracy and Efficacy Compared with Flow Probe and Transcutaneous Doppler (USCOM): An Ovine Cardiac Output Validation. Crit Care Res Pract. 2012;2012:621496.
15. Vandenbogaerde JF, Scheldewaert RG, Rijckaert DL, Clement DL, Colardyn FA. Comparison between ultrasonic and thermodilution cardiac output measurements in intensive care patients. Crit Care Med. 1986;14:294-7.
16. Pinsky MR, Cecconi M, Chew MS, De Backer D, Douglas I, Edwards M, et al. Effective hemodynamic monitoring. Crit Care. 2022;26:294.
17. Ait-Oufella H, Bige N, Boelle PY, Pichereau C, Alves M, Bertinchamp R, et al. Capillary refill time exploration during septic shock. Intensive Care Med. 2014;40:958-64.
18. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med. 2010;182:752-61.
19. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1795-815.
20. De Backer D, Cecconi M, Chew MS, Hajjar L, Monnet X, Ospina-Tascón GA, et al. A plea for personalization of the hemodynamic management of septic shock. Crit Care. 2022;26:372.
21. De Backer D, Vincent JL. Should we measure the central venous pressure to guide fluid management? Ten answers to 10 questions. Crit Care. 2018;22:43.
22. De Backer D, Aissaoui N, Cecconi M, Chew MS, Denault A, Hajjar L, et al. How can assessing hemodynamics help to assess volume status? Intensive Care Med. 2022;48:1482-94.
23. Teboul JL, Saugel B, Cecconi M, De Backer D, Hofer CK, Monnet X, et al. Less invasive hemodynamic monitoring in critically ill patients. Intensive Care Med. 2016;42:1350-9.

Turk J Intensive Care 2024;22:218-24
DOI: 10.4274/tybd.galenos.2024.00377

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Reasons for Intensive Care Unit Admission and Prognosis After Surgery for Gynaecologic Malignancies

Jinekolojik Malignite Cerrahisi Sonrası Yoğun Bakım Ünitesine Başvuru Nedenleri ve Prognoz

Received/Geliş Tarihi : 03.05.2024
Accepted/Kabul Tarihi : 05.06.2024

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ABSTRACT *Objective:* The aims of this study was to investigate factors associated with intensive care unit (ICU) admission and prognosis following surgical treatment of gynaecological malignancy.
Materials and Methods: This study was designed as a retrospective cohort analysis, which encompasses patients who were subjected to gynecologic oncological surgery and subsequently monitored in the ICU from December 1st, 2022, to December 1st, 2023.
Results: Data of 57 patients who underwent gynaecological oncological surgery and were admitted to ICU during the study period were analysed. Median age was 61.47 years, median body mass index 27 kg/m^2, American Society of Anaesthesiologists score 3±2.5. The most common indication for ICU admission was haemodynamic instability with 73.6% (n=42), followed by respiratory failure with 15.7% (n=9) and other reasons. Charlson comorbidity index, lactate and base deficit levels were higher and albumin values were lower in patients with ICU stay of 3 days or more (p=0.04, p=0.004, p=0.034, p=0.025). Only 2 patients (3.5%) developed mortality during the study period.
Conclusion: The most common indication for ICU follow-up after elective gynaecological oncology surgery is hemodynamic instability with low ICU mortality and short length of stay in general.
Keywords: Comorbidities, gynecologic oncology surgery, intensive care unit

ÖZ *Amaç:* Bu çalışmanın amacı jinekolojik malignitelerin cerrahi tedavisi sonrası yoğun bakım ünitesine (YBÜ) yatış ve prognoz ile ilişkili faktörleri araştırmaktır.
Gereç ve Yöntem: Bu çalışma, 1 Aralık 2022 ile 1 Aralık 2023 tarihleri arasında jinekolojik onkolojik cerrahi uygulanan ve sonrasında YBÜ izlenen hastaları kapsayan retrospektif bir kohort analizi olarak tasarlanmıştır.
Bulgular: Çalışma döneminde jinekolojik onkolojik cerrahi geçiren ve YBÜ kabul edilen 57 hastanın verileri analiz edildi. Medyan yaş 61,47, medyan vücut kitle indeksi 27 kg/m^2, Amerikan Anesteziyoloji Derneği skoru 3±2,5 idi. YBÜ kabul için en yaygın endikasyon %73,6 (n=42) ile hemodinamik instabilite iken, bunu %15,7 (n=9) ile solunum yetmezliği, %10,5 (n=6) yerine solunum yetmezliği ve diğer nedenler izlendi. Charlson komorbidite indeksi, laktat ve baz açığı düzeyleri 3 gün ve üzeri YBÜ'de kalan hastalarda daha yüksek, albümin değerleri ise daha düşüktü (p=0,04, p=0,004, p=0,034, p=0,025). Çalışma süresi boyunca sadece 2 hastada (%3,5) mortalite gelişti.
Sonuç: Elektif jinekolojik onkoloji cerrahisi sonrası YBÜ takibi için en yaygın endikasyon hemodinamik instabilite olup, genel olarak YBÜ mortalitesi düşük ve YBÜ yatış süresi kısadır.
Anahtar Kelimeler: Komorbiditeler, jinekolojik onkoloji cerrahisi, yoğun bakım ünitesi

Introduction

Gynaecological cancers are cancers of the female reproductive system and are the most common cancers among women worldwide. According to GLOBOCAN cancer data, gynaecological cancers account for approximately 40% of all cancer incidence in women worldwide. The estimated annual number of new cases worldwide is 604,127 for cervical cancer, 417,367 for endometrial cancer, 313,959 for ovarian cancer and 45,240 for vulvar cancer. Furthermore, gynecological cancers account for more than 30% of all cancer deaths among women. Surgical intervention is usually the preferred primary treatment modality for these cancers (1,2).

Gynaecological oncology surgery involves resection of tissues in both the lower and upper abdomen, especially in ovarian cancer. To ensure complete cytoreduction, surgery often goes beyond the removal of the uterus and ovaries (hysterectomy and adnexectomy). It may also involve removal of the bowel, bladder or liver, as well as the spleen (splenectomy), parts of the peritoneum (peritonectomy) or lymph nodes (lymphadenectomy) (3). These radical operations for gynaecological cancers can take a long time to complete and often result in a lot of blood loss. In the light of this information, these patients are at risk for serious complications that may result in postoperative morbidity and mortality (4). Therefore, postoperative intensive care unit (ICU) follow-up may be frequently required in this group of patients undergoing major surgical procedures. Optimising postoperative ICU management is crucial to improve patient outcomes. However, there are no clear criteria or risk factors that determine the optimal ICU admission strategy in this patient group. Furthermore, limited information is available on the epidemiology and prognosis of critical gynaecological oncology patients requiring postoperative ICU management (5-7).

The aim of this study was to evaluate the clinical characteristics, prognosis, ICU length of stay and associated factors in patients admitted to the ICU after gynaecological oncological surgery.

Materials and Methods

The current study was carried our in accordance with the Declaration of Helsinki and approved by the Clinical Researches Ethics Commitee of University of Health Sciences Turkey, Antalya Training and Research Hospital, Antalya, Turkey (decision no: 18/3 date: 28.12.2023).

It was designed as a retrospective cohort study and included patients who were followed up in the ICU after gynaecological oncology surgery between 01 December 2022 and 01 December 2023. The data of the patients were obtained from patient file database and the observation results noted to the patient ICU charts. Patient informed consent was waived due to the retrospective study design. Researchers analyzed only anonymized data.

Patients over 18 years of age who underwent surgery for gynaecological malignancies in our clinic and were admitted from the operating room to the ICU were included in the study. Patients younger than 18 years of age, patients who were not operated for gynaecological malignancy and patients who did not require postoperative ICU follow-up were excluded from the study.

Demographic and clinical data including age, body mass index, comorbidities, diagnosis of gynaecological malignancy, surgical resections performed, operative time (the time between the onset of anaesthesia and the completion of the surgical procedure), need for blood and blood product replacement, indication for ICU admission (haemodynamic instability, respiratory failure, heart failure), need for mechanical ventilation, need for inotropes, length of ICU stay and prognosis (exitus/survival) were obtained and analysed. Laboratory parameters (haemoglobin, base deficit, lactate, albumin) and arterial blood gas analysis (base deficit, lactate) were recorded.

Patients with one or more of the following criteria were considered haemodynamically unstable: Hypertension (20% increase in mean arterial pressure at baseline), hypotension (20% decrease in mean arterial pressure at baseline), tachycardia (heart rate ≥100), bradycardia (heart rate ≤60) (8,9). Respiratory failure was defined as arterial oxygen pressure (PaO_2) below 60 mmHg or arterial carbon dioxide pressure above 50 mmHg in room air or PaO_2 to inspired oxygen fraction ratio (PaO_2/FiO_2) below 300 (10,11).

Comorbidities were measured using the Charlson comorbidity index (CCI), a measure specifically designed to categorise the impact of comorbidities and their prognostic impact on mortality, which has been extensively validated in cohorts of patients with malignancies (12).

The acute physiology and chronic health evaluation-II (APACHE-II) and sequential organ failure assessment (SOFA) was used to measure the severity of a patient's

condition on admission to the ICU (13). The preoperative assessment of surgical risk, expressed by the American Society of Anaesthesiologists (ASA) score, was based on the physical status classification of the American Society of Anaesthesiology.

Statistical Analysis

In our study, analyses were performed using Statistical Package for the Social Sciences software version 21.0 (IBM Inc, Chicago, IL, USA). Descriptive statistics of numerical and qualitative (categorical) variables obtained in the study were analysed and numerical parameters were expressed as interquartile range (median, minimum and maximum) and categorical variables were expressed as frequency. Shapiro-Wilk test, histogram analyses and Q-Q plot graphs were used for the compatibility of numerical variables with normal distribution. For multiple group comparisons, One-Way analysis of variance (ANOVA) or Kruskal-Wallis H tests were performed. Distributional relationships between categorical parameters were evaluated by Pearson chi-square analysis or Fisher's Exact test. Pearson or Spearman's correlation analyses were used for correlation between numerical parameters. In the whole study, type-I error rate was taken as 5% and $p<0.05$ was accepted as significant.

Results

During the study period, there were 233 patients undergoing gynaecological cancer surgery and 59 patients were admitted to the ICU. Data from 57 patients who met the inclusion criteria were analysed (Figure 1).

Clinical and demographic characteristics of patients are presented in Table 1. The mean age was 61.47±12.13 years and 34 (59.65%) patients had comorbidities. The mean ASA score of the patients was III. Surgery was performed for ovarian cancer in 61.4%, endometrial cancer in 36.8% and colorectal cancer with isolated vaginal metastasis in 1 patient. Total hysterectomy and bilateral salpingo-oophorectomy were performed in 47 patients and systematic pelvic lymphadenectomy in 31 patients. Primary debulking was performed in 21 patients with ovarian cancer, interval debulking in 9 patients and secondary cytoreduction surgery in 5 patients. Splenectomy was performed in 8 patients with ovarian cancer, ureteroneocystostomy in 2 patients, peritonectomy in 12 patients and anastamosis of colorectal resection in 9 patients. Laparoscopic surgery was performed in 6 patients and all patients had endometrial cancer. Sentinel lymph node dissection was performed in 2 of these patients. The mean operative time was 300 (90-620) minutes and this time was longer in ovarian cancer surgery than in other surgeries ($p<0.001$). Blood product transfusion was required in 26 patients (45.6%) in the perioperative period, 24 patients required vasoactive drugs intraoperatively, and 2 of these patients continued to require vasoactive drugs postoperatively. Operative time was higher in this patient group ($p<0.001$).

The most common indication for ICU admission was haemodynamic instability (hypotension in 18 patients, hypotension with bradycardia in 2 patients, tachycardia with hypotension in 4 patients, hypertension in 6 patients, tachycardia with hypertension in 2 patients, tachycardia in 6 patients, bradycardia in 4 patients) with 73.6% (n=42), followed by respiratory failure with 15.7% (n=9) and other reasons. The mean APACHE-II and SOFA scores at ICU admission were 18.8±7.2 and 5±5.8, respectively. The mean PaO_2/FiO_2 at ICU admission was 320±55.6 mmHg and 36 (63.1%) patients required mechanical ventilation. Operative time was higher in this patient group ($p<0.001$). The mean length of stay on mechanical ventilation was 1 day (0-15). The median values of haemoglobin 11.83 g/dL (11.83±1.72), albumin 25.2 g/L (25.2±3.6), lactate 1.70 mmol/L (0.7-5.9) and base deficit 1.70 mmol/L (-10.2-19.4) are shown in Table 2. Patients who underwent ovarian cancer surgery had a longer operation time and a higher need for mechanical ventilator and blood product transfusion than patients who underwent endometrial cancer surgery ($p=0.007$, $p=0.026$, $p=0.024$).

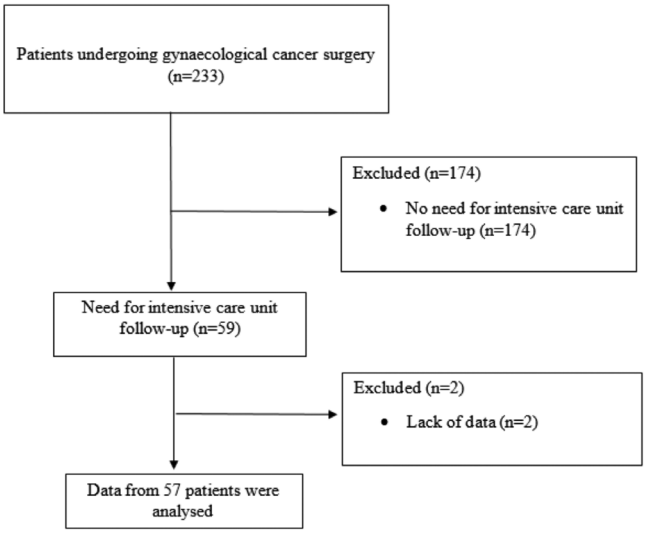

Figure 1. Study flow diagram

Table 1. Distribution summary of general descriptive data		
Parameters	**Frequency (n)**	**%**
Diagnosis		
Endometrium CA	21	36.84%
Over CA-periton CA	35	61.4%
Isolated vaginal metastasis of colon cancer	1	1.75%
Intraoperative replacements		
No	31	54.39%
Yes (ES and/or FFP)	26	45.61%
Mechanical ventilation		
No	21	36.84%
Yes	36	63.16%
Inotrope use*		
No	55	96.49%
Yes	2	3.51%
Presence of comorbidities		
No	23	40.35%
Yes	34	59.65%
Comorbidities$^{\Phi}$		
HT	12	21.1%
DM	8	14.0%
Asthma	2	3.5%
Hyperthyroidism	1	1.8%
CAD	4	7.0%
Epilepsy	2	3.5%
Elephantiazis	1	1.7%
CRF	1	1.8%
COPD	2	3.5%
Prognosis		
Alive	55	96.5%
Exitus†	2	3.5%
Operation$^{\Phi}$		
TAH-BSO	47	82.5%
Systematic pelvic, paraortic LN dissection	31	54.4%
Colorectal resection anastomosis	9	15.8%
Laparoscopy	6	10.5%
Splenectomy	8	14.0%
Interval debulking	9	15.8%
Secondary cytoreduction	5	8.8%
Primer debulking	21	36.8%
Peritonectomy	12	21.1%
Sentinal LN dissection	2	3.5%
Ureteroneocystostomy	2	3.5%

*Noradrenaline, †Causes of mortality: sepsis, ARF, ARDS and pulmonary embolism. $^{\Phi}$Some patients have more than one characteristic (comorbidity or type of operation performed). DM: Diabetes mellitus, HT: hypertension, CAD: coronary artery disease, CRF: chronic renal failure, HL: hyperlipidaemia, COPD: chronic obstructive pulmonary disease, CA: cancer (malignancy), ES: erythrocyte suspension, FFP: fresh frozen platelet, LN: lymph node, TAH-BSO: total abdominal hysterectomy bilateral salphingoopherectomy, ARDS: acute respiratory distress syndrome, ARF: acute respiratory failure

The median length of stay in the ICU was 2 (1-20) days. CCI, lactate and base deficit levels were higher and albumin values were lower in patients with ICU stay of 3 days or more (Table 3) (p=0.04, p=0.004, p=0.034, p=0.025). Only 2 patients (3.5%) developed mortality during the study period. Mortality was due to massive pulmonary embolism in 1 patient undergoing ovarian cancer surgery and intraobdominal sepsis/disseminated intravascular coagulation in 1 patient undergoing endometrial cancer surgery.

Discussion

The results of our study revealed that the most common indication for ICU follow-up after gynaecological oncology surgery was haemodynamic instability (73.6%) and ICU mortality was 3.5%. ICU length of stay was longer in patients with low albumin level, comorbidity, high lactate and base deficit.

Patients undergoing major gynaecological oncology surgery often require postoperative management in the ICU. In our study, 25.3% of patients who underwent gynaecological oncological surgery required ICU follow-up after surgery. Previous studies have also reported that 6% to 56% of patients require ICU follow-up after gynaecological cancer surgery (14-18). In a systematic review including 7 studies evaluating the factors affecting ICU admission after gynecologic oncology surgery, haemodynamic instability was reported to be the most common indication for ICU admission. Similar to the findings of this systematic review, the most common indication for ICU admission in our study was haemodynamic instability (19). In our study, the majority of patients had comorbidities and the mean CCI was 5 (2-10). Some studies evaluating the determinants of ICU admission in patients undergoing gynaecological oncology surgery have reported a significant association between high CCI scores and ICU admission (14,17). In parallel with these studies, the findings of our study reflect the fact that pre-existing comorbidities predispose to ICU admission in patients undergoing gynaecological oncology surgery.

In our study, the majority (61.4%) of the patients admitted to the ICU were patients who underwent surgery for ovarian cancer. Leath et al. (16) reported that the majority (39%) of 185 gynaecological oncology patients admitted to the ICU after surgery were patients who underwent surgery for ovarian cancer. Similarly, in a recent study in which the data of 666 patients admitted to the ICU after gynaecological

Table 2. General distribution characteristics of quantitative parameters			
Parameters	**Minimum**	**Maximum**	**Distribution†**
Age (years)	20	83	61.47±12.13
BMI (kg/m^2)	23	34	27±7.7
ASA (score)	1	4	3±2.5
Hb (g/dL)	6.7	16.4	11.83±1.72
Albumin (g/L)	18.3	37.1	25.2±3.6
APACHE-II (score)	5	34	18.8±7.2
SOFA (score)	0	11	5±5.8
PaO_2/FiO_2 (mmHg)	170	470	320±55.6
Parameters	**Q1**	**Q3**	**Median**
Base deficit (mmol/L)	-10.2	19.4	1.70 (-10.2-19.4)
Lactat (mmol/L)	0.70	5.90	1.70 (0.7-5.9)
Operation time (min)	90	620	300 (90-620)
ICU length of stay (days)	1	20	2 (1-20)
CCI (score)	2	10	5 (2-10)

†Age, Hb, BMI, ASA score, albumin, APACHE-II, PaO_2/FiO_2 (mmHg) and SOFA (score) parameters were expressed as mean ± standard devination. and other parameters were expressed as interquartile range. BMI: Body mass index (kg/cm^2), ASA: American Society of Anaesthesiologists, APACHE-II: acute physiological and chronic assessment-II, SOFA: sequential organ failure assessment, ICU: intensive care unit, CCI: Charlson comorbidity index, Hb: hemoglobin, PaO_2/FiO_2: Inspired oxygen fraction ratio

Table 3. Comparison of quantitative parameters according to intensive care unit length of stay				
	ICU length of stay			
	1 day (n=23, 40.4%)	**2 day (n=24, 42.1%)**	**≥3 day (n=9, 15.8%)**	**p-value**
Median (IQR)				
CCI (score)	4 (2-6)	5 (4-7)	7 (5-10)	**0.04**
Base deficit (mmol/L)	-2 (-7.5-3.5)	-3.05 (-10.2-2.4)	-4.9 (-8-19.4)	**0.034**
Lactate (mmol/L)	1.3 (0.8-3.6)	2 (0.7-4.6)	3.8 (1.5-5.9)	**0.004**
Operation time (min)	270 (90-450)	350 (100-620)	260 (120-420)	0.282
Mean ± standard devination†				
Age (years)	58.74±13.33	63.54±11.87	63.33±9.87	0.367
Hb (g/dL)	12.29±1.02	11.31±1.67	11.72±2.74	0.143
Albumin (g/L)	27.4±2.2	24.4±2.7	21.4±3.4	**0.025**
APACHE-II (score)	18.22±6.13	18.47±7.21	20.2±10.5	0.860
SOFA (score)	4.3±2.5	4±3.5	5±4.5	0.734
ASA (score)	2±1.7	2.3±1.7	2.8±1.2	0.687
BMI (kg/m^2)	26±4.3	26.5±5.1	26.9±3.3	0.610
PaO_2/FiO_2 (mmHg)	380±90.1	374±71	350±80.4	0.480

Parameters showing normal distribution characteristics were expressed as mean ± standard devination. Those not showing normal distribution characteristics were expressed as median (IQR). †One-Way analysis of variance (ANOVA), ‡Kruskal-Wallis H test, $p<0.05$ means statistical significance between all days. CCI: Charlson comorbidity index, APACHE-II: acute physiological and chronic assessment II, SOFA: sequential organ failure assessment, ASA: American Society of Anaesthesiologists, BMI: body mass index (kg/cm^2), IQR: interquartile range, Hb: hemoglobin, PaO_2/FiO_2: Inspired oxygen fraction ratio, ICU: intensive care unit

oncology surgery were included in the analysis, it was reported that approximately half of the patients were patients who underwent surgery for ovarian cancer (7). Ovarian cancer has the worst prognosis among gynaecological malignancies and is usualy diagnosed at late stage (stage III or IV) (20). Therefore, aggressive surgical procedures are often required in this patient group. As a result, prolonged operative time, the need for continuous volume resuscitation and the need for blood product transfusion may be frequent, and it is essential to perform the necessary replacements without causing haemodynamic instability.

In our study, ICU mortality was 3.5% and the mean APACHE-II score of the patients was 18.8±7.2. ICU mortality after gynaecological oncology surgery has been reported in a wide range (0-28%) in previous studies (5,14,16,21). Our study included patients who underwent elective surgery for gynaecological malignancy, and the mortality rate (3.1%) was similar to that reported by Krawczyk et al. (7). Van Le et al. (22) reported that the mortality rate in gynaecological oncology patients was 78% when the APACHE-II score was higher than 20 and 3% when it was lower than 20. Considering the mean APACHE-II score of our patient population in our study, our results confirm the analysis of Van Le et al. (22) The causes of mortality in our study were massive pulmonary embolism, sepsis and disseminated intravascular coagulation. Although the mortality rate was low, it should be kept in mind that this patient group is vulnerable to serious complications that may result in mortality and patients should be closely monitored in this respect.

In this patient group, dehydration, hypotension due to large intraoperative blood loss and the need for vasopressor agents may develop. Perioperative hypotension is known to be associated with unfavourable postoperative outcomes and increased mortality (23). Therefore, careful monitoring of the need for fluid resuscitation and blood product replacement to prevent hypotension is very important to prevent mortality. In our study, 45.6% of the patients received blood transfusion and vasopressor agents were needed in only 2 patients during postoperative period. In our clinic, we administer fluid and blood product transfusion to our patients in the peroperative period, including the preoperative period, taking into account haemodynamic parameters and clinical findings. One of the reasons for the low mortality rate may be the careful fluid and blood resuscitation to prevent hypotension in our clinic.

In our study, the length of ICU stay was generally short (median 2 days). The ICU length of stay reported by Heinonen et al. (5) was 5 days in both benign and malignant cases. Leath et al. (16) reported a median ICU length of stay of 2.2 days, which is similar to the results of our study. In a systematic review of patients undergoing gynecological oncology surgery, Thomakos et al. (19) reported that age, high CCI and blood loss levels and long operation time were associated with prolonged ICU stay. In a study of 95 patients to determine perioperative variables associated with length of stay in the surgical ICU and total cost of hospitalisation to optimise resource utilisation in patients operated for ovarian cancer, patient age ≥63 years was significantly associated with ICU stay ≥48 hours. In a multivariate analysis, Díaz-Montes et al. (24) showed that an albumin level <3.5 g/dL was significantly associated with prolonged ICU stay. In these studies, patients with ovarian cancer were evaluated in general. In our study, there were 9 patients with ICU length of stay of 3 days or more, and CCI, lactate and base deficit levels were higher and albumin values were lower in this patient group. In our study, the majority of our patient population consisted of patients with ovarian cancer, but there were also patients who underwent surgery for other gynecological cancers. Therefore, there may have been differences between the results of our study and the reported data in terms of factors that may cause prolonged hospitalisation.

This study has several limitations. It was a retrospective single centre study. We analysed data and ICU interventions without long-term outcomes and did not include the stage of neoplastic disease, which was outside the scope of the article. We are aware that the sample was not large enough to make a definitive conclusion about the outcomes of patients admitted to the ICU after gynaecological cancer surgery.

Conclusion

The most common indication for ICU follow-up after elective gynaecological oncology surgery is hemodynamic instability with low ICU mortality and short length of stay in general. However, ICU length of stay is longer in patients with low albumin level, comorbidity, high lactate and base deficit. Prospective studies with larger patient cohorts are needed to identify factors associated with ICU length of stay and to improve patient management and outcomes.

Ethics

Ethics Committee Approval: The current study was carried our in accordance with the Declaration of Helsinki and approved by the Clinical Researches Ethics Commitee of University of Health Sciences Turkey, Antalya Training and Research Hospital, Antalya, Turkey (decision no: 18/3 date: 28.12.2023).

Informed Consent: Since our study was retrospective, informed consent was not obtained from the patients.

Authorship Contributions

Surgical and Medical Practices: A.A., G.E.S., M.G., N.Y., I.Ü., T.T., Concept: N.K.Ö., T.T., Design: A.A., M.G., Data Collection and Process: T.T., Analysis or Interpretation: N.K.Ö., N.Y., Literature Search: A.A., Writing: A.A., I.Ü.

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

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

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71:209-49.
2. Wang S, Zheng R, Li J, Zeng H, Li L, Chen R, et al. Global, regional, and national lifetime risks of developing and dying from gastrointestinal cancers in 185 countries: a population-based systematic analysis of GLOBOCAN. Lancet Gastroenterol Hepatol. 2024;9:229-37.
3. Schwandt A, Andrews SJ, Fanning J. Prospective analysis of a fever evaluation algorithm after major gynecologic surgery. Am J Obstet Gynecol. 2001;184:1066-7.
4. Dhanis J, Keidan N, Blake D, Rundle S, Strijker D, van Ham M, et al. Prehabilitation to Improve Outcomes of Patients with Gynaecological Cancer: A New Window of Opportunity? Cancers (Basel). 2022;14:3448.
5. Heinonen S, Tyrväinen E, Penttinen J, Saarikoski S, Ruokonen E. Need for critical care in gynaecology: a population-based analysis. Crit Care. 2002;6:371-5.
6. Namendys-Silva SA, González-Herrera MO, Texcocano-Becerra J, Herrera-Gómez A. Outcomes of critically ill gynecological cancer patients admitted to intensive care unit. Am J Hosp Palliat Care. 2013;30:7-11.
7. Krawczyk P, Trojnarska D, Baran R, Lonc T, Swistek R, Tyszecki P, et al. Postoperative gynecologic oncology admissions to intensive care unit in the tertiary care center: an eight-year retrospective study. Ginekologia Polska. 2023;94:599-604.
8. Abebe MM, Arefayne NR, Temesgen MM, Admass BA. Incidence and predictive factors associated with hemodynamic instability among adult surgical patients in the post-anesthesia care unit, 2021: A prospective follow up study. Ann Med Surg (Lond). 2022;74:103321.
9. Reidy CM, Beach ML, Gallagher JD, Sites BD. Postoperative hemodynamic instability after simultaneous bilateral total knee arthroplasty. J Patient Saf. 2010;6:233-7.
10. Summers C, Todd RS, Vercruysse GA, Moore FA. Acute Respiratory Failure. Perioperative Medicine. 2022:576-86.
11. Canet J, Gallart L, Gomar C, Paluzie G, Valles J, Castillo J, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. Anesthesiology. 2010;113:1338-50.
12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373-83.
13. Zimmerman JE, Kramer AA. Outcome prediction in critical care: the Acute Physiology and Chronic Health Evaluation models. Curr Opin Crit Care. 2008;14:491-7.
14. Brooks SE, Ahn J, Mullins CD, Baquet CR. Resources and use of the intensive care unit in patients who undergo surgery for ovarian carcinoma. Cancer. 2002;95:1457-62.
15. Amir M, Shabot MM, Karlan BY. Surgical intensive care unit care after ovarian cancer surgery: an analysis of indications. Am J Obstet Gynecol. 1997;176:1389-93.
16. Leath C, Kendrick J, Numnum T, Straughn J, Rocconi R, Sfakianos G, et al. Outcomes of gynecologic oncology patients admitted to the intensive care unit following surgery: A university teaching hospital experience. Int J Gynecol Cancer. 2006;16:1766-9.
17. Ruskin R, Urban RR, Sherman AE, Chen L-l, Powell CB, Burkhardt DH, et al. Predictors of intensive care unit utilization in gynecologic oncology surgery. Int J Gynecol Cancer. 2011;21:1336-42.
18. Thomakos N, Zacharakis D, Rodolakis A, Zagouri F, Papadimitriou CA, Bamias A, et al. Gynecologic oncology patients in the surgical high dependency unit: an analysis of indications. Arch Gynecol Obstet. 2014;290:335-9.
19. Thomakos N, Prodromidou A, Haidopoulos D, Machairas N, Rodolakis A. Postoperative Admission in Critical Care Units Following Gynecologic Oncology Surgery: Outcomes Based on a Systematic Review and Authors' Recommendations. In Vivo. 2020;34:2201-2208.
20. Momenimovahed Z, Tiznobaik A, Taheri S, Salehiniya H. Ovarian cancer in the world: epidemiology and risk factors. Int J Womens Health. 2019;11:287-99.
21. Abbas FM, Sert MB, Rosenshein NB, Zahyrak ML, Currie JL. Gynecologic oncology patients in the surgical ICU. Impact on outcome. J Reprod Med. 1997;42:173-8.
22. Van Le L, Fakhry S, Walton LA, Moore DH, Fowler WC, Rutledge R. Use of the APACHE II scoring system to determine mortality of gynecologic oncology patients in the intensive care unit. Obstet Gynecol. 1995;85:53-6.
23. Hallqvist L, Granath F, Fored M, Bell M. Intraoperative Hypotension and Myocardial Infarction Development Among High-Risk Patients Undergoing Noncardiac Surgery: A Nested Case-Control Study. Anesth Analg. 2021;133:6-15.
24. Díaz-Montes TP, Zahurak ML, Bristow RE. Predictors of extended intensive care unit resource utilization following surgery for ovarian cancer. Gynecol Oncol. 2007;107:464-8.