TÜRK YOĞUN BAKIM DERGİSİ

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

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

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

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

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

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# YAZARLARA BİLGİ

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

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

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

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

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

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

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

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

Yayına kabul edilmeyen yazılar, sanatsal resimler hariç geriye yollanmaz.

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

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

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

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

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

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

### Makale Değerlendirmesi

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

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

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

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

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

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

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

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

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

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

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

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

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

#### 1) Başlık Sayfası (Sayfa 1)

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

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

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

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

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

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

**2) Özet (Sayfa 2)**

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

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

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

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

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

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

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Bulgular bölümü de çalışmanın tekrar edilebilmesine yetecek ayrıntıları içermelidir.

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

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

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

**Meryem Onay,**
**Ebru Karakoç,**
**Nurdan Çobaner,**
**Gizem Kurada,**
**Birgül Yelken**

# Investigation of the Effect of Heating Blanket Use on Bleeding and Long of Intensive Care Unit Stay After Major Open Urology Surgeries

## Isıtıcı Battaniye Kullanımının Açık Ürolojik Majör Cerrahilerde Kanama Miktarı ve Yoğun Bakımda Kalış Sürelerine Etkisinin İncelenmesi

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**ABSTRACT** *Objective:* Intraoperative hypothermia causes increased bleeding, increased transfusion risks, long of intensive care unit stay and subsequently higher medical costs. This study aimed to determine the effects of hypothermia on perioperative bleeding and intensive care unit stay duration in patients undergoing major oncological urology surgery.
*Materials and Methods:* Following approval of this study by the ethics committee, demographic characteristics, surgery type, operation time, lowest perioperative body temperature, hemodynamic parameters, the use of heating blanket during surgery, the amount of bleeding and transfusion, postoperative long of intensive care unit stay in patients who underwent open major urological surgery during 2015-2018 were retrospectively evaluated. Esophageal probe was used for temperature monitoring following anesthesia induction and a body temperature of <36 °C was considered to indicate hypothermia.
*Results:* A total of 68 patients without a heating blanket (n=57) and using a heating blanket (n=11) were included in the study. The intraoperative lowest recorded body temperature was 32.1 °C, and hypothermia (<36 °C) developed in 63.6% of patients for whom heating blankets were used and in 94% of patients for whom heating blankets were not used. The amount of intraoperative bleeding was significantly low in patients for whom heating blanket was used (p=0.03).
*Conclusion:* Perioperative hypothermia is a very frequent and preventable clinical condition that increases long of intensive care unit stay, mortality, and morbidity in geriatric patients and in patients undergoing major surgery. Based on our results, less bleeding and decreased need for intensive care unit stay were noted owing to the prevention of intraoperative hypothermia.
**Keywords:** Hypothermia, heating blanket, long of intensive care unit stay duration, intraoperative bleeding

**ÖZ** *Amaç:* İntraoperatif hipotermi, kan kaybında ve beraberinde transfüzyon risklerinde artış ve yoğun bakımda kalış sürelerinde uzamaya ve bunun sonucunda da maliyet artışına neden olmaktadır. Bu çalışmada majör onkolojik ürolojik cerrahi geçiren hastalarda hipoterminin perioperatif dönemde kanama, yoğun bakımda kalış süreleri üzerine etkisini görmeyi amaçladık.
*Gereç ve Yöntem:* Çalışmamızda etik kurul onayını takiben 2015 ile 2018 arası dönemde açık majör ürolojik cerrahi geçiren hastaların demografik özellikleri, geçirecekleri cerrahi türü ve operasyon süresi, perioperatif en düşük vücut sıcaklıkları, hemodinamik parametreleri, cerrahi sırasında ısıtıcı battaniye kullanılıp kullanılmadığı, kanama miktarları, transfüzyon miktarı ve postoperatif yoğun bakım ihtiyacı retrospektif olarak incelendi. Anestezi indüksiyonu sonrası ısı takibi için özofagus probu yerleştirilen hastalarda <36 °C hipotermi olarak kabul edildi.
*Bulgular:* Çalışmaya ısıtıcı battaniye kullanılmayan (n=57) ve ısıtıcı battaniye kullanılan (n=11) toplam 68 hasta kabul edildi. İntraoperatif en düşük vücut sıcaklığı 32,1 °C olup, ısıtıcı battaniye kullanılan hastaların %63,6, ısıtıcı battaniye kullanılmayan hastaların %94'ünde hipotermi (<36 °C ) görüldüğü tespit edildi. İntraoperatif kanama miktarı ısıtıcı battaniye kullanılan hastalarda anlamlı düzeyde az bulundu (p=0,03).
*Sonuç:* Perioperatif hipotermi, oldukça sık karşılaştığımız yaşlı hasta popülasyonunun ve majör cerrahi geçiren hastalarının yoğun bakımda kalış süresini mortalite ve morbiditesini artıran önlenebilir bir klinik tablodur. Bu çalışmada elde edilen sonuçlara göre intraoperatif hipoterminin önlenmesi ile daha az kanama izlenirken yoğun bakım ihtiyacı da azalmıştır.
**Anahtar Kelimeler:** Hipotermi, ısıtıcı battaniye, yoğun bakımda uzun kalış süresi, intraoperatif kanama

## Introduction

General and neuraxial anesthesia methods applied during surgeries disrupt thermoregulatory responses in patients who are not provided with external heat source (1). Normothermia is necessary for optimum metabolism and for maintaining physiological processes (2). Therefore, maintaining normothermia during anesthesia application requires attention to reduce comorbidities and postoperative complications (3). Perioperative hypothermia is defined as a body temperature of <36 °C 1 hour (h) preoperatively and within 24 h postoperatively and is a preventable adverse effect (4,5). The predictive factors include age, body mass index (BMI), American Society of Anesthesiologists (ASA) Physical Status score, sex, laparoscopic surgery, anesthesia method and heating techniques (4).

Intraoperative hypothermia causes increased blood loss and subsequent transfusion risks, increased surgical site infection, cardiovascular complications, organ failure, decreased clearance for various drugs, extended hospital and long of intensive care unit stay, consequently higher medical costs (6). Bleeding problems are common in patients who undergo major surgeries. Hemostatic mechanism is a result of the interaction between endothelial, thrombocyte, and plasma coagulation factors. Reduced thrombocyte functions and defects in coagulation cascade enzymes increase the amount of bleeding (1).

Perioperative hypothermia leads to decreased tissue perfusion and decreased motility of immune cells as well as scar formation, and these cause increased infection risk (1,7). The duration of action of some drugs used during anesthesia, especially muscle relaxants, is prolonged. The minimum alveolar concentration of volatile anesthetics required for unresponsiveness against surgical stimulants decreases with hypothermia. Metabolic rate decreases by 7-8% for each 1 °C decrease in body temperature (8). As a result, deeper anesthesia is induced and anesthesia recovery period is extended (7). Hypothermia stimulates the sympathetic nervous system, which increases tachycardia, hypertension, systemic vasoconstriction, and myocardial oxygen consumption. As a result, myocardial ischemia and arrhythmias occur (1,3).

Thus, the present study aimed to examine the effects of heating blanket use for intraoperative hypothermia on bleeding and long of intensive care unit stay. Through the retrospective review of patient medical records, we share our regular experiences regarding patients undergoing major urological surgeries and contribute to the prevention of potential complications by raising awareness in anesthesia and surgical teams for hypothermia.

## Materials and Methods

This retrospective study was approved by the Eskişehir Osmangazi University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (decision no: 20, date: 19.02.2019) and was conducted by examining the medical records of patients who had undergone major oncological surgeries between January 2015 and December 2018 at the urology clinic. The medical records of patients who aged >18 years, ASA Physical Status Classification I-III and had undergone major oncological surgery (nephrectomy, cystectomy, and prostatectomy) that lasted for >120 minutes (min) were included in the study. As heating blanket use for active heating recently began in our clinic, passive heating method had been used for patients prior to this. Patients were covered with sterile sheets during surgeries until the introduction of active heating. In active heating, patients were covered with heating blankets (Medwarm 190x50 cm warming bed + W-500D control unit) that were set at 39 °C before patients were taken to the operation table; this was maintained until patients left the operation table. The ambient temperature of the operation room was regulated by the central system and maintained at a routine temperature of 23 °C-24 °C at 40% humidity. Non-invasive monitoring (electrocardiogram, non-invasive blood pressure, and pulse oxymeter) was conducted before anesthesia induction for patients who had received premedication as per routine practices of our clinic. For general anesthesia induction, thiopental (5-7 mg/kg), rocuronium (0.6 mg/kg), and remifentanil (0.1-0.3 µg/kg were administered and endotracheal intubation was performed after an appropriate time for neuromascular blockade. For anesthesia maintenance, sevoflurane (2-3%), 50% air +50% oxygen (4 L/min), and remifentanil infusion (0.1-0.3 µg/kg) were administered. Invasive monitoring was performed by using radial artery and peripheral central venous pressure cathetarizations. During the surgery, invasive liquids (crystalloid and colloids) at room temperature were used. After intubation, esophageal temperature probes were placed, and patient body temperatures were recorded every 30 min. All surgeries were performed using the open laparotomy technique. The transfusion of blood products

was decided based on blood gas results, the calculated amount of bleeding, comorbidities, and clinician's judgment. The amount of bleeding was calculated by evaluating the aspirator, sponge used and the surgical field.

Age, sex, BMI, ASA score, surgery type, initial body temperature, lowest body temperature, systolic blood pressure, diastolic blood pressure, and mean arterial pressure values at the lowest body temperature, the amount of bleeding and transfusion, surgical duration, postoperative intensive care unit stay duration of the patients were retrospectively evaluated.

### Statistical Analysis

Continuous data have been presented as means ± standard deviations. Categorical data have been indicated as percentage. The Shapiro-Wilk's test was used for the normal distribution analysis of data. The Mann-Whitney U test was used for the cases with two groups in comparison of the non-normally distributed groups. Pearson Exact chi-square, and Fisher's Exact chi-square tests were used for analyzing the cross tables generated. The data were statistically analyzed using the SAS version 9.2 software (SAS Institute, Cary, North Carolina). P-values of <0.05 were considered statistically significant.

## Results

The medical records of 68 patients who had undergone major urological surgeries (prostatectomy, nephrectomy, or cystectomy) were included. The mean age of the patients was 70.2±7.59 in patients using a heating blanket, 61.5±8.15 in patients not using a heating blanket and BMI was 26.4±2.47 in patients using warming blanket, 26.0±4.69 in patients not using warming blanket (Table 1). Of all patients, underwent nephrectomy 32%, cystectomy 29% and prostatectomy 38%.

Operation room temperature was similar for both the groups. The lowest body temperature measured using the esophageal probe inserted after anesthesia induction was 35.1 °C. The initial body temperature measurement in 32% of the patients was <36 °C.

The lowest intraoperative body temperature was 32.1 °C. Intraoperative hypothermia threshold was accepted as a body temperature of 36 °C. The comparison of the two groups demonstrated that 63.6% of patients for whom heating blankets were used and 94% of patients for whom heating blankets were not used had hypothermia.

Intraoperative blood loss was significantly lower in patients for whom active heating used mean 586 mL±386.7 mL than in those for whom passive heating mean 1,161 mL±919.5 mL was used (p=0.03). The amount of transfusion was mean 0.18±0.60 (IU) in the group with active heating and mean 0.93±1.26 (IU) in the group without active heating (p=0.04). The lactate level between the groups was statistically significant (p=0.02) (Table 2).

The average lowest body temperature of patients for whom passive heating was used was 34.3 °C and that of patients for whom active heating was used was 35.4 °C; a statistically significant difference was noted between the groups (p<0.001).

**Table 1. Demographic data**

| Parameters | Heating blanket (+) (n=11) | Heating blanket (-) (n=57) | p-value |
|---|---|---|---|
| Age | 70.2±7.59 | 61.5±8.15 | 0.004* |
| **Gender** | | | |
| Male | 9 (82%) | 52 (91%) | 0.690 |
| Female | 2 (18%) | 5 (9%) | |
| BMI | 26.4±2.47 | 26.0±4.69 | 0.815 |
| **ASA** | | | |
| I | 1 (9%) | 20 (35%) | 0.057 |
| II | 6 (55%) | 31 (54%) | |
| III | 4 (36%) | 6 (11%) | |

ASA: American Society of Anesthesiologists, BMI: body mass index

**Table 2. Clinical data**

| Parameters | Heating blanket (+) (n=11) | Heating blanket (-) (n=57) | p-value |
|---|---|---|---|
| Initial body temperature (°C) | 36.0±0.58 | 36.0±0.49 | 0.953 |
| Initial lactate | 0.94±0.50 | 1.04±052 | 0.319 |
| Lowest body temperature (°C) | 35.4±0.70 | 34.3±0.96 | <0.001* |
| Lactate | 1.20±0.73 | 1.64±0.84 | 0.02* |
| Amount of bleeding (mL) | 586.3±386.7 | 1161.4±919.5 | 0.03* |
| Transfusion amount (IU) | 0.18±0.60 | 0.93±1.26 | 0.04* |
| SAP (mm/Hg) | 104.3±19.4 | 104.5±16.4 | 0.86 |
| DAP (mm/Hg) | 58.6±12.3 | 58.6±9.0 | 0.75 |
| MAP (mm/Hg) | 74.9±16.0 | 75.4±10.9 | 0.51 |
| Need of intensive care | 0 (0%) | 9 (15%) | 0.35 |

SAP: Systolic arterial pressure, DAP: diastolic arterial pressure, MAP: mean arterial pressure. *P<0.05 indicates statistically significant values

At the end of the surgery, no postoperative intensive care was required for patients for whom heating blankets were used; however, 9 of the 57 patients for whom heating blanket was not used required intensive care after surgery. There was no difference between the groups in terms of ASA (p=0.057) and surgical operation type (p=0.417). The mean age was statistically significant between the groups (mean age was 70.2±7.59 in the group with active heating, 61.5±8.25 in the group without active heating, p=0.004). The type of operation performed (p=0.417) and the mean operation time were similar between the groups; in the group with active heating was mean 3.72±1.27 h, in the group without active heating was mean 4.14±1.62 h (p=0.55).

## Discussion

Intraoperative hypothermia is a preventable clinical condition. The incidence of intraoperative hypothermia in patients who are not warmed is higher in major, longer, and complicated surgeries compared with that in shorter and minor operations. Especially geriatric patients; cachectic (with increased metabolism, such as in cancer) patients, who are at risk associated with anesthesia use (ASA III-IV); and burn patients are in the high-risk group for unwanted hypothermia. It has been reported that the incidence of unwanted hypothermia is between 50-90% (5). With the increase in the elderly population, the incidence of many chronic diseases, malignancies and oncological surgeries has increased. Similarly, a majority of patients undergoing major urological surgery have systemic diseases related to the geriatric respiratory and circulatory systems.

Perioperative hypothermia results in extended hospital stay duration, increased costs, and mortality. Achieving normothermia requires multimodal and multidisciplinary (physician, nurse, medical staff, and intensive care team) approaches and awareness (6). In the perioperative period, warming the patient and monitoring body temperature are crucial for the early detection of hypothermia and achieving normothermia (5). Patients are exposed to unwanted hypothermia during the perioperative period owing to many reasons such as low room temperature, the administration of cold intravenous liquids, and blood transfusion (9).

Advanced age is an independent risk factor of hypothermia; therefore, routine body temperature measurement and perioperative heating must be performed. Shivering encountered in the postoperative period is a common condition that increases oxygen consumption and potential complications in high-risk patients (10). In this study, the mean age of the patients was 62.9±8.46, and the average age was 70.2±7.59 and higher, especially in the group using heating blankets.

In a study that retrospectively analyzed the data of 2,574 adult patients who underwent planned abdominal surgery and for whom heating blankets were used, the determinant factors of intraoperative body temperature were examined. Body temperature decreased 1 h after surgical incision and then increased again. However, body temperature increase may not occur in surgeries longer than 3 h owing to thermoregulation mechanisms such as perspiration. Body temperature increase 1 h after surgical incision was associated with young age, increased BMI, male sex, laparoscopic surgery, and heating blanket use. Male sex and heating blanket use were strong predictive factors of preventing hypothermia 3 h after surgical incisions. Although the mechanism that prevents hypothermia in males is unclear, decreased conduction owing to higher subcutaneous adipose tissue in females may prevent hypothermia. In addition, compared with females, males have higher musculoskeletal mass, which participates in thermogenesis (4). The cause of continued decrease in body temperature after the first h depends on ambient temperature, the extent of the surgical procedure, patient-specific factors, insulation, and active heating (1). In our study, only 10.2% patients were female as only urological oncology cases were included. ASA, BMI, gender, type of operation and operation times ratios were similar in both groups. However, although there was no need for intensive care in the group in which a heating blanket was used, there was no significant difference between the groups (p=0.353).

Soysal et al. (9) investigated the effects of active and passive heating on perioperative hypothermia. For at least 20 min, active heating was applied for the first group (using carbon fiber resistive system - W500D + 190x50 cm) and passive heating (using blankets or socks) for the second group in the preoperative period. The third group was monitored as a control group. Body temperature of the active heating group until 3 h was significantly higher than that of the other two groups (p<0.001). Mean body temperatures were 36.2 °C±0.26 °C, 35.4 °C±0.49 °C, and 35.2 °C±0.47 °C, respectively. Body temperature in the perioperative period was not significantly different between the passive heating group and control group. A significant difference was

noted between the active heating and control groups regard to body temperature. Thus, active heating applied using the carbon fiber resistance system was an effective method. In our study, the average lowest body temperature of patients for whom active heating was not used was 34.3 °C and of those for whom active heating was used was 35.4 °C with a statistically significant difference (p<0.001); these results were similar to those reported in the literature.

In their study, Aksu et al. (10) examined 564 patients of the Kocaeli University; they defined hypothermia as a body temperature of <35 °C. They determined that the incidence of perioperative hypothermia was higher in the thorax and open abdominal surgery cases with general anesthesia. The incidence of perioperative hypothermia was 2.4% and that of postoperative hypothermia was 45.7%. Time required for normothermic and hypothermic patients to reach a satisfactory Aldrete score was 15 and 24.5 min, respectively. In the aforementioned study, age, surgery type and duration, and the amount of liquid administered were found to be the significant risk factors of hypothermia (10). In the present study, the lowest initial body temperature was 35.1 °C; of all patients, 32.3% had a body temperature of <36 °C and 64.8% developed hypothermia (<35 °C) when the lowest body temperatures were evaluated. These results may be explained by the fact that in our study, the mean age of patients was higher, surgical duration was longer, and all surgeries were open abdominal surgeries.

In a study that retrospectively investigated the time at which hypothermia develops in colectomies, a perioperative body temperature of >36.5 °C was directly proportional to a postoperative body temperature of >36 °C. It was highlighted that this relation was not affected by laparoscopic or open surgeries and that procedures designed for normothermia should be utilized before anesthesia induction and in the intraoperative period. Although some researchers have recommended the heating of intravenous fluids before administration, its efficacy is yet to be proven. Temperature measurements were performed using different methods via the oral route in pre- and postoperative periods and using esophageal heat probe during the intraoperative period (11). In our study, temperatures recorded using the esophageal heat probe inserted after intubation were considered as initial body temperatures. The lowest measured initial body temperature was 35.1 °C, which was considered to be affected by factors such as anesthesia induction and ambient temperature. While the entrance body temperature was similar between the groups, there was a significant difference between the lowest intraoperative body temperature.

A study conducted by Hassani et al. (12) found no difference between the effect of heating blankets set at 38 °C and those set at 40 °C on patients undergoing spinal fusion surgery under total intravenous anesthesia for preventing hypothermia-related complications during the induction, surgical, and recovery periods. However, hypothermia prevalence was lower in patients for whom heating blankets were set at 40 °C than in those for whom heating blankets were set at 38 °C (12).

Analysis based on current literature showed that each 1 °C decrease in body temperature with mild hypothermia increases blood loss by 16% and transfusion risk by 22% (1,13). A study assessing surgeries with high hypothermia risk such as hip and thorax surgeries demonstrated that the active heating group had less bleeding and hemoglobin decrease than the passive heating group; however, both the groups had similar transfusion requirements (6). In our study, intraoperative blood loss was also statistically significantly lower in the patients for whom active heating was used (mean 586 mL±386.7) than in those for whom passive heating was used (mean 1,161 mL±919.5) (p=0.03). The amount of transfusion was: 0.18±0.60 in the group with active heating, the mean amount of transfusion (IU) in the group without active heating (IU): 0.93±1.26, and it was statistically significant (p=0.04). Lactate level also supports this (p=0.02).

The study had its own limitations. First, the data were single-centered, retrospectively collected, and the distribution between groups was uneven. The lack of perioperative temperature measurements of the patients and the inability to access records of complications other than bleeding and the need for intensive care, which are thought to be related to this, limits the study. Although statistically significant results support other studies, it was not evaluated before the sample size because it was retrospective.

## Conclusion

Perioperative hypothermia is a clinically significant and preventable condition that can cause long-term complications. Our results suggest that perioperative hypothermia is a frequent and serious problem that is encountered in clinical practice. Therefore, we concluded

that temperature monitoring and the application of necessary active heating methods during the perioperative period can prevent hypothermia and deep anesthesia and mitigate serious complications such as bleeding.

## Ethics

**Ethics Committee Approval:** This retrospective study was approved by the Eskişehir Osmangazi University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (decision no: 20, date: 19.02.2019).

**Informed Consent:** Retrospective study.

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

## Authorship Contributions

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

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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# Effects of Different Gastric Residual Volume Thresholds on Morbidity and Mortality in Patients Receiving Intensive Care

## Yoğun Bakım Hastalarında Farklı Gastrik Rezidüel Volüm Eşiklerinin Morbidite ve Mortalite Üzerine Etkileri

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**ABSTRACT** *Objective:* Enteral feeding is often limited by gastrointestinal intolerance. However, there is no consensus on the threshold value of gastric residual volume (GRV) on adjusting the enteral feeding rate. This study aimed to determine the effects of GRV thresholds of 150 mL and 250 mL on reaching calorie and protein targets and to determine gastric intolerance in patients receiving intensive care and enteral feeding.

*Materials and Methods:* In this retrospective study, patients who were treated and followed in the intensive care unit (ICU) of our clinic between 2008 and 2017 were examined for 14 days after hospitalisation. Caloric values, protein values, presence of gastric intolerance, morbidity, and mortality factors of the patients, who were divided into two groups with 150 mL (group 1) and 250 mL (group 2) GRV thresholds, were examined.

*Results:* The amounts of calories and proteins provided after 14 days were significantly higher in group 2 ($p<0.001$), and the cumulative calorie and protein deficits were significantly less in group 2 ($p<0.001$). As regards morbidity and mortality, no significant difference was observed in aspiration pneumonia, anaemia, disseminated intravascular coagulation, septic shock, reintubation, intensive care mortality, 28$^{th}$ day mortality, and number of mechanical ventilation-free days between the two groups. The incidence of nosocomial infection ($p=0.002$) and ventilator-associated pneumonia ($p<0.001$) was significantly higher and the duration of mechanical ventilation ($p<0.001$) and length of stay in the ICU ($p<0.001$) was significantly longer in group 2 than in group 1. No statistically significant difference was observed between the two groups in terms of the development of gastrointestinal intolerance during follow-up ($p=0.896$).

*Conclusion:* Target nutritional values were reached in both groups. No pathological side effects of excessive intervention were observed in the group with lower tolerance. Similarly, no valuable morbidity or mortality result was obtained for the 250 mL threshold.

**Keywords:** Calories, enteral nutrition, gastric residual volume, intensive care, protein

**ÖZ** *Amaç:* Enteral beslenme sıklıkla gastrointestinal intolerans nedeniyle kısıtlanır. Enteral beslenme hızının gastrik rezidüel volüme (GRV) göre ayarlanmasının eşik değeri konusunda fikir birliği yoktur. Bu çalışmanın amacı enteral beslenme uygulanmakta olan yoğun bakım hastalarında, 150 mL ve 250 mL GRV eşiklerinin hedef kalori ve proteine ulaşma miktarını, morbidite ve mortaliteye etkilerinin saptanmasıdır.

*Gereç ve Yöntem:* Çalışma klinik retrospektif olarak planlandı ve 2008-2017 tarihleri arasındaki dönemde kliniğimiz yoğun bakım ünitesinde (YBÜ) takip ve tedavisi yapılan hastalar yatış anından itibaren 14 gün süreyle incelendi. GRV eşiğine göre 150 mL (grup 1) ve 250 mL (grup 2) olacak şekilde 2 gruba ayrılan hastaların kalori değerleri, protein değerleri, gastrik intolerans oluşumu, morbidite ve mortalite faktörleri incelendi.

*Bulgular:* On dört gün sonunda verilebilen kalori-protein oranları grup 2'de anlamlı olarak daha yüksekti ($p<0,001$) ve kümülatif kalori ve protein açığı anlamlı olarak grup 2'de daha azdı ($p<0,001$). Morbidite ve mortalite karşılaştırıldığında; aspirasyon pnömonisi, anemi, dissemine intravasküler koagülasyon, septik şok, reentübasyon, yoğun bakım mortalitesi, 28. gün mortalitesi ve mekanik ventilatör bağımsız gün sayısı açısından anlamlı fark gözlenmemiştir. Grup 2'de anlamlı olarak nozokomiyal enfeksiyon yüksek ($p=0,002$), ventilatör ilişkili pnömoni yüksek ($p<0,001$), mekanik ventilatörde kalış süresi ($p<0,001$) ve YBÜ'de yatış süresi ($p<0,001$) daha uzun olarak tespit edildi. Takip süresince gastrointestinal intolerans gelişimi açısından iki grup arasında istatistiksel olarak anlamlı fark gözlenmedi ($p=0,896$).

*Sonuç:* Her iki grupta da hedef beslenme değerlerine ulaşılmıştır, daha düşük tolerans grubunda aşırı müdahalede bulunmanın herhangi bir patolojik yan etkisiyle karşılaşılmamıştır, benzer şekilde 250 mL için de avantajlı bir morbidite ya da mortalite sonucuna ulaşılamamıştır.

**Anahtar Kelimeler:** Kalori, enteral beslenme, gastrik rezidüel volüm, yoğun bakım, protein

## Introduction

It is accepted that nutritional support given to patients in intensive care units (ICUs) is as important as the drug therapies prescribed (1). Nutrition is considered to be one of the most important controllable factors affecting morbidity and mortality (2,3).

It has been shown that wounds heal faster and the immune system is strengthened in patients with sufficient feeding, and morbidity and mortality increases in patients suffering from malnutrition (2,4,5). 40% of malnutrition observed in intensive care patients was associated with morbidity and mortality (6).

It is essential to calculate the energy and protein needs of patients to ensure sufficient nutritional support and to determine how this support will be provided. It can be given enterally and/or parenterally depending on the clinical condition of the patient (2,7). It has been shown that enteral feeding is a less costly and more physiologically appropriate feeding method, but its application is often limited by gastrointestinal intolerance [high gastric residual volume (GRV), regurgitation, vomiting, diarrhea, constipation, or abdominal distension]. In healthy adults, 10-100 mL of secretion (8) in the gastrointestinal tract remains in the stomach, but the amount of secretion remaining in the stomach increases in intensive care patients, where motility slows down (9). Complications such as vomiting, aspiration and ventilator-associated pneumonia (VAP) can be observed in patients with delayed gastric emptying. In order to reduce these risks, current guidelines suggest that GRV should be checked at regular intervals and enteral feeding should be adjusted according to GRV (10); however, there are different opinions regarding GRV thresholds.

New protocols are being created with current studies. By allowing high GRVs without signs of gastric distension, an increase in the target calories was observed as well as shortened lengths of hospital stays without increasing the risk of aspiration in the patients. However, gastrointestinal intolerance may go unnoticed with longer follow-up intervals (11).

This study aims to determine the effects of GRV thresholds of 150 mL and 250 mL on reaching calorie and protein targets and to determine gastric intolerance in intensive care patients receiving enteral feeding.

## Materials and Methods

This retrospective study was organized in accordance with the STROBE guidelines. After approval by the Clinical Trials Ethics Committee of the Karadeniz Technical University (decision no: 14, date: 13.11.2017), the patients who were followed up and treated in our Anesthesiology and Reanimation ICU between 2008 and 2017 were examined clinically and retrospectively.

The patients' demographic data, laboratory values, vital signs, development of VAP (12), presence of nosocomial infection (non-VAP) (13), development of aspiration pneumonia (14), anemia (15,16), disseminated intravascular coagulation (DIC) (17), presence of septic shock (18), length of stay in the ICU, length of stay on a mechanical ventilator (MV), development of reintubation, ICU mortality, values of Acute Pysiology and Chronic Health Evaluation-II (APACHE-II), The Sequential Organ Failure Assessment (SOFA), Glasgow coma scale (GCS), $PaO_2/FiO_2$ ratio (Horowitz index), protein and energy values attained, daily observations of gastrointestinal intolerance symptoms (vomiting/regurgitation, diarrhea, constipation), and prokinetic drug use were analyzed retrospectively over the first 14 days of admission into the ICU, and the relationship between nutritional status and the clinical results of GRV limits were examined.

Patients under 18 years of age, pregnant patients, patients with malignancies, intoxicated patients, those with less than 3 days of hospitalization, burn injuries, cases of renal failure and liver failure, those with a GCS value of 3, patients with return of spontaneous circulation (ROSC), and patients with severe malnutrition and conditions limiting the enteral feeding during the ICU admission were excluded from the study.

At the beginning of the study, it had been calculated that a minimum of 154 patients should be included in the study for each group at 80% strength. The groups were determined as group 1 (150 mL GRV) and group 2 (250 mL GRV). During their follow-up, GRV was measured by aspiration with 50 mL syringe every 6 hours and if feeding was not interrupted, the aspirate was given back. Groups (150 mL and 250 mL) were formed according to the amount of GRV.

Normal calorie requirements were calculated using the Harris-Benedict formula and taking into account the stress factors (19-21).

The protein requirement was determined as 1-2 gr/kg of protein per day in metabolically stressed patients,

as recommended by the current Society of Critical Care Medicine/American Society for Parenteral and Enteral Nutrition Clinical Practice Guidelines, as it was based on nutritional status, level of stress and ability to metabolize proteins physiologically (22).

On the 1st, 3rd, 7th, 10th and 14th days after admission into the ICU, APACHE-II scores, SOFA scores and GCS of the patients were recorded.

### Statistical Analysis

The data was analyzed using IBM SPSS V23. The suitability of the data for normal distribution was analyzed by the Shapiro-Wilk test. The independent samples t-test was used to compare the data suitable for normal distribution, and the Mann-Whitney U test was used to compare the data which was unsuitable for normal distribution. A comparison of categorical data according to group and mortality was performed with the chi-square test. Quantitative data was presented as arithmetic mean ± deviation, median (minimum-maximum), while qualitative data was expressed as frequency (percent). The significance level was taken as $p<0.05$.

## Results

Among 2,324 patients followed up in the department of anesthesiology and reanimation ICU of our clinic, 312 patients who met the criteria were included in the study and the patients were divided into two groups [group 1 (150 mL) and group 2 (250 mL)] according to their GRV limits. Patients under the age of 18 (n=127), pregnant patients (n=42), patients with malignancies (n=288), intoxicated patients (n=184), those with less than 3 days of stay (n=348), those suffering from burns (n=67), chronic kidney failure (n=206), and liver failure (n=59), patients with GCS equal to 3 (n=225), patients with ROSC (n=192), and patients with severe malnutrition (n=92) and other conditions preventing enteral feeding (n=182) during the hospitalization were excluded from the study, and when the number of patients meeting the criteria was reached, screening was terminated (Figure 1). The patients' gender, body weight, biochemical parameters at the time of hospitalization, vital signs, initial GCS values, Horowitz index, blood glucose level, prokinetic drug use, and the presence of diarrhea, constipation and vomiting/regurgitation did not indicate a statistically significant difference between the two groups. The median age values of the patients differed between the groups (p=0.005). While the median value was 48 years in group 1, it was 55.5 years in group 2. The median body mass index (BMI) values during the admissions to the ICU differed between the groups (p=0.011). While the median value was 28 kg $m^{-2}$ in group 1, it was 27 kg $m^{-2}$ in group 2. The median values of the APACHE-II score and the SOFA score on the first day differed between the groups (p=0.042; p=0.028, respectively) (Table 1).

The most common cause for admission of the patients to the ICU was trauma in both groups and was observed to be 42.3% in group 1 and 43.6% in group 2. Other causes of admission were determined to be postoperative period representing 28.8% and 16% in group 1 and group 2, respectively; hospitalization due to respiratory causes representing 16% and 30.8% in group 1 and group 2; neurological conditions representing 8.3% and 6.4% in group 1 and group 2; sepsis representing 3.2% and 1.9% in group 1 and group 2; and cardiac causes representing 1.3% in both groups, with a statistically significant difference (p=0.016, Table 2).

Concomitant diseases differed significantly between the groups (p=0.018). The number of patients without any concomitant disease was 89 (57%) in group 1 and 85 (55%) in group 2. Considering the existing concomitant diseases, the most common concomitant diseases in group 1 were of neurological origin (29.9%), while in group 2, the percentage of diseases with neurological origin was 24.7%. The most

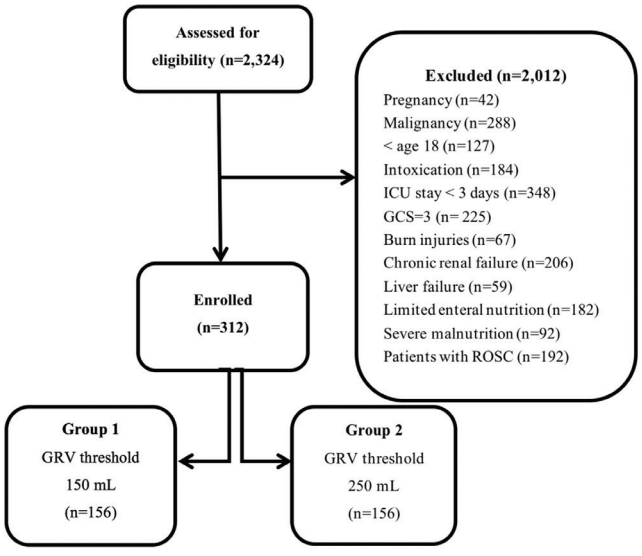


**Figure 1.** Flow chart of study population selection

GCS: Glasgow coma scale, GRV: gastric residual volume, ICU: intensive care unit, ROSC: return of spontaneous circulation

| Table 1. The comparison of demographic data and initial values | | | |
|---|---|---|---|
| | Group 1 (150 mL) | Group 2 (250 mL) | p-value |
| Gender [n (%)] | | | |
| Female | 48 (30.8) | 51 (32.7) | 0.715 |
| Male | 108 (69.2) | 105 (67.3) | |
| Weight (kg) | 83 (58-112) | 82 (56-108) | 0.106 |
| Age (year) | 48 (19-90) | 55,5 (18-89) | 0.005 |
| BMI (kg $m^{-2}$) | 28 (22-37) | 27 (19-35) | 0.011 |
| Creatinin (mg $dL^{-1}$) | 1 (0-5) | 1 (0-6) | 0.642 |
| Platelet ($mcL^{-1}$) | 166,500 (151-806,000) | 175,500 (23,000-649,000) | 0.171 |
| Total bilirubin (mg $dL^{-1}$) | 1 (0-77) | 1 (0-8) | 0.890 |
| Fever (ºC) | 37 (35-397) | 37 (35-39) | 0.170 |
| WBC (u $mcL^{-1}$) | 11,150 (4-89,000) | 10,800 (4-96,000) | 0.137 |
| Albumin (g $dL^{-1}$) | 3 (2-5) | 3 (2-5) | 0.754 |
| INR | 1 (1-3) | 1 (1-5) | 0.274 |
| ALT (IU L-1) | 22 (1-550) | 28.5 (1-950) | 0.175 |
| APACHE-II | 14 (2-31) | 14 (2-27) | 0.042 |
| SOFA | 6 (0-16) | 5 (0-12) | 0.028 |
| GCS | 10 (3-15) | 10 (4-15) | 0.416 |

BMI: Body mass index, WBC: white blood cell, INR: international normalized ratio, ALT: alanine aminotransferase, APACHE-II: Acute Pysiology and Chronic Health Evaluation-II, SOFA: The Sequential Organ Failure Assessment, GCS: Glasgow coma scale

| Table 2. The comparison of reason for admission and comorbid diseases | | | |
|---|---|---|---|
| | Group 1 (150 mL) n (%) | Group 2 (250 mL) n (%) | p-value |
| **Reason for admission** | | | |
| Cardiac | 2 (1.3) | 2 (1.3) | - |
| Neurological | 13 (8.3) | 10 (6.4) | - |
| Respiratory | 25 (16) | 48 (30.8) | 0.016 |
| Sepsis | 5 (3.2) | 3 (1.9) | |
| Trauma | 66 (42.3) | 68 (43.6) | - |
| Postoperative | 45 (28.8) | 25 (16) | - |
| **Comorbid disease** | | | |
| Hypertension | 7 (10.4) | 7 (8.2) | - |
| CAD | 5 (7.5) | 3 (3.5) | - |
| CHF | 2 (3) | 5 (5.9) | - |
| Diabetes Mellitus | 2 (3) | 6 (7.1) | 0.018 |
| COPD | 6 (9) | 23 (27.1) | |
| Neurological | 20 (29.9) | 21 (24.7) | - |
| Haematological | 5 (7.5) | 0 (0) | - |
| Others | 20 (29.9) | 20 (23.5) | - |

CAD: Coronary artery disease, CHF: congestive heart failure, COPD: chronic obstructive pulmonary disease

common concomitant disease in group 2 was chronic obstructive pulmonary disease (COPD) (27.1%), while in group 1, the percentage with COPD was 9%. The percentage of patients with hypertension was 10.5% and 8.2% in group 1 and group 2, respectively; those with concomitant cardiac disease was 10.5% and 9.4% in group 1 and group 2; and the rate of patients with diabetes mellitus known to compromise gastrointestinal motility was 3% and 7.1% in group 1 and group 2, respectively. Only group 1 included patients with hematological disorders with a rate of 7.5% (Table 2).

The two groups were compared in terms of calorie and protein intake. The amount of calories and proteins provided after fourteen days was significantly higher in group 2 ($p<0.001$). The cumulative calorie and protein deficit after fourteen days was significantly less in group 2 ($p<0.001$) (Table 3).

When the two groups were compared in terms of morbidity and mortality, no significant difference was observed in terms of aspiration pneumonia, anemia, DIC, septic shock, reintubation, intensive care mortality, 28$^{th}$ day mortality and number of mechanical ventilation free days. In group 2, nosocomial infection ($p=0.002$) and VAP ($p<0.001$) were significantly higher, duration of stay in the

MV (p<0.001) and length of stay in the ICU (p<0.001) were significantly longer (Table 4).

No statistically significant difference was observed between the two groups in terms of the development of gastrointestinal intolerance during follow-up (p=0.896) (Table 5).

## Discussion

Enteral feeding is defined as the continuous or intermittent administration of nutrients through nasogastric, nasojejunal, gastrostomy or jejunostomy routes in patients with normal gastrointestinal tract function who are suffering from malnutrition or expected to develop malnutrition (22). It is a safe and cost-efficient method that is suitable for human physiology (2,23). The most important cause of failure of enteral feeding is gastrointestinal motility disorder. As a result of this, GRV increases, and distention, vomiting,

**Table 3. The comparison of protein and calorie parameters**

| | Group 1 (150 mL) | Group 2 (250 mL) | p-value |
|---|---|---|---|
| EN (day) | 1 (1-14) | 3 (1-65) | <0.001 |
| PN (day) | 2 (0-14) | 3 (0-14) | 0.038 |
| Oral feeding (day) | 0 (0-9) | 0 (0-12) | 0.946 |
| Mean protein quantity (g $kg^{-1}$ $day^{-1}$)* | 1.30±0.21 | 1.51±0.22 | 0.001 |
| Percentage of protein that can be given** | 77 (55-90) | 86 (55-99) | <0.001 |
| 14-day total protein deficit (g) | 407.5 (157-590) | 238 (14-490) | <0.001 |
| Mean calorie quantity (kcal $kg^{-1}$ $day^{-1}$)* | 28.21±4.30 | 29.10±5.40 | 0.041 |
| Percentage of calorie that can be given** | 80 (74-96) | 90 (76-105) | <0.001 |
| 14-day total calorie deficit (kcal) | 7494 (1,666-11,070) | 3291 (0-10,389) | <0.001 |

EN: Enteral nutrition, PN: parenteral nutrition. *Mean ± standard deviation, other values are shown as median (minimum-maximum), **In the first 14 days of admission to intensive care. Mean protein quantity (g $kg^{-1}$ $day^{-1}$): The mean protein intake in a day. Percentage of protein that can be given: The mean 'protein intake percentages of the patients' for 14 days were compared. 14-day total protein deficit (g): The 14-day total protein deficits of the patients were compared. Mean calorie quantity (kcal $kg^{-1}$ $day^{-1}$): The mean calorie intake in a day. Percentage of calorie that can be given: The mean 'calorie intake percentages of the patients' for 14 days were compared. Fourteen-day total calorie deficit (kcal): The 14-day total calorie deficits of the patients were compared

**Table 4. Cross-group comparison**

| | Group 1 (150 mL) n (%) | Group 2 (250 mL) n (%) | p-value |
|---|---|---|---|
| **Nosocomial infection (non-VAP)** | | | |
| No | 94 (60.3) | 67 (42.9) | 0.002 |
| Yes | 62 (39.7) | 89 (57.1) | |
| **VAP** | | | |
| No | 136 (87.2) | 104 (66.7) | <0.001 |
| Yes | 20 (12.8) | 52 (33.3) | |
| **Aspiration pneumonia** | | | |
| No | 125 (80.1) | 135 (86.5) | 0.129 |
| Yes | 31 (19.9) | 21 (13.5) | |
| **Anemia** | | | |
| No | 128 (82.1) | 130 (83.3) | 0.765 |
| Yes | 28 (17.9) | 26 (16.7) | |
| **DIC** | | | |
| No | 115 (73.7) | 127 (81.4) | 0.103 |
| Yes | 41 (26.3) | 29 (18.6) | |
| **Septic shock** | | | |
| No | 120 (76.9) | 111 (71.2) | 0.245 |
| Yes | 36 (23.1) | 45 (28.8) | |
| **Reintubation** | | | |
| No | 144 (92.3) | 143 (91.7) | 0.835 |
| Yes | 12 (7.7) | 13 (8.3) | |
| **ICU mortality** | | | |
| No | 111 (71.2) | 104 (66.7) | 0.392 |
| Yes | 45 (28.8) | 52 (33.3) | |
| **$28^{th}$ day mortality** | | | |
| No | 113 (72.4) | 121 (77.6) | 0.296 |
| Yes | 43 (27.6) | 35 (22.4) | |
| MV free day | 2 (0-20) | 2.50 (0-40) | 0.165 |
| Duration of stay in MV* | 4 (0-37) | 9.5 (0-45) | <0.001 |
| Length of stay in ICU* | 7 (3-37) | 13 (3-70) | <0.001 |

VAP: Ventilator associated pneumonia, DIC: disseminated intravascular coagulopathy, ICU: intensive care unit, MV: mechanical ventilator, *median (minimum-maximum)

**Table 5. The comparison of total gastric intolerance presences of each patient for 14 days**

| | Median (min-max) | p-value |
|---|---|---|
| Group 1 (150 mL) | 0 (0-14) | 0.896 |
| Group 2 (250 mL) | 0.5 (0-12) | |

Min: Minimum, max: maximum

regurgitation, aspiration and diarrhea occurs. For this reason, GRV measurements are used in routine patient follow-ups to avoid complications. Increased GRV was identified as a cause of interruption to feeding, and 70% was found to be preventable (24,25).

Monitoring GRV at regular intervals in patients receiving enteral feeding is recommended (6,26). Although there is a clear consensus on the necessity of enteral feeding in intensive care patients, the method of application of this procedure, which has been adopted for 50 years, varies in the literature (6,27,28). There are studies indicating that GRV limits may be in the range of 50-500 mL in the follow-up of patients receiving enteral feeding (26,29). However, there are new studies showing that measuring GRV causes interruptions to enteral feeding, prolongs the time to reach target calories, and causes malnutrition; thus there is no need to measure GRV unless there are signs of gastric intolerance (26). In parallel with these studies, in the current study it was found that feeding in group 2 was interrupted less often; therefore enteral nutrition could be given for statistically significantly longer periods [median values are 0 (0-14) in group 150 and 3 (0-14) in group 250, p=0].

Based on the studies, the energy requirement should be 20-25 kcal/kg/day in the acute period and 25-30 kcal/kg/day in the recovery period (30). When the patients followed up in our ICU were analyzed retrospectively, it was found that group 2 were fed significantly more in terms of protein percentages and calorie requirements that were met during the first 14 days of their hospitalization (Table 4). When total protein and calorie deficits were analyzed in the same period, cumulative protein and calorie deficits were found to be significantly less in group 2, in which the patients could be fed enterally for a longer period of time (Table 4).

In our study, the median values of albumin at the 10$^{th}$ day in group 2 were found to be significantly higher in accordance with the protein and calorie percentages that were given to the patients during the 14-day follow-up (1-3-7-10-14 days) of the two groups [2 in group 1 (2-4), 3 (2-4) in group 2, p=0.009]. The median albumin value at the end of 14 days was 2.5 (1-4) in group 1 and 3 (1-4) in group 2 (p=0.126).

When previous studies were examined, 150 and 250 mL GRV threshold values were compared in terms of vomiting frequency and no difference was found between the two groups (11). In a recent study, 200 mL and 400 mL GRV threshold values were compared in terms of aspiration and regurgitation, and it was asserted that high GRV values did not increase the risk (27). Vomiting frequencies in patients with GRV>300 mL and GRV<300 mL were compared and it was reported that no significant difference was observed (8). No significant difference was found in a study examining the development of aspiration and pneumonia with high GRV values (31). Another study compared the 200 mL and 500 mL limits and reported that the high GRV limit was not associated with gastrointestinal complications in patients connected to the MV (29). A group without GRV measurements (with interruptions to feeding only when gastrointestinal intolerance occurred) and two groups with a 250 mL limit were compared, and it was found that the group without GRV measurements reached the target calories faster; and VAP, aspiration, diarrhea, and length of stay in the ICU were found to be similar in both groups (26). There was no difference in terms of vomiting or feeding intolerance in groups with and without GRV measurements (32). In one study, 100 mL and 200 mL GRV were compared and it was found that gastrointestinal system complications were less in the 100 mL group (33). In another study, diarrhea was observed at a rate of 29.5%. No significant difference was found between the two groups compared to the current study in terms of diarrhea, constipation, vomiting/regurgitation, aspiration and aspiration pneumonia (p=0.896) (11).

There are studies that have asserted that prokinetic drugs which accelerate gastric motility, such as metoclopramide and erythromycin, may be beneficial (34). On the other hand, in another study, the effects of prokinetic drug use on GRV were compared and it was determined that there was no significant difference between the groups (11). In the current study, it was found that the use of prokinetic drugs did not differ significantly in GRV (p=0.285). Reviews of the literature revealed that the number of studies on the drug-gastric motility relationship, or on the drugs that should be administrated by interrupting feeding, are limited (35,36). Steroid and insulin, which may affect gastric motility, were examined in the current study and no significant difference was found when the two groups were compared.

Scoring systems such as APACHE-II, Simplified Acute Physiology Score, Physiology Stability Index, SOFA and Therapeutic Intervention Scoring System are used to determine disease severity of intensive care patients (37,38). In the current study, the APACHE-II and SOFA scores were considered and similar results were obtained for the two groups. Similarly, in a study that undertook calorie and protein

monitoring, no correlation was found between APACHE-II scores and gastric intolerance symptoms (39).

In a study comparing VAP or new infection development, the length of ICU and hospital stay, organ failure scores, mortality rates in patients undergoing mechanical ventilation, similar results were found in patients with and without GRV follow-up (26). The development of sepsis and gastric intolerance (high GRV, diarrhea) was examined and a correlation was found between them ($p<0.001$) (40). In the current study, the rate of nosocomial infection (non-VAP) and VAP development were found to be higher in group 2. When the number of patients' MV free days was examined, it was observed that no difference was seen between the two groups and that initial APACHE-II and SOFA scores were similar, which suggested that the difference in VAP development may have been caused by regurgitation that went unnoticed. Having considered the causes of admission to ICU, it was thought that the higher age average in group 2, the significantly higher respiratory hospitalization rate, as well as the high rate of COPD as a concomitant disease, may have affected the length of hospital stay. In addition, the presence of significantly more postoperative patients in group 1 may have also affected the length of hospital stay. The causes of longer hospitals and MV stays in group 2 were attributed to the fact that the patients may be more susceptible to infections and late recovery despite their higher protein intake due to respiratory factors and age differences. In addition, as the number of postoperative patients in group 1 was higher, patients could be discharged earlier. Although the length of stay in MV differed, no significant difference was found in terms of ventilation when $PaO_2/FiO_2$ values were compared. It should also be remembered that there may be many causes that affect the length of ICU and MV stays. The fact that the target protein values were achieved in both groups, that more VAP cases were seen, and longer ICU and MV stays were observed in group 2 suggests that the 150 mL limit might actually be sufficient.

As for the length of stay in the ICU, a group of patients with a GRV threshold of 250 mL and without any GRV measurements had been compare previously; however, there was no difference in terms of their length of stay in ICU and MV (26). In another study, 200 mL and 500 mL GRV threshold values were compared and no difference was observed (29).

In one study, no difference was detected between the two groups with a GRV threshold value of 250 mL and without GRV monitoring in terms of duration of use of the MV (26). In a further study in which enteral feeding was evaluated in two groups, no significant difference was found in the duration of mechanical ventilation of patients (41).

Nutritional practices have a great effect on morbidity and mortality. On the other hand, enteral feeding is preferred as it strengthens the immune functions and is very beneficial in terms of reducing costs in developing countries like Turkey (3,42). In the current study, no significant difference was found between the groups in terms of ICU mortality and 28$^{th}$ day mortality ($p=0.392$, $p=0.296$). After examining all patients in this study, it was found that the increase in the number of days on which parenteral nutrition was given was associated with increased mortality ($p=0.004$), and the increase in the number of days of oral feeding was associated with decreased mortality ($p=0$).

Further studies on the evaluation of gastrointestinal intolerance in enteral feeding are ongoing. It is argued that the application of protocols allowing high GRV without any gastric distension symptoms will help increase target protein and calorie levels, and will shorten the length of hospital stay and the duration of mechanical ventilation, without causing an increased risk of aspiration.

Since our study was retrospective, higher GRV values or patients with no measured GRV values were not examined. In addition, energy and protein requirements were met according to the then current weights of the patients. For a more detailed evaluation, it is recommended that new studies should be conducted and compared based on the ideal weight of patients. After the study was completed, patients with higher GRV values began to be followed up in ICU. The difference between the BMI values measured during hospitalization yielded similar results in total protein and calorie amounts; however, when an evaluation was made in terms of the percentage of requirements met, based on the current weight, significant results were obtained.

## Conclusion

Target nutritional values were reached in both groups. No pathological side effects of excessive intervention were observed in the lower tolerance group. Similarly, no advantageous morbidity or mortality result was obtained for the 250 mL threshold. The results of this study have led to a belief that the current guidelines should be questioned

and prospective randomized controlled studies should be conducted involving more patients.

### Ethics

**Ethics Committee Approval:** The present study was approved by the Clinical Trials Ethics Committee of the Karadeniz Technical University (decision no: 14, date: 13.11.2017).

**Informed Consent:** It is a retrospective study. No need for consent.

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

### Authorship Contributions

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

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**ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA***

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# The Effects of the Position Changes of Critical Care Patients on Respiratory and Cardiac Parameters

## Yoğun Bakım Hastalarının Pozisyon Değişikliklerinin Solunum ve Kardiyak Parametreler Üzerindeki Etkileri

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**ABSTRACT** *Objective:* Position changes in patients requiring critical care aimed to mobilise secretions, prevent compression wounds and decrease the risk of ventilator-related pneumonia. This study aimed to investigate the effects of supine, left lateral, right lateral and Fowler positions on the respiratory and cardiac parameters with the $CO_2$ rebreathing technique using non-invasive cardiac output monitor.

*Materials and Methods:* Forty patients aged 18-65 years who were on invasive mechanical ventilator support and had a hospitalisation time >24 h were included in the study. Cardiac output was monitored with non-invasive cardiac output monitor. Patients were assisted on supine, left lateral, right lateral and Fowler positions. Respiratory and hemodynamic parameters of patients were measured at these positions with 1-h intervals.

*Results:* A significant difference was found among the measurements when the mean arterial pressure values measured at different times at the left lateral position were compared. Similarly, a significant difference was noted among $SpO_2$ values measured at the supine position at different times. However, this difference was not clinically significant. No significant differences were found within the groups as regards to other respiratory and cardiac parameters.

*Conclusion:* Position changes did not lead to a clinically significant change on respiratory mechanics, hemodynamic parameters and oxygenation in patients with stable hemodynamic who were on mechanical ventilator support.

**Keywords:** Critical care, patient position, cardiac output, hemodynamic monitoring, airway resistance

**ÖZ** *Amaç:* Yoğun bakım hastalarında pozisyon değişiklikleri ile sekresyonların hava yolunda mobilizasyonu, basınç ülserlerinin önlenmesi ve ventilatör ilişkili pnömoni riskinin azaltılması hedeflenmektedir. Sırtüstü (supin), sol lateral, sağ lateral ve Fowler pozisyonlarının solunum ve kardiyak parametreler üzerine etkilerini $CO_2$ yeniden soluma tekniği kullanan non-invaziv kardiyak debi (output) monitörü ile araştırmayı amaçladık.

*Gereç ve Yöntem:* Çalışmaya 24 saatten uzun süredir yoğun bakımda takip edilen, invaziv mekanik ventilatör desteği altındaki 18-65 yaş arası 40 hasta dahil edildi. Hastaların sırasıyla sırtüstü, sol yan, sağ yan ve Fowler pozisyonunda non-invaziv kardiyak debi monitörü ile kalp debisi izlendi. Hastaların solunum ve hemodinamik parametreleri bu pozisyonlarda bir saatlik aralıklarla ölçüldü.

*Bulgular:* Sol lateral pozisyonda farklı zamanlarda ölçülen ortalama arter basıncı değerleri karşılaştırıldığında ölçümler arasında anlamlı fark bulundu. Sırtüstü pozisyonlarda farklı zamanlarda ölçülen $SpO_2$ değerleri arasında önemli bir fark vardı. Ancak bu fark klinik olarak anlamlı değildi. Farklı zamanlarda ölçülen diğer solunum ve kalp parametreleri açısından gruplar arasında anlamlı farklılık bulunmadı.

*Sonuç:* Hemodinamisi stabil olan mekanik ventilatör desteği altındaki hastalarda pozisyon değişikliklerinin solunum mekanikleri, hemodinamik parametreler ve oksijenasyonda klinik olarak anlamlı bir değişikliğe yol açmadığını gördük.

**Anahtar Kelimeler:** Yoğun bakım, hasta pozisyonu, kardiyak debi, hemodinamik monitörizasyon, hava yolu direnci

## Introduction

Critical care patients are given different positions during the hospitalization due to several reasons including prevention of the compression wound, avoiding infections, clearing the respiratory tract secretions, increasing oxygenation, and improving blood circulation. Respiratory and hemodynamic changes may be seen during position changes (1,2).

Sustainable oxygen delivery is essential in order to maintain metabolism and vital functions in the organism. Oxygen delivery is determined by cardiac output (CO) and the changes in the oxygen content (3). Although thermodilution technique using pulmonary artery catheter is the gold standard for CO monitorization, there has been an increasing tendency to use alternative and non-invasive methods, because thermodilution is an invasive and difficult technique which measures with intervals and may cause severe complications during insertion of the catheter (4).

Non-invasive Cardiac Output (NICO) technique has been recommended as an alternative non-invasive CO measurement technique in patients receiving mechanical ventilation. NICO system is a new generation device which monitors CO using the partial rebreathing technique with pre-described data at short intervals through indirect Fick principle (5,6). Despite its advantages like a rapid and easy use, it has some limitations such as the use of an algorithm during the calculation of CO and inconsistency of the measurements especially in patients with severe respiratory failure (7).

In this study, we aimed to evaluate cardiac and respiratory effects of four different positions used for the care of patients in critical care units with NICO monitor.

## Materials and Methods

After approval by the Cumhuriyet University Ethics Committee (decision no: 2011-05/29, date: 31/05/2011) and informed consents of the patients, a total of 40 patients aged between 18 and 65 years old who were hospitalized in the critical care unit, intubated, and received mechanical ventilation with a hospitalization time longer than 24 hours were included in this prospective observational study. Patients receiving inotropic support, those with cardiac disease, morbid obesity, thoracic deformity, an injury that would prevent giving a position, abdominal distension, acute respiratory distress syndrome (ARDS), pulmonary infection, and patients with a history of facial surgery were excluded from the study. In addition, patients who developed a pulmonary infection, abdominal distension and ARDS, those needed cardiac support treatment, patients with disrupted hemodynamics and those with suspected pulmonary embolism were also excluded.

Sedoanalgesia was applied with fentanyl and midazolam during giving the position to the patients. Routine monitorization was performed with the electrocardiogram, peripheral oxygen saturation with a pulse oximeter probe, and invasive blood pressure with arterial cannulation using a 20 G cannula, from the radial artery. The height of the patients was measured with measuring tape, in centimeters. Patients' weight was measured with critical care patient weighing machine (RADWAG®,Wagi Elektroniczne, Poland), in kilograms.

A NICO (Novametrix Medical Systems Inc, Wallingford, CT, USA) monitor sensor was connected between the intubation tube and respiratory circuit of the patients. Patients' weight (kg), height (cm), hemoglobin values (g/dL), arterial blood oxygen pressure ($PaO_2$) and arterial blood carbon dioxide pressure ($PaCO_2$) values were entered to the NICO monitor and the device was reset. Measurement circuit of NICO was set based on the tidal volume (6-8 mL/kg) of the patients. The measurements were repeated at least three times and averaged. In order not to decrease the measurement precision of NICO, spontaneous respirations of the patients were suppressed and mechanical ventilation was applied in the controlled mode. Mechanical ventilator mode, respiratory rate, fraction of inspired oxygen ($FiO_2$), inspirium/expirium ratio and tidal volume were not changed during the study. Patients required changes were also excluded.

Patients were respectively given supine (S), 90° left side (L), 90° right side (R), and 45° Fowler (F) positions, and the measurements were read. For this purpose, the measures were read with one-hour intervals when patients were in the supine position. The measures were taken at the 1st, 2nd, and 3rd hours in the patients given L, R and finally F positions for 4 hours. The patients were taken to the S position back before shifting between the positions. Arterial blood gas was collected from the patients before the study at each position. $PaO_2$ and $PaCO_2$ values were entered to the monitor and reset process was done. CO measurement was made with one-hour intervals and recorded for each hour.

Data of each patient were divided into four groups as the S position, 90°L position, 90°R position, and 45 °C F position.

During the study mean arterial pressure (MAP), heart rate (HR), stroke volume (SV), CO, cardiac index (CI), oxygen saturation ($SpO_2$), peak inspiratory pressure (PIP), mean airway pressure (mPaw), dynamic compliance (Cdyn), airway resistance (Raw), and end-tidal carbon dioxide ($ETCO_2$) values were measured and recorded with one-hour intervals.

### Statistical Analysis

Data of our study was uploaded to the SPSS 14 Windows (Statistical Package for the Social Sciences, USA) software. Repeated measures analysis of variance was used in the comparison of the parameters measured for each position at the 1st, 2nd and 3rd hours. Bonferroni test was used to determine the measurement or groups causing the difference when significance was decided as a result of the analysis. P<0.05 values were considered statistically significant. In the study, considering $\alpha$=0.05 and $\beta$=0.20, 1-$\beta$=0.80, we decided to include 40 patients to the study. Power of the test was found as T: 0.80032.

## Results

Forty patients included in the study. Demographic data are given in Table 1.

Comparison values of cardiac parameters (MAP, HR, CO, CI, SV) within each group and among groups are given in Table 2. No statistically significant difference was found among the groups in terms of the cardiac parameters (p>0.05). Evaluation of the parameters within the groups showed only a significant difference MAP values at different times at the L position (p=0.006). MAP measurements at the L position in the paired comparisons, there was a significant difference between the 1st and 3rd hours (p=0.008) and between the 2nd and 3rd hours (p=0.011), while there was no significant difference between the 1st and 2nd hours (p=0.370).

Comparison values of respiratory parameters ($ETCO_2$, PIP, MAP, mPaw, Cdyn and Raw) within each group and among groups are given in Table 3. No significant difference was found between the groups in terms of the respiratory parameters (p>0.05). Evaluation of the parameters within the groups demonstrates a significant difference among $SpO_2$ values at different times at the S position (p=0.017).

**Table 1. Demographic distribution of the cases**

| Age (year) | Weight (kg) | Height (cm) | Body mass index | Gender male/female |
|---|---|---|---|---|
| 57.00±10.27 | 58.7±8.3 | 164±8.3 | 21.9±1.9 | 17/23 |

$SpO_2$ measurements at the S position in the paired comparisons, there was a significant difference between the 1st and 2nd hours (p=0.027) and between the 1st and 3rd hours (p=0.036), while there was no significant difference between the 2nd and 3rd hours (p=0.624). There was a significant difference between 1st hour $SpO_2$ values in all four groups (p=0.025). First-hour $SpO_2$ measurements in the paired comparisons, there was a significant difference between the S and L positions (p=0.007). There was also a difference between the S and R positions (p=0.050), while there was no difference between the other measurements (p>0.05). Whereas the highest $SpO_2$ values were obtained in the S position, the lowest measures were read at the R position.

## Discussion

The patient group in our study consisted of the patients without a pathology that would prevent pulmonary gas exchange and those we monitored with controlled respiration. In our study, we did not find a statistical or clinical difference with the position change in CO, CI and HR values that were measured with NICO. Although there was a statistically significant difference in MAP values measured at different times at the L position, and $SpO_2$ values measured at different times at the S position, these differences were not clinically significant as they did not affect the oxygen delivery to the tissues.

In a study by Giuliano et al. (8) with 26 critical care patients, no significant changes were found in CO, CI, SV, MAP and HR values measured at the 0th, 5th, and 10th minutes after giving 0 °C, 30 °C, and 45 °C semi-F position to the patients. In our study, S and 45 °C F positions were similar to that study. In our results also we did not found significant changes in CO, CI, SV, and HR values. Although there was a statistically significant difference in MAP values at the L position, this difference was not significant clinically. In a study by Banasik and Emerson (9) on 12 critical care patients with $PaO_2$≤70 mmHg and/or CI≤2.0, no significant effects of the right and left 45 °C lateral and supine position were found on CO, HR, and $SPO_2$ that are the main determinants of the tissue oxygen delivery. In our study, R and L positions were 90 °C, while no effects of S, F and L positions were found on CO and HR values. Although there were statistically significant differences between the groups and within group comparisons for each group in respect of

$SpO_2$ values, these differences were not clinically significant. Fink (10) reported that turning critical care patients from S position to the other positions with intervals significantly increased functional residual capacity and oxygenation. Whereas in the present study position changes significantly affected $SPO_2$, although this was not significant clinically. Unlike our study, in their study investigating effects of body positions on oxygen consumption and hemodynamics in critically ill patients, Jones and Dean (11) found HR higher in the F position compared to the L position. In another study investigating the effects of the L position on HR, there was a significant increase in HR at the L position, although this was not clinically significant (12). Since HR is one of the major determinants of CO, there is a direct association between oxygen delivery and CO. Whereas turning to the lateral position causes minimal physiological outcomes in healthy persons, this may lead to dramatic effects in the physical status in critical patients. Giving position to the critically ill patients may affect $O_2$ consumption, CO and gas exchange of the patient in a positive or negative direction. Increased HR upon turning to the lateral position and during the position changes is results from the increases in oxygen need and sympathetic stimulation. In general, positioning may lead to an increase in HR due to the stimulation ofthe autonomic nervous system and complex relationship of the stretch receptors. A decrease in mixed/central venous oxygen saturation ($SvO_2$) and an increase in HR response are expected with the increasing activity (12).

In a study, no significant difference was found between CO measures in supine positions reaching to 20 °C in

**Table 2. The cardiac parameters**

| | Group S | Group L | Group R | Group F | p |
|---|---|---|---|---|---|
| **MAP, (mmHg)** | | | | | |
| 1st h | 87.37±19.58 | 84.82±18.71 | 80.92±18.51 | 84.95±21.30 | 0.174 |
| 2nd h | 84.22±18.36 | 83.77±19.48 | 79.70±17.26 | 84.45±18.62 | 0.080 |
| 3rd h | 84.22±18.66 | 80.97±18.51 | 80.72±18.55 | 84.50±18.82 | 0.128 |
| p | 0.120 | 0.006 | 0.604 | 0.967 | |
| **HR, (beats/min)** | | | | | |
| 1st h | 97.80±19.55 | 97.75±18.32 | 95.35±21.57 | 94.80±19.70 | 0.346 |
| 2nd h | 95.87±17.05 | 96.50±22.36 | 98.92±25.12 | 94.27±18.92 | 0.241 |
| 3rd h | 96.70±19.79 | 97.27±21.84 | 98.17±22.31 | 94.40±21.93 | 0.291 |
| p | 0.483 | 0.717 | 0.091 | 0.930 | |
| **CO, (L/min)** | | | | | |
| 1st h | 5.77±1.67 | 5.63±1.67 | 5.74±1.90 | 5.58±1.87 | 0.580 |
| 2nd h | 5.85±1.74 | 5.79±1.97 | 5.75±1.89 | 5.53±1.85 | 0.331 |
| 3rd h | 5.72±1.84 | 5.69±2.00 | 5.71±1.85 | 5.58±1.92 | 0.879 |
| p | 0.724 | 0.398 | 0.906 | 0.767 | |
| **CI, (L/min/m²)** | | | | | |
| 1st h | 3.42±1.01 | 3.33±0.92 | 3.40±1.10 | 3.28±1.11 | 0.461 |
| 2nd h | 3.44±0.94 | 3.42±1.13 | 3.40±1.07 | 3.28±1.08 | 0.471 |
| 3rd h | 3.34±0.99 | 3.38±1.12 | 3.35±1.07 | 3.30±1.10 | 0.907 |
| p | 0.587 | 0.477 | 0.684 | 0.935 | |
| **SV, (mL)** | | | | | |
| 1st h | 62.97±19.68 | 59.80±17.48 | 63.12±19.03 | 61.22±18.74 | 0.269 |
| 2nd h | 61.50±16.53 | 61.70±20.00 | 62.42±19.31 | 62.25±20.04 | 0.959 |
| 3rd h | 60.40±16.88 | 62.17±19.80 | 62.35±18.91 | 61.45±20.03 | 0.761 |
| p | 0.344 | 0.165 | 0.799 | 0.662 | |

MAP: Mean arterial pressure, HR: heart rate, CO: cardiac output, CI: cardiac index, SV: stroke volume, S: supine, L: left side, R: right side, F: Fowler

patients receiving mechanical ventilation who were not administered positive end-expiratory pressure (PEEP) (13). In our study, the F position was 45 °C, and we administered PEEP of 5 cm $H_2O$ in all patients. In our study, we did not find a significant effect of position changes on CO values. Unlike our results, in another study, CO measured in 20 °C F position was significantly decreased in patients receiving mechanical ventilation (14). Wilson et al. (15) found statistically significant differences in CO and CI measurements between the position changes of 0 °C, 30 °C and the 45 °C, although these values were not clinically significant. Unlike our study, in a study by Driscoll et al. (16) including critical care patients a decrease by 11% was found between CO measures taken in the S position and those taken in 45 °C position in 70% of the patients. 40% of CO values obtained at 45 °C position was 10% lower, equal, or higher than the values obtained at S position. The mean CO at 0 °C was statistically higher than the mean CO at 45 °C. The authors stated that the use

**Table 3. The respiratory parameters**

| | Group S | Group L | Group R | Group F | p |
|---|---|---|---|---|---|
| **$SpO_2$ (%)** | | | | | |
| 1st h | 95.00±3.75 | 93.22±5.75 | 92.80±9.64 | 94.27±5.02 | 0.25 |
| 2nd h | 93.45±6.20 | 93.27±7.57 | 93.27±7.50 | 94.35±4.59 | 0.190 |
| 3rd h | 93.27±7.58 | 93.12±7.93 | 93.22±9.81 | 94.25±4.35 | 0.430 |
| p | 0.017 | 0.947 | 0.767 | 0.948 | |
| **$ETCO_2$, ($mmH_2O$)** | | | | | |
| 1st h | 43.77±12.00 | 45.60±12.48 | 45.62±10.98 | 45.45±11.89 | 0.221 |
| 2nd h | 45.57±11.07 | 44.82±9.80 | 45.85±11.52 | 45.35±10.83 | 0.709 |
| 3rd h | 4.12±10.98 | 46.27±12.86 | 47.00±13.87 | 45.72±11.25 | 0.097 |
| p | 0.198 | 0.394 | 0.332 | 0.895 | |
| **PIP, ($cmH_2O$)** | | | | | |
| 1st h | 20.17±5.39 | 20.50±5.58 | 19.60±5.82 | 19.20±6.30 | 0.291 |
| 2nd h | 19.77±4.77 | 19.92±6.61 | 19.52±7.03 | 19.65±5.54 | 0.966 |
| 3rd h | 19.42±4.88 | 20.15±6.31 | 20.15±5.56 | 19.72±6.67 | 0.691 |
| p | 0.288 | 0.686 | 0.610 | 0.632 | |
| **mPaw, ($cmH_2O$)** | | | | | |
| 1st h | 10.27±2.07 | 10.37±3.00 | 10.45±2.52 | 10.10±2.57 | 0.819 |
| 2nd h | 9.95±2.09 | 9.97±2.09 | 10.05±2.26 | 9.97±2.64 | 0.992 |
| 3rd h | 9.75±2.04 | 10.17±2.38 | 10.22±2.11 | 10.00±2.79 | 0.634 |
| p | 0.305 | 0.492 | 0.395 | 0.871 | |
| **Cdyn, ($mL/cmH_2O$)** | | | | | |
| 1st h | 46.30±20.64 | 47.97±22.77 | 46.30±20.64 | 47.85±21.89 | 0.622 |
| 2nd h | 47.55±22.94 | 47.17±20.34 | 47.55±22.94 | 47.40±20.81 | 0.767 |
| 3rd h | 45.52±20.35 | 47.05±19.93 | 45.52±20.35 | 46.05±20.31 | 0.839 |
| p | 0.529 | 0.886 | 0.529 | 0.425 | |
| **Raw, ($cmH_2O/L/s$)** | | | | | |
| 1st h | 11.07±8.19 | 11.45±7.87 | 11.80±8.74 | 11.12±7.80 | 0.663 |
| 2nd h | 11.25±8.06 | 10.35±6.65 | 11.80±9.20 | 11.02±7.76 | 0.244 |
| 3rd h | 11.05±7.67 | 10.82±6.97 | 11.80±8.70 | 11.07±8.68 | 0.526 |
| p | 0.867 | 0.099 | 1 | 0.984 | |

$SpO_2$: Pulse oximeter oxygen saturation, $ETCO_2$: end-tidal carbon dioxide, PIP: peak inspiratory pressure, mPaw: mean airway pressure, Cdyn: dynamic compliance, Raw: airway resistance, S: supine, L: left side, R: right side, F: Fowler

of vasoconstrictors might be the single variable showing a significant change in CO associated with position changes. In a study by Lange et al. (17) investigating effects of S and L positions on CO and intracardiac pressure in 24 patients, right ventricular peak systolic and end-diastolic pressures measured using a micrometer tip pigtail catheter were significantly higher at R and L positions compared to the S position in 17 patients. In addition, left ventricular end-diastolic pressures showed a higher increase in L position compared to the S and R positions. The variation between the results of different studies shows the importance of measuring CO which is among the major determinant of oxygen delivery to the tissues can be measured at bedside continuously without requiring any additional intervention. Therefore, because CO measurement can be made with NICO device easily and rapidly as in our study, CO monitoring can enable to take the necessary measures against the risk for impairment of oxygen delivery during bedsite applications such as positioning of the patients and physiotherapy.

In a study by Bein et al. (18) with critical care patients CI was significantly increased and the MAP was not changed at L position compared to the S position, while the MAP was significantly decreased and CI was not changed at R position compared to the S position. Whereas in our study there were significant changes between the MAP values measured at different times at the L position, these changes were not considered clinically significant, because the MAP values continued at a level enough to maintain tissue and organ perfusion. In our study, no significant effect of position changes was found on CI.

Thomas et al. (19) divided 34 patients receiving mechanical ventilation into three groups as those without pulmonary pathologies on chest X-ray, patients with unilateral infiltrates and those with acute lung injury/ARDS. The authors investigated theeffects of the lateral position of hemodynamics, oxygenation and respiratory mechanics of the patients. They demonstrated that the lateral position has no effect on gas exchange, HR and MAP. CI was found to be increased in the early phase of lateral position (T30). Cdyn was found to be increased at the lateral position in the group without pulmonary pathology and those with unilateral pulmonary pathology. In a study by Tanskanen et al. (20) with 56 operated patients, Cdyn was decreased in the patients turned to the prone and lateral positions from the supine position; no change occurred when given knee-elbow position, and the lowest PIP was found again in the knee-elbow position.

As a limitation of our study, we did not include patients with pulmonary pathology and hemodynamically unstable patients.

## Conclusion

We found that turning the patients from S position to L, R and F positions did not cause any significant change in CO, CI, HR, Raw, Cdyn, PIP and MAP values. We concluded that the measurement of CO with NICO monitor is reliable even in position changes. Further studies are needed on this subject.

### Ethics

**Ethics Committee Approval:** The study was approved by the Cumhuriyet University Ethics Committee (decision no: 2011-05/29, date: 31/05/2011).

**Informed Consent:** Informed consent was obtained from the patients.

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

### Authorship Contributions

Surgical and Medical Practices: İ.K., S.G., Concept: İ.K., İ.C., D.K., S.G., Design: İ.K., İ.C., D.K., S.G., Data Collection or Processing: İ.K., İ.C., D.K., Analysis or Interpretation: İ.K., İ.C., D.K., S.G., Literature Search: İ.K., İ.C., D.K., Writing: İ.K., İ.C., D.K.

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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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# Short-term Results of Patients with Spontaneous Subarachnoid Hemorrhage in Intensive Care Unit: Single-center Experience

## Yoğun Bakımda Spontan Subaraknoid Kanamalı Hastaların Kısa Dönem Sonuçları: Tek Merkez Tecrübeleri

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**ABSTRACT** *Objective:* Few studies have evaluated patients with spontaneous subarachnoid haemorrhage (sSAH) from an intensivist perspective. This study aimed to report the results of patients with sSAH in a high-volume centre monitored by a team experienced in the fields of brain surgery, interventional radiology and intensive care.
*Materials and Methods:* Data of patients with sSAH followed up between January 2014 and July 2018 in the intensive care unit (ICU) were retrieved from ICU patient observation charts, file records and hospital automated information system.
*Results:* This study enrolled 150 patients, of which 61 (40.7%) patients died despite receiving intensive care. Mortality rates between patients with (42.8%) and without (40%) vasospasm were comparable (p=0.917). Vasospasm developed in 37.8% of the 45 patients who underwent endovascular coiling and in 19.2% of those who underwent neurosurgical clipping (p=0.044). The median times that elapsed before endovascular or surgical procedures were 2.5 [interquartile range (IQR): 2-5] days in the surviving group and 2 (IQR: 1-5) days in the deceased group (p=0.164). Blood sodium and blood chloride levels were significantly higher in the deceased group from the third day onward. The median blood sodium level exceeded 142 mEq/L in the deceased group, but was lower than 142 mEq/L on the same day in the surviving group.
*Conclusion:* The results of this study suggest that Glasgow coma scale (GCS) at admission to the ICU is one of the important factors that affect treatment success. GCS is an important independent factor in selecting the timing or type of treatment (surgical clipping/endovascular coiling) and medical treatments such as nimodipine in patients with sSAH requiring intensive care. In addition, the incidence of vasospasm was higher in patients who underwent endovascular coiling. Increased sodium and chloride values during follow-up are the only parameters significantly associated with mortality.
**Keywords:** Endovascular procedures, intensive care unit, mortality, spontaneous subarachnoid haemorrhages, subarachnoid haemorrhage therapy, subarachnoid haemorrhage surgery

**ÖZ** *Amaç:* Spontan subaraknoid kanamalı (sSAK) hastaların yoğun bakımcılar gözüyle değerlendirildiği az sayıda çalışma mevcuttur. Çalışmamızda; mortalitesi ciddi oranda yüksek böyle bir hastalığın beyin cerrahisi, girişimsel radyoloji, yoğun bakım alanında deneyimli bir ekiple takip edildiği bir high volume center'daki takip sonuçlarını paylaşmayı amaçladık.
*Gereç ve Yöntem:* Yoğun bakım ünitemizde (YBÜ) Ocak 2014-Temmuz 2018 tarihleri arasındaki yaklaşık 5 yıl boyunca izlenen sSAK hastalarının verileri, YBÜ hasta izlem çizelgeleri, dosya kayıtları ve hastane otomasyon sistemi kullanılarak toplanmıştır.
*Bulgular:* Çalışmaya 150 hasta dahil edildi ve bunların 61'i (%40,7) yoğun bakıma kabul edilmesine rağmen öldü. Vazospazmı olan (%42,8) ve olmayan (%40) hastalar arasındaki ölüm oranları benzerdi (p=0,917). Endovasküler koil uygulanan 45 hastanın %37,8'inde ve beyin cerrahisi klipsleme işlemi yapılan hastaların %19,2'sinde vazospazm gelişti (p=0,044). Endovasküler veya cerrahi prosedürlerden önce geçen medyan süre, hayatta kalan grupta 2,5 [çeyrekler arası aralık (IQR): 2-5] gün ve kaybedilen 2 (IQR: 1-5) gündü (p=0,164). Üçüncü günden itibaren kaybedilen grupta kan sodyum ve kan klorür seviyeleri anlamlı ölçüde yüksekti. Medyan kan sodyum düzeyi kaybedilen grupta 142 mEq/L'yi aştı, ancak hayatta kalan grupta aynı gün 142 mEq/L'den düşüktü.
*Sonuç:* Bu çalışma ile YBÜ'ye kabulde Glasgow koma skalasının (GKS) tedavi başarısını etkileyen önemli etkilerden biri olduğunu söyleyebiliriz. GKS, yoğun bakım gerektiren sSAK hastalarının tedavisinde zamanlama veya tedavi türü (cerrahi/endovasküler klips) ve nimodipin gibi tıbbi tedavilere ek olarak önemli bir bağımsız faktörüdür. Takipteki sodyum ve klor değerlerinin artışı ise mortalite üzerinde anlamlı bulunan tek parametrelerdir.
**Anahtar Kelimeler:** Endovasküler prosedürler, yoğun bakım ünitesi, ölüm, spontan subaraknaoid kanama, subaraknoid kanama tedavisi, subaraknoid kanama cerrahisi

## Introduction

Subarachnoid hemorrhage (SAH) is a destructive event involving significant mortality and morbidity, frequently as high as 45%. Most SAH derives from ruptured intracranial saccular aneurysms. The presence of aneurysm is generally unexpected until the development of SAH. Following acute bleeding, rebleeding incidence is 3-4% in the first 24 h, and a 1-2% risk every day in the first month (1). One study reported an overall annual adjusted incidence rate of 10.3 per 100,000 person-years for spontaneous SAH (sSAH) [95% confidence interval (CI); 10.2-10.3] (2). Surgical or endovascular aneurysm repair is the only effective method of treatment (3). Crucial causes of mortality and morbidity are arterial vasospasm following acute treatment, delayed ischemic neurological deficits and cerebral infarction. This high-risk patient group must therefore be closely followed-up, particularly in the first 14 days after acute treatment. SAH management guidelines recommend prompt referral to high-volume centers. Decisions concerning aneurysm treatment should be taken by experienced surgeons, interventionalists, and neurological intensive care specialists (3). Although parameters of monitorization have been established in sSAH patients requiring intensive care follow-up, there is still no definite indication regarding which characteristics suggest that patients should be observed in intensive care. Although SAH is a disease with high mortality, the limited availability of intensive care beds makes it difficult for all patients to receive this care. This study aimed to examine the outcomes and characteristics of isolated sSAH patients followed up in intensive care.

## Materials and Methods

### Study Design

This study involved a retrospective examination of clinical data for patients admitted to the intensive care unit (ICU) of a high-volume university hospital due to sSAH. Ethical approval was granted by Ondokuz Mayıs University Clinical Research Ethics Committee (decision no: 2018/440, date: 28.09.2018). Data for sSAH patients enrolled between January 2014 and July 2018 were retrieved from ICU patient observation charts, records of file, and the hospital system. The study group consisted of 150 patients with the diagnosis of SAH whose data were available and accessible from patient record system during these years. Patients with insufficient data for analysis, traumatic SAH, or aged under 18 or stayed in brain surgery ward were excluded (Figure 1).

### Intensive Care Monitoring

Our unit is an 18-bed general ICU within a university hospital. All SAH patients are evaluated at the bedside at daily visits by the relevant member of the neurosurgery teaching staff. Decisions to perform surgical clipping or endovascular coiling are made by consultants from the interventional radiology and neurosurgery departments. This treatment is arranged as early as possible for all patients.

Admission criteria to the ICU for SAH patients are; who could not be extubated after postoperative period following emergency surgery, uncontrollable seizure, mechanical ventilation requirement due to neurological or respiratory instability without surgical or endovascular procedures having yet been performed, close monitoring requirements, hemodynamic instability, or a Glasgow coma score (GCS) <8.

### Patient Data

Patients' demographic data, diagnoses responsible for sSAH (aneurysm, arterial malformation, etc.), site of aneurysm, computed tomography (CT) findings other than SAH, treatments administered, timing of the surgical/endovascular procedure performed, vasospasm development, whether or not nimodipine was used, receipt

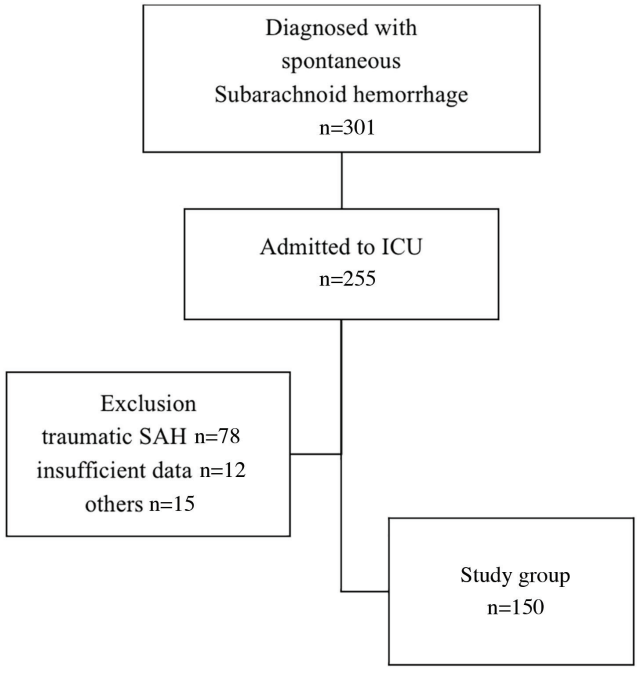


**Figure 1.** Study flow chart
ICU: Intensive care unit, SAH: subarachnoid hemorrhage

of inotrope/vasopressor therapy, mechanical ventilation requirement, GCS scores at presentation based on presence of neurological deficits according to the World Federation of Neurosurgeons scale (lowest value for each day) (4), length of stay in the ICU and mechanical ventilation, brain death and donation status, important laboratory tests during admission or for a maximum 28 days (Na, Cl, C-reactive protein, white blood cell values, haemoglobin/haematocrit, creatinine, and blood urea nitrogen), and outcomes were recorded.

### Clinical Follow-up

In our clinic, CT angiography (CTA) or digital subtraction angiography are performed on patients diagnosed with SAH using cerebral CT before surgical clipping or endovascular coiling procedures. Magnetic resonance imaging is not routinely performed at the preoperative period. After initial treatment all patients underwent early CT scanning, together with recurrent CT scans in the event of neurological instability. External ventricular drainage was applied for brain relaxation in case of patients with suspected intracranial hypertension.

Regulation of blood pressure was applied to ensure systolic blood pressure (SBP) <160 mmHg or mean arterial pressure <110 mmHg, and avoiding hypotension, in all cases. Intracranial pressure was not measured in all patients, only in case of clinical necessity or suspicion. Patients' hourly GCS values were recorded by nurses. Deep vein thrombosis prophylaxis was applied to all patients with pneumatic compression prior to aneurysm treatment. Prophylaxis continued after aneurysm treatment with low molecular weight heparin. Antiseizure drug therapy was not given routinely to all patients. Pain control and ulcer prophylaxis were applied in all cases.

The presence of vasospasm was determined on the basis of clinical and symptomatic criteria. Development of new focal or global neurological disorders that could not be explained in terms of states as hydrocephaly, bleeding, metabolic abnormalities, infection and surgical or endovascular complications was the defining of vasospasm (5,6).

CTA was generally performed to confirm vasospasm in suspected cases. Hypovolemia was avoided in the treatment of vasospasm, and fluid and vasopressor support was applied to establish SBP levels between 160 and 180 mmHg. Blood glucose was regulated in the limits of between 100-180 mg/dL. No patients followed-up due to SAH received nimodipine as a prophylaxis against vasospasm. Only patients with risk factors such as severe bleeding and close proximity to major intracerebral blood vessels, age <50, and hyperglycemia are started on nimodipine for vasospasm. The recommended therapeutic nimodipine dose is 60 mg every 4 h (7,8). No balloon angioplasty or intra-arterial vasodilators were employed for vasospasm treatment in any cases.

### Statistical Analysis

IBM SPSS V23 software (Chicago, USA) was used for data analyses. Normality of distribution was examined using the Shapiro-Wilks and Kolmogorov-Smirnov tests. The Kruskal-Wallis, Mann-Whitney U, Student's t, and chi-square tests were used for comparisons between the groups. General linear modeling, and the Wilcoxon and Friedman tests were used for serially measured data. Percentage, mean (± standard deviation), and median (25-75$^{th}$ quartile) values were used for data expressing. The chi-square test was applied to compare qualitative data. Categorical data were expressed as frequency and percentages.

## Results

One hundred fifty patients requiring intensive care and diagnosed with sSAH were enrolled in the study. Eighty-nine (59.3%) of the 150 patients were discharged from intensive care, while mortality in intensive care occurred in 61 (40.7%). Ninety (60%) of the 150 patients enrolled were female and 60 (40%) were male. Mean ages in the two groups were similar, at 56.7±13.4 years in the survived group and 56.8±16.79 in the non-survived group (p=0.966).

Aneurysm was the most common diagnosis responsible for SAH in both groups. Fifty-five (44.1%) of the aneurysmal SAH patients died, compared to 50% of patients with arteriovenous malformation related sSAH. No statistically significant difference was determined in mortality rates according to causes of SAH (p=0.361).

Localizations of aneurysm were predominantly in the anterior communicating artery (ACA). Twenty-one (32.8%) of the 64 patients with aneurysm in the ACA were lost, while the mortality rate in middle cerebral artery aneurysms was 13 (34.2%), and 3 (60%) in posterior communicating artery (PCA) aneurysms. Although the mortality rate was higher in PCA aneurysms, no statistically significant difference was determined in mortality rates (p=0.067). The most common accompanying non-SAH findings at CT were intracerebral hematoma and intraventricular hemorrhage, observed in 50 patients each.

Vasospasm developed in 35 (23.3%) of the 150 patients. The mortality rate in patients developing vasospasm (42.8%) was similar to that of the patients without vasospasm (40%) (p=0.917). There was no difference in mortality between the groups. Nimodipine was used in the treatment of 33 of the patients diagnosed of SAH, with mortality occurring in 14 (42.4%) of these. This rate was similar to that in the patients not using nimodipine during treatment (40.1%) (p=0.974).

Thirty-five (23.3%) patients were started on vasopressor/inotrope therapy, with mortality occurring in 30 (85.7%) of these. The mortality rate in patients not started on was 26.9%, significantly lower than in the group receiving vasopressor/inotrope therapy (p<0.001) (Table 1).

Calculation of times elapsed from first presentation to hospital with SAH to first endovascular or surgical procedures revealed a median value of 2 days (1-5 days). Median times were 2.5 days (2-5) and 2 days (1-5) in the survived and non-survived group respectively. The difference between the groups in terms of procedure times was not statistically different (p=0.164). There was no effect on the day of vasospasm development and mortality (p=0.114). These values were 3 days (2.25-5.75) in the survived group and 2 days (1-4) in the non-survived group. Vasospasm developed in 17 (37.8%) of the 45 patients undergoing endovascular coiling and in 14 (19.2%) of the 73 receiving neurosurgical clipping (p=0.044). No statistically significant relation was observed between mortality and duration spent in the emergency department before admission to the ICU. Median waiting duration were 10 h (5-22) in the survived group and 10 h (5-24) in the non-survived group (p=0.780). 81.3% of patients was treated with mechanical ventilation. Median mechanical ventilation duration was 5 days (3.25-8) in the non-survived group and 1 day (1-2.25) in the survived group (p<0.001). Lengths of ICU stay were similar in the two

**Table 1. Categorical comparison of the survived and non-survived groups**

| | | Mortality | | | |
|---|---|---|---|---|---|
| | | No | Yes | | |
| **Parameter** | | **n (%)** | **n (%)** | **Total** | **p** |
| Gender | Female | 54 (60) | 36 (40) | 90 | |
| | Male | 35 (58.33) | 25 (41.67) | 60 | 0.839 |
| Diagnosis | Aneurysm | 82 (59.9) | 55 (40.1) | 137 | |
| | AVM | 5 (50) | 5 (50) | 10 | |
| | Other | 2 (66.7) | 1 (33.3) | 3 | 0.361 |
| Site of aneurysm | ACA | 43 (67.19) | 21 (32.81) | 64 | |
| | MCA | 25 (65.79) | 13 (34.21) | 38 | |
| | PCA | 2 (40) | 3 (60) | 5 | |
| | Other | 19 (44.19) | 24 (55.81) | 43 | 0.067 |
| SAH CT findings | Intracerebral hematoma | 30 (60) | 20 (40) | 50 | |
| | Intraventricular hemorrhage | 25 (50) | 25 (50) | 50 | |
| | Subdural hematoma | 7 (58.33) | 5 (41.67) | 12 | |
| | Other | 27 (71.05) | 11 (28.95) | 38 | 0.263 |
| Treatment applied | Surgical | 55 (75.3) | 18 (24.7) | 73 | |
| | Endovascular | 31 (68.9) | 14 (27.1) | 45 | 0.58 |
| Vasospasm | No | 69 (60) | 46 (40) | 115 | |
| | Yes | 20 (57.14) | 15 (42.86) | 35 | 0.917 |
| Nimodipine use | No | 70 (59.83) | 47 (40.17) | 117 | |
| | Yes | 19 (57.58) | 14 (42.42) | 33 | 0.974 |
| Inotrope/vasopressor support | No | 84 (73.04) | 31 (26.96) | 115 | <0.001* |
| | Yes | 5 (14.29) | 30 (85.71) | 35 | |

SAH: Subarachnoid hemorrhage, CT: computed tomography, ACA: anterior communicating artery, AVM: arteriovenous malformation, MCA: middle cerebral artery, PCA: posterior communicating artery, *indicates statistical significance

groups (p=0.070) (Table 2). Six (17.6%) of the 34 patients with brain death became organ donors.

The median GCSs at presentation was 9. GCS scores were significantly lower in the first eight days of monitoring in the non-survived group compared to the survived group. At admission median GCS was 12 [interquartile range (IQR): 9-14] in the survived and 5 (IQR: 5-7) in the non-survived groups (p<0.001). In the follow-up days statistically significant different keep going (Figure 2). Both blood sodium and blood chloride levels were similar in the two groups in the first two days, but were significantly higher in the mortality group as of the third day. Median blood sodium levels exceeded 142 mEq/L in the non-survived group, but were lower than 142 mEq/L on the same days in the survived group. Median blood chloride levels were above 105 mEq/L in the non-survived group, but below 105 mEq/L in the survived group. Although statistically significant differences were determined on some days in other laboratory parameters, no significant trend was observed (Figure 2).

## Discussion

The present study analyzed data for patients with sSAH followed up in the ICU. While several studies have evaluated the pathophysiology and clinical characteristics of sSAH, uncertainties still exist regarding intensive care management (9-11). In terms of short-term outcome, one meta-analysis involving 33 studies reported mortality rates of 8.3-66.7% in patients with SAH (12). High mortality rate of 45% in cases of aneurysmal SAH was repoeted on the another study (1). Only sSAH patients with neurological, hemodynamic, or respiratory instability were admitted to the study. These patients' median GCS score at presentation was 9, and 81.3% required mechanical ventilation support. Our mortality rate of 40.7% in sSAH patients requiring intensive care management is therefore not surprising. This rate is compatible with general adult intensive care mortality, at between 30% and 65% (13-15). This result may be can explain with arterial vasospasm and delayed ischemic neurological deficits in addition to the severe condition of patients whose were admitted to the ICU. Besides of that SAH guidelines recommend that patients be referred to high-volume centers in the early period, but make no specific reference to the type of ICU (1,16). In the present study, length of stay in the emergency department for critical sSAH patients before admission to the ICU, the timing of the endovascular or surgical treatment applied, and the development of vasospasm had no effect on intensive care mortality. This may be related to all patients being in poor clinical condition and irrespective of rapid application of standardized protocols to all patients. Lott et al. (17) compared specialty ICUs with general ICUs and evaluated critical disease outcomes of various diagnoses. That study involved 124 ICUs and 11,984 patients. No difference was observed in mortality rates between general ICUs and specialty ICUs including neurological intensive care. Egawa et al. (18) reported improved neurological outcomes in SAH patients receiving intensive care including neurointensive care, but longer intensive care stays [median (IQR), 12 (9-14.3) days]. The median intensive care stay in the survived group in the present study was 5 (3-10) days, and 6 (4-12) days in the non-survived group. These short lengths of stay may be explained with correct circulation of intensive care. Our center is the best equipped neurosurgery center in the region, and has considerable experience with rapid diagnosis and treatment of unstable SAH patients being

**Table 2. Demographic comparison of the survived and non-survived groups**

| | Survived | Non-survived | Survived | Non-survived | p** |
|---|---|---|---|---|---|
| **Parameter** | **n (%)** | **n (%)** | | | |
| Age (year) | 89 (59.3) | 61 (40.7) | 56.7±13.4 | 56.8±16.79 | 0.966 |
| Endovascular/surgical procedure time (days) | 86 (72.9) | 32 (27.1) | 2.5 (2-5) | 2 (1-5) | 0.164 |
| Days to vasospasm development | 20 (57.14) | 15 (42.86) | 3 (2.25-5.75) | 2 (1-4) | 0.114 |
| Length of stay in emergency department (hours) | 89 (59.3) | 61 (40.7) | 10 (5-22) | 10 (5-24) | 0.780 |
| Duration of mechanical ventilation (days) | 62 (50.8) | 60 (49.2) | 1 (1-2.25) | 5 (3.25-8) | <0.001* |
| Length of intensive care stay (days) | 89 (59.3) | 61 (40.7) | 5 (3-10) | 6 (4-12) | 0.070 |

Number of patients are not same in all parameters, first two columns show number of patients. Normally distributed data expressed as mean ± standard deviation, non-normally distributed data expressed as median (25-75$^{th}$ quartile).
*Indicates statistical significance, **p value refers to comparison of durations (year, day, hour)

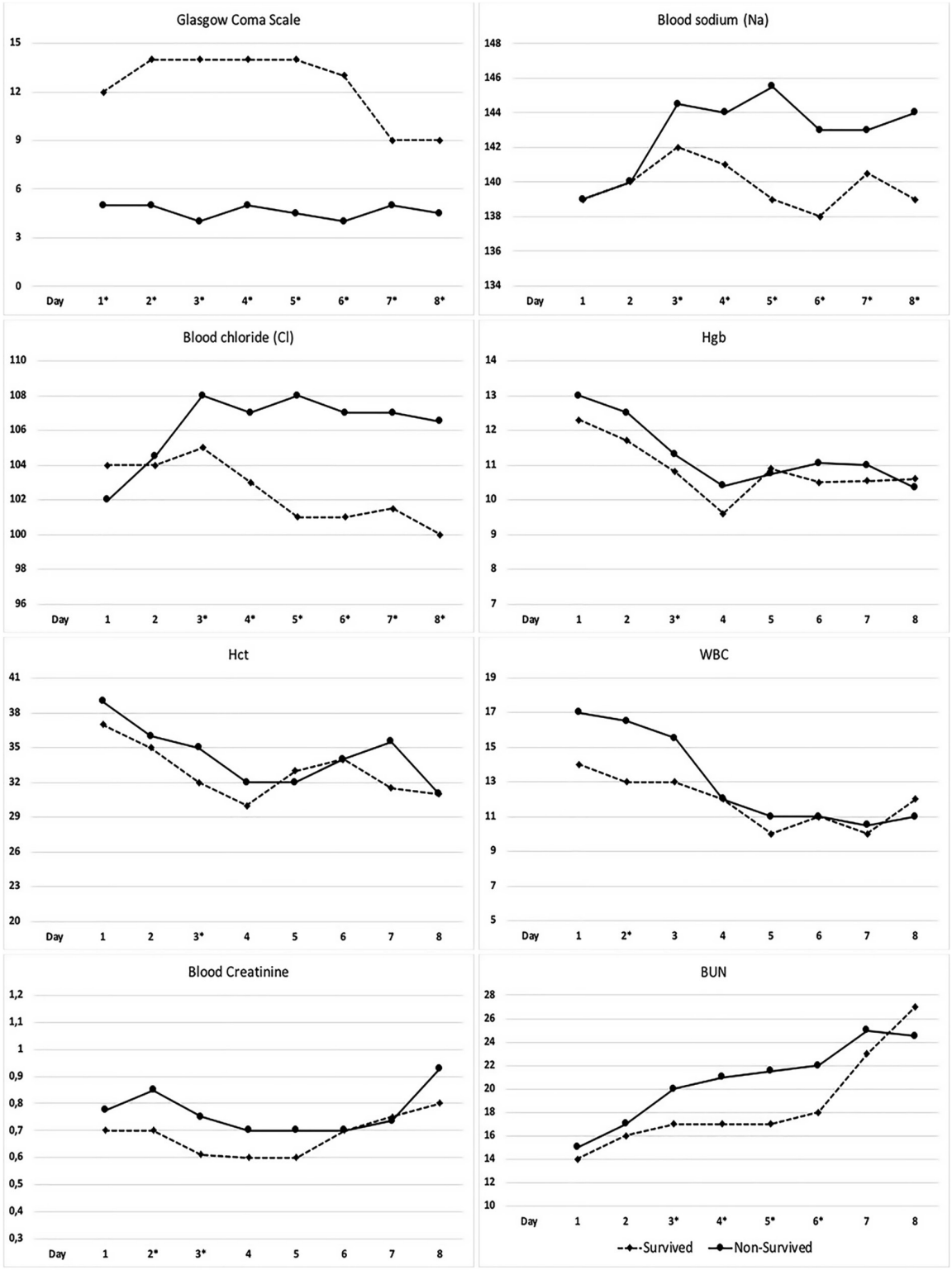


**Figure 2.** Plot graphs comparing laboratory parameters in the non-survived and survived groups
*Above the days indicates a statistically significant difference between the two groups.

Hgb: Haemoglobin, Hct: haematocrit, BUN: blood urea nitrogen, WBC: white blood cell
Units: Na: mEq/L, Cl: mEq/L, Hgb: g/dL, Htc: %, Leukocyte: $10^9$/L, Creatinine: mg/dL, BUN: mmol/L

referred to our ICU. All patients are therefore transferred to our ICU if indicated following rapid triage and stabilization. The great majority of SAH patients in our unit are admitted either postoperatively or in case of mechanical ventilation or requirement of close monitoring, hemodynamic instability, or GCS<8, while other patients are monitored on the ward or under emergency conditions. Patients responding to treatment are rapidly discharged from intensive care after extubation, while patients requiring palliative care are referred to surrounding hospitals and palliative units.

SAH represents 1-7% of all strokes (19). Aneurysm rupture is the cause in 85% of patients (20). The location of the aneurysm is frequently in the ACA (40%). Aneurysm was the most common cause of SAH at a rate of 91.3%, and 46.7% of aneurysms were located in the ACA in the present study. Surgical clipping or endovascular coiling are employed in treatment. Two randomized studies compared endovascular treatment with open surgery for intracranial aneurysms, the (21-24). Although both reported significantly greater obliteration rates and improved durability with open-surgery compared to endovascular procedures, better functional outcomes were achieved at 1 year with endovascular treatment. Surgery was performed on 48.6% of the patients in the present study, and endovascular treatment on 30%, depending on clinical indication. There was no significant difference in terms of short-term intensive care mortality between the two. Similarly, Koivisto et al. (25) were not find significant difference in terms of long-term mortality and morbidity between the two techniques. Whether aneurysm should be repaired using neurosurgical clipping or endovascular coiling depends on the patient's age, the presence of large intracranial hematomas requiring emergency extraction, clinical status, associated illnesses, the size, shape and location of the ruptured aneurysm, the available equipment and individual skills (26). One meta-analysis revealed that the risk of poor outcomes decreased to 23% at 1 year with coiling, compared to 34% following clipping (odds ratio: 1.48, 95% CI: 1.24-1.76), while no difference in mortality was observed (27). In the hands of an experienced surgeon surgical methods of cerebral aneurysms with the evolution of microsurgical techniques is an effective and safe procedure. Since our surgical team is highly experienced in critical cases, surgical rates may have been found to be high at the decision stage. On the other hand treatment at specialized neurosurgical centers is associated with better outcome compared with treatment at lower-volume centers. Aneurysm must be repaired as early as possible, and preferably within 24 h (3). No difference was determined in this study between non-survived patients within this period and surviving patients, and mean time to procedure was 48 h (1-5 days).

Delayed ischemic neurological deficit associated with arterial vasospasm and development of cerebral infarction affect patient outcomes following successful surgical or endovascular ruptured aneurysm repair. Vasospasm is believed to result from spasmogenic substances produced during the breakdown of subarachnoid blood. The cerebral arteries thus contract, and blood flow to the brain is reduced. Although not all patients are symptomatic, vasospasm develops in roughly 70% of SAH patients, with delayed cerebral injury (DCI) occurring in 40% of these (28). Angiographic vasospasm is seen in between 30% and 70% of angiograms performed on the seventh day following SAH, while in 20-30% of patients clinical or subclinical vasospasm is observed. Symptomatic vasospasm has been linked to clinical decline and worse prognosis (29,30). The incidence of development of symptomatic vasospasm was 23.3% and was similar with others. Vasospasm generally appears in 4-14 days, peaks in 7-10 days, and resolves by day 21 (31). Vasospasm was observed in the first seven days in all patients in our study. The current gold standard oral nimodipine, has been shown to decrease the risk of DCI and to be associated with better neurological outcomes (32). Patients are recommended to take nimodipine for 21 days in case of increased risk of DCI and vasospasm (33). However, it is not clear yet the evidence that nimodipine reduceses the incidence of vasospasm (7,8,34,35). In the present study, a low number of patients at risk of vasospasm used nimodipine, but no positive effect was observed on mortality.

SBP is recommended to be maintained at below 160 mmHg in all sSAH patients before aneurysm obliteration. On the other hand, triple-H therapy consists of hemodilution, hypervolemia, and hypertension (36). However, recent studies have shown that hypervolemia and hemodilution are associated with poorer outcomes. New evidence recommends euvolemic hypertension in order to increase cerebral blood flow (32). Other non-medical recommendations include balloon angioplasty and intra-arterial vasodilators. Although there is evidence that these treatments applied are not significantly effective in the prevention of vasospasm (7,8), a difference has been shown between methods in some studies. Mielke et al. (9) reported

that aneurysm clipping was associated with a greater incidence of vasospasm. Similarly in the present study, the incidence of vasospasm was higher in patients undergoing endovascular coiling (p=0.044). However, we could not find difference in mortality between the two groups of developing and non-developing vasospasm (p=0.974). This result can be explained by the prognosis of critical patients with sSAH who need intensive care is already worse than other SAH patients and perhaps there is an asymptomatic group in the group without vasospasm. Isolated asymptomatic angiographic vasospasm is traditionally not usually treated, unless the vasospasm is particularly severe.

Both hypo- and hypernatremia may be seen in the critical care management of SAH patients. Hyponatremia is associated with a longer hospital stay and cerebral infarction, although whether or not it affects neurological outcomes is still controversial (37). It frequently develops due to inappropriate anti-diuretic hormone secretion, cerebral salt loss, and glucocorticoid deficiency (38). We observed a significant increase in blood sodium and chloride levels in the non-survived group from day 3 onward. Median blood sodium levels in the non-survived group were above 142 mEq/L, while median chloride values in the same group were above 105 mEq/L. Similarly, studies have associated high sodium levels with poor neurological outcomes (39,40). In agreement with the present study, Okazaki et al. (41) showed that a cut-off point of 145 mEq/L was associated with poor outcomes. Our results are compatible with those findings. This has been attributed to SAH-related hypothalamic dysfunction triggering central diabetes insipidus (39). On the other hand, the resuscitation fluids selected in patients also affect biological changes.

There are a number of limitations to this study. First, since complete data could not be obtained due to its retrospective nature, pathologies at control CT performed on patients with suspected vasospasm could not be evaluated, and only the first CT findings were recorded. Second, only short-term results were evaluated, and long-term neurological status and mortality are unknown. Third, patients' neurological status was assessed using GCS only, other SAH evaluation scales were not employed. Age-related-co-morbidities capable off affecting patient outcomes were not evaluated. Finally, intracranial pressure was not measured in all cases, and data for all the cases in which it was performed were unavailable, and these were therefore not included in the analysis.

## Conclusion

Ours is one of the few studies to evaluate the intensive care outcomes of sSAH patients. While algorithms for the clinical monitoring and treatment of sSAH patients have been produced, interventions capable of reducing mortality in critical patients requiring intensive care are unknown. With this study we could say GCS at admission to ICU is one of the important effects which affects treatment success. GCS is an important independent factor as the timing or type of treatment (surgical clipping/endovascular coiling) and medical treatments such as nimodipine in the treatment of sSAH patients requiring intensive care. Besides in the present study, the incidence of vasospasm was higher in patients undergoing endovascular coiling. Early increased sodium and chloride values were associated with intensive care mortality. This finding shows the need for focus on other parameters in addition to the normal care standard in order to improve mortality in patients with clinically severe SAH, and for the planning of further intensive care prospective studies.

### Ethics

**Ethics Committee Approval:** Approval for the study was granted by the Ondokuz Mayıs University Clinical Research Ethics Committee (decision no: 2018/440, date: 28.09.2018).

**Informed Consent:** Retrospective study.

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

### Authorship Contributions

Surgical and Medical Practices: M.P.K., Ç.E.Ö., E.T., Concept: M.P.K., A.O.K., F.Ü., Design: M.P.K., Ç.E.Ö., A.O.K., E.T., F.Ü., Data Collection and Process: Ç.E.Ö., E.T., Analysis or Interpretation: M.P.K., A.O.K., F.Ü., Literature Search: M.P.K., Ç.E.Ö., F.Ü., Writing: M.P.K.

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

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ÖZGÜN ARAŞTIRMA / *ORIGINAL RESEARCH*

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# Yoğun Bakım Ünitesinde Uzun Yatış Süresi (≥90 Gün): Predispozan Faktörlerin ve Sonuçların Retrospektif Analizi

## Long Length of Stay in the Intensive Care Unit (≥90 Days): Retrospective Analysis of Predisposing Factors and Results

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**ÖZ** *Amaç:* Bu çalışmada yoğun bakım ünitesinde (YBÜ) çok uzun süre (≥90 gün) yatan hastaların klinik özelliklerini ve sonuçlarını saptayarak YBÜ'de kalma sürelerini etkileyen faktörlerin belirlenmesi amaçlandı.
*Gereç ve Yöntem:* Çalışmada Ocak 2015 ve Aralık 2018 tarihleri arasında YBÜ'de 90 gün ve üzeri yatan (n=98) hastaların dosyaları retrospektif olarak incelendi. Hastaların demografik verileriyle birlikte klinik özellikleri, sonuçları ve uygulanan ileri tedavi ve prosedürler, elektrolit bozuklukları, enfeksiyon özellikleri kayıt edildi. Hastaların YBÜ'de yatış süresini etkileyen prediktörler regresyon modeli ile belirlendi.
*Bulgular:* Hastaların yaş ortalamasının 70,10±18,55 yıl olduğu ve %77,6'sının hayatını kaybettiği belirlendi. Trakeostomi ve perkütan endoskopik gastrostomi işlemi uygulanan hastalarda ortalama yatış süresi anlamlı derecede yüksek bulundu (p<0,001). Hastalarda en sık ventilatör ilişkili pnömoni (%41,82) ve kan dolaşımı enfeksiyonu (%31,67) atakları görüldü. Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skoru, mekanik ventilatör süresi, kan transfüzyonu sayısı ve hipomagnezemi çok değişkenli regresyon modelinde uzun yatış süresini etkileyen prediktörler olarak belirlendi.
*Sonuç:* YBÜ'de çok uzun süre (≥90 gün) yatan hastalarda; yüksek APACHE-II skoru, uzun mekanik ventilatör süresi, kan transfüzyonu sayısı ve hipomagnezemi varlığının YBÜ'de uzun yatış süresi için bağımsız risk faktörleri olduğu belirlendi. Bu prediktörlerin daha iyi olası etkilerini göstermek için daha kapsamlı araştırmalar gereklidir.
**Anahtar Kelimeler:** Yoğun bakım ünitesi, yatış süresi, risk faktörleri

**ABSTRACT** *Objective:* This study aimed to determine factors affecting the duration of stay in the intensive care unit (ICU) by determining the clinical characteristics and results of patients with long ICU stay (≥90 days).
*Materials and Methods:* Data of patients (n=98) hospitalised in the ICU for ≥90 days between January 2015 and December 2018 were retrospectively analysed. Clinical characteristics, results, advanced treatments and procedures, electrolyte disturbances and infection characteristics were recorded together with the demographic data of the patients. The predictors affecting the length of ICU stay were determined using the regression model.
*Results:* The mean patient age was 70.10±18.55 years, and the mortality rate was 77.6%. The mean length of ICU stay was significantly higher in patients who underwent tracheostomy and endoscopic gastrostomy (p<0.001). The most common infections were ventilator-associated pneumonia (41.82%) and blood stream infections (31.67%). Acute Pysiology and Chronic Health Evaluation-II (APACHE-II) score, mechanical ventilator time, number of blood transfusions and hypomagnesaemia were determined as predictors affecting long ICU stay on the multivariate regression model.
*Conclusion:* In patients with a long ICU stay (≥90 days), high APACHE-II score, long mechanical ventilation duration, number of blood transfusions and hypomagnesaemia were determined to be independent risk factors for long ICU stay. More comprehensive research is required to show the potential effects of these predictors.
**Keywords:** Intensive care unit, length of stay, risk factors

## Giriş

Yoğun bakım üniteleri (YBÜ), kullanılan ileri teknolojiye sahip cihazlar ile kritik hastaların yakın takip ve tedavisinin yapıldığı hayat kurtarıcı ünitelerdir. Son dönemde kritik hastaların YBÜ yönetimi; YBÜ sayısının ve kalitesinin artması, ve tıbbi teknolojilere bağlı olarak önemli ölçüde iyileşmiştir (1,2).

Kronik kritik hastalık; uzun süre YBÜ'de tedavi gören veya uzun süreli mekanik ventilatör (MV) desteği alan hastalarda çoklu organ işlev bozuklukları gelişen bir hastalık durumu olarak tanımlanmaktadır (3). YBÜ'lerin hizmet verdiği önemli bir grup, kronik kritik hastalık durumudur. Bazı durumlarda, YBÜ'ler akut dönemde tedavilerden fayda göremeyen ve ölüm süreci uzayan kronik hastaların yattığı birimler haline gelmektedir (2-4).

YBÜ'de uzun yatış süresi (LOS) net olarak tanımlanmamıştır ve literatürde subjektif değerlendirmelere bağlı olarak farklı süreler (>7, >14, >21, >30) belirlenmiştir (5-8). Uzun süreli YBÜ hastalarını inceleyen çalışmalarda; hasta oranları tanım ölçütlerine göre ve merkezden merkeze farklılık göstermektedir (7,9-11). Bu sebeplerle kronik kritik hastaların gerçek insidansı net olarak bilinmemektedir (3,12,13). Bununla birlikte YBÜ'de LOS 30 gün üzeri olan hastalar çok nadirdir.

Literatürde uzun süreli YBÜ LOS'nin yüksek mortalite oranı, artmış enfeksiyon riski, elektrolit bozuklukları ve çeşitli komplikasyonlar ile ilişkili olduğu bildirilmiştir (1,14,15). Uzun süreli YBÜ LOS'si sağlık hizmetlerinin maliyetini artırmakta ve YBÜ ihtiyacı olan hastaların uygun sağlık hizmeti alamamasına yol açmaktadır (2,16). Ayrıca günümüzde dünyanın tümüne yayılan koronavirüs hastalığı-2019 salgını, özellikle YBÜ kaynakları üzerinde büyük yüke sebep olmaktadır. Bu sebeple YBÜ yataklarının akılcı kullanımı büyük öneme sahip olup bu alanda yapılacak çalışmaların bu sorunun çözümüne katkı sunacağı açıktır.

Bu çalışmada, YBÜ'de çok uzun süre (≥90 gün) tedavi gören hastaların klinik özelliklerini saptayarak YBÜ'de kalma sürelerini etkileyen faktörlerin belirlenmesi amaçlanmıştır.

## Gereç ve Yöntem

### Etik Beyan

Bu çalışma için etik kurul onayı Helsinki Bildirgesi'ne uygun olarak Malatya Klinik Araştırmalar Etik Kurulu'ndan alındı (karar no: 2019/137, tarih: 24.07.2019).

### Çalışmanın Tasarımı ve Çalışma Ortamı

Bu çalışma, Ocak 2015-Aralık 2018 tarihleri arasında 3. basamak bir tıp merkezi olan hastanemiz YBÜ'sünde tedavi gören 3.150 hastanın (>18 yaş) verileri retrospektif olarak incelenerek yapıldı. Hastanemiz YBÜ'sü 36 yataklı ve kapalı sistem olup tüm yetişkin dahili ve cerrahi kritik hastalara ileri düzeyde tedavi hizmeti sunmaktadır. Çalışmaya YBÜ'de 90 gün ve üzeri tedavi gören 98 (%3,11) hasta dahil edildi. Çalışmada koroner veya kalp-damar cerrahisi departmanlarına bağlı olarak YBÜ'de takip edilen hastalar hariç tutuldu.

### Çalışmanın Verileri

Hastaların demografik verileriyle birlikte YBÜ'ye kabul tipi (cerrahi veya medikal), kabul nedenleri, komorbiditeleri, YBÜ yatış süreleri, MV süreleri, YBÜ yatışı süresince saptanan elektrolit bozuklukları, renal replasman tedavileri, trakeostomi ve perkütan endoskopik gastrostomi (PEG) işlemleri ve işlem gün sayıları, kan transfüzyonu sayıları, mortalite ve taburculuk durumları değerlendirildi. Tüm hastaların YBÜ kabulleri esnasında hesaplanan Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skorları, giriş albümin ve laktat değerleri kayıt altına alındı. Hastaların YBÜ'ye kabul nedenleri Uluslararası Hastalık Sınıflandırması-10 (International Classification of Diseases-10) kodlarına göre sınıflandırıldı. Veriler hasta dosyalarından ve hastane bilgi sistemi otomasyon programından elde edildi. Kardiyak veya solunum arresti sonrası resüsitasyon uygulanan hastalar kardiyopulmoner resüsitasyon sonrası olarak gruplandırıldı. Komorbidite olarak alzheimer veya parkinson hastalığı olanlar nörodejeneratif hastalık grubuna dahil edildi. YBÜ yatış süresi boyunca herhangi bir zamanda karşılaşılan elektrolit bozuklukları kayıt edildi.

### Enfeksiyon Verileri

Hastaların tümüne MV desteği sağlanmış ve üretral sonda kullanılmıştır. Uygun hastalarda trakeostomi ve PEG işlemleri uygulanmıştır. Enfeksiyon hastalıkları bölümü tarafından YBÜ'ye günlük yapılan vizitlerde enfeksiyon tanıları, "Hastalık Kontrol ve Önleme Merkezleri" kriterlerine göre konuldu. Analiz edilen enfeksiyon ilişkili veriler; hasta dosyaları, hastane otomasyon sistemi, Ulusal Hastane Enfeksiyonları Sürveyans Ağı ve Ulusal Hastane Enfeksiyonları Sürveyans Programı veri tabanından elde edildi. Dökümante edilen veriler ventilatör ilişkili pnömoni, kan dolaşım enfeksiyonları, idrar yolu enfeksiyonları, yara yeri enfeksiyonları ve rektal kolonizasyon ile ilişkili vankomisin dirençli enterokok enfeksiyonları şeklinde sınıflandırıldı.

### İstatistiksel Analiz

Veri analizi SPSS 20.0 istatistik paket programı kullanılarak yapıldı. Verilerin analizinde frekans, ortalama ve standart sapma değerleri belirlendi. İstatistiksel olarak $p<0,05$ anlamlı kabul edildi. Kolmogorov-Smirnov testi ile değişkenlerin normal dağılıma uygunluğu değerlendirildi. Gruplar arasındaki farklılığı ortaya koymak için Student t ve Mann-Whitney U testi kullanıldı. Normal dağılmayan veya ordinal değişkenlerin olduğu durumlar Kruskal-Wallis testi ile değerlendirildi. Çok değişkenli bir lineer regresyon modeli kullanılarak farklı prediktörlerin YBÜ yatış süresine etkileri incelendi.

## Bulgular

### Hastaların Demografik ve Klinik Karakteristikleri

Hastaların 55'i (%55,1) erkek, 44'ü (%44,9) kadın ve yaş ortalaması 70,10±18,55 [minimum (min): 23, maksimum (maks): 102] yıl olarak bulundu. Yatış süresi ortalaması 160,44±68,70 (min: 90, maks: 376) gün olup, hastaların %77,6'sı hayatını kaybetti. Hastaların demografik özellikleri Tablo 1'de sunuldu. Hastaların 90'ı (%91,8) medikal, 8'i (%8,2) cerrahi nedenlerle YBÜ'ye kabul edildi. Cerrahi nedenle kabul edilen hastaların YBÜ LOS ortalaması 157,83±68,6 gün iken medikal hastalarda 189,75±66,9 gün olduğu görüldü. Komorbidite sayısı ortanca 2,18 (1-4) idi. Hastaların YBÜ'ye kabul esnasında ortalama APACHE-II skorunun 26,02±9,5, albümin değerinin 3,3±0,58 ve laktat değerinin 3,6±2,8 olduğu belirlendi (Tablo 1). Hastaların klinik karakteristikleri Tablo 1'de sunuldu.

### YBÜ'de Uygulanan Tedavi ve Prosedürler

YBÜ'de tüm hastalara MV desteği sağlanmış olup ortalama MV süresi 133,59±66,6/gün olarak bulundu (Tablo 2). Trakesostomi işlemi hastaların YBÜ yatışlarının ortalama 46,36±30,9 gününde, toplam 92 hastaya (%93,9) uygulandı. Trakeostomi uygulanan ve uygulanmayan hastaların ortalama yatış süreleri arasında anlamlı farklılık saptanmadı ($p=0,087$). PEG işlemi 68 hastaya uygulanmış olup işlem gün sayısı ortalaması 91,09±61,8 olarak bulundu. PEG uygulanan hastaların ortalama yatış süresi (189,42±11,92) uygulanmayanlara göre (140,75±7,35) anlamlı olarak yüksek bulundu ($p=0,024$). Tüm hastalara kan transfüzyonu uygulandı ve verilen ünite sayısının ortalaması 13,71±7,5 (1-38) olarak saptandı (Tablo 2).

### YBÜ'de Elektrolit Bozuklukları ve Enfeksiyon Karakteristikleri

Hastalarda en sık hipokalemi (%75,5) ve hipokalsemi (%73,5) gelişmiş olup bunu sırasıyla hipernatremi (%67,3), hiperkloremi (%57,1) izlemektedir. Hastaların elektrolit bozuklukları tabloda belirtildi (Tablo 3). Hipomagnezemi olan hastalarda ortalama yatış süresi 204,67±72,71 gün bulunmuş olup, olmayanlara göre anlamlı olarak daha uzun olduğu saptandı ($p\leq0,001$). Diğer elektrolit bozukluklarında yatış sürelerinde anlamlı farklılık saptanmadı.

Tüm hastalarda YBÜ'de yatışları süresince en az bir enfeksiyon atağı görülmüş olup toplam 483 defa enfeksiyon atağı geçirdikleri belirlendi (Tablo 4). Hastalarda 202 (%41,82) defa ventilatör ilişkili pnömoni, 153 (%31,67) defa kan dolaşımı enfeksiyonu, 82 (%16,97) defa idrar yolu enfeksiyonu, 26 (%5,38) defa yara yeri enfeksiyonu ve 20 (%4,14) defa rektal kolonizasyona bağlı enfeksiyon atakları tespit edildi (Tablo 4).

### YB'de Yatış Süresi İlişkili Faktörler

Çok değişkenli regresyon modelinde APACHE-II skoru, MV süresi, kan transfüzyonu sayısı ve hipomagnezemi yatış süresini belirleyen faktörler olarak belirlendi (Tablo 5). Hastaların APACHE-II skoru ve MV süreleri birlikte değerlendirildiğinde YBÜ'de yatış süresi varyansının %86'sını açıklamaktadır. Model istatistiksel olarak %99 güven seviyesinde önemli bulundu ($R^2=0,86$, $p\leq0,001$). Modelde kalan iki değişken ß katsayılarına göre değerlendirildiğinde; MV süresinin modele en güçlü katkıyı sağlayan değişken olduğu görülürken (0,78), diğer değişken olan APACHE-II skorunun modele daha az katkı (0,17) sağladığı görüldü. Modele dahil edilen yaş, komorbidite sayısı, albümin ve laktat değerleri, enfeksiyon atak sayısı, elektrolit bozukluk sayısı, trakeostomi ve PEG işlemlerinin YBÜ'de yatış süresini anlamlı şekilde yordamadığı görüldü.

## Tartışma

Bu çalışmada YBÜ'de tedavi gören hastaların %3,11'inin 90 gün ve üzerinde tedavi gördüğü ve sağkalım oranının (%22,4) çok düşük olduğu belirlendi. Ayrıca hastaların YBÜ'ye %91,8'inin dahili sebeplerle kabul edilmiş olduğu ve bu hastaların YBÜ LOS'nin cerrahi nedenlerle kabul edilenlere göre istatistiksel olarak anlamlı olmasa da yüksek olduğu tespit edildi. Arabi ve ark. (17) çalışmalarında YBÜ LOS'nin dahili hastalarda cerrahi hastalara göre daha fazla olduğunu belirtmiştir. Çalışmamıza benzer olarak Roedl ve

ark. (12) yaptıkları bir çalışmada; YBÜ'de tedavi alan hastaların %0,1'inin 90 gün ve üzeri kaldığı, hastaların yaş ortalaması 61/yıl olduğu ve hastaların üçte ikisinin hayatta kaldığı belirlenmiştir. Aynı çalışmada YBÜ'de sağkalım oranı yüksek bulunsa da çok uzun LOS'ye sahip hastaların YBÜ sonrası genel performanslarının daha kötü olduğu gözlenmiştir (12).

YBÜ'de uzun LOS'ye sahip hastalarda mortalitenin daha fazla olduğu ve LOS ile yaşam süresinin kısaldığı çeşitli çalışmalarla ortaya koyulmuştur (11,18). Ayrıca yaşlanmanın YBÜ'de LOS ve yüksek mortalite ile ilişkili olduğu da birçok çalışmada bildirilmiştir (19,20). Çalışmamızda da yaş ortalamasının yüksek olmasının hem yüksek mortalite oranına hem de ortalama yatış süresinin uzun olmasına katkı sunduğunu düşünmekteyiz. Bununla birlikte, YBÜ'de yatış süresi ve mortalite nedenleri çok faktörlü olup, YBÜ özelliklerine göre de değişkenlik göstermektedir (8,20,21).

Yapılan çalışmalarda hastaların yüksek APACHE-II skorunun uzun YBÜ LOS'nin önemli bir prediktif değeri

**Tablo 1. Hastaların demografik verileri ve klinik özellikleri (n=98)**

| Hasta özellikleri | | Yatış süresi (gün) | | p |
|---|---|---|---|---|
| | | Ortalama ± standart sapma | Ortanca (%25-75) | |
| Cinsiyet (n) | Erkek (54) | 170,59±73,18 | 141,5 (115,75-210) | 0,140* |
| | Kadın (44) | 147,97±61,30 | 126,5 (98,75-163) | |
| Hayatta kalma durumu (n) | Yaşayan (22) | 151,25±67,37 | 206,5 (119-255,75) | 0,013 |
| | Ölen (76) | 192,18±65,03 | 125 (112,25-159) | |
| YBÜ kabul tipi (n) | Medikal (90) | 157,83±68,6 | 127,5 (110-187,25) | 0,111* |
| | Cerrahi (8) | 189,75±66,9 | 187,5 (125-255,5) | |
| Kabul nedenleri (n) | Post-CPR (32) | 151,22±61,23 | 124,5 (112,25-174,5) | 0,584** |
| | Nörolojik hastalıklar (24) | 180,67±84,95 | 166,5 (99,75-249) | |
| | Solunum hastalıkları (18) | 153,39±78,65 | 128,5 (107,75-162,25) | |
| | Serebral hemoraji (8) | 128,25±19,53 | 123,5 (112,75-148,25) | |
| | Sepsis (6) | 139,83±18,93 | 150 (119-152,75) | |
| | Travma (4) | 192,50±80,85 | 191,5 (122,25-263,75) | |
| | Cerrahi (4) | 187,00±62,38 | 187,5 (132-241,5) | |
| | İntoksikasyon (2) | 202,00±2,82 | 202 (200-202) | |
| Komorbiditeler (n) | Hipertansiyon (50) | 160,28±66,80 | 129 (116,5-208,5) | 0,801* |
| | Nörodejeneratif hastalık (40) | 168,25±68,33 | 139 (107-240) | 0,618* |
| | Kalp yetmezliği (26) | 130,00±38,92 | 125 (106,25-138,75) | 0,025* |
| | Solunum hastalıkları (26) | 130,42±47,00 | 121 (106,75-134,25) | 0,010* |
| | Aritmi (21) | 132,95±58,18 | 110 (92-141,5) | 0,003* |
| | Koroner arter hastalığı (16) | 161,25±64,64 | 140 (107,5-234,75) | 0,962* |
| | Diabetes mellitus (5) | 154,70±53,04 | 152,5 (106,25-194) | 0,916* |
| | Kronik böbrek yetmezliği (4) | 121,25±7,89 | 123,5 (113-127,25) | 0,398* |
| | Diğer (22) | 184,71±86,92 | 133,5 (122,5-261,25) | 0,160* |
| Yaş (yıl)† | | 70,10±18,55 (23-102) | | |
| YBÜ yatış süresi (gün)† | | 160,44±68,70 (90-376) | | |
| Komorbidite sayısı† | | 2,18±0,9 (1-4) | | |
| APACHE-II skoru† | | 26,02±9,5 (6-42) | | |
| Albümin† | | 3,3±0,58 (1,8-4,5) | | |
| Laktat† | | 3,6±2,8 (0,49-12,79) | | |

APACHE-II: Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II, YBÜ: yoğun bakım ünitesi, post-CPR: kardiyopulmoner resüsitasyon sonrası, †ortalama ± standart sapma (minimum-maksimum), *Mann-Whitney U testi, **Kruskal-Wallis testi

**Tablo 2. Yoğun bakım ünitesinde uygulanan tedavi ve prosedürler**

| | | Yatış süresi (gün) | | p‡ |
|---|---|---|---|---|
| | | Ortalama ± standart sapma | Ortanca (%25-75) | |
| PEG | (+) (n=68) | 189,42±11,92 | 137,5 (115,25-241,5) | 0,024‡ |
| | (-) (n=30) | 140,75±7,35 | 122,5 (109,25-161) | |
| Renal replasman | (+) (n=14) | 154,93±14,15 | 123 (94,25-179,25) | 0,087‡ |
| | (-) (n=84) | 180,14±10,37 | 130,5 (115,25-210) | |
| Trakeostomi | (+) (n=94) | 178,13±69,75 | 130,5 (116,25-207,25) | 0,094‡ |
| | (-) (n=6) | 132,75±12,13 | 108,5 (94,25-155,5) | |
| PEG gün sayısı† | 91,09±61,8 (18-324) | | | |
| Kan transfüzyon sayısı† (Ü) | 13,71±7,5 (1-38) | | | |
| MV süresi† (gün) | 133,59±66,6 (25-370) | | | |
| Trakeostomi gün sayısı† | 46,36±30,9 (10-206) | | | |

PEG: Perkütan endoskopik gastrostomi, MV: mekanik ventilatör, †ortalama ± standart sapma (minimum-maksimum), ‡Mann-Whitney U testi

**Tablo 3. Yoğun bakım ünitesinde görülen elektrolit bozuklukları ve yatış süreleri**

| | n | % | Yatış süresi (ortalama ± standart sapma) (p)* |
|---|---|---|---|
| Hipokalemi | 74 | %75,5 | 153,38±58,59 (0,888) |
| Hipokalsemi | 72 | %73,5 | 151,18±60,57 (0,860) |
| Hipernatremi | 66 | %67,3 | 153,39±64,13 (0,248) |
| Hiperkloremi | 56 | %57,1 | 158,16±65,31 (0,682) |
| Hipomagnezemi | 33 | %33,7 | 204,67±72,71 (<0,001) |
| Hiponatremi | 29 | %29,6 | 169,76±64,40 (0,299) |
| Hiperkalemi | 24 | %24,5 | 159,45±65,96 (0,872) |
| Hipokloremi | 18 | %18,4 | 155,11±59,09 (0,971) |
| Hipermagnezemi | 2 | %2 | 93,50±2,12 (0,240) |

*Mann-Whitney U test

**Tablo 4. Yoğun bakım ünitesinde karşılaşılan enfeksiyon tiplerinin dağılımı**

| | n | % |
|---|---|---|
| Ventilatörle ilişkili pnömoni | 202 | 41,82 |
| Kan dolaşımı enfeksiyonu | 153 | 31,67 |
| İdrar yolu enfeksiyonu | 82 | 16,97 |
| Yara yeri enfeksiyonu | 26 | 5,38 |
| Rektal kolonizasyon (VRE) | 20 | 4,14 |

VRE: Vankomisin dirençli enterokok

olduğu bildirilmiştir (18,22,23). Çalışmamızda da APACHE-II skoru ortalamasının yüksek olmasının LOS ile ilişkili olduğu belirlenmiştir. Williams ve ark.'nın (10) çalışmasında APACHE-II skoru >11'in üzerinde olmasının YBÜ'de uzun LOS

**Tablo 5. Hastaların yoğun bakım ünitesinde yatış süresini açıklayan çok değişkenli doğrusal regresyon model tablosu (n=98)**

| $R^2$=0,868/F=73,78 | ß | Standart sapma | Beta | t | p |
|---|---|---|---|---|---|
| Değişkenler | | | | | <0,001 |
| APACHE-II skoru | 1,226 | 0,281 | 0,170 | 4,361 | <0,001 |
| MV süresi | 0,809 | 0,051 | 0,785 | 15,769 | <0,001 |
| Kan transfüzyonu sayısı | 22,066 | 6,132 | 0,153 | 3,598 | 0,001 |
| Hipomagnezemi | 1,464 | 0,411 | 0,161 | 3,563 | 0,001 |

MV: Mekanik ventilatör, APACHE-II: Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II

ile anlamlı düzeyde ilişkili olduğu bildirilmiştir. Farklı olarak bir çalışmada APACHE-II skorunun mortaliteyi öngörmede anlamlı olduğu fakat LOS ile ilişkili olmadığı gözlenmiştir (7). APACHE-II skoru hastaların YBÜ'de kalış süresi için prediktif bir parametre olup YBÜ'lerin akılcı yönetiminde bu paremetrenin gözardı edilmemesi gerekmektedir.

Birçok çalışmada enfeksiyon ile ilişkili olarak uzun MV süresinin kötü prognoza ve YBÜ'de uzun LOS'ye neden olduğu bildirilmiştir (7,13,24,25). Çalışmamızda tüm hastalara MV desteği sağlandığı ve MV süresinin YBÜ LOS'yi öngörmede en önemli parametre olduğu gözlenmiştir. YBÜ'de kritik hastaların 48 ila 72 saat içinde mekanik ventilasyondan ayrılamaması sonucu gelişen başarısız weaning durumunun altta yatan hastalığın şiddetini yansıttığı ve YBÜ'de yüksek mortalite oranına neden olduğu saptanmıştır (13). Bulgularımıza benzer olarak Wesch ve ark.

(21) cerrahi YBÜ'de 7 günde >14 saatten fazla MV desteği alınmasının, LOS'yi (>20 gün) öngörmede en etkili faktör olduğunu bildirmişlerdir.

Çeşitli çalışmalarda; hipoalbümineminin uzamış MV süresi, artmış mortalite, uzamış YBÜ LOS ve kronik hastalık durumunu öngörmedeki önemi vurgulanmıştır (23,26,27). Çalışmamızda YBÜ'ye giriş albümin düzeyi ortalama 3,3 mg/dL saptanmış olup hipoalbüminemi çoğu hastada gözlenmiştir. Kan laktat seviyesi YBÜ hastalarının prognozunu tahmin etmek için kullanılan parametrelerden biridir. Hiperlaktatemi, solunum ve dolaşım bozuklukları sonucu gelişen doku hipoksisine bağlı genellikle çok faktörlü bir durumdur (28). Adıyaman ve ark. (25) laktat >2 mmol L-1 olan hastalarda hem mortalitenin hem de YBÜ LOS'nin anlamı olarak daha uzun olduğunu saptamışlardır. Çalışmamız, çok uzun yatan hastalarda YBÜ'ye kabul esnasında hipoalbüminemi ve hiperlaktateminin görüldüğünü fakat bu laboratuvar parametrelerindeki bozulmaların yatış süresi ile ilişkili olmadığını göstermiştir.

Uzun süre yatan hastalarda malnütrisyon riski yüksek olup, bu durum nazokomiyal enfeksiyon ve multipl organ yetmezliği gibi komplikasyonlara neden olarak yatış süresini daha da uzatmaktadır (29). YBÜ'de 4 haftadan daha uzun süre enteral nütrisyon ile takip planlanan hastalarda PEG işlemi uygulanmaktadır (29,30). Diyabeti olan ve ileri yaş geriatrik hastalarda PEG ile beslenmenin faydalarının belirsiz olduğu ve sağkalım oranı düşük hastalarda PEG işlemine karar verirken daha seçici olunması gerektiği de bildirilmiştir (30,31). Kronik kritik hastalara 30-60 günlük bir nazogastrik beslenme süresi tanındıktan sonra hayatta kalırlarsa PEG düşünülebileceği belirtilmiştir (31). Çalışmamızda, hastalara yatış sürelerinin yaklaşık ortalama 90. gününde PEG işlemi uygulanmıştır. Çalışma popülasyonunun ileri yaş, kronik ek hastalıkları olan hasta grubu olmasından ve hasta yakınlarının onam vermede tereddüt etmesinden dolayı PEG işlemi uzun sürede gerçekleşmiştir. Ayrıca çalışmamızda PEG işlemi uygulanan hastalarda LOS anlamlı olarak daha uzun bulunmuştur. Benzer olarak, Dincer ve ark. (32) kronik bakım hastalarında PEG işlemi ile uzun LOS arasında anlamlı bir ilişkinin olduğunu ve çoğunu nörolojik hastaların oluşturduğunu bildirmişlerdir.

Tekrarlı weaning başarısızlığı ve uzamış MV süresi olan kronik kritik hastalarda trakeostomi ihtiyacı olabilir (17). Trakeostomili hastalarda LOS, entübe hastalara göre daha uzundur (17). Çalışmamızda uzamış mekanik ventilasyon nedeniyle hastaların %93,9'una trakeostomi işlemi uygulanmıştır. Bununla birlikte trakeostomi uygulanan hastalarda LOS'nin daha uzun olduğu fakat istatistiksel olarak anlamlı farklılığın olmadığı tespit edilmiştir. Farklı olarak ise Çevik ve Geyik (7) trakeostomi işleminin YBÜ'de LOS'nin ve mortalitenin prediktif bir faktörü olduğunu bildirmişlerdir.

Sonuçlarımıza göre uygulanan kan transfüzyonu sayısının uzun LOS'nin prediktörü olduğu belirlenmiştir. Tobi ve Amadasun (9) YBÜ'de uzun LOS'nin anemiye yatkınlığı artırdığını ve kan transfüzyonu ile kuvvetli ilişkili olduğunu bildirmişlerdir. Çalışmamızda görülen yüksek kan transfüzyonunun hastaların çok uzun LOS'ye sahip olmalarına ve geriatrik hasta popülasyonundan oluşmasına bağlı olduğunu düşünmekteyiz. Çünkü geriatrik hastalarda uzun LOS'ye bağlı olarak anemiye yatkınlığın geliştiği bilinmektedir (9,33). Çeşitli çalışmalarda, aneminin mortalite ve morbiditeye neden olduğu; tedavi amaçlı uygulanan kan transfüzyonun ise enfeksiyon artışı, mortalite ve uzun LOS ile ilişkilendirildiği gözlenmiştir (9,34).

Elektrolit bozuklukları, YBÜ'de kronik kritik hastalarda sık karşılaşılan ve olumsuz sonuçlara yol açabilen bir durumdur (35). Çalışmamızda dikkat çekici olarak hipomagnezeminin uzun LOS ile anlamlı ilişkisi tespit edilmiştir. Farklı çalışmalarda YBÜ'de hipomagnezemi sıklığının %20 ila %65 arasında değiştiği gözlenmiştir (15,36). Bu çalışmada hastaların %33'ünde hipomagnezemiye rastlanılmıştır. Hipomagnezeminin kritik hastalarda mortaliteyi öngördüğü ve normomagnezemiye göre LOS'nin daha uzun olduğu saptanmıştır (36). Bu durumun sebebi olarak; hipomagnezemiye bağlı kas güçsüzlüğü ve solunum yetmezliğinin geliştiği, böylece MV ihtiyacının arttığı ve uzamış weaninge neden olduğu belirtilmiştir (36).

Çalışmamızda en sık ventilatör ilişkili pnömoni (%41,82), kan dolaşımı enfeksiyonu (%31,67) ve idrar yolu enfeksiyonunun (%16,97) görüldüğü saptanmıştır. YBÜ'de uzun süre (>90 gün) yatan hastalarda gelişen enfeksiyonların incelendiği bir çalışmada; en sık kan dolaşımı enfeksiyonu (%48), ventilatör ilişkili pnömoni (%33), idrar yolu enfeksiyonu (%10) saptanmıştır. Aynı çalışmada enfeksiyon atak sayısının LOS'yi uzattığı sonucuna varılmıştır (37). Çalışmamızda hasta popülasyonunun çok uzun süre yatan, uzun süreli MV'ye bağlı, birçok girişimsel işlem uygulanan geriatrik hastalardan oluşmasından dolayı çok sayıda enfeksiyon atağı saptanmıştır. Bu durumun, hastaların LOS'ye katkı sunduğunu ve YBÜ kaynak tüketimini artırdığını düşünmekteyiz.

## Sonuç

Bu çalışmada, YBÜ'de çok uzun süre (≥90 gün) tedavi gören kronik kritik hastalarda mortalite oranının yüksek olduğu ve PEG işlemi uygulanan hastalarda yatış süresinin uzun olduğu saptandı. Bununla birlikte, yüksek APACHE-II skoru, uzun MV süresi, kan transfüzyonu sayısı ve hipomagnezemi varlığının YBÜ'de LOS için bağımsız risk faktörleri olduğu belirlendi. Sonuçlarımıza dayalı olarak, YBÜ'de kronik bakım hastalarında LOS'yi öngören faktörlerin önceden bilinmesi ve gerekli önlemlerin alınması YBÜ'lerin etkin kullanımına katkı sunabilecektir.

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OLGU SUNUMU / *CASE REPORT*

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# Postoperatif Dönem Yoğun Bakım Takibinde Kas Güçsüzlüğü Gelişen Hastanın Klinik Takibi

## Clinical Follow-up of a Patient with Muscle Weakness During the Postoperative Intensive Care Period

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**ÖZ** İnce bağırsak perforasyonu nedeniyle akut batın ameliyatı sonrası yoğun bakıma alınan hasta, postoperatif kas güçsüzlüğü nedeniyle tetkik edilmiş olup, ayırıcı tanı üzerine çalışılmıştır. Guillain-Barré sendromu akut enflamatuvar demiyelinizan bir polinöropatidir. Etiyolojide geçirilmiş enfeksiyonlar, cerrahi, transplantasyon ve malignite gibi durumlar suçlanmaktadır. Öykü, klinik muayene ve takip, laboratuvar tetkikleri ve elektrofizyolojik çalışmalar tanıda ve ayırıcı tanıda önemlidir. İntravenöz immünoglobulin ve plazmaferez tedavinin ana öğeleri olsa da destek tedavisi uzun süren tedavi sürecinde önemlidir. Bu olgu sunumunda cerrahi öyküsü olan ve gastrointestinal stromal tümörün nadir bir paraneoplastik sonucu olabileceğini düşündüğümüz hastaya yoğun bakımdaki yaklaşımımızı tartıştık.
**Anahtar Kelimeler:** Guillain-Barré sendromu, intravenöz immünoglobulin, plazmaferez, gastrointestinal stromal tümör

**ABSTRACT** The patient underwent intensive care after an acute abdominal surgery due to intestinal perforation. The patient was examined for postoperative muscle weakness, and the differential diagnosis was studied. Guillain-Barré syndrome is an acute inflammatory demyelinating polyneuropathy. Infection, surgery, and transplantation have been cited in its etiology. History, clinical examination and follow-up, laboratory tests, and electrophysiological studies are important in its diagnosis, as well as differential diagnosis. Intravenous immunoglobulin and plasmapheresis are the mainstays of care, and supportive care is important for long-term treatment. In this case report, an intensive care unit approach was discussed, in which the surgical paradigm and gastrointestinal stromal tumor were thought of as a rare paraneoplastic complication.
**Keywords:** Guillain-Barré syndrome, intravenous immunoglobulin, plasmapheresis, gastrointestinal stromal tumor

## Giriş

Yoğun bakım ünitesinde kas güçsüzlüğü hastanın yatış sebebi olabilirken, yoğun bakım takibi esnasında da bu durum ortaya çıkabilir. Akut ve subakut olarak ortaya çıkabilen bu durumlar iyi değerlendirilmeli ve tedavi açısından ayırıcı tanısı iyi yapılmalıdır. Guillain-Barré sendromu (GBS), 1,2-1,9/100.000 sıklıkta, erkeklerde 1,5-2 kat daha sık görülen, akut demiyelinizan bir polinöropatidir (1). Çeşitli enfeksiyonlar başta olmak üzere, cerrahi girişimler, malignite ve transplantasyon gibi durumlarda öyküde yer almaktadır. Gerek etiyolojik faktörler gerek klinik izlem gerekse laboratuvar bulguları açısından ayırıcı tanısının yapılması önemlidir. Biz bu olgu sunumumuzda birden fazla duruma bağlı olabileceğini düşündüğümüz olgumuzu literatür eşliğinde sunmaya çalıştık.

## Olgu Sunumu

Öyküsünde tip II diabetes mellitus dışında ek hastalık öyküsü olmayan 55 yaşında erkek hasta, karın ağrısı nedeniyle başvurduğu dış merkezde akut batın nedeniyle opere olmuş.

Terminal ileumunda kitle ve komşuluğunda perforasyon saptanan hastanın rezeksiyon ve anastomoz prosedürü tamamlanmış. Postoperatif 5. günde alt ekstremitelerden başlayan kas güçsüzlüğü gelişen hastaya metilprednizolon başlanmış, semptomları ilerleyen hasta entübe edilmiş, postoperatif 10. günde elektromiyografi (EMG) çekilmiş. Tetkik sonucu yaygın periferik nöropati ile uyumlu gelen hastaya 3 doz intravenöz immünoglobulin (IVIG) verilmiştir. Kliniğinde gerileme olmayan hasta postoperatif 15. günde periferik nöropati/miyopati ön tanısıyla kliniğimize kabul edildi. Hastanın yapılan ilk muayenesinde entübe, bilinci açık, bilateral ışık refleksleri alınıyordu, fasiyal sinir muayenesi doğaldı, yutkunma ve öksürük refleksleri yetersizdi. Kas gücü muayenesinde sağ üst ekstremite proksimal 2/5, sol üst ekstremite proksimal 3/5, her iki üst ekstremite distaller 3/5, alt ekstremite proksimaller 2/5, sol alt ekstremite distal 2/5, sağ alt ekstremite proksimal 1/5 bulundu. Derin tendon refleksleri alınamadı, duyu muayenesi doğaldı. Taşikardik, hipertansif olan hastanın kan basıncı değişiklikleri olmaktaydı, mekanik ventilatörde solunumu düzensizdi. Hastanın rutin monitörizasyonu yapıldı, tam kan sayımı, arter kan gazı, kan biyokimyası, tam idrar tetkiki çalışıldı. Trakea, kateter, idrar ve kan kültürleri çalışıldı. Kültürlerindeki üremelerine uygun antibiyoterapisi düzenlendi. Serum parathormon düzeyi 215 pg/mL ölçülen hastanın serum kalsiyum, 1,25-dihidroksivitamin D ve böbrek fonksiyon testleri normal idi. Beyin, torakal ve servikal manyetik rezonans incelemesinde belirgin patoloji saptanmadı. Lomber ponksiyon (LP) ile yapılan beyin omurilik sıvısı (BOS) incelemesinde hücre saptanamadı, BOS glukoz düzeyi 85 mg/dL olarak ölçüldü, eş zamanlı kan glukoz düzeyi 165 mg/dL ölçüldü. Kültüründe üreme olmadı. Protein düzeyi 46 mg/dL ölçülen hastaya EMG çekilemedi.

Hasta GBS kabul edilip 5 seans plazmaferez yapıldı. Hastanın tedavi sürecinde ileumundan cerrahi olarak eksize edilen kitlesinin patolojik incelemesi gastrointestinal stromal tümör (GİST) olarak geldi. Tıbbi onkoloji kliniğine konsülte edildi. Hasta fizik tedavi ve rehabilitasyon programına alındı. Beş seans plazmaferez uygulaması ve fizik tedavisi yapılan hastanın takiplerinde kas gücünde anlamlı bir iyileşme olmadı. Mekanik ventilatör desteği ihtiyacı giderilemeyen hastanın EMG'si yapıldı, motor ileti hızlarında yavaşlama ve periferik nöropati tespit edildi. LP ile BOS bakısı tekrarlandı. BOS mikroskopisinde hücre görülmeyen hastanın glukoz düzeyi normaldi, proteini 66 mg/dL olarak ölçülen hastanın 2. defa 5 seanslık plazmaferezi planlandı. İkinci 5 seanslık plazmaferez uygulamasından sonra hastanın kas gücü dramatik şekilde arttı. Mekanik ventilatörde takipli hastanın basınç ayarlı senkronize aralıklı zorunlu ventilasyon modda 15 $cmH_2O$ tepe basıncı ile tidal volümü 7-8 mL/kg düzeylerindeydi. Solunumu düzenli hale gelen hastanın taşikardisi ve hipertansiyonu geriledi. Hastanın başarılı ekstübasyonu ve takibinde solunum fizyoterapisi ile solunumsal açıdan stabil hale geldi. Hastanın periferik kas gücü muayenesinde asimetrisi geriledi, kas gücü arttı, ağız yolu ile normal beslenmeyi tolere etti. Hasta tedavisinin tamamlanması için fizik tedavi ve rehabilitasyon kliniğine devredildi. Hastadan onam formu alınmıştır.

## Tartışma

Tanısal açıdan iyi tanımlanmış bazı akut ve subakut başlangıçlı kas güçsüzlüğü nedenleri detaylı olarak incelenmelidir.

Kritik hastalık nöropatisi çoğunlukla sepsisten >2 hafta sonra klinik olarak ortaya çıkarken, EMG'de akson kaybı beklenir (2). Yoğun bakım hastalarında ciddi nekrotizan miyopati de görülebilir. İlk olarak status astmatikus için yüksek doz steroid (>1 gram metilprednizolon) ve uzun süreli nöromüsküler bloker ajan kullanılan hastalarda tanımlanan yoğun bakım akut miyopatisi, klinik olarak hastalar mekanik ventilatörden geç ayrıldığında fark edilir (3,4).

Myastenia gravis olgularında ise oküler, bulber tutulum, proksimal kas güçsüzlüğü ve EMG'de tek lif iletiminde geçici değişme patognomoniktir (5).

Botulismus olgularında ise EMG'de motor ileti hızı normal olup yanıtlar artma eğilimindedir (6).

Kene felci, kabuklu deniz hayvanları zehirlenmesi ve organofosfat zehirlenmeleri ise hastalık öncesi maruziyet öyküsü nedeniyle dışlanabilmektedir. Kas güçsüzlüğü ve duyuların korunduğu post poliyomiyelit olgularında yapılan BOS incelemelerinde görülen pleositoz ayırıcı tanıda dikkat çeker (7).

Kraniyal sinirlerin ve solunumun korunduğu, anormal serum potasyum düzeylerinin görüldüğü periyodik paraliziler akılda tutulmalıdır (8).

Bizim olgumuzun öykü, klinik ilerleyiş, fizik muayene, kan ve BOS tetkikleri, görüntüleme ve elektrofizyolojik değerlendirmeler sonucunda bahsedilen tanılardan uzaklaştığını düşündük.

GBS akut kas güçsüzlüğünün ön planda olduğu otoimmün poliradikülonöropatidir (9). Dünya çapında GBS insidansı 1,2-1,9/100.000'dir (1). Hastaların yaklaşık üçte

ikisinde 6 hafta içinde *Campylobacter jejuni*, *Haemophilus influenzae*, Epstein-Barr virüs, Sitomegalovirüs, *Mycoplasma pneumoniae* ve influenza virüs enfeksiyon öyküsü bulunmaktadır (10). Enfektif organizmanın veya antijenlerin B ve T-hücre aracılı immün yanıtı uyarması ile miyelin kılıfta hasarlanma olduğu kabul görmektedir. Histopatolojide, nöronlar içinde ve perivasküler dokuda monosit ve lenfosit infiltrasyonu görülmekte olup, serumda IL-2, IL-6, TNF-alfa ve IF-gama artışı bu durumun destekleyicisidir (11). İmmünolojik çalışmalar GBS'nin patogenezine tam bir ışık tutamamıştır. Hastalığın erken evresinde makrofajlar aktive olmaktadır ve antigangliosid antikorlar mevcuttur (12). Biz teknik yetersizlik nedeniyle bu tetkikleri yapamadık. GBS'nin farklı cerrahi prosedürler sonrasında çıkabileceği olgu sunumları ile de raporlanmıştır (13). Yapılan çalışmalarda GBS tanısı alan hastalarda malignensi riskinin normal popülasyonla karşılaştırıldığında daha yüksek olduğu belirtilmiş, Hodgkin hastalığı, non-Hodgkin lenfoma, malign melanom gibi bazı malignensilerin nadir de olsa GBS ile prezente olabildiği olgular görülmüştür (14-16). Tanı öncesinde ve tedavi esnasında GBS gelişmiş küçük hücreli akciğer kanseri olguları bildirilmiştir (17). Yaptığımız literatür taramalarında altta yatan GİST tanısı almış hastalarda paraneoplastik sendrom tanısı çok nadir olmakla birlikte nefrotik sendrom (18) ve GBS (19) tanılı birer adet olgu sunumu bulabildik. Bizim hastamızın yakın öyküsünde ishal veya enfeksiyon bulunmamaktaydı. Kas güçsüzlüğünden 5 gün önce gelişen acil cerrahi girişim ve rezeksiyon materyalinin patolojisi sonucunda tanıladığımız GİST bizim için predispozan faktörler açısından önemlidir.

GBS tanısal spesifik testler bulunmadığı için, ayrıntılı klinik öykü, detaylı fizik muayene, hastalığa özgü klinik belirtiler ve nörofizyolojik testlerle desteklenen klinik bir tanıdır. Klasik olarak hastalığın seyri ekstremitelerde kas güçsüzlüğü ve reflekslerde zayıflamanın aşağıdan başlayıp yukarı doğru ilerlemesidir. Yutma güçlüğü ve hava yolu açıklığını sağlamada güçlük çekilebilir. Yoğun bakım tedavisine gerek duyulan hastalarda otonom sinir sistemi tutulumu yaygındır. Kan basıncında dalgalanma, disritmi ve postural hipotansiyon vazomotor kontrolün bozulmasıyla ilişkilidir (20). Bizim hastamızda klinik başlangıcın dış merkezde olması sebebiyle öykü ve klinik takip konusunda eksiklik olabilir. Hasta yakını, ilgili hekim ile görüşmeler ve eski epikriz incelemeleri ile bu eksikliği gidermeye çalıştık. Hastamızın refleks kaybı ve kas güçsüzlüğünün alt ekstremiteden başlaması, solunum işlevinin yetersizliği, taşikardisinin mevcudiyeti ve kan basıncının düzensiz olması klinik açıdan önemliydi.

GBS'nin karakteristik laboratuvar özelliklerinden birisi albüminositolojik dissosiasyon (pleositoz olmaksızın yükselmiş protein) gösteren anormal BOS bulgusudur. İlk 48 saatte normal olup 1 hafta içinde 1 g/dL seviyelerine kadar artabilirken, nadiren haftalar sonra bile BOS proteini normal kalabilir (21). Glukoz düzeyleri normal bulunurken, hücre sayısı genellikle 10 hücre/$mm^3$'den az olur. GBS, insan bağışıklık yetmezliği virüsü enfeksiyonu veya Lyme hastalığının bir belirtisi olarak ortaya çıkarsa hücre sayısı 25-50 hücre/$mm^3$ düzeylerine ulaşır. Bizim hastamızda dış merkezde yapılan IVIG tedavisi sonrası alınan ilk örnekte BOS protein düzeyi hafif artmış bulunmuştu. İlk yaptığımız 5 seanslık plazmaferez uygulaması sonrası yapılan tetkikte ise protein düzeyi yüksekti. Yaptığımız her iki incelemede glukoz düzeyleri normal iken, hücre sayısı da anlamlı olarak normaldi. GBS'de EMG tetkikinde proksimal sinir segmentleri boyunca sinir ileti hızında yavaşlama gösterir. Uyarılmış motor yanıtların amplitüdü azalır (21). Bizim hastamızda yaptığımız tetkikte sinir ileti hızında yavaşlama gösterildi.

GBS seyrinde güçsüzlükle birlikte birçok klinik problem ortaya çıkabilir. Bunların bazıları hastaların yaşam kalitesini etkilerken, bazıları prognoz ve mortaliteyi etkileyebilmektedir. Yedi günden önce başvuru, öksürememe, ayak ve el bilek güçsüzlüğü, boyun kasları güçsüzlüğü ve karaciğer testleri artmış ise mekanik ventilasyon desteği gerekebilir (22). En sık problem olan taşikardiye, 120 atım/dk'yi aşmadığı sürece müdahale edilmemelidir. Hipertansiyon ve taşikardiye kısa etkili esmolol ve nitroprussid ile müdahale edilebilir. Yutma güçlüğü varsa, beslenmede nazogastrik sonda ile enteral yol tercih edilmelidir. Eklem ve solunum fizyoterapisi ön planda olmalıdır. Hastaların büyük çoğunluğu ağrıdan şikayetçidir, non-steroid anti-enflamatuvar ilaçlar ve opioidler kullanılabilir (23).

Yüksek doz kortikosteroid kullanımının denendiği çalışmalar olumlu sayılabilecek etkileri öne sürmekle birlikte, ventilasyon süresi, mortalite, 28 gün ve 365 gün sonrası iyileşme oranlarını etkilemediği gösterilmiştir (24). IVIG ve plazmaferez etkinliğin benzer olduğu gösterilmiştir. IVIG ulaşım kolaylığı, uygulaması basit olması ve yan etkilerin az olması nedeniyle ilk tercih edilebilir (25). Klinik uygulamada 2 gr/kg total doz 5 günde verilmelidir. Motor fonksiyonların kazanımı, morbidite, mortalite, mekanik ventilasyon süresi üzerine olumlu etkileri gösterilen ilk tedavi rejimi plazmaferezdir (26). Etki gücü ilk haftada daha belirgindir, 1 aya kadar uygulamaya başlanabilir. Günaşırı 5 uygulama, 50 mL/kg/uygulama ya da 200-250 mL/kg total olarak uygulanır.

Albümin taze donmuş plazmaya oranla daha az yan etki potansiyeliyle birliktedir. Bizim hastamızda dış merkezde önce düşük doz steroid verilmiş akabinde 3 doz IVIG ile tedaviye devam edilmiş olup herhangi bir klinik yanıt alınamamıştır. Biz hastayı kabulümüzden sonra hastaya plazmaferez uyguladık. Yanıtsız olan 1'inci 5 kürlük tedaviden sonra yaptığımız 2'nci 5 günlük kürden dramatik yanıt aldık.

GBS, öncesinde geçirilmiş enfeksiyon, cerrahi girişim, transplantasyon gibi durumların sorumlu tutulabildiği otoimmün bir polinöropatidir. GİST'nin paraneoplastik etkilerinin olmadığı kabul edilmekle birlikte nadir olgu sunumları bulunmaktadır. Biz olgumuzda geçirilmiş cerrahi prosedür ve GİST tanısını etken olarak suçlayabiliriz. Sonuç olarak GBS, erken tanı, yoğun bakımda multidisipliner yaklaşım ve uygun destek tedavisi ile hastalar açısından yüz güldürücü şekilde sonuçlanabilmektedir.

### Etik

**Hasta Onamı:** Hastadan onam formu alınmıştır.

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

### Yazarlık Katkıları

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CASE REPORT / *OLGU SUNUMU*

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# Encephalitis and Toxic Hepatitis Caused by Bee Sting: An Unusual Case Report

## Arı Sokmasına Bağlı Ensefalit ve Toksik Hepatit: Alışılmadık Bir Olgu Sunumu

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**ABSTRACT** A bee sting can be a serious problem that affects people all over the world. Several clinical manifestations of bee sting have been described elsewhere. Furthermore, local allergic reactions are more common, causing pain, redness, and swelling of soft tissue within a few hours. In some cases, severe neurological deficits that can lead to death have been reported. According to the literature, the onset of neurological symptoms can range from 30 seconds to 96 hours. Herein, we present the case of a 48-year-old man who developed allergic encephalitis and toxic hepatitis as a result of multiple bee stings.
**Keywords:** Bee sting, bee venom, encephalitis

**ÖZ** Arı sokması, dünya çapında görülen ciddi bir tıbbi durumdur. Arı sokması sonrası gelişen çeşitli klinik tablolar tanımlanmıştır. Lokal alerjik reaksiyonlar daha yaygındır ve birkaç saat içinde yumuşak dokuda ağrı, kızarıklık ve şişmeye neden olabilir. Nadiren ölüme yol açabilen ciddi nörolojik defisitler bildirilmiştir. Literatürde bildirildiği üzere nörolojik semptomların başlangıcı 30 saniye ile 96 saat arasında değişmektedir. Burada, birden çok arı sokmasına bağlı gelişen alerjik ensefalit ve toksik hepatit ile başvuran 48 yaşında bir erkek hastayı bildiriyoruz.
**Anahtar Kelimeler:** Arı sokması, arı zehiri, ensefalit

## Introduction

Various clinical presentations after a bee sting have been described in the literature. Bee stings often cause local dermal allergic reactions. However, various systemic involvements can result in serious complications (1). Anaphylaxis is a serious systemic involvement that causes sudden death. Anaphylactic shock, acute kidney failure, myocardial infarction, atrial fibrillation are other unusual systemic manifestations that can occur. Also, there have been prior reports of neurological reactions including epileptic seziures, peripheral neuropathies and cerebrovascular disease. The clinical signs of neurological involvement associated with bee sting vary depending on underlying immunological, ischemic or toxic mechanisms (2). Here, we present a case with encephalitis complicated with toxic hepatitis, which is an extremely rare neurological involvement due to bee sting.

## Case Report

A 48-year-old male patient was brought to the emergency department as he experienced a sudden loss of consciousness soon after stung by a bee while working in the rural area. His family history revealed subjects with similar systemic reactions after a bee sting. His father died due to systemic complications after bee sting during the follow-up in the intensive care unit. The patient's vital signs were a temperature of 36.7 °C, blood pressure of 130/90 mmHg, and respiratory rate of 16/min. The physical examination revealed localised allergic reaction findings suggesting multiple bee stings at the neck and left arm. On the neurological examination, the patient exhibited reduced consciousness with stupor. He had dysarthric speech. Neck rigidity and Kerning's sign were positive. The horizontal saccadic eye movements were slow, and

partial gaze restrictions were noted. He had quadriparesis with brisk deep tendon reflexes and Babinski sign on the right. Cardiac and respiratory examinations were normal. The biochemistry and hemogram tests were within normal limits. The cerebrospinal fluid (CSF) examination revealed higher protein levels (79 mg/dL). The opening pressure was within normal limits. The CSF colour was bright, and there were no cells. Magnetic resonance imaging showed T2W and fluid-attenuated inversion recovery images hyperintense lesions involving lateral temporal lobes bilaterally suggesting cortical oedema (Figure 1). Electroencephalography was unremarkable. The patient was started to follow-up the intensive care unit as encephalitis due to exposure to bee stings. He was treated by antihistaminics, high dose corticosteroids (1 mg/kg/day) and antibiotics. However, his clinical findings showed progression he developed vegetative state and complicated with gastrointestinal haemorrhage on the third day of the follow-up. The massive increase in serum liver enzymes (aspartate aminotransferase: 880 U / L, alanine aminotransferase: 2,200 U/L, gamma-glutamyltransferase: 430 U/L) and abnormal coagulation tests [partial thromboplastin time (PTT): 34 sec, activated PTT: 61 sec, international normalized ratio: 2.6] were observed. The patient died despite the intervention and supportive treatments. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

## Discussion

Local allergic reactions due to bee sting in the form of pain, redness and swelling are self-limiting. Sometimes it may represent severe clinical findings. Among these, the most known is anaphylactic shock, with severe clinical conditions such as myocardial infarction, acute pulmonary oedema, gastrointestinal haemorrhages, and acute organ dysfunctions (1,2). Rare neurological clinical findings include ischemic stroke, polyneuropathy, parkinsonism, encephalitis, Guillain-Barré syndrome and toxic encephalopathy (2,3).

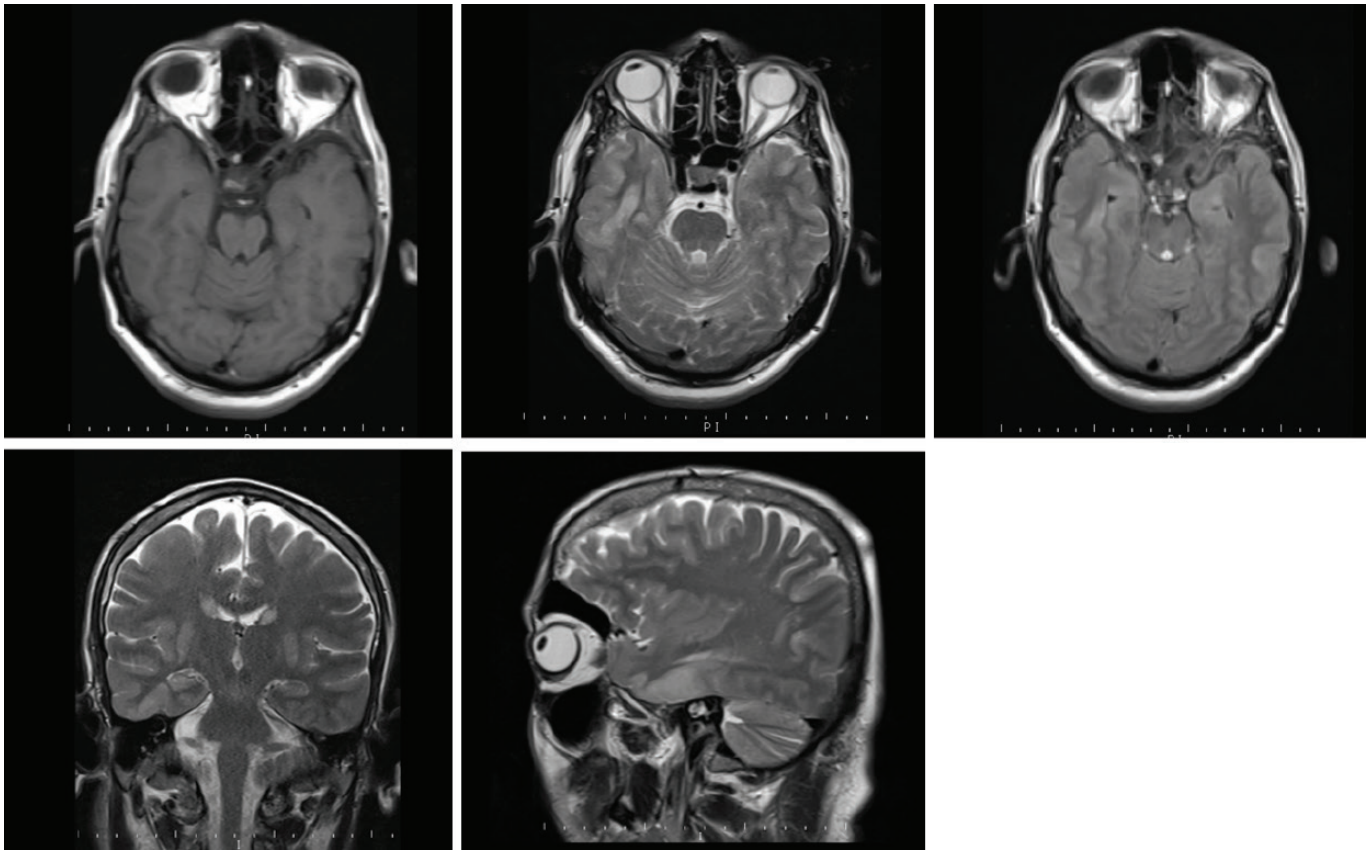

**Figure 1.** T2W and FLAIR hyperintense, T1W hypointense lesions involving lateral temporal lobes bilaterally suggesting cortical oedema
FLAIR: Fluid-attenuated inversion recovery

The amount of venom injected with the sting of a single bee is 0.33 mg. If more than one bee stings, the amount of venom entering the systemic circulation increases. In our patient, it can be thought that with the sting of more than one bee, more venom enters the systemic circulation and the severity of the clinical picture is related to this condition. Bee venom contains various amines and enzymes (4). More immunological reactions are induced compared to the immune sensitivity of individuals. Specific IgE antibodies are bound to high-affinity IgE receptors on the surface of mast cells in individuals who become sensitive to the venom of the bee after a bee sting. These surface antibodies that encounter antigen initiate signal transmission by forming bridging. Microflames move the granules towards the microtubules or plasma membrane. These granules are released out of the cell by exocytosis. Various mediators and cytokines are released at different times as a result of the activation of the mast cell. Ready-to-release mediators; proteases such as histamine, tryptase, chymase, cathepsin G, carboxypeptidase, acid hydrolases and heparin. The mediators that can be released in the early and late stages are leukotrienes B4 and C4, prostaglandin D2, platelet-activating factor (PAF), thromboxane B2, and adenosine. Tumour necrosis factor-alpha, granulocyte-monocyte colony-stimulating factor and transforming growth factor-beta are released in the late period. Among these products, in the first few minutes, pre-synthesized mediators such as mainly histamine, tryptase, heparin, chymase and newly created mediators such as leukotrienes, prostaglandins, PAF; IL-4 is released at the third hour and IL-13 later. Early released substances are responsible for the vascular manifestations of anaphylaxis, and ischemic stroke, which can be seen as neurological involvement, is a result of this mechanism. Substances released in the late period are responsible for immunological inflammation symptoms (5,6).

Possible mechanism mentioned in neurological involvement; although Guillain-Barré syndrome is directly associated with immunological damage as in encephalitis and encephalomyelitis and encephalopathies, it may also result from the direct interaction of enzymes and amines such as phospholipases, hyaluronidase, histamine, serotonin, dopamine, norepinephrine, and acetylcholine receptors (7). In the literature, there have been only 4 reports of a bee sting-induced allergic encephalitis; 2 in Russia, 1 in India and 1 in USA (8-10). Clinical presentation in one of the reports included headache, generalized seizures and response to steroids was observed (7). The other case with similar complaints, had to be treated by multiple anticonvulsants adding to steroids because of the refractory gelastic seizures (10). In our case, seizures were not observed. Similar to the case of Shasaitov and Parkhomenko (8), the clinic manifestations of our case developed by more than one bee stings. In this case, unlike the other case reports, there were systemic and neurological involvements that occurred as a result of different mechanisms related to multiple bee sting. It is thought that causes of the death are the encephalitis by the immunological mechanisms and secondary coagulation factor deficiency based on toxic hepatitis directly caused by bee venom. Our case is precious as it is a demonstrative presentation showing that neurological and systemic involvement due to bee sting develops with many different mechanisms.

## Ethics

**Informed Consent:** Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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

## Authorship Contributions

Concept: Ö.Ö., A.H.A., Design: Ö.Ö., A.H.A., Literature Search: Ö.Ö., Writing: Ö.Ö.

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

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CASE REPORT / *OLGU SUNUMU*

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# An Exceptional Etiology of a Rare Disease: Pneumatosis Intestinalis in the Intensive Care Unit due to Chronic Graft-Versus-Host Disease

## Ender Bir Etiyoloji ile Beraber Nadir Bir Hastalık: Yoğun Bakım Ünitesinde Kronik Graft-Versus-Host Hastalığına Bağlı Pnömatozis İntestinalis

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**ABSTRACT** Pneumatosis intestinalis (PI) is a rare disease, which presents a wide range of severity. Numerous etiologies, including trauma, inflammation, infections, autoimmunity, drugs, and mechanical procedures, gave rise to this complication. Abdominal computerized tomography is the preferred diagnostic tool with high sensitivity. The diagnosis depends on free air detection in the intramural portion of the gastrointestinal system and main and intrahepatic branches of the portal venous structures. However, the exact mechanism is unknown. The clinical scenario may vary from benign to life-threatening. One of the etiological factors that cause PI is the chronic graft-versus-host disease (cGVHD), which must be considered in patients with solid organ or hematological malignancies. Especially, patients who received long-term immunosuppressive therapies and were diagnosed with cGVHD are prone to developing a PI. Many patients experience unnecessary operational risks if underdiagnosed. A multidisciplinary approach by the primary physician, general surgeon, and radiology specialist is necessary for the proper treatment of these patients. This case report aimed to discuss the clinical presentation of PI in the course of cGVHD in the intensive care unit.
**Keywords:** Chronic graft versus host disease, pneumatosis intestinalis, intensive care

**ÖZ** Pnömatozis intestinalis (PI) nadir ve hafiften ağıra değişen geniş bir klinik yelpazede ortaya çıkabilen bir hastalıktır. Travma, enflamasyon, enfeksiyonlar, otoimmünite, ilaçlar ve mekanik işlemleri içeren çok farklı etiyolojiler bu klinik komplikasyona yol açabilir. Abdominal bilgisayarlı tomografi yüksek sensitivite ile tercih edilen tanı aracıdır. Tanı, gastrointestinal kanalın intramural kısımlarında ve portal venin ana gövdesinde ve intrahepatik dallarında serbest hava saptanmasına dayanır. Hastalığın kesin ortaya çıkış mekanizması bilinmemektedir. Klinik bulgular hafiften hayatı tehdit edici durumlara kadar değişiklik gösterebilir. PI'ya neden olabilen ve özellikle solid organ ve hematolojik maligniteli hastalarda akılda tutulması gereken etiyolojik faktörlerden birisi de kronik graft-versus-host hastalığıdır (cGVHD). Uzun süre immünosüpresif ilaç kullanımı öyküsü ve tanı konulmuş cGVHD olan hastalar özellikle bu komplikasyona yatkındır. Doğru tanı konulamaz ise pek çok hasta gereksiz operasyonel risklerle karşı karşıya kalabilir. Bu hastaların uygun tedavileri için hastanın sorumlu hekimi, genel cerrahi uzmanı ve radyoloji uzmanını kapsayan ekibin multidisipliner ortak yaklaşımı gereklidir. Bu olgu sunumunun amacı yoğun bakım ünitesinde cGVHD seyrinde ortaya çıkan PI kliniğini tartışmaktır.
**Anahtar Kelimeler:** Kronik graft-versus-host hastalığı, pnömatozis intestinalis, yoğun bakım

## Introduction

Pneumatosis intestinalis (PI) is a rare disease radiologically characterized by collection of gas in the intestinal wall (1). In some cases, gas can also be seen in intraperitoneal and extra peritoneal spaces and organs (2), and in more severe cases it can be seen in portal venous system which usually accompanies intraabdominal pathologies often associated with surgical conditions (3). Although PI and/or portal venous gas (PVG) can be easily detected by computerized tomography (CT), its clinical significance remains to be a challenge as a wide range of etiologies from benign to catastrophic might be the cause (4,5). PI might have traumatic, inflammatory, mechanical, autoimmune, pulmonary, infectious, drug-related causes. It can also occur as a complication of bacterial or viral infections, interventional procedures such as colonoscopy, chronic obstructive pulmonary disease, gastrointestinal obstructions, immunodeficiency or cancer treatment. One of the most uncommon causes of PI that won't be easily considered in the intensive care unit (ICU) is graft versus host disease (GVHD) (6), unless medical history is well questioned.

The purpose of this case report is to discuss a clinical presentation of PI in the course of chronic GVHD (cGVHD) in the ICU.

## Case Report

A 19-year-old male patient was diagnosed with T-cell acute lymphoblastic leukemia in April 2013 at the age of fifteen. He underwent an HLA 7/10 matched haploidentical transplantation from his mother in February 2014. Due to development of stage 2 skin GVHD on day 20 of transplant, 2 mg/kg methylprednisolone was started. He was discharged on the 30$^{th}$ day with complete donor chimerism. However, diarrheae emerged on day 70 posttransplant during steroid taper. Daily 1.5 liters stool with no microbiological cause led to diagnose stage 3 gastrointestinal GVHD. With the history of skin and intestinal GVHD, ongoing skin changes like hypo-hyperpigmentated areas and pruritic erythematous changes and new onset oral GVHD, the patient was diagnosed as moderate cGVHD. Hepatic GVHD developed on day 517 posttransplant. Photopheresis was scheduled. On day 1,144 posttransplant, at age 19, a skin biopsy was performed, which was reported as cGVHD.

While taking mycophenolate mofetil and metylprednisolone for chronic GVHD, he was admitted to the emergency room with high fever, anorexia, nausea, dyspnea, cough, sputum and syncope. The patient who had a cachectic appearance was also suffering from abdominal pain and diarrhea. Although his abdomen was tender to palpation, neither defence nor rebound was detected. Procalcitonin was 30 ng/mL, C-reactive protein: 211 mg/L in the laboratory values. The patient was transferred to a 3$^{rd}$ stage ICU with the diagnosis of septic shock. Piperacillin-tazobactam, levofloxacin, teicoplanin and voriconazole was commenced immediately after his transfer.

Bilateral pneumonic infiltrations were detected in thorax CT. Intramural air was observed in the stomach wall in abdominal CT scan: Milimetric free-air densities were observed within the perigastric fat tissue adjacent to the cardio-esophageal junction and major curvature of the stomach (Figure 1). Intravascular air was seen in the main portal vein lumen and intrahepatic portal veins, which were more prominent in the arteriolar phase images (Figure 2). Local heterogeneity and increased density were observed in peripancreatic and perigastric fat tissue planes and minimal free peritoneal fluid was observed in this region. The radiologic findings was suggesting early phase of perforation.

An emergency operation planned initially was cancelled after considering his medical history together with his current physical examination. Chronic gastrointestinal GVHD was considered as a potential cause of PI and a conservative aproach was preferred in the follow up with the consensus of intensive care, hematology, general surgery and radiology teams. Enteral feeding was stopped and nasogastric decompression was performed.

Levofloxacin-sensitive *Streptococcus pneumoniae* grew in his blood culture. Cytomegalovirus DNA was also

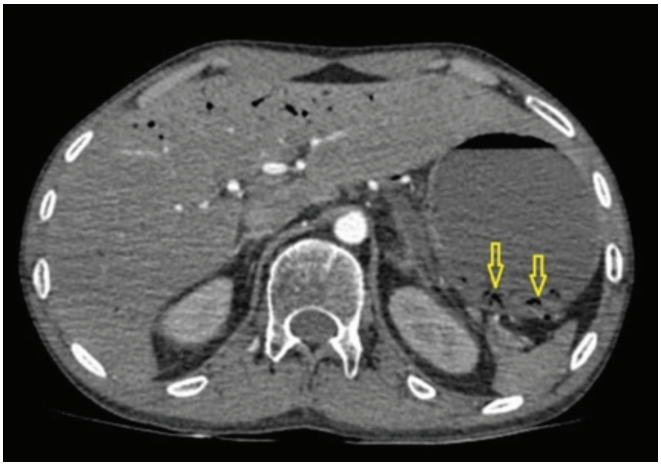

**Figure 1.** Millimetric air densities in the stomach wall

found positive. There was no growth in the urine and stool cultures. The treatment was supplemented with ganciclovir IV 2x5 mg metylprednisolone was continued. Non-invasive mechanical ventilation (NIMV) support was initiated because of hypoxemia. Despite NIMV support, respiratory distress worsened and the patient was electively intubated. On the 4th day of ICU *Acinetobacter* grew in tracheal secretory culture. Antibiotic therapy was switched to colistin intravenous 2x2.5 mg/kg and colistin inhaler 2x75 mg.

The patient was successfully extubated on the 8th day of intubation after he met the weaning criteria. Approximately 20 days after the first CT, control abdominal tomography revealed that the free air densities in the stomach, liver and portal system had resolved (Figure 3).

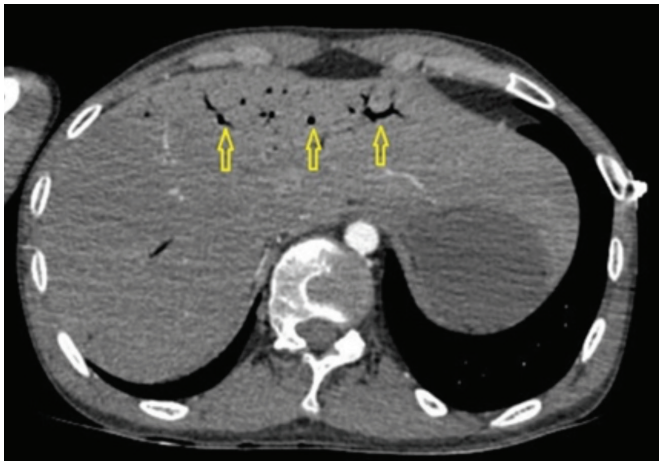

**Figure 2.** Intravascular air in the main portal vein lumen and intrahepatic portal veins

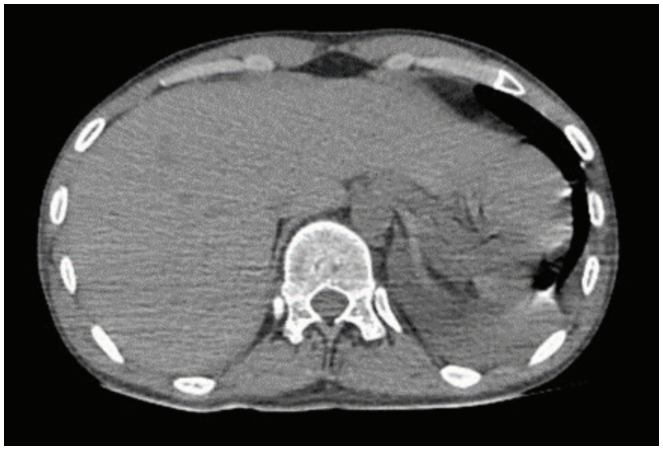

**Figure 3.** Normal appearance on tomography. Air densities have disappeared

## Discussion

PI may be idiopathic (15%) or more frequently secondary (85%) to gastrointestinal or non-gastrointestinal etiologies (7). It can occur in very different clinical situations. It can be asymptomatic in some cases (2), but most patients present with nausea, vomiting, diarrhea and abdominal pain.

Our patient was admitted to the ICU with septic shock. PI was detected in the initial abdominal CT. Some major diseases considered in the differential diagnosis: Intestinal perforation, intraabdominal sepsis, or cGVHD.

Because of the presence of *S. pneumoniae* in blood culture and pneumonic infiltrates in thorax CT, lung was thought to be the primary source of infection. Although there was a possibility of intraabdominal infection, there were no clinical features suggesting an underlying acute abdominal emergency and intraabdominal sepsis. The patient had mild physical examination findings; no signs of peritonitis on abdominal exam (eg, abdominal rigidity, rebound tenderness), no ileus, no metabolic acidosis and low lactate levels in arterial blood gas.

Intraabdominal sepsis related PI is a very rare condition in ICU. PI more often occurs after a major abdominal surgery or endoscopic procedure or during intraabdominal catastrophes (eg, intestinal obstruction, ischemia, infarction, perforation, necrotizing enterocolitis, typhlitis). In one of the two reported cases of intraabdominal sepsis, it was seen that PI was accompanied by paralytic ileus (8). In the other case the diagnosis of septic shock was due to ischemic bowel (9).

GVHD is a very common complication of allogeneic stem cell or bone marrow transplantation and emerges when immunocompetent donor cells recognize recipient cells as foreign. The chronic form of the disease usually occurs a few months after transplantation and is associated with the release of autoreactive T-cells and the induction of antibody production by autoreactive B-cells. Clinical manifestations of chronic GVHD include skin involvement; oral mucosa; gastrointestinal tract; and high serum bilirubin. Reported incidence rates of chronic GVHD range from 6 to 80 percent, depending upon the presence of risk factors and the diagnostic criteria used (10). The skin, liver, gastrointestinal tract, musculoskeletal system and lungs are the principal target organs (11). Among patients with small bowel and colonic involvement, common symptoms and signs include anorexia, nausea, vomiting, chronic diarrhea, malabsorption and weight loss. A scoring system for cGVHD was created by the National Institutes of Health in 2005 and revised in 2014

(10,12). The overall severity is scored as mild, moderate, or severe.

Considering the multi organ involvement and a major disability, our patient appeared to have severe cGVHD. cGVHD in the gastrointestinal tract leads to mucosal atrophy, bacterial and fungal superinfections, fibrosis and malabsorption syndromes with ulcer formation. Intestinal mucosal injury, concomitant infections, infiltration of inflammatory cells and defect in the connective tissue related with steroid therapy, are the predisposing factors to PI (6).

Although PI appears to be based on many factors, its exact cause is unknown. Several theories have been proposed in the literature. Mechanical theory: Gas dissects into the wall of the bowel from the luminal surface or through the serosal surface by tracking along mesenteric blood vessels (13,14). Bacterial theory: PI results from gas-forming bacteria gaining access to the submucosa. Biochemical theory: Luminal bacteria produce excessive amounts of hydrogen gas through fermentation of food. In addition cancer treatment or steroid administration in immunosuppressed patients can lead to impaired lymphatic drainage. It can also cause mucosal injury and aspiration of air through the intestinal lumen. It was obvious that our patient had long-term steroid use and accompanying immunosuppression.

Emergent exploratory laparotomy indications for PI are reported to be 1. Signs of peritonitis (eg, abdominal rigidity, rebound tenderness), 2. Metabolic acidosis (arterial pH<7.3, $HCO_3$<20 mmol/L), 3. Lactate >2.0 mmol/L, 4. PVG (7,15). None of them were present in our patient except PVG. Our decison was conservative treatment. Combination of antibiotics and an elemental diet referaining from enteral feeding was our protocol.

cGVHD, should be considered as an etiological factor in the differential daignosis of PI with ischemic mucosal lesions and possible gastrointestinal perforation and treatment plan should be made with caution. The presence of free air and fluid in the peritoneal cavity is not always an evidence of perforation, and can be seen as a complication of PI. For this reason, close colloboration with radiology, surgery and intensive care doctors might be life saving.

Regardless of the underlying pathologic factor, PI has a wide ethiological spectrum from life-threatening to benign. For this reason management can range from emergency surgery to observation. Clinicians need to interpret the radiographic findings in accordance with the clinical scenario so that they can make a correct diagnosis and apply appropriate treatment. In patients with gastrointestinal GVHD, PI or pneumoperitoneum is not always related with a perforation and conservative approach should always be the primary approach unless perforation is proved, to mimimize unnecessary surgical interventions. Early recognition of the clinical picture is perhaps the most important factor in deciding whether to distinguish critically dangerous and life-threatening causes from non-urgent causes effectively.

## Ethics

**Informed Consent:** An informed consent form was obtained.

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

## Authorship Contributions

Concept: T.Ç., Design: T.Ç., M.K., Data Collection and Process: T.Ç., H.Ö., B.T.E., V.U., Analysis or Interpretation: T.Ç., H.Ö., M.K., V.U., Y.S., B.C., Literature Search: T.Ç., H.Ö., B.T.E., Writing: T.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.

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