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AMAÇ

Türkiye'de ve yurtdışında anestezi, algoloji, yoğun bakım ve cerrahi bilimler alanlarında yapılan nitelikli araştırma çalışmalarını, vaka sunumlarını ve derlemeleri ulusal ve uluslararası bilim ortamına sunarak duyurmak ve paylaşmak; ayrıca sürekli bir eğitim platformu oluşturarak bilimsel iletişimin gelişimine katkıda bulunmaktır.

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AIM

The aim of the journal is to announce offering of national and international scientific environment and share high quality research studies, case studies and reviews conducted in the field of anesthesia, pain medicine, intensive care and surgical sciences both in Turkey and abroad; and to contribute to the development of scientific communication by establishing a continuous educational platform.

SCOPE

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1. Yazarlar

Yazarlar, bu belgenin IIA ve B bölümlerinde ayrıntılı olarak belirtilen tüm yazarlık ilkeleri ve çıkar çatışması bildirimlerine uymalıdır.

a. Yırtıcı veya Sahte Dergiler

Sayıları günümüzde hızla artan adı 'bilimsel dergi' olan ama kar amacı güden herhangi bir eleme olmaksızın ücret karşılığı tüm gönderileri yayınlayan dergiler nedeniyle ki bunlara predetör dergiler denilmektedir. Bilimsel dergicilikte bazı standartları korumak daha önemli hale gelmiştir. Bu nedenle dergimiz ICMJE, COPE ve WAME gibi kuruluşların önerilerini takip etmekte ve standartlarına uymaktadır.

2. Dergiler

a. Gizlilik

Dergilere gönderilen yazılar, yazarın özel, gizli mülkü olan ayrıcalıklı iletişimdir ve yazarlar, bir yazının ayrıntılarının herhangi birinin veya tamamının erken ifşa edilmesiyle zarar görebilir.
Bu nedenle editörler, el edilip edilmediği ve incelenip değerlendirilmediği, inceleme sürecindeki içeriği ve durumu, gözden geçirenlerin eleştirisi ve nihai kaderi de dahil olmak üzere yazarlar ve gözden geçirenler dışındaki kimseyle paylaşılmamalıdır. Üçüncü şahıslardan yazılar ve yasal işlemlerde incelemeleri kullanma talepleri kibarca reddedilmeli ve editörler mahkeme celbi olarak bu tür gizli materyalleri temin etmemek için elinden geleni yapmalıdır.
Editörler, hakemlerin yazıları, ilgili materyalleri ve içerdikleri bilgileri kesinlikle gizli tutmaları gerektiğini de açıkça belirtmelidir. Hakemler ve editoryal personel, yazarın çalışmasını kamuya açık olarak tartışmamalı ve hakemler, makale yayınlanmadan önce yazarların fikirlerini uygun görmemelidir. Hakemler makaleyi kişisel kullanımları için saklamamalı ve makalelerin basılı kopyalarını imha etmeli ve incelemelerini gönderdikten sonra elektronik kopyaları silmelidir.
Bir makale reddedildiğinde, yerel yönetmeliklerde saklama gerekmedikçe dergilerin kopyalarını editör sistemlerinden silmeleri en iyi yöntemdir. Reddedilen yazıların kopyalarını tutan dergiler, bu uygulamayı Yazarlar Bilgilendirmesinde açıklamalıdır.
Bir makale yayınlandığında, dergiler, çalışmalarla ilgili gelecekteki soruları cevaplamak için, yerel düzenlemelere bağlı olarak, asıl başvuru, gözden geçirme, gözden geçirme ve yazışmaların kopyalarını en az üç yıl süreyle ve muhtemelen kalıcı olarak saklamalıdır.
Editörler hakemlerin ve yazarların izni olmadan hakemlerin yorumlarını yayınlamamalıdır. Dergi politikası yazarları gözden geçirenin kimliğine karşı koruyacaksa ve yorumlar imzalanmadıysa, söz konusu kimliği hakemlerin ifade ettiği yazılı izin olmadan yazara veya başkalarına ifşa edilmemelidir.
Sahtekârlık veya sahtekarlık iddiası varsa gizliliğin ihlal edilmesi gerekebilir, ancak editörler yazarları veya hakemleri bu konuda istekli olduklarını bildirir ve gizlilik aksi takdirde onurlandırılmalıdır.

b. Zamanlama

Editörler yazıların kendileri için mevcut kaynaklarla zamanında işlenmesini sağlamak için ellerinden geleni yapmalıdır. Eğer editörler bir makale yayınlayacaksa, zamanında yapmayı denemeli ve planlanan gecikmeler yazarlarla müzakere edilmelidir. Bir derginin bir makaleye devam etme niyeti yoksa, editörler, yazarın farklı bir dergiye göndermelerine izin vermek için makaleyi en kısa sürede reddetmeye çalışmalıdır.

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c. Hakem Değerlendirmesi

Hakem değerlendirmesi, dergilere sunulan yazıların, genellikle editoryal personelin bir parçası olmayan uzmanlar tarafından eleştirel bir değerlendirmesidir. Tarafsız, bağımsız, eleştirel değerlendirme, bilimsel araştırma da dahil olmak üzere tüm bilimsel çalışmaların özünü oluşturduğu için,hakem incelemesi, bilimsel sürecin önemli bir uzantısıdır.
Hakem değerlendirmesinin gerçek değeri tartışılmaktadır, ancak süreç bilimsel topluluk üyeleri arasında bir makale için adil bir duruşma yapılmasını kolaylaştırmaktadır. Daha pratik olarak, editörlerin hangi yazıların dergileri için uygun olduğuna karar vermelerine yardımcı olur. Hakem değerlendirmesi genellikle yazarların ve editörlerin raporlama kalitesini iyileştirmelerine yardımcı olur.
Sistemlerin yerinde olmasını sağlamak derginin sorumluluğundadır.
Uygun hakemlerin seçimi için hakemlerin, sadece e-posta için ek materyaller de dahil olmak üzere, makalenin değerlendirilmesine ilişkin tüm materyallere erişebilmesini sağlamak ve hakem değerlendirmelerinin bağlamda uygun bir şekilde değerlendirilmesini ve yorumlanmasını sağlamak editörün sorumluluğundadır.
Hakemli bir dergi, gözden geçirilmek üzere gönderilen makaleleri göndermekle yükümlü değildir ve eleştirmenlerin önerilerini olumlu veya olumsuz olarak izlemekle yükümlü değildir. Bir derginin editörü sonuçta tüm içeriğin seçiminden sorumludur ve editöryal kararlar, derginin uygunluğu gibi bir makalenin kalitesiyle ilgili olmayan konulardan haberdar edilebilir. Bir editör, eserin bütünlüğü ile ilgili endişeler ortaya çıktığında kabul edildikten sonra da dahil olmak üzere herhangi bir anda herhangi bir makaleyi reddedebilir.
Dergiler, incelemeye gönderdikleri yazıların sayısı ve türleri, her bir yazı için aradıkları gözden geçirenlerin sayısı ve türleri, inceleme sürecinin açık veya kör olması ve inceleme sürecinin diğer yönleri bakımından farklılık gösterebilir. Bu nedenle ve yazarlara sunulan bir hizmet olarak dergiler, hakem inceleme sürecinin bir tanımını yayınlamalıdır.
Dergiler bir makaleyi kabul etme veya reddetme kararını nihai olarak gözden geçirmeli ve hakemlerin hakemlerinin dergilerine katkısını kabul etmelidir. Editörler, hakemlerin yorumlarını aynı makalenin hakemleri ile paylaşmaya teşvik edilir, böylece hakemler inceleme sürecinde birbirlerinden öğrenebilirler.
Hakem değerlendirmesinin bir parçası olarak, editörlerin araştırma protokollerini, protokolden ayrıysa istatistiksel analiz planlarını ve / veya projeye özgü çalışmalarla ilgili sözleşmeleri incelemeleri teşvik edilir. Editörler, yayın için bu tür çalışmaları kabul etmeden önce yazarları bu tür belgeleri yayın sırasında veya sonrasında kamuya açık hale getirmeye teşvik etmelidir. Bazı dergiler, bu belgelerin kamuya kabul edilmesinin bir koşulu olarak ilan edilmesini gerektirebilir.
Bağımsız veri analizi ve kamuya açık verilerin mevcudiyeti için günlük gereklilikleri, bu revizyon sırasında yayınlanmıştır; bu, yayın öncesi ve sonrası hakem incelemesi için verilerin mevcudiyetinin önemine dair gelişen görüşleri yansıtmaktadır. Bazı dergi editörleri şu anda yayın için çalışmaları kabul etmeden önce bağımsız bir biyoistatistikçi tarafından deneme verilerinin istatistiksel analizini talep etmektedir. Diğerleri yazarlardan çalışma verilerinin üçüncü şahıslar tarafından görüntülemek ve / veya yeniden analiz etmek için kullanıp kullanamayacağını belirtirken, başkaları da yazarların verilerini gözden geçirmek veya yeniden analiz için başkalarıyla paylaşmasını teşvik eder veya talep eder. Her dergi, potansiyel yazarların kolayca erişebileceği bir yerde veri analizi ve kayıt için kendi spesifik gereksinimlerini oluşturmalı ve yayınlamalıdır.
Bazı insanlar gerçek bilimsel hakem değerlendirmesinin sadece bir bildiri yayınlandığı tarihte başladığına inanmaktadır. Bu bağlamda, tıbbi dergiler, okuyucuların yayınlanmış makaleler hakkında yorum, soru veya eleştiriler sunma mekanizmasına sahip olmalı ve yazarların uygun şekilde cevap vermeleri ve dergi verilerinin talepleri ile işbirliği yapmaları ya da bildiri ile ilgili ek bilgi talep etmeleri gerekir. yayından sonra ortaya çıkar (bkz. Bölüm III).

d. Bütünlük

Editöryal kararlar, bir yazının dergiye uygunluğuna ve yazının orijinalliği, kalitesi ve önemli sorular hakkındaki kanıtlara katkısına dayanmalıdır. Bu kararlar ticari çıkarlardan, kişisel ilişkilerden ya da gündemlerden ya da olumsuz ya da kabul gören bilgeliği inandırıcı bir şekilde sorgulayan bulgulardan etkilenmemelidir. Ayrıca, yazarlar yayın için sunmalı ya da kamuya açık bir şekilde sunmalı ve editörler yayın dikkate alınmamalı, istatistiksel olarak anlamlı olmayan veya sonuçsuz bulguları olan bulgularla yapılan çalışmaları kapsam dışı bırakmamalıdır. Bu tür çalışmalar, meta-analiz yoluyla diğer çalışmalarla bir araya getirildiğine dair kanıtların hala önemli soruların cevaplanmasına yardımcı olabileceğine dair kanıt sağlayabilir ve bu tür olumsuz ya da sonuçsuz bulguların halka açık bir şekilde kaydedilmesi, çabanın istenmeyen şekilde çoğaltılmasını önleyebilir ya da benzer çalışmaları düşünen diğer araştırmacılar için değerli olabilir. Dergiler, temyiz sürecini açıkça belirtmeli ve temyiz ve şikayetlere cevap verecek bir sisteme sahip olmalıdır.

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Editöre Mektup

Olgu Sunumları

JoCASS
Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

COMPARISON OF FASCIOCUTANEOUS FLAPS AND GRACILIS MUSCLE FLAPS IN ISCHIAL PRESSURE ULCER RECONSTRUCTION

İSKİAL BASI ÜLSERLERİNİN ONARIMINDA GRASİLİS KAS FLEBİNİN FASYOKUTAN FLEPLERLE KARŞILAŞTIRILMASI

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Abstract

Aim: The reconstruction options for pressure ulcers have been widely reported, but there is still a need for ideal method in ischial pressure ulcer reconstruction. The aim of this study is to compare the development of recurrence and wound site complications and length of stay in two different patient groups who were treated for ischial pressure ulcers with a combination of gracilis muscle flap and fasciocutaneous flap procedures and those who were treated only with local fasciocutaneous flaps.

Methods: Between 2016 and 2022, a total of 34 patients with Grade 3 and 4 ischial pressure ulcers were analyzed retrospectively in the Plastic, Reconstructive, and Aesthetic Surgery Clinic of Çukurova University's Faculty of Medicine. Of this total patient group, 18 were treated with a combination of gracilis muscle flap and fasciocutaneous flap procedures (Group 1) and 16 were treated with local fasciocutaneous flaps (Group 2).

Results: The mean age of the patients was 39 in Group 1 and 44.5 in Group 2. Group 1 patients had a mean length of stay of 9 days, while those in Group 2 had a mean length of stay of 15 days. Early postoperative complications such as dehiscence and hematoma occurred in both patient groups. While complications occurred in 6 patients in Group 1 (33.3%), 7 patients experienced complications in Group 2 (43.8%).

Conclusions: Reconstruction of ischial pressure ulcers is very problematic due to high recurrence rates. Therefore, a wide range of repair options have been defined. Fasciocutaneous flaps may be insufficient to obliterate the dead space alone. In addition to a skin flap, gracilis muscle flap can be an effective option for the ischial cavity with better surgical outcomes.

Keywords: Ischial pressure ulcer, gracilis muscle flap, reconstruction

Öz

Amaç: Bası ülserlerinin onarımı için birçok seçenek rapor edilmekle birlikte iskial bası ülserlerinin onarımında hala ideal bir yöntem bulunmamaktadır. Bu çalışmanın amacı; iskial bası ülseri nedeniyle gracilis kas flebi ve fasyokutan flep kombinasyonuyla onarım yapılan ve sadece lokal fasyokutan fleplerle onarım yapılan iki ayrı hasta grubunun yara yeri komplikasyon gelişimi ve yatış süresi açısından karşılaştırılmasıdır.

Yöntemler: Çukurova Üniversitesi Tıp Fakültesi Plastik, Rekonstrüktif ve Estetik Cerrahi Kliniğinde, 2016-2021 yılları arasında grade 3 ve 4 iskial bası ülseri nedeniyle gracilis kas flebi ve fasyokutan flep kombinasyonu ile onarım yapılan 18 hasta (Grup1), lokal fasyokutan fleplerle onarım yapılan 16 hasta (Grup2) olmak üzere toplam 34 hasta retrospektif olarak incelenmiştir.

Bulgular: Hastaların yaş ortalaması Grup1'de 39, Grup 2'de 44,5'ti. Ortalama yatış süresi Grup1'de 9 gün iken, Grup 2'de 15 gündü. Hastalarda sütur ayrışması ve hematom gibi erken postoperatif komplikasyonlar gelişti. Grup1'de 6 hastada komplikasyon gelişirken (%33,3), Grup2'de 7 hastada komplikasyon gelişti (%43,8).

Sonuç: iskial bası ülserlerinin onarımı yüksek nüks oranları nedeniyle oldukça sorunludur. Bu nedenle onarımda çok sayıda seçenek tanımlanmıştır. Tek başına fasyokutan fleplerle yapılan onarımlar iskial bölgedeki bası ülseri poşunu doldurmada yetersiz kalabilir. Gracillis kasını iskial poşa yerleştirip üzerine fasyokutan fleplerle kombine etmek erken postoperatif komplikasyonları ve nüks gelişimini azaltmak için dikkate alınması gereken bir seçenektir.

Anahtar Kelimeler: İskial bası ülseri, gracilis kas flebi, rekonstruksiyon

Introduction

Pressure sores develop as a result of ischemic damage to the skin and subcutaneous tissues caused by constant exposure to external pressure and friction[1]. Although early-stage pressure sores can be treated with conservative methods, those in advanced stages such as Grades 3 and 4 are treated with surgery. In these patients, the principles of surgical treatment include complete excision of the ulcer and bursa, removal of infected bones or bones that may cause future pressure, and covering of the region with well-blooded tissue[2]. Recurrence rates vary widely in long-term follow-up after surgical treatment[3,4]. The development of recurrence, which can be explained by a variety of factors that vary depending on the wound and the patient, has an impact on the life quality of patients and continues to be a significant issue for the health system due to rising costs.

In the sitting position, the ischial tuberosity is the area that is exposed to the most pressure, and ischial pressure sores are common in patients who spend a lot of time in wheelchairs[5,6]. There are numerous surgical options for closing ischial pressure sores, including V-Y advancement flaps, perforator flaps, gluteus maximus, gracilis, hamstring muscle flaps, and free flaps[7-10]. There is no ideal method, and each method has advantages, disadvantages, and varying rates of recurrence[11]. In the literature, a wide variety of muscle flaps are used in the surgical treatment of pressure sores to fill the dead space. The aim of this study is to investigate whether the gracilis muscle flap, which is used to fill the dead space in addition to the traditional fasciocutaneous flaps in the reconstruction of ischial pressure ulcers, causes changes in the recurrence rates and length of stay.

Materials and Methods

The study was conducted in accordance with the Helsinki Declaration principles. The ethics committee approval was granted on 09.07.2021 by the Çukurova University Faculty of Medicine Clinical Research Ethics Committee (meeting:113, decision:52). 34 patients who underwent surgery for ischial pressure ulcer between January 2016 and January 2022 were retrospectively evaluated from the medical records and surgical logbooks. All patients underwent surgery in the Plastic Reconstructive and Aesthetic Surgery Clinic at Çukurova University's Faculty of Medicine. All patients participating in the study provided written consent. Patients with ischial pressure ulcers who were treated with a combination of gracilis muscle flap and fasciocutaneous flap procedures during this period were classified as Group 1, and patients who only received fasciocutaneous flaps were classified as Group 2. Etiological and demographic characteristics of the patients, repair methods, development of dehiscence in the early postoperative period, and length of stay were recorded. The patients in the two groups were compared in terms of complications developed and the length of stay. Patients with poor health condition and a short life expectancy were excluded from the study.

- *Operation technique*

All the patients had received conservative treatment with antibiotherapy before the operation. The operations were performed in the prone position under general anesthesia. First, the ulcer and bursa were completely excised. Bony spurs were softened if necessary. Gracilis muscle was identified from its origin, then detached from its insertion point through a distal thigh skin incision. Gracilis was dissected to the main pedicle, then transposed to ischial cavity under the subcutaneous tunnel (Figures 1-2). The muscle was passed through the tunnel and sutured to fill the dead space (Figures 3-4).

The muscle was sutured appropriately by covering it using a fasciocutaneous flap procedure such as V-Y advancement,

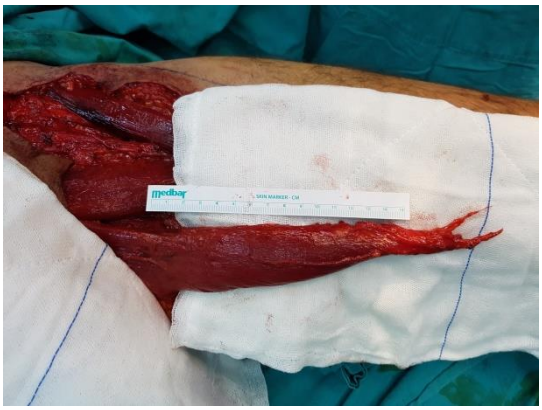

Figure 1. Preparation of the gracilis muscle flap

Figure 4. Suturation of the muscle

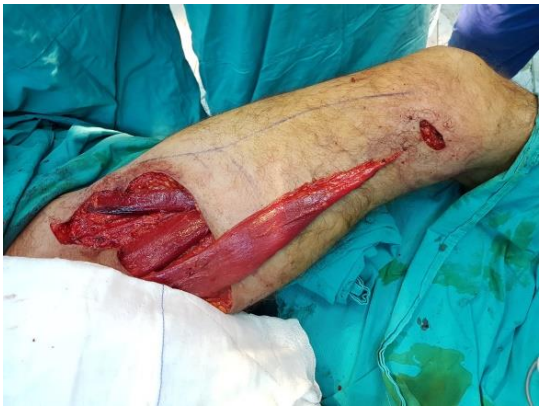

Figure 2. Donor site of the gracilis muscle flap

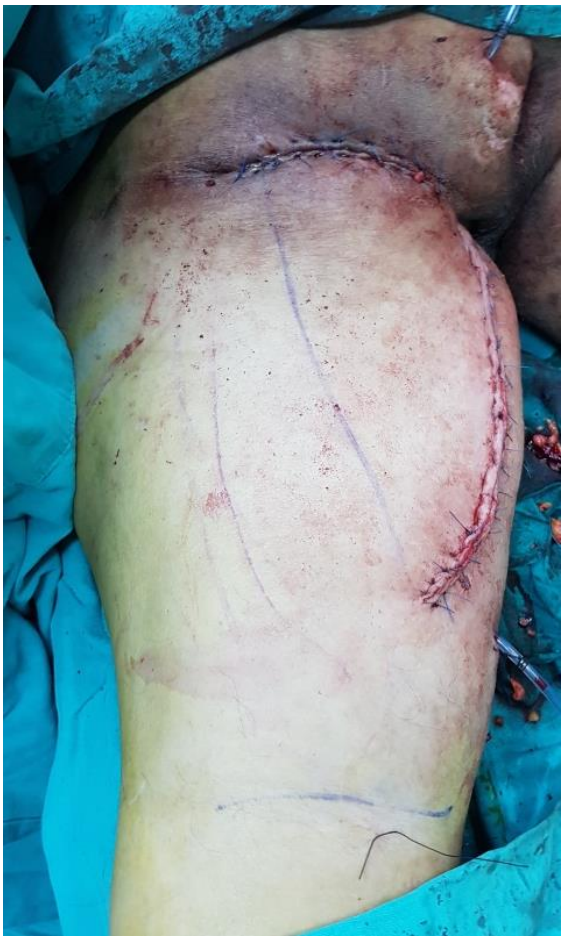

Figure 5. Covering the muscle flap with fasciocutaneous rotation flap

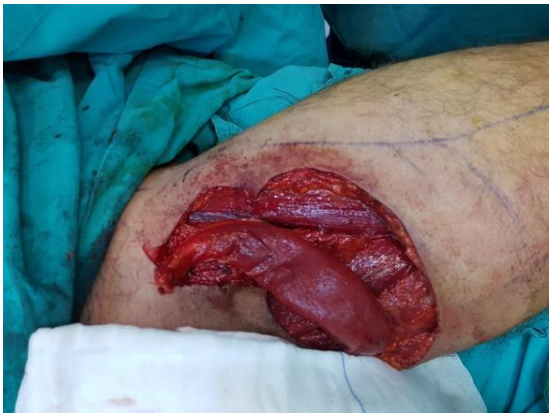

Figure 3. Filling the dead space with the muscle flap

hatched, SGAP (superior gluteal artery perforator), and IGAP (inferior gluteal artery perforator) (Figure 5).
A hemovac drain was placed under the flap and in the donor area. In Group 2 patients, the reconstruction was performed using only fasciocutaneous flaps without the gracilis muscle.
A standard diet program was applied after surgery. The patients were positioned appropriately to prevent pressure on the flap in the postoperative period. While hospitalized, the patients were checked for early complications with twice-daily visits. They were evaluated at 1 week, 1 month, 3 months, and 6 months outpatient clinic controls after discharge.

- *Statistical analysis*

Data were analyzed using the IBM SPSS 25.0 program. The assumption of normality was accepted when the skewness and kurtosis values of the variables were between -1.5 and +1.5 (B.G. Tabachnick, L.S. Fidell Using Multivariate Statistics (sixth ed.) Pearson, Boston, 2013).
The Mann Whitney U test was used to determine whether the non-normally distributed variables differed by group in terms of their medians. Medians and quartiles are used as representations (shown as Median (1st Quartile-3rd Quartile) (Field, A. 2013. Discovering statistics using IBM SPSS statistics. Sage).
Fisher Exact statistics were used if the expected number of observations was less than 5, and Yate's statistics were used if it was between 5 and 25.

Results

Eighteen of the 34 patients in the study (52.9%) were in Group 1, and 16 (47.1%) were in Group 2. The overall F/M ratio was 13/21. The etiological data of the patients are listed in Table 1. The median age values were 39 and 44.5 for Group 1 and 2, respectively, and no statistically significant difference in median age was found between the groups (p=0.31). The median length of stay durations were 9 and 15 days for Group 1 and 2, respectively, and no statistically significant difference in median length of stay duration was found between the groups (p=0.01). The duration of hospitalization of the patients in Group 2 was longer than Group 1. Suture dehiscence and recurrence were seen in 6 patients (33.3%) in Group 1, and 7 patients (43.8%) in Group 2. In this respect, no statistical difference was found between the two groups (Table 2).

Table 1. General Patient Characteristics

	Group 1	Group 2	Total
Number of Patients	18 (52.9)	16 (47.1)	34 (100)
Sex (F/M)	6/12	7/9	13/21
Etiology			
• Traffic accident	6	7	13 (38.2)
• Fall from height	6	1	7 (20.6)
• Meningomyelocele	3	3	6 (17.6)
• Cerebrovascular incident	2	2	4 (11.8)
• Occupational accident	0	2	2 (5.9)
• Vertebral mass	1	1	2 (5.9)

Table 2. Analysis of Quantitative Variables

	Group 1	Group 2	
Age	39 (28.5-53.25)*	44.5 (38.25-56.75)*	p=0.31 U=64.5
Length of Stay	9 (6.75-12)*	15 (10.25-21.5)*	Z=-2.75 p=0.01
Sex	n (%)	n (%)	
• Male	12 (66.7)	9 (56.3)	x2=0.07
• Female	6 (33.3)	7 (43.8)	p=0.79a
Complications	n (%)	n (%)	
• No	12 (66.7)	9 (56.3)	x2=0.07
• Yes	6 (33.3)	7 (43.8)	p=0.79a

a; Yate's Statistics, * Median (1st quartile-3rd quartile), the p<0.05 value was accepted as significant.

Discussion

There are a variety of reasons why treatment of pressure sores in the ischial region is more difficult than in the sacral and trochanteric regions. Pressure sores in the sacral and trochanteric regions occur in the supine position, whereas pressure sores in the ischial region occur as a result of sitting for a long time. In the sitting position, the pressure on the ischial region is greater than the pressure on the sacral region in the supine position[11,12]. In other words, the ischial region is exposed to a greater burden. Because the dead space in the ischial region is larger than in other areas, infection is more prevalent in this region[3]. Furthermore, contamination and maceration with urine and feces are more common due to anatomical susceptibility[13]. Due to these disadvantages, surgeons often look for different flap options in the reconstruction of ischial pressure sores. The most commonly used flaps are fasciocutaneous, musculocutaneous, and, more recently, perforator flaps. Fasciocutaneous flaps are considered by some to be insufficient to fill the dead space in the ischial region and some argue that moving muscle to the region will provide sufficient volume to fill the dead space and that richer vascularity can control infection[9,14]. Indeed, muscle flaps can be a good option for closing the dead space and controlling infection in pressure ulcers with deep pouches[15]. In general, hamstring and gluteus maximus muscle flaps are preferred in this region[9,14,16,17].

The rich vascularity of muscle flaps provides an advantage; however, these flaps have been questioned due to studies showing that the muscle atrophies significantly over time[18,19]. Loss of muscle function is disadvantageous in non-paraplegic patients[20]. Experimentally, compression of musculoskeletal flaps causes tissue hypoxia, resulting in muscle necrosis without skin necrosis[21]. For these reasons, there is still no consensus about whether muscle flaps should be used in the reconstruction of pressure sores[22].

In the present research, gracilis muscle flaps together with other fasciocutaneous flaps were preferred in the reconstruction of ischial pressure sores. As a long muscle, the gracilis provides sufficient volume to fill the dead space. The preparation of the muscle flap is simple. It is possible to cut the distal insertion region with a small incision in the distal thigh after locating the

proximal part, pass the muscle through the tunnel, and fill the defect easily. Since this procedure does not cause extensive scar development, it will not limit future flap options. Also, blood loss is minimal.
Muscle reconstruction was carried out using a fasciocutaneous hatched flap, V-Y thigh flap, or IGAP flap. There was no difference between the groups in terms of suture dehiscence and recurrence in the early postoperative period. However, the length of stay was shorter in patients on whom muscle flaps were used. Restoration was easier when there was suture dehiscence in the muscle flap group due to the fact that the muscle filled the dead space, allowing the fasciocutaneous flap to adapt to the defect more easily. When suture dehiscence and recurrence developed in the group treated using only fasciocutaneous flaps, the dead space could not be filled completely, and secondary procedures become difficult. The belief is that the long length of stay in Group 2 is related to this situation.
The limitations of this study are that it is retrospective, and the accuracy of the study depends on the accuracy of the medical records. Furthermore, the presence of more than one surgeon, the fact that flap choice was determined by the surgeon, and the inability to standardize factors such as nutrition and antibiotic prophylaxis of the patients before the surgery are other disadvantages of the study. Moreover, a further disadvantage of the technique used in this research is that in some patients, the tone and volume of the gracilis muscle may have been insufficient.

Conclusion

Reconstruction of ischial pressure ulcers is very difficult due to high recurrence rates. The gracilis muscle flap can be considered an alternative option in this type of reconstruction because it is a simple technique that causes minimal donor site morbidity and does not limit future flap options.

Author contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

Authors declared no financial support.

Ethical approval

This study, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
The study was approved by the Çukurova University Faculty of Medicine Clinical Research Ethics Committee (09.07.2021, meeting:113, decision:52)

References

1. Mimura M, Ohura T, Takahashi M, et al. Mechanism leading to the development of pressure ulcers based on shear force and pressures during a bed operation: influence of body types, body positions, and knee positions. Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society 2009;17(6):789-96. doi: 10.1111/j.1524-475X.2009.00540.x
2. Kwon R, Janis J. Pressure sores. In: Neligan PC, ed. Plastic Surgery. 3rd ed. Philadelphia, PA: Saunders Elsevier, 2013.
3. Yamamoto Y, Tsutsumida A, Murazumi M, et al. Long-term outcome of pressure sores treated with flap coverage. Plastic and reconstructive surgery 1997;100(5):1212-17. doi: 10.1097/00006534-199710000-00021
4. Disa JJ, Carlton JM, Goldberg NH. Efficacy of operative cure in pressure sore patients. Plastic and reconstructive surgery 1992;89(2):272-78. doi: 10.1097/00006534-199202000-00012
5. Cushing CA, Phillips LG. Evidence-based medicine: pressure sores. Plastic and reconstructive surgery 2013;132(6):1720-32. doi: 10.1097/PRS.0b013e3182a808ba
6. Kim YS, Lew DH, Roh TS, et al. Inferior gluteal artery perforator flap: a viable alternative for ischial pressure sores. Journal of plastic, reconstructive & aesthetic surgery : JPRAS 2009;62(10):1347-54. doi: 10.1016/j.bjps.2008.03.026
7. Lee SS, Huang SH, Chen MC, et al. Management of recurrent ischial pressure sore with gracilis muscle flap and V-Y profunda femoris artery perforator-based flap. Journal of plastic, reconstructive & aesthetic surgery : JPRAS 2009;62(10):1339-46. doi: 10.1016/j.bjps.2007.12.092

8. Higgins JP, Orlando GS, Blondeel PN. Ischial pressure sore reconstruction using an inferior gluteal artery perforator (IGAP) flap. British journal of plastic surgery 2002;55(1):83-85. doi: 10.1054/bjps.2001.3713
9. Demirseren ME, Ceran C, Aksam B, et al. Clinical Experience With the Combination of a Biceps Femoris Muscle Turnover Flap and a Posterior Thigh Fasciocutaneous Hatchet Flap for the Reconstruction of Ischial Pressure Ulcers. Annals of plastic surgery 2016;77(1):93-96. doi: 10.1097/SAP.0000000000000290
10. Lemaire V, Boulanger K, Heymans O. Free flaps for pressure sore coverage. Annals of plastic surgery 2008;60(6):631-34. doi: 10.1097/SAP.0b013e31812c1465
11. Keys KA, Daniali LN, Warner KJ, et al. Multivariate predictors of failure after flap coverage of pressure ulcers. Plastic and reconstructive surgery 2010;125(6):1725-34. doi: 10.1097/PRS.0b013e3181d51227
12. Foster RD, Anthony JP, Mathes SJ, et al. Ischial pressure sore coverage: a rationale for flap selection. British journal of plastic surgery 1997;50(5):374-79. doi: 10.1016/S0007-1226(97)90548-8
13. Vohra RK, McCollum CN. Pressure sores. BMJ (Clinical research ed) 1994;309(6958):853-57. doi: 10.1136/bmj.309.6958.853
14. Burm JS, Hwang J, Lee YK. A New Option for the Reconstruction of Primary or Recurrent Ischial Pressure Sores: Hamstring-Adductor Magnus Muscle Advancement Flap and Direct Closure. Annals of plastic surgery 2018;80(4):400-05. doi: 10.1097/SAP.0000000000001280
15. Gosain A, Chang N, Mathes S, et al. A study of the relationship between blood flow and bacterial inoculation in musculocutaneous and fasciocutaneous flaps. Plastic and reconstructive surgery 1990;86(6):1152-62; discussion 1163
16. Bertheuil N, Aillet S, Heusse JL, et al. Ischial pressure ulcers: long-term outcome of 2 surgical techniques. Annals of plastic surgery 2014;73(6):686-91. doi: 10.1097/SAP.0b013e31828587f0
17. Ku I, Lee GK, Yoon S, et al. A dual padding method for ischial pressure sore reconstruction with an inferior gluteal artery perforator fasciocutaneous flap and a split inferior gluteus maximus muscle flap. Archives of plastic surgery 2019;46(5):455-61. doi: 10.5999/aps.2019.00031
18. Daniel RK, Faibisoff B. Muscle coverage of pressure points--the role of myocutaneous flaps. Annals of plastic surgery 1982;8(6):446-52. doi: 10.1097/00000637-198206000-00002
19. Yamamoto Y, Ohura T, Shintomi Y, et al. Superiority of the fasciocutaneous flap in reconstruction of sacral pressure sores. Annals of plastic surgery 1993;30(2):116-21. doi: 10.1097/00000637-199302000-00004
20. Verpaele AM, Blondeel PN, Van Landuyt K, et al. The superior gluteal artery perforator flap: an additional tool in the treatment of sacral pressure sores. British journal of plastic surgery 1999;52(5):385-91. doi: 10.1054/bjps.1999.3101
21. Nola GT, Vistnes LM. Differential response of skin and muscle in the experimental production of pressure sores. Plastic and reconstructive surgery 1980;66(5):728-33. doi: 10.1097/00006534-198011000-00008
22. Thiessen FE, Andrades P, Blondeel PN, et al. Flap surgery for pressure sores: should the underlying muscle be transferred or not? Journal of plastic, reconstructive & aesthetic surgery : JPRAS 2011;64(1):84-90. doi: 10.1016/j.bjps.2010.03.049

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EVALUATION OF MORTALITY RISK WITH CURB-65 AND PSI IN PATIENTS WITH AND WITHOUT GERIATRIC COVID-19 PNEUMONIA

GERİATRİK COVID-19 PNÖMONİSİ OLAN VE OLMAYAN HASTALARDA CURB-65 VE PSI İLE MORTALİTE RİSKİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: The evaluation and management of pneumonia resulting from the infections of coronavirus disease 2019 (COVID-19) urgently require assessing disease severity to decide on the hospital admission and determine the therapeutic needs and options. This study compared the effectiveness of the CURB-65 scoring system and pneumonia severity index (PSI) to evaluate the mortality risk in the geriatric group having COVID-19 pneumonia and with other non-COVID-19 pneumonia.

Methods: 527 patients in ages 65 years or older, whose computerized tomography scans showed ground glass densities, were selected among 21,134 patients who applied for laboratory confirmation of COVID-19. All demographic, clinical, and laboratory data were retrospectively scanned, and selected patients having COVID-19 pneumonia or non-COVID-19 pneumonia were followed up.

Results: The overall mortality rate among all patients was 25.6%, the ratio of the patients having COVID-19 pneumonia was 14.3%, and the ratio of patients having non-COVID-19 pneumonia was 29.2%. ROC analysis showed that PSI>group III among COVID-19 patients had an effective discriminative effectiveness in predicting mortality with 77.8% sensitivity, 73.2% specificity, PPV 32.6%, NPV 95.2% (AUC:0.800, 95% CI: 0.720–0.866; P<0.0001). In predicting mortality in COVID-19 pneumonia patients with a CURB-65 score >2, sensitivity was 66.7%, PPV 60% specificity, and NPV 94.3% (AUC: 0.857, 95% CI: 0.783–0.913; P<0.0001).

Conclusions: For pneumonia patients with a PSI score greater than three and CURB-65 score greater than two, COVID-19 and non-COVID-19 infections are powerful scores in predicting mortality. Each scoring system has its advantages in stratifying geriatric patients on admission and hospitalization.

Keywords: COVID-19, CURB-65, geriatric, pneumonia, pneumonia severity index, mortality

Öz

Amaç: 2019 koronavirüs hastalığı (COVID-19) enfeksiyonlarından kaynaklanan pnömoninin değerlendirilmesi, yönetimi, hastaneye kabule karar vermek, terapötik ihtiyaçları ve seçenekleri belirlemek için acilen hastalık şiddetinin değerlendirilmesi gerektirmektedir. Bu çalışma, COVID-19 pnömonisi olan geriatrik grupta ve diğer COVID-19 olmayan pnömonilerle mortalite riskini değerlendirmek için CURB-65 skorlama sistemi ve pnömoni şiddet indeksinin (PSI) etkinliğini karşılaştırdı.

Yöntemler: COVID-19 laboratuvar teyidi için başvuran 21.134 hasta arasından, bilgisayarlı tomografi taramalarında buzlu cam yoğunlukları görülen 65 yaş ve üzeri 527 hasta seçildi. Tüm demografik, klinik ve laboratuvar verileri retrospektif olarak tarandı ve COVID-19 pnömonisi olan veya COVID-19 dışı pnömonisi olan hastalar seçilip takip edildi.

Bulgular: Tüm hastalar arasında genel ölüm oranı %25,6, COVID-19 pnömonisi olan hastalarda oran %14,3 ve COVID-19 dışı pnömonisi olan hastalarda oran %29,2 idi. ROC analizi, COVID-19 hastaları arasında PSI>grup III'ün mortaliteyi tahmin etmede %77,8 duyarlılık, %73,2 özgüllük, %32,6 PPV, %95,2 NPV'idi. (AUC:0,800, %95 GA: 0,720-0,866; P<0,0001).

CURB-65 skoru >2 olan COVID-19 pnömoni hastalarında mortaliteyi tahmin etmede duyarlılık %66,7, PPV %60 özgüllük ve NPV %94,3 idi. (EAA: 0,857, %95 GA: 0,783–0,913; P<0,0001).

Sonuç: PSI skoru üçten büyük ve CURB-65 skoru ikiden büyük olan COVID-19 ve COVID-19 olmayan enfeksiyonlara sahip pnömoni hastaları için mortalite tahmininde güçlü skorlamalardır. Geriatrik hastaların kabul ve yatışlarına göre sınıflandırılmasında her bir skorlama sisteminin avantajları vardır.

Anahtar Kelimeler: COVID-19, CURB-65, geriatri, pnömoni; pnömoni şiddet indeksi, mortalite

Introduction

The severe acute respiratory syndrome known as SARS-CoV-2 resulted in the recent coronavirus disease 2019 (COVID-19), turning into a worldwide pandemic in a short period. According to the recent data reported by the World Health Organization (WHO), starting on February 25, 2022, there were roughly 428,5 million confirmed cases and 5,9 million deaths[1]. One of the major problems in the combat against COVID-19 is the lack of a feasible risk scale to use in prognosis, which could alleviate the burden of such settings as primary care or general practice[2].

The evaluation and management of pneumonia due to viral infections urgently require assessing the disease severity to decide on admission or hospitalization in inpatient services or intensive care units (ICU) and determine the therapeutic needs and options. The high prevalence of COVID-19, especially in Turkey with a comprehensive healthcare system giving a medical treatment free of charge for all residents during the outbreak, requires a simple scoring system to quickly triage severe patients[3]. One of these systems, the pneumonia severity index (PSI), scores and classifies patients having pneumonia into five groups in line with their features and risk of mortality[4]. Despite yielding a detailed, precise classification of severity with the calculating a score using 20 variables, PSI is not likely to be efficiently used as a routine application in emergency rooms or primary care for which time effectiveness is of due significance. Moreover, this index is suggested to evaluate outpatients with a low mortality risk rather than in-patients having pneumonia in severe degrees when they are admitted to the hospital[5].

Another scoring system, the CURB-65 score, is commonly used in management of community-acquired pneumonia (CAP), including five parameters which can be easily obtained: namely, age, blood pressure, confusion, blood urea nitrogen (BUN), and rate of respiration[6]. CURB-65 has also been beneficial in effectively predicting the clinical results of CAP by viral infection and 14-day mortality for hospital-acquired pneumonia[7,8].

Besides these scoring systems, prognostic factors, including the presence of comorbidities, age and gender have also been cited as a having correlation with the severity and mortality in COVID-19 infection[5,9]. The guidelines of Turkish Ministry of Health orders that any possible patient in age 50 and over having any comorbidities must be categorized as eligible for hospitalization regardless of computed tomography (CT) findings, vital signs and laboratory results[10]. Thus, these criteria for admission and hospitalization includes a high number COVID-19 patients, which may result in an additional burden for the healthcare system and health professionals during the outbreak[3]. Therefore, a practical scoring system such as PSI or CURB-65 should first be implemented in geriatric patients to diminish the burden of hospitalization. However, age may play a role in mortality. A recent report about some clinical manifestations of cases with COVID-19 including not only elderly but also young patients indicated PSI scores were found to be higher in the former in comparison to the latter group[11]. Another study reported that older patients having a CURB-65 score of 2 or above could not survive COVID-19 infection compared with young patients. Nevertheless, these predictive criteria sets have not been compared for geriatric patients having COVID-19. As such, the present study compared the CURB-65 and PSI ability to evaluate the mortality risks of geriatric patients with pneumonia resulting from COVID-19 and non- COVID-19 infections.

Materials and Methods

- *Study Design and Patients*

The present study designed in retrospective manner was conducted in a tertiary hospital (Antalya, Turkey), a designated tertiary hospital fully equipped for COVID-19 patients. Totally 1,886 elderly patients (ages 65 or older) were selected from 21,134 patients who applied for laboratory confirmation of COVID-19 by real-time reverse transcription-polymerase chain reaction (real-time RT–PCR) test and computerized tomography (CT) for a timeline from March 11, 2020, (the date of the first case reported in Turkey) to August 25, 2020. The WHO interim guidance was utilized as the diagnostic criteria of COVID-19, confirmed through RT-PCR detection of the SARS-CoV-2 in an onsite clinical laboratory[12]. 527 participants whose CT scans showed ground glass densities consistent with COVID-19 pneumonia comprised the study group (Fig. 1).

126 patients having positive RT-PCR obtained from nasopharyngeal swab were clustered as COVID-19 pneumonia, and 401 patients with negative results were clustered as non-covid-19 pneumonia. Patients under age 65, patients whose thoracic CT scans did not show any ground glass densities, patients whose findings showed no suspicion of pneumonia (negative CT scan), and patients whose findings exhibited no suspicion of COVID-19 infection were excluded from the study.

The present study received approval; the requirement for informed consent was waived by the Ethics Commission of Antalya Training and Research Hospital (No: 2020-256- l3/8 Date: August 27, 2020). This study was carried out in line with the Declaration of Helsinki.

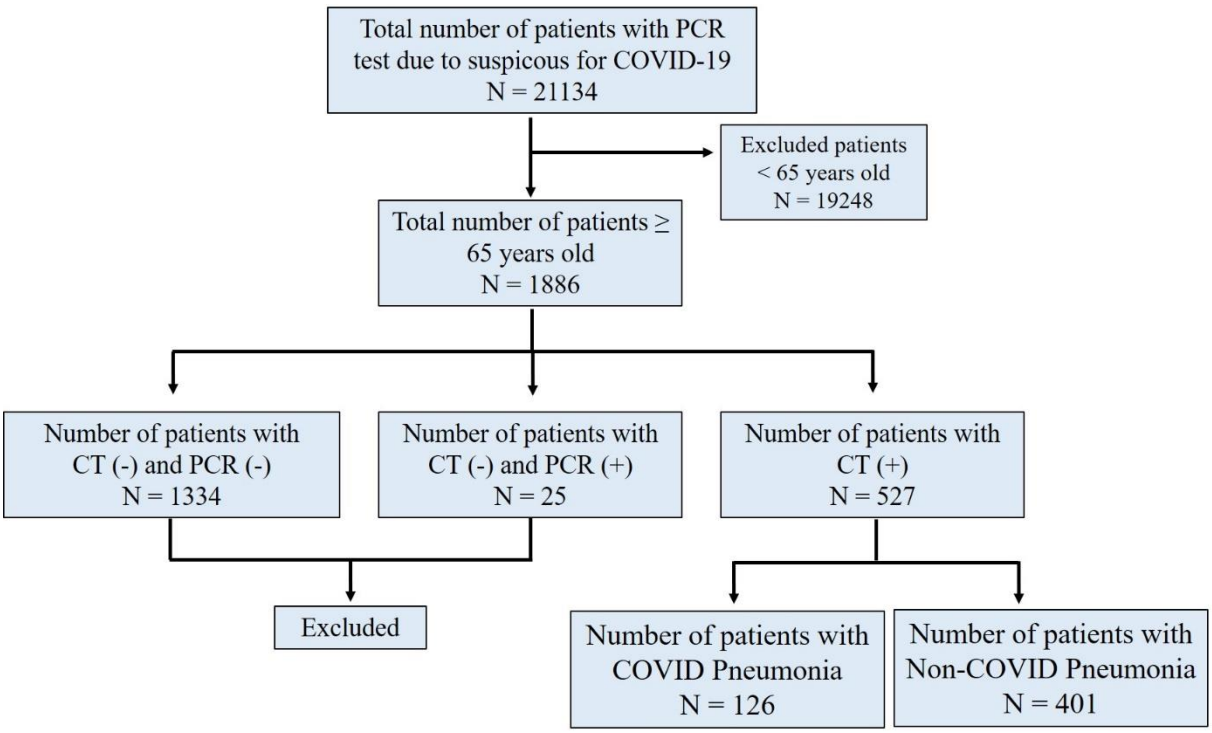

Figure 1. The flow chart of selection of the patients for the study

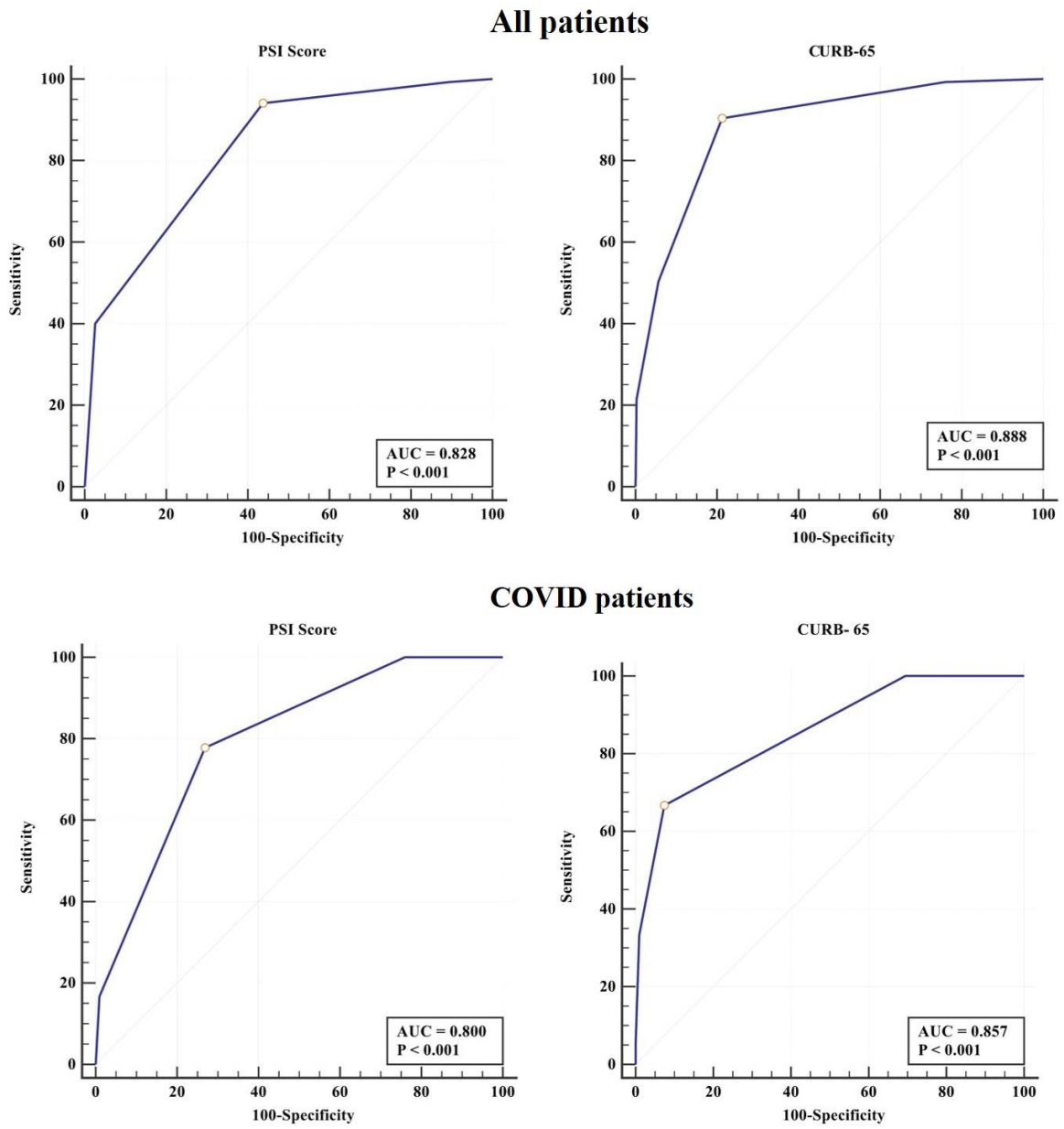

Figure 2. Receiver operator characteristic (ROC) curves for the PSI and CURB-65 scores to predict the mortality among all patients and COVID-19 patients (AUC: Area under curve)

- *Data collection*

All demographic data, presenting symptoms, comorbidities, triage vital signs (including blood pressure, fever, oxygen saturation at rest, respiratory and heart rate), clinical and laboratory data collected at the first admission of the patients, and resulting data were obtained from electronic medical records through a standardized data collection form. The data were controlled by two physicians, and another expert reevaluated possible differences in evaluation between the two reviewers.

The initial outcome was the type of pneumonia, classified as either due to COVID-19 infection or to other infections, including bacteria or other viruses. As the severity scores for pneumonia, PSI and CURB-65 scores collected at hospital admission were calculated. The CURB-65 comprises five variables (with 1 point

attributed for each item): new-onset confusion; urea >7 mmol/L; respiratory rate ≥30/minute, systolic blood pressure <90 mmHg and/or diastolic blood pressure ≤60 mmHg, and age ≥65 years, all criteria were defined in line with the related literature[13]. PSI scores were categorized into groups I, II, III, IV, and V, according to the literature[3].

- *Laboratory assay and scanning*

According to the clinical examination findings, nasopharyngeal swabs were obtained from 527 patients suspected of SARS-CoV-2 infection for the RT-PCR test. The samples were stored at 2–8°C for up to 72 hours after collection. The technique and its safety requirements were in accordance with the literature[14].
A CT scanner (Canon Aquilion Lightning 160 slice/80 detector row Ultra Helical CT) was used for thoracic CT scanning of the patients with pneumonia findings on clinical examination.
Blood samples were obtained right after their admission to conduct usual laboratory tests. All evaluations were conducted within 2 hours after the collection of blood samples. In the evaluation of the nasopharyngeal swabs and blood samples, only the samples collected in admission were utilized.

- *Hospitalization and Treatments*

In line with the regulations of the Turkish Ministry of Health, suspected patients over 65 years old with a comorbidity (e.g., hypertension, chronic renal disease, diabetes, mellitus, cardiopulmonary disease, immunosuppressive/immunomodulatory conditions, or malignancy) or with tachypnea (respiratory rate >22/min), tachycardia (pulse >125/min), hypoxemia (Spo2 <93%), hypotension (<90/60 mmHg) were admitted to the hospital[10] .
The COVID-19 Diagnosis and Treatment Protocol, established by the Turkish Ministry of Health, was used to treat all of the hospitalized patients[10].

- *Statistical Analysis*

Chi-square test was utilized to evaluate the categorical variables, and the Mann-Whitney U test was utilized to evaluate the continuous variables. The Spearman Rank Correlation was performed to determine the correlation between the two continuous variables. These statistical analyses were conducted using the GraphPad InStat Version 3.6. $P<0.05$ was accepted as statistically significant.
In order to determine the cut-off value for PSI and CURB-65 scores for predictions of patients' mortality, Number Cruncher Statistical System 2007 (NCSS, Kaysville, Utah, USA) program was utilized. Diagnostic screening tests (sensitivity, specificity, PPV, NPV) were used, and receiver operating characteristic (ROC) curve analyses were plotted using each of the following disease severity measures as predictors of mortality to calculate the cut-off for the parameters. $P<0.001$ level was accepted as significant.

Results

- *Demographic, Clinical, and Laboratory Findings*

Totally, 527 patients were included in the research. The mean age was 75.2 ± 7.9 years. ($P <0.0001$). 60.3% of the patients were male and the groups exhibited significant differences according to the pneumonia type ($P = 0.0279$).
The mean systolic blood pressure (SBP), oxygen saturation (SpO2), and Glasgow coma score (GCS) were all significantly higher; alternatively, the respiratory rate was lower in patients having COVID-19 pneumonia in comparison to non-COVID-19 patients ($P<0.01$). The comparison of the

Table 1. Demographic and clinical features of the patients in comparison to the type of pneumonia

Variable	Total N = 527	COVID-19 N = 126	NON-COVID-19 N = 401	P value
Age (year), Mean±SD	75.2 ± 7.9	72.2 ± 6.9	76.1 ± 8.0	<0.0001
Gender, n (%)				
• Male	318 (60.3)	65 (51.6)	253 (63.1)	0.0279
• Female	209 (39.7)	61 (48.4)	148 (36.9)	
Comorbidities, n (%)				
• Hypertension	382 (72.5)	93 (73.8)	289 (72.1)	0.789
• Diabetes Mellitus	206 (39.1)	53 (42.1)	153 (38.2)	0.497
• COPD/Asthma/Bronchitis	168 (31.9)	23 (18.3)	145 (39.2)	0.0003
• Malignity	95 (18.0)	7 (5.6)	88 (21.9)	<0.0001
• Cardiovascular diseases	212 (40.2)	32 (25.4)	180 (44.9)	0.0002
• Cerebrovascular diseases	123 (23.3)	13 (10.3)	110 (27.4)	0.0001
• Chronic renal failure	67 (12.7)	8 (6.3)	59 (14.7)	0.0212
• Chronic liver disease	18 (3.4)	4 (3.2)	14 (3.5)	0.864
• Coronary Failure	76 (14.4)	7 (5.6)	69 (17.2)	0.0019
Symptoms at diagnosis, n (%)				
• Fever	311 (59.0)	85 (67.5)	226 (56.4)	0.0352
• Malaise	337 (63.9)	113 (89.7)	224 (55.9)	<0.0001
• Dry cough	269 (51.0)	83 (65.9)	186 (46.4)	0.0002
• Sore throat	232 (44.0)	91 (72.2)	141 (35.2)	<0.0001
• Dyspnea	360 (68.3)	74 (58.7)	286 (71.3)	0.0111
• Chest pain	53 (10.1)	9 (7.1)	44 (11.0)	0.282
• Headache	47 (8.9)	16 (12.7)	31 (7.7)	0.127
• Dizziness	39 (7.4)	12 (9.5)	27 (6.7)	0.396
• Diarrhea	22(4.2)	8 (6.3)	14 (3.5)	0.253
• Nausea	46 (8.7)	18 (14.3)	28 (7.0)	0.0186
• Myalgia	122 (23.1)	72 (57.1)	50 (12.5)	<0.0001
• Purulent sputum	512 (97.2)	122 (96.8)	390 (97.3)	0.799
Clinical Findings, Mean±SD				
• Fever °C	37.3 ± 0.7	37.4 ± 0.7	37.4 ± 0.6	0.056
• Pulse	93.3 ± 18.8	94.2 ± 16.7	93.0 ± 19.5	0.234
• SBP mmHg	116.2 ± 20.5	121.4 ± 18.4	114.6 ± 20.9	0.0013
• DBP mmHg	69.2 ± 12.4	70.8 ± 11.2	68.7 ± 12.7	0.125
• Respiratory rate /min	24.7 ± 4.2	23.5 ± 3.5	25.0 ± 4.3	0.0005
• SpO_2 (%)	92.6 ± 6.1	94.5 ± 4.5	91.9 ± 6.4	<0.0001
• GCS	14.5 ± 1.5	14.9 ± 0.4	14.4 ± 1.7	0.0018

SD: Standard deviation, SBP: Systolic blood pressure, DBP: diastolic blood pressure, SpO2: Oxygen saturation, COPD: Chronic obstructive pulmonary disease, GCS: Glasgow Coma Scale

Table 2. Laboratory findings of the patients in comparison to the type of pneumonia

Parameters	Total N = 527	COVID-19 N = 126	NON-COVID-19 N = 401	P value
Blood groups				
• A	96 (18.2)	24 (19.0)	72 (18.0)	<0.0001
• AB	13 (2.5)	3 (2.4)	33 (8.2)	0.081
• B	41 (7.8)	8 (6.3)	10 (2.5)	0.0207
• 0	79 (15.0)	12 (9.5)	67 (16.7)	0.201
Undefined	322 (61.1)	81 (64.3)	219 (54.6)	
Rh				
• Negative	25 (4.7)	9 (7.1)	16 (4.0)	
• Positive	204 (38.7)	38 (30.2)	166 (41.4)	0.077
Glucose (mg/dL)	154.9 ± 89.5	140.5 ± 67.6	159.5 ± 95.1	0.0056
Renal Functional Tests				
• BUN (mg/dL)	29.6 ± 21.7	22.9 ± 12.1	31.7 ± 23.6	0.0001
• Creatinine (mg/dL)	1.3 ± 0.9	1.15 ± 0.7	1.36 ± 0.97	0.112
Na (mmol/L)	136.2 ± 6.4	135.8 ± 3.7	136.3 ± 7.0	0.824
K (mmol/L)	4.4 ± 5.9	5.2 ± 11.7	4.2 ± 0.6	0.730
Liver Metabolism				
• ALT (U/L)	40.0 ± 167.4	27.8 ± 19.1	44.0 ± 192.2	0.0041
• AST (U/L)	58.2 ± 279.8	35.7 ± 18.2	65.6 ± 321.9	0.0004
• CK (U/L)	162.3 ± 338.3	146.1 ± 145.6	166.5 ± 372.3	0.072
• CK-MB (U/L)	23.9 ± 26.2	22.0 ± 29.5	24.7 ± 24.6	0.0278
• Total bilirubin (mg/dL)	0.98 ± 2.1	0.6 ± 0.3	1.08 ± 2.4	0.0027
• Direct bilirubin (mg/dL)	0.35 ± 1.1	0.17 ± 0.1	0.39 ± 1.3	0.0357
CRP (mg/L)	79.2 ± 89	67.7 ± 72.9	82.9 ± 93.4	0.834
Total Blood Counts				
• WBC (103/mm3)	10.9 ± 8.3	6.5 ± 3.5	12.3 ± 8.9	<0.0001
• HBG (g/dL)	11.8 ± 2.3	12.5 ± 1.7	11.6 ± 2.4	<0.0001
• HTC (%)	36.0 ± 6.8	37.4 ± 4.5	35.6 ± 7.4	0.001
• PLT (103/mm3)	242.2 ± 115.8	217.5 ± 87.9	250.3 ± 122.5	0.0007
• PLR	210.7 ± 143.2	262.1 ± 159.3	206.2 ± 141.2	0.105
• NEU (103/mm3)	8.7 ± 8.9	4.6 ± 3.4	9.97 ± 9.7	<0.0001
• LYM (103/mm3)	1.9 ± 2.6	1.27 ± 0.5	2.04 ± 3.0	0.084
• MON (103/mm3)	1.0 ± 2.3	0.58 ± 0.3	1.13 ± 2.6	<0.0001
• NLR	8.4 ± 11.6	4.8 ± 6.0	9.5 ± 12.7	<0.0001
• LMR	2.8 ± 5.6	2.56 ± 1.5	2.9 ± 6.4	0.0012
Troponin T (ng\L)	91.6 ± 419.4	19.2 ± 43.8	119.8 ± 490.8	<0.0001
Procalcitonin (ng/ml)	10.1 ± 79.9	0.75 ± 2.3	12.5 ± 89.7	0.0211
Myoglobulin (ng/ml)	143.8 ± 364.2	122.9 ± 210.9	156.4 ± 432.3	0.519
Clothing Metabolism				
• aPTT (sec)	31.5 ± 9.4	30.5 ± 4.2	31.9 ± 10.8	0.928
• PT (sec)	14.6 ± 7.7	12.7 ± 2.4	15.3 ± 8.9	<0.0001
• INR	1.3 ± 0.8	1.1 ± 0.2	1.4 ± 0.98	<0.0001
• D-dimer (µg/L)	1213.8 ± 3611.2	466.2 ± 709.1	1526.0 ± 4238.9	<0.0001
Sedimentation (mm/h)	48.4 ± 80.9	46.3 ± 43.6	49.5 ± 94.2	0.405
Fibrinogen (mg/dL)	493.5 ± 211.0	471.9 ± 178.3	505.5 ± 226.9	0.446
Iron (µg/L)	31.6 ± 23.4	27.9 ± 15.6	32.8 ± 25.4	0.955
Ferritin (µg/L)	291.1 ± 449.3	223.5 ± 216.4	314.2 ± 634.4	0.689
TIBC (µg/L)	267.9 ± 133.5	295.8 ± 111.5	258.9 ± 139.3	0.0151
Blood Gas Parameters				
• pH	7.4 ± 0.1	7.4 ± 0.06	7.4 ± 0.1	0.228
• PaCO2 (mm Hg)	39.5 ± 9.8	36.0 ± 9.8	40.0 ± 9.8	0.0229
• PaO2 (mm Hg)	66.3 ± 10.9	71.0 ± 9.7	64.8 ± 10.9	<0.0001
• HCO3 (mmol/L)	22.6 ± 4.3	22.3 ± 3.5	22.6 ± 4.4	0.813
• Lactate (mmol/L)	2.36 ± 1.9	1.75 ± 0.7	2.5 ± 1.98	0.198

All parameters are given as mean ± standard deviation.

BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CK: Creatinine kinase, CK-MB: Creatinine kinase isoenzyme MB, CRP: C reactive protein, WBC: White blood cells, HBG: Hemoglobin, HTC: Hematocrit, PLT: Platelets, PLR: Platelet/lymphocyte ratio, LYM: Lymphocyte, NEU: Neutrophil, MON: Monocyte, LMR: Lymphocyte/Monocyte, NLR: Neutrophil/Lymphocyte ratio, aPTT: activated partial prothrombin time, PT: Prothrombin time, INR: international normalized ratio, TIBC: Total Iron Binding Capacity, ABG: Arterial Blood Gases

patients in terms of their demographic and clinical features can be seen in Table 1.
Type A was the most common blood type among all patients, and the percentage of COVID-19 patients having the A-type was significantly higher in comparison to those of non-COVID-19 patients (P<0.0001).
Among renal functional tests, the mean concentration of blood urea nitrogen (BUN) of COVID-19 patients was significantly higher in comparison to those of non-COVID-19 ones (P<0.001). Nearly all parameters of liver metabolism (i.e., liver enzymes), except for creatine kinase, were significantly lower among COVID-19 patients (P<0.05). The difference between the mean CRP was not statistically significant among the groups (P=0.834). The laboratory findings showed that the mean glucose level in COVID-19 patients was significantly higher than in non-COVID-19 patients (P<0.01). The parameters of total blood counts, including white blood cells (WBC), hematocrit (HTC), platelets (PLT), neutrophil (NEU), monocyte (MON), Neutrophil/Lymphocyte ratio, were significantly lower among COVID-19 patients compared with those of non-COVID-19 patients (P<0.001). Troponin T and procalcitonin levels were also lower among COVID-19 patients (P<0.0001 and P=0.0211, respectively).
Almost all parameters of clotting as prothrombin time (PT), international normalized ratio (INR), D-dimer, were far lower among COVID-19 patients compared with those of non-COVID-19 patients (P<0.0001). Among blood gas parameters, the mean PaCO2 was significantly lower (P=0.0229), while PaO2 was significantly higher among COVID-19 patients in comparison to non-COVID-19 ones (P<0.0001; Table 2).

- *Follow-up Outcomes*

From the 527 patients who were admitted to the hospital, 94 (21.7%) were transferred to their house for containment after their treatment in emergency department. According to the instructions of the Ministry of Health of Turkey, 94 patients with COVID-19 clinical symptoms and ground glass density detected in CT scans were taken into isolation at home so that their treatments and clinical course were closely followed. (Table 3). The mortality rates among non-COVID-19 patients were higher among those hospitalized directly in ICU. Mean duration of hospitalization in inpatient settings was significantly longer among patients having non-COVID-19 pneumonia than those having COVID-19 (P=0.0122). However, the mean duration in ICU of non-COVID-19 patients was shorter in comparison to those of COVID-19 patients (P=0.0028; Table 3). The COVID-19 and non-COVID-19 patients receiving oxygen therapy and surviving to discharge were significantly higher in number in comparison to the non-surviving patients who received the same therapy (P<0.0001).

- *Correlations with the mortality rates of patients with COVID-19 pneumonia*

Patients' age, symptoms at diagnosis including malaise and dyspnea, clinical findings including pulse, DBP, respiratory rate, SpO2 and GCS, Na levels, parameters of liver metabolism including creatine kinase isoenzyme MB (CK-MB) and direct bilirubin, CRP levels, total blood counts of WBC, NEU, LYM and MON, NLR and LMR, concentrations of troponin T, procalcitonin, myoglobulin, D-dimer, fibrinogen, blood gas parameters, and lactate were found to be significantly in correlation to the mortality rates among COVID-19 patients (P<0.05; Table 4).

- *PSI and CURB-65*

Patients were divided into five different groups in accordance with pneumonia severity ranging from I (no disease) to V (most severe) on the PSI and 1 to 5 on the CURB-65. Out of all the patients, 42

patients (7.97%) were categorized into group II, 186 (35.3%) were in group III, 234 (44.4%) in group IV, and 64 (12.1%) in group V (Table 3). The mortality rates among all patients for both types of pneumonia were dramatically higher in groups IV and V (P<0.0001). Non-COVID-19 patient's mortality rates in groups IV and V were significantly higher in comparison to the COVID-19 patients in the same groups (P<0.0001; Table 3). PSI scores also were significantly in correlation to the mortality rates of COVID-19 patients (P<0.0001; Table 5). ROC analysis showed that the PSI greater than group III among COVID-19 patients also had a good discriminative efficiency in predicting mortality with 77.8% sensitivity, 73.2% specificity, PPV of 32.6%, and NPV of 95.2% (AUC = 0.800, 95% CI 0.720 – 0.866; P<0.0001; Table 5; Fig. 2).

A total of 95 (18.0%) patients gave a CURB-65 score of 1, only one of whom (0.7%) died during follow-up. A CURB-65 score ≥2 was obtained in 432 patients (82.0%). Of these, 134 patients (25.4%) died during follow-up. CURB-65 scores were significantly in correlation to the mortality rates of COVID-19 patients (P<0.0001; Table 4).

ROC analysis showed a CURB-65 score of >2 among COVID-19 patients, having a discriminative effectiveness in predicting mortality with 66.7% sensitivity, 92.6% specificity, PPV of 60%, and a NPV of 94.3% (AUC: 0.857, 95% CI 0.783 – 0.913; P<0.0001; Table 5).

Discussion

COVID-19 associated mortality is a multifaceted entity, including myriad factors as the age and any underlying disease, which has resulted in a healthcare burden during the pandemic[15]. The present study evaluated and compared the efficiencies of two prognostic scoring systems in predicting mortality risks in a geriatric group of patients with pneumonia and compared the outcomes among patients having COVID-19 pneumonia or non-COVID-19 pneumonia (bacterial or viral pneumonia). These measures functioned reliably in both COVID-19 and Non-COVID-19 pneumonia. The average mortality rate among all patients was 25.6%; the rate among patients having COVID-19 pneumonia was 14.3%, and that of patients having non-COVID-19 pneumonia was 29.2%. PSI scores above III showed better sensitivity (77.8% vs. 66.7%) but lower specificity (73.2% vs. 92.6%) and PPV (32.6% vs. 60%) and a comparable NPV (96.2% vs. 94.3%) in predicting mortality among all patients compared with a CURB-65 score above 2.

In a meta-analysis for community-acquired pneumonia, the PSI and CURB-65 score systems were shown to have high negative predictive values in predicting mortality. Similar results were found in non-COVID-19 pneumonias in our study [16].

COVID-19 related mortality rate has been cited between 11.7% and 28.2% [9,17-20]. The mortality rates of geriatric patients having COVID-19 pneumonia in the present study (14.3%) were inconsistent with these reports, and Turkish reports, with a mortality rate between 2.1% and 19% [3,20-21].

This wide range in mortality rate may be due to differences in the demographic and clinical features of study groups, the hospitalization criteria, the treatment strategies, and the measures of mortality rates. On the other hand, ground-glass appearance can be seen in chronic interstitial lung diseases, acute alveolar diseases, cardiogenic edema as well as viral atypical pneumonias. This may be due to the older age, more frequent comorbidities, and worse clinical findings in respiratory rate and saturation in the non-COVID-19 group.

For patients with infection resulting from SARS-CoV-2, developing prognostic rating scales with the ability to yield consistent predictions is necessary[24].

Table 3. Treatments, follow-up and mortality scores of the patients in comparison to the type of pneumonia and the mortality

Parameters	Total N = 527			COVID-19 N = 126			NON-COVID-19 N = 401			P value*
Mortality, n (%)		135 (25.6)			18 (14.3)			117 (29.2)		0.0013
	Survivor N = 392	Mortality N = 135	P value	Survivor N = 108	Mortality N = 18	P value	Survivor N = 284	Mortality N = 117	P value	
Oxygen therapy, n (%)	148 (37.8)	129 (95.6)	<0.0001	25 (23.1)	17 (94.4)	<0.0001	123 (43.3)	112 (95.7)	<0.0001	<0.0001
Mechanic Ventilation, n (%)										
• Non-invasive	25 (6.4)	29 (21.5)	<0.0001	1 (0.9)	4 (22.2)	0.0003	24 (8.5)	25 (21.4)	0.0006	0.0126
• Invasive	17 (4.3)	108 (80)	<0.0001	5 (4.6)	14 (77.8)	<0.0001	12 (4.2)	94 (80.3)	<0.0001	0.0126
Endpoint, n (%)										
• Discharge from ES	93 (23.7)	1 (0.7)	<0.0001	33 (30.6)	0 (0)	0.0147	60 (21.1)	1 (0.9)	<0.0001	0.0075
• Hospitalization in service	251 (64.0)	57 (42.2)	<0.0001	72 (66.7)	13 (72.2)	0.846	179 (63.0)	44 (37.6)	<0.0001	0.0244
• ICU	47 (12.0)	77 (57.0)	<0.0001	3 (2.8)	5 (27.8)	0.0005	44 (15.5)	72 (61.5)	<0.0001	<0.0001
• Transfer to ICU	18 (4.6)	50 (37.0)	<0.0001	5 (4.6)	9 (50)	<0.0001	13 (4.6)	41 (35.0)	<0.0001	0.592
Duration (day)										
• In service	6.2 ± 4.1	8.2 ± 7.7	0.997	7.7 ± 4.3	5.3 ± 4.3	0.0199	6.1 ± 4.1	8.8 ± 8.1	0.248	0.0122
• In ICU	8.8 ± 10.7	10.99 ± 12.9	0.123	15.3 ± 10.6	15.3 ± 15.9	0.647	8.0 ± 10.5	10.4 ± 12.3	0.144	0.0028
PSI Score, n (%)										
• I	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)		
• II	41 (10.5)	1 (0.7)		26 (24.1)	0 (0)		15 (5.3)	1 (0.9)		
• III	179 (45.8)	7 (5.2)	<0.0001	53 (49.1)	4 (22.2)	<0.0001	126 (44.4)	3 (2.6)	<0.0001	<0.0001
• IV	161 (41.1)	73 (54.1)		28 (25.9)	11 (61.1)		133 (46.8)	62 (53.0)		
• V	10 (2.6)	54 (40)		1 (0.9)	3 (16.7)		9 (3.2)	51 (43.6)		
CURB-65										
• 1	94 (24.0)	1 (0.7)		33 (30.6)	0 (0)		61 (21.5)	1 (0.9)		
• 2	214 (54.6)	12 (8.9)	<0.0001	67 (62.0)	6 (33.3)	<0.0001	147 (51.8)	6 (5.1)	<0.0001	<0.0001
• 3	61 (15.6)	54 (40)		7 (6.5)	6 (33.3)		54 (19.0)	48 (41.0)		
• 4	21 (5.4)	39 (28.9)		1 (0.9)	5 (27.8)		20 (7.0)	34 (29.1)		
• 5	1 (0.3)	29 (21.5)		0 (0)	1 (5.6)		1 (0.4)	28 (23.9)		

ES: Emergency Service, ICU: Intensive care unit, PSI, Pneumonia Severity Index, CURB-65: 5-point score based on confusion, urea, respiratory rate, blood pressure, and age 65.
*Giving the comparison between all COVID patients and all Non-COVID patients regardless of the mortality

Table 4. Correlation of the demographic, clinical and laboratory findings of COVID-19 patients with the mortality rates

Variable	Spearman r	95% CI	P value
Age	0.287	0.113 – 0.444	0.0011
Gender	0.0584	-0.123 – 0.236	0.516
Symptoms at diagnosis			
• Fever	0.041	-0.140 – 0.220	0.645
• Malaise	-0.542	-0.811 – 0.086	0.0201
• Dry cough	-0.089	-0.265 – 0.093	0.323
• Sore throat	-0.051	-0.229 – 0.131	0.573
• Dyspnea	0.204	0.025 – 0.370	0.0219
• Chest pain	0.062	-0.120 – 0.240	0.492
• Headache	-0.088	-0.263 – 0.093	0.329
Clinical Findings			
• Fever °C	0.046	-0.136 – 0.224	0.612
• Pulse	0.249	0.072 – 0.411	0.005
• SBP mmHg	-0.100	-0.275 – 0.081	0.264
• DBP mmHg	-0.223	-0.387 – -0.045	0.0121
• Respiratory rate	0.261	0.085 – 0.421	0.0032
• SpO2	-0.406	-0.546 – -0.244	<0.0001
• GCS	-0.594	-0.699 – -0.463	<0.0001
CRP	0.394	0.232 – 0.534	<0.0001
Total Blood Counts			
• WBC	0.265	0.091 – 0.424	0.0033
• HBG	-0.062	-0.238 – 0.118	0.499
• HTC	-0.134	-0.310 – 0.051	0.144
• PLT	-0.032	-0.212 – 0.151	0.727
• PLR	0.270	-0.173– 0.622	0.212
• NEU	0.390	0.221 – 0.536	<0.0001
• LYM	-0.253	-0.417 – -0.073	0.0051
• MON	0.198	0.020 – 0.364	0.0295
• NLR	0.415	0.249 – 0.557	<0.0001
• LMR	-0.300	-0.458 – -0.123	0.0008
Troponin T	0.281	0.098 – 0.446	0.0023
Procalcitonin	0.342	0.071 – 0.566	0.0123
Myoglobulin	0.344	0.089 – 0.557	0.0076
CK-MB	0.286	0.025 – 0.511	0,028
D-dimer	0.283	-0.090 – 0.456	0.0036
Sedimentation	-0.025	-0.286 – 0.240	0.851
Fibrinogen	0.233	0.006 – 0.438	0.0385
Blood gas parameters			
• pH	-0.029	-0.141 – 0.366	0.887
• PaCO2	-0.267	-0.595 – 0.138	0.179
• PaO2	-0.139	-0.224 – 0.051	0.0015
• HCO3	-0.224	-0.565 – 0.182	0.262
• Lactate	0.630	0.246 – 0.843	0.0029
Endpoint	0.347	0.178 – 0.496	<0.0001
Transfer to ICU	0.479	0.299 – 0.626	<0.0001
Duration (day)			
• In service	-0.252	-0.443 – -0.039	0.0178
• In ICU	-0.108	-0.516 – 0.341	0.633
PSI Score	0.390	0.226 – 0.533	<0.0001
CURB-65 Score	0.488	0.337 – 0.614	<0.0001

BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CK: Creatinine kinase, CK-MB: Creatinine kinase isoenzyme MB, CRP: C reactive protein, WBC: White blood cells, HBG: Hemoglobin, HTC: Hematocrit, PLT: Platelets, PLR: Platelet/lymphocyte ratio, LYM: Lymphocyte, NEU: Neutrophil, MON: Monocyte, NLR: Neutrophil/Lymphocyte ratio, aPTT: activated partial prothrombin time, PT: Prothrombin time, INR: international normalized ratio, TIBC: Total Iron Binding Capacity, ABG: Arterial Blood Gases

Table 5. Comparative scores of PSI and CURB-65 in predicting the mortality among all patients

Score		Cut-off	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	AUC [95% CI]	P value
All patients	PSI	>III	94.1 88.7 - 97.4	56.3 51.2 - 61.2	42.6 39.7 - 45.6	96.5 93.3 - 98.2	0.828 0.793 - 0.859	<0.0001
	CURB-65	>2	90.4 84.1 - 94.8	78.8 74.4 - 82.7	59.5 54.6 - 64.2	96.0 93.4 - 97.6	0.888 0.858 - 0.913	<0.0001
Covid patients	PSI	>III	77.8 52.4 - 93.6	73.2 63.8 - 81.2	32.6 24.5 - 41.8	95.2 89.2 - 97.9	0.800 0.720 - 0.866	<0.0001
	CURB-65	>2	66.7 41.0 - 86.7	92.6 85.9 - 96.7	60.0 41.7 - 75.9	94.3 89.6 - 97.0	0.857 0.783 - 0.913	<0.0001

ROC: Receiver operating characteristic, PPV: Positive Predictive Value, NPV: Negative Predictive Value, AUC: Area under ROC curve, CI: Confidence Interval. PSI, Pneumonia Severity Index, CURB-65: 5-point score based on confusion, urea, respiratory rate, blood pressure, and age 65.

Among them, PSI, was associated with the clinical features and results of elderly and young patients with COVID-19, and this was found to be higher in the elderly group in comparison to young patients[11]. Another score, CURB-65, was also reported to be considerably higher in non-surviving patients due to COVID-19 [9]. A Turkish report by Satici et al. evaluated CURB-65 and PSI's performance in 30-day mortality prediction among COVID-19 patients regardless of age groups[3]. They determined the PSI ≥ 4 group had 80% sensitivity and 89% specificity, while CURB-65 scores of ≥ 2 had 73% sensitivity and 85% specificity[3]. However, in the present study, a PSI score over III showed better sensitivity, but a CURB-65 score above 2 showed better specificity for all pneumonia patients, including COVID-19 patients, likely to be resulting from the fact that our geriatric study population was over the age of 65.

The significant correlation of the present study regarding the findings of COVID-19 patients shows parallelism with the report showing a significant association between higher CRP levels and increases in mortality risk[2,25]. In another study, older age, low lymphocyte count, comorbidities, and a high score of lung edema radiographic assessment were cited as independent factors linked to elevated mortality risk[26].

In this study, the rate of Neutrophil lymphocyte was found to be high in covid-19 patients[27]. Unlike the literature, lower neutrophil/lymphocyte ratios were found in COVID-19 pneumonia patients. The reason for this may be due to some additional diseases as our patient group, which we included in the study, is geriatric. Because many reasons such as abnormal thyroid functions, metabolic syndrome, acute coronary syndrome, diabetes mellitus, hypertension kidney and malignancies, liver dysfunction, systemic infections, and the use of drugs affecting hematological parameters might have an influence on the neutrophil-lymphocyte ratio [28,29]. Algorithms based on multiple machine-learning by Yadaw et al. recommended such prognostic predictors as O2 saturation, age, patient type and body temperature[30]. A large retrospective study from China reported that age and the comorbidities of the patients were indicated to have a link with COVID-19 patients' mortality rates[31]. Another report in Turkey showed that dyspnea, the presence of comorbidities, pulse O2 saturation and CRP level have a

potential to predict mortality depending on the severity of the disease[22]. Especially, an association was found between any comorbid disease and dyspnea in the patients and an increased mortality rate.

The correlation between elevated mortality and advanced age has become well-established finding presently. One of the initial reports in China indicated that the mortality rate could be three times higher for older patient group, specifically for those 80 and older[32]. An Italian report demonstrated that the rate of mortality was 26% in the ICU, whereas it was 36% after 65 years of age[33]. Another crucial point is that the average survival time in days from the manifestation of symptoms to loss of life due to COVID-19 was fewer in older patients[34]. In the present study, the percentage of geriatric patients having COVID-19 pneumonia transferred to the ICU during follow-ups significantly correlated considering the mortality rates. Patients with COVID-19 may be first hospitalized in inpatient services, but if their prognosis deteriorates rapidly and unexpectedly, they may be transferred to the ICU due to declining health status. Moreover, the duration of hospitalization in inpatient services also significantly correlated with the mortality rates among COVID-19 patients, but the ICU duration did not.

In a study for COVID-19 mortality, it was stated that the PSI and CURB-65 scores scales in the emergency department did not have sufficient decision-making power for hospitalization[35].

In our study, PSI scores above group III and CURB-65 scores above 2 are powerful tools for predicting pneumonia patients' mortality rates due to COVID-19 infections. Both scoring systems assist healthcare providers in the emergency departments in their decisions regarding the discharge or hospitalization of patients with geriatric COVID-19 pneumonia. Using these two scoring systems in emergency departments, geriatric COVID-19 pneumonia patients with a high mortality risk can be identified, further and given treatment to improve healthcare services and reducing mortality rates.

The limitations of this study mostly depend on its retrospective nature. We did not perform multivariate analysis on all clinical and laboratory data correlated with the mortality rates. Additionally, the prognostic scores of patients were not determined prospectively. Though, the majority of the Turkish clinical institutes have routinely been collecting the demographic and clinical data starting from the onset of the pandemic. Another limitation of the study was the missing laboratory data, which were not parts of the discharged patients' routine evaluation. Ground glass was detected in thorax CT in all patients included in the study. But the ground glass appearance can be seen in chronic interstitial lung diseases, acute alveolar diseases, cardiogenic edema as well as viral atypical pneumonias. There is a limitation in this sense.

Conclusion

In conclusion, this present study designed in retrospective manner with a large cohort of geriatric COVID-19 patient group and patients with non-COVID-19 pneumonia collected from a single-center, indicated that PSI scores over group III and CURB-65 over 2 are potent tools for predicting mortality rates in patients having pneumonia accompanied by COVID-19 infections or not. Both scores have advantages in stratifying the geriatric patients on admission and hospitalization.

Author contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

The present study received approval; the requirement for informed consent was waived by the Ethics Commission of Antalya Training and Research Hospital (No: 2020-256- l3/8 Date: August 27, 2020). This study was carried out in line with the Declaration of Helsinki.

References

1. WHO, Data last updated: February 25, 2022. Available at: https://covid19.who.int/. Accessed February 25, 2022.
2. Pan A, Liu L, Wang C, et al. Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. JAMA. 2020;323(19):1915-23. doi:10.1001/jama.2020.6130.
3. Satici C, Demirkol MA, Sargin Altunok E, et al. Performance of pneumonia severity index and CURB-65 in predicting 30-day mortality in patients with COVID-19. Int J Infect Dis. 2020;98:84-9. doi:10.1016/j.ijid.2020.06.038.
4. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med. 1997;336(4):243-50. doi:10.1056/NEJM199701233360402.
5. Guo J, Zhou B, Zhu M, et al. CURB-65 may serve as a useful prognostic marker in COVID-19 patients within Wuhan, China: a retrospective cohort study. Epidemiol Infect. 2020;148:e241. Published 2020 Oct 1. doi:10.1017/S0950268820002368.
6. Singanayagam A, Chalmers JD. Severity assessment scores to guide empirical use of antibiotics in community acquired pneumonia. Lancet Respir Med. 2013;1(8):653-62. doi:10.1016/S2213-2600(13)70084-5.
7. Zhou F, Wang Y, Liu Y, et al. Disease severity and clinical outcomes of community-acquired pneumonia caused by non-influenza respiratory viruses in adults: a multicentre prospective registry study from the CAP-China Network. Eur Respir J. 2019;54(2):1802406. doi:10.1183/13993003.02406-2018.
8. Oktariani, Pitoyo CW, Singh G, et al. CURB 65 score as a predictor of early mortality in hospital-acquired pneumonia. Egypt J Chest Dis Tuberc 2019;68 (2):231-5. doi: 10.4103/ejcdt.ejcdt_146_18
9. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in Lancet. 2020;395(10229):1054-62. doi:10.1016/S0140-6736(20)30566-3
10. Bilim Kurulu Çalışması. COVID-19 (SARS-CoV-2 enfeksiyonu) Rehberi. TC. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü (2 Nisan 2020) Ankara. 2020. Available at: https://covid19rehberi.com/wp-content/uploads/2020/04/COVID19_Eriskin_Hasta_Tedavisi_02042020.pdf Accessed February 20, 2021.
11. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect. 2020;80(6):e14-e18. doi:10.1016/j.jinf.2020.03.005
12. WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. 2020b. January 2, 2020. Available at: https://www.who.int/publications-/i/item/10665-332299 Accessed December 15, 2021.
13. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377-82. doi:10.1136/thorax.58.5.377
14. Pondaven-Letourmy S, Alvin F, Boumghit Y, Simon F. How to perform a nasopharyngeal swab in adults and children in the COVID-19 era. Eur Ann Otorhinolaryngol Head Neck Dis. 2020;137(4):325-7. doi:10.1016/j.anorl.2020.06.001
15. Ji Y, Ma Z, Peppelenbosch MP, Pan Q. Potential association between COVID-19 mortality and health-care resource availability. Lancet Glob Health. 2020;8(4):e480. doi:10.1016/S2214-109X(20)30068-1
16. Loke YK, Kwok CS, Niruban A, Myint PK. Value of severity scales in predicting mortality from community-acquired pneumonia: systematic review and meta-analysis. Thorax. 2010;65(10):884-90. doi:10.1136/thx.2009.134072
17. Giacomelli A, Ridolfo AL, Milazzo L, et al. 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study. Pharmacol Res. 2020;158:104931. doi:10.1016/j.phrs.2020.104931

18. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in Lancet. 2020 Jan 30;:]. Lancet. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
19. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China [published correction appears in JAMA Intern Med. 2020 Jul 1;180(7):1031]. JAMA Intern Med. 2020;180(7):934-43. doi:10.1001/jamainternmed.2020.0994
20. Görgülü Ö, Duyan M. Effects of Comorbid Factors on Prognosis of Three Different Geriatric Groups with COVID-19 Diagnosis. SN Compr Clin Med. 2020;2(12):2583-94. doi:10.1007/s42399-020-00645-x
21. Bulut C, Kato Y. Epidemiology of COVID-19. Turk J Med Sci. 2020;50(SI-1):563-570. Published 2020 Apr 21. doi:10.3906/sag-2004-172
22. Aksel G, İslam MM, Algın A, et al. Early predictors of mortality for moderate to severely ill patients with Covid-19. Am J Emerg Med. 2021;45:290-6. doi:10.1016/j.ajem.2020.08.076
23. Duyan, M, Ozturan IU. Comparıng the effects of hydroxychloroquıne, favıpıravır, and hydroxychloroquıne plus favıpıravır on survıval of gerıatrıc populatıon wıth covıd-19-related pneumonıa: a propensıty score-matched analysıs. Turkish Journal of Geriatrics, 2022, 25.1. doi: 10.31086/tjgeri.2022.271
24. Wynants L, Van Calster B, Collins GS, et al. Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal [published correction appears in BMJ. 2020 Jun 3;369:m2204]. BMJ. 2020;369:m1328. doi:10.1136/bmj.m1328
25. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020;50(4):332-4. doi:10.1016/j.medmal.2020.03.007
26. Ciceri F, Castagna A, Rovere-Querini P, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol. 2020;217:108509. doi:10.1016/j.clim.2020.108509
27. Bastug A, Bodur H, Erdogan S, et al. Clinical and laboratory features of COVID-19: Predictors of severe prognosis. Int Immunopharmacol. 2020;88:106950. doi:10.1016/j.intimp.2020.106950
28. Bedel C, Selvi F. Association of Platelet to Lymphocyte and Neutrophil to Lymphocyte Ratios with In-Hospital Mortality in Patients with Type A Acute Aortic Dissection. Braz J Cardiovasc Surg. 2019;34(6):694-8. doi:10.21470/1678-9741-2018-0343
29. Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A. Neutrophil Lymphocyte Ratio and Cardiovascular Disease Risk: A Systematic Review and Meta-Analysis. Biomed Res Int. 2018;2018:2703518. doi:10.1155/2018/2703518
30. Yadaw AS, Li YC, Bose S, et al. Clinical predictors of COVID-19 mortality. medRxiv : the preprint server for health sciences, 2020.05.19.20103036. doi: 10.1101/2020.05.19.20103036
31. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51. doi:10.3760/cma.j.issn.0254-6450.2020.02.003
32. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42. doi:10.1001/jama.2020.2648
33. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy [published correction appears in JAMA. 2021 May 25;325(20):2120]. JAMA. 2020;323(16):1574-81. doi:10.1001/jama.2020.5394
34. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. J Med Virol. 2020;92(4):441-7. doi: 10.1002/jmv.25689
35. Preti C, Biza R, Novelli L, et al. Usefulness of CURB-65, pneumonia severity index and MULBSTA in predicting COVID-19 mortality. Monaldi Arch Chest Dis. 2022;10.4081/monaldi.2022.2054. doi:10.4081/monaldi.2022.2054

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EFFECTS OF TRADITIONAL TURKISH MUSIC EDUCATION ON VOICE RANGE PROFILE AND VOICE QUALITY

GELENEKSEL TÜRK MÜZİĞİ EĞİTİMİNİN SES ALANI VE SES KALİTESİ ÜZERİNE ETKİSİ

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Abstract

Aim: The aim of this study; to investigate whether traditional Turkish music education is as effective on voice range profile and voice quality as classical music education.

Methods: Twenty volunteers in the Conservatory and 10 volunteers the Turkish Amateur Music Choir were included in the study. Digital recordings of the subjects' voices were obtained before and after 8 months of voice training. Voice recordings were analyzed with the Dr. Speech voice analysis program. Voice analysis results were compared between groups.

Results: Voice range profile was found expanded as 3, 2, and 5 semitones in group 1 (29 to 32 semitones), group 2 (30 to 32 semitones) and group 3 (23 to 28 semitones), respectively. The parameters of harmonic component of voice such as HNR, SNR, and NNE improved in all groups after voice training. GRBAS scores were normal in the conservatory group before training and improved following training in all groups, with the amateur group being the most obvious. When the alterations were compared between the groups, no significant differences were observed between the first and second conservatory groups, whereas a significant difference was observed between the amateur group and the first and second conservatory groups in seven parameters (amplitude tremor, HNR, SNR, NNE and GRBAS).

Conclusions: This is the first study about the effects of traditional Turkish music education on subjective and objective parameters of the singing voice. Our research shows that traditional Turkish music education improved the singing voice improvements as much as with classical music.

Keywords: Quantitative voice assessment, voice, voice range profile, voice training

Öz

Amaç: Bu çalışmanın amacı; geleneksel Türk müziği eğitiminin ses alanı profili ve ses kalitesi üzerinde klasik müzik eğitimi kadar etkili olup olmadığını araştırmaktır.

Yöntemler: Çalışmaya Konservatuar'dan 20 gönüllü ve Türk Müziği Amatör Korosundan 10 gönüllü alındı. 8 aylık ses eğitimi öncesi ve sonrasında deneklerin seslerinin dijital kayıtları alındı. Ses kayıtları Dr. Speech ses analiz programı ile analiz edildi. Ses analizi sonuçları gruplar arasında karşılaştırıldı.

Bulgular: Ses aralığı profili sırasıyla Grup 1'de (29- 32) 3 yarım ton, grup 2'de (30- 32) 2 yarım ton ve grup 3'te (23- 28) 5 yarım ton genişletilmiş bulundu. HNR (harmonic to noise ratio), SNR (signal to noise ratio), NNE (normalized noise energy) gibi sesin harmonik bileşenlerinin parametreleri, ses eğitimi sonrası tüm gruplarda düzeldi. GRBAS skorları, konservatuvar grubunda ses eğitimi öncesi normaldi ve amatör grupta diğer gruplara göre daha belirgin düzeldi. Gruplar arasındaki değişimler karşılaştırıldığında, birinci ve ikinci konservatuvar grupları arasında anlamlı bir farklılık gözlenmezken amatör grup ile birinci ve ikinci konservatuvar grupları arasında yedi parametrede (amplitüd tremor, HNR, SNR, NNE ve GRBAS) anlamlı farklılıklar izlendi.

Sonuç: Bu çalışma geleneksel Türk müziği eğitiminin ses alanı ve ses kalitesi üzerindeki etkilerini inceleyen ilk çalışmadır. Araştırmamız, geleneksel Türk müziği eğitiminin, ses alanı ve ses kalitesi üzerinde klasik müzik kadar etkili olduğunu göstermektedir.

Anahtar Kelimeler: Sayısal ses değerlendirmesi, ses, ses aralığı profili, ses eğitimi

Introduction

With the rapidly developing technology and the reflection of technology in the field of medicine, research on language and speech disorders, which has gained more importance in recent years, has accelerated. The Dr. Speech voice analysis program and Praat are the most frequently used programs that provide a technological and objective evaluation of voice This is an important feature, especially for professional voice performers[1,2].

Many subjective and objective methods are used to evaluate voice. The grade, roughness, breathiness, asthenia, strain (GRBAS) scale can be used for perceptual evaluation and is a subjective method[3,4]. Parameters such as fundamental frequency (F0), jitter (frequency perturbation), shimmer (amplitude perturbation), standard deviation of fundamental frequency (SD-f), standard deviation of amplitude (SD-amp), harmonic to noise ratio (HNR), signal to noise ratio (SNR), normalized noise energy (NNE), tremor of frequency (F-tremor), and tremor of amplitude (A-tremor) are mainly measured in objective evaluation[5,6]. The aim of classical music education is to teach how to use voice correctly and effectively. Vocal education includes correct learning of anatomy and physiology, posture, breathing, relaxation exercises, phonation, resonance, and articulation[7].

Turkish music is among the most popular genres of music. Popular music includes Turkish music, Classical music, and Far Eastern-Central Asian music [1]. The universal sets of this musics are different. The factor that creates the difference is the distance between the voice range profile in this set. In Far Eastern-Central Asian music, an octave is divided into six unequal ranges, in classical music it is divided into 12 equal semitones, and in traditional Turkish music, it is divided into 24 unequal ranges. This segmentation is one of the most influential elements both on the creation of melody and on performance and style. Music is universal and culturally expresses local customs and traditions.

This assertion may be about musical systems. Traditional Turkish music has emerged as a product of Central Asia, Seljuk, and especially the Ottoman civilization; it has become a very rich type of music both in terms of the number of melodies, forms, and methods. In traditional Turkish music, melodies follow each other without repeating themselves, whereas classical music repeats simultaneously or sequentially. When a Turkish, Chinese or an Australian artist performs the same note, they sing it in different styles [7,8].

Although the effects of classical music education have been investigated many times, the effects of traditional Turkish music education on the vocal range profile and vocal quality have not been investigated. In this study, the effects of Turkish music education on the vocal range profile and voice quality between conservatory students and an amateur choir were examined.

Materials and Methods

- *Research Group*

Twenty students from the Singing Class of Ege University Turkish Musical State Conservatory Voice Training Department and 10 volunteers from Celal Bayar University Turkish Music Amateur Choir participated in the study. The conservatory students had passed the conservatory acceptance examination, had a high voice range profile, and high voice quality, and had already received training. Eleven of the conservatory students (6 males and 5 females) were in the first year (group 1) and nine (3 males and 6 females) (group 2) were in the second year. In the amateur choir (1 male and 9 females) (group 3), volunteer students and staff were trained by a laryngologist, who is a knowledgeable professor about the anatomy and physiology of voice. All students participated in the training and study for 8

months between October 2011 and May 2012.

Eleven students from the conservatory indicate only group 1 participated in 16 hours of singing lessons per week (4 hours singing technique, 6 hours basic music solfege in normal speech tones and basic music theory, 6 hours Turkish music solfege and theory). Nine students from the conservatory indicate only group 2 participated in 27 hours singing training program per week (2 hours singing technique, 8 hours basic music solfege in speech tones and basic music theory, 6 hours Turkish music solfege and theory, 7 hours classical Western music technique repertoire, 4 hours classical Turkish music chorus work).

Ten people who attended the amateur choral performed breathing, relaxation, trill exercises aloud. (Trill without losing tension between half ton range; this goes up and down quickly or rather it goes up and down, which can be achieved by vibrating tongue and palate the sound of ‘‘r’’), and Turkish music singing 2-3 hours per week during the study period. They performed tongue trills exercises at home instructed by conductor. These participants had not been trained on notes at the conservatory like conservatory students. They were taught in the classic Turkish music style, call and response. Songs were sung by a laryngologist trained in vocal anatomy and physiology, and the amateur choir tried to sing it by listening. The amateur choir has no hobbies related to other types of music.

- *Data Collection Process*

A voluntary written proclamation form was obtained from the subjects. A general ear, nose, and throat (ENT) examination was performed. The participant form questioned identity information, smoking habits, hearing problems and reflux, whether the participants had undergone any surgery on otolaryngology, and previous voice training.

At the beginning of the first semester, videolaryngostroboscopy (VLS) was performed using a Storz 8020 laryngoscope to identify whether the participant had laryngeal pathologies. Those who were found to have closing defects, vocal nodules, sulcus vocalis, Reinke’s edema, vocal polyps, traumatic corditis in the vocal cords in stroboscopic examinations were excluded from the study. In all groups, students who did not participate in voice training courses for any reason and smoking, had hearing problems and reflux, undergone any surgery on otolaryngology, in the last three months were excluded. Students who regularly attended conservatory and amateur choir trainings, whose voice recordings were completed and whose GRBAS scores were normal, were included in the study.

Voice recordings were performed in a quiet room using a computer, the Cool Edit program, and a Philips condenser microphone. Voices were recorded using mono, 44.100 Hz sample rate and 16-bit sample depth. Ten minutes of vocal warm up exercise was performed before the student’s voice recordings. The microphone was held at a distance of 10 cm by a researcher, and a total of 40-90 seconds of recording was taken by keeping the speech tone and a few low and high pitched sounds for 5-10 seconds.

Vocal range refers to the full spectrum of pitches that a human voice can produce, starting from the lowest note and reaching to the highest note. The vocal range of the students was identified using a Yamaha Porta Sound PC 100 branded piano by a professional conservatory lecturer. Musically acceptable bass and high-pitched notes were identified with semi-tone sensitivity. Modal registers for boys and girls were included in the vocal range profile. The same procedures were repeated at the end of the study corresponded to 8th month in both groups.

The instrumental and perceptual evaluation was done by the same person who was unaware of the results before and after for

all participants. For GRBAS scoring, audio samples were listened to by 2 separate people and averaged. Their average scores were accepted for statistical analysis; 0=normal, 1=mild impairment, 2=medium impairment, and 3=worst.

- *Voice analysis*

After all the audio recordings were taken, all audio was listened to again, and the 3-4 second tracks with high musicality tone were recorded as a separate audio file. Among them, at least three voice recordings were selected, which were the best for pre- and post-training. It was decided which voice recording would be chosen by listening to the recorded voices of the students and the amateur choir by the two researchers according to the clarity of the voice. The clarity of the voice was depended to the decreased noise ratio. That is: as the noise ratio in the environment decreases, the clarity of the voice increases. The same vowel is chosen for all recordings and all singers.
The same passages were used in the pre and post tests for each singer. A total of six fragmented averages (three first semesters and three second semesters) for each student were analyzed using the Dr. Speech Voice analysis program (Tiger DRS Inc, Seattle, WA). The results of this analysis were used for the statistical analysis. By performing voice analysis on each recording, F0, jitter, shimmer, SD-f, SD-amp, HNR, SNR, NNE, f-tremor, and a-tremor data were found. These parameters are the most frequently used parameters that give information about the quality of the voice. Jitter and shimmer % values are the average values of the others.
In this study, parameters such as mean F0, max-min F0, mean amplitude, max-min amplitude, mean period, and max-min period, which were measured using the Dr. Speech Voice Analysis program, were not evaluated statistically because these parameters vary according to the sex of the person, the voice they produce, the duration of the sound, the intensity, the microphone characteristics, and the distance. Therefore, these parameters may not be suitable for measuring the effect of voice training on voice quality.

- *Statistical Analysis*

Analysis of the data was performed using the SPSS 11.5 package program. In the data obtained by counting, frequency (percentage) was accepted as descriptive measures, and in variables obtained by measurement, mean, standard deviation, median, minimum-maximum were accepted as descriptive measures. $p<0.05$ was considered statistically significant. The Mann Whitney U test and Wilcoxon Signed Ranks test was used for comparison between groups.

- *Ethical Approval*

This study was approved by the local ethics committee with the decision dated 23.03.12 and numbered 114.

Results

Three groups joined the study. The average ages were 20.8 years for group 1, 21.1 years for group 2, and 26.7 years for group 3. Group 1 consisted of five females and six males, group 2 was consisted by six females and three males, and group 3 consisted of nine females and one male. There was no statistically significant difference between the groups in terms of age and gender.
The mean values of pre-training data were compared among the groups using the Mann Whitney -U test. There was no significant difference in the parameters between the first and second groups before the training. The comparison between group1, group2, and group3, significant differences were found in voice range profile, jitter %, shimmer %, A-tremor, HNR, SNR, NNE, hoarseness, roughness,

Table 1. Averages of groups' pre-training data and comparisons between the groups.

	GROUP 1		GROUP 2		GROUP 3	
	Mean (min-max) SD	P between 1- 2	Mean (min-max) SD	P between 2- 3	Mean (min-max) SD	P between 1-3
Voice range profile (Semi-tone)	29,2±3.3 (25-34)	0.56	29.8±2.8 (23-32)	0.01	22.8 ±5.7 (14-33)	*0.01*
Jitter %	0.07±0.02 (0.02-0.1)	0.32	0.1 ±0.04 (0.06-0.2)	0.01	0.2±0.1 (0.1-0.4)	<0.001
Shimmer %	1.04±1.1 (0.80-1.30)	*0.88*	1.1±0.5 (0.50-2)	0.02	2.2±1.2 (0.3-5.1)	<0.001
F-tremor	2.1±1.1 (1-4.90)	0.79	2.4±0.3 (1-4.50)	0.39	3.6 ±3.4 (1.1-12)	0.32
A-tremor	1.8±0.9 (1-4.50)	0.16	1.5±0.7 (1-3.40)	<0.001	6 ±4 (1-12)	<0.001
HNR	27.5 ±2.7 (24-33)	0.97	27.2±4.4 (20-33)	<0.001	20.1±4 (14-26)	<0.001
SNR	25.8±3 (20-31)	0.54	26.7±3.9 (20-32)	<0.001	18.9±4 (13-25)	<0.001
NNE	-17.1±2.9 (-23, -18)	0.22	-19.1±3.9 (-25, -13)	<0.001	-9.3 ±4 (-16,-5)	<0.001
Hoarseness	0.09 ±0.3 (0-1)	0.88	0.1±0.3 (0-1)	<0.001	0.9±0.3 (0-1)	<0.001
Roughness	0.09±0.09 (0-1)	0.88	0.1 ±0.3 (0-1)	0,60	0.2±0.4 (0-1)	0.49
Breathiness	0 ±0 (0-0)	0.999	0±0 (0-0)	<0.001	1.8±0.3 (0-3)	<0.001

Mann Whitney U test, F-tremor: Tremor of frequency, A-tremor: Tremor of amplitude, HNR:The harmonic-to-noise ratio , SNR:The signal-to-noise ratio , NNE: Normalized noise energy, GRBAS: The grade, roughness, breathiness, asthenia, strain

breathiness, and general sound quality (GRBAS) parameters before voice training (Table 1).

The pre-training and post-training values of each group were assessed separately. The averages of the data before the participants' training and the data after the training were one of 14 parameters in group 2, and seven of 14 parameters in group 3 were positively and compared with Wilcoxon signed ranks test. It was seen that four of 14 parameters in group 1, significantly changed. It was observed that the voice range profile expanded by three semitones in the first group, from 29 to 32 semitones; by two semitones in the group 2, from 30 to 32 semitones; and by 5 semitones, from 23 to 28 semitones in the group 3. It was observed that the voice range profile increased by an average of 2- 5 semitones and the greatest expansion was in the amateur choir. The values before and after training in jitter, shimmer, F-tremor, A-tremor, SD-f, SD-amplitude, which are among the objective parameters, were already within normal limits in groups 1 and 2. Therefore, the improvements that occurred were not considered significant. in group 2. Significant improvements were seen in voice range profile and A-tremor in group 3. In the HNR, SNR, and NNE parameters related to the harmonic component of the sound, the changes in groups 1 and 2 were not significant in the values before and after

Table 2. Comparison of groups' mean of pre-training data and post-training data

PARAMETER	GROUP 1			GROUP 2			GROUP 3		
	Before Mean ±SD (min-max)	After Mean ±SD (min-max)	P	Before Mean ±Sd (min-max)	After Mean ±SD (min-max)	P	Before Mean ±SD (min-max)	After Mean ±SD (min-max)	P
Voice range profile (Semi-tone)	29,2±3.3 (25-34)	31,9 ±3.7 (27-38)	*0.007*	29.8±2.8 (23-32)	32.2±4.1 (26-39)	0.105	22.8±5.7 (14-33)	27.2±5.9 (19-36)	*0.005*
Jitter %	0.07±0.02 (0.02-0.1)	0,1±0.1 (0-0.40)	0.623	0.1 ±0.04 (0.06-0.2)	0.07 ±0.03 (0-0.20)	0.141	0.1±0.1 (0.1-0.4)	0.1±0.1 (0-0.40)	0.292
Shimmer %	1.±0.1 (0.80-1.30)	1.5±0.3 (1.10-2.1)	*0.003*	1.1±0.5 (0.50-2)	1.6±0.5 (1.1-2)	0.066	2.2±1.2 (0.3-5.1)	2±0.8 (1.16-3.3)	0.838
F-tremor	2.1±1.1 (1-4.90)	1.70 (1-3.20)	0.292	2.4±0.3 (1-4.50)	1.4±0.7 (1-3.10)	0.063	3.6±3.4 (1.1-12)	2.3±1.7 (1-5.3)	0.415
A-tremor	1.8±0.9 (1-4.50)	0.86 1.3±0.3 (1-1.90)	*0.050*	1.5 ±0.7 (1-3.40)	2.6±1.4 (1.10-5)	0.097	6 ±4 (1-12)	1.2 ±0.2 (1-1.8)	*0.008*
SD-f	1.3±0.8 (0.50-3)	1.3±0.5 (0.80-2.3)	0.766	1.8 ±0.9 (0.60-4)	1.8±0.8 (0.80-3)	0.635	2.3±1.2 (0.9-4.9)	1.8±0.8 (0.8-4.07)	0.283
SD-amp	7 ±1.7 (4.70-1)	5 ±0.6 (4-6)	*0.005*	7.3±2.2 (5-12)	±1.1 (2-6.50)	*0.008*	4.8±2 (0.5-6.7)	5.8 ±2.7 (1-10)	0.203
HNR	27.5±2.7 (24-33)	28.7±1.4 (25-31)	0.181	27.2 ±4.4 (20-33)	27.2±2.6 (24-31)	0.999	20.1±4 (14-26)	26.5±3 (21-31)	*0.012*
SNR	25.8±3 (20-31)	27±2.4 (22-30)	0.109	26.7±3.9 (20-32)	26.1 ±2.5 (23-30)	0.495	18.9±3.7 (13-25)	25.8 ±3.2 (20-30)	0.11
NNE	-17.1±2.9 (-23, -18)	-17.3±3.5 (-23 ,-11)	0.894	-19.1±3.9 (-25, -13)	-17.1±2.9 (-22, -13)	0.154	-9.3 ±4 (-16,-5)	-15.9 ±5 (-25 , -10)	*0.008*
Hoarseness	0.09 ±0.3 (0-1)	0±0 (0-0)	0.317	0.1±0.3 (0-1)	0 ±0 (0-0)	0.317	0.90 (0-1)	0.10 (0-1)	*0.005*
Roughness	0.09±0.09 (0-1)	0±0 (0-0)	0.317	0.1±0.3 (0-1)	0 ±0 (0-0)	0.317	0.2±0.4 (0-1)	0.1±0.3 (0-1)	0.564
Breathiness	0 ±0 (0-0)	0.09±0.9 (0-1)	0.317	0±0 (0-0)	0±0 (0-0)	0.999	1.8±0.3 (0-3)	0.2 ±0.4 (0-1)	*0.016*
GRBAS (Overall Voice Quality)	0,2±0.6 (0-2)	0.09±0.3 (0-1)	0.655	0.2±0.6 (0-2)	0±0 (0-0)	0.317	2.9±1.2 (0-4)	0.5±0.9 (0-3)	*0.011*

Wilcoxon Signed Ranks test SD-f: The standard deviation of the fundamental frequency , SD-amp:The standard deviation of amplitude , F-tremor: Tremor of frequency , A-tremor: Tremor of amplitude, HNR:The harmonic-to-noise ratio , SNR:The signal-to-noise ratio , NNE: Normalized noise energy, GRBAS: The grade, roughness, breathiness, asthenia, strain

the training, but these values were significant group 3. In the parameters of hoarseness, breathiness, and GRBAS scale regarding the perceptual analysis of voice, the changes in groups 1 and 2 were not significant but were significant in the group 3. An increase in modal register width was observed in all groups after voice training (Table 2).

The changes following voice training were investigated among the groups. The difference between the pre- and post-training values of each parameter was found for each participant; and the averages of the groups were compared using the Mann - Whitney U test. There was no significant difference between groups 1 and 2 in any parameters, but significant differences were found *between group 3* and the other groups. When the amateur choir and the first year and the second-year students of the conservatory were compared, there was a significant difference in *seven parameters including a-tremor, HNR, SNR, NNE, and GRBAS* ($p<0.05$) (Table 3).

Discussion

The education and training of the singing voice in an esthetically pleasing manner takes years and can only be achieved based

Table 3. Comparison between the groups: the average of differences between pre- and post-training values.

PARAMETER	Group 1 Mean± (min-max)	group 1-3 p	Group 2 Mean± (min-max)	group 2-3 p	Group 3 Mean± (min-max)	group 1-3 p
Voice range	2.6 ±0.1 (0-9)	0.281	3.4 ±0.8 (0-7)	0.506	4.4 ±1.3 (1-8)	0.075
Jitter %	-0.2±0.4 (-0.3, -0.1)	0.432	0.2±0.7 (-0.2, 0.1)	0.897	0.3±0.8 (-0.10, 0.20)	0.429
Shimmer %	-0.5±0.2 (-1, -0.1)	0.939	-0.5±.8 (-2, 0.90)	0.165	0.2±0.1 (-1.06, 3.2)	0.120
F-Tremor	0.4±1.1 (-1.5, 3.40)	0.490	1 ±0.7 (-1.2, 3)	0.437	1.2±0.8 (-2.9,11.3)	0.916
A-tremor	0.4 ±0.8 (-0, 2.90)	0.023	-1.1±0.9 (-4, 1.5)	*0.001*	4.7±1.7 (0-11)	*0.002*
HNR	-1.1±0.9 (-6, 2)	0.422	0.0 (-6, 6)	*0.011*	-6.4±1.4 (-12, 0)	*0.019*
SNR	-1.2±0.4 (-6, 1)	0.206	0.6±0.2 (-5, 7)	*0.003*	-6.8 ±0.8 (-12, 0)	*0.004*
NNE	0.1±0.4 (-8, 9)	0.380	-2 ±0.5 (-8, -4)	*0.004*	6.6 ±1.4 (-1, 15)	*0.012*
Hoarseness	0,09±0.1 (0-1)	0.084	0,1±0.1 (0-1)	0.003	8±0.7 (0-1)	*0.001*
Roughness	0.09±0.1 (0-1)	0.084	0.1±0.1 (0-1)	0.999	0.1±0.1 (-1, 1)	0.918
Breathiness	-0.1 ±0.8 (-1, 0)	0.343	0 ±0 (0-0)	*0.003*	1.6±0.6 (0-3)	*0.002*
GRBAS (Overall voice quality)	0.1±0.3 (-1, 2)	0.553	0.2±0.7 (0-2)	*0.003*	2.4 ±0.5 (0-4)	*0.002*

Mann Whitney U test, F-tremor: Tremor of frequency, A-tremor: Tremor of amplitude, HNR: The harmonic-to-noise ratio , SNR: The signal-to-noise ratio , NNE: Normalized noise energy, GRBAS: The grade, roughness, breathiness, asthenia, strain

on capability. Voice training and voice rehabilitation are also exceptionally useful in correcting pathologies that result from poor performance of the professional voice [9]. The effects of classic music education on voice field and voice quality have been researched before. Previous studies have generally compared professional voice users who received voice training with a control group, but we could not find any studies that compared voice quality and voice range profile before and after vocal training in Turkish music. In this study, the effects of professional Traditional Turkish music education in conservatory and amateur choral, on objective and subjective voice parameters were examined.

It is not possible to obtain a completely improved objective measurement of aspects learned by voice training. Normally, 2 to 4 years of voice training improves the voice. However, voice training given in a short period such as 6 months also affects the voice quality and range positively [10,11]. Voice training can improve breathing, position (body posture while singing), posture, sound intensity, resonance, smoothness, and timbre, and other factors

improve with singing training. The parameters we used in this study: voice range, jitter (%), shimmer (%), HNR, NNE, SNR, were used to evaluate voice quality in many previous studies [12,13,14]

In group 1, the vocal range expanded by three semitones (29 to 32), in group 2 two semitones (30 to 32), and in group 3 by 5 semitones (23 to 28). we observed. Conservatory students are generally students who have passed the conservatory exam and have a wider vocal range than the amateur choir. Therefore, the expansion of the vocal range in the conservatory group is less than in the amateur choir.

Siupsinskien et al. examined the effects of voice training on vocal capabilities in vocally healthy age and gender differentiated groups measured by voice range profile (VRP). When compared with nonsingers, both genders of trained adult and child singers exhibited increased mean pitch range, highest frequency, and VRP area in high frequencies ($p < 0.05$)[15]. Voice training has significant positive effects on vocal capability parameters measured by VRP, Suipsinskien et al. in contrast, we saw more VRP increases in the amateur choir in our study. This may be because the amateur choir initially had a lower VRP.

In our study, the amateur choir sang using the traditional Turkish method 2-3 hours per week after 5-10 minutes of warm-up exercises (trill, vibration of lip- palate and tongue). As a result of the ongoing 8-month voice training study, a clear improvement in the voice quality parameters and a 5 half-tone expansion in the voice range profile were observed. This showed that with training, the singers could expand their voice range profile even by singing, and that they could produce a higher quality voice. In addition, in some studies; It has also been claimed that an 18-month long-term study is needed for voice training to cause a significant change in voice quality [11].

In the HNR, SNR, NNE parameters, the changes in groups 1 and 2 were not significant in the pre- and post-training values, in group 3 these changes were significant. We observed a significant difference in seven parameters (a-tremor, HNR, SNR, NNE, hoarseness, breathiness, GRBAS) in the amateur choir compared with the conservatory first year students and second year students in post-training results. The harmonic values of the voice were positively affected in all groups. The lack of significant change in the jitter% value in our study (group 1, 2 and 3) may be due to the short duration of the voice training, Objective parameters, jitter, shimmer, A-tremor, F-tremor, SD-amp, and SD-F were already close to the minimum in groups 1 and 2 and the improvement after the voice training showed no significance. Conservatory students have a certain musical ear, and they can play at least one musical instrument and pass the acceptance exam. It is difficult to improve an already high musicality tone voice in 8 months. However, the quality of the amateur choir students was worse than that of the conservatory students, and the short-term voice training was sufficient to change their voice quality positively. Moreover, it has been shown that a significant improvement in voice range and quality could be possible with 3 hours of training and singing in traditional Turkish music, once per week for 8 months [8].

There are some limitations in the study. By making similar studies in the future with larger study groups, the effects of voice education on voice range profile and voice quality can be evaluated in greater detail. We used the VLS in the exclusion of organic voice pathologies. Our study was

not designed for comparing VLS values. After the voice training, studies that evaluate with VLS can be planned. During the 8-month vocal training, some students left the school and the choir, could not attend regular lessons and choral work, and could not be recorded for the second voice analyses, which affected the ratio of women to men among the groups. Self-perception assessment was not used in the education of groups. The records were only seen by the investigators for the study and were not shared. Therefore, the positive effects of visualization of singers were not implemented. Finally, if the goal was to verify how Turkish music increases the vocal range profile, no comparison has been made with another musical genre, if able to have the same effects.

Conclusion

This is the first study about the effects of traditional Turkish music education on subjective and objective parameters of the singing voice. Our research shows that traditional Turkish music education improved the singing voice, as much as with classical music education. İmprovements were observed both in conservatory students and amateur chorus, but excellent changes in voice range profile was observed in amateur chorus.

Some part of this study was presented as oral presentation at "24th International Rhinocamp 2021" held in Marmaris, entitled as "Effects of Traditional Turkish Music Education on Voice Range Profile and Voice Quality'

Author contributions

Concept A.K., A.V.Y., Design – A.K., Supervision A.K., A.V.Y., Materials – A.K., Data collection &/or processing – A.K., A.V.Y., Analysis and/or interpretation -A.K., Literature search – A.K., Writing – A.K., Critical review – AK.
All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

Permission was obtained from the Celal Bayar University, Medical Faculty Clinical / Human Research Ethics Committee for this study, and Helsinki Declaration rules were followed to conduct this study.(decision dated 23.03.12 and numbered 114)

References

1. Wendler J. Singing and science. Invited lecture at the 7th Pan-European voice conference (PEVOC7), Groningen, August 28 to September 1, 2007. Folia phoniatrica et logopaedica : official organ of the International Association of Logopedics and Phoniatrics (IALP).2008;*60*(6), 279–87.
doi: 10.1159/000170076
2. Dos Santos P, Vieira MN, Sansão J, et al. Effect of Auditory-Perceptual Training With Natural Voice Anchors on Vocal Quality Evaluation. Journal of voice : official journal of the Voice Foundation.2019;*33*(2):220–5.
doi: 10.1016/j.jvoice.2017.10.020
3. Nowosielska-Grygiel J, Olszewski J. The usefulness of the acoustic and the capacity analysis of singing voice. Otolaryngologia polska = The Polish otolaryngology. 2019;*73*(3): 16–25.
doi: 10.5604/01.3001.0013.1534
4. Ma EP, Yiu E. M. Multiparametric evaluation of dysphonic severity. Journal of voice : official journal of the Voice Foundation. 2006;*20*(3): 380–90.
doi: 10.1016/j.jvoice.2005.04.007
5. Brown WS, Jr Rothman HB, Sapienza CM. Perceptual and acoustic study of professionally trained versus untrained voices. Journal of voice : official journal of the Voice Foundation. 2000;*14*(3):301–9.
doi: 10.1016/s0892-1997(00)80076-4
6. Svec JG, Sundberg J, Hertegård S. Three registers in an untrained female singer analyzed by videokymography, strobolaryngoscopy and sound spectrography. The Journal of the Acoustical Society of America. 2008;*123*(1):347–53.
doi: 10.1121/1.2804939
7. Van Lierde KM, D'haeseleer E, Baudonck N, et al. The impact of vocal warm-up exercises on the objective vocal quality in female students training to be speech language pathologists. Journal of voice : official journal of the Voice Foundation. 2011;*25*(3):e115–e121.
doi: 10.1016/j.jvoice.2009.11.004

8. Costicova ND. Gagauz's Trıo "Oglan" As The Brıghtest Example Of Gagauzıan Musıc Culture . İnönü University Culture and Art Journal . 2017;3(1):187-97.
doi: 10.22252/ijca.337024
9. Sielska-Badurek EM, Sobol M, Olszowska K, et al. Contemporary Commercial Music Singing Students-Voice Quality and Vocal Function at the Beginning of Singing Training. Journal of voice : official journal of the Voice Foundation. 2018;*32*(6): 668–72.
doi: 10.1016/j.jvoice.2017.08.027
10. Brown WS, Jr Rothman HB, Sapienza CM. Perceptual and acoustic study of professionally trained versus untrained voices. Journal of voice: official journal of the Voice Foundation. 2000;*14*(3):301–9.
doi: 10.1016/s0892-1997(00)80076-4
11. Timmermans B, De Bodt MS, Wuyts FL, et al. Training outcome in future professional voice users after 18 months of voice training. Folia phoniatrica et logopaedica: official organ of the International Association of Logopedics and Phoniatrics (IALP). 2004;*56*(2):120–9.
doi: 10.1159/000076063
12. Van Lierde KM, D'haeseleer E, Baudonck N, et al. The impact of vocal warm-up exercises on the objective vocal quality in female students training to be speech language pathologists. Journal of voice: official journal of the Voice Foundation. 2011;*25*(3):e115–e121.
doi: 10.1016/j.jvoice.2009.11.004
13. Lundy, D. S., Roy, S., Casiano, R. R., et al. JAcoustic analysis of the singing and speaking voice in singing students. Journal of voice : official journal of the Voice Foundation.2000;*14*(4): 490–493.
doi: 10.1016/s0892-1997(00)80006-5
14. Heuillet-Martin G, Danoy MC, Florentin L, et all. Voir le "timbre" en voix chantée: éducation et rééducation [Seeing the timbre in the singing voice: training and retraining]. Revue de laryngologie - otologie – rhinologie. 1990;*111*(4):365–70.
15. Siupsinskiene NL. Effects of vocal training on singing and speaking voice characteristics in vocally healthy adults and children based on choral and nonchoral data. Journal of voice : official journal of the Voice Foundation. 2011;*25*(4):e177–e189.
doi: 10.1016/j.jvoice.2010.03.010

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BRAIN DEATH AND ORGAN DONATION DURING THE COVID-19 PANDEMIC: A RETROSPECTIVE OBSERVATIONAL STUDY

COVID-19 PANDEMİSİNDE BEYİN ÖLÜMÜ VE ORGAN BAĞIŞI: RETROSPEKTİF GÖZLEMSEL ÇALIŞMA

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Abstract

Aim: Transplantation processes were impacted worldwide due to the COVID-19 pandemic. The present study investigates brain death and cadaveric organ donation during the pandemic at a large referral hospital in Turkey.

Methods: All brain death cases diagnosed between 11.3.2020 and 11.3.2021 in our center were retrospectively evaluated. Patient data were analyzed, including demographic characteristics, family consent rates, and additional COVID-19 tests for donor eligibility. In addition, declaration and donation times, the number of donors, and the usability of organs were studied. Furthermore, the patients whose organs could not be used despite family consent were considered regarding the medical reasons for that outcome.

Results: 26 adult brain death cases were included in the study. Family consents were granted in seven (26.9%) patients. The organs of three of the seven cases with family consent were transplanted. In one of the remaining four, the second RT-PCR test was positive. In the other ones, both RT-PCR tests were negative, but COVID-19 could not be ruled out through laboratory tests and chest tomography, and bacteremia were evident in blood cultures. The non-donor's lymphocyte count (0.665 $\times 10^9$/L [0.340-0.770]) was significantly lower than that of donor (1.182 $\times 10^9$/L [1.050-1.780]) ($p < 0.05$). Besides, procalcitonin levels were significantly higher among non-donors (10.48 µg/L [3.19-26.68]) ($p < 0.05$).

Conclusions: The COVID-19 pandemic has drastically affected transplantation processes. Prolonged stays due to additional evaluations for COVID-19 may pose the risk of intensive care acquired infections in donors and should be careful in terms of donor loss due to infections.

Keywords: COVID-19, brain death, organ transplantation

Öz

Amaç: COVİD-19 pandemisi dünya genelinde olduğu gibi ülkemizde de organ nakli süreçlerini etkilemiştir. Bu çalışma ile pandemi döneminde bölgedeki en büyük referans pandemi hastanesindeki beyin ölümü ve kadaverik organ donasyonu olgularının değerlendirilmesi amaçlanmıştır.

Yöntemler: 11.3.2020-11.3.2021 tarihleri arasında hastanemizde tanı koyulan tüm beyin ölümü olguları retrospektif olarak değerlendirilmiştir. Demografik özellikler, aile onay oranları ve COVID-19 ekartasyonu açısından yapılan ek değerlendirmeler dahil olmak üzere hasta verileri analiz edildi. Deklarasyon ve donasyon süreleri, donor sayısı ve organların kullanılabilirlik oranları incelenmiştir. Ayrıca, aile onayı olmasına rağmen tıbbi nedenlerle organları kullanılamayan olgular, bu sonucun altta yatan nedenleri açısından değerlendirildi.

Bulgular: Çalışmaya 26 erişkin beyin ölümü olgusu dahil edilmiştir. Yedi (%26,9) hastada aile onayı mevcuttu. Aile onamı olan 7 olgunun 3'ünün organları transplante edilmiştir. Geri kalan olgulardan bir olgunun alınan ikinci RT-PCR testi pozitifti. Diğer olgularda her iki RT-PCR negatif olmasına rağmen laboratuar tetkikleri ve donasyon öncesi çekilen toraks tomografilerinde COVID-19 ekarte edilememişti, ayrıca kan kültürlerinde bakteriyemi mevcuttu. Donor olmayanların medyan lenfosit sayısı (0,665 × 109/L [0,340-0,770]), donorlere göre (1,182 ×109/L [1,050-1,780]) anlamı olarak düşüktü ($p < 0,05$). Ayrıca prokalsitonin düzeyleri donor olmayanlarda (10.48 µg/L [3.19-26.68]) anlamlı olarak daha yüksek saptandı ($p < 0,05$).

Sonuç: COVID-19 pandemisi transplantasyon süreçlerini büyük oranda etkilemiştir. Bu dönemde COVID-19 ekartasyonu açısından yapılan ek değerlendirmelere bağlı uzamış yoğun bakım yatış süreleri ve beraberinde gelişebilecek yoğun bakım kaynaklı enfeksiyonların, donor kaybı oranlarını artırabileceği göz önünde bulundurulmalıdır.

Anahtar Kelimeler: COVID-19, beyin ölümü, organ nakli

Introduction

Ongoing developments in transplantation present a life-saving treatment option for end-stage organ failures. However, donor pools for cadaveric organ transplantation remain limited. Accurate detection of brain death (BD) cases is critical for expanding organ donations and, hence, ensuring the continuity of transplantation processes, particularly those of heart and lung that can be performed via cadaveric donors.

The COVID-19 pandemic has impacted organ transplant processes worldwide. Similar situations had arisen during past viral disease outbreaks such as Ebola, West Nile Virus, SARS-CoV, and influenza A/H1N1, necessitating a series of arrangements to minimize setbacks in transplantation procedures. These include measures taken to screen donors for infectious diseases and avoid the risk of transmission to recipients, as well as healthcare professionals[1,2].

The COVID-19 pandemic has affected the whole world, resulting in the infection of more than 270 million people and the death of 5 million people as of December 2021[3]. The first COVID-19 case in Turkey was reported in March 2020; since then, healthcare resources and workforce have mainly been assigned to pandemic units to treat COVID-19 cases. In a similar vein, most intensive care unit (ICU) beds have been allocated for COVID-19 treatment, resulting in a lower overall number of BD cases that typically constitute the main supply of cadaveric donors. Besides, factors such as the necessity of immunosuppressant use after transplantation and the risk of asymptomatic COVID-19 in donors or recipients have also influenced transplantation processes negatively.

Current literature on COVID-19 is vast; however, there are limited studies on BD during the pandemic. The present study investigates BD cases and cadaveric organ donation during the pandemic at Ankara City Hospital, a large regional referral center. Accordingly, the study analyzes the relevant BD diagnosis rates, additional COVID-19 tests and consultations required for donor eligibility, the effect of these evaluations on declaration and donation times, and the resulting number of donors and usable organs.

Materials and Methods

This single-center, retrospective, observational study was conducted at a tertiary training and research hospital in Ankara, Turkey. Local ethics committee approval was obtained for the investigation (approval number: 2021/E2-21-391). All patient data were accessed through electronic medical records and files.

All BD cases diagnosed between 11.3.2020 and 11.3.2021 were retrospectively evaluated. Pediatric cases were excluded (age <18). Patient data were analyzed, including demographic characteristics, comorbidities, acute physiology and chronic health evaluation II (APACHE II) and Glasgow Coma Scale (GCS) scores at ICU admission, BD etiologies, clinical testing and radiological imaging, and laboratory findings.

In our center, BD diagnoses are made by the BD commission as per the criteria specified in the Organ and Tissue Transplantation Services Regulation, the Ministry of Health, Turkey (Official Gazette 01.02.2012, 28191)[4]. All patients having the preconditions for BD diagnosis undergo an apnea test (AT). If this is not feasible, computed tomography (CT) cerebral angiography is performed to assess cerebral blood circulation according to the Turkish Neurological Society, Diagnostic Guidelines for Brain Death[5]. After the diagnosis of BD, family interviews for donation consent are conducted by our hospital's organ and tissue transplantation coordinators. Then, the results of the interviews and patient data are submitted by the coordinators to the National Coordination Center for Organ Transplantation for further consideration. The present study covers the final outcomes of these assessments and the rates of donation and usable organs.

In Turkey, potential donors are evaluated during the COVID-19 pandemic as per the recommendations of the Ministry of Health, The Coronavirus Scientific Advisory Board. The Department of Tissue, Organ Transplantation Services requires from the donors at least two consecutive negative results for COVID-19 reverse transcription-polymerase chain reaction (RT-PCR) test from endotracheal aspirate with a minimum interval of 24 hours. Besides, the donors are inquired about disease symptoms and history of contact and travel. Furthermore, all donors are required chest CT and pulmonary diseases and infectious diseases consultations[6].

The analysis for the present study included all laboratory tests, chest CT imaging results, and additional evaluations for COVID-19 required from the donors, as mentioned above. The patients whose organs could not be used despite family consent, i.e., non-donors, were evaluated regarding the medical reasons for that outcome, laboratory values were compared. The investigation also covers the time from ICU admission to BD diagnosis and the time from family consent for donation to organ procurement.

• *Statistical analysis*

All statistical analyses were performed via the IBM SPSS Statistics 25.0 software package. The Shapiro-Wilk test, skewness and kurtosis values, and histograms were used to determine the conformity of variables to the normal distribution. Numerical variables with normal distribution are expressed as mean±standard deviation, and those without normal distribution as median (minimum-maximum [min-max]).

Categorical variables are presented as numbers and percentages. The Mann-Whitney U test was used to compare the medians of donor and non-donor laboratory values. A p-value <0.05 was considered statistically significant.

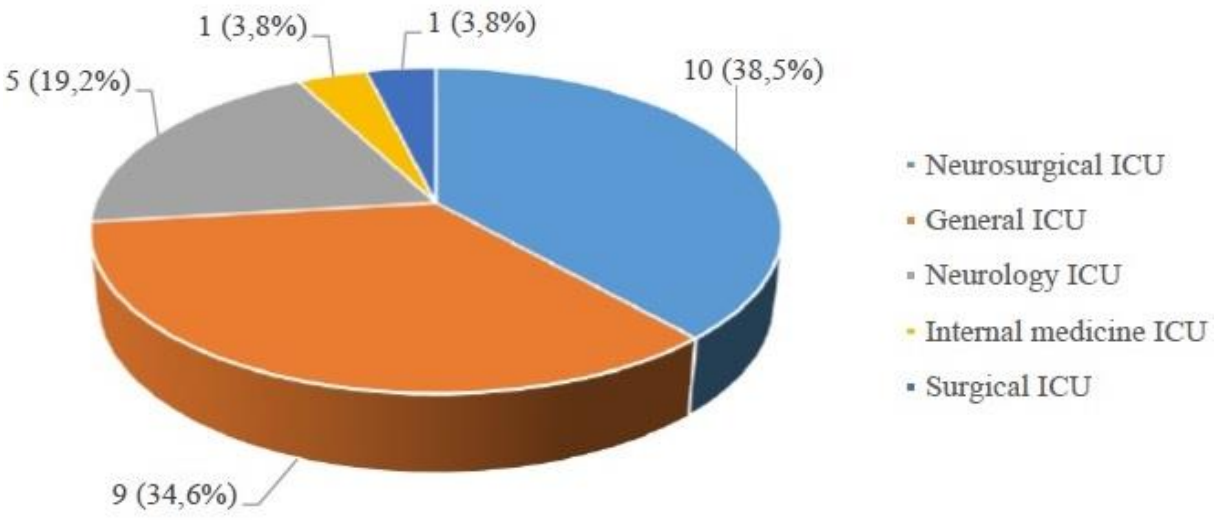

Figure 1. Intensive Care Units Where Patients Followed

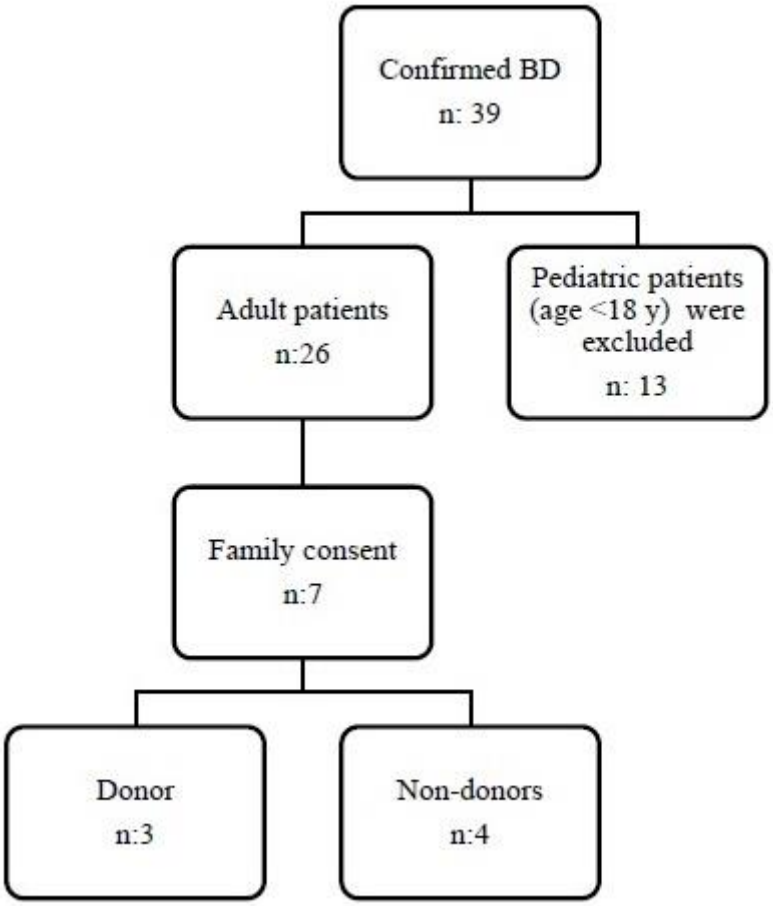

Figure 2. Brain Death, Family Consent and Donors in the First Year of the Pandemic

Results

There were 39 cases of confirmed BD in our center between 11.3.2020 and 11.3.2021, the initial year of the COVID-19 pandemic. 13 patients of age <18 were excluded. The median age of the remaining 26 BD cases was 46 (min-max, 20-78). 13 (50%) of these were male. Regarding ICUs and their respective departments, BD diagnosis was most frequent in neurosurgical ICU with 10 (38.5%) cases and least in internal medicine ICU and surgical ICU with one case each (3.8%) (Figure 1). The median ICU length of stay was 7.5 (min-max, 2.0-37.0) days. The median APACHE II and GCS scores at ICU admission were 26.5 (min-max, 17-50) and 5 (min-max, 3-7), respectively. Hypertension was the most frequent comorbidity, seen in nine (34.6%) cases (Table 1). The most common ICU admission diagnosis among BD cases was subarachnoid hemorrhage, followed by intraparenchymal hemorrhage (Table 2).

Five (19.2%) patients had undergone neurosurgery during their ICU stay. Three (11.5%) patients had trauma history.

17 patients having the preconditions for BD diagnosis had undergone AT. The median AT duration was 10 (min-max, 8-14) minutes. AT had been terminated in five (19.2%) patients due to hemodynamic instability. The CT angiography was performed as an ancillary test in 25 (96.2%) patients and transcranial Doppler in one patient. The families of confirmed BD cases were invited by our hospital's organ and tissue transplantation coordinators for interview.

Table 1. Demographic and Clinic Characteristics and Comorbidities of Patients

Age, median (min-max), y	46 (20-78)
Male, No. (% of total)	13 (50%)
LOS ICU (days) median (min-max)	7.5 (2.0-37.0)
GCS, median (min-max)	5 (3-7)
APACHE II, median (min-max)	26.5 (17-50)
Comorbidities of Patients, No. (% of total)	
Hypertension	9 (34.6)
Diabetes mellitus	2 (7.7)
Chronic obstructive pulmonary disease	2 (7.7)
Cardiovascular disease	3 (11.5)
Chronic renal failure	2 (7.7)
Cerebrovascular disease	6 (23.1)
Others*	5 (19.2)

APACHE II: acute physiology and chronic health evaluation-II scores, GCS: Glasgow Coma Scale, ICU: intensive care unit, min-max: minimum to maximum, LOS: length of stay
*Others: Chrone diesase, chronic liver failure, hyperlipidemia, systemic lupus erythematosus

Family consent was granted in seven (26.9%) patients; one patient was excluded from donor evaluation due to being foreign national as per the decisions of the Ministry of Health, the National Coordination Center for Organ Transplantation; the families of five (19.3%) patients declined multiple invitations for interview, and those of 13 (50%) patients refused to consent to donation. None of our BD cases had an organ donation card beforehand. The most common blood group among our patients was A (42.3%). Table 3 shows patient laboratory findings at the time of BD diagnosis. The Department of Tissue, Organ Transplantation Services published instructions on 20.3.2020 to rule out COVID-19 in potential donors. Two of our cases diagnosed before this date had no COVID-19 RT-PCR tests but had not been donors either. The testing was performed in all subsequent BD cases. COVID-19 RT-PCR positivity was detected in 3 patients. 23 (88.5%) cases diagnosed with BD underwent chest CT imaging for COVID-19 screening. All donors had chest CT scans and two consecutive negative RT-PCR test results at least 24 hours apart. In the end, the organs of three of the seven cases with family consent were transplanted (Figure 2).

Table 2. Etiology of Brain Death

	No. (% of total)
Subarachnoid hemorrhage	12 (46.2)
Intracerebral hematoma	5 (19.3)
Ischemic stroke	4 (15.4)
Metanol intox	2 (7.7)
Postcardiorespiratory arrest	1 (3.8)
Meningitis	1 (3.8)
Intracranial tumor	1 (3.8)

Table 3. Laboratory Tests of Patients at Diagnosis of Brain Death

Hemoglobin, g/dL	9.7±2.6
WBC, $\times 10^9$/L	13.6±7.0
Lymphocytes, $\times 10^9$/L	1.334±0.664
Platelets, $\times 10^9$/L	187.5 (37.0-451.0)
CRP, g/L	0.18 (0.01-0.55)
PCT, μ g/L	1.24 (0.03-49.37)
Glucose, mg/dL	135.5 (65.0-292.0)
LDH, U/L	537 (227-7658)
Serum creatinine, mg/dl	1.90 (0.42-5.28)
Urea mg/dl	75 (16-201)
AST, U/L	186.5 (25.0-1046.0)
ALT, U/L	59.5 (10.0-451.0)
Sodium, mEq/L	151.1±14.5
Blood groups No. (%)	
A	11 (42.3)
B	4 (15.4)
AB	3 (11.5)
0	8 (30.8)

Abbreviations: ALT: alanine aminotransferase, AST: aspartate aminotransferase, CRP: C-reactive protein, LDH: lactate dehydrogenase, PCT: procalcitonin * Numerical variables with normal distribution are expressed as mean±standard deviation, and those without normal distribution as median (minimum-maximum).

The heart and kidneys were used for transplant in the first case; the heart, liver, kidneys, and corneas in the second case; and the heart, kidneys, and corneas in the third.

The patients whose organs could not be used despite family consent, i.e., non-donors, were evaluated regarding the medical reasons for that outcome. In one of these non-donors, the second RT-PCR test was positive. In the other ones, both RT-PCR tests were negative, but COVID-19 could not be ruled out through laboratory tests and chest CT, and positive blood cultures indicated bacteremia. Therefore, these patients had been considered ineligible for organ donation by the National Coordination Center for Organ Transplantation.

Donor and non-donor some infection laboratory values measured at evaluation day were also compared. The non-donor's median absolute lymphocyte count (0.665 $\times 10^9$/L [min-max, 0.340-0.770]) was significantly lower than that of donor (1.182 $\times 10^9$/L [min-max, 1.050-1.780]) ($p < 0.05$). Besides, procalcitonin levels were significantly higher among non-donors (μg/L: 10.48 [min-max, 3.19-26.68]) ($p < 0.05$) (Table 4).

Table 4. Donor and Non-donor's Some Infection Laboratory Values

	Donor n=3	**Non-donor n=4**	**p-value***
WBC, $\times 10^9$/L	14.00 (11.00-17.57)	14.76 (4.35-16.95)	0.724
Lymphocytes, $\times 10^9$/L	1.182 (1.050-1.780)	0.665 (0.340-0.770)	0.034
LDH	620 (306-991)	743 (469-1297)	0.724
PCT, μ g/L	0.29 (0.13-0.38)	10.48 (3.19-26.68)	0.034
CRP, g/L	0.08 (0.07-0.16)	0.31 (0.13-0.40)	0.077

CRP: C-reactive protein, LDH: lactate dehydrogenase, min-max: minimum to maximum, PCT: procalcitonin, WBC: white blood cell, *Mann-Whitney U test, $P < .05$, statistically significant.

Finally, the time intervals relevant to BD diagnosis and organ procurement were considered. The median time from ICU admission to BD diagnosis was 4 (min-max, 1.0-36.0) days. In the donors, the time from family consent for donation to organ procurement was 18.5 hours in the first case, 18.2 hours in the second, and 6.2 hours in the third.

Discussion

Transplant procedures have been a drastically affected area of healthcare during the COVID-19 pandemic. The number of organ transplantations decreased worldwide, as well as in Turkey, especially in the early stages of the pandemic[7,8]. In the present study, BD was diagnosed in 26 adult patients between 11.3.2020 and 11.3.2021. As our center is the largest pandemic hospital in the region, the vast majority of ICU beds were reserved for COVID-19 treatment. BD most frequently occurred in our neurosurgical ICU. However, the number of beds in the neurosurgical ICU had decreased from 48 to 16 during pandemic. The case was similar for general ICU and neurological ICU bed capacity. This reduction seems to be the main reason for the low number of donors during the pandemic. Besides, cases of trauma, which typically constitute the primary BD etiology, were referred to other hospitals in Ankara since the trauma resuscitation area in our emergency clinic had also been allocated for COVID-19 patients. This has been another reason for the low rate of BD cases.

The appointment of healthcare professionals, such as organ and tissue transplant coordinators and transplant surgeons, in COVID-19 services has also impacted transplantation processes. There are nine transplant coordinators in our center, and they continued to work in their unit during the pandemic to maintain the processes of donor identification and transplantation and minimize the risk of viral transmission. During the pandemic, family interviews have generally been conducted via telephone worldwide[9]. However, the transplant coordinators in our center continued face-to-face interviews, observing protective measures against infection[10]. Open and effective communication is key in obtaining family consent for organ donation in BD cases. Otherwise, high refusal rates are inevitable[11]. The family consent rate for organ donation was 26.9% (n = 7/26) among our BD cases. In contrast, the Ministry of Health, Department of Tissue, Organ Transplantation Services data for 2020 indicate a family consent rate of 18.9% (n = 263/1385)[12]. This difference is most likely related to continued face-to-face family interviews in our center.

AT, the cardinal method for BD diagnosis, was performed on all cases that met the preconditions. Due to the pandemic, physicians may be reluctant to apply any technique producing aerosols that increase transmission risk, but ancillary tests are not recommended instead of AT since they can yield false positive and negative results[13]. Whenever feasible, AT should be performed for clinical confirmation of BD, even in cases with COVID-19[14]. Before the pandemic the most preferred AT approach is apneic oxygenation, which involves delivering oxygen into the trachea by placing a cannula into the endotracheal tube after weaning from ventilation[15]. In order to prevent aerosol formation and COVID-19 transmission risk, it is recommended to perform the AT either by a T-piece and attaching a filter to the expiratory limb, or via continuous positive airway pressure (CPAP)[16]. Among our cases, three had positive COVID-19 RT-PCR test results, only one of these met the preconditions for AT. Physicians wearing personal protective equipment applied the test in a negative pressure room by a T-piece and attaching a filter to the expiratory limb. In our hospital, RT-PCR tests were obtained from all cases before ICU admission. Nevertheless, as a precaution against possible false negatives, our medical staff paid utmost attention to personal protection during patient examinations, and no

COVID-19 transmission occurred among our members.

The pandemic has necessitated various arrangements for the continuity of transplantation activities. In Turkey, additional tests and consultations are requested in donor evaluation, as per the recommendations of the Ministry of Health, The Coronavirus Scientific Advisory Board[6]. In the present study, the RT-PCR test was positive in one of the four cases whose organs were unusable for medical reasons. In the other 3 cases, COVID-19 could not be ruled out by laboratory tests and chest CT, and bacteremia was evident in blood cultures. As long as the pandemic continues, further studies on organ donor evaluations are crucial. Currently, there are conflicting views regarding donor organ use in cases of suspected infections or bacteremia. Some studies advocate proceeding with transplantation under appropriate antibiotic therapy in these cases[17-19].

Prolonged ICU stays due to additional evaluations on donors potentially increase the risk of ICU-acquired infections. Physicians should be wary of complications in patients on mechanical ventilation and invasive hemodynamic monitoring, such as ventilator-associated pneumonia and catheter-related infection. Infection control measures, prompt screening of blood cultures, and, if necessary, appropriate antibiotic therapy can reduce donor loss.

In the present study, a comparison of donor and non-donor laboratory values revealed significantly lower lymphocyte counts in the non-donors. Published literature recommends referring to lymphocyte count in the haemogram test to evaluate COVID-19 suspicion, severity, or prognosis[20,21]. In a study on haematological parameters in the diagnosis of COVID-19, Peng et al.[22] found significantly lower lymphocyte count in positive cases compared to healthy individuals. The authors have indicated 88.05% specificity and 70.97% sensitivity for lymphocyte count $< 0.870\times10^9$/L in detecting acute respiratory distress syndrome due to COVID-19. COVID-19 should be diligently ruled out in cases accompanied by severe lymphopenia.

Procalcitonin, a primary inflammatory marker, was significantly higher among the non-donors in the study. However, the studies have shown that inflammatory markers can be elevated despite the absence of infection in BD cases due to increased sympathetic activity[23]. In contrast, a study on the relationship between procalcitonin level and infection in BD cases has indicated procalcitonin >9 ng/mL as a significant inflammatory marker[19]. Among our non-donors, the median procalcitonin level was 10.48 μg/L, and these cases were also bacteremic. In sum, a detailed scanning for the focus of infection can be helpful in evaluating potential donors with procalcitonin levels above a particular cutoff value.

Among our donors, the time from family consent for donation to organ procurement was median 18.25 (min-max, 6.25-18.50) hours. Concerning the same parameter, Caliskan et al.[24] reported a pre-pandemic mean of 8.5 ± 2.12 hours and a pandemic mean of 54 ± 11.53 hours. Prolonged time to organ procurement during the pandemic can be associated with protective measures, as well as additional tests and consultations required from donors.

The main limitations of this study are its single-center design and low number of cases. Besides, since our hospital is a recently established one, data is unavailable to compare pandemic and pre-pandemic statistics for BD and organ donation. On the other hand, our center is Turkey's largest pandemic hospital; therefore, the results of this study can prove valuable for future studies on BD and deceased organ donation during the COVID-19 pandemic.

Conclusion

In countries like Turkey, where cadaveric donation is only possible after BD, accurate detection of BD cases is vital for the continuity of transplantation processes. Prolonged intensive care stays due to additional evaluations for COVID-19 may pose the

risk of intensive care acquired infections in donors and should be careful in terms of donor loss due to infections. Further studies on BD detection and donor evaluation are imperative, as the end of the pandemic is still unforeseeable.

Author contributions

Author read and approved the final manuscript.

Conflict of interest

Author declares that they have no conflict of interest.

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Ethical approval

Ethics committee approval was received for this study from the University of Health Sciences, Ankara City Hospital Clinical Research Ethics Committee (Approval Date: April 7, 2021; Approval Number: 2021/E2-21-391).

References

1. Kumar D, Humar A. Pandemic influenza and its implications for transplantation. Am J Transplant. 2006;6(7):1512-7. doi:10.1111/j.1600-6143.2006.01364.x
2. Kaul DR, Mehta AK, Wolfe CR, et al. Ebola virus disease: implications for solid organ transplantation. Am J Transplant. 2015;15(1):5-6. doi:10.1111/ajt.13093
3. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int/ (accessed date: 22 December 2021)
4. Organ and Tissue Transplantation Services Regulation, the Ministry of Health, Turkey. Available from: https://www.mevzuat.gov.tr/mevzuat?MevzuatNo=15860&MevzuatTur=7&MevzuatTertip=5 (accessed date: 01 February 2012)
5. Arsava EM, Demirkaya Ş, Dora B, et al. Turkish Neurological Society diagnostic guidelines for brain death. Turk J Neurol. 2014;20:101-4.
6. Republic of Turkey Ministry of Health. Coronavirus Screening for Potential Donors. Available from: https://organ.saglik.gov.tr/AllNews.aspx?q=4V/Rsua850c21xrT4j071HUy38dyQWoNzy1FpkcjwsZtuynTX65bvLnZPVXqGaYQ (accessed date: 20 January 2021)
7. Ahmed O, Brockmeier D, Lee K, et al. Organ donation during the COVID-19 pandemic. Am J Transplant. 2020;20(11):3081-8. doi:10.1111/ajt.16199
8. Angelico R, Trapani S, Manzia TM, et al. The COVID-19 outbreak in Italy: Initial implications for organ transplantation programs. Am J Transplant. 2020;20(7):1780-4. doi:10.1111/ajt.15904
9. Valdes E, Agarwal S, Carroll E, et al. Special considerations in the assessment of catastrophic brain injury and determination of brain death in patients with SARS-CoV-2. J Neurol Sci. 2020;417:117087. doi:10.1016/j.jns.2020.117087
10. Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic. CDC. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html (accessed date: 10 September 2021)
11. Kentish-Barnes N, Siminoff LA, Walker W, et al. A narrative review of family members' experience of organ donation request after brain death in the critical care setting. Intensive Care Med. 2019;45(3):331-342. doi:10.1007/s00134-019-05575-4
12. Republic of Turkey Ministry of Health. Tissue, Organ Transplantation and Dialysis Services. Donations and Donors. Available from: https://organkds.saglik.gov.tr/dss/PUBLIC/Brain_Death.aspx (accessed date: 10 January 2021)
13. Young GB, Lee D. Acritique of ancillary tests for brain death. NeurocritCare 2004;1(4):499-508. doi:10.1385/NCC:1:4:499
14. Migdady I, Rae-Grant A, Greer DM. Brain death evaluation during the pandemic. Neurology. 2020;95(15):693-694. doi:10.1212/WNL.0000000000010544
15. Wijdicks EFM, Varelas PN, Gronseth GS, et al. American Academy of Neurology. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2010;74(23):1911-8. doi:10.1212/WNL.0b013e3181e242a8
16. Radaideh Y, Garg R, Abdalla AA, et al. Challenges in brain death determination and apnea testing for patients with COVID-19. J Stroke Cerebrovasc Dis 2020;29(12):105419. doi:10.1016/j.jstrokecerebrovasdis.2020.105419
17. Lumbreras C, Sanz F, González A, et al. Clinical significance of donor-unrecognized bacteremia in the outcome of solid-organ transplant recipients. Clin Infect Dis. 2001;33(5):722-6.

doi:10.1086/322599
18. Paredes D, Gambra MP, Cervera C, et al. Characterization of the organ donor with bacteremia. Transplant Proc. 2007;39(7):2083-5. doi:10.1016/j.transproceed.2007.07.050
19. Rangeard O, Audibert G, Perrier JF, et al. Relationship between procalcitonin values and infection in brain-dead organ donors. Transplant Proc. 2007;39(10):2970-4. doi:10.1016/j. transproceed.2007.02.101
20. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parameters in patients with COVID-19 infection [published correction appears in Am J Hematol. 2020 Nov;95(11)-:1442]. Am J Hematol. 2020;95(6):E131-E134. doi:10.1002/ajh.25774
21. Zhao Q, Meng M, Kumar R, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. Int J Infect Dis. 2020;96:131-5. doi:10.1016/j.ijid.2020.04.086
22. Peng J, Qi D, Yuan G, et al. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): A multicenter, cross-sectional study. J Clin Lab Anal. 2020;34(10)-:e23475. doi:10.1002/jcla.23475
23. Watts RP, Thom O, Fraser JF. Inflammatory signalling associated with brain dead organ donation: from brain injury to brain stem death and posttransplant ischaemia reperfusion injury. J Transplant. 2013;521369. doi:10.1155/2013/521369
24. Caliskan G, Sayan A, Kilic I, et al. Has the COVID-19 Pandemic Affected Brain Death Notifications and Organ Donation Time? [published online ahead of print, 2021 Aug 9]. Exp Clin Transplant. 2021;10.6002/ect.2021-.0090. doi:10.6002/ect.2021.0090

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EVALUATION OF RISK FACTORS FOR CARDIAC COMPLICATIONS AFTER LUNG RESECTION

AKCİĞER REZEKSİYONU SONRASI KARDİAK KOMPLİKASYONLAR İÇİN RİSK FAKTÖRLERİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: The aim of this study is to evaluate cardiac complications (CC) and risk factors associated with these complications in patients after lung resection.

Methods: Cardiac complications were observed in 136 (11.4%) of 1186 patients who underwent lung resection in a single center between 2017 and 2020. 136 patients who developed complications in the same period and 215 patients who had consecutive operations and did not develop complications were included in the study

Results: 287 (81.7%) of the patients were male and the mean age was 58.9 years. There is a statistically significant relationship between cardiac complications after lung resection with geriatric age, male gender, presence of hypertension (HT), presence of lung cancer, neoadjuvant therapy, high SOFA score, chronic obstructive pulmonary disease (COPD), and cerebrovascular accident (CVA). In addition, CVA, EF<60%, neoadjuvant therapy, pneumonectomy, high Sequential Organ Failure Assessment score (SOFA) and intraoperative blood transfusion were found to be independent risk factors for the development of complications. Among the intraoperative factors, pneumonectomy (p<0.001), thoracotomy (p=0.002), intraoperative blood product use (p<0.001) and inotropic use (p<0.001) were correlated with CC. In multiple logistic regression analysis, preoperative thyroid disease (p=0.04), CVA (p=0.001), neoadjuvant therapy (p=0.002), EF<60% (p=0.01), pneumonectomy (p=0.003), intraoperative blood transfusion (p<0.0001) and high SOFA score (p<0.0001) emerged as independent risk factors affecting the development of cardiac complications.

Conclusions: There is significant relationship between cardiac complications after lung resection with geriatric age, male sex, HT, lung cancer presence, neoadjuvant therapy, high SOFA score, COPD, CVA presence. In addition, CVA, EF< 60%, neoadjuvant therapy, pneumonectomy and high SOFA score and intraoperative blood transfusion were identified as independent risk factors in the development of complications.

Keywords: Lung resection, cardiac complications, atrial fibrillation, thoracotomy, video-assisted thoracoscopic surgery

Öz

Amaç: Bu çalışmanın amacı akciğer rezeksiyonu sonrası hastalarda görülen kardiyak komplikasyonlar (KK) ve bu komplikasyonlarla ilişkili risk faktörlerini değerlendirmektir.

Yöntemler: 2017-2020 yılları arasında tek bir merkezde akciğer rezeksiyonu yapılan 1186 hastanın 136'sında (%11,4) kardiyak komplikasyon gözlendi. Aynı dönemde komplikasyon gelişen 136 hasta ve ardışık ameliyat olan ve komplikasyon gelişmeyen 215 hasta çalışmaya dahil edildi.

Bulgular: Hastaların 287'si (%81,7) erkekti ve yaş ortalaması 58,9'du. Geriatrik yaş, erkek cinsiyet, hipertansiyon (HT), akciğer kanseri varlığı, neoadjuvan tedavi, yüksek SOFA skoru, kronik obstrüktif akciğer hastalığı (KOAH) ve serebrovasküler olay (SVO) ile akciğer rezeksiyonu sonrası kardiyak komplikasyonlar arasında istatistiksel olarak anlamlı bir ilişki vardır. Ayrıca SVO, EF<%60, neoadjuvan tedavi, pnömonektomi, Sıralı Organ Yetmezliği Değerlendirme Skoru (SOFA) ve intraoperatif kan transfüzyonu komplikasyon gelişimi için bağımsız risk faktörleri olarak bulundu. İntraoperatif faktörlerden pnömonektomi (p<0,001), torakotomi (p=0,002), intraoperatif kan ürünü kullanımı (p<0,001) ve inotrop kullanımı (p<0,001) KK ile korele idi. Çoklu lojistik regresyon analizinde, preoperatif tiroid hastalığı (p=0,04), SVO (p=0,001), neoadjuvan tedavi (p=0,002), EF<%60 (p=0,01), pnömonektomi (p=0,003), intraoperatif kan transfüzyonu (p<0,0001) ve yüksek SOFA skoru (p<0,0001) kardiyak komplikasyon gelişimini etkileyen bağımsız risk faktörleri olarak gözlendi.

Sonuç: Geriatrik yaş, erkek cinsiyet, HT, akciğer kanseri varlığı, neoadjuvan tedavi, yüksek SOFA skoru, KOAH, SVO varlığı ile akciğer rezeksiyonu sonrası kardiyak komplikasyonlar arasında anlamlı ilişki vardır. Ayrıca SVO, EF<%60, neoadjuvan tedavi, pnömonektomi ve yüksek SOFA skoru ve intraoperatif kan transfüzyonu komplikasyon gelişmesinde bağımsız risk faktörleri olarak gözlendi.

Anahtar Kelimeler: Akciğer rezeksiyonu, kardiyak komplikasyonlar, atriyal fibrilasyon, torakotomi, video yardımlı torakoskopik cerrahi

Introduction

Patients who have undergone thoracotomy with lung resection encounter cardiac problems that cause high postoperative morbidity and mortality in the perioperative period. Despite advances in surgical technique and approach, the mortality rate is in the range of 2-12% [1]. Despite advanced and aggressive perioperative management, various types of arrhythmias, hemodynamic instability, acute coronary disease, angina, myocardial infarction, heart failure (HF) and thromboembolism can still be observed. These complications bring along many problems such as increased mortality and mortality rate, long-term hospitalization, need for intensive care, and increased costs [2,3]. Risk factors for perioperative mortality such as being over 70 years old, forced expiratory volume in 1 second less than 41%, cardiac disease, chronic diseases such as chronic obstructive pulmonary disease and diabetes, right hemithorax surgery, unsuccessful extubation and perioperative fluid management have been identified [4]. However, it is difficult to determine the effect of these factors on results independently because the number of studies on this subject is limited.

The primary aim of this study is to detect and evaluate the cardiac complications of patients who underwent lobectomy and pneumonectomy for lung resection within 30 days postoperatively.

Materials and Methods

- *Patients and Perioperative Management*

A total of 1186 patients who were operated for lung resection (lobectomy, pneumonectomy) at Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital between January 2017 and January 2020 were included in the study. We aimed to evaluate the postoperative cardiac complications (PCC) occurring within 15 days postoperatively between these dates. Data of 136 patients who developed PCC during the specified study period were analyzed. 215 patients who were operated in the same period and who did not develop any cardiac complications and who underwent lung resection were randomly selected and evaluated as a control group. The data of these 215 patients were included in the study because they were found to be reliable. Thirty-two patients with preoperative cardiac arrhythmia who were on antiarrhythmic therapy and whose arrhythmia continued after the operation were excluded from the study.

Preoperative clinical cardiological and anesthesia evaluation, PA Chest X-ray, computed tomography (CT), 12-lead electrocardiography (ECG) and pulmonary function tests (PFT) were applied to all patients. Operation capability was determined according to the determined surgical guidelines. Lung resections were performed by open thoracotomy or video-assisted thoracic surgery (VATS).

Surgical and anesthesia teams, standard surgical approach and anesthesia management were used throughout the study period and remained constant throughout the study. Short-term antibiotic prophylaxis was routinely administered intravenously (iv) (ampicillin / sulbactam 3 g) before anesthesia. Premedication was performed with midazolam before the induction of general anesthesia. After applying propofol 2 mg / kg, fentanyl 2-3 mcg / kg, rocuronium bromide (0.5 mg / kg) and endotracheal intubation with a double lumen tube, anesthesia was maintained with 50% 02, 50% air and 2% sevoflurane. Pathological lung cancer staging was evaluated according to the TNM classification. At the end of the operation, two chest tubes were placed in the thoracic cavity and removed when there was no air leak, and the pleural drainage output was <150 mL / 24 hours.

Unless contraindicated, 0.1 mg / kg of morphine, 1000 mg of paracetamol, and 1 mg / kg of tramadol hydrochloride were

administered iv to all patients for pain relief near the end of the operation. During the intensive care follow-up, pain control was provided as patient-controlled analgesia with 300 mg tramadol hydrochloride / 24 hours iv. The pain levels of the patients were evaluated with a visual pain scale. Care was taken to keep the pain level between 0-4 points. Low molecular weight heparin was given for 2-4 weeks postoperatively.

Postoperative patients were transferred to the general intensive care unit (ICU) and were followed up for 24 hours. To prevent hypoxia, nasal (1-2 L / min) or continue positive airway pressure (CPAP) approach was used when necessary. The PO_2 value of the cases was tried to be maintained between 70-100 mmHg and PCO_2 value between 40-55 mmHg. Heart rate (HR), ECG, oxygen saturation (SPO_2), central venous-arterial pressures and arterial blood gases were continuously monitored during the stay at the ICU. Central venous pressure (CVP) was monitored at regular intervals. If ventricular contraction was significantly impaired, inotropic support was provided with norepinephrine bitartarate, dopamine HCl or doputamine HCl. The perioperative need for blood products was determined on an individual, patient basis; In general, blood transfusions were administered when hemoglobin was <8.5 g / dl, efforts were made to keep the hemoglobin value above 10 g / dl. Postoperative fibro-bronchoscopy (FBS) was performed in the case of lung atelectasis and to obtain bronchial secretion samples for microbiological examinations. An active postoperative respiratory physiotherapy program, including deep breathing exercises, was applied to all patients. Mechanical ventilation support was started in case of respiratory failure. Early oral nutrition and mobilization was initiated.

Approval was obtained from the Ethics Committee of Istanbul Yedikule Chest Diseases and Chest Surgery Training and Research Hospital for this study (2020-34) . All patients have written consent for the use of their medical information after the operation.

- *Cardiac monitoring and definition*

Cardiac monitoring was followed by the daily practice of an integrated clinic that shared the same routine and data collection system over heart rhythm, arterial blood pressure, CVP, SPO_2, and included ICU and service level. Patients were monitored with continuous ECG for at least 24 hours postoperatively. Additional records were collected in the presence of a cardiac pathology. Arrhythmia was defined by physician evaluation based on a radiotherapy strip or a 12-lead ECG recording. Arrhythmias are classified as atrial fibrillation (AF), supraventricular tachycardia (SVT), ventricular extra systole (VES), bradycardia, ventricular fibrillation (VF), and ventricular tachycardia (VT). Patients with abnormal cardiac findings were evaluated by a cardiologist with echocardiography (ECHO), and treatments were planned according to the results of the consultation. Amiodarone, administered orally or iv, has formed the standard pharmacological treatment of AF. Amiodorone was administered as a 24-hour infusion after the loading dose. Diltiazem HCI and metoprolol ampoule intravenous forms were also used when necessary. In the case of recurrence of AF, the same protocol was used. In the case of hypotension, sympathomimetic agents (norepinephrine bitartarate, dopamine HCI, doputamine HCI) were administered at the appropriate dose. In the case of hypertension, treatment was provided by iv glyceryl trinitrate or oral antihypertensive drugs.

- *Collection of data*

In 384 patients, demographic data from preoperative, intraoperative and post-operative variables, accompanying diseases, lung function, neoadjuvant therapy, type and degree of cancer, type of surgical procedure and postoperative

complications were recorded retrospectively. Study data were obtained from patients' preoperative anesthesia evaluation form, laboratory information, consultations, intraoperative patient records, service and intensive care follow-up forms. Cardiac complications were collected under the headings of arrhythmias, hemodynamic instability, acute coronary disease, angina, heart failure (HF) and thromboembolism. Non-cardiac complications accompanying cardiac complications were recorded as respiratory failure, pneumonia, renal failure (RF), cerebrovascular accident (CVA), and pulmonary embolism. Patients with chronic heart rhythm disorder were not included in the evaluation.

- *Statistical analysis*

The demographic characteristics of the patients and the collected data were entered into IBM® SPSS® (the Statistical Package for the Social Sciences) Statistics version 23. Variables were characterized using mean, maximum, and minimum values, percentages were used for qualitative variables. Normal distributions were reported as mean ± SD, and Student's t-test was used for comparisons between groups. For the analysis of qualitative variables, Pearson's chi-square test, if the group was small, Fisher's exact test was used. Nonparametric continuous variables were recorded as median and spatial distribution and compared using Mann-Whitney U tests. A $p < 0.05$ value was considered statistically significant. Parametric and nonparametric values were compared in terms of postoperative cardiac complications (PCC). In multivariate analysis, parametric and nonparametric variables were evaluated using only the parametric and nonparametric variables that were statistically revealed to have an effect on PCC development in single variable analysis, and independent risk factors were determined.

Results

Demographic, preoperative, peroperative and postoperative data of the patients in the study are shown in Table 1.

Cardiac arrhythmias include AF (n = 90, 66.2%), SVT (n = 20, 14.8%), Asystole (n = 6, 4.4%), VES (n = 7, 5.1%), and VF/VT (n = 8, 6%) was observed. Hemodynamic instability developed in 27.9% of those who developed PCC, heart failure in 9 (6.6%), angina in 8 (5.9%) and MI in 5 patients (3.7%). Additional complications developed in 45 (33.1%) of the patients who developed PCC. Respiratory failure in 30 (22.1%) patients, pneumonia in 6 (4.4%), CVA in 5 (3.7%), and RF in 3 (2.2%) patients. Mechanical ventilator support (intubation, CPAP) was applied for an average of 1.4 days in the patients who developed respiratory failure.

Considering the preoperative findings, over 65 years old ($p = 0.001$), male ($p = 0.02$), ASA III-IV ($p < 0.001$), CHF ($p < 0.001$), CAD ($p = 0.003$), HT ($p = 0.002$), hyperlipidemia ($p < 0.001$), COPD ($p < 0.001$), thyroid disease ($p = 0.003$), CRF ($p = 0.03$), CVA ($p < 0.001$), rhythm disturbance presence ($p < 0.001$), lung cancer ($p = 0.008$), neoadjuvant ($p < 0.001$) and EF values <60% ($p < 0.001$) were statistically significantly associated with cardiac complication. Considering the peroperative findings, VATS ($p = 0.02$), pneumonectomy ($p < 0.001$), left-sided disease ($p = 0.04$), intraoperative inotropic ($p < 0.001$), intraoperative blood transfusion ($p < 0.001$), and revision due to bleeding ($p < 0.001$) were associated with cardiac complication. It was observed that patients who developed PCC were older than those who did not (62.2 ± 9.9 years versus 56.7 ± 13.0 years, $p < 0.001$). There was no significant difference between patients with and without PCC in terms of other variables (Table 1).

Table 1. Comparison of demographic and pre/intraoperative data in patients with and without postoperative cardiac complications (PCC)

Variables		Total (n=351)	Non-PCC (n=215)	PCC (n=136)	*Odds Ratio*	*95% CI*	*p value*
			Preoperative				
Age (years), n (%)	<65	226 (64.4%)	153 (71.2%)	73 (53.7%)	2.130	1.361-3.333	0.001
	≥65	125 (35.6%)	62 (28.8%)	63 (46.3%)			
Gender, n (%)	Male	287 (81.8%)	168 (78.1%)	119 (87.5%)	0.511	0.280-0.933	0.02
	Female	64 (18.2%)	47 (21.9%)	17 (12.5%)			
CHF, n (%)	yes	43 (12.3%)	8 (3.7%)	35 (25.7%)	0.112	0.050-0.249	<0.001
	no	308 (87.7%)	207 (96.3%)	101 (74.3%)			
CAD, n (%)	yes	61 (17.4%)	27 (12.6%)	34 (25.0%)	0.431	0.246-0.754	0.003
	no	290 (82.6%)	188 (87.4%)	102 (75.0%)			
HT, n (%)	yes	122 (34.8%)	61 (28.4%)	61 (44.9%)	0.487	0.311-0.763	0.002
	no	229 (65.2%)	154 (71.6%)	75 (55.1%)			
HL, n (%)	yes	25 (7.1%)	7 (3.3%)	18 (13.2%)	0.220	0.089-0.543	<0.001
	no	326 (92.9%)	208 (96.7%)	118 (86.8%)			
DM, n (%)	yes	59 (16.8%)	35 (16.3%)	24 (17.5%)	0.907	0.513-1.605	0.738
	no	292 (83.2%)	180 (83.7%)	112 (82.4%)			
COPD, n (%)	yes	158 (45.0%)	83 (38.6%)	75 (55.1%)	0.511	0.089-0.543	<0.001
	no	193 (55.0%)	132 (61.4%)	61 (44.9%)			
Thyroid disease, n (%)	yes	16 (4.6%)	4 (1.9%)	12 (8.8%)	0.196	0.062-0.621	0.003
	no	335 (95.4%)	211 (98.1%)	124 (91.2%)			
CRF, n (%)	yes	6 (1.7%)	1 (0.5%)	5 (3.7%)	0.122	0.014-1.060	0.03
	no	345 (98.3%)	214 (99.5%)	131 (96.3%)			
CVA, n (%)	yes	28 (8.0%)	4 (1.9%)	24 (17.6%)	0.088	0.030-0.261	<0.001
	no	323 (92.0%)	211 (98.1%)	112 (82.4%)			
MI/Angio/Bypass, n (%)	yes	24 (6.8%)	12 (5.6%)	12 (8.8%)	0.610	0.266-1.402	0.241
	no	327(93.2%)	203 (94.4%)	124 (91.2%)			
Operation reason, n (%)	Lung cancer	328 (97.8%)	195 (90.7%)	133 (97.8%)	0.220	0.064-0.755	0.008

	Bronchiectasis	23 (6.6%)	20 (9.3%)	3 (2.2%)			
Neoadjuvant therapy, n (%)	yes	31 (8.8%)	8 (3.7%)	23 (16.9%)	0.190	0.082-0.438	<0.001
	no	320 (91.2%)	207 (96.3%)	113 (83.1%)			
EF, n (%)	≥ 60%	230 (65.5%)	173 (80.5%)	57 (41.9%)	5.709	3.535-9.219	<0.001
	< 60%	121 (34.5%)	42 (19.5%)	79 (58.1%)			
Intraoperative							
Operation mode, n (%)	Thoracotomy	259 (73.8%)	168 (78.1%)	91 (66.9%)	1.768	1.092-2.862	0.02
	VATS	92 (26.2%)	47 (21.9%)	45 (33.1%)			
Operation mode, n (%)	Lbc/segm	277 (78.9%)	188 (87.4%)	89 (65.4%)	3.677	2.151-6.287	<0.001
	Pnmc	74 (21.1%)	27 (12.6%)	47 (34.6%)			
Operation side, n (%)	Right	160 (45.6%)	107 (49.8%)	53 (39.0%)	1.522	1.003-2.400	0.04
	Left	191 (54.4%)	108 (50.2%)	83 (61.0%)			
Inotrope use, n (%)	yes	23 (6.6%)	1 (0.5%)	22 (16.2%)	0.024	0.003-0.182	<0.001
	no	328 (93.4%)	214 (99.5%)	114 (83.8%)			
Blood product received, n (%)	yes	75 (21.4%)	9 (4.2%)	66 (48.5%)	0.046	0.022-0.098	<0.001
	no	276 (78.6%)	206 (95.8%)	70 (51.5%)			
Revision due to hemorrhage, n (%)	yes	13 (3.4%)	1 (0.4%)	12 (8.8%)	0.048	0.006-0.376	<0.001
	no	338 (96.6%)	214 (99.6%)	124 (91.2%)			

*CHF, congestive heart failure; CAD, coronary artery disease; HT, hypertension; HL, hyperlipidemia; DM, diabetes mellitus; COPD, chronic obstructive pulmonary failure; CRF, chronic renal failure; CVA, cerebrovascular accident; MI, myocardial infarction; EF, Ejection fraction; VATS: video-assisted thoracoscopic surgery; lbc, lobectomy; segm, segmentectomy; pnmc, pneumonectomy; CI, confidence interval.

Table 2. Relationship between patients' baseline parameters and postoperative cardiac complications (PCC)

Variables	Total (n=351)	Non-PCC (n=215)	PCC (n=136)	*p*
BMI, mean ± SD	26.4±4.4	26.5±4.5	26.2±4.2	0.688
APACHE II, mean ± SD	8.5±3.5	7.6±2.6	10.0±4.2	<0.001
SOFA, mean ± SD	0.56±1.67	0.12±0.35	1.27±2.49	<0.001
FEV1 (L), mean ± SD	2.29±0.63	2.39±0.64	2.14±0.59	<0.001
Procedure time (hours), mean ± SD	3.8±0.8	3.7±0.7	3.8±1.0	0.097
Ventilation time (days), mean ± SD	1.1±0.6	1.0±0.0	1.3±0.9	<0.001
Intensive care LOS (days), mean ± SD	1.7±1.4	1.0±0.0	2.9±1.8	<0.001

BMI, body mass index; SOFA, Sequential Organ Failure Assessment Score; APACHE, Acute Physiology and Chronic Health Evaluation Score II;
FEV1, forced expiratory volume in the first second, LOS, length of stay; SD, standard deviation

When the relationship between some basal parameters of the patients and the development of PCC was examined, APACHE II (p <0.001) and SOFA scores (p <0.001) were higher in patients with PCC, while FEV1 (p <0.001) and hemoglobin (Hg) (p = 0.04) levels were higher in patients without PCC. (Table 2). Patients who developed PCC had longer operation time than those who did not. However, the difference was not statistically significant (p = 0.097). It was observed that patients who developed PCC had longer periods of ventilation and ICU hospitalization (p <0.001, for both).

Multiple logistic regression analysis was performed using the independent variables determined to affect the development of PCC in Tables 1 and 2. Presence of preoperative thyroid disease (p=0.04), presence of CVA (p=0.0001), use of neoadjuvant (p=0.002), EF <60% (p=0.01), pneumonectomy (p=0.003), intraoperative blood transfusion (p<0.0001) and high SOFA (p<0.0001) were found to be independent risk factors affecting the development of PCC (Table 3). It was observed that the presence of preoperative CHF (p=0.07) and intraoperative inotrope use (p=0.06) were close to significant in terms of affecting the development of PCC.

Discussion

In our study, the relationship between PCC occurring after lung resection and the patient's peroperative factors was investigated. Age, gender, RF, HT, COPD and lymph node dissection may be risk precursors for cardiopulmonary complications [5, 6]. Significant multivariate predictors of postoperative PCC were male sex, advanced patient age, a history of congestive heart failure, a history of arrhythmias, and a history of peripheral vascular disease [7]. In our study, CVA, EF< 60%, neoadjuvant therapy, pneumo-nectomy and high SOFA score and intraoperative blood transfusion were identified as independent risk factors in the development of PCC.

On the other hand, in a retrospective study of 379 patients over 80 years of age who underwent lung resection, male gender and the presence of previous infarction were positive risk factors for morbidity, while age was not evaluated in the same category[7]. Age alone is not one of the risk factors in the ASA classification, but the increase in coronary artery disease (CAD),

Table 3. Multivariate logistic regression analysis for postoperative cardiac complications

Variables	Odds ratio	95% CI	p value
Age ≥ 65 years	0.580	0.233-1.440	0.204
Gender (male)	1.703	0.585-4.959	0.328
CHF	3.392	0.874-13.154	*0.07*
CAD	0.490	0.169-1.421	0.189
HT	1.746	0.805-3.788	0.158
HL	0.747	0.152-3.654	0.719
COPD	1.527	0.706-3.301	0.281
Thyroid disease	5.544	1.079-28.485	0.04
CRF	2.770	0.088-86.335	0.561
CVA	26.952	5.331-136.253	0.0001
Arrhythmia	2.461	0.815-7.399	0.108
Lung cancer	2.232	0.278-17.900	0.449
Neoadjuvant therapy	6.701	1.927-23.306	0.002
EF < 60%	2.997	1.255-7.155	0.01
VATS	1.792	0.606-5.302	0.291
Pneumonectomy	5.315	2.168-13.031	0.003
Left-side operation	1.791	0.806-3.982	0.152
Inotrope use (intraop)	8.654	0.899-83.224	*0.06*
Blood product use (intraop)	12.404	4.506-34.140	<0.0001
Reoperated due to hemorrhage	3.948	0.359-43.355	0.261
APACHE II	0.946	0.800-1.161	0.700
SOFA	6.389	2.766-14.757	<0.0001
FEV1	1.072	0.551-2.086	0.837
Hg	0.873	0.721-1.004	0.891

***** CHF, congestive heart failure; CAD, coronary artery disease; HT, hypertension; HL, hyperlipidemia; COPD, chronic obstructive pulmonary failure; CRF, chronic renal failure; CVA, cerebrovascular accident; EF: Ejection fraction; VATS, video assisted thoracoscopic surgery; intraop: intraoperative; APACHE II, Acute Physiology and Chronic Health Evaluation Score II; SOFA, Sequential Organ Failure Assessment Score; FEV1, forced expiratory volume in the first second; Hg, hemoglobin; EF, ejection fraction; *CI, confidence interval*

DM, HT and peripheral vascular diseases increases with aging [8]. In our study, being over the age of 60 and male gender were among the risk factors.

Fernandes et al. observed that the presence of COPD, hypoxemia, anemia and pneumonectomy increased PCC after lung resection [9]. In our study, the most common chronic diseases of the patients were listed as COPD (45%), HT (34.8%), CAD (17.8%), DM (16.8%) and CHF (12.3%). The incidence of CAD in patients scheduled for lung resection is between 7-16%. The presence of CAD manifests itself with increased morbidity and mortality rates following the operation [10]. If a CAD is diagnosed in a person who has undergone thoracotomy, the risk of cardiac complications is 6%, otherwise 1% [10].In studies, if the EF is below 35%, the perioperative MI risk is 80%, if the EF is 35-56% it is 20%, if the EF is above 56%, the perioperative MI risk is 0% [8]. In our study, a significant relationship was observed between an EF of <60% and complications.

The markers of mortality and morbidity after lung cancer resection are listed as BMI, male gender, renal dysfunction, chemotherapy, pneumonectomy, bilobec-

tomy, and emergency surgery [3,11]. However, it is difficult to assess the effectiveness of which factor independently. In our study, a positive correlation was found between neoadjuvant therapy and complications. Major clinical conditions that increase the perioperative cardiovascular risk are unstable coronary syndromes, decompensated CHF, prominent arrhythmia and severe valvular disease [8]. In our study, a positive relationship was found between HT and arrhythmia. In non-small cell cancers, the incidence of HT in patients with AF is 52% [12]. HT was detected in 44.9% of our complicated patients, and this is consistent with the literature.

The type of lung resection is one of the factors that determine the degree and nature of cardiac complications. Pneumonectomy is associated with higher morbidity and mortality rates compared to other lung resections [3]. While the incidence of AF after pneumonectomy is 40%, this rate may vary between 10-20% after lobectomy [12]. The incidence of AF in left lobectomies was higher than in right lobectomies (62% & 38%) [13]. In our study, while the rate of complication development in left side surgery was 61%, this rate was 39% on the right side. The incidence of respiratory complications after pneumonectomy can be observed in the range of 11-49% [3] . In our study, 25% of 47 pneumonectomy patients who developed cardiac complications also developed respiratory failure.

VATS surgery is characterized by less hospital stay and postoperative pain compared to thoracotomy [14]. Defined by Swanson et al. VATS is more conservative than thoracotomy and relies on the guidance of national and international centers with extensive experience. VATS is preferred in the treatment of early non-small cell lung cancer because it is less invasive than thoracotomy [10,15]. 259 (73.8%) of our cases were operated by thoracotomy, 92 (26.2%) by VATS method. The complication rate of patients who underwent thoracotomy was 1.7 times higher than those with VATS.

Supraventricular arrhythmias are common rhythm disturbances after pulmonary surgery. Its frequency varies between 3.2-30% in various studies, its common form is AF [7,14, 16, 17]. Risk factors for arrhythmia are listed such as male gender, advanced age (> 60 years of age), presence of chronic lung disease, type of lung resection, postoperative hemorrhage, rethoracotomy, paroxysmal AF and pain [16,17]. These arrhythmias appear clinically as hemodynamic problems, potential for systemic embolization, long-term prophylactic drug use, and increased hospital costs. Increased cardiac enzyme level, myocardial ischemia / infarction and hypotension can be observed in 38% of patients with arrhythmia [17]. Postoperative AF is characterized by a 3-6-fold increase in intensive care admission and hospital mortality, and it may extend the hospital stay for 2-3 days [13]. In our study, the average length of stay in the intensive care unit for patients with AF was observed to be 2.9 days. Postoperative AF usually starts in the first 24 hours and peaks on the 2nd and 3rd days [13, 14, 17,18]. In our study, the arrhythmia occurrence time ranged from 1 to 7 days, and the average was found to be 2.29 days.

Amiodarone, metoprolol and diltiazem are frequently used in the treatment of arrhythmias. Although the effectiveness of prophylactic arrhythmia treatment has not yet been proven, there are supporting studies on the use of amiodarone and diltiazem [14,19]. The most preferred drug in our study was amiodarone (69.3%), which has recently become popular and preferred both for treatment and prophylaxis [13, 19]. Amiodarone tablet 2 * 1 po was given to our patients as a prophylactic after the use of amiodarone. The success with Amiodarone was 89.5%. The most common side effects associated with the use of amiodarone are hypotension, bradycardia and respiratory complications [19]. Hypotension developed due to amiodarone treatment in our 5 patients.

Other cardiac complications occurring following the arrhythmia were listed as hemodynamic instability, heart failure, and angina. Preoperative diagnosis of CHF was present in 25% of our patients. In our study, HF / MI findings emerged in 26 patients. In a series of 598 patients who underwent thoracic surgery, transient ischemic changes detected by echocardiography in 23 (3.8%) patients and MI were noted in 7 (1.2%) patients [2]. If the patient has a history of previous infarction, the risk of having a perioperative MI is between 2.8% and 17%, and if there is no cardiac history, it is 0.13% [2]. Nine patients who developed angina symptoms were referred to the cardiology unit for further treatment.

In our study, 25% of the patients who developed PCC had respiratory failure symptoms, and these patients were given mechanical ventilation support. Pulmonary edema is an uncommon complication after lung resection and its incidence is usually 2.5-4% after pneumonectomy. Because it is a precursor of perioperative pulmonary edema, CHF is an important risk factor affecting mortality [8]. Preoperative diagnosis of CHF was present in 58% of our patients who developed respiratory failure.

Limitation of the study: The study was conducted in a single center and in a certain time period.

Conclusion

In summary, this study showed that many factors are effective in the occurrence of cardiac complications after lung resection. Cardiac complications after lung resections are among the most common causes of mortality and morbidity. Geriatric age, male gender, HT, lung cancer, neoadjuvant therapy, high SOFA scores and pneumonectomy operation have been observed to increase the risk of complications. In addition, presence of goiter and CVA disease, EF <60%, presence of neoadjuvant, pneumonectomy, high SOFA score and high correlation between intraoperative blood transfusion and PCC were found. Appropriate preoperative approach, qualified evaluation of patients who are candidates for complications, and proper collaboration of treatment units are of vital importance in minimizing morbidity and mortality.

Author contributions

All authors contributed to the study conception and design.
All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

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References

1. Stéphan F, Boucheseiche S, Hollande J, et al. Pulmonary complications following lung resection: a comprehensive analysis of incidence and possible risk factors. Chest. 2000; 118(5):1263-70. doi: 10.1378/chest.118.5.1263
2. De Decker K, Jorens PG, Van Schil P. Cardiac complications after noncardiac thoracic surgery: an evidence-based current review. Ann Thorac Surg. 2003; 75(4):1340-8. doi: 10.1016/s0003-4975(02)04824-5
3. Rena O, Papalia E, Oliaro A, Casadio C, et al. Supraventricular arrhythmias after resection surgery of the lung. Eur J Cardiothorac Surg. 2001; 20(4):688-93. doi: 10.1016/s1010-7940(01)00890-9
4. Algar FJ, Alvarez A, Salvatierra A, et al. Predicting pulmonary complications after pneumonectomy for lung cancer. Eur J Cardiothorac Surg. 2003;23(2):201-8. doi: 10.1016/s1010-7940(02)00719-4
5. Fu D, Wu C, Li X, Chen J. Elevated preoperative heart rate associated with increased risk of cardiopulmonary complications after resection for lung cancer. BMC Anesthesiol. 2018;25;18(1):94. doi: 10.1186/s12871-018-0558-9
6. Erol Y, Ergönül AG, Özdil A, et al. Assessment of Cardiac Complications in Patients Undergoing

Pulmonary Resection. Heart Lung Circ. 2019;28(7):1099-1101.
doi: 10.1016/j.hlc.2018.08.019
7. Dominguez-Ventura A, Allen MS, Cassivi SD, et al. Lung cancer in octogenarians: factors affecting morbidity and mortality after pulmonary resection. Ann Thorac Surg. 2006;82(4):1175-9.
doi: 10.1016/j.athoracsur.2006.04.052
8. Smilowitz NR, Berger JS. Perioperative Cardiovascular Risk Assessment and Management for Noncardiac Surgery: A Review. JAMA. 2020;324(3):279–290.
doi: 10.1001/jama.2020.7840.
9. Fernandes EO, Teixeira C, Silva LC. Thoracic surgery: risk factors for postoperative complications of lung resection. Rev Assoc Med Bras. 2011;57(3):292-8.
doi: 10.1590/s0104-42302011000300011
10. Sandri A, Petersen RH, Decaluwé H, et al. Coronary artery disease is associated with an increased mortality rate following video-assisted thoracoscopic lobectomy. J Thorac Cardiovasc Surg. 2017;154(1):352-357.
doi: 10.1016/j.jtcvs.2017.03.042
11. Duc H, Humberto C, Katrina Z, et Al. Association Of İmpaired Heart Rate Recovery With Cardiopulmonary Complications After Lung Cancer Resection Surgery. J Thorac Cardiovasc Surg. 2015;149:1168-73.
doi: 10.1016/j.jtcvs.2014.11.037
12. Cardinale D, Martinoni A, Cipolla CM, et al. Atrial fibrillation after operation for lung cancer: clinical and prognostic significance. Ann Thorac Surg. 1999;68(5):1827-31.
doi: 10.1016/s0003-4975(99)00712-2
13. Imperatori A, Mariscalco G, Riganti G, et al. Atrial fibrillation after pulmonary lobectomy for lung cancer affects long-term survival in a prospective single-center study. J Cardiothorac Surg. 2012 10;7:4.
doi: 10.1186/1749-8090-7-4
14. Ivanovic J, Maziak DE, Ramzan S, et al. Incidence, severity and perioperative risk factors for atrial fibrillation following pulmonary resection. Interact Cardiovasc Thorac Surg. 2014;18(3):340-6.
doi: 10.1093/icvts/ivt520
15. Agostini PJ, Lugg ST, Adams K, et al. Risk factors and short-term outcomes of postoperative pulmonary complications after VATS lobectomy. J Cardiothorac Surg. 2018 12;13(1):28.
doi: 10.1186/s13019-018-0717-6
16. Pedoto A, Amar D. Perioperative Arrhythmias and Acute Right Heart Failure in Noncardiac Thoracic Surgery. Curr Anesthesiol Rep. 2014; 4:142–149.
17. Vretzakis G, Simeoforidou M, Stamoulis K, et al. Supraventricular arrhythmias after thoracotomy: is there a role for autonomic imbalance? Anesthesiol Res Pract. 2013; 413985.
doi: 10.1155/2013/413985
18. Figas-Powajbo E, Gawor Z, Kozak J. Perioperative cardiac arrhythmias in patients undergoing surgical treatment for lung cancer. Pol Arch Med Wewn. 2007;117(7):290-6.
19. Tisdale Je, Wroblewski Ha, Wall Ds. A Randomized Trial Evaluating Amiodarone For Prevention Of Atrial Fibrillation After Pulmonary Resection. Ann Thorac Surg. 2009;88(3):886-93.
doi: 10.1016/j.athoracsur.2009.04.074

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ÜÇÜNCÜ BASAMAK BİR SAĞLIK MERKEZİNİN PERKÜTAN ENDOSKOPİK GASTROSTOMİ DENEYİMİ

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY EXPERIENCE OF A TERTIARY HEALTH CENTER

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Abstract

Aim: Percutaneous endoscopic gastrostomy (PEG) is a low-risk, inexpensive, accessible and technically easier enteral procedure that can be performed in endoscopy units or at the bedside, in which intravenous or local agents can be used for sedation. In our study, we aimed to evaluate the indications, complications and outcomes of the patients who underwent PEG in our clinic.

Methods: Patients who underwent percutaneous endoscopic gastrostomy (PEG) procedure between January 2015 and March 2021 in the general surgery endoscopy unit of a tertiary healthcare center were included in the study. The clinical data of the cases, complications due to PEG, and mortality were investigated.

Results: Of 260 patients with PEG, 158 (60.7%) were male and 102 (39.3%) were female. The mean age of the patients was 65.23 years (range 18-92 years). The clinic that requested PEG most frequently was the anesthesia and reanimation intensive care clinic (n=146; 56.1%). The most common indication for PEG was oral intake disorder due to cerebrovascular disease (n=194, 74.6%). Complications (6 early and 10 late) developed in 16 (6.1%) patients after PEG application. The most common early complication was peristomal infection (n=4, 1.5%). The most common late complication (n=7; 2.7%) was PEG catheter occlusion. While no mortality was observed in any patient due to PEG application, mortality secondary to primary disease was observed in 62 (23.8%) patients in the first 30 days.

Conclusions: Percutaneous endoscopic gastrostomy is a fast, safe and cost-effective method that does not require general anesthesia and can be performed by an experienced team in patients who require enteral nutrition.

Keywords: Percutaneous endoscopic gastrostomy, complication, mortality.

Öz

Amaç: Perkütan endoskopik gastrostomi (PEG) endoskopi ünitelerinde veya yatak başında uygulanabilen, sedasyon için intravenöz veya lokal ajanların kullanılabildiği, düşük riskli, ucuz, ulaşılabilir ve teknik olarak daha kolay bir enteral işlemdir. Çalışmamızda; kliniğimizde PEG uyguladığımız hastaların endikasyonlarını, komplikasyonlarını ve sonuçlarını değerlendirmeyi amaçladık.

Yöntemler: Üçüncü basamak bir sağlık kuruluşunun genel cerrahi endoskopi ünitesinde Ocak 2015-Mart 2021 tarihleri arasında perkütan endoskopik gastrostomi (PEG) işlemi uygulanan olgular çalışmaya dahil edildi. Olguların klinik verileri, PEG'ye bağlı gelişen komplikasyonlar ve mortalite durumu araştırıldı.

Bulgular: PEG takılan 260 hastanın 158'i (%60,7) erkek, 102'si (%39,3) kadındı. Hastaların yaş ortalaması 65,23 yıl (yaş aralığı 18-92 yıl) idi. En sık PEG açılması isteyen klinik, anestezi ve reanimasyon yoğun bakım kliniği (n=146; %56,1) idi. En sık PEG endikasyonu serebrovasküler hastalık (n=194; %74,6) nedeniyle oral alım bozukluğu idi. PEG uygulaması sonrası toplam 16 (%6,1) hastada komplikasyon (6'sı erken dönem ve 10'u geç dönem) gelişti. En sık erken dönem komplikasyon peristomal enfeksiyon (n=4; %1,5) idi. Geç dönem komplikasyonu olarak en sık görülen (n=7; %2,7) PEG kataterinin tıkanması idi. PEG uygulanmasına bağlı hiçbir hastada mortalite gözlenmez iken; ilk 30 günde 62 (%23,8) hastada primer hastalığı sekonder mortalite gözlendi.

Sonuç: Perkütan endoskopik gastrostomi enteral beslenme istenen hastalarda, genel anestezi gerektirmeyen, deneyimli ekip tarafından hızlı, güvenli ve düşük maliyetle uygulanabilecek bir yöntemdir.

Anahtar Kelimeler: Perkütan endoskopik gastrostomi, komplikasyon, mortalite.

Giriş

İnsan, yaşamın devamlılığı için gıdaya ihtiyaç duyar. Bazı hastalık durumlarında gıda alımı ağız yoluyla sağlanamaz ve hastaları alternatif yollardan beslemek gerekir. Bu durumda beslenme enteral veya parenteral yollarla sağlanabilir. Parenteral beslenme; gastrointestinal sistemin (GİS) anatomik veya fonksiyonel olarak bütünlüğünün bozulması veya enteral yol ile yeterli enerji gereksinimine ulaşılamaması durumunda gerekli olan besin öğelerinin damar yoluyla verilmesi işlemidir[1]. GİS fonksiyonları normal olan hastalarda ise enteral beslenme en ideal olanıdır. Enteral beslenme ile mukozal bütünlük ve bariyer fonksiyonu korunmakta, mukozal atrofi önlenmekte, intestinal immün yanıt ve normal floranın devamlılığı sağlanmaktadır. Enteral yolda en fizyolojik olan gastrik beslenmedir. Bu amaçla hastalarda midenin dışarı ağızlaştırılması (gastrostomi) işlemi uygulanır. Gastrostominin en sık endikasyonları; otuz günden fazla beslenme desteğine ihtiyaç duyan hastalar, nörolojik hastalar ve baş-boyun kanseri olan hastalardır[2]. Gastrostomi işlemi radyolojik, cerrahi veya endoskopik olarak uygulanabilir. Radyolojik yöntem sayılı merkezlerde uygulanmakta, cerrahi yöntem ise hastanın morbidite ve mortalitesini önemli derecede artırmaktadır. Bu nedenle tercih edilen yöntem perkütan endoskopik gastrostomi (PEG) yöntemidir.

PEG endoskopi ünitelerinde veya yatak başında uygulanabilen, sedasyon için intra venöz veya lokal ajanların kullanılabildiği, düşük riskli, ucuz, ulaşılabilir ve teknik olarak daha kolay bir işlemdir. Bu nedenle günümüzde gastrostomi için en sık tercih edilen yöntemdir[3].

Çalışmamızda; kliniğimizde PEG uyguladığımız hastaların endikasyonlarını, komplikasyonlarını ve sonuçlarını değerlendirmeyi amaçladık.

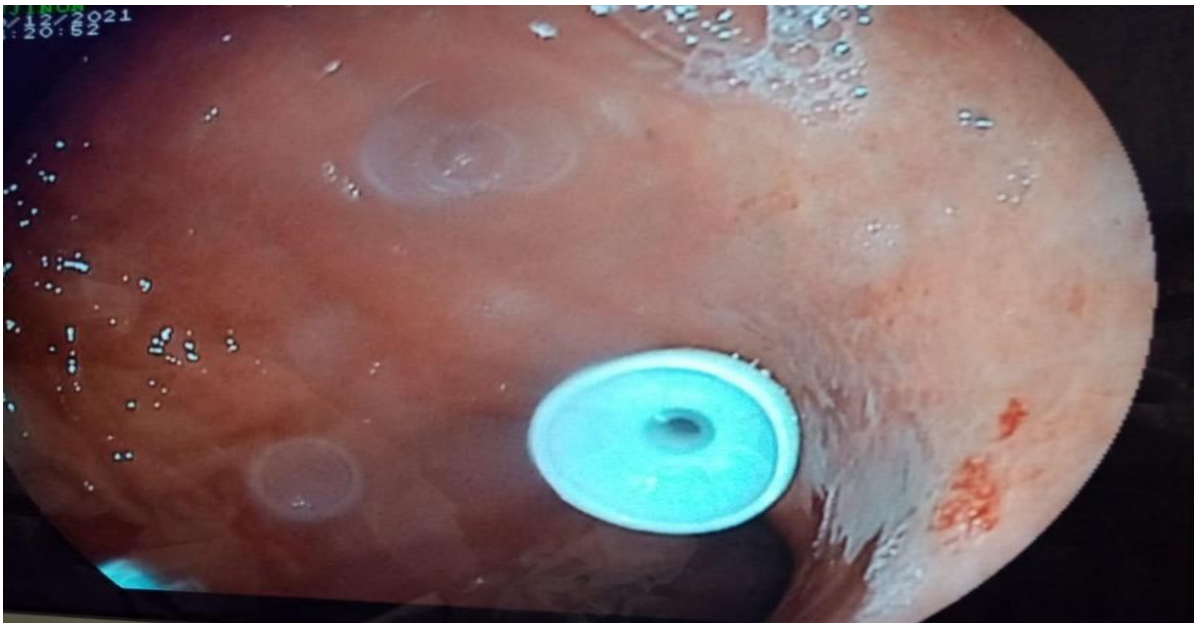
Materyal ve Metot

Çalışmamıza etik kurul onayı alındıktan sonra başlanılmış olup; Erzurum Bölge Eğitim ve Araştırma Hastanesi Genel Cerrahi Endoskopi Ünitesi'nde Ocak 2015-Mart 2021 tarihleri arasında perkütan endoskopik gastrostomi (PEG) işlemi uygulanan 260 hasta dahil edildi. Hastaların verileri hasta dosyalarından ve elektronik arşiv sisteminden retrospektif olarak incelendi. Hastaların yaşları, cinsiyeti, primer hastalıkları, PEG takılma endikasyonları, PEG'ye sekonder meydana gelen komplikasyonları kaydedildi. Komplikasyonlar ilk 30 günde meydana geldi ise erken dönem komplikasyon, ilk 30 günden sonra meydana gelmiş ise geç dönem komplikasyon olarak gruplandırıldı. Ayrıca PEG kataterinin çıkması, tıkanması, kırılması, çevresinden sızıntı olması, peristomal enfeksiyon veya kanama gibi komplikasyonlar minör komplikasyon olarak; gastrokolik fistül, ileus, perforasyon, aspirasyon pnömonisi gibi komplikasyonlar major komplikasyon olarak adlandırıldı.

Hastaların mortalite durumu da değerlendirildi. Mortalitenin PEG komplikasyonuna mı bağlı yoksa primer hastalığa mı bağlı olduğu araştırıldı. Ayrıca, PEG takılması sonrası ilk 30 günlük ve ilk 3 aylık mortalite oranları belirlendi.

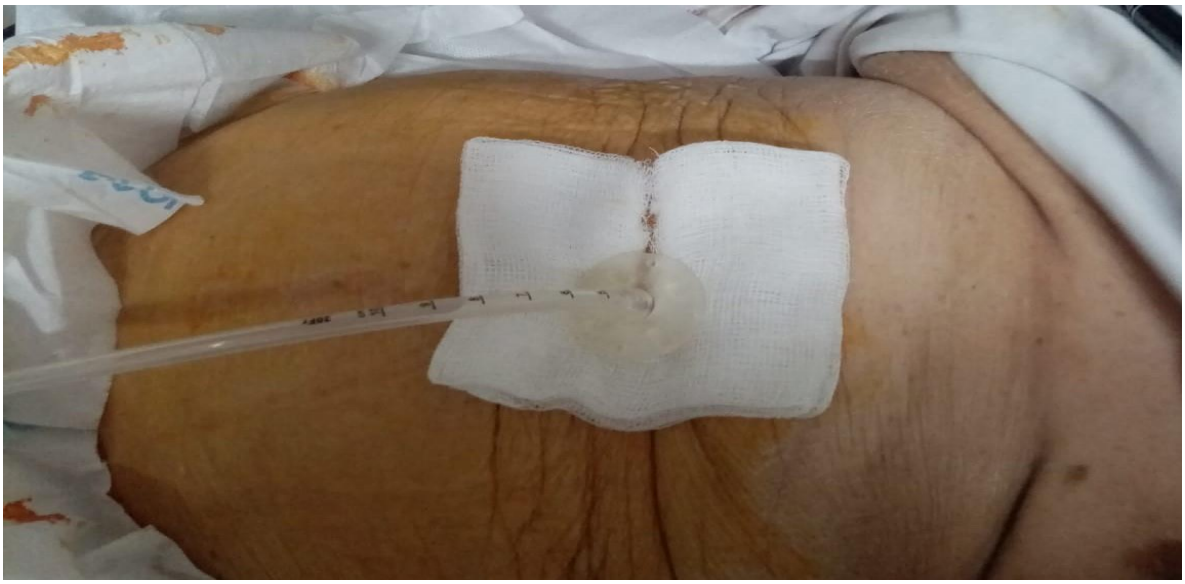
- *Perkütan endoskopik gastrostomi uygulaması*

PEG işlemi uygulanan hastaların standart olarak işlemden önce rutin tetkikler değerlendirildi ve işlemden sekiz saat önce nazogastrik beslenme varsa kesildi. Primer hastalık nedeniyle antibiyotik kullanıl-mayan hastalarda işlemden 30 dk. önce profilaktik amaçla intra venöz olarak 2. kuşak seftriakson türü antibiyotik (1 gram sefazolin) yapıldı.



Figür 1. PEG takılması sonrasında özofagogastroduodenoskop ile midenin kontrolü

İşlemler endoskopi ünitesinde veya yatak başında uygulandı. Entübe olmayan hastalarda PEG uygulaması bir anestezist (anestezi teknikeri ve/veya doktoru) gözetiminde, sedo-analjezi (intra venöz midazolam veya ketamin eşliğinde hastanın kilosuna uygun dozlarda) eşliğinde uygulandı. PEG işlemi tüm hastalarda Gauderer ve arkadaşları tarafından belirtilen Pull yöntemi ile yapıldı. İşlemlerin tümünde 20 F'lik PEG kiti kullanıldı. İşlem tamamlandıktan sonra özofagogastro-duodenoskop ile tüpün intra gastrik kısmının mukozaya tam olarak yerleştiğinden ve kanama olmadığından emin olmak için kontrol edildi (Figür 1). PEG takıldıktan 12 saat sonra 50 cc sıvı verilerek hastalarda karın ağrısı, PEG çevresinden sızdırma veya sıvı verilmesinden sonra kusma olup olmadığı değerlendirildi (Figür 2). 24 saat sonra 20 cc ile beslenmeye başlandı ve tedrici olarak artırılarak enteral beslenme başlandı.



Figür 2. PEG kataterinin dışardan görüntüsü.

Bulgular

Perkütan endoskopik gastrostomi (PEG) uygulanan hastaların 158'i (%60,7) erkek, 102'si (%39,3) kadındı. Hastaların yaş ortalaması 65,23 yıl (yaş aralığı 18-92 yıl) idi. En sık PEG açılması istenen klinik anestezi ve reanimasyon yoğun bakım kliniği (n=146; %56,1) olup; Tablo 1'de PEG takılmasını isteyen klinikler ve hasta sayıları gösterilmiştir. Hastalar yattığı kliniklerde yatış etiyolojilerine göre değerlendirildiğinde; en sık yatış etiyolojisi serebrovasküler hastalık (SVH) (n=194; %74,6) idi. Tablo 2'de hastaların primer yatış etiyolojileri gösterilmiştir.

Toplam 6 (%2,3) hastada PEG takılma işleminde başarısızlık olması nedeniyle bu hastalara cerrahi olarak gastrostomi uygulandı. Bu hastaların 2'sinde özofagusa invaze olan akciğer kanseri, 2'sinde larinks kanseri ve 2'sinde özofagus lümenini tamamen tıkayan özofagus kanseri mevcuttu. Cerrahi olarak gastrostomi uygulanan hiçbir hastada komplikasyon görülmedi. PEG uygulaması sonrası toplam 16 (%6,1) hastada komplikasyon gelişti. Bu 16 komplikasyonun 6'sı erken dönem komplikasyon ve 10'u geç dönem komplikasyondu.

Tablo 1. PEG takılmasını isteyen klinikler ve hasta sayıları

PEG Takılmasını İsteyen Klinik	Hasta sayısı (%)
Anestezi ve Reanimasyon Yoğun Bakım Kliniği	146 (%56,1)
Palyatif Bakım Kliniği	58 (%22,3)
Nöroloji Kliniği	28 (%10,8)
İç Hastalıkları Kliniği	25 (%9,6)
Beyin Cerrahi Kliniği	2 (%0,8)
Radyasyon Onkoloji Kliniği	1 (%0,4)

Tablo 2. Etiyolojik nedene göre PEG hastalarının dağılımı.

Etiyoloji	Hasta sayısı (%)
Serebrovasküler Hastalık	194(%74,6)
Alzheimer/Demans/ Parkinson	28(%10,8)
Hipoksik/İskemik Ensefalopati	14 (%5,4)
Kranial Travma	11 (%4,2)
Özofagus Kanseri	7 (%2,7)
Larinks Kanseri	2 (%0,8)
Akciğer Kanseri	2 (%0,8)
Nöroşirurji Operasyonu Sonrası	2 (%0,8)

Erken dönem komplikasyonlar peristomal kanama (n=2; %0,8) ve peristomal enfeksiyon (n=4; %1,5) idi. Peristomal kanaması olan hastalarda baskılı tampon uygulandı, kullanılan antikoagülan tedaviler kesilerek hastalar takip edildi ve ek müdahaleye gerek kalmadan peristomal kanamanın durduğu gözlendi. Peristomal enfeksiyon gelişen hastalarda ise PEG kataterleri çekildi, hastalara parenteral tedavi başlandı. Hem aerobik mikroorganizmaları hem de anaerobik mikroorganizmalara etki edecek antibiyotikler ile peristomal enfeksiyonlar yönetildi. PEG katater yara yerleri tamamen iyileşen hastalara, farklı alanlardan PEG katateri takıldı.

Geç dönem komplikasyonu olarak 7 (%2,7) hastada PEG kataterinin tıkanması ve 3 (%1,2) hastada PEG kataterinin tamamen çıkması meydana geldi. Tüpü tıkanan hastaların beşinin PEG kanülü basınçlı su yardımıyla açıldı. Lümeni açılamayan 2 hastada PEG katateri değiştirildi. Hasta uyumsuzluğu olması nedeniyle 3 hasta PEG kataterini çıkardı. Bu hastalara yeniden PEG uygulaması yapıldı.

Meydana gelen tüm komplikasyonlar minör komplikasyon olup (%6,1); hiçbir hastada majör komplikasyon görülmedi. Ayrıca PEG uygulamasına bağlı hiçbir hastada mortalite gözlenmez iken; primer hastalığa bağlı ilk 30 günlük mortalite oranı %23,8 (n=62) iken; üç aylık mortalite oranı %28,8 (n=75) idi.

Tartışma

Hastalıkların tedavi sürecinde beslenme açısından destek sağlanması en önemli basamaklardan biridir. Beslenme için kullanılan yöntem tercih edilirken, gastrointestinal sistem (GİS) fonksiyonları ve anatomik bütünlük göz önüne alınmalıdır. Oral yoldan beslenemeyen ancak GİS fonksiyonları normal olan hastalarda en uygun beslenme yöntemi; bakteriyel translokasyonu azaltması, normal flora devamlılığını sağlaması ve daha fizyolojik olmasından dolayı PEG ile enteral beslenmedir[4]. PEG yöntemi cerrahi yönteme göre daha hızlı, güvenli ve düşük maliyetlidir. Ayrıca işlemden sonra sağlık profesyonellerine ihtiyaç duyulmadan beslenmenin devam ettirilebilmesi ve hastaların yaşam kalitesini artırması önemli bir avantajdır.

Oral beslenmenin zorlaştığı durumlar olan hasta bilincinin azalması, kaybolması durumlarında ve genel durumunun kötü olduğu durumlarda PEG'ye ihtiyaç artmaktadır. Bu tür hasta popülasyonu anestezi ve reanimasyon yoğun bakım kliniği, nöroloji kliniği ve palyatif bakım kliniği gibi kliniklerde fazla olduğundan PEG takılması konsültasyonu ile karşılaşılması daha olasıdır. Tuncer ve arkadaşlarının yapmış oldukları bir çalışmada; PEG uygulanan hastalar konsülte edilen kliniğe göre değerlendirilmiş ve en sık konsültasyon %36,7 ile anestezi ve reanimasyon yoğun bakım kliniğinden, ikinci olarak %16,3 ile radyasyon onkolojisi kliğinden olduğu bildirilmiştir[5]. Şenlikçi ve arkadaşlarının yapmış olduğu başka bir çalışmada ise hem anestezi ve reanimasyon yoğun bakım kliniği hem de nöroloji kliniğinden konsülte edilen hasta oranı eşit olarak (%42,3) bildirilmiştir[6]. Temiz ve arkadaşlarının 2008-2014 yılları arasındaki PEG hastalarını değerlendirdiği çalışmasında da en sık PEG takılması için konsültasyon istenen klinik %48,4 oranında anestezi ve reanimasyon yoğun bakım kliniği idi[7]. Bizim çalışmamızda ise literatürle uyumlu olarak en sık konsültasyonun %56,1 ile anestezi ve reanimasyon yoğun bakım kliniğinden olduğu görüldü.

Serebrovasküler hastalık, serebral palsi, kafa/beyin travması, baş-boyun ve özofagus tümörleri, politravma hali ve uzun süreli koma hali PEG endikasyonları arasındadır. PEG uygulanan hastaların çoğunluğunu nörolojik hastalığı olanlar oluşturmaktadır. Çünkü kranial hasarlanmaya bağlı hastaların yutma fonksiyonları ve yeme fonksiyonları etkilenmekte ve oral alımda sorunlar olmaktadır. Şít ve arkadaşlarının yapmış olduğu çalışmada olguların %60'ında[8], Rahmani ve arkadaşlarının yapmış olduğu başka bir çalışmada ise olguların %77'sinde nörolojik hastalığın olduğu tespit edildi[9,10]. Bizim çalışmamızda ise en sık görülen PEG takılma endikasyonu %76,4 ile serebrovasküler hastalıklar idi.

PEG işlemi cerrahi gastrostomi yöntemine kıyasla morbidite ve mortalitesi daha az olması nedeniyle tercih edilmektedir. PEG işlemi uygulanan hastalar genellikle hipertansiyon, diyabetes mellitus, koroner arter hastalığı, solunum problemleri gibi kronik ek hastalıkları olan hastalardır ve bu durum genel anestezi uygulanması için önemli risk oluşturmaktadır. Ayrıca PEG işlemi ameliyathane şartları gerektirmeyen, kısa süreli ve lokal/hafif sedasyon ile yapılabilen bir işlem olduğundan; bu hastalarda anestezi riskleri minimalize edilmiş olur.

PEG minimal invaziv bir işlem olmasına karşın; PEG takılması sonrasında PEG kataterinin çıkması, tıkanması, kırılması, çevresinden sızıntı olması, peristomal enfeksiyon veya kanama gibi minör komplikasyonlar veya gastrokolik fistül, ileus, perforasyon, aspirasyon pnömonisi gibi major komplikasyonlar da görülebilmektedir. Literatürde minör komplikasyon oranı %6-33; major komplikasyon oranı ise %0-2,8 olarak bildirilmiştir[2,11]. Bizim çalışmamızda minör komplikasyon görülme oranı %6,1 olup; en sık görülen minör komplikasyon PEG kataterinin tıkanmasıdır (%2,7). Buna karşın majör komplikasyon oranımız %0 idi.

PEG işlemine bağlı mortalite nadiren görülmekte olup; mortalite oranı %1'in altındadır. PEG ihtiyacı olan hastalar genel durumu kötü hastalar oldukları için, bu

hastalarda işlem dışı sebeplere bağlı mortalite yüksek oranda görülmektedir. Yapılan çalışmalarda işlem sonrası ilk 30 günde mortalite oranı, işlem dışı nedenlere bağlı olarak %8-26,8 arasında değişmektedir. 3 aylık mortalite ise %15,7 ila %42 arasında değişmektedir[12-14]. Bizim çalışmamızda işleme bağlı mortalite görülmemiş olup; işlem dışı nedenlerle hastaların ilk otuz günlük mortaliteleri 62 (%23,8), üç aylık mortaliteleri ise 75 (%28,8) olduğu görüldü.

Sonuç

Perkütan endoskopik gastrostomi enteral beslenme istenen hastalarda, genel anestezi gerektirmeyen, deneyimli ekip tarafından hızlı, güvenli ve düşük maliyetle uygulanabilecek, komplikasyon ve mortalite riski diğer girişimsel yöntemlere nazaran az olan bir yöntemdir. Uygulanabilirliği kolay olan bu yöntem, tamamen obstrüktif üst gastrointestinal sistem hastalıklarında ne yazık ki uygulanamamakta, bu tür hasta gruplarında cerrahi olarak beslenmenin sağlanması kaçınılmaz olmaktadır.

Yazar katkısı

Tüm yazarlar çalışmanın tasarımına ve yazılmasına katkıda bulundular. Tüm yazarlar çalışmanın son halini gözden geçirip kabul ettiler.

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Kaynaklar

1. Çelebi D, Yılmaz E. Cerrahi Hastalarda Enteral ve Parenteral Beslenmede Kanıta Dayalı Uygulamalar ve Hemşirelik Bakımı. İstanbul Gelişim Üniversitesi Sağlık Bilimleri Dergisi. 2019(7):714-31. doi:10.38079/igusabder.546979
2. Demirci H, Çaycı HM, Erdoğdu UE, et al. Palyatif Bakım ve Perkütan Endoskopik Gastrostomi, Turkiye Klinikleri J Fam Med-Special Topics. 2017;8(4):263-71.
3. Yıldırım O. Perkütan endoskopik gastrostomi (PEG) uygulanan hastaların endikasyon, komplikasyon ve sonuçlarının değerlendirilmesi. Tez, İnönü Üniversitesi, Malatya, 2011.
4. Arslan M. Yoğun Bakım Hastasında Enteral Beslenmenin Önemi: Enteral Mukoza: Bariyer mi? Geçirgen mi? Yoğun Bakım Dergisi, 2002;e58:1-6
5. Tuncer K, Kılınçsoy N, Demirağ EL et al. Perkütan endoskopik gastrostomi sonuçlarımız: 49 olgunun irdelenmesi. Akademik Gastroenteroloji Dergisi. 2003;2(2).
6. Şenlikçi A, Kuzu U, Fatma D, Et al. İkinci basamak hastanede perkütan endoskopik gastrostomi deneyimlerimiz. Endoskopi Gastrointestinal. 2018;26(3):95-8. doi: 10.17940/endoskopi.502900
7. Temiz A, Aslan OB, Albayrak Y, et al. Perkütan endoskopik gastrostomi: endikasyon ve komplikasyonlar. Akademik gastroenteroloji dergisi. 2015;14(3):113-6.
8. Şit M, Kahramansoy N, Tekelioğlu ÜY, et al. Perkütan endoskopik gastrostomi uygulamalarındaki deneyimlerimiz. JAREM. 2013;3(2):66-8.
9. Rahnemai-Azar AA, Naghshizadian R, Kurtz A, et al. Percutaneous endoscopic gastrostomy: indications, technique, complications and management. World J Gastroenterol. 2014;20(24):7739-51. doi: 10.3748/wjg.v20.i24.7739
10. Demirci H, Kilciler G, Öztürk K, et al. Perkütan endoskopik gastrostomi uygulamalarındaki tecrübelerimiz. Endoskopi Gastrointestinal. 2015;23(3):73-6.
11. Bravo JG, Ide E, Kondo A, et al. Percutaneous endoscopic versus surgical gastrostomy in patients with benign and malignant diseases: a systematic review and meta-analysis. Clinics (Sao Paulo). 2016;71(3):169-78. doi: 10.6061/clinics/2016(03)09
12. Lucendo AJ, Friginal-Ruiz AB. Percutaneous endoscopic gastrostomy: An update on its indications, management, complications, and care. Rev Esp Enferm Dig. 2014;106(8):529-39.
13. Tsaousi G, Stavrou G, Kapanidis K, et al. Unsedated Outpatient Percutaneous Endoscopic Gastrostomy in Stroke Patients: Is It Feasible and

Safe? Surg Laparosc Endosc Percutan Tech. 2019;29(5):383-8.
doi: 10.1097/SLE.0000000000000661

14. Fagundes RB, Cantarelli JC, Jr., Fontana K, et al. Percutaneous endoscopic gastrostomy and peristomal infection: an avoidable complication with the use of a minimum skin incision. Surg Laparosc Endosc Percutan Tech. 2011;21(4):275-7.
doi: 10.1097/SLE.0b013e318221c3f1

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COVID-19 ENFEKTE HASTALARDA CERRAHİ OPERASYONLAR, PROGNOZ-MORTALİTE DEĞERLENDİRMESİ

SURGICAL OPERATIONS IN COVID-19 INFECTED PATIENTS, ASSESSMENT OF PROGNOSIS-MORTALITY

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Abstract

Aim: Since the beginning of the pandemic, several articles have reported negative results in the surgery of patients infected with COVID-19. However, new data are required with respect to insufficient numbers and case diversity. The aim of the current study is to report the prognosis of COVID-19 patients in the perioperative period following the operation.

Methods: In individuals who had undergone surgery, patients who were found to have COVID-19 by Polymerase Chain Reaction (PCR) on their nasopharyngeal swabs up to 14 days before or 14 days after surgery, or who had contact history and symptoms, or those with symptoms of COVID-19 in their thoracic tomography, were included in the study. The data of the patients were obtained from patient files and digital records.

Results: A total of 3093 patients were operated; 40 of these patients were included in the study as COVID-19 (+) or COVID-19 suspect; 5 (12.5%) of the 40 operated patients died in the postoperative period. The average age of the patients who died was 69.6 years old. Of the patients who died, 4 (80%) were male and 1 (20%) was female. Comorbid diseases were present in 4 of the patients who died. None of the operating suite employees experienced COVID-19 infection associated with these patients who underwent surgery.

Conclusions: We found that the postoperative mortality rate of patients infected with COVID-19 in our hospital is slightly lower than the reported rate in the literature. Elective cases should be postponed, except for emergency surgical cases. Male gender, advanced age, presence of 2 or more comorbidities are risk factors for adverse postoperative outcomes in COVID-19(+) patients.

Keywords: COVID-19, SARS-CoV-2, pandemic, surgery, elective

Öz

Amaç: Pandeminin başlangıcından bu yana çeşitli makalelerde SARSCoV-2 ile enfekte hastaların cerrahisinde olumsuz sonuçlar bildirilmiştir. Ancak sayıların yetersizliği ve vaka çeşitliliği açısından yeni verilere ihtiyaç duyulmaktadır. Bu çalışmanın amacı, perioperatif dönemde SARSCoV-2 ile enfekte hastaların, ameliyat sonrası prognozlarını bildirmektir.

Yöntemler: Ameliyat geçirmiş bireylerde, ameliyattan 14 gün öncesine veya ameliyattan 14 gün sonrasına kadar nazofarengeal süürüntülerinde Polimeraz Zincir Reaksiyonu (PCR) ile COVID-19 (+) oldukları tespit edilen veya temas öyküsü bulunup semptomları olan ya da çekilen toraks tomografilerinde COVID-19 bulgusu saptanan hastalar çalışmaya dahil edildi. Hastaların demografik verileri, PCR test sonuçları, toraks tomografi bulguları, ASA skorları, ek hastalıkları, cerrahi tipi, operasyon süreleri, anestezi türü, hastaların taburculuk günü ve yoğun bakım/servis yatış günleri hasta dosyaları ve elektronik kayıtlardan elde edildi.

Bulgular: Hastanemizde toplam 3093 hasta opere edilmiştir. Bu hastalardan 40'ı kesin veya olası COVID-19 olarak çalışmaya dahil edildi. Opere edilen 40 hastadan 5'i (%12,5) operasyon sonrası dönemde eksitus olmuştur. Eksitus olan hastaların yaş ortalaması 69,6 idi. Ölen hastalarda 4'ü (%80) erkek, 1'i (%20) kadın cinsiyetinde idi. Ölen hastaların 4'ünde eşlik eden hastalıklar mevcuttu. Hiçbir ameliyathane çalışanı cerrahi geçiren bu hastalarla ilişkili COVID-19 enfeksiyonu geçirmemiştir.

Sonuç: Hastanemizde SARSCoV-2 ile enfekte hastaların cerrahi sonrası ölüm oranlarının literatürden biraz daha düşük olduğunu saptadık. Çalışmamızdan elde edilen veriler ışığında, acil cerrahi vakalar dışında elektif vakalar ertelenmelidir. Erkek cinsiyet, ileri yaş, 2 veya daha fazla eşlik eden hastalığın varlığı, COVID-19 (+) hastalarda ameliyat sonrası olumsuz sonuçlar için risk faktörleridir.

Anahtar Kelimeler: COVID-19, SARS-CoV-2, pandemi, cerrahi, elektif

Giriş

Tespit edildiği günden itibaren hızla yayılan ve yüksek mortalite ile seyreden COVID-19 tüm dünyanın korkulu rüyası olmaya devam etmektedir. Ağır pnömoni ile seyreden vakaların yanında asemptomatik vakaların sayısı da çok fazladır. Semptom vermeyen bu grup bulaş için ciddi risk oluşturmaktadır. COVID-19'un seyri uzundur ve COVID-19 kuluçka döneminde bile oldukça bulaşıcıdır[1].

Ülkemizde hastane kaynaklarının korunmasına yardımcı olmak, gereksiz yatak işgallerini en aza indirmek ve hastalığın yayılmasını yavaşlatmaya yardımcı olmak amacıyla Mart 2020 tarihinde tüm elektif veya acil olmayan ameliyatlara ara verildi[2]. Bununla beraber opere olması gereken kanser hastaları, travma olguları, hastanın konforunu bozan cerrahi gerektiren vakalar sekteye uğramış, operasyonlarının iptal edilmesi veya ertelenmesi, muhtemelen morbidite ve mortalitenin artmasına neden olmuştur[3]. Tüm dünyada, pandeminin 12 haftalık zirvesinde 28 milyondan fazla (%72,3) planlanmış ameliyat prosedürünün iptal edildiği tahmin edilmektedir[4].

Ameliyatların ertelenmesinin bir başka sebebi de COVID-19(+) hastalardaki cerrahi süreci tam olarak bilememektir. COVID-19(+) hastalarda yüksek perioperatif mortaliteye ilişkin erken raporlar, operasyonlardan yaygın bir şekilde kaçınmayı teşvik etmiştir. Cerrahi operasyon ile COVID-19 hastalarının genel durumlarının bozulduğuna dair görüşler olmasına rağmen hala yeterli veriler ortaya konmamıştır.

Bu çalışmada, SARSCoV-2 ile enfekte hastalarda cerrahi operasyonların morbidite ve mortalite oranlarını saptayıp, literatüre ışık tutmayı hedefledik.

Materyal ve Metot

Çalışma Helsinki Deklarasyonu Prensiplerine uygun olarak yapıldı. Akdeniz Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu'ndan 26.05.2021 tarihli (karar no:KAEK-338) etik kurul onayı alındı. Hastanemizde 01.08.2020-01.03.2021 tarihleri arasında COVID-19(+) veya şüpheli olup opere edilen hastalar retrospektif olarak incelendi. Hastaların COVID-19 olası/kesin olgu sınıflamaları hastaneye başvuruları sırasında geçerli olan Sağlık Bakanlığı rehberlerine göre düzenlendi[5]. Çalışmanın yapıldığı dönemi kapsayan aralıktaki Sağlık Bakanlığı rehberlerine göre olgu tanımları şöyledir:

Olası Olgu A: Ateş veya akut solunum yolu hastalığı belirti ve bulgularından en az biri (öksürük ve solunum sıkıntısı) ve klinik tablonun başka bir neden/hastalıkla açıklanamaması ve semptomların başlamasından önceki 14 gün içerisinde kendisi veya yakınının yurtdışında bulunma öyküsü varlığı.

Olası Olgu B: Ateş veya akut solunum yolu hastalığı belirti ve bulgularından en az biri (öksürük ve solunum sıkıntısı) ve semptomların başlamasından önceki 14 gün içerisinde doğrulanmış COVID-19 olgusuyla yakın temas etme öyküsünün varlığı.

Olası Olgu C: Ateş ve ağır akut solunum yolu enfeksiyonu belirti ve bulgularından en az biri (öksürük ve solunum sıkıntısı) ve hastanede yatış gerekliliği varlığı ("severe acute respiratory infections"- ağır akut solunum yolu enfeksiyonları, SARI) ve klinik tablonun başka bir neden/hastalıkla açıklanamaması durumu.

Olası Olgu D: Ani başlangıçlı ateşle birlikte öksürük veya nefes darlığı olması ve burun akıntısı olmaması.

Kesin Olgu: Olası olgu tanımına uyan olgulardan moleküler yöntemlerle SARS-CoV-2 saptanan olgular.

Ameliyat geçirmiş bireylerden, ameliyattan 14 gün öncesine veya ameliyattan 14 gün sonrasına kadar nazofarengeal sürüntüntülerinde polimeraz zincir reaksiyonu (PCR) ile COVID-19 oldukları tespit edilen veya temas öyküsü bulunup semptomları olan ya

da çekilen toraks tomografilerinde COVID-19 bulgusu rastlanan hastalar çalışmaya dahil edildi.
Hastaların demografik verileri, PCR test sonuçları, toraks tomografi bulguları, ASA (American Society of Anesthesiologist sınıflandırması) skorları ek hastalıkları, cerrahi tipi, operasyon süreleri, anestezi türü, hastaların taburculuk günü ve yoğun bakım/servis yatış günleri hasta dosyaları ve elektronik kayıtlardan elde edildi[6].

Bulgular

Hastanemiz ameliyathanesinde 01.08.2020-01.03.2021 tarihleri arasında toplam 3093 hasta opere edilmiştir. Bu hastalardan 40'ı olası veya kesin COVID-19 olarak çalışmaya dahil edildi. Hastalardan 26'sının (%65) PCR testi pozitif iken, 14'ünün (%35) PCR testi negatif ancak temaslı-semptomlu ya da tomografi bulguları COVID-19 lehine idi. Evden gelen hastalar Sağlık Bakanlığının güncel tedavi rehberi doğrultusunda tedavi almaktaydı. Hastane yatışları sırasında COVID-19 tanısı alan hastalara da Sağlık Bakanlığının güncel tedavi rehberi doğrultusunda tedavi başlanmıştır.
Opere edilen 40 hastanın 15'i (%37,5) erkek, 25'i (%62,5) kadın idi. Hastaların yaş ortalamasının 39,8±12,3 olduğu görüldü. Ortalama cerrahi süresi 53,37±27,4 dakika olarak saptandı (Tablo I). Hastalardan 29'u ASA I, 6'sı ASA II, 5'i ASA III olarak operasyona alındı. Eşlik eden ek hastalıklar Tablo I' de verilmiştir. Hastaların ortalama servis yatış günü 2,77 idi. Sadece 2 hastanın servis yatışı olmayıp yoğun bakım yatışı mevcuttu. Operasyon sonrası yoğun bakımda takip edilen hasta sayısı 4 (%10) idi, bu 4 hastanın ortalama yoğun bakım yatış günü 24,74 olarak saptandı. Postoperatif 30 günlük dönemde yoğun bakım takibi gereken 4 hastadan 3'ünün eksitus olduğu görüldü.
Opere edilen 40 hastadan 5'i (%12,5) operasyon sonrası dönemde eksitus olmuştur. Eksitus olan hastaların yaş ortalaması 69,6 idi.

Tablo 1. Katılımcıların demografik verileri

Demografik veriler	Ort ±SS	
Yaş Ortalaması	39,8±12,3	
Ortalama Cerrahi Süresi	53,37±27,4	
Toplam Hasta	*Sayı*	*%*
Kadın	25	62,5
Erkek	15	37,5
Ek hastalık	*Sayı*	*%*
Hipertansiyon	29	72,5
**KOAH	7	17,5
Diyabetes Mellitus	3	7,5
Kardiyovasküler Hastalık	3	7,5
Serebrovasküler Hastalık	3	7,5
	2	5

* Örneklem sayısı toplam sayıdan fazladır
**KOAH: Kronik Obstrüktif Akciğer Hastalığı

Ölen hastalardan 4'ü (%80) erkek, 1'i kadın (%20) cinsiyetinde idi. Ölen hastaların 4'ünde eşlik eden hastalıklar mevcuttu (Tablo 2).
Eksitus olan hastalardan 3'ü Ortopedi kliniği tarafından femur fraktürü nedeniyle, 1'i Beyin Cerrahi kliniği tarafından beyin tümörü nedeniyle, 1'i de Genel Cerrahi kliniği tarafından mide perforasyonu nedeniyle opere edilmişti. Bu 5 hastadan 4'ü postoperatif dönemde yoğun bakımda takip edilmişti. Hastaların operasyondan ortalama 19,20 gün sonra eksitus oldukları saptandı. Bu hastaların 3'ü (%60) genel anestezi altında opere edilirken, 2'si (%40) spinal anestezi altında opere edilmiştir (Tablo II).
İncelenen grupta; Genel Cerrahi kliniği tarafından 11 hasta (%27,5), (7 apendektomi, 2 inguinal herni, 1 barsak perforasyonu, 1 mide perforasyonu), Ortopedi kliniği tarafından 7 hasta (%17,5), (4 femur fraktürü, 1 metakarp fraktürü , 1 tibia fraktürü), Kadın Hastalıkları kliniği tarafından 18 hasta (%45) (17 sezeryan ,1 küretaj), Beyin Cerrahi kliniği tarafından 2 hasta (%5) (1 lomber stabilizasyon, 1 beyin tümörü), Üroloji kliniği tarafından 2 hasta (%5) (1 anorektal apse, 1 Ureteroscopy) hasta opere edilmiştir (Tablo III).

Tablo 2. Operasyondan Sonra Eksitus Olan Hastaların Dağılımı

Yaş	Cinsiyet	PCR	BT	Geçirilen operasyon	Anestezi türü	ASA	Ek Hastalık	Eksitus Zamanı (Postop/gün)
87	E	Neg	Buzlu cam	Femur fraktürü	Spinal	3	KOAH, KAH	20
52	E	Poz	Buzlu Cam	Femur fraktürü	Genel	2	HT	8
67	E	Neg	Buzlu cam	Mide perforasyonu	Genel	3	KOAH, HT	33
68	K	Poz	Buzlu cam	Femur fraktürü	Spinal	1	Yok	7
74	E	Poz	Buzlu cam	Beyin Tümörü	Genel	2	HT, DM	28

Hastaların 33'ü (%82,5) spinal anestezi altında, 7'si (%17,5) genel anestezi altında opere olmuştur.
Hastalardan 39'u acil şartlarda operasyona girerken, 1 hastada elektif lomber stabilizasyon operasyonundan 1 gün sonra PCR pozitifliği saptanmıştır.

Tablo 3. Cerrahi uygulayan klinik

Klinik	Sayı	%
Kadın Doğum	18	45
Genel Cerrahi	11	27,5
Ortopedi	7	17,5
Beyin Cerrahi	2	5
Üroloji	2	5

Tartışma

Toplum bağışıklığı yeterli düzeyde sağlanmadığı müddetçe, cerrahi ihtiyaçları olan hastaların eş zamanlı COVID-19 olma olasılığı artmaktadır. Amerikan Anestezi Uzmanları Derneği ve Anestezi Hasta Güvenliği Vakfı, elektif cerrahi geçiren hastaların, özellikle salgın durumunun yüksek olduğu bölgelerde, planlanan prosedürden kısa bir süre önce COVID-19 için test edilmesini önermektedir7. Biz de elektif olarak opere edilecek her hastaya 24 saat önce PCR testi uyguladık. Hastaların tanı almaları hem anestezi planlaması hem de operasyona girecek sağlık ekiplerinin güvenliği açısından çok önemlidir.

Peri-operatif COVID-19 enfeksiyonu bulunan hastalarda cerrahi sonrası ölüm oranlarında artış olduğu yapılan çalışmalarda bildirilmiştir[3,8,9].
Serimizde 5 (%12,5) hastada 19,2 ± 8,2 gün sonra postoperatif ölüm kaydettik. Çalışmamızda aynı dönemde elektif vakalar operasyona alınmadığı için COVID-19 olmayan hastalarla karşılaştırma grubu oluşturulamadı. Ancak, hastanemizde 2019-2020 tarihleri arasında opere edilip yoğun bakıma alınan hastaların prognozlarını sunan bir çalışmada, hastaların mortalite oranlarının %5,88 olduğu bildirilmişti. Bu kıyaslama SARSCoV-2 ile enfekte hastalarda mortalitenin arttığını açıkça göstermektedir[10].
Lei ve arkadaşları[11] elektif cerrahi uygulanan 34 asemptomatik COVID-19 hastasında; %20,5 postoperatif ölüm, %44,1 YBÜ yatış oranı ve %100 postoperatif pulmoner komplikasyon bildirmiş. Pandeminin başında yapılan cerrahi girişimlerden 161 COVID-19 (+) ve 342 COVID-19 (-) hastanın karşılaştırmalı incelendiği başka bir çalışmada; COVID-19 (+) hastaların 30 günlük genel postoperatif mortalite oranı (%16), negatif kontrol grubuna (%4) kıyasla daha yüksek saptanmıştır[9]. Ameliyattan 7 gün önce veya 30 gün sonra COVID-19 enfeksiyonu doğrulanmış 1128 cerrahi hastanın (elektif cerrahi: %24,8, acil cerrahi: %74,0) değerlendirildiği bir çalışmada; bu hastalarda mortalite %23,.8 ve pulmoner komplikasyonlar %51,2 oranında saptanmıştır[12]. Mortalite oranımızı literatüre göre daha düşük saptadık. Bu

düşüklüğü hastalarımızın pulmoner tutulumlarının az olması, seçilen uygun anestezi teknikler ve postoperatif dönemde yoğun bakım ihtiyacının düşük olmasına bağladık. Hastalarımızın %45'i sezaryen operasyonu geçiren ek hastalığı bulunmayan genç hastalardı. Hastalarımıza pulmoner komplikasyonlardan kaçınmak için %82,5 oranında spinal anestezi uyguladık.

ASA III-IV gibi yüksek ASA skoru olan geriatrik hastalarda cerrahi sonrası mortalitenin daha yüksek oranda görüldüğü bilinmektedir[13,14]. Acil kalça kırığı operasyonu geçiren 65 yaş üstü 16695 hastanın operasyon verileri incelendiğinde, mortalite oranı %2,1 bulunmuş ve genel anestezi uygulanan hastalar mortalite açısından daha yüksek riskli saptanmıştır[15]. Hastalarımızdan 5'i ASA III olup bu hastaların 2'si postoperatif dönemde eksitus oldu. Eksitus olan hastalarda birden fazla hastalığın eşlik ettiği gözlendi. Yüksek ASA skorlu hastaların ek olarak SARSCoV-2 ile enfekte olmaları, pulmoner komplikasyonların gelişmesini ve mortalite oranlarını arttırmaktadır. Bu hastaların preoperatif dönemde iyi hazırlanması, genel anesteziden ziyade rejyonel tekniklerin tercih edilmesi gerekir.

COVID-19 (+) 294 hastanın dahil edildiği çok merkezli bir çalışmada postoperatif pulmoner komplikasyonların, perioperatif COVID-19 enfeksiyonu olan hastaların yarısında ortaya çıktığı ve yüksek mortalite ile ilişkili olduğu sonucu ortaya konulmuştur. COVID-19 salgını sırasında ameliyatlar özellikle 70 yaş ve üstü erkeklerde daha riskli saptanmıştır. Çalışmanın sonucunda, ameliyat ihtiyacını geciktirmek veya önlemek için acil olmayan prosedürlerin ertelenmesi ve ameliyatsız tedavinin teşvik edilmesi gerektiği belirtilmiştir[12]. Çalışmamızdaki hastalardan, 4'ünde (%10) YBÜ takibi gerekti. Bizim çalışmamızda da benzer şekilde eksitus olan hastaların yaş ortalaması 69,6 idi ve %80'ni erkek cinsiyet oluşturmaktaydı. Hastaların hepsi acil şartlarda operasyona alınmıştı. Biz de çalışmamızın sonuçlarına dayanarak SARSCoV-2 ile enfekte, 70 yaş üzeri, acil opere edilen erkek cinsiyetinde mortalitenin daha yüksek olduğunu söyleyebiliriz.

COVID-19 geçiren hastaların mortalitesinin incelendiği başka bir çalışmada da; 3127 SARSCoV-2 enfekte cerrahi geçiren hastada 30 günlük mortalite oranı %9,1 olarak saptanmıştır. Aynı dönemde COVID-19 olmayan hastalarda cerrahi sonrası mortalite oranı %1,4 olarak bulunmuştur. Aynı çalışmada mortalite oranlarının zamanla ilişkili olduğu ve COVID-19 enfeksiyonundan 7 hafta sonra mortalite oranlarının COVID-19 olmayan hastalarla bir farkı kalmadığı belirtilmiştir16. Chong ve arkadaşlarının çalışmasında, ameliyat öncesi PCR (-) olup operasyon planlanan hastalar, 2 hafta hastanede izolasyon sağlandıktan sonra opere edilmiş ve ameliyat sonrası 30 günlük tüm nedenlere bağlı ölüm oranı %1,26 (5/398) olarak saptanmıştır. Chong ve arkadaşları[17] öneri olarak operasyon planlanan hastaların tam izolasyonu ile cerrahilerin güvenle devam edebileceklerini bildirmişlerdir. SARSCoV-2 ile enfekte vakalarda mortalitenin artışı aşikâr iken elektif vakalar ertelenmeli ve bu esnada hastalar mümkün olduğunca izole edilmelidir.

Verilerimiz daha önce yayınlanmış kanıtlardan istatistiksel olarak daha iyi sonuçlar ortaya koydu. Hastalarımızda mümkün olduğunca rejyonel anestezi yöntemleri tercih edilmiştir. Bu tercihteki amacımız: akciğer fonksiyonlarını bozmamak, hastalığın progresyonunun ağırlaşmasını engellemek, mümkün olan en kısa hastanede yatış sürelerini sağlamak ve sağlık personeli bulaşını en aza indirmektir.

Hastanemizde her vaka için sağlık personelleri kişisel koruyucu ekipman kullanmış olup, cerrahi prosedürlerden sonra hiçbir sağlık çalışanında cerrahi ile ilişkili COVID-19 enfeksiyonu saptanmadı.

Sonuç

Hastanemizde SARSCoV-2 ile enfekte hastaların cerrahi sonrası ölüm oranlarının literatürdekinden istatistiksel olarak daha düşük olduğunu saptadık. Ancak daha önceki

ölüm oranlarına kıyasla SARSCoV-2 ile enfekte hastalarda postoperatif mortalitenin arttığı aşikardır. Acil cerrahi vakalar dışında elektif vakalar ertelenmelidir. Preoperatif tarama ve kişisel koruyucu ekipman kullanımının benimsenmesi zorunlu tutulmalıdır. Pulmoner komplikasyonlar çoğunlukla ölümden sorumludur. Pulmoner komplikasyonların zararlı etkilerini azaltan stratejiler benimsemek çok önemlidir. Erkek cinsiyet, ileri yaş, 2 veya daha fazla eşlik eden hastalığın varlığı, COVID-19 pozitif hastalarda ameliyat sonrası olumsuz sonuçlar için risk faktörleridir.

Yazar katkısı

Tüm yazarlar çalışmanın tasarımına ve yazılmasına katkıda bulundular. Tüm yazarlar çalışmanın son halini gözden geçirip kabul ettiler.

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Kaynaklar

1. Yu P, Zhu J, Zhang Z, et al. A familial cluster of infection associated with the 2019 novel coronavirus indicating possible person-to-person transmission during the incubation period. J Infect Dis. 2020; 221(11): 1757-61. doi: 10.1093/infdis/jiaa077
2. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü [Internet]. Covid-19 (SARS-CoV-2 İnfeksiyonu) Rehberi. Bilim Kurulu Çalışması. 12 Nisan 2020. [erişim 12 Nisan 2020]. https://ohsad.org/wp-content/uploads/2020/04/COVID-19_Rehberi-1.pdf.
3. Patel NG, Reissis D, Mair M, et al. Safety of major reconstructive surgery during the peak of the COVID-19 pandemic in the United Kingdom and Ireland – multicentre national cohort study. J Plast Reconstr Aesthet Surg. 2021; 74(6): 1161-72. doi: 10.1016/j.bjps.2020.12.032
4. COVIDSurg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans: Elective surgery during the SARS-CoV-2 pandemic. Br J Surg. 2020; 107(11): 1440-49.
5. T.C. Sağlık Bakanlığı COVID-19 Rehberleri [İnternet]. Ankara: T.C. Sağlık Bakanlığı [erişim 13 Ekim 2020]. https://covid19bilgi.saglik.gov.tr/tr/
6. American Society of Anesthesiologists Clinical Information [Internet]. Schaumburg, IL: American Society of Anesthesiologists; 2020. ASA Physical Status Classification System [Erişim:10 Eylül 2021]. https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system
7. American Society of Anesthesiologist, Anesthesia Patient Safety Foundation [Internet]. The ASA and APSF joint statement on perioperative testing for the COVID-19 virus. [erişim 13 Ekim 2020] https://www.asahq.org/about-asa/newsroom/news-releases/2020/04/asa-and-apsf-joint-statement-on-perioperative-testing-for-the-covid-19-virus.
8. Glasbey JC, Nepogodiev D, Simoes JFF, et al. Elective cancer surgery in COVID-19-free surgical pathways during the SARS-CoV-2 pandemic: an international, multicenter, comparative cohort study. J Clin Oncol. 2021; 39(1): 66-78. doi: 10.1200/JCO.20.01933
9. Jonker PKC, van der Plas WY, Steinkamp PJ, et al. Perioperative SARS-CoV-2 infections increase mortality, pulmonary complications, and thromboembolic events: a Dutch, multicenter, matched-cohort clinical study. Surgery. 2021; 169(2): 264-74. doi: 10.1016/j.surg.2020.09.022
10. Coşkun AS. Postoperatif Yoğun Bakıma Kabul Edilen Hastaların 1 Yıllık İncelenmesi. Acta Med Nicomedia. 2020; 3(3): 105-8.
11. Lei S, Jiang F, Su W, et.al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020; 21: 100331. doi: 10.1016/j.eclinm.2020.100331
12. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. COVIDSurg Collaborative. Lancet. 2020; 396(10243): 27-38. doi: 10.1016/S0140-6736(20)31182-X
13. Li SG, Sun TS, Liu Zet al. Factors influencing postoperative mortality one year after surgery for

hip fracture in Chinese elderly population. Chin Med J (Engl). 2013; 126(14): 2715-9.
doi: 10.3760/cma.j.issn.0366-6999.20122986
14. Liu JL, Wang XL, Gong MW, et al. Comparative outcomes of peripheral nerve blocks versus general anesthesia for hip fractures in geriatric Chinese patients. Patient Prefer Adherence. 2014; 8: 651-9.
doi: 10.2147%2FPPA.S61903
15. Qiu C, Chan PH, Zohman GL, et al. Impact of Anesthesia on Hospital Mortality and Morbidities in Geriatric Patients Following Emergency Hip Fracture Surgery. J Orthop Trauma. 2018; 32(3): 116-23.
doi: 10.1097/BOT.0000000000001035
16. COVIDSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia. 2021; 76(6): 748-58.
doi: 10.1111/anae.15458
17. Chong SMY, Hung RKY , Gwozdz A, et al. 30-Day postoperative COVID-19 outcomes in 398 patients from regional hospitals utilising a designated COVID-19 minimal surgical site pathway. Annals 2021; 103(6): 395-403.
doi: 10.1308/rcsann.2020.7072

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RELATIONSHIP BETWEEN SERUM ASYMMETRIC DIMETHYLARGININE LEVEL AND OBSTRUCTIVE SLEEP APNEA SYNDROME SEVERITY

SERUM ASİMETRİK DİMETİL ARJİNİN DÜZEYİ VE OBSTRUKTİF UYKU APNE SENDROMU AĞIRLIĞI ARASINDAKİ İLİŞKİ

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Abstract
Aim: The repetitive hypoxemia can induce oxidative stress mechanisms. Oxidative stress increases serum asymmetric dimethylarginine (ADMA) levels in patients with obstructive sleep apnea syndrome (OSAS). To investigate the relationship between serum levels of ADMA and OSAS severity.
Methods: 330 patient's records, who underwent overnight polysomnography (PSG) were retrospectively examined. The patients who had an abnormal serum glucose, lipid, thyroid, renal and liver function tests levels, had excluded. 72 patients had participating criteria. Patients were categorized into five groups according to apnea/hipopnea index (AHI). Measurement of ADMA levels were performed by ELISA kit.
Results: The mean age was 44,19 ± 14,24 years. 31,9 % of the patients were female. Patients in normal group, severe, medium, mild and positional–REM dependent OSAS group were 26,4%, 25%, 6,9 %, 16,7% and 25%; respectively. A significant positive correlation was found between AHI and ADMA (r= 0,483; p<0,001). Appropriate cut-off criterion was set at 1,39 for ADMA. Sensitivity for this value was 73,58 % (95 % Confidence Interval (CI): 61,71- % 85,45 %) and specificity was 94,74 % (95 % CI: 84,70- % to 100%). Accuracy or correct classification rate was found to be 79,17 %. The positive predictive value was 97,5 % and negative predictive value was 56,25 %. The positive likelihood ratio (LR +) was 13,98 (LR + > 10) and the negative likelihood ratio was (LR-) 0,28 (R- <1).
Conclusions: ADMA was found to be a strong and good diagnostic tool among patients with normal levels for glucose, lipid, TSH, creatinine and liver function tests.

Keywords: Obstructive sleep apnea, hypoxemia, ADMA

Öz
Amaç: Obstrüktif Uyku Apne Sendromu (OUAS) olan hastalarda ortaya çıkan tekrarlayan hipoksemi ve reoksijenasyon oksidatif stres mekanizmalarını tetikleyebilir. Oksidatif stres OUAS hastalarında Asimetrik dimetilarginin (ADMA) düzeylerini artırır. Çalışmamızda Serum Asimetrik Dimetil Arjinin (ADMA) düzeyi ve Obstrüktif Uyku Apne Sendromu (OUAS) ağırlığı arasındaki ilişkiyi incelemeyi amaçladık.
Yöntemler: Polisomnografi yapılan 330 hasta kayıtları retrospektif olarak değerlendirildi. Anormal serum glukozu, lipid, tiroid, böbrek ve karaciğer bozuklukları olan hastalar çalışma dışı bırakıldı. Kabul kriterleri 72 sağladı. Hastalar apne hipopne indekslerine göre beş gruba ayrıldılar. Asimetrik Dimetil Arjinin ölçümleri ELİSA kiti ile yapıldı.
Bulgular: Ortalama yaş 44,19 ± 14,24 idi. Hastaların %31,9'u kadındı. Hastalar normal, ağır, orta, hafif, rem-pozisyonel olarak gruplandığında; %26, %25, %6,9, %16,7 ve %25 oranlarındaydılar. AHI ve ADMA arasında anlamlı korelasyon saptandı (r= 0,483; p<0,001). ADMA için uygun cut-off değeri 1,39 olarak belirlendi. Bu değer için duyarlılık %73,58 (%95 güven aralığı (CI): 61,71- %85,45 %), özgünlük %94,74 (95 % CI: 84,70- %100%) idi. Doğruluk ya da doğru sınıflandırma oranı %79,17 olarak bulundu. Pozitif kestirim değeri %97,5 ve negatif kestirim değeri ise %56,25 idi. Pozitif olabilirlik oranı (LR+) 13,98 (LR+>10) ve negatif olabilirlik oranı (LR-) 0,28 (LR-<1) olarak saptandı.
Sonuç: ADMA test yöntemi; normal glukoz, lipid, tiroid, karaciğer ve böbrek fonksiyon testine sahip hastalarda, güçlü ve iyi bir tanı testi kriteri olma özelliklerine sahip olabilir.

Anahtar Kelimeler: Obstrüktif uyku apne sendromu, hipoksemi, ADMA

Introduction

Obstrucive Sleep Apnea Syndrome (OSAS) is the most commonly observed reason for the lack of sleep (insomnia) in the adulthood phase, concerning many systems in the body, which progresses along with the repeating obstruction of the upper airway during sleep[1-3]. OSAS is also the source of serious morbidity and mortality with its cardiovascular results as well as its social and neuropsychological results[4-6].

Hypoxia and reoxygenation which show up and repeat in the patients suffering from an obstructive sleep apnea induce oxidative stress mechanisms[7].

Decreasing dimethylarginine dimethylaminohydrolase (DDAH) and increasing Protein arginine N-methyltransferase 1 (PRMT-1) enzymes as a result of the oxidative stress appeared in the OSAS cause the Asymmetric Dimethylarginine (ADMA) level rise, increased ADMA serum levels decrease Nitric acid (NO) levels inhibiting Endothelial NOS (e-NOS) activity and causes endothelial dysfunction with the said mechanism.

Golden standard in OSAS is Polysomnography (PSG)[8]. However, the technical hardware requirement and the fact that the survey takes a long time causes that the process when the patients with obstructive sleep apnea syndrome take diagnosis and start the treatment is prolonged.

Our purpose is to investigate the employability of the ADMA in foreseeing the presence and severity of OSAS.

Materials and Methods

This study has been carried out on successive 330 persons who have been applied to the Sleep Clinic of Chest Diseases in the Medical Faculty of Düzce University between August 2011 and August 2013 with complaints of sleep disorders and undergone a polysomnography throughout the night with the informed consent of the relevant patients. A 9 ml of blood taken for hemogram and biochemistry has been put into K3 EDTA and biochemistry tubes in the morning at the end of the night through which the polysomnography was applied. Other parameters than ADMA have been studied without losing time by means of the Pentra DX 120-Pentra XL 80 devices available in the Microbiology-CBC-Biochemistry Laboratories. Samples taken to be able to measure ADMA values have been frozen at 80° C after they were centrifuged and their plasma has been extracted by a single physician. ADMA levels have been directly measured from the blood of the selected patient group employing ELISA kit (from Immunodiagnostik AG), enzyme-linked immunosorbent assay method.

Patient files have been examined retrospectively. Cases with apnea-hypopnea index ≥ 5 were considered to be OSAS. Three patients due to their central sleep apnea, and 253 persons because of their laboratory anomalies such as high glucose, lipid levels have been extracted from the study. According to the AHI indexes, 72 patients involved in the study have been divided into groups with the following numbers: 19 normal, 12 light sleep apnea, 5 mild sleep apnea, 18 severe sleep apnea and 18 positional/REM-related sleep apnea.

The descriptive statistics have been calculated for all data in the study (mean, standard deviation, median, minimum, maximum, percent values). Levene and Shapiro-Willk tests have been carried out in order to control the homogeneity of variances and normality assumptions. One-Way ANOVA (post hoc Tukey test) and Kruskal-Wallis (post-hoc Dunn's test) tests have been employed in the comparison between the groups. McSweeney and Porter's Rank ANCOVA (post hoc Bonferroni test) tests have been carried out in order to eliminate the effects of confounding factors between the groups. Fisher-Freeman-Halton test has been utilized in order to examine the relationships between categorical variables. Degree and direction of the relationship between two variables have been found by Partial Correlation test while controlling the effect of confounding factor. ROC analysis

has been performed in order to determine the suitable cut-off value for the diagnostic test. p<0.05 was considered to be statistically significant. PASW 18 software program and specially written macros have been utilized. The Research and Ethics Committee of the Düzce University approved the study (March 2012/93).

Results

Our patients were grouped as 26.4% normal (n=19). 25% severe (n=18), 25% positionrem dependent (n=18), 16,7% mild (n=12), 6.9% moderate (n=5) OSAS according to AHI. Mean age was 44.19±14.24. There was a statistically significant difference between the groups as of age (p=0.041). The difference was detected between the normal and moderate groups (p=0.035). The age variable was detected as the confounding factor. 3. 9% of the patients participating in our survey were women (n=23). No statistically significant difference was detected between the groups in respect of gender (p=0.525). There was not a difference between the groups in respect of BMI (p=0.551). There was a difference between REM, N1, N2, N3 durations of the groups (p=0.093).

Statistical analysis was performed by eliminating the age effect in all group comparisons. When the effect of confounding factor (age) and average and minimum oxygen values are under control, a positive correlation was detected between the ADMA and AHI values (r= 0.483, p<0.001).

In respect of ADMA levels, it was seen that there was a statistically significant difference between the groups (p<0.001) (Table 1). As a result of multiple-comparisons, a statistically significant difference was detected between the severe and positionalrem dependent patient groups and normal, mild and moderate, moderate vs severe, OSAS patient groups. The results of comparison of differences between the groups in respect of min SO_2, mean SO_2, desaturation index, nighttime passed as <%90 was given Table 2. It was found that there were statistically significant difference between the groups in respect of mean SO_2, min SO_2 desaturation index, night time passed as <%90 levels. Moreover, negative correlations were detected between ADMA and average SO_2 (r=-0.311, p=0.011) and Min SO_2 (r=-0.291, p=0.014). A positive correlation was detected between ADMA and desaturation index (r= 0.439, p<0.001). But the significant relationship between the percentage of nighttime saturation as <90 and ADMA was not detected (p>0.05).

Table 1. ADMA levels of the groups

Group	n	Mean± SD	Median	Min	Max	p
Normal	19	0,87±0,34	0,88	0,28	1,41	
Mild	12	1,24±0,71	0,94	0,38	2,26	
Moderate	5	0,89±0,13	0,89	0,71	1,04	<0,001
Severe	18	2,19±0,16	2,17	1,98	2,47	
Pos-Rem	18	2,02±0,50	2,13	0,08	2,41	
Total	72	1,55±0,71	2,02	0,08	2,47	

SD: Standard Deviation; p<0.001 values for the comparison of normal vs. severe, pos-rem, mild vs. severe, moderate vs. severe; p=0.004 value for the comparison of moderate vs. pos-rem; p=0,011 value for the comparison of mild vs. pos-rem

Table 2. The descriptive statistics of Min SO2, mean SO2, desaturation index, nighttime passed as <%90 according to groups

	Normal (n=19)	Mild (n=12)	Moderate (n=5)	Severe (n=18)	Pos-rem (n=18)	Total (n=72)	p
			meanSO₂ *				
Mean± SD	96,11±1,05	95,25±1,71	95,60±0,55	94,17±1,92	96,00±0,97	95,42±1,57	
Median	96	96	96	95	96	96	0,001
(min- max)	(94-98)	(91-97)	(95-96)	(89-96)	(95-98)	(89-98)	
			minSO₂ £				
Mean± SD	87,68±6,31	86,58±3,48	85,00±5,10	75,28±10,55	84,83±6,58	83,50±8,63	
Median	89	86,5	84	80	86	85	<0,001
(min- max)	(73-95)	(79-92)	(78-90)	(55-88)	(71-94)	(55-95)	
			desaturation index ¥				
Mean± SD	2,69±3,49	7,23±4,23	14,78±14,97	51,26±29,77	14,58±9,67	19,40±24,85	
Median	1,4	7,05	8,6	58,6	16,6	8,15	<0.001
(min- max)	(0-14,5)	(1,3-15,4)	(1,5-39,1)	(0-104,3)	(0,8-34)	(0-104,3)	
			uykudesattime Ω				
Mean± SD	0,65±0,97	2,38±1,66	4,82±4,65	20,76±13,24	5,20±4,03	7,39±10,54	
Median	0,2	2,4	2,1	19,5	4,9	2,5	<0.001
(min-max)	(0-3,8)	(0,3-6,4)	(0,6-11,4)	(0-41)	(0-13,8)	(0-41)	

SD: Standard Deviation, Min-Max: Minimum-Maximum; *: p=0.002 value for the comparison of normal vs. severe; p=0.005 value for the comparison of severe vs. pos-rem; £: p<0.001 value for comparison of normal vs. severe; p=0.004 value for the comparison of mild vs. severe; p=0.010 value for the comparison of severe vs. pos-rem; ¥: p≤0.001 value for the comparison of normal vs. severe and pos-rem; p=0.001 value for the comparison of groups mild vs. severe; p=0.019 value for the comparison of severe vs. pos-rem; Ω: p<0.001 value for the comparison of normal vs. severe and pos-rem; p=0.001 value for the comparison of mild vs. severe; p=0.017 value for the comparison of severe vs. pos-rem

The differences between the groups in respect of serum glucose (p=0.727), total cholesterol (p=0.504) and ldl (p=0.518) values were not significant.

It was determined that ADMA test method can be used as a diagnosis criteria (area under the curve (AUC)=0.84, p<0.001). Best cut-off value for ADMA was determined as 1.39. For this value, the sensitivity was 73.58% (95% Confidence Interval (CI): %61.71-%85.45) and Specificity was 94.74% (95% CI: 84.70%-100%) (Figure 1). Accuracy or true classification rate was found as 79.17%. Positive predictive value was 97.5% and negative predictive value was 56.25%. Positive likelihood ratio (LR+) was detected as 13.98 (LR+>10) and negative likelihood ratio (LR-) was detected as 0.28 (LR-<1). According to the results, ADMA test has the properties of a strong and good diagnostic test.

Discussion

As a result of our study, a significant correlation has been observed between minimum oxygen saturation, mean oxygen saturation, Oxygen desaturation Index and AHI values. It has been determined that the ADMA test method has the features to be a strong and good diagnostic test criteria in people whose fasting blood glucose, LDL, triglyceride, TSH, creatinine, liver function tests are within normal limits.

OSAS is a disease characterized by recurred airflow restriction or block due to contraction of the airways[9,10]. Excessive daytime sleepiness arising due to fragmentation of sleep gives rise to failure at work, work and traffic accidents, repetitive nocturnal hypoxia leads to certain physiological diseases.

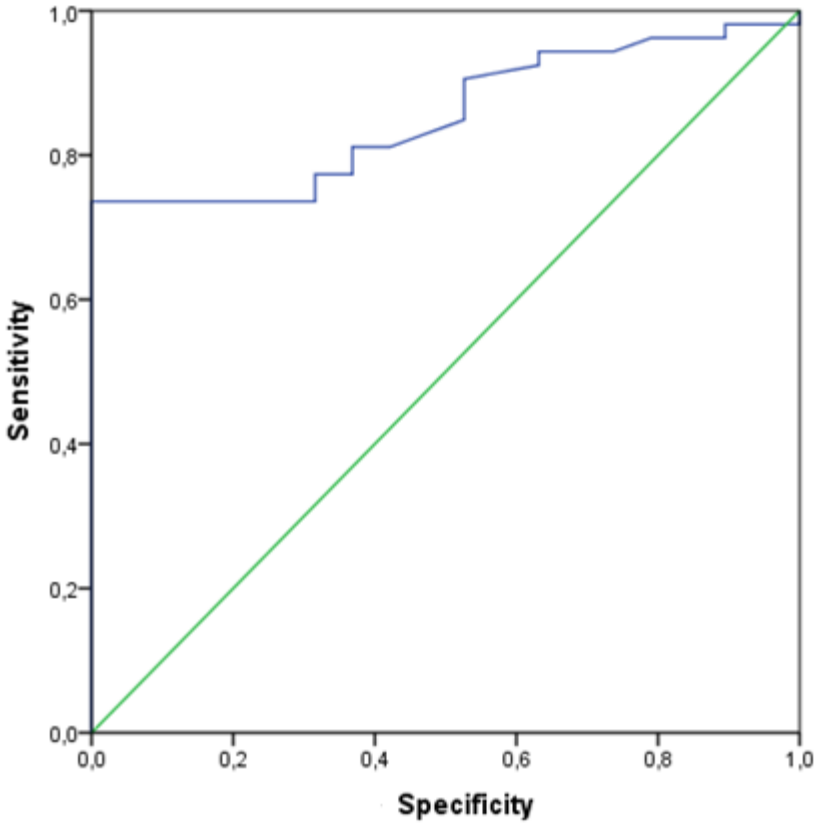

Figure 1. ROC curve of ADMA test

Therefore, patients with OSAS have a high incidence of hypertension, arrhythmias, coronary artery diseases and congestive heart failure[11,12]. Polysomnography PSG) is considered the hold standard in the diagnosis of sleep disordered breathing and is recommended by the American Sleep Disorders Association [American Sleep Disorders Association (ASDA)][13,14].

As polysomnography is a difficult to reach, had to apply, laborious and expensive test, alternative additional diagnosis methods are being investigated. We do not have a good preliminary test, which shall foresee to which patients primary PSG shall be applied. In our working group, ¼ of the patients to whom PSG was applied were detected to be normal. And this prevents us from making use of the laboratories effectively, diagnosis and treatment for real patients are delayed.

ADMA is a methylated arginine derivative whose importance is increasing, and which occurs as a result of the protein arginine methyl transferase (PRMT) enzyme adding methyl groups following synthesis with regulation to the arginine residue in the nucleoproteins, and the destruction of these proteins[15]. The protein bound ADMA which occurs as a result of the methylation of the protein bound arginine has no inhibitor effect on the NOS enzyme. For this inhibition, free ADMA caused by the proteolysis of methylated protein is required.

A large portion of the free ADMA which occurs in the cell as a result of proteolysis, is immediately destroyed by the dimethylaminohydrolase (DDAH) enzyme in the cell. A small portion however escapes

intracellular degradation and enters the bloodstream. This small amount of ADMA entering the bloodstream, is either excreted unchanged through the kidneys in urine, or is taken back into the cells through liver and kidneys and is metabolized by the DDAH enzyme[16]. In cases of increased oxidative stress in the body, an increase in ADMA levels occurs. This increase in ADMA levels may be due to a decrease in DDAH enzyme activity. In the reduction of activity, the oxidation of cysteine in the active area of DDAH is important. This oxidation can be accomplished by NO and thus its activity can be recycled and reduced[17,18]. Inducible NOS (iNOS) activity increases greatly with inflammation, and NO is produced in very large quantities. The produced NO combines with superoxide (O^-) radicals, becoming peroxynitrite ($ONOO^-$) and reduces the half-life of NO (19). The formation of peroxynitrite occurs faster than the capture of superoxide radicals by superoxidedismutase (SOD). Peroxynitrite binds to the active area of DDAH and reduces its activity, thus leading to an increase in ADMA amount and a reduction in NO levels. Oxidative stress changes the activity of enzymes with a role in ADMA production and leads to a change in ADMA amounts[19]. PRMT activity is increased with reactive oxygen species and ADMA levels increase[20].

In a study by Christou et al, the antioxidant capacity of patients with OSAS were found to be close to the antioxidant capacity of health individuals. However, in patients with severe OSAS diagnosis, as a reflection of extreme oxidative stress, low antioxidant capacity has been determined[21].

Some researchers have displayed those pigs exposed to hypoxia have inhibited DDAH activity. DDAH activity and expression has lowered in newborn primary pulmonary hypertension. This explains the reduction of NOS activity in patients and the increased ADMA levels[22].

We also believe that increased ADMA in OSAS can also be explained with another mechanism. The low oxygen levels occurring in OSAS, leads to an increase in hypoxia-inducible factor 1 (HIF-1) levels providing the activation of genes responsible for EPO, VEGF, glucose transporter and glycolytic enzyme transcription. Studies have shown that, with intracellular and extracellular oxidative stress of erythropoietin reduces DDAH enzyme activity[23]. Erythropoietin levels have been shown to be higher in OSAS patients than healthy group[24]. These results are suggestive of increased erythropoeitin levels secondary to hypoxia in OSAS patients and oxidative agents inhibition of DDAH enzyme may raise ADMA levels.

Setting off from the point of could there be another alternative examination to PSG, have considered that increased erythropoeitin levels secondary to hypoxia in OSAS patients and oxidative agents inhibition of DDAH enzyme may raise ADMA levels and have seen that the results of our study and information in literature support our hypothesis.

When health, mild, moderate, severe, Positional-Rem dependent OSAS groups were compared in our study, we determined a significant difference in terms of ADMA levels between the groups

We determined a significant positive correlation between AHI, defined as the number of apnea and hypopnea, forming the basis of hypoxia in OSAS patients, per sleep hour and ADMA values. In a study by A. Barcelo et al, a tendency to increased ADMA levels in severe OSAS patients was found, but a statistical difference could not be determined. This result is suggestive of increased

ADMA in OSAS patients being due to obesity and metabolic disorders[25,26].

However, in our study groups there was no significant difference in terms of BMI and metabolic parameters, and any parameters that could impact the determined ADMA values such as age, average, minimum oxygen values were controlled. Despite the serum markers studied in patients being different, the mediator release mechanism being based on our oxidative stress hypothesis supports our results.

In the study conducted by In et al, a positive correlation was determined between ADMA levels and the duration when the saturation was <%90[26]. According to our findings, when the confounding factors (age) are eliminated and the groups compared, a significant difference has been determined between the groups in terms of average oxygen saturation (SO_2) and minimum SO_2. When the confounding factor impact (age) is controlled, a significant negative correlation has been determined between ADMA and minimum SO_2. An increase in ADMA with the increased lowest oxygen saturation measured overnight of patients has shown a result consistent with our hypothesis.

We have determined a significant positive correlation between the oxygen desaturation index, defined as the number of oxygen desaturations per hour during sleep and ADMA.

Conclusion

In our study, it was determined that ADMA test method has the properties of being a strong and good diagnosis test criteria for people, whose fasting blood glucose, ldl, trigliceride, tsh, creatinine, liver function tests are at normal levels.

PSG is expensive, having limited accessibility and a time-consuming technique. Employment of such technique in the properly selected patient groups will lessen the laboratories patient loads and prevent the real patients from being destitute of diagnosis and therapy for a long time. A study related to this very subject is required, which will be prospective, have more advanced control and also include the results of therapy.

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Author contributions

Both all authors contributed to the drafting and revising of the article. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

The Research and Ethics Committee of the Düzce University approved the study (March 2012/93).

References

1. Dempsey JA, Veasey SC, Morgan BJ, et al. Pathophysiology of sleep apnea. Physiol Rev. 2010 Jan;90(1):47-112. doi: 10.1152/physrev.00043.2008
2. Riha RL. Defining obstructive sleep apnoea syndrome: a failure of semantic rules. Breathe (Sheff). 2021 Sep;17(3):210082. doi: 10.1183/20734735.0082-2021
3. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med*. 2002;165(9):1217-39. doi:10.1164/rccm.2109080
4. Sedeek MH, Llinas MT, Drummond H, et al. Role of reactive oxygen species in endothelin-induced hypertension. Hypertension. 2003;42(4):806-810. doi:10.1161/01.HYP.0000084372.91932.BA
5. Parish JM, Somers VK. Obstructive sleep apnea and cardiovascular disease. Mayo Clin Proc. 2004;79(8):1036-46. doi:10.4065/79.8.1036

6. Eisele HJ, Markart P, Schulz R. Obstructive Sleep Apnea, Oxidative Stress, and Cardiovascular Disease: Evidence from Human Studies. Oxid Med Cell Longev. 2015;-608438. doi:10.1155/2015/608438
7. May AM, Mehra R. Obstructive sleep apnea: role of intermittent hypoxia and inflammation. Semin Respir Crit Care Med. 2014;35(5):531-44. doi:10.1055/s-0034-1390023
8. Semelka M, Wilson J, Floyd R. Diagnosis and Treatment of Obstructive Sleep Apnea in Adults. Am Fam Physician. 2016;94(5):355-60.
9. Lugaresi E, Plazzi G. Heavy snorer disease: from snoring to the sleep apnea syndrome--an overview. Respiration. 1997;64(1):11-4. doi:10.1159/000196730
10. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. Journal of Clinical Sleep Medicine. 2017;13:479–504.
11. Pansani AP, Schoorlemmer GH, Ferreira CB et al. Chronic apnea during REM sleep increases arterial pressure and sympathetic modulation in rats. Sleep. 2021;14;44(5):zsaa249. doi: 10.1093/sleep/zsaa249
12. Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. Practice parameters for the indications for polysomnography and related procedures. Sleep. 1997;20:406-22.
13. Standards of Practice Committee of the American Sleep Disorders Association. Practice parameters for the use of portable recording in the assessment of obstructive sleep apnea. Sleep 1994;17:372-7.
14. Sleep related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. The report of the American Academy of Sleep Medicine Task Force. Sleep 1999;22:667-89.
15. Kovács K, Karvaly GB, Farkas R, et al. Clinical and diagnostic relevance of asymmetric and symmetric dimethyl arginine (ADMA/SDMA). Orv Hetil. 2022;163(13):500-5. doi:10.1556/650.2022.32394
16. Teerlink T. ADMA metabolism and clearance. Vasc Med. 2005;10:S73-S81. doi:10.1191/1358863x05vm597oa
17. Leiper J, Murray-Rust J, McDonald N, et al. S-nitrosylation of dimethylarginine dimethyl-aminohydrolase regulates enzyme activity: further interactions between nitric oxide synthase and dimethylarginine dimethylaminohydrolase. Proc Natl Acad Sci. 2002;99(21):135272. doi:10.1073/pnas.212269799
18. Valkonen VP, Laaksonen R. Asymmetric dimethylarginine (ADMA) and acute vascular events. Clin Chim Acta. 2004;348(1-2):9-17. doi:10.1016/j.cccn.2004.05.020
19. Noris M, Perico N, Remuzzi G. Mechanisms of disease: Pre-eclampsia. Nat Clin Pract Nephrol. 2005;1(2):98-120. doi:10.1038/ncpneph0035
20. Sydow K, Münzel T. ADMA and oxidative stress. Atheroscler Suppl. 2003;4(4):41-51. doi:10.1016/s1567-5688(03)00033-3
21. Christou K, Moulas AN, Pastaka C, Gourgoulianis KI. Antioxidant capacity in obstructive sleep apnea patients. Sleep Med. 2003;4(3):225-228. doi:10.1016/s1389-9457(02)00253-8
22. Arrigoni FI, Vallance P, Haworth SG, et al. Metabolism of asymmetric dimethylarginines is regulated in the lung developmentally and with pulmonary hypertension induced by hypobaric hypoxia. Circulation. 2003;107(8):1195-201. doi:10.1161/01.cir.0000051466.00227.13
23. Winnicki M, Shamsuzzaman A, Lanfranchi P, et al. Erythropoietin and obstructive sleep apnea. Am J Hypertens. 2004;17(9):783-6. doi:10.1016/j.amjhyper.2004.04.011
24. Barceló A, Piérola J, de la Peña M, et al. Day-night variations in endothelial dysfunction markers and haemostatic factors in sleep apnoea. *Eur Respir J*. 2012;39(4):913-8. doi:10.1183/09031936.00039911
25. Hannemann J, Böger R. Dysregulation of the Nitric Oxide/Dimethylarginine Pathway in Hypoxic Pulmonary Vasoconstriction-Molecular Mechanisms and Clinical Significance. *Front Med (Lausanne)*. 2022;9:835481. doi:10.3389/fmed.2022.835481
26. İn E, Özdemir C, Kaman D, et al. Heat Shock Proteins, L-Arginine, and Asymmetric Dimethylarginine Levels in Patients With Obstructive Sleep Apnea Syndrome. Arch Bronconeumol. 2015;51(11):544-50. doi:10.1016/j.arbres.2015.02.020

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CİDDİ DÜŞÜK EJEKSİYON FRAKSİYONLU KALP YETMEZLİĞİ OLAN BİR OLGUDA PERİOPERATİF YÖNETİM

PERIOPERATIVE MANAGEMENT IN A CASE OF HEART FAILURE WITH SEVERE LOW EJECTION FRACTION

Pınar Ergenoğlu

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Editöre Mektup

Sayın Editör;

Radikal sistektomi kasa invaziv non-metastatik mesane kanserleri için standart tedavidir[1]. Kasa invaziv mesane kanserli hastalarda sıklıkla eşlik eden kardiyovasküler komorbidite, diyabet, obezite gibi hastalıklar dolayısıyla artmış cerrahi komplikasyon oranı söz konusudur[2]. Bu hastalarda preoperatif dönemden postoperatif takibe kadar her evrede multidisipliner yaklaşım gereklidir. Kalp yetmezliği ventriküler dolum veya kan ejeksiyonunun herhangi bir yapısal veya fonksiyonel bozukluğundan kaynaklanan karmaşık bir klinik sendromdur. Kalp yetmezliğinin başlıca belirtileri, egzersiz toleransını sınırlayabilen nefes darlığı ve yorgunluk ve pulmoner ve/veya splanknik konjesyona ve/veya periferik ödeme yol açabilen sıvı tutulmasıdır. Ejeksiyon fraksiyonunun ≤%40 olması düşük ejeksiyon fraksiyonlu kalp yetmezliği olarak tanımlanmaktadır[3] .

Bu olguda kasa invaziv mesane kanseri nedeni ile radikal sistektomi üriner diversiyon cerrahisi geçiren ciddi düşük ejeksiyon fraksiyonlu kalp yetmezliği bulunan 52 yaşında erkek hastamızda perioperatif anestezi yönetimimiz sunulmaktadır. Hastanın medikal hikayesinde Tip II diabetes mellitus, iskemik kalp hastalığı, konjestif kalp yetmezliği ve kronik böbrek hastalığı mevcuttu.

Radikal sistektomi ileal loop operasyonundan 1 yıl önce inferior myokard infarktüsü geçirdiği öğrenildi. Ekokardiyografik değerlendirmesinde sol ventrikül sistolik ve diyastolik disfonksiyonu, global hipokinezisi mevcuttu. Ejeksiyon fraksiyonu %10, pulmoner arter basıncı 35 mmHg idi. Hasta preoperatif dönemde üroloji kliniğine yatırılarak nefroloji, kardiyoloji ve endokrinoloji kliniklerine konsülte edildi. Preoperatif kan şekeri regülasyonu yapıldı. Yetmezlik açısından kardiyak medikasyonları yeniden düzenlendi. Optimum şartlarda operasyona alındı. Anestezi indüksiyonunda tüm ilaç dozları minimalize edilerek 0,04 mg/kg midazolam, 1mg/kg ketamin, 1mcg/kg fentanil, 0,5 mg/kg rokuronyum bromür uygulandı. İndüksiyon sonrasında hipotansiyon gözlenmedi. Anestezi idamesinde %50 oksijen %50 hava ve %0,5-2 sevofluran kullanıldı. İndüksiyon sonrası santral venöz kateter, radial arter kanülasyonu uygulanarak operasyon boyunca invaziv arteriyel basınç, nabız kontur kardiyak debi ve santral venöz basınç monitörizasyonu yapıldı. Hastaya peroperatif dönemde ortalama arteriyel basıncı 60 mmHg'nın üzerinde tutacak şekilde vazopressör olarak noradrenalin infüzyonu başlandı. Ciddi düşük ejeksiyon fraksiyonlu kalp yetmezliği nedeniyle hedefe yönelik sıvı tedavisi protokolü uygulandı; 500 ml kritalloid sıvı infüzyonu, 3 ünite eritrosit süspansiyonu ve 3 ünite taze donmuş plazma transfüzyonu yapıldı. Operasyon boyunca hedefe yönelik sıvı tedavisini düzenlemek amacı ile nabız kontur kardiyak debi için PiCCO® system (Pulsion Medical Systems, Munich, Germany) monitörü kullanıldı. Yapılan ölçümler ile hastanın sıvı ve inotrop ajan tedavisi düzenlendi. Kan gazı takiplerine göre hastanın hemoglobin seviyesi ≥ 10 mg/dl olacak şekilde kan transfüzyonu yapıldı. Ortalama arteriyel basıncın 60 mmHg'nın altına düşmesine izin verilmedi. Operasyon süresi 248 dakika idi. Operasyon sonunda hemodinamisi stabil olan hasta ekstübe edilerek postoperatif yakın takip ve tedavi amacıyla reanimasyon ünitesine çıkarıldı. Yoğun bakım takibinde hemodinamisi stabil seyreden inotropik ajan ihtiyacı olmayan hasta postoperatif 2. günde servise alındı. Postoperatif ürolojik cerrahi takibi tamamlandıktan sonra hastaya ciddi düşük ejeksiyon fraksiyonlu kalp yetmezliğine bağlı ölümcül aritmilerin önlenmesi endikasyonuyla kardiyoloji tarafından intrakardiak defibrilatör implantasyonu gerçekleştirilerek taburcu edildi.

İskemik kalp hastalığı, dünya çapında morbidite ve mortalitenin en yaygın nedenleri arasındadır[4]. Kalp yetmezliğine, perikard, miyokard, endokardiyum, kalp kapakçıkları, damar sistemi veya metabolizmayı etkileyen hastalıklar dahil olmak üzere pek çok bozukluk neden olur. Düşük ejeksiyon fraksiyonlu kalp yetmezliğinin en yaygın nedenleri arasında idiyopatik dilate kardiyomiyopati, koroner kalp hastalığı (iskemik), hipertansiyon ve kalp kapak hastalığı bulunmaktadır[5]. Radikal sistektomi, ürolojide önemli bir cerrahi zorluğu temsil eder. Cerrahi tekniğin standardizasyonuna, iyileştirilmiş anestezi ve perioperatif bakım protokollerine rağmen, bilateral pelvik lenf nodu diseksiyonu ve üriner diversiyon veya mesane rekonstrüksiyonu ile açık radikal sistektomi sonrası morbiditenin %30-64'e kadar çıktığı bildirilmektedir[6]. ERAS (Enhance Recovery after Surgery- Cerrahi Sonrası Gelişmiş İyileşme) Derneği'nin yayınladığı radikal sistektomi üriner diversiyon cerrahisinde protokol önerilerinde preoperatif komorbiditelerin düzeltilmesi, intraoperatif dönemde aşırı hidrasyondan kaçınılması, hedefe yönelik sıvı tedavisi, arteriyel hipotansiyonu önlemek amacı ile vasopressör tedavisi uygulaması yer almaktadır[7]. Biz de hastamızda ERAS önerileri doğrultusunda bakım planı oluşturarak perioperatif dönemde hastanın mevcut tüm risklerini kontrol altına almayı başardık. İmplante edilebilir kardiyoverter defibrilatör (ICD), semptomatik kalp yetmezliği ve sol ventrikül ejeksiyon fraksiyonu (LVEF) %35 veya daha az olan hastalarda mortaliteyi azaltmak için etkili bir tedavidir[8]. Bu nedenle hastamıza postoperatif dönemde ICD implantasyonu uygulanmıştır.

Sonuç olarak yüksek riskli hastaların anestezi ve cerrahi yönetiminde, mevcut kılavuzlar eşliğinde multidisipliner ileri tedavi ve takiplerinin yapılmasının faydalı olabileceğini düşünmekteyiz.

Yazar katkısı
Yazar çalışmanın son halini gözden geçirip kabul etmiştir.

Etik onam
Bu sunu için hastadan onay alınmıştır. Editöre mektup için etik onam şartı aranmamıştır.

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Kaynaklar

1. Vetterlein MW, Gild P, Kluth LA, et al. Perioperative allogeneic blood transfusion does not adversely affect oncological outcomes after radical cystectomy for urinary bladder cancer: a propensity score-weighted European multicentre study. BJU Int. 2018;121:101-10. doi: 10.1111/bju.14012
2. Joensen UN, Maibom SL and Poulsen AM. Surgical Management of Muscle Invasive Bladder Cancer: A Review of Current Recommendations. Semin Oncol Nurs. 2021;37:151104. doi: 10.1016/j.soncn.2020.151104
3. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013;128:e240-327. doi: 10.1161/CIR.0b013e31829e8776
4. Moroni F, Gertz Z and Azzalini L. Relief of Ischemia in Ischemic Cardiomyopathy. Curr Cardiol Rep. 2021;23:80. doi: 10.1007/s11886-021-01520-4
5. Malik A, Brito D, Chhabra L. Congestive Heart Failure. In: StatPearls Publishing, 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK574497/ Erişim tarihi:15.12.2021
6. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55:164-74. doi: 10.1016/j.eururo.2008.07.031
7. Cerantola Y, Valerio M, Persson B, et al. Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS((R))) society recommendations. Clin Nutr. 2013;32:879-87. doi: 10.1016/j.clnu.2013.09.014
8. Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. 2009;-361:1329-38. doi:10.1056/NEJMoa0906431

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A RARE CAUSE OF MATERNAL CARDIAC ARREST: IDIOPATHIC VENTRICULAR FIBRILLATION

NADİR BİR MATERNAL KARDİYAK ARREST NEDENİ: İDİYOPATİK VENTRİKÜLER FİBRİLASYON

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Letter to editor

Dear editor;

Severe preeclampsia is one of the serious hypertensive disorders of pregnancy and is significantly associated with cardiovascular morbidity during delivery. Also, the risk of cardiac arrest is higher in this patients[1]. Sudden cardiac arrest (SCA) usually develops due to ventricular fibrillation (VF) or rapid ventricular tachycardia (VT) in the presence of cardiac pathologies[2]. Idiopathic VF (IVF) is a resuscitated cardiac arrest with documented VF without known cardiac, respiratory, metabolic, toxicological etiology[3]. Maternal cardiac arrest (MCA) is a rare condition but may occur even in the best medical health care systems; fast and specified intervention is required[4].

In this case report, we aimed to present our postpartum patient who developed cardiac arrest due to IVF, which is rare in maternal cardiac arrest, and underwent successful cardiopulmonary resuscitation.

A 29-year-old, 25-week-old preeclamptic, twin pregnancy female patient was admitted to the intensive care unit after a cesarean section. It was learned that the patient was pregnant with in vitro fertilization and did not have any systemic disease. The patient, hospitalized in the obstetrics clinic due to severe preeclampsia and

albuminuria at the 24th week of pregnancy, was discharged with alpha-methyldopa after blood pressure regulation. She was readmitted to the hospital with hypertensive crisis and acute renal failure one week later. One of the fetuses was intrauterine exitus; the patient underwent cesarean section (C/S) with spinal anesthesia. The operation was completed with no complications. The patient was accepted to the intensive care unit (ICU) with hypertensive crisis, acute renal failure, oliguria, hyperkalemia (Serum potassium level: 6.6 mmol/ L), and diplopia in the early postoperative period. In the ICU, blood pressure was regulated with glyceryl trinitrate infusion, hyperpotassemia treated with glucose-insulin infusion, and during the follow-up, renal failure regressed without dialysis. The patient was examined with cerebral magnetic resonance imaging because of diplopia to exclude neurological disorders, and no pathology was detected. At the 6th hour of ICU follow-up, the patient developed witnessed VF. A successful cardiopulmonary resuscitation (CPR) was applied. Two milligrams of adrenalin were applied during CPR, and after the second defibrillation return of spontaneous circulation was observed. The patient was extubated with complete neurological recovery at the 8th hour of successful CPR. In electrocardiographic evaluation, the QT interval was found to be normal (corrected QT: 367 ms-Figure 1). The patient was diagnosed with IVF due to the absence of an electrolyte abnormality or structural cardiac abnormality in echocardiography. On the further cardiologic evaluation, an indication for ICD implantation was made. Nevertheless, the patient did not accept ICD insertion. After six days in ICU, the patient was transferred to the obstetric ward.

Severe preeclampsia is one of the serious hypertensive disorders of pregnancy and is significantly associated with cardiovascular morbidity during delivery. It is reported that preeclampsia develops 2-3 times more in twin pregnancies compared to singleton pregnancies, progresses more severely. Also, the risk of cardiac arrest is higher in this patients[1].

SCA usually develops due to VF or rapid VT in the presence of cardiac pathologies such as cardiomyopathy, long QT syndrome, valvular or congenital heart diseases[2].

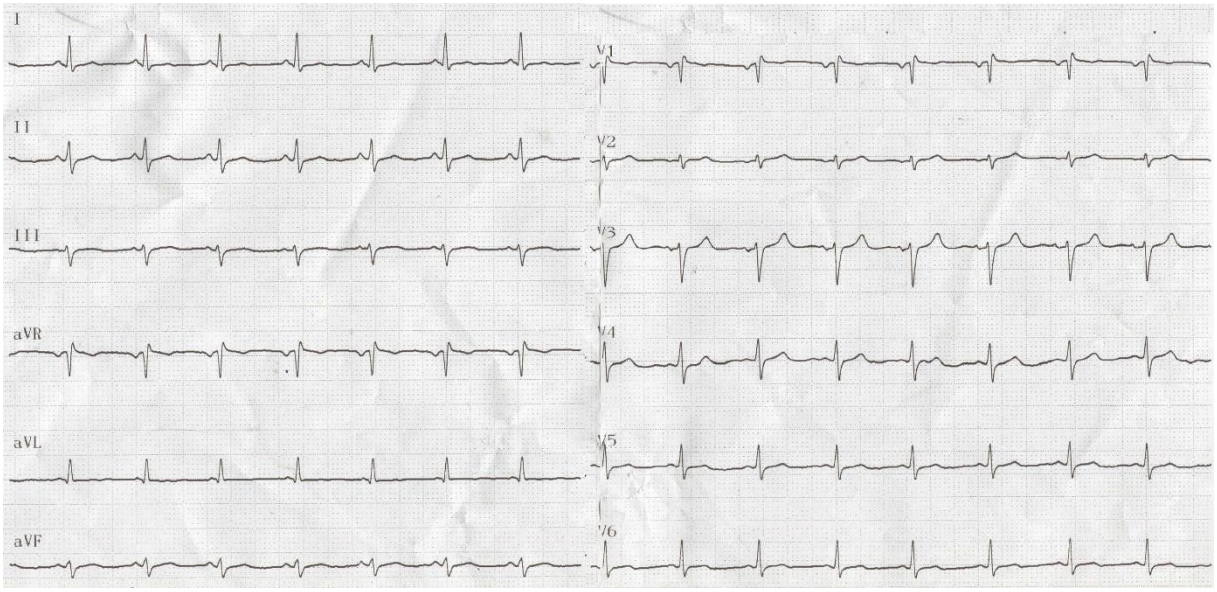

Figure 1. Example of a full 12-lead electrocardiogram (ECG)

IVF is a resuscitated cardiac arrest with documented VF without known cardiac, respiratory, metabolic, toxicological etiology[3]. During the last three decades, distinct clinical entities have been recognized, and the spectrum of IVF has been narrowed. Diagnostic assessment of SCA survivors and genetic analysis contributed to this development.

Diagnoses such as Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and long QT syndrome are not interpreted as 'idiopathic' anymore[5]. Extensive diagnostic assessment is essential in unexplained SCA survivors. There was no structural cardiac pathology defined in our patient, and she was diagnosed with IVF.

Maternal cardiac arrest (MCA) is a rare condition but may occur even in the best medical health care systems; fast and specified intervention is required[4]. MCA is reported in approximately 1 in 12000 deliveries in the USA, mostly due to hemorrhage, heart failure, amniotic fluid embolism, sepsis, and anesthesia complications. Although survival depends on the underlying etiology of arrest, outcomes are defined better than the other causes of cardiac arrest[6,7].

In our patient, the development of witnessed cardiac arrest in the intensive care unit and rapid intervention resulted in successful CPR.

We present our postpartum patient who developed idiopathic ventricular fibrillation, one of the rare causes of MCA. Rapid and successful intervention in cardiac arrest in the intensive care unit has determined the maternal prognosis. We think that this case will contribute to raising awareness about the causes of MCA.

Ethical Approval:
For this study, it is a letter to the editor and does not need the approval of the ethics committee. Approval was obtained from the patient for this letter.

Conflict of Interest:
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References

1. Wang Y, Wu N, Shen H. A Review of Research Progress of Pregnancy with Twins with Preeclampsia. Risk Manag And Health Policy. 2021;14:1999–2010. doi: 10.2147%2FRMHP.S304040
2. John RM, Tedrow UB, Koplan BA, et al. Ventricular arrhythmias and sudden cardiac death. Lancet. 2012;380(9852):1520-9. doi: 10.1016/s0140-6736(12)61413-5
3. Almahameed ST, Kaufman ES. Idiopathic Ventricular Fibrillation: Diagnosis, Ablation of Triggers, Gaps in Knowledge, and Future Directions. JICRM. 2020;11:4135–46. doi: 10.19102/icrm.2020.110604
4. Lipowicz AA, Cheskes S, Gray SH, et al. Incidence, outcomes and guideline compliance of out-of-hospital maternal cardiac arrest resuscitations: A population-based cohort study. Resuscitation. 2018;132:127–32. doi: 10.1016/j.resuscitation.2018.09.003
5. Conte G, Giudicessi JR, Ackerman MJ. Idiopathic ventricular fibrillation: the ongoing quest for diagnostic refinement. Europace. 2021;23:4–10. doi: 10.1093/europace/euaa211
6. Mhyre JM, Tsen LC, Einav S, et al. Cardiac arrest during hospitalization for delivery in the United States, 1998-2011. Anesthesiology. 2014 ;120:810–8. doi: 10.1097/aln.0000000000000159
7. Heviz Y, Einav S. Maternal cardiac arrest. Curr Opin Anaesthesiol. 2014;32:298–306. doi: 10.1097/aco.0000000000000719

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A PATIENT WHO DEVELOPED GABAPENTIN-RELATED ATRIOVENTRICULAR COMPLETE BLOCK AFTER ANESTHESIA INDUCTION: A VERY RARE CASE

ANESTEZİ İNDÜKSİYONU SONRASI GABAPENTİNE BAĞLI ATRİYOVENTRİKÜLER TAM BLOK GELİŞEN BİR HASTA: ÇOK NADİR BİR OLGU

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Case Report

Abstract

In noncardiac surgeries, the development of complete atrioventricular block during general anesthesia is a very rare condition. The possibility of developing atrioventricular block may increase with the presence of cardiac pathology or drugs or metabolic predisposing factors that affect cardiac conduction and the anesthetic agents may also contribute. In this case, we aimed to present a patient with left bundle branch block, using gabapentin, and developed atrioventricular block during general anesthesia induction.

Keywords: Anesthesia, gabapentin, atrioventricular block

Öz

Nonkardiyak cerrahilerde, genel anestezi sırasında atriyoventriküler tam blok gelişmesi çok nadir görülen bir durumdur. Kardiyak patoloji veya kardiyak iletiyi etkileyen ilaç ya da metabolik predispozan faktörlerin varlığı ile atriyoventriküler blok gelişme olasılığında artış görülebilir. Bu durumda, kullanılan anestezik ajanlar da blok gelişimine katkıda bulunabilir. Biz de bu olguda, sol dal bloğu olan ve gabapentin kullanan bir hastada genel anestezi indüksiyonu sırasında atriyoventriküler tam blok gelişen hastayı sunmayı amaçladık.

Anahtar Kelimeler: Anestezi, gabapentin, atriyoventriküler blok

Introduction

Left bundle-branch block (LBBB) is a conduction disorder among healthy individuals[1]. Third-degree atrioventricular (AV) block is the failure to conduct the electrical activity in the atrium to the Purkinje fibres and is defined as AV complete block. Atrium and ventricle contract independently; junctional or ventricular escape rhythm maintains the perfusion[2].
Gabapentin is usually used to treat neuropathic pain, restless leg, and focal epileptic activities[3]. Efficacy is related to the blockage of the α2δ subunit of presynaptic voltage-gated calcium channels essential for membrane depolarization, decreased excitatory neurotransmitter release[4], and blockage voltage-activated sodium channel results with high-frequency action potential firing limiting[5,6].
In this case report, we aimed to present our patient with LBBB and receive gabapentin that complete AV block developed after the induction of general anesthesia.

- *Case report*

Our patient was a 72-year-old female. Thyroidectomy was planned with the suspicion of follicular neoplasia. In the preoperative evaluation, laboratory tests were normal, and she was euthyroid. There were no known cardiac pathologies. On her cardiac evaluation, LBBB on electrocardiogram and left ventricular hypertrophy on ECHO were detected. In her medical history, the use of 800 mg gabapentin for neuropathic pain due to spinal stenosis was detected. The patient was accepted as ASA III, and premedication was done with 0.03 mg/kg midazolam. General anesthesia induction was applied with 1 mg/kg propofol, 1mcg/kg fentanyl, 0.5 mg/kg rocuronium. Anesthesia maintenance was provided with %2 sevoflurane in 50% oxygen-nitrous oxide mixture. Deep hypotension and bradycardia developed after 5 minutes of general anesthesia induction. Heart rate decreased to 35 beats/min; blood pressure decreased to 45/25 mmHg. 0.5 mg of atropine and 10 mg of ephedrine were administered. A total of 3 mg of atropine sulfate was administered. Deep bradycardia sustained; complete AV block observed, and temporary pacemaker was applied immediately. The patient consulted with cardiology concurrently. The operation was postponed, and the patient awakened. The patient was admitted to the ICU, and a permanent pacemaker was implanted. After one week of ICU admission the patient discharged with full recovery.

Discussion

There are several causes of complete AV block. AV-nodal blocking agents such as calcium channel blockers, beta-blockers, and digoxin in inferior myocardial infarction are the leading causes. The atrium and ventricle contract independently if the complete AV block occurs, and junctional or ventricular escape rhythm maintains the perfusion [2].
LBBB is a conduction disorder in less than 1% of the population, and hypertension, left ventricular hypertrophy, and coronary artery disease usually accompanies it. Patients with isolated LBBB have an increased risk of overt cardiovascular disease and cardiac mortality[1].
Gabapentin alters voltage-activated sodium channels and the use of antiepileptic drugs acting on sodium channels is a risk factor for sudden cardiac death[5-7]. Gabapentin indications include neuropathic pain, restless leg, or focal epileptic activities[3]. In the population, the use of gabapentin is not rare, and the prevalence is also increasing; unfortunately, the rate of misuse is increasing[8].Some of the cardiac side effects of gabapentin are worsening heart failure, atrial fibrillation, hypotension, and bradycardia. These side effects are rare, mild, and temporary. AV block is indicated as one of the rare side effects of gabapentin (<0.1%) due to drug information[9]; in the literature, the number of studies on this issue is not

satisfying. Gabapentin acts by inhibiting calcium influx and subsequent release of excitatory neurotransmitters[10]. Possible mechanisms for the haemodynamic effects of gabapentin include direct action that causes vasodilation by inhibiting voltage-gated calcium channels in the vessels, and effects on the descending noradrenergic and spinal alpha-2 adrenergic systems. It has been reported that the combination of gabapentin and opioids is associated with more frequent side effects[11]. The known hemodynamic mechanisms of action of gabapentin and its opioid interaction may have potentiated the conduction disorder in our patient and may have caused the development of a complete AV block.

Conclusion

In this case report, we present our patient who developed AV complete block immediately after the induction of anesthesia due to gabapentin use. We think that great care should be taken in the induction of anesthesia in patients using gabapentin and having cardiac conduction disorders.

Ethical Approval:
For this study, it is a letter to the editor and does not need the approval of the ethics committee. Approval was obtained from the patient for this letter.

Conflict of Interest:
Authors declared no conflict of interest.

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References

1. Fahy GJ, Pinski SL, Miller DP, et al. Robinson K. Natural history of isolated bundle branch block. Am J Cardiol. 1996;77:1185-90. doi: 10.1016/s0002-9149(96)00160-9
2. Kerola T, Eranti A, Aro AL, et al. Risk Factors Associated With Atrioventricular Block. JAMA Netw Open. 2019;2:e194176. doi: 10.1001/jamanetworkopen.2019.4176
3. Gee NS, Brown JP, Dissanayake VU, et al.The novel anticonvulsant drug, gabapentin (Neurontin), binds to the alpha2delta subunit of a calcium channel. J Biol Chem. 1996;271:5768-76. doi: 10.1074/jbc.271.10.5768
4. Benarroch EE. What Is the Mechanism of Therapeutic and Adverse Effects of Gabapentinoids? Neurology. 2021;96:318-21. doi: 10.1212/wnl.0000000000011424
5. Liu Y, Qin N, Reitz T, et al. Inhibition of the rat brain sodium channel Nav1. 2 after prolonged exposure to gabapentin. Epilepsy Res. 2006;70-:263-8. doi: 10.1016/j.eplepsyres.2006.03.007
6. Tamil AW, Mclean MJ. Limitation by gabapentin of high frequency action potential firing by mouse central neurons in cell culture. Epilepsy Res. 1994;17:1-11. doi: 10.1016/0920-1211(94)90074-4
7. Bardai A, Blom MT, van Noord C, et al. Sudden cardiac death is associated both with epilepsy and with use of antiepileptic medications. Heart. 2015;101:17-22. doi: 10.18553/jmcp.2020.26.3.246
8. Pauly NJ, Delcher C, Slavova S, et al. Trends in gabapentin prescribing in a commercially insured US adult population, 2009-2016. J. Manag.Care.Spec.Pharm. 2020;26:246-52. doi. 10.18553/jmcp.2020.26.3.246
9. Medically reviewed by Drugs.com.. Gabapentin Side Effects. Last updated on 28.08.2021 Available from: https://www.drugs.com/sfx/gabapentin-side-effects.html Date of access: 03.03.2022
10. Bockbrader HN, Wesche D, Miller R, Chapel S, et al. A comparison of the pharmacokinetics and pharmacodynamics of pregabalin and gabapentin. Clin pharmacokin. 2010:49;661-9. doi: 10.2165/11536200-000000000-00000
11. Tanabe M, Takasu K, Kasuya N, et al. Role of descending noradrenergic system and spinal α2-adrenergic receptors in the effects of gabapentin on thermal and mechanical nociception after partial nerve injury in the mouse. Br J Pharmacol. 2005:144;703-14. doi: 10.1038%2Fsj.bjp.0706109