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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.

KAPSAM

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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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EVALUATION OF RISK FACTORS FOR RECURRENCE IN HAND ENCHONDROMAS, THE EFFECT OF PATHOLOGICAL FRACTURE AND GRAFT SELECTION ON CLINICAL RESULTS

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Abstract

Aim: Enchondroma is the most common tumor of phalanx and metacarpus. Various techniques and methods have already been investigated for a long time. We aimed to examine the clinical and radiological results of curettage and bone substitute used in a broad spectrum of patients with an enchondroma.

Methods: Forty-seven patients operated with the diagnosis of enchondroma were included in the study. Curettage and filling of the cavity with bone substitutes were performed. The mean age of the patients was 29.32±15.08 years, and follow-up was 28.47±25.10 months. Patients who did not comply with standard follow-up protocol were excluded. An experienced orthopedic surgeon evaluated radiological results, and MRI reports and images for patients with recurrences were extracted from the hospital database. Clinical assessment was made according to ROM and observed deformity.

Results: Mean consolidation time was 3.08±2.19 months. The recurrence rate was 6.4%. There was no difference between groups admitted with fracture and w/o fracture, allograft and autograft group in terms of clinical and radiological results.

Conclusions: Curettage and grafting was still an upcoming and safe method for enchondroma.

Keywords: *Enchondroma, curettage, bone substitute*

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Introduction

Enchondroma is the hand's most common primary bone tumor[1]. Due to their benign nature, they usually do not give any symptoms. In clinical practice, the diagnosis is often made incidentally by radiographs obtained after trauma or other reasons[2]. It can be diagnosed by plane radiographs and, MRI and CT images[3]. Although the treatment is intralesional, curettage alone or placement of autograft, allograft, or other bone substitutes into the cavity is often sufficient. Although enchondromas are defined under the class of benign tumors, the need for treatment is summarized under three main purposes. 1. Confirming histopathological diagnosis, 2. Eliminating the risk of fracture, and 3. preventing the progression of the deformity[4].

Previously, only curettage was recommended for treatment[5-6]. Afterward, it was suggested that the cavity formed after curettage should be filled by the bone substitute[7-8]. Theoretically, the accumulation of osteoprogenitor cells in this region by hematoma due to iatrogenic fracture after curettage and new bone may make this approach rational[4]. However, the weakness of the bone and the time it takes to heal have made it attractive to use bone substitutes to increase mechanical support[9].

In case of fracture at the time of diagnosis, the approach may vary according to different schools. Accordingly, while some authors state that it would be appropriate to wait for the healing of the fracture and to perform curettage and grafting after the union is achieved, they suggest that if surgery is planned after the diagnosis of the fracture, the immobilization period required by the fracture should be included in the immobilization period after the surgery[10].

Two problems encountered in follow-up are tumor recurrence or weakened bone fractures. Although malignant transformation is not typical, it is generally more expected in advanced ages and areas other than the hand. In this article, we retrospectively evaluated the enchondromas encountered at hand.

Materials and Methods

Patients treated with standard curettage with or without graft for hand enchondroma between 2011 and 2020 were retrospectively analyzed, after obtaining ethical approval from the ÇÜTF institute with the decision number 125/21. A total of 47 patients (table 1) were included in the study. Thirty (63.8%) patients were female and 17 (36.2%) were male. Considering the patient's complaints, the first symptoms were pathological fractures in six (12.8%) patients and a painful mass in eleven (23.4%) patients. Pathology was found incidentally in 30 (63.8%) of the patients. In 21 (44.7%) patients, the pathology was seen on the right hand, while in 26 (55.3%) patients on the left. The mean follow-up period was 28.47±25.10 months. Patients without direct radiographs during the pre- and postoperative period, and magnetic resonance images before the operation were not included in the study. The histopathological results of the patients were taken as the criterion for definitive diagnosis. The volume of enchondromas was measured by MRI (figure 1) before the intervention. This guided us in determining the amount of allograft and autograft to be used.

Surgical technique

Indications for patients who underwent surgery were pain, progressive deformity, or enchondroma causing problems using the involved finger. Informed consent forms have also elucidated the patients regarding graft material. The choice of allograft or autograft was left to the patient. Autograft was used in 37 (78.7%) patients and allograft was used in five (10.6) patients. X-ray examinations were taken with a standard cartridge, and a digital low dose to determine the presence of calcification in the bone and accompanying soft tissue. To determine the natural structure of the deformed bone, ra-

diographs were obtained bilaterally. Evaluation of the ultimate pathology was made according to size, shape, contour, extent, and topography. In adult patients, if an autograft will be used, the graft will be taken from the iliac wing of the patient, so the surgery was performed under general anesthesia. In pediatric patients, general anesthesia was used regardless of the type of bone replacement. Regional anesthesia was used in 9 patients. General anesthesia was applied to 38 patients.

After determining the proximal and distal borders of the mass under the fluoroscopy imaging device, appropriate incisions were made. The window was created equal to the tumor size to see the entire lesion (figure 2). An angled or ring-shaped curette was used. Curettage with bone burr was added to contribute to mechanical curettage in all cases. Thermal damage was achieved with electrocautery inside the cavity. Afterward, the cavity was filled with autograft or allograft. The construct was strengthened with two crossed K wires or a plate if there was a concomitant pathological fracture or severe weakening of the bony cortex. The previously removed cover was also subjected to the processes that the cavity was exposed to and placed in its original place. The periosteal repair was performed first, and the remaining layers were adequately closed. A short arm splint was applied for pain and edema control for three weeks.

Follow-up

The patients who had no problems after the operation were discharged after wound dressing on the first day. The sutures were removed in the 2nd week, and the splint was removed in the 3rd week. After the splint, a gentle passive motion was started. The active movement was started after consolidation seen on X-ray or fracture healing.

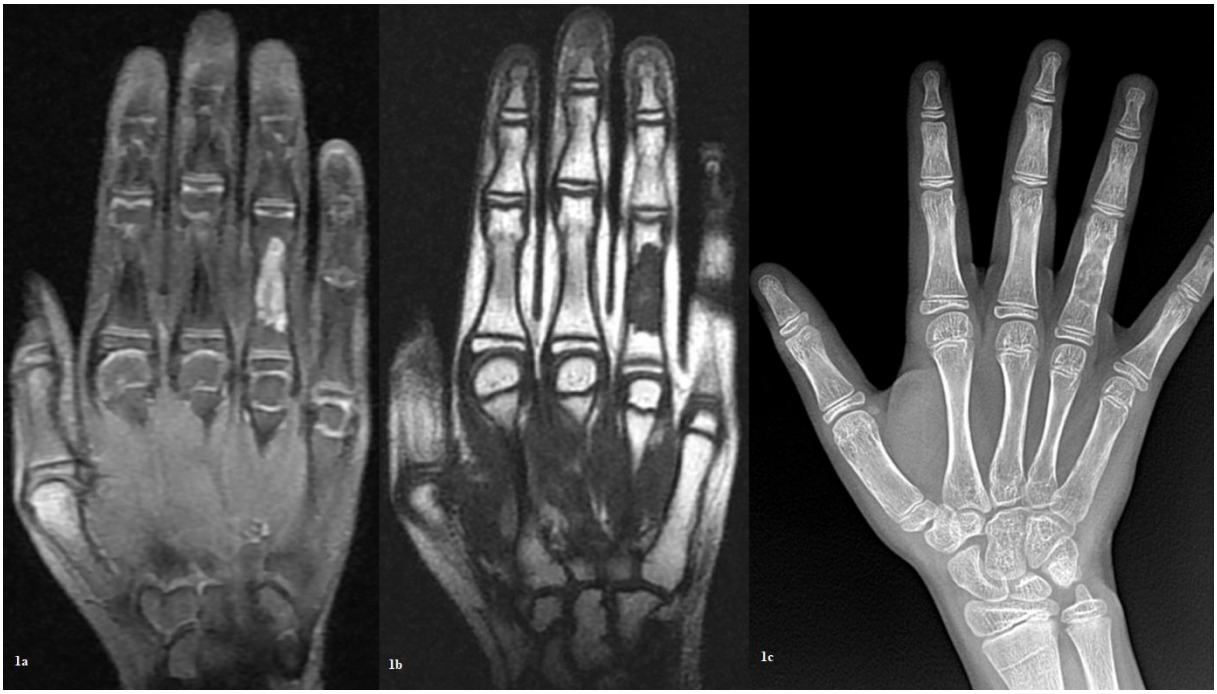

Figure 1. MRI and X-ray samples of a patient with enchondroma in the fourth metacarpal
1a: MRI T2 sequence image
1b: MRI T1 sequence image
1c: X-Ray image

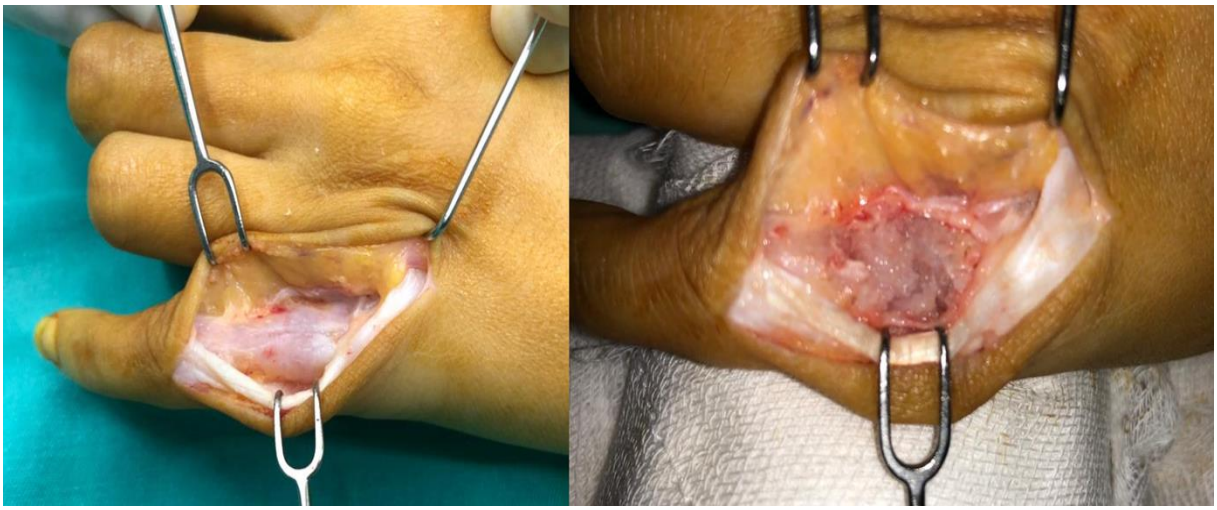

Figure 2. Intraoperative view of the patient who was operated for enchondroma in the left-hand 5th metacarpal

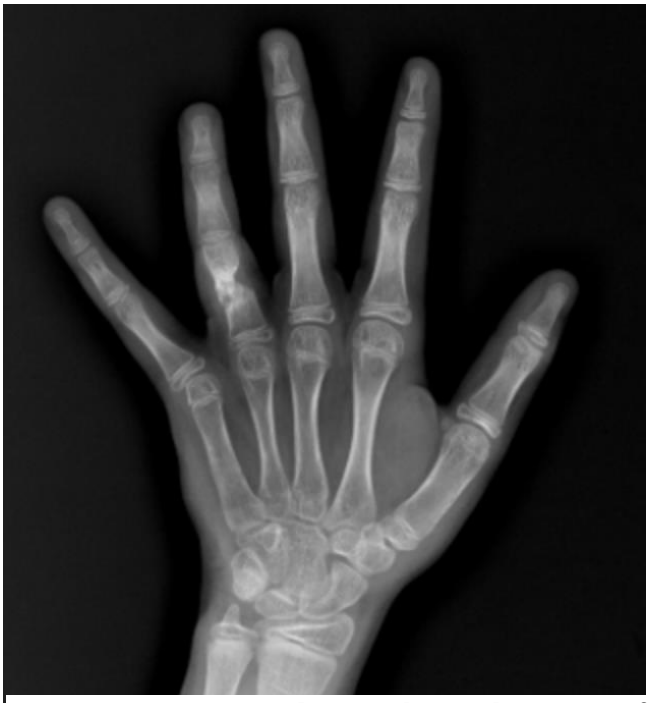

Figure 3. Recurrence direct radiography image of the patient who was operated for 4th finger proximal phalanx enchondroma

Patients were called to the outpatient clinic on the 6th, 12th,18th, 24th week, and every three months for regular follow-up. X-rays of the patients were obtained. MRI was requested if there was a finding suggestive of recurrence in or around the curetted and grafted area. Criteria for functional assessment were loss of motion (<20% compared to the contralateral limb), scar formation, residual deformity and classified as good, fair and poor[6].

Statistics

SPSS 23 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). Chi-square test or Fischer test statistics were used to compare categorical variables. In the comparison of continuous measures between the groups, the distributions were controlled, the Student T test was used for the variables that met the parametric distribution prerequisite, and the Mann Whitney U test was used for the MCA variable that did not meet the parametric distribution prerequisite. Repeated Measurement Variance analysis was used in the pre- and postoperative evaluations of AI. Statistical significance level was taken as 0.05 in all tests.

Table 1. Patients characteristics

PATIENTS	AGE	GENDER	FOLLOW-UP	BONE	SIZE	LAST DEFORMITY	SUBSTITUTE	SIDE	RECURRENCE	FRACTURE	HİSTOPATHOLOGY	FIXATION	CONSOLIDATION	FUNCTION
1	24	M	92	METACARP	32	NA	OTO	LEFT	NA	ACUTE	ENCHONDROMA	PLATE	4 MONTHS	GOOD
2	23	M	38	PHALANX	18	NA	OTO	LEFT	8 MONTHS	ACUTE	ENCHONDROMA	PLATE	6 MONTHS	GOOD
3	39	F	112	METACARP	19	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	4 MONTHS	MODERATE
4	27	F	30	METACARP	26	40 DEGREE FLEX	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	5 MONTHS	GOOD
5	31	F	108	METACARP	21	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	5 MONTHS	GOOD
6	25	M	8	PHALANX	23	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	PLATE	2 MONTHS	GOOD
7	20	F	25	PHALANX	20	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	5 MONTHS	GOOD
8	23	F	24	PHALANX	10	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	13 MONTHS	GOOD
9	49	F	76	PHALANX	15	18 DEGREE FLEX	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	5 MONTHS	GOOD
10	38	M	23	PHALANX	24	14 DEGREE EXT	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	8 MONTHS	GOOD
11	40	M	27	PHALANX	15	NA	ALLO	LEFT	NA	INTACT	ENCHONDROMA	NA	4 MONTHS	MODERATE
12	10	F	32	PHALANX	28	PSEUDO 32 DEGREE FLEX	ALLO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
13	37	M	24	METACARP	11	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
14	10	M	36	METACARP	28	NA	OTO	LEFT	NA	ACUTE	ENCHONDROMA	NA	1.5 MONTHS	GOOD
15	4	M	28	PHALANX	17	NA	ALLO	RİGHT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
16	4	F	36	PHALANX	28	NA	ALLO	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
17	25	F	25	PHALANX	9	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	MODERATE
18	34	M	18	PHALANX	12	18 DEGREE EXT	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
19	41	M	28	PHALANX	18	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	6 MONTHS	MODERATE
20	33	F	36	PHALANX	15	NA	AMP	RİGHT	NA	INTACT	ENCHONDROMA	NA	NA	NA
21	2	F	18	METACARP	5	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
22	54	M	18	PHALANX	28	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
23	46	F	62	METACARP	8	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
24	26	F	12	PHALANX	35	NA	AMP	LEFT	NA	INTACT	ENCHONDROMA	NA	NA	NA
25	62	F	50	METACARP	16	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	MODERATE
26	7	F	12	PHALANX	32	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	MODERATE
27	44	F	45	METACARP	12	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
28	14	F	12	PHALANX	18	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
29	19	F	14	PHALANX	19	10 DEGREE EXT	OTO	LEFT	NA	INTACT	ENCHONDROMA	PLATE	1.5 MONTHS	GOOD
30	31	M	24	PHALANX	14	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	GOOD
31	29	F	6	METACARP	10	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
32	19	F	12	PHALANX	22	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
33	54	F	9	METACARP	9	NA	NA	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
34	18	F	22	METACARP	16	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	4 MONTHS	GOOD
35	43	F	35	METACARP	16	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
36	43	M	6	METACARP	19	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	4 MONTHS	MODERATE
37	11	F	36	METACARP	8	NA	NA	LEFT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
38	17	M	36	METACARP	24	NA	OTO	LEFT	NA	ACUTE	ENCHONDROMA	K-WIRE	3 MONTHS	GOOD
39	26	F	6	PHALANX	7	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	MODERATE
40	31	M	18	PHALANX	20	NA	ALLO	LEFT	NA	INTACT	ENCHONDROMA	NA	3 MONTHS	POOR
41	30	F	13	PHALANX	15	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
42	14	F	6	METACARP	9	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
43	9	F	12	PHALANX	14	NA	OTO	LEFT	3 MONTHS	ACUTE	ENCHONDROMA	NA	6 MONTHS	POOR
44	48	F	4	PHALANX	6	NA	OTO	RİGHT	NA	ACUTE	ENCHONDROMA	NA	1.5 MONTHS	MODERATE
45	43	M	6	PHALANX	5	NA	OTO	LEFT	NA	INTACT	ENCHONDROMA	NA	1.5 MONTHS	GOOD
46	42	F	12	PHALANX	15	NA	OTO	RİGHT	NA	INTACT	ENCHONDROMA	NA	2 MONTHS	GOOD
47	51	M	6	METACARP	18	25 DEGREE FLEX	OTO	LEFT	3 MONTHS	INTACT	ENCHONDROMA	NA	6 MONTHS	MODERATE

Results

The mean postoperative consolidation time was 3.09±2.19 months. Recurrence (figure 3) was seen in three patients (6.7%) during the follow-up period. The mean time to recurrence was four months. No chondrosarcoma or an alternative pathology was detected in any patient. No correlation was found between enchondroma size and recurrence (p=0.677) Deformity was observed in seven patients (14.9%) at the last follow-up. Flexion (20.3 degrees) deformity was observed in three patients, and extension (18.5 degrees) deformity was observed in four patients. Flexion deformity was observed in three patients and extension deformity was observed in four patients. Fixation was applied to five (10.6%) patients. While deformity was observed in one patient who was fixated, deformity was observed in 6 of 36 patients who were not fixated. It was shown that the application or non-application of fixation did not cause a significant difference in the development of deformity (p=0.571). There was no significant difference in union time in patients who used allograft and autograft. Two (4%) patients underwent amputation at the appropriate level. Two (4.25%) patients had poor results due to dense scar tissue on the dorsum of the hand. While moderate results were obtained in 10 (21.27%) patients, good results were obtained in 33 (70.21%) patients. Two amputated patients were not included in the functional evaluation. Whether there was a fracture at the time of admission and whether fixation was applied or not had no effect on the functional outcome.

Discussion

In the historical process, many studies have been carried out on the treatment of patients with enchondroma. In our study, we showed that curettage and grafting are effective methods in hand enchondromas. Enchondroma was diagnosed in all patients included in the study as a result of X-ray and MRI, and histopathology was consistent with enchondroma in all patients. In this context, we believe that direct X-ray and MRI will be sufficient to diagnose enchondroma. In addition, we found that surgery performed without waiting for union in the presence of pathological fractures did not differ from surgery performed after union in terms of postoperative complications or long-term deformity. Regarding selected graft materials, using autograft or allograft did not affect the treatment results.

Treatment of enchondromas of the hand was initially reported as a plan with curettage alone. However, placing a bone substitute into the created cavity has become popular, although it has remained a debatable topic[4-11]. We put a bone substitute in the cavity in patients, and we believe that such an approach would be more reliable, considering that the consolidation period is not long, which will pose a risk in terms of fractures and deformities that may occur after the cavitary wall is thin in patients. However, we did not ignore the necessity of supporting these two approaches with randomized controlled studies.

At the time of diagnosis, accompanying pathological fracture with existing pathology is common in hand enchondromas. About 40% of the patients are admitted to the hospital with fractures. The fracture rate of the patients in our study was %12.8. Our institute is a tertiary health institute, and patients with fractures could be treated in other institutes since they were admitted to the emergency department. In our research, most cases were either referred from other institutes or preferred to be treated in tertiary health centers. This could explain the inconsistency with the literature. While some authors advocate simultaneous surgery for fracture and pathology, some recommend surgery for pathology following the healing of the fracture[12-14]. We generally think that the view in the first part would be more practical and logical. We are considering that the majority of the fractures occurring in the finger fractures are unstable and the possibility of reduction loss in the

follow-up with conservative treatment; when the union occurs, the deformity caused by the pathology may make the subsequent surgery more complicated due to the additional deformity risk of malunion that will appear as a result of fracture healing. The similar cosmetic and functional outcomes in our patients with acute fractures at the time of diagnosis can be explained by the fact that the consolidation time of the bone placed in the cavity and the time required for fracture healing is similar. In the literature, recurrence rates in enchondromas range from 0% to 13%. Two propositions stand out in this regard[15]. First, relapse cases are usually seen in the early postoperative period and require more frequent follow-up of patients in the early postoperative period. Second, recurrent enchondromas may be low-grade chondrosarcomas. Of the patients we included in our study 6.7% There were recurrences. The mean recurrence time was 4 months. This is consistent with the first proposition. The mean age of the patients with recurrence was 11.67. Considering the age of the patients and the fact that none of them had Ollier's disease, which increased the susceptibility to malignancy, we think this situation does not comply with the second proposition. Moreover, the histopathology results of the patients support this situation.

There are studies on the relationship between the difference in graft materials used and the recurrence rates[16]. Although some studies have reported that recurrence rates are higher in patients using allografts, there are also publications showing that autograft use also increases recurrence rates[15]. In a study evaluating the clinical results of using different grafts, it was revealed that the recurrence rates in both groups were similar and even similar to the placebo groups that did not use a bone substitute[16]. Our study shows that it is not related to the use of different bone substitutes in terms of recurrence rates. At this point, we think that using any of the graft options to be preferred in hand enchondromas will not make a difference in patient outcomes.

One weakness of the study was significant differences between number of cases in each group. X-Rays, MRI were evaluated by single surgeon which could lead to bias. Besides, study groups were purified. The patients with osteochondromatosis, Ollier, and Mafucci disease were excluded which could lead to the misinterpretation of the results in cases of recurrences or possible malignancy. These are the main weakness of the study.

Enchondromas are among the most common cases encountered in the clinical practice of clinical orthopedic and hand surgeons. The fact that it can cause pathological fracture and deformity depending on its progression confirms the need for treatment. In this context, surgical curettage and placement of bone substitutes into the cavity are sufficient in terms of clinical and radiological results, regardless of the nature of the placed substitute, whether there is an accompanying fracture or not at the time of application.

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

This study was approved by the Institutional Investigation and Ethics Committee with the approval number of "125/21" -2022 and conducted at Cukurova University in Turkey

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CORRELATION OF PATIENT FEATURES OF COVID-19, LABORATORY TESTS AND COMPUTED TOMOGRAPHY FINDINGS: SINGLE-CENTER RETROSPECTIVE STUDY

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Abstract

Aim: Computed Tomography (CT) findings, clinical and laboratory data are very important in the diagnosis and treatment process of Coronavirus Disease 2019 (COVID-19). In this study, the relationship between these findings was investigated.

Methods: 93 patients with positive Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) test for SARS-CoV-2 were included in the study. CT findings, laboratory tests, and the World Health Organization Clinical Progress Scale (WHO-CPS) were evaluated.

Results: Of the patients, 52 were male and 41 were female. The mean age was 46. The most common laboratory finding is high CRP levels (67.74%). GGO, consolidation, halo sign and air bronchogram were most frequent CT findings. The mean of CT score was 4.91. A statistically significant positive correlation was found between CT score and age, D-dimer, CRP, ferritin and fibrinogen. There was a significant negative correlation between CT score, lymphocyte count and oxygen saturation. There was no correlation between CT score and procalcitonin, gender and presence of comorbid disease. There was a moderate negative correlation between CT score and IL-6 blocker use and corticosteroid therapy, and a mild negative correlation between CT score and favipravir use. The correlation between CT score and immunosuppressant use was not significant. We also found a moderate positive correlation between WHO-CPS and CT scores.

Conclusions: The CT score is correlated with some laboratory and clinical markers, and we think that these findings indicate that CT is a very useful test in the diagnosis as well as in the follow-up.

Keywords: *COVID-19, CT, laboratory findings*

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Introduction

The new type of coronavirus (SARS-CoV-2), which can cause severe disease in humans, was officially identified on January 2020 and named coronavirus disease 2019 (COVID-19)[1]. COVID-19 can present as upper respiratory tract infection, pneumonia, encephalitis, pulmonary or systemic emboli formation, acute respiratory distress syndrome, respiratory failure, systemic inflammatory response or sepsis[2]. The gold standard method for the diagnosis is the polymerase chain reaction (PCR) test[3]. However, the PCR test may show negative results, especially in the early period[4]. In the diagnosis of COVID-19, computed tomography (CT) can be helpful, and show positive findings even before the onset of symptoms[5,6]. Clinical findings and laboratory data are also very important in the diagnosis and treatment process[7]. In this study, we investigated the correlation between laboratory data, clinical findings and CT findings of patients with COVID-19.

Materials and Methods

Patients

A total of 148 patients who were applied to our hospital, between March 2020 to June 2020, with the symptoms such as fever, fatigue, myalgia, cough, loss of taste and smell, and were suspected for COVID-19 included in this retrospective study. Because of negative real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2, 55 patients were excluded from the study. In addition, pediatric patients were not included into the study. Finally, we included 93 patients (41 female, 52 male) who had positive result of RT-PCR test for SARS-CoV-2. All the patients have thin-sectional non-contrast chest CT. This study approved by our institutional ethical committee and Ministry of Health COVID-19 Science Committee.

Image Acquisition and Chest CT Evaluation

Thin-sectional non contrast chest CT was performed with a 4-slice CT scanner (Asteion Super 4, Canon). To minimize motion artifacts, patients were scanned on single breath hold, on inspiratory phase in the supine position. The associated parameters were used: tube voltage, 120 kV; automatic tube current modulation, 100–250 mAs; slice thickness, 1.25 mm without interslice gap.

The major CT findings were based on the standard glossary for thoracic imaging reported by the Fleischner Society[8]. The evaluated CT features were ground glass opacity (GGO), consolidation, reticular pattern, halo and reversed halo signs, crazy paving, air bronchogram, vascular enlargement, subpleural line, mediastinal lymphadenopathy and pleural effusion that were defined for SARS-CoV-2 pneumonia by novel literature. Also bilaterality, peripheral or central involvement, multilobar distribution of the lesions were estimated. The outer one-third of the lung was accepted as peripheral, the remaining locations were accepted as central.

A semi-quantitative CT severity scoring system was used, described by Pan et al (1). Each of the five lung lobes were visually scored on a scale 0 to 5.

0 means no involvement.
1, less than 5% involvement.
2, 5%-25% involvement.
3, 26%-49% involvement.
4, 50%-75% involvement.
5 for more than 75% involvement.

The total score was the sum of the lobar scores and ranged 0 to 25. Image analysis was performed by two radiologists with 15- and 5-years' experience. Final scores were decided by common consensus.

Patient characteristics and laboratory data

We retrospectively collected the laboratory data including lymphocyte count, lymphocyte percentage, D-dimer, C-reactive protein (CRP), ferritin and procalcitonin levels. Also, the drugs which needed for the treatment: corticosteroid, IL-1 blocker, IL-6 blocker and favipravir were recorded. Patient characteristics were sex, age, presence of comorbid disease. Information about patient characteristics is given in the Table 1. We calculated the WHO Clinical Progression Scale (WHO-CPS)[9]. The scale provides a measure of illness severity across a range from 0 (not infected) to 10 (dead) with data elements that are rapidly obtainable from clinical records. The features and scores used in the scale are given in Table 2.

Statistical analysis

Patient findings are given as frequencies and percentages in categorical variables; mean ± standard deviation in numerical variables is given as minimum-maximum values. Correlation analysis was performed by Pearson Correlation Test. $p<0.05$ was considered significant in all comparisons. Analyzes were performed with SPSS 20.0.

Results

Of the 93 included patients with COVID-19, 52 (55.9%) were male and 41 (44.1%) were female, and the mean age was 46±16,77 (range 21-83) years old. All patients have symptoms like fever, cough and weakness, myalgia and 46 (49.5%) patients have comorbid disease and 7 (7.5%) of them have a history of immunosuppressant treatment.
The results of laboratory tests were often abnormal, the most frequent abnormalities were mildly decreased lymphocyte count, lymphocyte percentage and increased CRP, D-dimer, procalcitonin, fibrinogen levels (Table 3).

Table 1. Demographic data and patient characteristics

Parameters		n	%
Gender	Female	41	44,1
	Male	52	55,9
Intubation status	+	6	6,5
	-	87	93,5
Additional disease	+	47	50,5
	-	46	49,5
Immunsuppressive drug use	+	7	7,5
	-	86	92,5
IL-1 Blocker use	+	7	7,5
	-	86	92,5
IL-6 Blocker use	+	12	12,9
	-	81	87,1
Corticosteroid use	+	19	20,5
	-	74	79,5
Favipiravir use	+	62	66,7
	-	31	33,3

The most common laboratory finding is high CRP levels (n=63, 67.74%). Fibrinogen was high in 53 patient and 35 patient has high D-dimer levels (37.63%). 25 of 83 patients had high ferritin level (24.71%). Also 21 (22.58%) of 93 patients had lymphopenia and lymphocyte percentage was low in 37 patient (39.78%). The interval from onset symptoms to PCR test and chest CT scan was 4±3.2 (range 1-17) days.
Twenty patients had normal chest CT findings. GGO, consolidation, halo sign and air bronchogram were the most frequent CT findings, respectively (Table 4). The mean of CT score was 4.91 (range, 0-21) and CT score was compared with age, gender and laboratory findings. When the involvement patterns and frequencies were evaluated, it was found that bilateral lung involvement, multilobar and peripheral involvement were the most common (Table 5).
Statistically significant positive correlation were found between CT score vs age ($p<0.05$, $r=0.487$), D-dimer ($p<0.05$, $r=0.331$), CRP ($p<0.05$, $r=0.587$) (Graphic A), ferritin ($p<0.05$, $r=0.653$) (Graphic B) and fibrinogen ($p<0.05$, $r=0.592$) levels.

Table 2. WHO clinical progression scale[9]

Patient State		Descriptor	Score
Uninfected		Uninfected • no viral RNA detected	• 0
Ambulatory mild disease		Asymptomatic • viral RNA detected Symptomatic • independent • assistance needed	• 1 • 2 • 3
Hospitalized	moderate disease	• no oxygen therapy* • oxygen by mask or nasal prongs	• 4 • 5
Hospitalized	severe diseases	Hospitalized • oxygen by NIV or high flow • Intubation and mechanical ventilation, pO2/FiO2 ≥150 or SpO2/FiO2 ≥200 • Mechanical ventilation pO2/FIO2 <150 (SpO2/FiO2 <200) or vasopressors • Mechanical ventilation pO2/FIO2 <150 and vasopressors, dialysis, or ECMO • Dead	• 6 • 7 • 8 • 9 • 10

ECMO=extracorporeal membrane oxygenation. FiO2=fraction of inspired oxygen. NIV=non-invasive ventilation. pO2=partial pressure of oxygen. SpO2=oxygen saturation. *If hospitalised for isolation only, record status as for ambulatory patient.

Statistically significant negative correlation were found between CT scores vs. lymphocyte count and lymphocyte percentage ($p<0.05$, $r=-0.317$) (Graphic C) and oxygen saturation ($p<0.05$, $r=-0.606$).
There was no significant correlation between CT score and procalcitonin ($p > 0.05$, $r= - 0.033$) levels, confirming that this disease is transmitted by a virus.
No significant relationship was found between CT score vs. gender ($p > 0.05$, $r = 0.148$), presence of comorbid disease ($p > 0.05$, $r = - 0.097$).
IL-1 and IL-6 blockers were used for 7 (7.5%) and 12 (12.9%) patients, respectively. 19 (20.4%) patients have used corticosteroids and favipravir.

Table 3. Laboratory findings

Findings	n=93
Lymphocyte count ($10^3/\mu$lt), mean (SD)	1.391 (7.3)
Lymphocyte percentage (%)	23.6 (12.5)
CRP (mg/L), mean (SD)	45.9 (81.1)
Ferritin, mean (SD)	388.7 (811)
Procalcitonin (ng/ml), mean (SD)	1.3 (10.3)
D-dimer level (mg/L), mean (SD)	1.0 (1.8)
Fibrinogen (mg/dl), mean (SD)	418.5 (160.7)
Oxygen saturation (%),mean(SD)	94.9 (4.6)

When we looked for relationship between CT score and the required drugs for the treatment, statical analyses showed moderate negative correlation between usage of IL-6 blocker ($p<0.05$, $r=0.627$) and corticosteroid therapy ($p<0.05$, $r=0.496$). There was a mild negative correlation between CT score and use of favipravir ($p<0.05$, $r=0.378$).
The correlation between CT score and use of immunosuppressant was non-significant ($p > 0,05$, $r = -0,071$). We found a mild negative correlation between CT score and intubation ($p<0.05$, $r=0.388$), 6 (6.45%). Patients had needed intubation, 4 (4.30%) of them died because of COVID-19. Also, we found moderate positive correlation between the WHO-CPS score and CT score ($p<0.05$, $r = 0.571$) (Graphic D).

Table 4. CT features

Features	n(%)
Ground-glass opacity	68 (73.1)
Consolidation	38 (40.9)
Crazy paving	14 (15.1)
Reticular	19 (20.4)
Air bronchogram	32 (34.4)
Pleural thickening	13 (14.0)
Subpleural lines	10 (10.8)
Bronchiectasis	7 (7.5)
Halo sign	34 (36.6)
Vascular enlargement	24 (25.8)
Mediastinal lymphadenomegaly	9 (9.6%)
Pleural effusion	3 (3.2%)

Table 5. Involvement patterns of lung

	n (%)
Involvement of lungs	
• bilateral	63 (88.7)
• unilateral	8 (11.3)
Involvement of the lobes	
• multilobar	63 (88.7)
• unilobar	8 (11.3)
Distribution of pulmonary lesions	
• peripheral	28 (39.4)
• central	1 (1.40)
• peripheral and central	43 (60.6)

Discussion

COVID-19 pandemic started in 2019 and become most important public health-care problem in whole world since then. Most cases are asymptomatic but around 1-2% of COVID-19 infection could result with significant morbidity and even mortality. Though, well-known diffuse systemic involvement of different organs were reported, lung was the far most common involved organ in COVID-19 infection and mainly diagnosed by chest CT. The most common CT findings of COVID-19 were reported as GGOs with or without consolidation in significant number of studies[2]. With the current study we looked for whether there was correlation with patient characteristics', common laboratory values, and CT findings or not. We found the most frequent laboratory data is high CRP levels (67.74%) in accordance with the literature[10]. Bilateral multilobe involvement, peripheral (including peripheral and central) distribution and GGO appearance were the most common chest CT findings of COVID-19. These results are similar to the CT findings of COVID-19 reported in the literature[3].

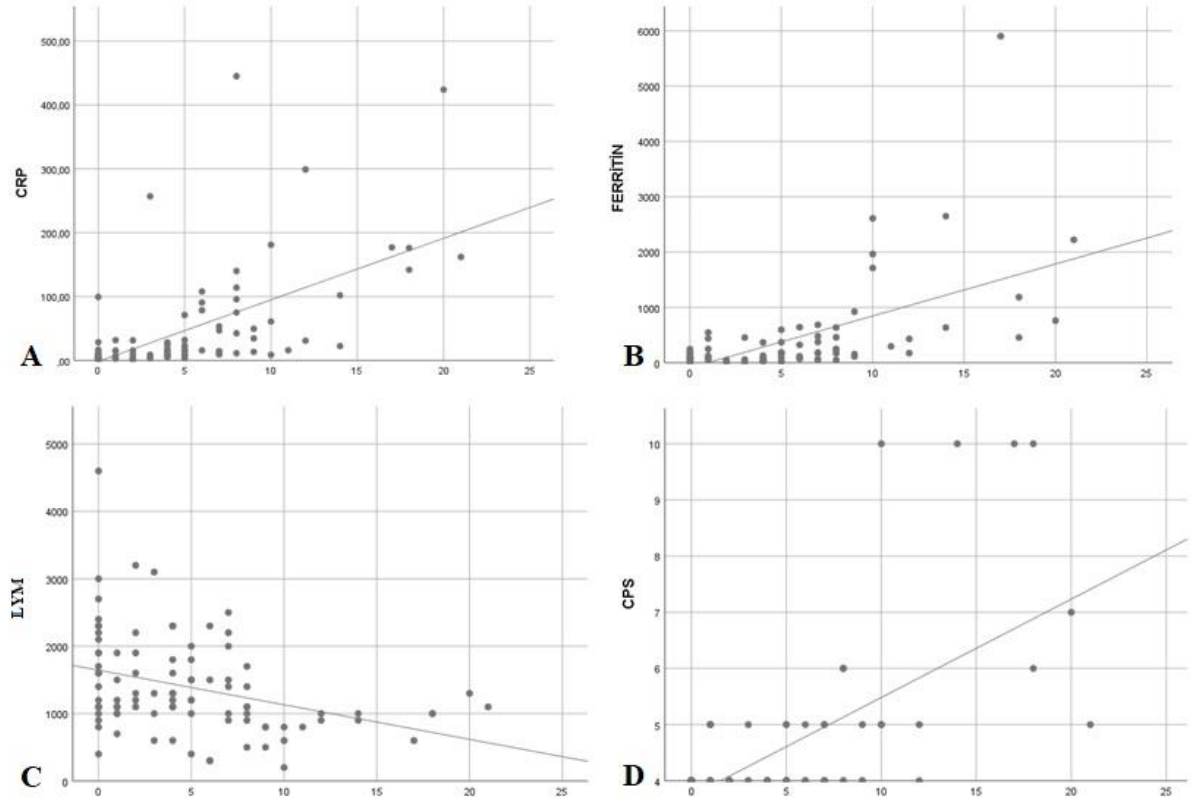

Figure 1. Correlation graphics
A Correlation between CT score and CRP
B Correlation between CT score and ferritin
C Correlation between CT score and lymphocyte count
D Correlation between CT score and WHO-CPS

In our study, a significant correlation was observed between the CT score vs age. This result is consistent with the presentation of the disease with more severe findings in the elderly and is correlated with the literature. No significant relationship was found between CT score and gender. It is already known that CT findings are detected at similar rates in both genders[11].

Statistically significant negative correlation were found between CT score vs. lymphocyte count and lymphocyte percentage and oxygen saturation. It has been showed that severe COVID-19 patients have significantly higher levels of CRP, and there is a relationship with high CRP levels and mortality. Beside increasing CRP, the lymphocyte count decreases with increasing disease severity. By being in correlation with CRP levels and lymphocyte counts, CT score may predict disease severity and be used as a tool for management of the treatment[12-14].

The limitations of our study are that it was single-centered and the number of cases was small, the number of patients using IL blockers was low, and the lack of optimization in laboratory data, since we did not know on which day of the disease the patients applied.

According to results of our study, a mild negative correlation detected between CT score and favipravir therapy. In the literature, there are studies advocating and not advocating that the treatment is effective[15]. However, no significant correlation was observed in our study, and the use of favipravir in the following periods became very controversial, especially in patients with mild signs, it was shown that it isn't effective for treatment[16].

In our study, it was determined that D-dimer levels and CT score were correlated. Similarly, in the studies of Zhu J et al., D-dimer and CRP levels were found to be correlated with the CT score[17]. Ferritin and fibrinogen levels are also a commonly used parameter to evaluate the severity of the disease. In our study, correlation was found between CT score and ferritin and fibrinogen level, and literature information supports our results[18,19]. In follow-up, the CT score may be useful in correlating infection severity.

Conclusion

The correlation of CT score with laboratory and clinical findings such as D-dimer, CRP, lymphocyte count and lymphocyte percentage, oxygen saturation and WHO-CPS highlights the importance of CT findings in the diagnosis as well as in the method. In order to better define this relationship, multicenter studies with a larger number of patients are required

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

This study was approved by the Institutional Investigation and Ethics Committee with the approval number of "99/05" -2020 and conducted at Cukurova University in Turkey

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THE VALUE OF INTEGRATED PULMONARY INDEX MONITORING AFTER ELECTROCONVULSIVE THERAPY

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Abstract

Aim: The Integrated Pulmonary Index (IPI) is an algorithm integrated 4 major parameters [end-tidal carbon dioxide ($EtCO_2$), respiratory rate (RR), oxygen saturation (SpO_2), and pulse rate (PR)] measured by commercially available monitors in order to provide a simple indication of the patient's overall ventilatory status. IPI provides to determine the need for additional clinical assessment or intervention by evaluating respiratory status of patient. The aim of the study was to study the value of IPI monitoring for assessment of respiratory status and recovery from anesthesia after electroconvulsive therapy (ECT).

Methods: Total 64 patients, ranging in age from 18 to 65 years and undergoing ECT for various psychiatric disorders, were enrolled in this prospective observational study. All patients were anesthetized with a standardized technique. After the return of spontaneous breathing, in addition to the standard monitoring, all patients were monitored with microstream $EtCO_2$, is a portable bedside monitor that continuously monitors a patient's $EtCO_2$, RR, SpO_2, PR and IPI. All those parameters and Modified Aldrete Score (MAS) were recorded during the first 5 minutes immediately after neuromuscular blockage recovery and the first 10 minutes in the post anesthesia care unit (PACU) stay, at 1-min intervals. Supplemental oxygen requirement, any interventions improving the patency of airway and any complications such as apnea, bradypnoea, tachypnoea etc. were also recorded.

Results: There were 1088 IPI readings ranging from 1 to 10. IPI values during 5 minutes of recovery period were significantly lower in the respiratory intervention group, and significantly low in patients who needed supplement oxygen in the PACU. Additionally, significant correlations were found between IPI and MAS or SpO_2 during follow-up in PACU.

Conclusions: The IPI monitorization can be useful over the standard monitorization in terms of better evaluation of respiratory status, and provide to make decision about PACU recovery, after ECT.

Keywords: *Integrated pulmonary index, end-tidal carbon dioxide, electroconvulsive therapy, Modified Aldrete Score.*

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Introduction

Accurate assessment of patient's respiratory status is an essential requirement of good patient care in all clinical settings: from pre-hospital and emergency care, through the spectrum of acute care within the hospital, and finally on the general medical surgical ward, respiratory status is a cornerstone of patient management.[1] Spot checks of respiratory rate and percentage of oxygen saturation cannot provide a complete picture of respiratory status. Continuous monitoring of oxygenation and ventilation using capnography and pulse oximetry allows providers to review trends in respiratory parameters not captured by intermittent monitoring and promotes timely medical intervention that may prevent a respiratory complications and arrest.[2]

The Integrated Pulmonary Index (IPI) is an algorithm that integrated 4 major parameters: end-tidal carbon dioxide ($EtCO_2$), respiratory rate (RR), oxygen saturation (SpO_2), and pulse rate (PR) measured by commercially available monitors in order to provide a simple indication of the patient's overall ventilatory status.[3]

It gives results in a single value representing respiratory status on a scale of 1 (critical respiratory insufficiency) to 10 (optimal respiratory status). IPI provides to determine the need for additional clinical assessment or intervention by evaluating respiratory status of patient (Table 1).[3]

This is the first commercially available tool incorporating ventilation and oxygenation into a single respiratory index score, and also the first example of a fused respiratory vital signs index based on implementing an expert rule system using fuzzy logic.[3]

Electroconvulsive therapy (ECT) is a unique therapy that intentionally provokes seizure by applying electrical current to the human central nervous system.[4] Although respiratory care during ECT can be completed within 10 min, inappropriate management interferes with the efficacy of the therapy and increases the risk of complications.[5-7]

Table 1. Classification of the patient status according to the IPI score.[3]

IPI	Patient status
10	Normal
8-9	Within normal range
7	Close to normal range, requires attention
5-6	Requires attention and may require intervention
3-4	Requires intervention
1-2	Requires immediate intervention

Abbreviations: IPI, integrated pulmonary index.

In this context, a prospective observational trial was designed to study the value of IPI monitoring for assessment of respiratory status (primary outcome) and recovery from anesthesia (secondary outcome) after electroconvulsive therapy.

Materials and Methods

This study was approved by the Institutional Investigation and Ethics Committee with the approval number of 12/90 in July 2019 and conducted at Cukurova University in Turkey.

Patients and intervention

For this prospective observational clinical study, sixty-four American Society of Anesthesiologists (ASA) physical status class I-II patients over the age of 18 who needed ECT due to various psychiatric problems were included in their first ECT sessions, between August 2019 and February 2020. Patients with cerebrovascular disease, ischemic heart disease, severe pulmonary disease that limits patient's daily activities, body mass index over 35 kg / m^2, and age over 65 were excluded from the study.

Patients who were taken to the ECT room after 6 hours of fasting, were monitored by electrocardiogram (ECG), pulse oximeter,

non-invasive blood pressure (BP), and non-invasive microstream $EtCO_2$ monitoring (*Medtronic capnostream 35*). Microstream $EtCO_2$ monitoring is a portable bedside monitor that continuously monitors a patient's $EtCO_2$, RR, SpO_2, PR and IPI. $EtCO_2$ monitoring was performed using a combined nasal cannula, one side of which was used to sample CO_2 for measurement of $EtCO_2$, whereas the other delivered low-flow oxygen (2L/min).

Outcome and follow-up

The initial baseline BP, PR, $EtCO_2$, SpO_2, RR and IPI values, and age, gender, ASA score, psychiatric diagnosis, weight and height of the patients were recorded. Standard general anesthesia protocol for ECT was applied to all patients. Anesthesia was induced with 3-5 mg/kg intravenous (iv) thiopental sodium until the response for verbal command and the eyelash reflex disappeared. After loss of consciousness, 1 mg/kg iv succinylcholine chloride was administered, and ventilation was assisted using a face mask and 100% oxygen. Ventilation was performed by anesthesia residents with more than 2 years' experience in the position. One minute after the injection of succinylcholine, an electrical stimulus was applied bilaterally for 5 seconds at the minimal stimulus intensity by a trained psychiatrist using an ECT stimulator.

After the return of spontaneous breathing, in addition to the standard monitoring, all patients were monitored again with microstream $EtCO_2$ monitoring. All parameters measured by $EtCO_2$ monitoring (IPI, SpO_2, $EtCO_2$, RR, PR) and also Modified Aldrete Score (MAS) (Table 2)[8] were recorded during the first 5 minutes immediately after neuromuscular blockade recovery which was evaluated by return of spontaneous respiration and body movement, and the first 10 minutes in the post-anesthesia care unit (PACU) stay, at one minute intervals. Any interventions to improve respiratory status such as supplemental oxygen, mask ventilation, jaw-thrust maneuver to open the airway, and any complications such as apnea, bradypnoea, hypopnea, tachypnoea and hypercapnia etc. were recorded during these periods.

Table 2. Modified Aldrete Score[8]

Criteria	Characteristics	Points
Activity	Able to move 4 extremities	2
	Able to move 2 extremities	1
	Unable to move extremities	0
Respiration	Able to breathe deeply and cough freely	2
	Dyspnea or limited breathing	1
	Apneic	0
Circulation	BP +/- 20% of pre-anesthetic level	2
	BP +/- 20-49% of pre-anesthetic level	1
	BP +/- 50% of pre-anesthetic level	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
Oxygen saturation	Able to maintain O2 saturation >92% on room air	2
	Needs oxygen to maintain O2 saturation >90%	1
	O2 saturation <90% even with supplemental oxygen	0

The descriptions of the respiratory events to be treated and the types of intervention were as follows:

Events:

- Apnea: Absence of an $EtCO_2$ waveform for 10 seconds
- Bradypnea: RR<8/min + $EtCO_2$ > 50 mmHg
- Hypopnea: RR<12/min + $EtCO_2$ < 30 mmHg
- Tachypnea: RR>25/min
- Hypercarbia: $EtCO_2$>50 mmHg
- SpO_2 < 93% (in operation room)
- SpO_2 < 90% (in PACU)
- Apnea episodes detected by clinical observation

Interventions:

- Jaw thrust maneuver (JT)
- Assisted mask ventilation (AMV)
- JT + AMV
- Supplemental oxygen

Statistical analysis

Statistical analysis of the study was performed using SPSS software (version 23; IBM, New York, USA). Data are expressed as mean (SD) and categorical variables as count (%). Statistical differences between groups were evaluated using independent sample t tests. Relationship between IPI and MAS or SpO_2 was tested with Pearson correlation test. The statistical significance value was accepted as $p<0.05$.

Results

Eighty-two patients who were in the first session of their ECT were evaluated for the study within six months. 18 patients were excluded from the study because of not meeting inclusion criteria or declined to participate. Thus, 64 patients (36 female, 28 male) in the ASA I-II status, aged 18-65 years (mean age 39.86 ± 12.76 years), were included in the study. Total 1088 IPI readings ranging from 1 to 10 were consecutively recorded for these 64 patients. Descriptive statistics of IPI values and corresponding physiological parameters were presented in table 3.

A total of 38 (59.3%) patients requiring intervention were documented in the first 5 minutes of the follow-up. Of these events 16 (42%) were for SpO_2 < 93, 14 (37%) were for IPI <6, 8 (21 %) were for other reasons.

Table 3. Mean physiological parameters corresponding to IPI values

IPI	n	SpO_2[a]	$EtCO_2$[a]	Respiratory rate[a]	Heart rate[a]
1	3	88.00±9.17	29.33±10.21	14.00±13.11	97.33±28.87
2	3	93.67±6.81	31.33±20.55	11.67±12.42	102.00±13.00
3	2	91.50±9.19	31.00±18.38	14.50±9.19	100.00±21.21
4	24	92.04±4.13	34.17±15.39	19.21±7.96	100.00±14.18
5	39	92.38±3.73	41.21±9.59	21.69±10.09	98.74±12.78
6	76	93.36±2.45	41.88±9.13	19.68±7.74	96.79±12.21
7	203	93.30±2.42	41.61±7.68	20.34±6.55	94.05±11.19
8	268	94.82±1.74	39.98±6.72	20.87±6.22	94.75±11.44
9	239	93.71±1.79	38.90±4.65	18.37±3.60	92.64±10.42
10	229	96.97±1.80	38.84±4.21	16.66±3.50	89.66±12.27

Abbreviations: IPI, integrated pulmonary index; SpO_2, peripheral oxygen saturation; $EtCO_2$, end-tidal carbondioxide.
[a]Values are given as mean±standard deviation.

Table 4. Comparison of the IPI, SpO_2, $EtCO_2$, RR, and HR values for the first five minutes between the intervention group and the non-intervention group

Parametres	Intervention group[a] n=38	Non-intervention group[a] n=26	p value
Baseline IPI	9.63±0.71	9.77±0.58	0.41
Baseline SpO_2	97.84±1.58	98.23±1.75	0.36
Baseline $EtCO_2$	35.63±4.37	35.38±4.57	0.95
Baseline RR	17.08±4.76	16.62±3.34	0.67
Baseline HR	84.05±15.70	80.73±15.62	0.40
1. min IPI	6.05± 1.94	7.81± 1.20	0.00*
1. min SpO_2	95.92± 3.23	97.12± 3.10	0.14
1. min $EtCO_2$	38.92±13.14	42.42±6.91	0.00*
1. min RR	14.95±9.03	18.92±7.27	0.07
1. min HR	99.61±16.19	93.38±13.63	0.11
2. min IPI	7.03±2.41	7.92±1.23	0.06
2. min SpO_2	95.26±4.48	96.46±2.92	0.23
2. min $EtCO_2$	39.13±3.67	42.96±5.61	0.18
2. min RR	17.37±8.54	20.77±6.51	0.91
2. min HR	99.26±14.26	91.12±21.14	0.70
3. min IPI	6.63±2.31	8.38±1.13	0.00*
3. min SpO_2	94.34±3.54	96.23±2.68	0.02*
3. min $EtCO_2$	40.32±12.72	40.12±6.96	0.94
3. min RR	18.79±8.71	20.19±5.76	0.47
3. min HR	98.32±14.24	93.92±12.73	0.21
4. min IPI	6.92±2.04	8.42±1.06	0.00*
4. min SpO_2	93.84±3.77	96.12±2.70	0.01*
4. min $EtCO_2$	40.68±8.94	40.77±7.07	0.96
4. min RR	19.89±6.25	19.85±5.14	0.97
4. min HR	97.66±13.42	93.19±11.34	0.17
5. min IPI	7.58±1.65	8.54±1.02	0.00*
5. min SpO_2	94.18±3.14	95. 38±2.49	0.10
5. min $EtCO_2$	40.79±6.80	40.08±6.51	0.67
5. min RR	20.00±5.45	19.81±4.29	0.88
5. min HR	97.18±12.21	94.00±10.91	0.29

Abbreviations: IPI, integrated pulmonary index; SpO_2, peripheral oxygen saturation; $EtCO_2$, end-tidal carbon dioxide; RR, respiratory rate; HR, heart rate.
[a]Values are given as mean±standard deviation.
**These values indicate statistical significance ($p<0.05$).*

The distribution of the IPI, SpO_2, $EtCO_2$, RR, and HR values for the first five minutes between the intervention group and the non-intervention group was shown in table 4. IPI values at 1, 3, 4 and 5 minutes were significantly lower in the intervention group (Figure 1). SpO_2 values were also significantly lower in the intervention group at 3 and 4 minutes, but all mean saturation percentages were greater than 94 for the first 5 minutes (Figure 2). At that period, mean $EtCO_2$ values were similar between the groups and were within the normal range. According to this table, SpO_2 or $EtCO_2$ alone cannot determine the need for intervention in the early recovery period as much as IPI. Modified Aldrete Scores were also similar between intervention groups.

During the follow-ups in the PACU, it was observed that 15 (23.4%) patients needed intervention in the first 10 minutes. Since the patients were classified as those with and without supplemental oxygen requirement in the PACU, IPI values were significantly lower in the group requiring supplemental oxygen at 1, 2, 4, and 6 minutes. However, the mean IPI values were 6 and above at all times, except for 1 minute (Table 5).

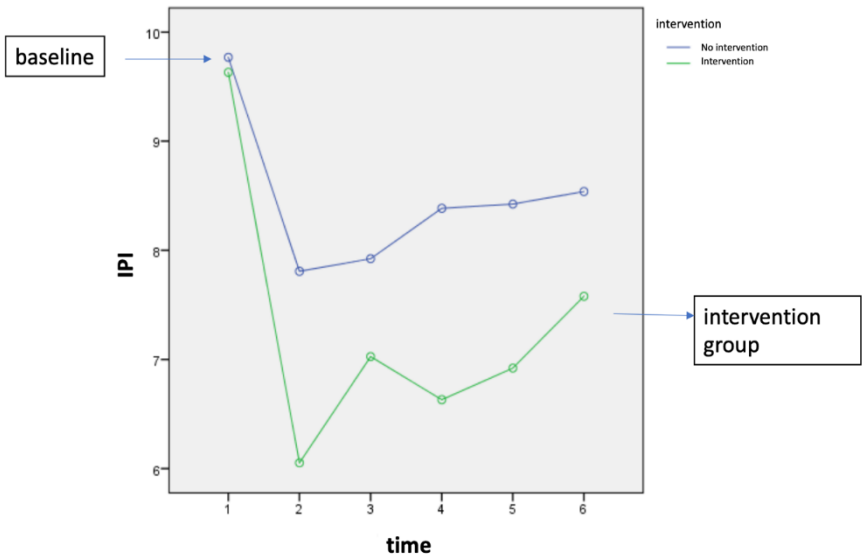

Figure 1. Time distribution of IPI values between the intervention group and the non-intervention group.

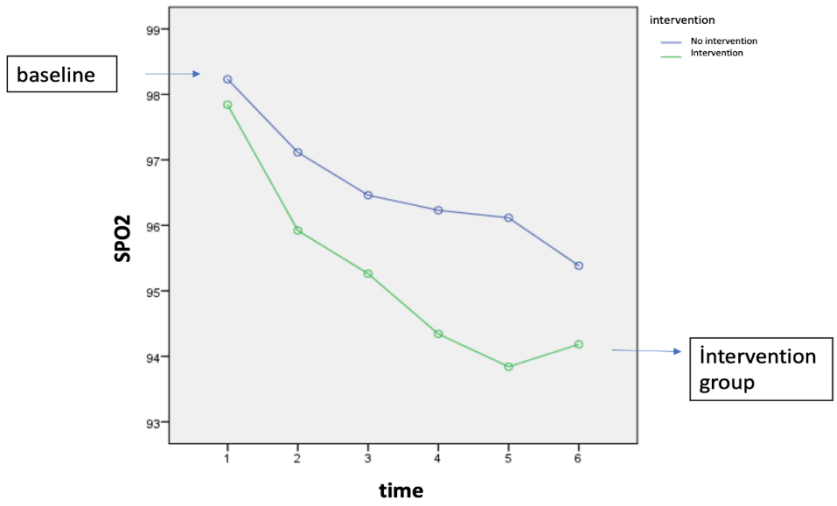

Figure 2. Time distribution of SpO_2 values between the intervention group and the non-intervention group.

When the correlation between IPI and SpO_2 or MAS was evaluated, there was a significant correlation between IPI and SpO_2 in the first 5 minutes of recovery, but there was no correlationbetween IPI and MAS except for 5 minutes (Table 6). In PACU, there was a significant correlation between IPI and SpO_2 or MAS at all follow-up periods (Table 7). The overall incidence of respiratory complications is summarized in table 8.

Discussion

In this prospective observational study, in patients requiring respiratory intervention during the recovery period after ECT, integrated pulmonary index monitoring was found to be an accurate and easier indicator than SpO_2 or $EtCO_2$ monitoring alone. While there was no significant difference or

abnormality in $EtCO_2$ and SpO_2 in patients who needed intervention, IPI levels were found to be significantly lower. Moreover, in the PACU, the IPI was measured low in patients who needed supplement oxygen in the early post-anesthesia period. While there was no correlation between IPI and MAS in the first 5 minutes of recovery, there was a significant correlation between IPI and MAS in follow-ups in PACU. It was detected that this significant correlation also existed between IPI and SpO_2.

Activation of the autonomic nervous system and related hemodynamic changes and alterations in cerebrovascular dynamics as a physiological response to ECT, as well as complications related to the respiratory system, are common problems during anesthesia management.[7] Although the restoration of the respiratory system during ECT is relatively short, careful monitoring of all systems is vital during this process, which results in the activation of many physiologic systems in the body. Capnography can be used to determine the adequacy of ventilation in mechanically ventilated or unconscious patients, or in patients undergoing procedural sedation.[9] The presence of a normal waveform indicates a patent airway and spontaneous breathing, and normal $EtCO_2$ levels (35 to 45 mmHg) indicate adequate ventilation and perfusion.[10] Several systematic reviews and meta-analyses show that early intervention through capnography monitoring reduces the incidence of adverse respiratory events such as hypoxemia.[11-13] As a consequence, proper monitoring of the respiratory system can reduce respiratory complications and furthermore, it has been reported that $EtCO_2$ monitoring can stabilize hemodynamic changes during ECT and it is thought to be useful for safe and effective anesthesia management of patients undergoing ECT.[5]

Table 5. Relationship between supplement oxygen requirement and IPI at PACU

IPI	Supplement Oxygen requirement[a]	No supplement Oxygen requirement[a]	p value
1. min at PACU	9(14%) 5.44±1.01	55(86%) 7.89±1.67	0.00*
2. min at PACU	7(11%) 6.00±0.81	57(89%) 8.25±1.25	0.00*
3. min at PACU	4(6%) 8.00±1.41	60(94%) 8.23±1.22	0.71
4. min at PACU	6(9%) 7.67±0.51	58(91%) 8.33±1.17	0.02*
5. min at PACU	2(3%) 8.00±0.00	62(97%) 8.19±1.11	0.17
6. min at PACU	9(14%) 7.00±0.70	55(86%) 8.62±1.06	0.00*
7. min at PACU	4(6%) 9.00±0.00	60(94%) 8.53±1.29	0.00*
8. min at PACU	3(5%) 8.33±1.15	61(95%) 8.57±1.00	0.68
9. min at PACU	1(2%) 8.00±0.00	63(98%) 8.52±1.20	0.66
10. min at PACU	1(2%) 7.00±0.00	63(98%) 8.75±0.99	0.08

Abbreviations: IPI, integrated pulmonary index; PACU, post-anesthesia care unit.
[a]*Values are given as n(%) and mean±standard deviation.*

Table 6. Correlation of IPIs with SPO_2 and MAS at the first 5 minutes after recovery

Time	Correlation coefficient (r) IPI ~ SPO2	Correlation coefficient (r) IPI ~ MAS
1. min	0.13	0.04
2. min	0.35**	0.28*
3. min	0.35**	0.23
4. min	0.66**	0.20
5. min	0.50**	0.37**

Abbreviations: IPI, integrated pulmonary index; SpO_2, peripheral oxygen saturation; MAS, Modified Aldrete Score
**Correlation is significant at the 0.05 level (2-tailed).*
***Correlation is significant at the 0.01 level (2-tailed).*

Table 7. Correlation of IPIs with SPO_2 and MAS at PACU

Time	Correlation coefficient (r) IPI ~ SPO2	Correlation coefficient (r) IPI ~ MAS
1. min at PACU	0.62**	0.44**
2. min at PACU	0.72**	0.53**
3. min at PACU	0.31*	0.28*
4. min at PACU	0.62**	0.31*
5. min at PACU	0.60**	0.33**
6. min at PACU	0.52**	0.30*
7. min at PACU	0.42**	0.38**
8. min at PACU	0.14	0.33**
9. min at PACU	0.48**	0.43**
10. min at PACU	0.39**	0.18

Abbreviations: IPI, integrated pulmonary index; PACU, post-anesthesia care unit; SpO_2, peripheral oxygen saturation; MAS, Modified Aldrete Score
**Correlation is significant at the 0.05 level (2-tailed).*

Moreover, in a trial conducted in the pediatric population, it was reported that $EtCO_2$ monitoring was more sensitive than peripheral oxygen saturation monitoring in determining the need for respiratory support in the seizure and postictal period, and capnography evaluation showed a high correlation with blood gases.[14]

In ECT procedures, airway management is maintained with mask ventilation instead of endotracheal intubation unless there is a risk of aspiration. However, there is always a risk of ineffective ventilation during mask ventilation, particularly in patients with obesity, beard or obstructive sleep apnea disorder, despite appropriate ventilation technique.[15]

Table 8. Incidence of overall respiratory complications

Complication	n (%)
Bradypnea	5 (7.8%)
Hypopnea	9 (14.1%)
Tachypnea	28 (43.8%)
Hypercarbia	18 (28.1%)
Apnea	12 (18.7%)

On the other hand, monitorization of end-tidal CO_2 is important in ECT, because the increased carbon dioxide tension due to apnea episode immediately after the electrical stimulation, accelerated cerebral metabolism during the electrically induced seizure, or muscle fasciculations caused by succinylcholine may contribute the adverse respiratory outcomes.[5]

Therefore, instead of evaluating respiratory functions only with SpO_2 during recovery from anesthesia, following patients with capnography improves patient outcomes in ECT procedures. In addition, to evaluate the respiratory status of the patient, instead of interpreting the individual parameters such as respiratory rate, SpO_2 or $EtCO_2$ level on the monitor, ensuring this aim with a single variable like IPI, which is a newly developed index for non-invasive respiratory monitoring, provides the chance for faster and timely intervention. In this study, SpO_2 or $EtCO_2$ monitoring alone did not always guide the group in need of respiratory intervention. IPI monitoring appears to be a simple and rapid trigger for response to respiratory adverse events.

In the current study, statistical analysis have shown that, among the physiological parameters of patients, $EtCO_2$, RR and HR are mostly unchanged at different IPI values or respiratory intervention groups. These findings revealed that the IPI algorithm alone could drive the intervention requirement. Similarly, other previous studies have reported that IPI correlates with the respiratory physiological parameters of patients undergoing procedural sedation.[16,17]

In a study in which IPI was used to evaluate the respiratory status of postoperative patients, it was reported that IPI monitoring increased the number of interventions to improve the patients' respiratory conditions compared to standard clinical care.[18] In the present study, although the number of patients requiring intervention in the PACU was low, IPI was significantly lower in patients requiring supplement oxygen.

There are some studies reporting that the incidence of adverse respiratory events for 24 hours is 46-47% in patients followed up with capnograph in the postoperative period.[18,19] However, these studies were conducted in patients receiving general anesthesia using long-acting opioids. The ECT procedure is accompanied by a superficial and short-term anesthesia application, and opioids are often not needed. Therefore, the respiratory system is restored also in a short period. In this study, the incidence of apnea, hypercarbia, and hypopnea in the early recovery period, within the first 5 minutes of the postictal period, was found to be 18.7%, 28.1%, 14.1%, respectively, and none of the patients developed late-stage respiratory depression, despite the fact that their clinical relevance is uncertain. The PACU course progressed smoothly in almost all patients. Except for the first 2 minutes, IPI and MAS levels were always high in PACU. For this reason, we are in the opinion that the IPI monitoring will not contribute significantly to the care of patients with ECT in the late period. Nevertheless, significant correlations were found between IPI and MAS or SpO_2 during follow-up in PACU and further, monitoring the respiratory system with more than one method does not affect the incidence of adverse respiratory events and improves exactly patient safety. Similarly, in a study conducted in high-risk patients receiving general anesthesia, it was shown that IPI can predict the occurrence of respiratory complications in the PACU. For this reason, it has been reported that it may be useful for respiratory monitoring in PACUs and intensive care units after general anesthesia.[20]

This study had some limitations. First, since we did not have comparable arms, such as the IPI monitor arm and the standard monitor arm, assured comparison of events occurrences and interventions was not completely achieved. Second, our relatively small sample size was insufficient to identify additional risk factors for adverse respiratory events. Third, study was not blinded. Although most of the care giver were not accustomed to IPI monitor, anesthesiologists and PACU staff were not blinded of all parameters (IPI, $EtCO_2$, RR) displayed by $EtCO_2$ monitoring. This may have caused bias. Finally, we could not determine threshold values for IPI because the follow-up period was short and patients were relatively free of the risk of residual effects of anesthesia. On the other hand, it was valuable that we evaluated interventions by eliminating opioid use, which is a major risk factor for respiratory adverse events.

Conclusion

Although electrically induced seizure in ECT is self-limiting and adverse outcomes are uncommon, application of an end-tidal carbon dioxide monitoring is considered beneficial for safe and effective anesthesia management for patients undergoing ECT. The objective of the IPI algorithm is to simplify patient monitoring through real-time analysis of $EtCO_2$, RR, SpO_2, and PR, providing a single number that accurately indicates a patient's respiratory status in a simple and objective manner. The IPI monitorization can be useful over the standard

monitorization in terms of better evaluation of respiratory status. On the other hand, the presented data in this study are limited, thus, prospective comprehensive large sample sized studies are required to investigate the value of routine use of IPI monitoring during ECT.

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
This study was approved by the Institutional Investigation and Ethics Committee with the approval number of 12/90 in July 2019 and conducted at Cukurova University in Turkey.

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DIFFICULT AIRWAY ANTHROPOMETRIC MEASUREMENTS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA ACCORDING TO SLEEP ENDOSCOPY SCORES

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Abstract

Aim: The aim of the study was to determine the measures to evaluate difficult intubation and predictors of intubation difficulties in the preoperative period in patients undergoing obstructive sleep apnea syndrome (OSAS) surgery. With these measurements, both the modified Cormack Lehane score and obstructions during sleep endoscopy were evaluated.

Methods: The study included 40 patients who presented at the outpatient clinic with the complaint of snoring, underwent polysomnography, and were diagnosed with OSAS between August 2018 and December 2019. Measurements were taken of the modified Mallampati Index, mouth opening, thyromental distance, and sternomental distance. The modified Cormack Lehane scoring system was applied after anesthesia induction.

Results: A statistically significant correlation was observed between thyromental distance and the Modified Cormack Lehane Scoring-system (MCLS) (p= 0.017) and between intubation time and MCLS (p= 0.012). As MCLS increased, the average intubation time increased. A statistically significant correlation was observed between external compression and MCLS (p= 0.001) and between the number of intubation trials and MCLS (p= 0.035). A positive correlation was found between MCLS and the desaturation index (p= 0.035, r= 0.343) and between the MCLS and the hypopnea index (p= 0.031, r= 0.342)

Conclusions: There was found to be interdependence with the measurements related to difficult intubation according to both the sleep position and the apnea hypopnea index and hypopnea index.

Keywords: *Sleep apnea, difficult intubation, sleep endoscopy, thyromental distance, modified Cormack Lehane scoring system, airway management*

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a common disease that affects all age groups. Patients with OSAS are prone to obstruction of the upper airway during sleep, which causes them to wake because of the extra breathing effort required to restore the airway which has collapsed due to apnea. These events repeat at a recurring frequency throughout the sleep time. The same events occur when sedative and anesthetic agents suppress consciousness. Both functional and anatomic abnormalities may play a role in the pathogenesis of disorders in patients with OSAS syndrome[1-3].

Anesthesia management is difficult in patients with OSAS syndrome due to cardiac arrhythmia, myocardial ischemia, cerebrovascular insufficiency and intracranial hypertension, and difficult intubation is an important problem in the induction period of general anesthesia. Studies on the theoretical explanation of the relationship between OSAS and difficult intubation are not common, and those which have been published on this subject in literature have generally been retrospective[1-3]. The Modified Mallampati score (MMS) is an important measurement for the evaluation of anatomic variations of the upper airway. The MMS is an effective method in evaluating tongue root and narrow mouth opening, i.e. the oropharynx [4]. The relationship between a high MMS and difficult intubation in patients with OSAS has been proven in studies[5]. The Stop-Bang score in patients with OSAS, the Modified Cormack and Lehane scoring system (MCLS), and thyromental and sternomental distances have also been associated with difficult intubation[3].

Identification and diagnosis of difficult intubation in the preoperative period reduces complications in OSAS patients. The aim of this study was to evaluate predictive factors for difficult airway in OSAS patients (Han's scoring, modified Mallampati Index, MCLS, neck circumference, thyromental distance, sternomental distance, upper lip bite test) together with sleep endoscopy findings and polysomnography data.

Materials and Methods

Approval for the study was granted by the Local Ethics Committee (protocol no: 298; dated: 25/07/2018). All the study subjects provided informed consent for voluntary participation in accordance with the Helsinki Declaration. This prospective study was conducted with OSAS patients who were planned to undergo surgery between August 2018 and December 2019.

Study Population

Patients aged >18 years, who were referred to the Sleep Disorders Clinic of the Otolaryngology Department and underwent diagnostic polysomnography (PSG) for any reason between August 2018 and December 2019, were reviewed for participation in the study. A total of 40 patients who were scheduled to undergo surgery were included in the study for analysis. Neck circumference (cm) was measured with a flexible tape-measure, horizontally at the upper margin of the laryngeal prominence with the patient positioned with head erect and eyes facing forward. Height and weight were measured with the subject without shoes or heavy outer garments. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared.

In all the patients, the MMS was determined as the measurement of mouth opening. The distance between the thyroid notch and mentum was recorded as the thyromental distance, and the distance between the sternal notch and the mentum as the sternomental distance. Patients were asked to complete the STOP-BANG questionnaire. STOP-BANG stands for S – history of snoring, T – history of tiredness, O – observed apneas during sleep, P – blood pressure (hypertension), B – body mass index (BMI) >35 kg/m2, A – age >50 years, N – neck circumference >40 cm, G – gender is male.

Each positive response is given one point and the total points provide the total score. Patients were evaluated with drug-induced sleep endoscopy (DISE) before the operation. MCLS was applied after anesthesia induction[6].

Modified Cormack and Lehane scoring system (MCLS)[6]

Grade 1: Most of the glottic opening can be seen
Grade 2a: Partial view of the vocal cords
Grade 2b: Only the arytenoids and epiglottis seen.
Grade 3: Only the epiglottis is visible
Grade 4: Neither the glottis nor the epiglottis can be seen

Han's mask ventilation grading scale made[7]

Grade1: Ventilated by mask
Grade 2: Ventilated by mask plus oral airway adjuvant ± muscle relaxant
Grade 3: Difficult to mask ventilate despite above, inadequate or unstable, requiring two providers
Grade 4: Unable to mask ventilate with or without the use of muscle relaxants

Modified Mallampati scoring

The airway is classified according to the structures seen, as follows: class I, soft palate, fauces, uvula, pillars; class II, soft palate, fauces, uvula; class III, soft palate, base of uvula; class IV, soft palate not visible at all (Modified Mallampati)[8].

Measurement of mouth opening

Mouth opening was measured by asking the subject to open their mouth as wide as possible, while the examiner measured the maximum distance from the incisal edge of the maxillary central incisors to the incisal edge of the mandibular central incisors at the midline[9].

Measurement of sternomental thyromental distance

During the airway assessment, sternomental distance was measured as the straight distance between the upper border of the manubrium sterni and the bony point of the mentum with the head in full extension and the mouth closed[10].
The height was measured between the anterior border of the thyroid cartilage and the anterior border of the mentum, with the head in a neutral position and the mouth closed[11].

Upper lip bite test

Classification of the jaw protrusion was made with the upper lip bite test. Patients are asked to bite their upper lip with the lower incisors and the classification is applied as Grade I: lower incisors can bite the upper lip above the vermilion line; Grade II: lower incisors can bite the upper lip below the vermilion line; Grade III: lower incisors cannot bite the upper lip. Grades I and II predict easy intubation, while Grade III predicts difficult intubation[12].

Jaw protrusion

Temporomandibular joint mobility is assessed by asking the patient to open the mouth fully and then place their lower incisors as far forward as possible (subluxation).

A: Lower teeth can be placed in front of the upper teeth
B: Lower teeth can be placed in line with the upper teeth
C: Lower teeth cannot be placed in line with the upper teeth

The laryngoscope used during intubation was recorded and whether or not videolaryngoscope, Gem elastic bougie, and external compression were used.

Sleep Endoscopy Protocol

After the patients were taken to the operating room, an intravenous (i.v.) 0.9% NaCl infusion was started at the rate of 3 ml/kg/h. During the procedure, patients were given nasal O2 (2 L / min), and electrocardiography (ECG), pulse oximetry, and non-invasive blood pressure monitoring were performed. The bispectral index (BIS), electroencephalography (EEG) electrodes (BIS QUATRO; Covidienlc, 15 Hampshire Street, Mansfield, MA, USA) were placed on the patient's forehead for monitorization. The BIS recording time was set to 15 seconds. For sedation, an iv propofol infusion was started at a dose of 100 µg / kg / min. The propofol infusion was continued until the patient became unconscious and snoring started, then the velopharyngeal region obstruction was evaluated. The BIS value was evaluated between 50-60 (deep sedation) with flexible nasopharyngo-laryngoscope and obstruction areas of the patients were evaluated by the otolaryngologist (Bilal N.). The vellum, oropharynx, tongue, epiglottic regions were evaluated according to the VOTE classification as 0: no obstruction, 1: partial obstruction, 2: full obstruction[13,14].
Patients were excluded from the study if they had American Society of Anesthesiologists (ASA) physical classification of ≥3, food allergies such as xylocaine, propofol, eggs, beans, milk, moderate or severe chronic obstructive pulmonary disease, epilepsy or cerebrovascular disease, or were aged <18 years.

Sleep Studies and Polysomnography Scoring

The sleep of the patients overnight was evaluated with an Embla® S4500 PSG amplifier (Flaga, Reykjavik, Iceland). A total of 21 signals were recorded with the PSG device, respiratory signals, electroencephalography (EEG), electrocardiography (ECG), electro-oculography (EOG), electromyography (EMG), snoring and patient position. Obstructive hypopnea is defined as a decrease in air flow of at least 30% lasting at least 10 seconds and a 3% decrease in accompanying arousal in SaO_2. Apnea is defined as a minimum 90% reduction in airflow amplitude and respiratory events lasting at least 10 seconds[15].
According to the International Classification of Sleep Diseases (ICSD-3), the diagnosis of OSAS was made from the determination of one or more of the diagnostic criteria of apnea hypopnea index (AHI) > 5 from the result of PSG report and snoring, witnessed apnea or daytime sleepiness [10]. According to AHI, the severity of OSAS was evaluated as AHI of 5-14.9 points: mild, AHI of 15-29.9 points: medium, and AHI of ≥30 points: severe. Those with AHI <5 were considered as the control group.

Statistical Evaluation

Data obtained in the study were analyzed statistically using IBM SPSS ver. 22 and R 3.3.2. software. Conformity of the data to normal distribution was examined with the Shapiro-Wilk test. Comparisons of 3 or more groups of variables with normal distribution were made with One Way Anova, and post hoc tests of Tukey HSD and Tamhane T2. In the comparisons of 3 or more groups of non-normally distributed variables, the Kruskal Wallis H test was applied. The Exact test was applied to determine relationships between categorical variables. Correlations between quantitative variables were investigated using the Pearson correlation test. Statistical significance was accepted as $p < 0.05$.

Results

Evaluation was made of a total of 40 patients comprising 31 males and 9 females with a mean age of 41.2± 9.9 years. The demographic data of the patients are given in Table 1.

Table 1. Demographic data of patients

Gender	Male Female	*n(%)*	31(77,5) 9(22,5)
Age BMI		*Mean±SD*	41,2±9,9 29,6±3,7
STOP BANG	Low High	*n(%)*	7(17,5) 33(82,5)
Stop bang scala AHI		*Mean±SD*	4,35±0,7 20,0±4,8
HI		*Median±SD*	6,07±5,43
AI Total sleep time Sleep eficiency		*Mean±SD*	13,7±9,8 384,4±80,7 89,3±6,6
Desaturation index		*Median±SD*	10,9±10,3
Minimum oxygen saturation Mean O_2 saturation Mean heart rate		*Mean±SD*	85,6±5,9 95,5±2,1 68,0±9,2
Arousal index		*Median±SD*	21,5±19,2
Propofol Remifentanyl Intubation time		*Mean±SD*	182,0±43,28 107,0±38,02 57,9±54,8

The surgeries performed for patients undergoing sleep endoscopy were anterior palatoplasty in 5 (12.5%) cases, anterior palatoplasty + lateral palatoplasty in 3 (7.5%), anterior palatoplasty + lower concha radiofrequency in 1 (2.5%), open approach septorhinoplasty in 5 (12.5%), expansion sphincter pharyngoplasty in 10 (25%), lower turbinate radiofrequency in 1 (2.5%), and septoplasty in 14 (35%).

The average STOP-BANG score was calculated as 4.35 ± 0.5, with distribution as 2 points in 4 patients, 3 points in 3 patients, 4 points in 12, 5 points in 17, and 6 points in 4.

Postoperative complications were determined as desaturation in 5 patients, of which 1 was applied nasal airway due to the development of apneas during awakening. CPAP was performed in one patient due to desaturation, and then followed up in the intensive care unit (ICU). Tachycardia developed in 5 patients. One patient had elevated blood pressure and increased lactate level, so was followed up in the ICU. Blood pressure recovered with artery therapy. One patient developed suspected myocardial infarction (MI) and was followed up, but there was no increase in cardiac enzymes. Bleeding developed in 1 patient.

The intubation of 29 (72.5%) patients was completed at the first attempt, in 8 (20%) at the second attempt and in 3 (7.5%) at the third attempt.

There was no statistically significant difference between MCLS and BMI (p = 0.373). As the MCLS increased, the BMI average increased. There was no statistically significant difference between MCLS scoring and neck circumference (p = 0.174). As the MCLS increased, the average neck circumference increased. A statistically significant difference was observed in the relationship between thyromental distance and MCLS (p = 0.047). A statistically significant difference was observed between those intubated with gum elastic bougie and MCLS (p = 0.001). A statistically significant difference was observed in the relationship between intubation time and MCLS (p = 0.007). As MCLS increased, the average intubation time increased. A statistically significant difference was observed between external compression and MCLS (p < 0.001). As MCLS increased, the number of external compressions increased.

Table 2. Evaluation of patients' measurements according to modified Cormack and Lehane scoring system

		1	2A	2B	3	4	p
BMI, Median (Q1-Q3)		25,90 (24,10-28,70)	28,40 (27,30-31,60)	29,80 (28,50-31,00)	30,30 (28,70-34,50)	30,15 (27,80-32,70)	0.373
ASA	2,0	3,00(60,00)	5,00(83,33)		5,00(83,33)	15,00(83,33)	0.674
	3,0	2,00(40,00)	1,00(16,67)		1,00(16,67)	3,00(16,67)	
Modified mallampati score	1,0	1,00(20,00)	1,00(16,67)		0,00(0,00)	0,00(0,00)	0.519
	2,0	1,00(20,00)	2,00(33,33)		2,00(33,33)	5,00(27,78)	
	3,0	3,00(60,00)	2,00(33,33)		3,00(50,00)	12,00(66,67)	
	4,0	0,00(0,00)	1,00(16,67)		1,00(16,67)	1,00(5,56)	
Neck Circumference Median (Q1-Q3)		39,00 (36,00-41,00)	41,00 (37,00-41,00)	38,75 (37,50-41,00)	40,50 (38,00-43,00)	42,50 (40,00-43,00)	0.174
Thyromental Distance Median (Q1-Q3)		10,00 (10,00-10,00)[d]	9,00 (8,00-10,00)	9,00 (8,00-9,00)	7,50 (6,00-9,00)[a]	9,00 (8,00-10,00)	0.047
Sternomental Distance Median (Q1-Q3)		18,00 (16,00-18,50)	17,00 (15,00-17,00)	16,50 (16,00-17,00)	16,00 (16,00-16,00)	16,00 (15,00-19,00)	0.865
Mouth Opening Median (Q1-Q3)		7,00 (6,00-7,00)	7,00 (6,50-7,00)	6,75 (6,00-7,00)	6,50 (6,00-7,00)	7,00 (6,00-7,00)	0.969
Upper Lip Bite Test	0,0	0,00(0,00)	0,00(0,00)		0,00(0,00)	1,00(5,56)	1.00
	1,0	5,00(100,00)	6,00(100,00)		6,00(100,00)	17,00(94,44)	
Jaw protrusion	A	5,00(100,00)	6,00(100,00)		6,00(100,00)	17,00(94,44)	1.00
	B	0,00(0,00)	0,00(0,00)		0,00(0,00)	1,00(5,56)	
STOP BANG score, Median (Q1-Q3)		4,00 (4,00-5,00)	4,00 (4,00-5,00)	5,00 (4,00-5,00)	4,50 (3,00-5,00)	5,00 (4,00-5,00)	0.922
Laryngoscope Type	Mac.	2,00(40,00)	2,00(33,33)		0,00(0,00)	8,00(44,44)	1.00
	Mil.	3,00(60,00)	4,00(66,67)		6,00(100,00)	10,00(55,56)	
Video-Laryngoscope	,0	3,00(60,00)	2,00(33,33)		3,00(50,00)	9,00(50,00)	0.327
	1,0	2,00(40,00)	4,00(66,67)		3,00(50,00)	9,00(50,00)	
Gum elastic bougie	,0	1,00(20,00)	4,00(66,67)		0,00(0,00)	1,00(5,56)	p<0.001*
	1,0	4,00(80,00)	2,00(33,33)		6,00(100,00)	17,00(94,44)	
Intubation time (sec) Median (Q1-Q3)		15,00 (14,00-30,00)[e]	35,00 (15,00-35,00)[e]	26,00 (17,00-125,00)[e]	20,00 (15,00-25,00)[e]	65,00 (35,00-140,0)[a,b,c,d]	0.007*
External compression	,0	1,00(20,00)	5,00(83,33)		0,00(0,00)	1,00(5,56)	p<0.001*
	1,0	4,00(80,00)	1,00(16,67)		6,00(100,00)	17,00(94,44)	
Number of attempts	1,0	5,00(100,00)	5,00(83,33)		6,00(100,00)	8,00(44,44)	0.080
	2,0	0,00(0,00)	1,00(16,67)		0,00(0,00)	7,00(38,89)	
	3,0	0,00(0,00)	0,00(0,00)		0,00(0,00)	3,00(16,67)	

A statistically significant difference was observed between the number of attempts and MCLS (p = 0.080).As MCLS increased, the number of attempts increased (Table 2). When Han's mask was evaluated according to the ventilation grading scale, a statistically significant difference was observed between BMI, intubation time and number of attempts, respectively (p = 0.056, p = 0.011, p = 0.035). As the Han mask ventilation grading scale increased, the number of attempts, intubation time, and BMI increased (Table 3). When the findings of sleep endoscopy were examined, superior thyroid notch (Adam's apple) was observed to be statistically significant in patients with complete collapse in the vellum. Neck circumference was 41cm (39.0-43.0) in patients with complete collapse. In those with partial collapse, the average neck circumference was calculated to be 39.3 cm (34.5-41.8). Neck circumference in patients without collapse was calculated as mean 33.5 cm (33.5-33.5). Thyromental distance was measured as 9 cm (8.0-10.0) in patients with complete collapse, and 8.5 cm (7.5-10.5) in those with partial collapse, and 6 cm (6.0-6.0) in those without collapse.

Table 3. Evaluation of patients' measurements according to Han's mask ventilation grading scale scoring

			Han's mask ventilation scale scoring						p
			1.0		2.0		3.0		
BMI[a]		Median (Q1-Q3)	28,8 (25,4-30,5)		28,6 (27,5-32,0)		32,0 (29,5-33,9)		0.056
ASA	2.0	n(%)	10	83.3	14	87.5	9	75.0	0.869
	3.0		2	16.7	2	12.5	3	25.0	
Modified mallampati score	1.0	n(%)	2	16.7	1	6.3	1	8.3	0.830
	2.0		3	25.0	5	31.3	3	25.0	
	3.0		7	58.3	9	56.3	6	50.0	
	4.0		0	0.0	1	6.3	2	16.7	
Neck Circumference[a]		Median (Q1-Q3)	39,0 (36,8-42,0)		41,0 (37,5-42,0)		43,0 (40,5-44,0)		0.051
Thyromental Distance[a]		Median (Q1-Q3)	9,0 (7,0-10,0)		9,0 (8,3-10,0)		9,0 (8,0-10,0)		0.946
Sternomental Distance[a]		Median (Q1-Q3)	16,0 (15,0-18,3)		16,0 (16,0-17,5)		16,5 (15,5-18,0)		0.871
Mouth Opening[a]		Median (Q1-Q3)	7,0 (6,0-7,0)		7,0 (6,3-7,0)		6,8 (6,0-7,0)		0.955
Upper Lip Bite Test	.0	n(%)	0	0.0	1	6.3	0	0.0	1.00
	1.0		12	100.0	15	93.8	12	100.0	
Jaw protrusion	A	n(%)	12	100.0	15	93.8	12	100.0	1.00
	B		0	0.0	1	6.3	0	0.0	
STOP-BANG Score	2.0	n(%)	2	16.7	2	12.5	0	0.0	0.144
	3.0		2	16.7	0	0.0	1	8.3	
	4.0		3	25.0	6	37.5	3	25.0	
	5.0		2	16.7	8	50.0	7	58.3	
	6.0		3	25.0	0	0.0	1	8.3	
Laryngoscope Type	Miller	n(%)	5		8		2		0.218
	Macintosh		7		8		10		
Video-Laryngoscope	.0	n(%)	7	58.3	11	68.8	3	25.0	0.085
	1.0		5	41.7	5	31.3	9	75.0	
Gum elestic bougie	.0	n(%)	4	33.3	3	18.8	4	33.3	0.737
	1.0		8	66.7	13	81.3	8	66.7	
Intubation time(sec)		Median (Q1-Q3)	22,5 (15,0-35,0)		33,0 (22,5-50,0)		117,5 (63,0-145,0)		0.011
External pressure	.0	n(%)	6	50.0	4	25.0	2	16.7	0.213
	1.0		6	50.0	12	75.0	10	83.3	
Number of attempts	1.0	n(%)	11	91.7	12	75.0	6	50.0	0.035
	2.0		1	8.3	4	25.0	3	25.0	
	3.0		0	0.0	0	0.0	3	25.0	

Sternomental distance was measured as 7 cm (7.0-7.0) in those with full collapse, 6.8 (6.0-7.0) cm in those with partial collapse, and 6.0 cm (6.0-6.0) in those without collapse evaluated as (Table 4).

When evaluated with sleep endoscopy at the level of epiglottis, tongue root, and oropharynx, no statistically significant difference was determined in the difficult airway predictive values (modified Mallampati, HAN score, CMLS, neck circumference, thyromental distance, sternomental distance, upper lip bite test).

A positive correlation was found between MCLS and the desaturation index ($p = 0.035$, $r = 0.343$) (Figure 1).

A positive correlation was found between MCLS and the hypopnea index ($p = 0.031$, $r = 0.342$) (Figure 2).

Table 4. Evaluation of difficult intubation measurements according to sleep endoscopy findings

			Vellum						P
			No Collapse		Partial Collapse		Fully Collapse		
Modified Mallampati	1,0	n(%)	0	0,0	2	25,0	2	6,5	0,228
	2,0		1	100,0	0	0,0	10	32,3	
	3,0		0	0,0	6	75,0	16	51,6	
	4,0		0	0,0	0	0,0	3	9,7	
Han's scoring	1,0	n(%)	1	100,0	4	50,0	7	22,6	0,207
	2,0		0	0,0	3	37,5	13	41,9	
	3,0		0	0,0	1	12,5	11	35,5	
Adam's apple protrusion	No	n(%)	1	100,0	2	25,0	21	67,7	0,042
	Yes		0	0,0	6	75,0	10	32,3	
Modified Cormack Lehane Scoring-system	1,0	n(%)	0	0,0	1	12,5	4	12,9	0.154
	2A		0	0,0	3	37,5	2	6,5	
	2B		0	0,0	1	12,5	5	16,1	
	3,0		1	100,0	1	12,5	4	12,9	
	4,0		0	0,0	2	25,0	16	51,6	
Neck Circumference		Median (Q1-Q3)	33,50 (33,50-33,50)		39,3 (34,5-41,8)		41,0 (39,0-43,0)		0,173
Thyromental Distance		Median (Q1-Q3)	6,00 (6,00-6,00)		8,5 (7,5-10,5)		9,0 (8,0-10,0)		0,790
Sternomental Distance		Median (Q1-Q3)	14,00 (14,00-14,00)		16,5 (15,0-17,5)		16,0 (16,0-18,0)		0,620
Mouth Opening		Median (Q1-Q3)	6,00 (6,00-6,00)		6,8 (6,0-7,0)		7,0 (6,0-7,0)		0,588

Figure 1. Positive correlation between Cormack Lehane score and desaturation index

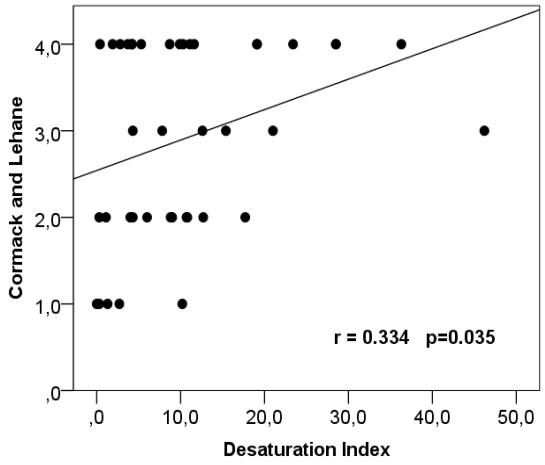
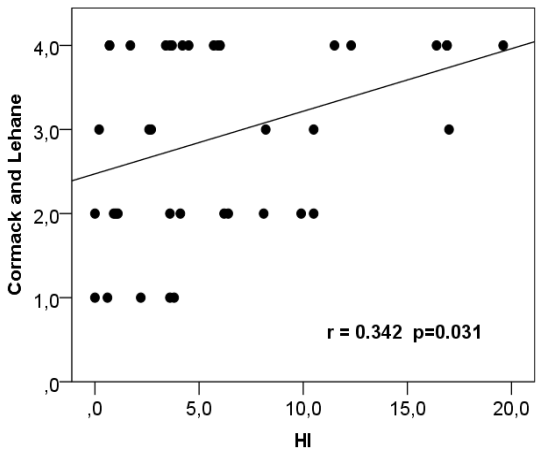


Figure 2. Cormack Lehane score correlation curve of hypopnea index



Discussion

The results of this study demonstrated that the statistical significance of the MCLS used for difficult intubation with thyromental distance, intubation time, number of attempts and external compression is an important criterion in the management of OSAS anesthesia.

The Cormack-Lehane and the Modified Cormack -Lehane scoring systems were developed for the evaluation of the hypopharynx using direct laryngoscopy[16-18]. The grading of these scoring systems is based on the extent to which hypopharyngeal obstruction affects the visualization of fixed laryngeal structures. The aim of this study was to determine whether a similar grading system could be used during DISE for the assessment of hypopharyngeal obstruction in patients with OSAS.

OSAS concerns most branches as well as anesthetists. In the preoperative examination, the upper airway should be evaluated anatomically in order to detect pathologies that may cause difficulty in the upper airway opening under endotracheal intubation and anesthesia[19]. A high STOP-BANG score obtained in the anamnesis shows that the patient may have difficult airway management. In this study, no statistically significant difference was observed when the STOP-BANG score was evaluated with MCLS and the HAN score. No statistically significant correlation was determined.

Difficult intubation is an important problem during general anesthesia. While difficult intubation has been reported at a rate of 2.2% in low-weight patients, this rate is 15.5% in obese patients[16]. Obesity and OSAS are interdependent. The average BMI of the current study patients was 29.6±3.7, neck circumference was measured as 40.12±12.1 cm, and 47.5% of the patients were evaluated as morbidly obese.

In a study conducted by Siyam et al.[17], the ratio between OSAS and difficult intubation was reported to be 21.9%. In the current study, according to MCLS, when difficult intubation was accepted as level 3 and 4[7], it was found to be 60%.

There is evidence that OSAS causes peroperative morbidity and mortality. In particular, upper airway surgery, which may be accompanied by intraluminal obstruction such as surgeries that may cause hematoma, tubes such as nasogastric catheters and nasal tampons, and narrowing of the upper airway, such as postoperative edema, are of great importance in terms of OSAS[18-20]. Sleep endoscopy performed before upper airway surgery contributes greatly to evaluations made by both the surgeon and the anesthetist in terms of areas with collapse[21,22].

In the current study, when obstruction levels (vellum, oropharynx, tongue root, epiglottis) in sleep endoscopy were compared with MCLS, the Han score and the modified Mallampati score, no statistically significant difference was found with these scores.

Eggerstedt et al.[23] observed a statistically significant difference of 6.5cm in the thyromental distance of patients with full obstruction in the epiglottis region. In the current study, the average thyromental distance was determined to be 9 cm in patients with complete obstruction in the vellum region in patients undergoing sleep endoscopy. The sleep endoscopy findings and difficult intubation findings were evaluated together, but the only significant result determined was in respect of evident Adam's apple. The difficulty of evaluating obstructions at all levels with difficult intubation findings has been previously stated in literature[23].

Sleep-related breathing difficulties can affect all age groups and can be seen with some diseases and syndromes. Studies on how the pathologies of these affect the duration of anesthesia and surgery are still in the initial stages[2].

The most important point for anesthesiologists is to be aware of patients with OSAS symptoms and diagnosis and to

take due care in the perioperative management of these patients.

Conclusion

In patients with obstructive sleep apnea, difficult intubation was re-evaluated with BMI, the modified Mallampati score, STOP-BANG, and the Cormack Lehane scoring system. There was found to be interdependence with the measurements related to difficult intubation according to both the sleep position and the apnea hypopnea index and hypopnea index.

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 study's ethical approval was given by the Kahramanmaraş Sütçü İmam University Local Ethics Committee (protocol no: 298; dated: 25/07/2018)

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MANAGEMENT OF GROIN HERNIORRHAPHY-RELATED CHRONIC POSTSURGICAL PAIN: GENERAL SURGEONS' UNDERSTANDING, ATTITUDES, AND EXPERIENCES

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Abstract

Aim: Groin herniorrhaphy is a common surgical procedure worldwide. Groin herniorrhaphy-related chronic postsurgical pain (GHCPSP) has a negative effect on quality of life. This survey evaluated general surgeons' knowledge, attitudes, and experiences with GHCPSP.

Methods: A survey on GHCPSP was designed by two experienced general surgeons and a pain physician and reviewed by an experienced hernia surgeon. The survey included four questions to assess demographic characteristics of the respondents; four questions related to understanding of pain characteristics of GHCPSP and the effectiveness of pain treatments for GHCPSP; five questions about attitudes towards management of early postoperative pain and GHCPSP; five questions related to experience of surgical techniques for groin herniorrhaphy, consultation rates to pain and psychiatry clinics for multidisciplinary management of GHCPSP, and working collaboration with a pain clinic. The survey was emailed to all members of the Turkish Surgical Society.

Results: The study included 259 respondents. The majority (248/95.8%) of respondents prescribed non-opioid medications for early postoperative pain control. 42% of the respondents favored paracetamol and/or NSAIDs for GHCPSP, and 42.9% favored multimodal agents for GHCPSP. 20% of the respondents stated that a validated scale or questionnaire is used to assess GHCPSP. 17.5% of the surgeons stated that neuropathic pain may be a component of GHCPSP. 90% of the respondents thought that referral to a pain physician may be useful in terms of pharmacological and interventional therapies in the management of patients suffering from refractory GHCPSP. The average consultation rates of respondents to pain and psychiatry clinics for GHCPSP was 30% and 1%, respectively.

Conclusions: General surgeons have adequate awareness of early postoperative pain and GHCPSP. On the other hand, the assessment of pain characteristics needs to be improved and the value of a multidisciplinary approach to pain management needs to be more recognized.

Keywords: Herniorrhaphy, chronic postsurgical pain, neuropathic pain, multidisciplinary management, pain medicine

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Introduction

Groin herniorrhaphy is a common procedure worldwide, with approximately 2 million procedures performed each year [1]. After surgery, some patients may experience persistent pain. In 2008, Macrae defined chronic pain that develops in areas that are not the continuation of the preoperative process and may be associated with the surgical site 2 months after surgery as chronic postsurgical pain (CPSP) [2]. It has been concluded that pain must persist for at least 6 months to fulfill the definition of CPSP associated with hernia repair, as inflammation in the area surrounding the mesh used in hernia repair continues up to the third postoperative month [3]. The incidence of groin herniorrhaphy-related CPSP (GHCPSP) was reported to be 3.8-12.4% [4] [5], regardless of the severity of pain, and GHCPSP was reported to have negative effects on quality of life, such as relations with others, work, and exercise [6].

Patients with GHCPSP may experience both nociceptive pain, which is described as aching, stabbing, throbbing, sharp and gnawing, and neuropathic pain, which is described as burning, and stinging. In the development of neuropathic pain, neuroma, sutures or postoperative adhesions, nerve entrapment or direct trauma that may occur in the ilioinguinal nerve, iliohypogastric nerve, the genitofemoral nerve and the lateral femoral cutaneous nerve in the perioperative process play a role. Pain may increase with hip joint hyperextension and decrease with flexion and radiate to the scrotal/labial area, upper leg, or lower back. GHCPSP can be triggered by contact with the wound site, coughing, abdominal breathing, bowel movements. There may also be loss of sensation in the leg and/or groin and painful ejaculation [7].

GHCPSP is one of the reasons patients sue surgeons, and litigation results sometimes cause economic losses for surgeons [8]. The European Hernia Society has outlined predictive factors and recommended management strategies for GHCPSP [9]. There have been no assessment of general surgeons, practicing hernia surgery, experience, knowledge, attitudes to the GHCPSP.

This study aimed to evaluate general surgeons' understanding of the pathophysiology of GHCPSP, the effectiveness of pain clinics for GHCPSP, management of early pain, experience of surgical techniques for groin herniorrhaphy, preference of mesh type, consultation rates to pain and psychiatry clinics for multidisciplinary management of GHCPSP and working collaboration with a pain clinic.

Materials and Methods

This cross-sectional survey was conducted in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was performed from January to February 2021 after obtaining ethics approval from the local ethics committee (No: 2020/3040, date: 22 December 2020).

Intervention

Two experienced general surgeons and one pain physician designed a survey to evaluate GHCPSP, focusing on general surgeons' knowledge, attitudes, and experiences. Clinicians designed this survey considering the topics and recommendations in The European Hernia Society Groin Hernia Surgery Guideline[8].

The survey was subsequently reviewed by an experienced hernia surgeon. The physician based the questions to address important topics related to GHCPSP. The survey included four questions to assess demographic characteristics (years of experience in general surgery, type of health facility were they're employed, availability of a pain clinic in the hospital and city where

they work) of the respondents; four questions related to understanding of neuropathic pain component in groin GHCPSP and the effectiveness of different types of pain treatments for CPSP after groin herniorrhaphy; five questions about attitudes towards management of early postoperative groin herniorrhaphy-related pain and GHCPSP with their prescription preferences; five questions related to experience of surgical techniques for groin herniorrhaphy, preference of mesh type, consultation rates to pain and psychiatry clinics for multidisciplinary management of GHCPSP, and working collaboration with a pain clinic (Appendix). The survey was designed using Google Survey and mailed to all members of the Turkish Surgical Society, also we sent personal reminders.

Participants

Only general surgeons with at least 2 years of experience in the field of general surgery were included. The general surgeons included in the study used either the classic open herniorrhaphy (Lichtenstein) technique or laparoscopic herniorrhaphy (laparoscopic totally extraperitoneal *or* transabdominal preperitoneal) method in groin herniorrhaphy.

Statistics

Statistical analyses were performed using SPSS, version 20.0 (IBM Corp., Armonk, NY). There were no missing data. The Shapiro–Wilk test was used to evaluate the distribution of the data. Variables with nonnormal distributions were summarized as medians and interquartile ranges (25–75%), and confidence intervals of the median differences were calculated at 95%. Categorical data were summarized as numbers and percentages. The relationship between numerical variables was evaluated using Spearman's correlation analysis. Point-biserial correlations between nominal variables and continuous variables were determined. A value of $P < 0.05$ was considered statistically significant.

A post-hoc power analysis was performed after finalization of the study. The G-power software package, version 3.1.6 (Franz Faul, Kiel University, Kiel, Germany) was used for the power analysis. Two hundred fifty-nine general surgeons were included in the final analysis. The power of the study was calculated as 0.97, with an effect size of 0.3 and significance level of 0.05.

Results

Of 1600 number of general surgeons had been contacted, 264 physicians agreed to participate in the study, giving a response rate of 16.5%. After exclusion of those with less than 2 years of experience in general surgery ($n = 5$), the final study included 259 participants. The average number of years' experience in general surgery was 13 (8.0–20.0) (95% CI, 13.36–15.34) years. Table 1 provides information on type of health facilities where the respondents (N = 259) were employed. Eighty-six (33.2%) respondents reported that they worked in a clinic in collaboration with the pain clinic in their residency program, 182 (70.3%) had a pain physician in the hospital where they currently worked, and 244 (94.32%) had a pain physician in the city where they worked.

Table 1. Type of health facilities where the general surgeons ($n = 259$) were employed.

Type of health facility	Percentage (number, *n*)
Public hospital	16.7 (43)
Private hospital	18.7 (49)
Training and research hospital	43.3 (112)
University hospital	21.3 (55)
Total	100% (259)

Table 2. Pain relief prescribing practices of the general surgeons (*n* = 259)

Pain relief medications	Percentage (number, n)
Paracetamol	11.6% (30)
NSAIDS*	74.5% (193)
Paracetamol plus NSAIDS*	12.7% (33)
Combinations with opioids	1.2% (3)
Total	100% (259)

** Nonsteroidal anti-inflammatory drugs*

The average practicing laparoscopic technique rate of the respondents was 20% (2.0–60.0) (95%CI, 29.77–38.25). When asked about their preference regarding mesh type in herniorrhaphy. The respondents stated that their average rate of using standart mesh was 99% (80.0–100.0, 29.77–38.25), bioabsorbable mesh 0% (0–1.0) (95%CI, 2.10–4.58), and light mesh at 0% (0–15) (95%CI, 12.15–19.10).

Most of the respondents (248/95.8%) stated that they prescribed postoperative pain control medication at the time of patient discharge after herniorrhaphy. Their choices of pain relief drugs for early postoperative pain are shown in Table 2.

The respondents were also asked about neuropathic pain. The level of agreement with the following statements was evaluated on a Likert 5-point scale: "Neuropathic pain may accompany chronic pain after hernia repair," and "I am competent in evaluating neuropathic pain, questioning patients about neuropathic pain, and assessing neuropathic pain symptoms." The responses of the respondents are shown in Table 3. Survey respondents used a validated scale or questionnaire to assess GHCPSP in 20% (0–70) (31.55–40.78).

The pain relief prescription practices of the respondents for GHCPSP are shown in Table 4.

Respondents stated their average consultation rate of 30% (1-70) (95% CI, 34.55-43.48) and 1% (0-10) (95% CI, 8.74-13.21) to pain and psychiatry clinics.

Table 3. Respondents' understanding of neuropathic pain.

Scores on a 5-point Likert scale*	Percentage (number, *n*)	
	Questioning and examination **	Being a component of CPSP***
1	13.5% (35)	2.3% (6)
2	34.4% (89)	3.5% (9)
3	34.7% (90)	17.8% (46)
4	10.0% (26)	40.5% (105)
5	7.3% (19)	35.9% (93)
Total	100.0% (259)	100% (259)

**A score of 1 on the Likert scale denoted strongly disagree, whereas a score of 5 denoted strongly agree.*
***"I have knowledge and experience in evaluating, questioning, and examining neuropathic pain which be a component of groin herniorrhaphy related CPSP." Do you agree with this statement?*
****"Neuropathic pain may be a component of groin herniorrhaphy-related chronic postsurgical pain." Do you agree with this statement?*

Table 4. Respondents' (*n* = 259) preferences in terms of pain relief medications after herniorrhaphy

Pain relief medications	Percentage (number, *n*)
Paracetamol and/or NSAIDS*	42.9 (111)
Antidepressants	0.8 (2)
Gabapentinoids	6.6 (17)
NSAIDS plus antidepressants	7.7 (20)
NSAIDS plus gabapentinoids	27.4 (71)
NSAIDS plus antidepressants plus gabapentinoids	12.4 (32)
Combinations with opioids	2.3 (6)
Total	100 (259)

** Nonsteroidal anti-inflammatory drugs*

The attitudes of the respondents toward GHCPSP were assessed by presenting them with the following case. "Twelve months after undergoing hernia repair, a patient presents with persistent pain in the inguinal area. After excluding possible pain-related causes, such as mesh-related infection, fluid collection, mesh migration, and a recurrent hernia, I consider on the management of

chronic pain." They were then asked whether they agreed with this statement. The level of agreement was evaluated on a Likert 5-point scale. Table 5 shows the responses of these questions.

The respondents were also questioned about groin GHCPSP, with their level of agreement with various statements assessed using a 5-point Likert scale. Table 6 provides a summary of the answers.

There was a moderate positive correlation between the rate of referring patients with GHCPSP to pain physicians and responders' collaboration with a pain clinic during responders' residency program (p = 0.04, r = 0.55). There was a weak positive correlation between the rate of referring patients with GHCPSP to pain physicians and the respondents' views on pharmacological options that pain physicians may have for GHCPSP (p = <0.001, r = 0.22).

There was a weak positive correlation between the rate of referring patients with GHCPSP to pain physicians and the respondents' views on interventional treatment options that pain physicians can utilize for CPSP (p = <0.001, r = 0.31).

There was no correlation between respondents' rate of referrals of patients with GHCPSP to a pain physician and the presence of a pain medicine clinic in the hospital where the respondent currently worked (p = 0. 084, r = 0.18).

Table 5. Respondents' (n = 259) attitudes toward CPSP after herniorrhaphy.

Scores on a 5-point Likert scale*	Percentage (number, n)
1	2.3 (6)
2	15.8 (41)
3	8.9 (23)
4	20.5 (53)
5	52.5 (136)
Total	100 (259)

**A score of 1 on the Likert scale denoted strongly disagree, and a score of 5 denoted strongly agree.*

Table 6. Respondents' thoughts on the effectiveness of different types of pain treatments for CPSP after herniorrhaphy

Scores on a 5-point Likert scale*	Percentage (number, n)	
	Pharmacological treatments**	Interventional treatments***
1	1.2% (3)	1.5% (4)
2	1.5% (4)	4.2% (11)
3	7.7% (20)	7.7% (20)
4	27.8% (72)	23.9% (62)
5	61.8% (160)	62.5% (162)
Total	100.0% (259)	100.0% (259)

**A score of 1 on the Likert scale denoted strongly disagree, and a score of 5 denoted strongly agree.*
*** "General surgeons can prescribe appropriate and adequate pharmacological treatment, but pain physicians can recommend alternative pharmacological treatments." Do you agree with this statement?*
***"General surgeons can prescribe appropriate and adequate pharmacological treatment, but pain physicians can utilize interventional treatments." Do you agree with this statement?*

There was no correlation between the number of years of experience in general surgery and the rate of referrals of patients with GHCPSP to a pain physician (p = 0.07, r = 0.26).

Discussion

In this study, 95.8% of the respondents stated that they routinely prescribed pain relief medication to patients at the time of discharge after groin herniorrhaphy. They stated that they generally prescribed pain relief medications, such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs), as early postoperative pain control and that they prescribed opioids only rarely. Poor control of pain in the early postoperative period was reported to be a predictive factor for the development of GHCPSP and GHCPSP-related limitations of activity [4 10]. Tan et al.[10] reported a high rate of opioid prescription at discharge after abdominal surgery [11]. Increased opioid prescriptions can result in opioid misuse and even death due to an overdose [12]. In the pre-

sent study, the control of early postoperative pain by general surgeons seemed good. In this study, 90% of the respondents thought that referral to a pain physician may be useful in terms of pharmacological and interventional therapies in the management of patients suffering from refractory GHCPSP. In addition, 30% of general surgeons stated that they referred patients with GHCPSP to pain clinics. Courtney et al.[6] reported that GHCPSP can be prevented by timely referral of patients to pain clinics. Other research found that pain relief was possible via the application of tender area local anesthetic injection [13], ilioinguinal and iliohypogastric nerve blocks, radiofrequency therapy [14], and Th12-L2 dorsal root ganglion pulsed radiofrequency treatment in pain clinics [15]. Lai et al.[15] determined that 50% of surgeons considered that acute postoperative pain should be managed using a multidisciplinary approach. In addition, they revealed that the majority of surgeons need training on pain and in a multidisciplinary pain management [16].

The European Hernia Society recommends a multidisciplinary approach to pain management [9]. To the best of our knowledge this is the first study on surgeons' understanding and experience of GHCPSP and their attitudes toward a multidisciplinary approach to GHCPSP management. In the present study, despite the positive opinions of general surgeons about the usefulness of pain clinics, the rate of referrals to pain clinics was low. The low rate of referrals may be explained by successful management of pain by the respondents themselves, patients changing their physicians, or patients refusing alternative treatment methods. Multicenter clinical studies and data from patient interviews could help to shed light on the factors underlying the low rate of patient referrals.

In our study, only 20% of the respondents stated that they used the laparoscopic technique. The open technique has been reported to be a risk factor for the development of GHCPSP. In addition, chronic activity-related pain was found to be more severe in patients who underwent open repair than laparoscopic surgery [10]. The risk of GHCPSP with the laparoscopic technique, which is strongly recommended by the European Hernia Society, was reported to be lower than with the open technique [9]. Encouraging the uptake of a laparoscopic approach to groin hernia repair among general surgeons could help to reduce incidence of GHCPSP.

In this study, the majority of the respondents (99%) stated that they used a standard mesh in groin herniorrhaphy. Previous research found that light meshes were advantageous in terms of reducing early postoperative pain but not GHCPSP [9]. Considering that most of the surgeons in this study used the Lichtenstein technique, they followed the recommendations of the European Hernia Society regarding the use of a standard mesh with Lichtenstein technique.

In our study, 17.5% of the surgeons stated that neuropathic pain may be a component of GHCPSP. Previous research reported that neuropathic pain may develop as a result of tension, compression, electrical damage, or contusion of genitofemoral or ilioinguinal nerves [17]. Studies also showed that 38.5–55% of patients with GHCPSP experienced neuropathic pain [7, 18]. The present study shows that neuropathic pain is a neglected area of GHCPSP.

In this study, just 20% of the respondents said that they used a validated scale or questionnaire to assess GHCPSP. The Inguinal Pain Questionnaire, which is a validated scale, can be used to assess GHCPSP [19]. Other pain assessment tools and validated scales for GHCPSP include the Short Form-36 and Carolinas Comfort Scale, both of which evaluate the effect of pain on functionality [20], and the Surgical Pain Scale, which assesses the intensity of pain at rest and during normal activities, physical activities, and work-related activities, as well as pain-related discomfort [21]. In this study, the rate of use of validated scales in assessments of GHCPSP was low. As reported previously, inadequate assessments of pain represent a major barrier in pain manage-

ment [22]. Using a validated pain scale to assess the severity of pain and its impact can improve the management of GHCPSP.

In this study, just 1% of the respondents declared that they referred patients with GHCPSP to psychiatric clinics. Previous research highlighted the relationship between GHCPSP and psychological problems, such as anxiety, depression, catastrophizing, and kinesiophobia [23]. Acceptance and commitment therapy have been found to be useful treatments for CPSP [24]. General surgeons should consider consulting more frequently with psychiatry clinics in pain management of patients with GHCPSP.

A limitation of our study was that the surgeons were not directly questioned about their views on the utility of multidisciplinary teams and training programs in pain management. Lai et al.[15] reported that the majority of surgeons considered that training on pain and pain management should take place via meetings with a pain team. In future studies, the effect of multidisciplinary meetings and educational programs on surgeons' clinical approaches to GHCPSP management can be evaluated. Participant bias may be another limitation of our study. Participants who felt confident about their knowledge and experience of GHCPSP may have been more likely to have participated in the study.

Conclusion

General surgeons have sufficient awareness of early postoperative pain and GHCPSP. However, understanding of GHCPSP in evaluations of pain-related characteristics, including pain severity, and the effect of pain on quality of life needs to be improved. Furthermore, greater acceptance of the value of a multidisciplinary approach to pain management is needed.

Author contributions

- Conception or design of the work: 1, 2, 3
- Data collection: 1, 2, 3
- Data analysis and interpretation: 1
- Drafting the article: 1, 2, 3
- Critical revision of the article: 1, 2, 3
- Final approval of the version to be published: 1, 2, 3
- Guarantor: 1

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Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

This cross-sectional study was conducted in accordance with the Declaration of Helsinki and in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The study was performed in January 2020 after obtaining ethics approval from Necmettin Erbakan University Ethics Committee (No: 2020/3040, date: 22 December 2020).

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SLEEP DISORDERS IN THE FOLLOW-UP OF COVID-19 INFECTION: A SINGLE CENTER EXPERIENCE

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Abstract

Aim: This study aims to investigate sleep-related disorders and their possible causes after COVID-19 infection.

Methods: The data of patients over the age of 18 with a history of COVID-19 infection who applied to our Sleep Disorders Unit in the last 3 months were obtained retrospectively from anamnesis, laboratory, imaging, and polysomnography examinations. The data of Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale and Beck anxiety inventory (BAI) tests of patients were included in the study.

Results: After COVID-19 infection, in all patients, reason for admitting to our Sleep Disorders Unit was complaints of insomnia. Another sleep-related disorder was determined in 64% of the patients (Obstructive Sleep Apnea Syndrome (OSAS) is the most common with 52%). The history of the chronic cardiorespiratory, cerebral, endocrine-metabolic disease was significantly higher in patients having complaints of insomnia and another accompanying sleep-related disorders (68% vs 0%, p=0.001). Also, the history of hospitalization in these patients was higher, although not statistically significant (50% vs 11%, p=0.088). For all patients, the median BAI value and the mean PSQI value were high (13 and 11.6, respectively), but no correlation was found between them (p=0.336).

Conclusions: The most common reason for sleep-related admission after COVID-19 infection is complaints of insomnia and if there is a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization because of COVID-19 infection, another accompanying sleep-related disorders, especially OSAS, should investigate. Also, the severity of anxiety disorder as a cause of insomnia complaints is not correlated with the deterioration in sleep quality.

Keywords: *Insomnia, COVID-19, comorbidity, polysomnography.*

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Introduction

Coronavirus disease (COVID-19) was accepted as a pandemic by the World Health Organization on March 11, 2020. Severe psychiatric and neuropsychiatric diseases in patients with history of COVID-19 infection have been reported between 14% to 61% during infection and between 14.8% and 76.9% after infection similar to other coronavirus pandemics, such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [1]. Primary mental health disorders in affected individuals include depression, anxiety disorder, post-traumatic stress disorder (PTSD), insomnia, and sleep disorders.

The prevalence of insomnia varies between 3.9% and 22% worldwide [2]. The community-based studies have shown the prevalence of insomnia during the COVID-19 pandemic is close to or higher than the upper limit of the worldwide prevalence of insomnia, varying between 19.1% and 37% [3–5].

Anxiety and depression stand out as the primary cause of insomnia during the COVID-19 pandemic [6]. In both cases, increased cognitive arousals and changing cerebral monoamine concentrations, as well as an increase in proinflammatory cytokines caused by psychological stressors such as C-reactive protein (CRP), Tumor-necrosis factor (TNF) and interleukin-6 (IL-6), neuroinflammation, irregularity of the hypothalamic-pituitary-adrenal axis, genetic factors and circadian rhythm irregularity may play a role in the pathophysiology of insomnia [7–9]. However, it is known that sleep-related disorders, which can cause poor sleep quality such as insomnia, lead to increased susceptibility to depression and infectious processes by increasing these proinflammatory cytokines and causing changes in T lymphocyte expression and proliferation [10,11]. For this reason, early diagnosis and treatment of sleep-related disorders, especially insomnia that may occur during and after COVID-19 infection, is essential in terms of neurological, immunological and psychological processes.

This study aimed to evaluate possible sleep-related disorders retrospectively in our patients who were followed up in the Sleep Disorders Unit of our hospital in the last three months and who had a history of COVID-19 infection.

Materials and Methods

After the approval of Eskişehir Osmangazi University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 26.10.2021, No: 05), the study was organized according to the Principles of the Declaration of Helsinki. All patients over 18 who applied to Eskişehir City Hospital Sleep Disorders Unit between 15.01.2021 and 15.04.2021 and had a history of COVID-19 Polymerase Chain Reaction (PCR) test positivity were retrospectively screened and included in the study. The exclusion criteria were being younger than 18 years of age, being pregnant, using medication that may cause sleep disturbance, not having a sleep disorder complaint, not having a history of COVID-19 infection and insufficient data.

In all patients fulfilling including criteria in the study, the reason for admitting to our Sleep Disorders Unit was complaints of insomnia. In addition, age, gender, characteristics and duration of sleep disturbance complaints, body mass indices, history of hospitalization or intensive care unit admission due to COVID-19 infection, presence of an additional sleep-related disease, chronic cardiac, respiratory, cerebral, endocrine-metabolic disease and psychiatric disorders were recorded. Data for this study were collected using the hospital information management system in detail from patient's history, anamnesis, laboratory, imaging and polysomnography (PSG) examinations. All medications used by the patients were noted. The data obtained from the Pittsburgh sleep quality index test (PSQI), Epworth sleepiness scale (ESS) and Beck anxiety inventory (BAI)

tests were included in the study. A clinical neurophysiology specialist applied these tests to all patients who applied with complaints of insomnia.

The PSQI test, developed by Buysse et al. [12], is a scale consisting of 24 questions evaluating sleep quality and disturbance in the past month. Nineteen questions are self-report questions, and five questions are answered by spouse or roommates of the patient. Questions answered by the spouse or roommates are not included in the scoring. PSQI includes seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping pills, and daytime dysfunction. The score obtained from these components varies between 0-21. A total score above 5 indicates "poor sleep quality".

ESS, developed by Johns et al. [13], is a scale consisting of 8 questions and indicates daytime sleepiness. In each question, the scoring method is the same. The probability of falling asleep is calculated with scale. On an ordinary day when the patient is not excessively tired is given 0 points if there is no probability of falling asleep, 1 point if it is a low probability, 2 points if it is a medium probability, and 3 points if it is a high probability. A total score of 10 and above indicates the presence of excessive daytime sleepiness.

BAI, developed by Beck et al. [14], is a scale consisting of 21 questions in total and in which each question scoring between 0-3 is used to measure the anxiety of the individual. A total score of 8-15 indicates a mild level of anxiety, between 16-25 indicates moderate anxiety, and between 26-63 indicates a high level of anxiety.

The data of type 1 PSG performed during all night in laboratory conditions as well as scored and reported according to the guideline organized by American Academy of Sleep Medicine (AASM) in 2020 [15] were included in the study in the patients applying with complaints of insomnia accompanied by symptoms including snoring, witnessed apnea, waking from sleep with shortness of breath, night sweats, nocturia, restless sleep, and fatigue.

Statistical evaluation was analyzed using the SPSS-24 (Statistical Package for the Social Sciences) program. Categorical data were compared using Fisher's exact test. Non-parametric data were evaluated with the Mann-Whitney U test, and parametric data were evaluated with the Student-t and One-way ANOVA test. Pearson correlation analysis was used in the correlation analysis of parametric data. According to the analysis results, the p-value of 0.05 and below was accepted as statistically significant.

Results

A total of 25 patients who applied with the complaints of insomnia after COVID-19 infection between 15.01.2021 and 15.04.2021 were included in the study.

In the study, the first set of questions aimed to evaluate the baseline characteristics of the patients. As shown in Table 1, 16 (64%) of the patients were female, and 9 were male. Their mean age was 48±14 years, and the median duration of insomnia complaints was two months (Interquartile Range [IQR]: 1.5-3 months). The mean body mass index was 27±5.7 kg/m^2.

A total of 9 patients (36%) had a history of hospitalization due to COVID-19 infection, and 2 (0.5%) patients needed treatment in the intensive care unit (Table 1).

PSG examination was performed all night in laboratory conditions in 16 patients (64%) who had insomnia complaints accompanied by symptoms such as snoring, witnessed apnea, awakening from sleep with shortness of breath, night sweats, nocturia, restless sleep, and fatigue during the day. According to the result of PSG and clinical evaluation, at least one other sleep-related disease accompanying insomnia complaints was observed in 16 (64%) patients. Further analysis showed the presence of obstructive sleep apnea syndrome (OSAS) in 13 patients (52%),

Table 1. Demographic characteristics of all patients presenting with complaints of insomnia

Demographic characteristics (n=25)	
Gender, female/male, n (%)	16/9 (64/36)
Age, years, mean (SD)	48 (14)
Insomnia duration, months, median (IQR)	2 (1.5-3)
Body mass index, kg/m2, mean (SD)	27 (5.7)
Number of patients with a history of hospitalization, n (%)	9 (36)
Number of patients treated in the Intensive Care Unit, n (%)	2 (8)
Duration of hospitalization, days, mean (SD)	17.1 (13.7)

SD, Standard deviation; IQR, interquartile range
Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.

restless legs syndrome / Willis-Ekbom disease (RLS/WED) in 3 patients (12%), periodic limb movement disease (PLMD) in 2 patients (8%), and central sleep apnea syndrome associated with Cheyne-Stokes respiration in 1 patient (4%). According to clinical and PSG data, while 10 patients (40%) had a history of cardiorespiratory and/or endocrine-metabolic diseases, 2 patients (8%) had a generalized anxiety disorder, and 1 patient (4%) had epilepsy (Table 2).

Patients who applied with the complaint of insomnia after COVID-19 infection were divided into those with and without accompanying sleep-related disorders. Demographic and clinical data of these two groups were compared. Further statistical tests revealed that chronic cardiorespiratory/endocrine-metabolic/cerebral disease history was significantly higher in the group with a history of the concomitant sleep-related disease (p=0.001). The history of hospitalization was also higher in this group, although not statistically significant (p=0.088). Two patients with a history of hospitalization in the intensive care unit were also in this group. Other demographic and clinical data between the two groups were similar and detailed in Table 3.

When sleep-related data were evaluated, it was noted that the median value of subjective sleep latency (sSL) was 60 minutes and increased, while the mean value of subjective total sleep time (sTST) was 312 minutes and decreased. The mean PSQI value was found to be high with 11.6±3.2 and indicated poor sleep quality and also, the median value of the BAI score was high with 13 (IQR:6-26.5). The mean ESS score was 4.6±3.7 and was low, indicating decreased daytime sleepiness, consistent with insomnia complaints (Table 4).

According to BAI scores, 5 patients had mild anxiety, 5 patients had moderate anxiety, and 6 patients had high anxiety (10.8±3.1, 19.8±2.7, and 35.8±3.7, respectively). The mean PSQI score of each group was found to be high (11±2.5, 11.4±5.1 and 12.5±5.6, respectively), but no significant difference was found between the groups in terms of PSQI score (p=0.803). Similarly, no correlation was found between BAI and PSQI scores in all patients with insomnia and with or without anxiety (p=0.336).

Patients with insomnia complaints were divided into two groups: those with a history of hospitalization (n: 9, 36%) and those without (n: 16, 64%). Both groups had a high BAI score (18.2±12.2 and 9 [IQR:5.2-27.7], respectively, p=0.452) and PSQI score (12 [IQR:9.5-16] and 11.1±2.9, respectively, p=0.357).

However, no statistically significant difference was found between the two groups.

Patients with insomnia were also divided into two groups: those with comorbid sleep-related respiratory disorders (n:14, 56%) and those without (n:11, 44%). When all sleep-related data were compared, it was observed that both groups had low sTST,

Table 2. Distribution of comorbidities in patients presenting with complaints of insomnia

All patients diagnosed with insomnia (n:25)	
Presence of sleep-related illness, n (%)*	16 (64)
Mild OSAS (AHI:5-14), n (%)	1 (4)
Moderate-severe OSAS (AHI≥15), n (%)	12 (48)
CSAS associated with Cheyne-Stokes respiration, n (%)	1 (4)
RLS/WED, n (%)	3 (12)
PLMD, n (%)	2 (8)
Presence of chronic cardiorespiratory/endocrine disease, n (%)	10 (40)
Presence of chronic cerebral disease, n(%)	1 (4)
Presence of psychiatric disorder, n (%)	2 (8)

OSAS, obstructive sleep apnea syndrome; AHI, apnea hypopnea index; CSAS, central sleep apnea syndrome; RLS/WED, Restless legs syndrome / Willis-Ekbom disease; PLMD, periodic limb movement disorder
**Subgroup analysis indicates the presence of more than one accompanying sleep-related disease in a patient.*

Table 3. Comparison of demographic characteristics of all patients with and without accompanying sleep disorder diagnosed with insomnia

Groups, n (%)	Patients without concomitant sleep disorder 9 (36)	Patients with concomitant sleep disorders 16 (64)	p
Demographic characteristics			
Gender, female/male, n (%)*	5/4 (55/45)	11/5 (68/32)	0.671
Age, years, mean (SD)**	43 (11.9)	50.8 (14.6)	0.187
Insomnia duration, months, mean (SD)**	2 (0.9)	2.4 (1.4)	0.513
Body mass index, kg/m2, mean (SD)**	25.9 (3.9)	28.5 (6.4)	0.290
Presence of chronic cerebral/endocrine/cardiorespiratory disease, n (%)*	0 (0)	11 (68)	0.001
Presence of psychiatric disorder, n (%)*	0 (0)	2 (12.5)	0.520
Number of patients with a history of hospitalization, n (%)*	1 (11)	8 (50)	0.088
Number of patients treated in the Intensive Care Unit, n (%)*	0 (0)	2 (12.5)	0.520

SD, Standard deviation; *Fisher's Exact test was used.**Student T test was used. Mean values (SD) were used for parametric (normally distributed) data.

Table 4. Analysis of sleep-related data of all patients presenting with complaints of insomnia

Sleep-related data	
sSL, minutes, median (IQR)	60 (60-165)
sTST, minutes, mean (SD)	312 (109.2)
Pittsburgh sleep quality index score, mean (SD)	11.6 (3.2)
Epworth sleepiness scale score, mean (SD)	4.6 (3.7)
Beck anxiety inventory score, median (IQR)	13 (6-26.5)

SD, Standard deviation; IQR, interquartile range; sSL, subjective sleep latency; sTST, subjective total sleep time, Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.

Table 5. Comparison of sleep-related data in patients with and without sleep-related respiratory disorder who presented with complaints of insomnia

	Patients without sleep-related breathing disorders (n=11)	Patients with sleep-related breathing disorders (n=14)	p
sSL, minutes, median (IQR)*	60 (60-180)	75 (60-157.5)	0.851
sTST, minutes, mean (SD)**	316.3 (146.5)	308.5 (73.8)	0.874
Pittsburgh sleep quality index score, mean (SD)**	11.1 (3.6)	12 (2.9)	0.540
Epworth sleepiness scale score, mean (SD)**	4.4 (3.2)	4.7 (4.1)	0.831
Beck anxiety inventory score, median (IQR)/mean (SD)*	8 (6-36)	15.2 (11.5)	0.687

SD, Standard deviation; IQR, interquartile range; sSL, subjective sleep latency; sTST, subjective total sleep time;
** Mann-Whitney U test was used. **T-test was used. Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.*

high sSL, PSQI and BAI scores, but no statistically significant difference was found between the two groups (Table 5).

Discussion

Insomnia is a condition characterized by complaints about sleep, which can occur alone or as a result of many diseases such as anxiety, depression, chronic pain, and sleep apnea [16]. Insomnia is diagnosed by the presence of symptoms associated with sleep causing deterioration in at least one of the patient's cognitive, mental, behavioral, social, occupational, and familial functions such as difficulty initiating sleep, inability to continue sleep, waking up early in the morning, resistance to going to bed at the appropriate sleep time [17]. For the diagnosis of acute insomnia, these sleep-related complaints that occur at least 3 times a week should continue less than 3 months, and for the diagnosis of chronic insomnia, these complaints should continue longer than 3 months. The prevalence of insomnia varies between 3.9% and 22% worldwide [2].
It has been shown in studies that mental disorders and sleep-related disorders, especially insomnia, occur during and after COVID-19 infection in people who are infected with COVID-19. In these studies, it has been reported that the prevalence of depression is three times higher (15.97% vs 4.4%), anxiety disorder is four times higher (3.6% vs 15.15%), and PTSD is five times higher (21.94% vs 4%) in people infected with COVID-19 compared to the general population [18–20]. Community-based studies have shown that the prevalence of insomnia during the COVID-19 pandemic is close to or higher than the upper limit of the worldwide prevalence of insomnia. It varied between 19.1% and 37% [3–5]. In our study, the reason for admission in all patients who applied to our Sleep Disorders Unit after COVID-19 infection in the last 3 months was complaints of insomnia and these results were consistent with the literature. In our study, the mean duration of insomnia complaints was determined as 2 months. Consistent with general population, in this study it was observed that the patients who applied with insomnia complaints were predominantly female and were in the middle-advanced age group [21]. After detailed questioning of these patients who applied with insomnia complaints, PSG examination was performed on 16 patients. According to clinical, PSG and laboratory data, two-thirds (64%) of the patients had another sleep-related disorder accompanying the complaints of insomnia, and the most common sleep-related disorder was found to be obstructive sleep apnea syndrome (OSAS)

with 52%. The prevalence of OSAS is around 10-15% in the general population in this age group, and complaints of insomnia in OSAS cases can reach up to 50% [22,23]. According to our results, it was seen that the frequency of OSAS in the COVID-19 population is higher than the prevalence of OSAS in the general population, and one of the most important symptoms in these patients may be insomnia rather than daytime sleepiness. In our study, the patients were divided into two groups as those with or without a concomitant sleep-related disorder; it was observed that the rate of chronic cardiorespiratory, cerebral and endocrine-metabolic diseases was significantly higher in the group with a concomitant sleep-related disorder. Also, it was observed that the history of hospitalization was higher in this group, although not statistically significant. This has demonstrated that the patients applying with complaints of insomnia after COVID-19 infection should be evaluated in detail in terms of other underlying sleep-related disorders, especially OSAS, if they have a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization. In this group, effective treatment of comorbid sleep-related respiratory disorders suggested that it could both improve insomnia complaints and reduce the number and duration of hospitalizations during COVID-19 infection by controlling the systemic effects of other comorbid chronic diseases.

Objective sleep tests such as polysomnography and actigraphy in diagnosing insomnia have less sensitivity and specificity than the self-reports used to define insomnia [24]. Based on the self-reports of the person, the diagnosis of insomnia can be mentioned if the sleep latency and duration of wakefulness after sleep onset are over 30 minutes [25]. However, the PSQI is a test used effectively to evaluate sleep quality and complaints of insomnia. Consistent with the literature, in our study, the median value of sSL is high and 60 minutes and also the mean sTST has reduced and is 312 minutes in patients who applied insomnia complaints after COVID-19 infection. In this study, the mean PSQI test score has been determined as 11.6 in these patients, indicating poor sleep quality. In previous study have reported that 40% of insomnia patients fulfill the criteria of any psychiatric disorders; this rate is 23% for major depression and 24% for anxiety disorders [26]. And also insomnia has determined in 90% of the patients with major depression [27]. Studies have shown that the prevalence of anxiety disorder in people with COVID-19 infection is four times higher than the general population (3.6% vs 15.15%) [18]. Consistent with this, in our study, the median value of the BAI score used in evaluating anxiety disorder as a cause of insomnia was found to be 13 and increased. However, no correlation was found between the severity of anxiety disorder and sleep quality. In addition, in our study, although high anxiety levels and poor sleep quality were detected in those with a history of hospitalization as a cause of anxiety and those with respiratory disorder associated with sleep, no significant difference was found compared to those who did not. In a study, PSQI scores of healthcare workers employed in COVID-19 services show correlation with BAI scores positively [28]. In contrast, according to our results, the association between PSQI and BAI scores suggests that the effect of level of anxiety disorders on deterioration of sleep quality is subjective and this suggests that treating mild anxiety disorder after COVID-19 infection could effectively ameliorate severe insomnia complaints.

The limited number of patients and the fact that PSG was not performed on all patients can be counted among the limitations of the study. Our study is single-center, and we consider that it would be beneficial to expand our study with a multicenter study, including more patients. In addition, PSG was not routinely applied to patients with only insomnia complaints, except for the patients in whom considered a diagnosis of paradoxical insomnia as well as the patients with symptoms accompanying insomnia complaints and suggesting the presence of an-

other sleep-related disease. Therefore, we consider that a prospective study in which PSG will be performed as a routine will provide more objective data about complaints associated with sleep of the patients. Thus, we believe that a multicenter and prospective study will support our study. In this study, the demographic and clinical characteristics of all patients with complaints of insomnia were compared to the literature. And also, patients with complaints of insomnia and concomitant sleep-related disorders generated the control group of study and, therefore, in the second stage of the study, the demographic and clinical characteristics of all patients with insomnia complaints were evaluated according to the presence of accompanying sleep-related disorders.

Conclusion

In summary, the study showed that the most common sleep-related symptom after COVID-19 infection was insomnia. If these patients presenting with complaints of insomnia have a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization, should investigate in terms of another sleep-related disease, especially OSAS. The effective treatment of these comorbid sleep-related diseases provides improving complaints of insomnia and also can play an effective role in reducing the number and duration of hospitalizations due to COVID-19 infection via controlling the systemic effects of other chronic diseases. In addition, it has been shown that anxiety disorder occurring after COVID-19 infection causes different levels of insomnia and thus poor sleep quality in patients. Therefore, we also suggest that treating mild anxiety disorder after COVID-19 infection may effectively cure severe insomnia complaints.

Author contributions
Concepts: 1,2
Design:1,2
Literature search:1
Clinical studies:1
Data acquisition:1,2
Data analysis:1
Statistical analysis:1
Manuscript preparation:1
Manuscript editing:1
Manuscript review:1,2

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
Eskişehir Osmangazi University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 26.10.2021, No: 05), the study was organized according to the Principles of the Declaration of Helsinki.

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A COMPARISON OF THE EFFECTS OF PRE-EMPTIVE AND INTRAOPERATIVE INTRAVENOUS ACETAMINOPHEN ADMINISTRATION ON PAIN MANAGEMENT AFTER CIRCUMCISION

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Abstract

Aim: The aim of this study was to compare the efficacy of the pre-emptive and intraoperative use of intravenous acetaminophen in post-circumcision pain in children.

Methods: The records of patients who had undergone circumcision were retrospectively evaluated using our database in the Samsun University, Samsun Training and Research Hospital, Department of Pediatric Surgery, Turkey, from May 2021 to May 2022. Patients were divided into two groups based on administration of pre-emptive (Group 1) and intraoperative (Group 2) acetaminophen. Baseline characteristics, vital signs, outcomes, and Face, Legs, Activity, Cry, and Consolability (FLACC) scale scores were then compared between the groups.

Results: Two hundred four patients, 95 (46.6%) in Group 1 and 109 (53.4%) in Group 2, were enrolled in the study. No significant difference was determined in terms of mean body mass index, age, length of stay in the recovery room, operative time, or length of hospital stay. Vital findings exhibited no difference in preoperative, induction, intraoperative, or postoperative recordings. Significant differences were observed between the groups' mean pain scores 30 minutes after surgery ($p = 0.024$). However, no such significant differences were observed at one and three hours after surgery ($p = 0.063$ and $p = 0.708$, respectively). Rescue analgesia was performed in 13 (13.7%) cases in Group 1 and 17 (15.6%) in Group 2 ($p = 0.7$).

Conclusions: Pre-emptive intravenous acetaminophen reduced pain 30 minutes after circumcision. Pre-emptive and intraoperative use of acetaminophen resulted in similar and acceptable efficacy in pain relief one and three hours after surgery.

Keywords: *Acetaminophen, pre-emptive, circumcision, pain, analgesia, pediatrics*

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Introduction

Male circumcision involves the excision of the foreskin from the glans of the penis and is one of the most frequently performed surgical procedures worldwide[1]. However, in common with all surgical procedures, circumcision is a painful event. Post-operative pain is the most frequent side-effect of circumcision, and this and the complications there of are a source of concern on the part of surgeons and anesthesiologists[2]. Increasing awareness of the problem and endeavors to improve pain management in children, both intra- and postoperatively, led to the publication of guidelines in 2018 by the European Society for Paediatric Anaesthesiology Pain Committee[3].

Pre-emptive analgesia, the administration of analgesic medications prior to surgical incision, has been recommended under various surgical conditions by numerous studies. However, the efficacy of pre-emptive analgesia remains unknown, although the results of clinical trials in humans have consistently described it as beneficial[4]. The pre-emptive approach entails the management of pain before it actually occurs, the objective being to minimize postoperative pain by disrupting afferent input. The most efficacious pre-emptive agents in terms of lowering central sensitization are analgesics that act on pain resulting from injuries due to incisions and related inflammation[5].

Similarly, to non-steroidal anti-inflammatory drugs, acetaminophen exhibits both central and peripheral effects. Acetaminophen is a safe analgesic and administered in different forms and by various routes. Its use is particularly recommended for postoperative pain management and in the form of a single therapy aimed at relieving mild postoperative pain without causing major adverse effects[6]. The analgesic effects of intravenous (IV) acetaminophen administration have also been widely examined, especially in children, and acetaminophen has been recommended for pre-emptive analgesia[7].

It is important to identify a cost-effective analgesic agent with acceptable pain-reducing capabilities. The pre-emptive or intraoperative use of acetaminophen can produce differing outcomes in terms of pain relief. However, no previous studies have compared the analgesic effects of these two methods. The purpose of this study was to compare the effects of pre-emptive and intraoperative IV acetaminophen administration on postoperative pain in boys after circumcision.

Materials and Methods

Two hundred four patients who underwent circumcision at the Samsun University, Samsun Training and Research Hospital, Department of Pediatric Surgery, Turkey, between May 2021 and May 2022 were included in the study.

Patient evaluation and selection

All children in the study received 15 mg kg^{-1} IV acetaminophen for pain control, either prior to circumcision (Group 1) or immediately after the incision was made (Group 2).

Inclusion criteria

- Age 1-7 years,
- Being operated using the dorsal slit technique under general anesthesia, and
- Receipt of pre-emptive or intraoperative IV acetaminophen.

Exclusion criteria

- Children aged under one year or over seven,
- Children undergoing circumcision other than with the dorsal slit technique (guillotine, sleeve resection, Plastibell, Mogen clamp, etc.),
- Patients receiving analgesic therapy other than acetaminophen,
- Patients receiving postoperative IV acetaminophen,

- Patients using analgesic, antiepileptic, or sedative drugs, and
- Patients undergoing additional procedures together with circumcision (herniorrhaphy, tonsillectomy, orchiopexy, appendectomy, etc.) were excluded from the study.

Preoperative preparation

Patients were given standard maintenance fluids, depending on their body weight. Group 1 received IV acetaminophen 30 minutes prior to circumcision.

Anesthesia management

All patients were monitored throughout the surgical procedure in terms of electrocardiography, respiratory rate, non-invasive arterial blood pressure, and pulse oximetry. General anesthesia was induced in all cases through the administration of a combination of fentanyl l-2 µg/kg and 1% propofol 2-3 mg/kg. A mixture of 50% nitrous oxide, 50% oxygen, and 2-3% sevoflurane was also employed during anesthesia. Postoperatively, the laryngeal mask was removed once the child began to breathe spontaneously, and all cases were transferred to the recovery room.

Surgical technique

The dorsal slit method was employed in all cases. This entails the separation of the adhesions between the prepuce and the glans. Artery forceps are placed at 10 and 1 o'clock, and both layers of the prepuce are then incised at the 12 o'clock position, leaving a few millimeters of skin proximal to the corona. The surgical method is described in Figure 1. Dorsal slit circumcision was performed on all children's by the same surgeon (SSB).

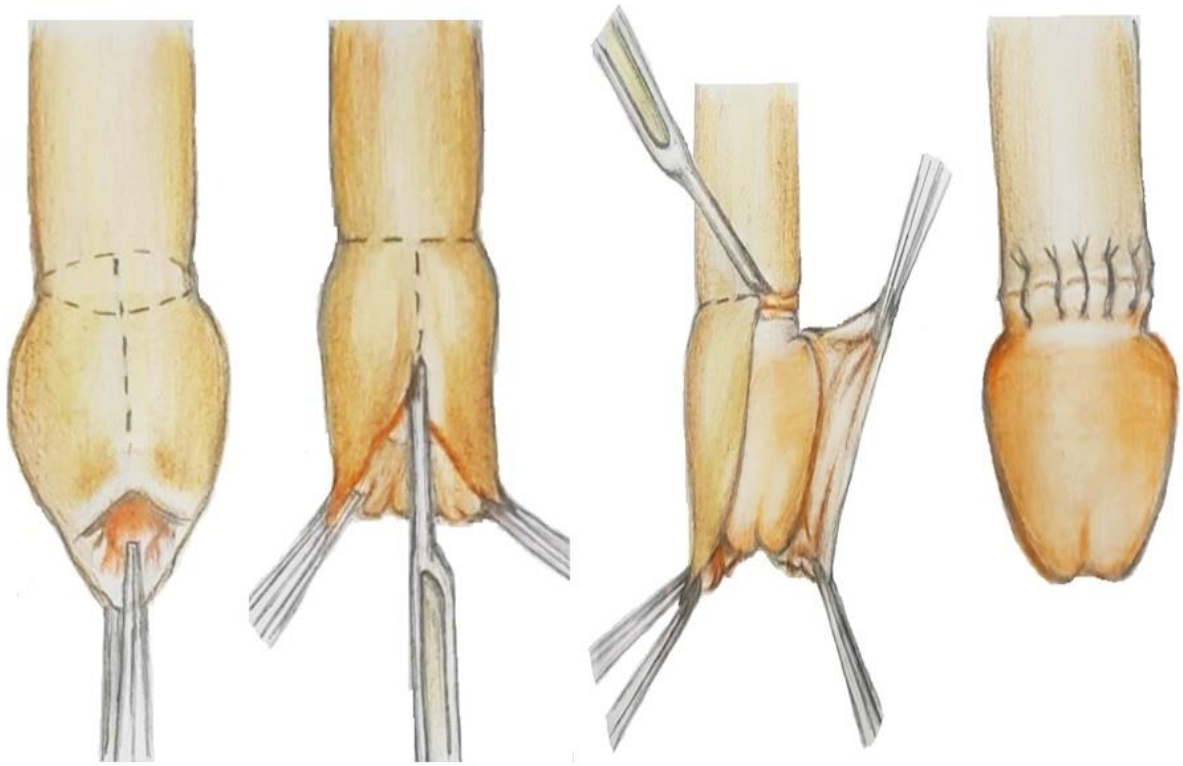

Figure 1. Technic of dorsal slit circumcision (a: The incision line is marked; b: Grasp the foreskin with two artery forceps and the foreskin is cut the dorsal midline; c: The preputial skin is resected leaving a 0.5 cm sleeve to the corona; d: Penil skin is then sutured to the coronal sleeve)

Categories	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting, back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Figure 2. Face, Legs, Activity, Cry, Consolability (FLACC) Scale

Evaluation of postoperative pain

Patient pain was assessed using the Face, Legs, Activity, Cry, Consolability (FLACC) scale. This consists of five domains (face, legs, activity, crying, and consolability), each of which is scored 0, 1, or 2, yielding a total scale score from 0 to 10 (Figure 2). Total FLAAC scores were calculated. A score of 0 is interpreted as relaxed/comfortable, 1–3 as mild discomfort, 4–6 as moderate pain, and 7–10 as severe discomfort/pain[8]. Pain scores were recorded 30 minutes, and one and three hours after surgery. Rescue analgesia (IV tramadol, 1-2 mg kg^{-1}) was administered in cases with high postoperative FLAAC scores (>4).

Data collection

Clinical data were analyzed, including body mass index (BMI), age, respiratory rate, heart rate, saturation rate, pain scores, length of stay in the recovery room, rescue analgesia requirements, operative time, and length of hospital stay.

Statistical analysis

Data analysis was performed on SPSS version 25 software (Statistical Package for Social Sciences- IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was employed to determined normality of distribution of measurable data. Continuous data as mean ± standard deviation, and nominal data were expressed as frequencies and percentages. Nominal variables were evaluated using the Chi-square test, while the independent Samples T test was applied to determine the presence of a statistically significant difference between the two groups. A p values lower than 0.05 were regarded as significant.

Table 1. Detailed information of all patients in the study.

Variables	Group 1 (N = 95)	Group 2 (N = 109)	p value
Age (years), mean ± SD	4.1 ± 2.29	3.98 ± 2.27	0.7
Body mass index (kg/m²), mean ± SD	18.62 ± 3.06	18.22 ± 3.29	0.371
Operative time (minute), mean ± SD	26.4 ± 4.37	25.94 ± 3.76	0.426
Recovery time (minute), mean ± SD	35.4 ± 6.12	35.33 ± 5.8	0.874
Hospital stay (hour), mean ± SD	9.04 ± 0.98	9.06 ± 0.94	0.871

Abbrevation: SD, standard deviation.

Results

Two hundred four patients with a mean BMI value was 18.16 ± 3.12 kg/m^2 were included in the study. The patients' mean age of 4.03 ± 2.29 years, mean operative time was 26.15 ± 4.05 minutes, and mean length of hospital stay was 9.05 ± 0.96 hours.

No statistically significant differences were observed between the groups in terms of patient BMI, age, length of stay in the recovery room, operative time, and length of hospital stay. Patient outcomes and characteristics are presented in Table 1. Comparison of children's heart, respiratory, and saturation rates between the groups revealed no difference in preoperative, induction, intraoperative, or postoperative recordings (p >0.05). The vital findings are shown in Table 2. The groups' FLAAC values at 30 min, one hour, and three hours postoperatively were 2.22 ± 1.24 vs. 2.61 ± 1.21, 1.10 ± 0.91 vs. 1.33 ± 0.80, and 0.71 ± 1.34 vs. 0.78 ± 1.43, respectively.

Significant differences were observed between the groups' mean scores of pain immediately after 30 minutes (p = 0.024). However, no such significant differences were observed at one and three hours after surgery (p = 0.063 and p = 0.708, respectively). The detailed FLAAC scores of the groups are shown in Table 3.

During postoperative observation, rescue analgesia was not performed for the first postoperative three hours in order to evaluate the efficacy of acetaminophen administration. Rescue analgesia was applied to patients with higher FLAAC scores (FLAAC >4), 13 (13.7%) children in Group 1 and 17 (15.6%) in Group 2 (p = 0.7). Additionally, no adverse effect of acetaminophen was observed. All of the patients were discharged from the hospital after an uneventful six-hour period.

Table 2. The vital findings of patients in groups. Values are presented as mean ± standard deviation.

Variables	Group 1 (N = 95)	Group 2 (N = 109)	p value
Preoperative heart rate (beats/minutes)	128.5 ± 18.28	125.11 ± 14.99	0.148
Preoperative breath rate (breath/minutes)	24.88 ± 4.78	24.04 ± 5.30	0.24
Preoperative saturation rate (%)	99.68 ± 0.51	99.66 ± 0.49	0.738
Induction heart rate (beats/minutes)	122.21 ± 14.05	120.87 ± 16.45	0.536
Induction breath rate (breath/minutes)	25.30 ± 5.48	24.56 ± 4.85	0.31
Induction saturation rate (%)	99.87 ± 0.33	99.85 ± 0.40	0.696
Intraoperative heart rate (beats/minutes)	118.31 ± 20.26	127.45 ± 85.20	0.309
Intraoperative breath rate (breath/minutes)	24.20 ± 4.90	23.23 ± 4.61	0.151
Intraoperative saturation rate (%)	99.92 ± 0.26	99.87 ± 0.33	0.201
Postoperative heart rate (beats/minutes)	118.27 ± 11.46	118.09 ± 11.03	0.908
Postoperative breath rate (breath/minutes)	24.18 ± 4.32	23.11 ± 4.08	0.068
Postoperative saturation rate (%)	99.85 ± 0.38	99.77 ± 0.44	0.163

Table 3. Pain scores measured on the Face, Legs, Activity, Cry, and Consolability (FLACC) scale at different times.

FLACC scores	Group 1 (N = 95)	Group 2 (N = 109)	p value
30 minutes after surgery, mean ± SD	2.22 ± 1.24	2.61 ± 1.21	0.024
1 hour after surgery, mean ± SD	1.10 ± 0.91	1.33 ± 0.80	0.063
3 hours after surgery, mean ± SD	0.71 ± 1.34	0.78 ± 1.43	0.708

Abbrevation: SD, standard deviation

Discussion

The present study examined the effects of pre-emptive and intraoperative use of IV acetaminophen on postoperative pain relief in children. While the greatest analgesic effect during the first 30 minutes after circumcision was observed in the pre-emptive group, both applications of acetaminophen exhibited similar and acceptable efficacy in pain relief one hour after surgery.

Acetaminophen is frequently employed in the treatment of urological surgery-related postoperative pain[6]. IV, oral, or rectal acetaminophen administration are frequently used to provide analgesia after circumcision, with rare side-effects associated with the use of acetaminophen including anaphylaxis, liver disorders, hypotension, and tachycardia[9]. McNicol et al.[10]'s systematic review and meta-analysis showed that 37% of patients receiving IV acetaminophen experienced a 50% decrease in pain severity over four hours (vs. 16% among those receiving placebo). Additionally, the administration of IV acetaminophen was associated with a lower additional analgesic requirement. The FLAAC scoring system was used for pain evaluation in the present study. Scores of 4-6 are interpreted as representing moderate pain under this system. Mean FLAAC scores were below 3 at all-time points in both groups. Additional analgesia was given to 13 (13.7%) children in Group 1 and 17 (15.6%) in Group 2. In agreement with the previous literature, acetaminophen was seen to provide effective treatment of post-circumcision pain.

Pre-emptive analgesia occupies a dominant place among the various alternatives available for improving postoperative pain control. Pre-emptive analgesia involves analgesic medication being administered prior to tissue injury, in other words before the reception, transmission, modulation, and nociception of the aggressive stimulus, the objective being to prevent hyperalgesia and the resulting pain-amplifying stimulus[11]. Pre-emptive analgesia has been used as an effective pain control method in pediatric surgeries, and acetaminophen is one of the most commonly used drugs for pre-emptive analgesia in pediatric patients[7,9,12-14].

The quality of acetaminophen-related postoperative analgesia methods in circumcision has been investigated in a number of previous studies[15]. Munevveroglu and Gunduz[15] compared the effects of penile block, caudal block, subcutaneous ring block, IV tramadol, and IV acetaminophen on pain management after circumcision. No differences were observed between the pain scores of the five groups at 30, 60, 120, or 180 minutes after surgery. The findings of that study showed that IV acetaminophen provided similar pain palliation to that of invasive analgesia methods.

An examination of the literature shows that the IV form of acetaminophen has generally been compared with the rectal or oral forms[7,14,16,17]. IV acetaminophen has been found to exhibit its analgesic effect more rapidly than the oral and rectal forms. This is attributed to the IV form of acetaminophen reaching peak plasma concentrations and entering the central nervous system more rapidly than the other types[16,18]. The efficacy of IV acetaminophen may vary depending on whether use is preoperative, intraoperative, or postoperative. Pre-emptive use of the IV form of acetaminophen was therefore compared with IV form intraoperative use in the present study. Our search of the literature revealed no previous studies comparing these two methods with one another.

Previous studies have shown that IV acetaminophen can be safely used without causing any pathology in vital findings[9,14]. However, pre-emptive IV acetaminophen use is also thought to be capable of causing various changes in the patient's vital signs during surgery. In the present research, patients' vital signs were therefore recorded in the preoperative, induction, intraoperative and postoperative periods, and no clinically significant abnormality was observed between the groups.

There are a number of limitations to this study, one being its retrospective and sin-

gle-center nature. In addition, the observation and pain recording period was limited to the first three hours postoperatively, and it might have been useful to have extended this to 24 hours. Nonetheless, we think that our research is particularly valuable in terms of its large patient number and role as a pioneering study investigating the effectiveness of IV acetaminophen used for analgesia at different time points.

Conclusion

In conclusion, pre-emptive acetaminophen provides more effective analgesia in the first 30 minutes postoperatively but loses this advantage after one hour. Considering the analgesic efficacy and limited half-life of IV acetaminophen, administered either pre-emptively or intraoperatively, its use may be recommended for effective postoperative pain management in children undergoing circumcision.

Author contributions
All authors read and approved the final manuscript.
SA: Conception of the work, analyzing and acquisition of data, drafting the work, final approval.
SSB: Acquisition of data, literature search, drafting the work, final approval.
GE: Design of the work, acquisition of data, drafting the work, final approval.
EP: Conception of the work, acquisition of data, drafting the work, final approval.
HSC: Design of the work, literature search, analysis of data, drafting the work, final approval.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
This study was carried out in line with the Declaration of Helsinki and it was approved by Samsun University, Clinical Research Ethics Committee (No: 2022/2/1, Date: 01.06.2022).

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THE RELATIONSHIP BETWEEN COVID-19 RELATED COAGULOPATHY WITH ORGAN DAMAGE AND PROGNOSIS

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Abstract

Aim: Coagulopathy and thromboembolic complications are frequently seen in COVID-19. We aimed to evaluate the relationship of coagulopathy with organ dysfunction and mortality in COVID-19.

Methods: COVID-19 patients requiring intensive care for treatment and follow-up were retrospectively analyzed. In the definition of coagulopathy, the International Society on Thrombosis and Hemostasis (ISTH) overt disseminated intravascular coagulation (DIC) scoring system was used. Patients were divided into three groups according to the ISTH scores as follows; patients with no coagulopathy (ISTH score <2), patients with non-evident abnormal coagulation (ISTH score = 2), and patients with evident abnormal coagulation (ISTH score > 2) and mechanical ventilation requirement, acute kidney injury (AKI), acute hepatic injury (AHI) and mortality rates were compared between these groups.

Results: One hundred fifty-five critically ill adult patients with COVID-19 were included in the study. An abnormal coagulation profile developed in 94 (60.6%) patients; of those, 56 (36.1%) patients had non-evident abnormal coagulation, and 38 (24.5%) had evident abnormal coagulation. While there was a significant difference between the groups regarding coagulopathy and development of AKI, requirement for mechanical ventilation, and mortality, no significant difference was found in AHI and length of stay in the intensive care unit. Both mortality and development of AKI increased in correlation with the severity of coagulopathy. ISTH score and development of AKI and AHI were risk factors for both mortality and mechanical ventilation requirement.

Conclusions: COVID-19-related coagulopathy, as determined by the ISTH overt DIC scoring system, is a predictor of organ damage and mortality.

Keywords: *Coagulopathy, Coronavirus disease 2019 (COVID-19), critical illness, mortality, organ damage.*

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Introduction

Coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a remaining global epidemic. The spectrum of clinical manifestations is broad and varies from asymptomatic to severe respiratory failure in different individuals.[1] Although most severe patients initially present with single-organ failures, such as respiratory failure, the disease later progresses to a systemic involvement manner, and multi-organ dysfunction may occur. Organ dysfunction is a common and mortal complication in COVID-19.[2] Many mechanisms such as inflammatory response (cytokine storm), shock, and disseminated intravascular coagulation (DIC) may contribute to organ dysfunction in COVID-19. Coagulopathy is one of the most important prognostic factors for these patients' outcomes.[3] There is increasing evidence that coagulopathy and thrombosis are common complications, particularly in COVID-19 patients who do not survive.[2,4] Although the hypercoagulable state associated with COVID-19 has been termed by some as disseminated intravascular coagulation (DIC)-like state, it differs from DIC in terms of some clinical and laboratory findings. COVID-19-associated coagulopathy (CAC) usually exhibits coagulation abnormalities with elevated fibrinogen and D-dimer levels, mild thrombocytopenia, and thrombosis in arterial and venous systems.[5] Unlike the classical DIC pattern resulting from bacterial sepsis or trauma, activated partial thromboplastin time (aPTT) and/or prothrombin time (PT) prolongation is minimal in COVID-19.[6] Therefore, finding effective hematology and coagulation parameters and predicting prognosis in patients with COVID-19 is a priority. The International Society on Thrombosis and Hemostasis (ISTH) overt DIC scoring systems[7] can be used to establish a risk classification and manage coagulopathy in COVID-19 patients at admission. In this study, we retrospectively analyzed the effects of COVID-19 associated coagulopathy on the requirement for mechanical ventilation, acute kidney injury (AKI), acute hepatic injury (AHI), and mortality in COVID-19 patients treated in the intensive care unit.

Materials and Methods

The study was registered at the Adana City Training and Research Hospital Clinical Research Ethics Committee on 27 January 2022 and approved with the approval number of 1758. In this study, COVID-19 patients requiring intensive care for treatment and follow-up, who were hospitalized in the Republic of Turkey Ministry of Health Adana City Training and Research Hospital between October 1, 2020 - October 1, 2021, were retrospectively analyzed. Since the study was retrospective, informed consent was not obtained from the subjects. Exclusion criteria included a history of liver disease or failure, chronic kidney disease or failure, known hematological disease or coagulation disorder, glomerular filtration rate (GFR) <90 mL min^{-1} at admission to the hospital, missing data on hematological, biochemical, and coagulation parameters. Patients' data on COVID-19-related symptoms, signs, and laboratory parameters were obtained from electronic medical records. Demographic characteristics of patients (age, gender, etc.), parameters of blood tests (e.g., complete blood count, kidney and liver function tests, coagulation parameters, blood gas analysis), additional diseases including hypertension, diabetes, cerebrovascular disease, malignancy, coronary artery disease (CAD), presence of chronic obstructive pulmonary disease (COPD), Acute Physiology and Chronic Health Assessment (APACHE) II score calculated within the first 24 h after hospital admission, Glasgow Coma Scale (GCS) score were recorded for all patients. ISTH overt DIC scoring systems were used to define coagulopathy.[7] Coagulopathy was graded by dividing the patients into three groups: patients with ISTH score <2 with no coagulopathy (Group non-coagulopathy), patients with

ISTH score=2 with non-evident abnormal coagulation (Group NEAC), and patients with ISTH score>2 with evident abnormal coagulation (Group EAC). The requirement for mechanical ventilation, AKI, AHI, and mortality rates were compared between these three groups. Kidney Disease: Improving Global Outcomes (KDIGO)[8] definition and staging system was used for AKI diagnosis. Acute hepatic injury was defined as the alanine aminotransferase (ALT) level exceeding twice the upper limits of normal (ALT > 80 U/L) according to Schiff's liver diseases.[9] The primary outcomes were to compare the requirement for mechanical ventilation, the development of AKI and AHI between the groups, and secondary outcomes included length of stay in the intensive care unit and mortality.

Statistical analysis

Statistical analysis of the study was performed using SPSS version 23. Demographic data were given as mean, standard deviation, and number and percentage. The normal distribution for continuous variables was checked with the Kolmogorov–Smirnov test. Statistical differences between groups were evaluated using Fisher's exact and ANOVA tests. Variables were expressed as mean ± SD, and survival analysis was performed using the Kaplan-Meier test. Logistic regression analysis was applied for the relationship of risk factors with mortality and mechanical ventilation. The statistical significance value was accepted as $p<0.05$.

Table 1. Demographics and baseline characteristics of COVID-19 patients

		Group non-coagulopathy (n=61)	Group NEAC (n=56)	Group EAC (n = 38)	p-value
Gender	Male	39(%63.9)	34(%60.7)	16(%42.1)	
	Female	22(%36.1)	22(%39.2)	22(%57.9)	
Age		56.13±17.02	54.79±20.34	56.21±18.01	0.906
Comorbidities		30(%49.2)	22(%39.3)	21(%55.3)	0.291
GCS		14.26±2.02	13.30±3.31	12.84±3.60	0.050
APACHE II score		13.02±4.75	15.39±3.07	14.89±6.56	0.126
Hospitalization Day		13.26±11.18	14.39±12.54	18.92±15.85	0.099
Mortality		12(%19.17)	22(%39.3)	20(%52.6)	0.002*
Acute Kidney Injury	Total	10(%16.4)	17(%30.4)	17(%44.7)	0.009*
	Stage 1	1(%1.6)	3(%5.4)	4(%10.5)	0.153
	Stage 2	6(%9.8)	7(%12.5)	10(%26.3)	0.067
	Stage 3	3(%4.9)	7(%12.5)	3(%7.9)	0.337
Mechanical Ventilation	Total	39(%63.9)	44(%78.6)	33(%86.8)	0.027*
	Invasive	16(%26.2)	26(%46.4)	23(%60.5)	0.002*
	Noninvasive	23(%37.7)	18(%32.1)	10(%26.3)	0.502
Acute Hepatic Injury		24(%39.3)	24(%42.9)	21(%55.3)	0.291

*Data are shown as the number and percentages of patients n(%) or mean±SD; *p<0.05 compared to groups; NEAC: non-evident abnormal coagulation; EAC: evident abnormal coagulation; GCS: Glasgow coma scale; APACHE: Acute Physiology and Chronic Health Assessment*

Table 2. Laboratory parameters of COVID-19 patients on admission.

	Group non-coagulopathy (n=61)	Group NEAC (n=56)	Group EAC (n = 38)	p-value
PCT (µg L-1)	0.78±3.27	1.72±7.89	1.83±3.87	0.552
CRP (mg L^{-1})	83.42±66.56	106.78±99.12	147.57±106.72	0.003*
WBC (10^3 μL^{-1})	10.23±4.98	11.08±4.19	14.07±14.29	0.068
Hb (g dL^{-1})	12.76±2.01	11.95±2.13	11.52±1.78	0.008*
Neutrophil (10^3 μL^{-1})	9.00±4.50	9.87±4.02	10.70±6.48	0.241
Lymphocyte (10^3 μL^{-1})	0.61±0.68	0.60±0.48	0.66±0.50	0.881
Monocyte (10^3 μL^{-1})	0.58±0.70	0.51±0.45	0.49±0.35	0.686
PLT (10^3 μL^{-1})	233.39±85.72	244.30±94.36	256.82±127.35	0.526
Albumin (g L^{-1})	31.36±4.30	29.52±4.61	28.32±3.43	0.002*
Bilirubin (mg dL^{-1})	0.55±0.23	0.80±0.51	0.89±0.64	0.001*
ALT (U L^{-1})	36.79±22.94	34.79±28.97	37.53±29.46	0.871
AST (U L^{-1})	41.51±21.55	42.95±22.59	49.97±33.49	0.250
BUN (mg dL^{-1})	39.70±15.91	34.59±17.31	43.24±20.28	0.058
Creatinine (mg/dl)	0.63±0.18	0.54±0.18	0.64±0.18	0.009*
GFR (mL min^{-1} 1.7^{-1})	108.44±17.50	116.86±23.92	108.34±16.38	0.042
PT (sec)	13.92±10.39	12.87±2.68	14.42±2.96	0.525
aPTT (sec)	24.65±8.13	24.21±7.12	26.09±9.14	0.524
INR	1.03±0.10	1.41±2.70	1.20±0.27	0.464
D-Dimer (µg L^{-1})	572.00±231.59	1718.75±511.05	8913.42±13055.46	0.000*
Fibrinogen (mg dL^{-1})	560.35±187.43	500.95±193.27	551.01±178.19	0.202
PH	7.44±0.06	7.43±0.07	7.42±0.07	0.159
PO2 (mmHg)	72.96±24.82	73.98±28.54	79.34±39.71	0.574
PCO2 (mmHg)	38.88±9.73	39.70±13.58	39.46±15.66	0.939

*Data are shown as mean±SD or number of patients (n); *p<0.05 compared to groups; PCT: procalcitonin, CRP: C-reaction protein; WBC: white blood cell; Hb: Hemoglobin; PLT: Platelet; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; GFR: glomerular filtration rate; PT: prothrombin time; aPTT: activated partial thromboplastin time; INR: International Normalized Ratio*

Results

This retrospective study recruited two hundred thirty-one COVID-19 patients requiring intensive care for treatment and follow-up. Seventy-six patients who did not fulfill the inclusion criteria were excluded from the study.

So, the data of 155 adult patients admitted to the intensive care unit with the diagnosis of COVID-19 were analyzed. 61 (39.8%) patients had no abnormal coagulation profile (group non-coagulopathy), while 94 (60.6%) had coagulopathy according to the ISTH overt DIC scoring system. Of the patients with coagulopathy, 56 (36.1%) had non-evident abnormal coagulation (group NEAC), and 38 (24.5%) had evident abnormal coagulation (group EAC).

The mean age of the patients was 55.66±18.41 years. The number of males was higher in both groups with non-coagulopathy and non-evident abnormal coagulation [39 (63.9%) and 34 (60.7%), respectively].

Approximately half of the patients (47%) had at least one comorbidity (Table 1).

While there was a significant difference between the groups regarding the development of AKI, requirement for mechanical ventilation, and mortality, there was no sig-

nificant difference in AHI and length of stay in the intensive care unit. The death occurred in the intensive care unit in 54 patients; 12 (19.7%) of those were in the group non-coagulopathy, 22 (39.3%) were in the group NEAC, and 20 (52.6%) were in the group EAC (Figure 1). The development of AKI and mechanical ventilation requirements were statistically significantly higher in subjects with abnormal coagulation than in subjects with non-coagulopathy ($p<0.009$ and $p<0.027$, respectively). AKI developed in 44 patients; 10 (16.4%) of them were in the group non-coagulopathy, 17 (30.4%) were in the group NEAC, and 17 (44.7%) were in the group EAC. Mechanical ventilation was required in 116 patients; 39 of them (63.9%) were in the group non-coagulopathy, 44 (78.6%) were in the group NEAC, and 33 (86.8%) were in the group EAC. It was observed that the development of AKI, the requirement for mechanical ventilation, and mortality increased in correlation with the severity of coagulopathy. Although there was no significant difference in the length of stay in the intensive care unit ($p<0.099$), it was observed that the length of hospital stay was longer in patients with evident abnormal coagulation (18.92±15.85) (Table 1).

There were significant differences between the groups in the laboratory findings of the patients in the levels of CRP, hemoglobin, albumin, total bilirubin, and D-dimer. CRP was significantly higher in groups with abnormal coagulation than in patients with non-coagulopathy ($p<0.003$). Hemoglobin and albumin were significantly lower in the group EAC than in the other groups ($p<0.008$ and $p<0.002$, respectively). D-dimer was significantly higher in patients with abnormal coagulation than with non-coagulopathy ($p<0.000$). It was also observed that D-dimer increased in correlation with the severity of coagulopathy (Table 2). ISTH score and development of AKI and AHI were risk factors associated with mortality and mechanical ventilation requirement.

At the same time, the APACHE score ($p<0.000$) was a risk factor associated with mortality, and the elevation of AST ($p<0.001$) and ALT ($p<0.022$) were risk factors significantly associated with the requirement for mechanical ventilation (Table 3).

Table 3. Risk factors associated with mortality and mechanical ventilation

	Mortality		Mechanical Ventilation	
Variable	OR (%95 CI)	p-value	OR (%95 CI)	p-value
Age	1.03 (1.01, 1.05)	0.020*	0.99 (0.97, 1.01)	0.462
ISTH Score	1.54 (1.18, 2.01)	0.001*	1.51 (1.12, 2.04)	0.006*
AKI	23.25 (9.29, 58.18)	0.000*	22.38 (2.96, 168.90)	0.003*
AHI	5.36 (2.60, 11.03)	0.000*	8.36 (3.05, 22.92)	0.000*
Comorbidity	1.89 (0.97, 3.69)	0.061	0.60 (0.29, 1.26)	0.180
AST	1.01 (0.99, 1.02)	0.302	1.03 (1.01, 1.05)	0.001*
ALT	0.99 (0.98, 1.07)	0.290	1.02 (1.00, 1.04)	0.022*
Creatinine	1.18 (0.20, 6.96)	0.851	0.48 (0.07, 3.35)	0.462
APACHE II score	1.11 (1.05, 1.18)	0.000*	1.01 (0.95, 1.06)	0.734

*Data are shown as odds ratio(range of values); *p<0.05 for risk factors of mortality or indication of mechanical ventilation; OR: odds ratio; CI: confidence interval; ISTH: International Society on Thrombosis and Hemostasis; AKI: Acute Kidney Injury; AHI: Acute Hepatic Injury; AST: aspartate aminotransferase; ALT: alanine aminotransferase; APACHE: Acute Physiology and Chronic Health Assessment.*

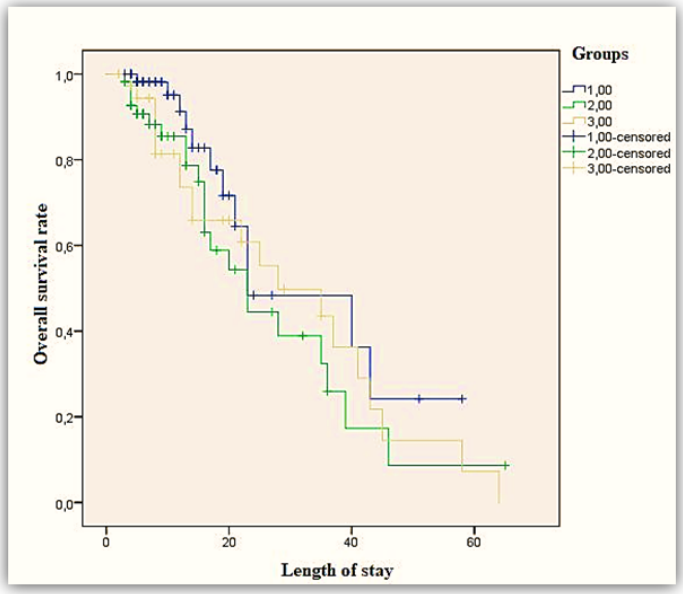

Figure 1. Illustrated survival rates of non-coagulopathy patients, non-evident abnormal coagulation patients, and evident abnormal coagulation patients during hospitalization.
Group 1: non-coagulopathy;
Group 2: non-evident abnormal coagulation;
Group 3: evident abnormal coagulation.

Discussion

Our study showed that as the severity of coagulopathy increased in critically ill COVID-19 patients, AKI and mortality rates gradually raised. It was also shown that the ISTH score was significantly associated with the requirement for mechanical ventilation (OR 1.51, 95% CI 1.12-2.04 P=0.006) and mortality (OR 1.54, 95% CI 1.18-2.01 P=0.001). All results suggested that ISTH overt DIC scoring systems may be used to establish a risk stratification and manage coagulopathy in COVID-19 patients.

COVID-19 is a disease caused by SARS-CoV-2 and may affect multiple organ systems. SARS-CoV-2 causes lung inflammation that progresses to a cytokine storm in severe cases. Alveolar and interstitial inflammation is observed in the lungs of COVID-19 patients.[10] In COVID-19 patients, the immune system is overactivated, numerous inflammatory mediators are released, and activation of platelets occurs.[11] Severe pulmonary inflammation can damage pulmonary vascularity and trigger pulmonary thrombosis in the early stages of the disease.[12] Processes of inflammation and coagulation are the primary defense mechanisms of the body. Both increase in correlation with disease severity and harm the patient.[13]

Unlike classical DIC and sepsis-induced coagulopathy (SIC), patients with COVID-19 have some different abnormal coagulation characteristics. Fibrinolysis is generally suppressed in DIC and SIC, leading to fibrin deposition in the microcirculation and ultimately to organ damage.[14] In these coagulation disorders, the two most helpful laboratory parameters used in estimating SIC are a decrease in platelet count and a prolongation of PT. Additionally, abnormal increases in D-dimer are not expected because fibrinolysis is suppressed in DIC. Patients with COVID-19 pneumonia usually have abnormal coagulation parameters, elevated fibrinogen and D-dimer levels, and mild thrombocytopenia. In COVID-19, D-dimer levels are disproportionately elevated compared to abnormalities seen in other coagulation parameters. This process may be explained by the up-regulation of local fibrinolysis in the alveoli by urokinase-type plasminogen activator (u-PA) released from alveolar macrophages.[15] Tang et al.[4], in a study examining abnormal coagulation parameters, identified markedly elevated D-dimers as one of the predictors of mortality. In an analysis of laboratory-confirmed clinical cases with COVID-19 from more than

550 hospitals in China, which includes data on 1099 patients, D-dimer ≥ 0.5 mg L^{-1} was recorded in 260/560 (46.4%) patients, disease in patients tested if not severe, only 43% had D-dimer elevated, and approximately 60% had severe disease.[3] Similarly, in a large epidemiological study conducted in China, it was observed that D-dimer increased during disease progression in approximately 50% of patients with COVID-19, and this rate increased to approximately 100% in patients who died.[16] Huang et al.[17] reported that in patients who needed intensive care support, D-dimer levels [median D-dimer level of 2.4 mg L^{-1} (0.6-14.4)] at admission were higher compared with those who did not require intensive care support [median D-dimer level of 0.5 mg L^{-1} (0.3–0.8), p = 0.0042]. Our study shows that D-dimer levels reach abnormal levels as the severity of coagulopathy increases. Transiently increased D-dimer levels may be used as an indication of the need for more aggressive treatment and intensive care.

Consumptive coagulopathy seen in SIC and DIC is not seen in the early stage of COVID-19. Spiezia et al.[18] affirmed that patients with COVID-19 and acute respiratory failure present with severe hypercoagulation rather than hypocoagulation (i.e., consumptive coagulopathy). The same study identified that PT and APTT were within the normal range in most patients at presentation, as hypercoagulation occurs in the early stages of COVID-19. Several studies have reported that patients with COVID-19 are in a hypercoagulable state, manifested by decreased PT and aPTT and elevated D-dimer levels.[3,19] In our study, PT was lower in patients with non-evident and evident abnormal coagulation than in patients with non-coagulopathy, which was interpreted in favor of hypercoagulation.

Acute kidney injury (AKI) occurs in 0.5-9% of patients with COVID-19 and is a major complication of COVID-19. AKI develops in 10-30% of critically ill patients.[20] SARS-CoV-2 binds to the ACE2 receptor in the kidney and causes deregulation of the angiotensin mechanism. In COVID-19, this results in hypoxia and hypotension via hypercoagulation and microangiopathy, leading to acute kidney injury.[21] Although AKI development is considered a predictor of disease severity and an unfavorable prognostic factor for survival, few studies have reported a significant relationship between AKI and mortality during the COVID-19 pandemic.[22] In our study, the development of AKI was seen as a risk factor associated with mortality (OR 23,25, %95 CI 9,29-58,18 P=0.000).

Liver dysfunction is more common in severe COVID-19 patients, and patients with liver dysfunction are also at risk of developing severe illness.[23,24] In some studies, the simultaneous increase in ALT and D-dimer was noted in most patients indicating that liver injury may be induced, at least in part, by potential intrahepatic microvascular thrombosis.[25] Although there was no significant difference in our study, it is seen that the development of AHI is higher, especially in patients with evident abnormal coagulopathy.

Conclusion

COVID-19 associated abnormal coagulation is initially localized in the lung, but later systemic involvement may progress to CAC and SIC/DIC. Although the abnormal coagulation state associated with COVID-19 has some similarities to DIC, including a marked increase in D-dimer and mild thrombocytopenia, and meets the criteria for probable DIC in the ISTH scoring system, coagulation parameters like high fibrinogen and factor VIII activity are unlike from DIC.[26] Therefore, just like in DIC, the diagnosis of coagulopathy is made clinically in COVID-19 patients. There is no single test or combination of pathognomonic tests for DIC and CAC. However, the ISTH scoring system, which has high sensitivity and specificity based on expert opinion, may be used in COVID-19 as a guide in preventing, diagnosing, and treating coagulopathy.

In our study, the primary determinant of ISTH was a significant increase in D-dimer levels. In the light of these data, we suggest that patients with a 2 to 5-fold increase in D-dimer levels for COVID-19 associated coagulopathy should be evaluated for intensive care and aggressive treatment, already in the lack of other severe symptoms.

Author contributions
All authors read and approved the final manuscript. Concepts 1,2, Design 1,2, Definition of intellectual content 1,2, Literature search 1,2, Clinical studies 1, Experimental studies 1, Data acquisition 1,2 Data analysis 1,2, Statistical analysis 2, Manuscript preparation 1, Manuscript editing 1,2, Manuscript review 1, Guarantor 2.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
The study's ethical approval was given by the Adana City Training and Research Hospital Clinical Research Ethics Committee on 27 January 2022 and approved with the approval number of 1758.

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A RETROSPECTIVE STUDY ABOUT INCONTINENCE AND ENURESIS IN THE SHADOW OF COVID19 PANDEMIC

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Abstract

Aim: Enuresis and/or incontinence are one of the most common problems that families seek professional help. In this study we wanted to evaluate the patients who applied to pediatric nephrology outpatient clinics with enuresis and/or urinary incontinence during Covid19 pandemic.

Methods: We retrospectively evaluated the patients with the ICD diagnoses of "Non-organic enuresis" and "Urinary incontinence". The data regarding two hundred and four patients were analyzed and compared via dividing them into two groups as Group A (Primary enuresis nocturna) and Group B (other enuresis and incontinence types such as dysfunctional voiding, secondary enuresis, bladder and bowel dysfunction etc.).

Results: Mean age was significantly higher in Group A when compared with Group B (9.57 (± 2.78) vs. 8.67 (±3.27), p=0.036). In Group A male/female ratio was 61/43, in Group B male/female ratio was 36/64 (p<0.001). Family history was more prevalent in Group A (72% vs 31%) (p<0.001). In Group B, 25% of the patients had a history of at least one symptomatic urinary tract infection, and it is significantly higher than Group A (p=0.012). One-hundred and nine over 204 patients had applied for a control visit (53%). Overall treatment success rate in patients having at least one control visit was 82% and 72% in Group A and B respectively.

Conclusions: Urinary incontinence and enuresis are common problems in children. There are certain differences between nocturnal enuresis and day time incontinence in terms of their characteristics and the treatments as well. We usually demand a control visit since the treatment of enuresis and incontinence requires close follow-up, however only 53% of the patients applied for a control visit. This low rate of control visit might be attributed to the Covid19 pandemic since patients and families might have avoided to apply to hospitals with this "less serious" complaints when compared with an important contagious disease.

Keywords: *Covid19, enuresis, incontinence, bed-wetting*

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Introduction

Urinary incontinence is the uncontrolled leakage of urine, and enuresis is the urinary incontinence during sleep including naps. Diurnal enuresis (or enuresis diurna) is an obsolote term replaced with "functional daytime urinary incontinence" nowadays. Primary enuresis defines the habit of bedwetting since the time of toilet training. Secondary enuresis is bedwetting of a person who had been "dry" for at least six months[1-3]. The prevalence of daytime urinary incontinence in children varies from 3.2% to 9%[1,4-6]. Prevalence decreases with age, and is higher in girls[1,4-7]. Prevalance of nocturnal enuresis is reported to be as 7.2-8% in children[8].

Enuresis and/or urinary incontinence are caused by several etiologies. The largest group of patients applying to pediatric nephrology and urology clinics are the ones with monosymptomatic enuresis nocturna. Those patients do not have any other symptoms except bedwetting. Non-monosymptomatic nocturnal enuresis defines bedwetting with daytime lower urinary tract symptoms[1,2]. On the other hand, secondary enuresis may be the result of urinary tract infections, pinworms or psychosocial problems. Diabetes mellitus, as well as diabetes insipitus, and renal insufficiencies may also present as urinary incontinence[3].

In a child with enuresis and/or daytime incontinence, lower urinary system should be evaluated. Together with incontinence, the presence of urgency, frequency or recurrent urinary tract infections might indicate lower urinary tract dysfunction. Overactive bladder, dysfunctional voiding, underactive bladder, postponing of the voiding, stress incontinence, giggle incontinence, vesico-vaginal reflux are the most possible diagnoses in a child with lower urinary tract dysfunction[1]. Nocturnal enuresis have been attributed to several reasons such as nocturnal polyuria, detrusor overactivity, increased arousal threshold during sleep, and genetic factors[1,3].

In this study we aimed to evaluate the profile of the patients with enuresis and/or incontinence in the shadow of Covid-19 pandemic.

Materials and Methods

Pediatric patients who applied to the outpatient clinics of pediatric nephrology department of Kayseri City Hospital between December 2019 and August 2021, during the most overwhelming times of Covid19 pandemic, with the ICD diagnoses of "Non-organic Enuresis" and/or "Urinary Incontinence" were retrospectively evaluated. Among all patients with those ICD codes, 204 patients who had detailed anamnesis on the online records of the hospital were chosen as study group. Since enuresis is defined by ICCS (International Children's Continence Society) in children who had passed their fifth birthday[10], we evaluated the data of patients older than 5 years of age.

We recorded and analyzed the demographic data, laboratory data (kidney function tests, complete blood count, and urine density), radiological findings (urinary ultrasounds), the history of recurrent urinary tract infections, the main complaint at application, the presence of bowel dysfunction (in terms of constipation and fecal incontinence), the final diagnoses, the treatment modalities, and data regarding improvement of the symptoms.

The patients were divided into two groups as "primary enuresis nocturna group (defined as Group A)" and "other incontinence&enuresis types (defined as Group B)", since primary enuresis nocturna can be speculated as a more benign condition. The data regarding the two groups were compared.

The data of 204 patients were evaluated with IBM SPSS for Windows (SPSS version 17.0). For the analysis of the categorical data in Group A and Group B Chi-square (χ^2) test was used. Student t test was performed for normally distributed data, and Mann-Whitney U test for nonnormally

distributed data. Frequencies and percentages were used as descriptive values in the categorical data.
Arithmetical mean±standard deviation was used for the normally distributed data, and median and interquartile range (IQR) were used for the non-normally distributed data. Statistical significance was accepted as 0.05.
Local Ethic Committee of Kayseri City Hospital approved the study, on 18 March 2021, with the decision number 331.

Results

Among 204 patients, 97 of them were male (47.5%), 107 were female (52.5%). Mean age of the patients were 9.1 years (±3.05). Mean age of the girls were 9.02 years whereas mean age of the boys were 9.2 years. Mean age for toilet training was 2.5 years (±0.8) (min-max: 1,5-5).
One-hundred and nineteen (58.3%) patients applied to the hospital with the complaint of bedwetting during sleep, 17 (8.3%) patients with daytime incontinence, 67 patients applied with the complaints of both nocturnal and day-time incontinence and one patient's complaint was incontinence during laughing. When the patients and their parents were questioned, 51% of the patients had the habit of postponing the voiding. Family history of an enuretic relative was found in 55% of the patients.

Table 1. Diagnoses of the patients

	n(%)
Primary enuresis nocturna	104 (51%)
Secondary enuresis nocturna	22 (10.8%)
Dysfunctional voiding	37 (18.1%)
Overactive bladder	12 (5.9%)
Enuresis diurna	14 (6.9%)
Giggle incontinence	3 (1.5%)
Bladder and Bowel Dysfunction	8 (3.9%)
Mental retardation and Learning disabilities	3 (1.5%)
Neurogenic bladder	1 (0.5%)

Constipation was an accompanying condition in 23 (11%) of the patients and fecal soiling in 14 (6.8%) patients. Among 197 patients who had at least one urinary ultrasonographic investigation in the medical records of the hospital's system, 165 (83.7%) had normal findings. Fourteen patients (6.8%) had thickening of the urinary bladder wall, whereas 7 patients (3.5%) were found to have hydronephrosis. Five patients had structural anomalies in kidneys and the urinary tract (excluding hydronephrosis). One patient with daytime urinary incontinence had an ultrasound imaging supporting ureterovaginal fistula, and that patient was referred to pediatric urology for further follow-up and treatment. Incidentally two patients were found to have microlithiasis and one patient was found to have unilateral simple kidney cyst. When we evaluate the medical history of the patients 36 (17.6%) of them had at least one symptomatic urinary tract infection in their life.
One-hundred and four patients (51%) were diagnosed as primary enuresis nocturna, 37 patients (18.1%) as dysfunctional voiding, 22 patients (10.8%) as secondary enuresis nocturna, 14 patients (6.9%) as enuresis diurna, 12 patients (5.9%) as overactive bladder. Eight patients were found to have bladder and bowel dysfunction (previously known as dysfunctional elimination syndrome), three patients were diagnosed as giggle incontinence, and another three patients had the diagnosis of specific learning disabilities. One patient was diagnosed as neurogenic bladder (Table 1).
When we divide the patients into two groups as primary enuresis nocturna (Group A) and other incontinence&enuresis types-(Group B); mean blood urea nitrogen (BUN), serum creatinine, serum sodium, potassium, glucose, hemoglobin levels and mean urine density were similar between the two groups.

Table 2. Clinical and laboratory data of the groups.

	Group A	Group B	p value
N	104	100	
Age (years), Mean(±SD)	9.57 (± 2.78)	8.67 (±3.27)	0.036
Male/Female ratio (n/n)	61/43	36/64	0.001
BUN (mg/dL)	10.3	10.8	>0.05
Serum creatinine (mg/dL)	0.47	0.45	>0.05
Serum sodium (mmol/L)	139	138	>0.05
Serum potassium (mmol/L)	4.5	4.4	>0.05
Serum glucose (mg/dL)	88	84	>0.05
Hemoglobin (g/dL)	13.5	13.2	>0.05
Hematocrit (%)	38.4	38.9	>0.05
MCV (fL)	78.6	78.5	>0.05
Urine density	1020	1019	>0.05
Toilet training age (years)(Mean)	2.5	2.5	>0.05
Family history (n)	45/62 (72%)	14/45 (31%)	<0.001
History of UTI (n of patients)	12/104 (11%)	24/95 (25%)	0.012
Voiding postponement (n)	29/104 (27.8%)	67/100 (67%)	<0.001
Constipation (n)	7/104 (6%)	16/93 (17%)	0.024
Fecal soiling (n)	-	14/94	<0.001
Urinary anomaly (including hydronephrosis)	5	7	
Bladder thickening	-	14	
Comorbid Conditions			
Epilepsy	-	4	
ADHD	1	2	
Obesity	1	3	
Diabetes mellitus	1 (MODY 5)	1 (Type 1 DM)	

Mean age in Group A was significantly higher than the mean of the Group B (9.57 years (± 2.78) vs. 8.67 years (±3.27) p=0.036). Mean toilet training age was similar between the two groups (2.5 years). In Group A male/female ratio was 61/43, however in Group B female patients were dominant with a ratio of male/female ratio of 36/64. The difference is significant with a p value of 0.001.

Postponing of the voiding was seen in 29 patients (27.8%) in Group A, whereas 67 patients (67%) in Group B were found to have void postponement. This difference is also significant (p<0.001). In Group A, family history was found in 45 of 62 patients (72%), in Group B family history was found in 31% of the patients (14/45) (p<0.001).

The history of having at least one symptomatic urinary tract infections was found in 12/204 patients (11%). Among group B, 24 of 95 patients (25%) had a history of urinary tract infection, the rate of urinary tract infections was significantly higher in that group when compared with the primary enuresis nocturna group (Group A) (p=0.012). Fecal incontinence was prominent in 14 patients among 94 patients in Group B whereas none of the patients had fecal incontinence in Group A (p<0.001). Constipation was seen in 7/104 (6%) in Group A whereas it was more prevalent in Group B 16/93 (17%) (p=0.024) (Table 2).

Among all patients, oral desmopressin was administered to 86 patients (42%), behavioral modifications were the choice of treatment in 68 patients (33%), daily calendar in 18 (8%) patients, and 9 patients (4.4%) had been administered oxybutynin. Desmopressin was also the choice of medication in 10 patients with secondary enuresis nocturna, 7 of them benefited from the treatment, remaining three did not have a control visit. Desmopressin was administered after having the detailed anamnesis

and work-up to elucidate the exact etiology of secondary enuresis and when the behavioral modifications fail.

In Group A 76 patients were administered desmopressin treatment, 15 patients were treated with calendar method and 3 patients with alarm method. Ten patients only had suggestions about voiding with no other treatment methods applied. In Group B, 9 patients diagnosed as overactive bladder later, were administered oxybutynin and 58 patients were given advices on voiding habits and postures, with behavioral therapy (Table 3).

Totally, 109 over 204 patients had applied for a control visit (53%). Sixty-nine patients (66%) among 104 patients in Group A had at least one control visit. Among those 69 patients who had control visits, 57 of them were discovered to have responded well to therapy, making the success rate 82% in patients having control visits in Group A. Among 53 patients in Group A having desmopressin and applied for a control visit, 41 patients benefited from desmopressin treatment making the success rate 77%. Twelve among 15 patients benefited from calendar method (success rate is 80%) and 4 patients benefited from lifestyle modifications. In Group B, only 40 of 100 patients had control visits, and among those 40 patients 29 had benefited from the treatment the success rate 72% in this group. In Group A, one patient had been discovered to have a rotational anomaly in his right kidney. An atrophic left kidney with a non-obstructive ureterovesical junction obstruction in right kidney was diagnosed in another patient. Two patients were discovered to have unilateral hydronephrosis, two patients had microlithiasis, one patient with unilateral kidney cyst had the diagnosis of MODY 5 with a HNF1Beta mutation. Two patients in Group A had renal microlithiasis. In Group B, 14 patients had thickening in bladder wall on their urinary ultrasound imaging, whereas none of the patients had thickened bladder wall in Group A. A 5-year-old girl with diurnal enuresis was found to have ectopic ureter opening to vagina wall and referred to pediatric urology. A patient with unilateral right renal agenesis and another one with unilateral two cysts in left kidney were the other urinary anomalies detected in ultrasound in Group B. Three patients had been found to have microlithiasis incidentally. Five patients had hydronephrosis in Group B.

Eight among 104 patients in Group A were referred to pediatric urology department due to unresponsiveness to desmopressin treatment. Twenty patients in Group B were referred to pediatric urology with the suspicion of bladder dysfunction and with the need of uroflowmetric and urodynamic tests.

Table 3. Treatment modalities and the prognosis of the patients

	Group A N (%)	Group B N (%)	p value
Behavioral modifications	10 (9.6%)	58 (58%)	<0.001
Desmopressin	76 (73%)	10 (10%)	<0.001
Oxybutynin	-	9 (9%)	0.001
Calendar Method	15 (7.3%)	3 (3%)	0.008
Alarm	3 (2.8%)	-	>0.05
Urology consultation	8 (unresponsive to desmopressin) (7.6%)	20 (20%)	0.019
Child psychiatry consultation	-	5 (5%)	0.031
Control visit	69/104 (66%)	40/100 (40%)	<0.001
Improvement with treatment modalities	57/69 (82%)	29/40 (72%)	>0.05
Total	104	100	

When we evaluate the comorbid conditions, in Group A there was one patient with obesity, whereas there were three obese patients in Group B. Four patients had epilepsy in Group B. Established diagnosis of attention deficit hyperactivity disorder (ADHD) was found in three patients (one in Group A vs two in Group B). Two patients (one in Group A and one in Group B) were on the follow-up of pediatric psychiatry with the diagnoses of generalized anxiety disorder and were on selective serotonin reuptake inhibitors treatment. One of them responded well to behavioral modifications and the other one benefited from desmopressin treatment. One patient in Group B had the established diagnosis of Type 1 diabetes and applied with the complaint of both daytime incontinence and nocturnal enuresis. The patient had a bad control on her blood sugar and benefited from behavioral modifications together with strict sugar control. Two patients with secondary enuresis with the suspicion of sibling rivalry disorder and three patients with possible learning disorder were referred to pediatric psychiatry department.

Discussion

Nocturnal enuresis is defined as urinary incontinence during sleep in children older than the age of five[10-12]. Primary nocturnal enuresis can be defined when the child has never been dry more than 6 months. Enuresis can be further separated into monosymptomatic or non- monosymptomatic based on the presence of lower urinary tract symptoms or bladder dysfunction[10-12]. Prevalence of nocturnal enuresis in children at 7 years of age changes between 15–22% among male children and 7–15% among female children[9,13]. In align with that, in our cohort we also found a male dominance in primary nocturnal enuresis group (Group A) with a male/female ratio of 61/43. In a recent data, 10% of the children were found to have enuresis and at the age of seven 1% of the children presented with secondary enuresis[14,15]. Among our cohort 22 patients (10.8%) had secondary enuresis nocturna. Genetic predisposition, abnormally large production of urine, developmental issues, heavily sleeping, male gender, constipation, and low socioeconomic status are the known general risk factors associated with nocturnal enuresis[9].

On the other hand, daytime urinary incontinence is an important issue in especially school-aged children affecting their quality of life[1]. Day-time wetting accounts for 4.2%–32% of the total incontinence cases[16]. Daytime urinary incontinence in 7-year-old children has an overall prevalence rate of 3.2-9.0%, and almost 1% of the children experience daytime urinary incontinence in a considerable extent[1,4-6]. Prevalence gets lower with increasing age. Prevalence of daytime urinary incontinence is higher in girls when compared with the boys, this discrepancy might be attributed to the dissimilarities in the anatomy of different genders[1,5-7]. We also found a significant female predominance in Group B in which most of the patients have daytime urinary incontinence.

Family history might be positive for both enuresis nocturna and daytime urinary incontinence. In nocturnal enuresis heritance is more prevalent. Genes 8q, 12q, and 13q are demonstrated to be related with nocturnal enuresis[17]. In our cohort 72% of the patients in Group A (primary enuresis nocturna) had positive family history, whereas only 31% of the patients in Group B had a family member with incontinence. Our findings are consistent with previous data.

Urinary incontinence might also be associated with behavioral issues. Among incontinent children, increased prevalence of anxiety, attention, hyperactivity problems, and oppositional behavior were found when compared with continent children[1,18]. Studies document that several developmental disorders such as ADHD has an association with enuresis[14,18,19]. In addition, enuresis nocturna is associated with psychological disorders, and ADHD is present in as much as 20% of children with nocturnal enuresis[2,9]. Despite the unclearness of the mech-

anism it is speculated that a delay in neuronal maturation might be related with it[14,18,20,21]. In our study three patients had the established diagnosis of ADHD. Anxiety and psychological stress are known causes of overactivity in bladder[22]. In our study, two patients had the diagnosis of anxiety disorder and were using medications prescribed by a pediatric psychiatrist.

Dysfunctional voiding, overactive bladder, underactive (lazy) bladder, voiding postponement, stress incontinence, giggle incontinence, vesico-vaginal incontinence are the subtypes of daytime incontinence. In our study 37 patients had dysfunctional voiding, 12 patients had overactive bladder, 8 patients had bladder and bowel dysfunction, and three patients were found to have giggle incontinence. The signs and symptoms of dysfunctional voiding are post-void residue (poor bladder emptying), staccato or interrupted voiding, incontinence, enuresis, constipation, recurrent urinary tract infections. There is a functional incontinence arising from failure in coordinating the urinary tract between the detrusor and the sphincter ending in a dysfunction in the urinary phase. Overactivity in the pelvic muscles leads to infravesical obstruction[16,23].

Postponing the micturition via holding maneuvers defines voiding postponement and it is associated with low voiding frequency, urgency, and possible urge incontinence[1]. Hydronephrosis may be seen in the children with holding maneuvers. Upper urinary system is strained by the dyssynergic lower urinary tract. In our cohort hydronephrosis was prevalent in 7 (3.3%) patients (two in Group A, five in Group B).

Stress incontinence is defined by the uncontrolled leakage of urine during a physical activity increasing intraabdominal pressure such as coughing or sneezing. Giggle incontinence (or enuresis risoria) is a rare, benign and self-limiting condition, seen usually in females, in which wetting occurs during laughing, although bladder function is otherwise normal. It is thought to be arised from centrally mediated and related to a receptor imbalance of cholinergic and monoaminergic systems that results in loss of the muscle tone[16,24]. Among our study group there were three cases with giggle incontinence. For both stress and giggle incontinence, exact causes are unknown[1].

Another type of incontinence is vesico-vaginal (or urethro-vaginal) reflux or post-void dribbling especially in obese prepubertal girls. During urination, urine might flow towards vagina due to the compression of the thighs and wetting of the underwear occurs after urination[2,16].

Functional constipation develops in almost 50% of children with dysfunctional voiding[2,10-12]. Constipation was found in 11% of our total cases (6% in primary enuresis group (Group A) vs 17% in Group B). Dysfunctional elimination syndrome term, used previously, is now replaced by the term “bladder and bowel dysfunction”, and the new nomenclature is also recommended by The International Children’s Continence Society[2,10-12]. We had 8 patients diagnosed as bladder and bowel dysfunction which had daytime urinary and fecal incontinence.

Anamnesis of the patient (including extensive history of urination and history of febrile urinary tract infections), physical examination (including the inspection of urogenital system to detect congenital malformations, and lumbosacral region examination), voiding diaries, questionnaires, uroflowmetry, and ultrasound are the diagnostic tools. According to ICCS guidelines, the diagnosis of overactive bladder does not require a test such as urodynamics. However if the physician is suspicious of autonomic dysfunction (detrusor overactivity), which is an important etiology of overactive bladder in childhood, cystometrics will be helpful[10-12]. Urinary stream is recorded as a graphic in uroflowmetry, and it gives us data about urine volume, flow time, velocity at the beginning of micturition, maximum flow rate (mL/s), and flow pattern. A normal flow will have a bell-shaped pattern and will be completed within 20 seconds[1,2].

Treatment differs according to the types of enuresis and the etiology of daytime incontinence. Generally, clinicians tend to treat

primary enuresis nocturna cases with both behavioral therapy and medications. Behavioral therapy consists of recommendations on regular water intake and timed voiding during daytime and decreasing the amount of fluid intake in the evening. The calendar method in which the child marks the wet and dry nights is also helpful. We also found a success rate of 80% among patients with calendar method.

Desmopressin is known as the best medication for nocturnal enuresis. Due to the risk of water intoxication, patients must be warn about not drinking large volumes of fluid with the drug[12]. Previous studies concludes the response rate of desmopressin in monosymptomatic enuresis as 60–80%. In our study 77% of the patients among the ones with a control visit in Group A responded well to desmopressin treatment. Despite alarms are known as effective methods for the treatment of enuresis, in our patient group alarm method was not the mostly preferred one due to several known factors such as technical problems related with it such as child's sweat causing false alarms, or low battery time[25]. We only had three patients treated with alarm method in our cohort. Most of the parents of enuretic children tend to prefer the combination of behavioral modifications and taking medications[9]. We did not prefer imipramine, which is originally a tricyclic antidepressant drug, due to its possible cardiac effects.

First choice of treatment of daytime enuresis is urotherapy which is a non-invasive treatment consisting of the education of the child, behavioral modifications and lifestyle changes regarding the arrangement of voiding frequencies, voiding habits and posture, and fluid intake in order to prevent incontinence episodes[1]. Fecal impaction can cause pressure on bladder neck and urethra, resulting in lower urinary tract dysfunction, therefore medication for constipation may be added to urotherapy[1,26-28]. In our patient group, 23 patients (11%) had constipation and were administered constipation therapy together with suggestions about life-style modifications as well as nutritional advices.

Since regular visits are recommended to evaluate progress and to prevent prolonged treatment (or change the treatment if necessary) we usually demand a control visit for our patients. A control visit will also identify the benefits of the treatment, motivate the patient and parents, and the physician will find the opportunity to strengthen the recommendations as well. However only 53% of the patients had the control visit in our cohort. We speculate that, this low control rate might be attributed to the ongoing Covid19 pandemic. Patients and families might have felt uncomfortable to go to hospitals with this "less serious" complaints regarding enuresis and urinary incontinence, when compared with a life threatening contagious disease.

The control rate was significantly higher in Group A, and the treatment success was also higher in this group. This may be related with the need of a prescription since medical treatment rate (mainly desmopressin) is higher in group A. In the shadow of a pandemic affecting the whole world, families might have been evaluated enuresis and/or incontinence as a benign condition and refused to apply to the hospital for a second visit. Due to the fact that anxiety is known as an enuretic issue, Covid19 pandemic might have an additional effect on incontinence and/or enuresis cases via causing anxiety in children, as well as treatment failure.

The limitation of our study is its retrospective nature. We have few missing data regarding the anamnesis of the patients. Besides we were not able to show the trends (whether there is increase or decrease) in the applications of incontinence and/or enuresis and we could not compare the patients with the number of total applications (per year) before the pandemic.

Conclusion

Treatment for enuresis and/or incontinence is multidisciplinary and requires expert knowledge. Urotherapy is a conservative treatment, which is the first choice for all

types of daytime incontinence. Primary enuresis nocturna can be treated with desmopressin and/or calendar method. We recommend to obtain routine biochemical tests and urinary ultrasound to identify urinary system anomalies and other conditions that may present as incontinence.

We believe that Covid-19 pandemic had affected the number of control visit applications as well as compatibility to treatment. Therefore, our study reconfirms the information of delayed health seeking behavior during pandemic. More studies are essential to show the effect of Covid19 on incontinence and/or enuresis.

Author contributions
OYA and FB were involved in the collection of the data and the clinical follow-up of the patients. OYA is the major contributor in writing the manuscript. 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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BIOMECHANICAL COMPARISON OF PROXIMAL FEMORAL NAIL (PFN) WITH ANTI-ROTATORY LAG SCREW AND PROXIMAL FEMORAL NAIL WITH BLADE LAG SCREW IN PROXIMAL FEMUR FRACTURES

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Abstract

Aim: It was evaluated whether nail systems with different lag screws used to treat proximal femoral fractures caused a change in durability in axial loading.

Methods: 14 bone models with femoral fractures of type AO/OTA 31/A2 were randomly divided into two groups, seven bones in each group. Bone models in the first group were fixed with the proximal femur nail which has a blade lag screw, while bone models in the second group were fixed with the proximal femur nail which has an anti-rotatory lag screw. Axial cyclic force at a speed of 5 mm/min was applied to the femoral heads of all bone models in accordance with the femoral mechanical axis. The test was continued until implant failure developed or the bone model was broken.

Results: Bone models in the PFN group were broken with a minimum force of 908 N and a maximum of 1195 N, while their average was 1050 N; the bone models in the A-PFN group were broken with a minimum force of 847 N and a maximum 1219 N, while their average was 1096 N. There was no statistically significant difference between fracture-forming forces after axial loading of the bones in the two groups ($p=0.95$; $p>0.05$)

Conclusions: There were no cut-out and varus collapse complications in the proximal femoral nails applied in the correct position by providing complete reduction in unstable intertrochanteric femoral fractures. After these results, it was predicted that both models of nails could be used safely in unstable intertrochanteric femoral fractures

Keywords: *PFN, intertrochanteric femur fractures, unstable*

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Introduction

The number of hip fractures due to osteoporosis, which occurs after the aging of the world population, is increasing day by day. While the incidence of hip fracture was 1.6 million worldwide in the early 1990s, it is predicted that this count will be approximately 6 million in 2050[1,2].
Fractures of the intertrochanteric region of the femur are frequently seen in patients over 65 years of age as a result of low-energy traumas. It is one of the most common fractures due to osteoporosis in the elderly patient group[2,3]. The incidence of these fractures is currently between 8% and 10%. The incidence of femoral intertrochanteric fractures is also accelerating with increasing life expectancy. In this context, it can be said in general manner that more than 75% of intertrochanteric fractures occur as a result of simple falls during walking or standing in the elderly, while a small percentage occur as a result of high-energy traumas such as traffic accidents and falls from high seen in younger ages[4].
While systems such as DHS and proximal hip plates or proximal femoral nails are recommended for the surgical treatment of intertrochanteric fractures, which are thought to be stable according to preoperative imaging, proximal femoral nails (PFN) are recommended for the surgical treatment of intertrochanteric fractures that are thought to be unstable due to their biomechanical advantages [5].
The condition of success in the treatment of intertrochanteric femur fractures hinge on the patient's general condition and additional diseases, pre-fracture mobilization capacity, osteoporosis level, patient-related factors such as patient expectation, as well as parameters such as fracture type, surgical timing (early-late), implant type used, reduction quality and surgeon's experience. Proximal femoral nails are preferred majorly in intertrochanteric femoral fractures[6].
In this biomechanical study, it was evaluated whether using different lag screws in the proximal femoral nails used in the treatment of proximal femur fractures to prevent rotation causes a change in the durability of the nail under axial loading.

Materials and Methods

This study was approved by the Istanbul Medeniyet University Göztepe Training and Research Hospital Ethics Committee with its decision dated 24.08.2022. In our study. 14 third generation synthetic bone models (Synbone AG indust. Switzeland®, model 2221) with a head-neck angle of 135 degrees, anteversion of 15 degrees, a height of 337 mm, a head diameter of 48 mm and a canal diameter of 10 mm were used (Figure 1).

Figure 1. Synbone synthetic bone model, model 2221

All bone models are 31A2 type fracture models according to AO/OTA classification. This type of fracture is a comminuted pertrochanteric femur fracture, describing a fracture with a loss of lateral wall continuity (≤20.5 mm), with several fragments extending more than 1 cm distal to the trochanter minor, and is included in the group of unstable fractures.
14 bone models with femoral fractures of type AO/OTA 31/A2 were randomly di-

vided into two groups, seven bones in each group. Bone models in the first group were fixed with the proximal femur nail which has a blade lag screw (PFN, Zimed®), while bone models in the second group were fixed with the proximal femur nail which has an anti-rotatuary lag screw (A-PFN, Zimed®). During this fixation, in order to send the lag screw from the center, firstly a Kirschner wire guide was sent until it came out from the middle of the head and then a lag screw was sent over it. Thus, tip-apex distance (TAD) of the lag screw, whose length was planned in advance according to the size of the model, was precisely adjusted and sent in the appropriate position (Figure 2).

Figure 2. Lag screw differences of proximal femoral nails used in bone models
A: lag screw with blade
B: anti-rotatory lag screw

All fracture models were tested under vertical compression forces on the Shimadzu Autograph AGS Tester. First of all, two bone models without any procedure were placed in the test device at 15° valgus in accordance with the vertical loading axis and pilot study was made. Assistance was received from metallurgical and material engineers during all the applications. After the pilot study was found to be successful, axial cyclic force at a speed of 5 mm/min was applied to the femoral heads of all bone models in accordance with the femoral mechanical axis. The test was continued until implant failure developed or the bone model was broken (Figure 3).

Figure 3. Bone model during axial loading

This experiment was repeated for each model and all data were recorded via the computer program attached to the machine for later analysis. The location where the models were broken, and the form of the fracture were noted.

Statistical Analysis

Categorical variables were presented as numbers and percentages, and continuous

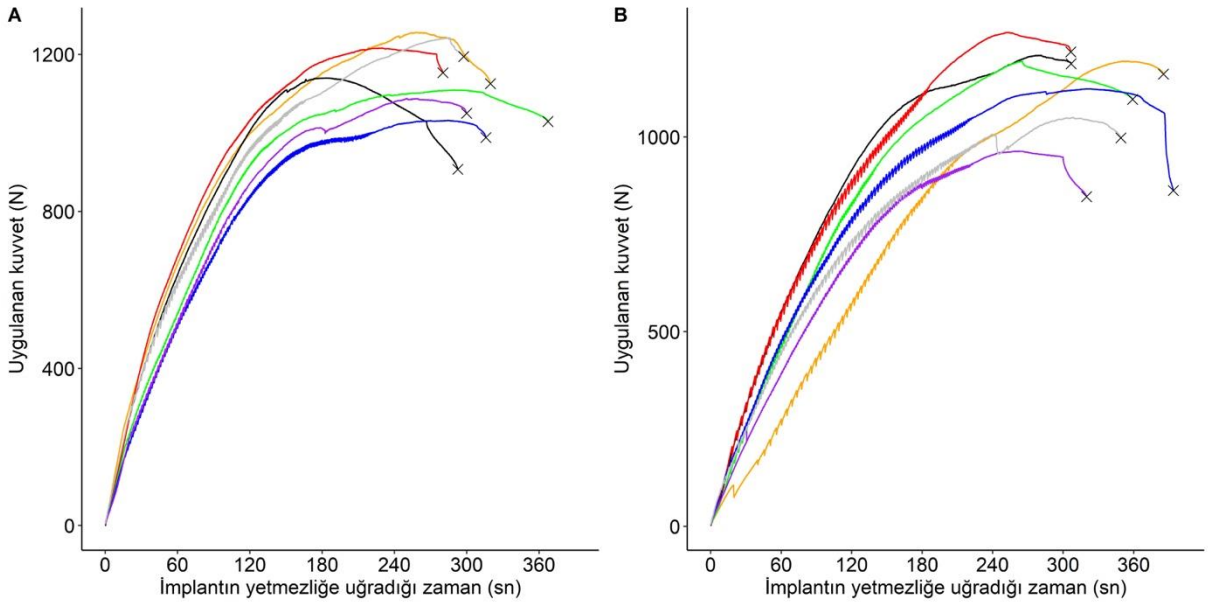

Figure 4. Force timeline at which bone models are broken
A: Bone models fixed with PFNA B: Bone models fixed with PFN with bladed lag screw

variables as mean±standard deviation. The measurements between the two groups were compared with the Mann-Whitney U test. Situations with a two-way p value of <0.05 were considered statistically significant. Analyzes were performed with R version 4.2.1 (https://www.r-project.org/).

Results

Axial loading was applied to both groups of bones until fracture occurred. The bones in the PFN group were fractured with a minimum force of 908 N and a maximum of 1195 N, with a mean of 1050 N. The bones in the A-PFN group were fractured with a minimum force of 847 N and a maximum of 1219 N, with a mean of 1096 N (Figure 4). There was no statistically significant difference between the forces that caused fractures after axial loading on the bones in the two groups (p=0.95; p>0.05) (Table 1). All bones were fractured in a transverse manner from the distal of the existing implant after the application of axial force (Figure 5). No new fractures occurred in any bone during nailing. While axial loading was applied to the fixed fractured bones, no cut-out was observed in any of the bones in both groups. There was no varus deformity in the bones as well.

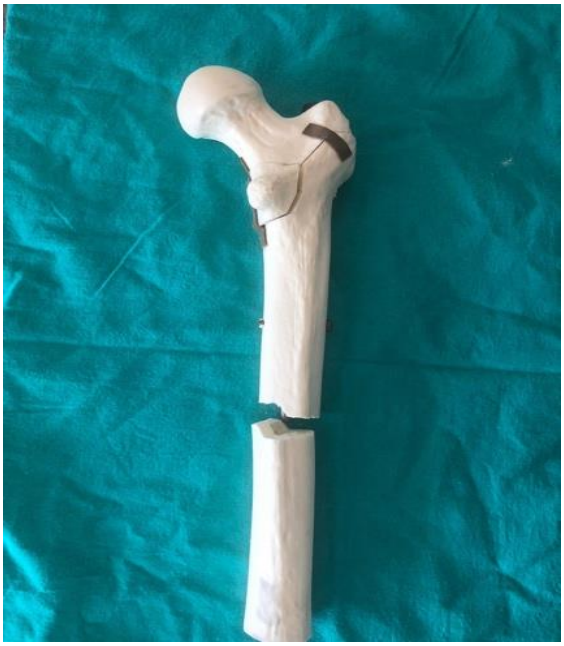

Figure 5. Transverse fractured bone model from the just distal of implant after axial loading

Table 1. Comparison of the axial forces applied between the groups at the moment of fracture. No significant difference in force applied for implant failure between Type 1 and Type 2 (p=0.95)

	Total, n=14	Group 1, n=7	Group 2, n=7	p
Force, median (min-max)	1073 [847;1219]	1050 [908;1195]	1096 [847;1219]	0.95
Force (mean±SD)	1073 [991;1159]	1050 [1009;1140]	1096 [930;1175]	0.95
Force, median (%25-%75)	1059 (125)	1064 (100)	1053 (153)	0.95

Discussion

Treatment of intertrochanteric femur fractures has become an increasingly important issue due to the increasing number of patients. There are mechanical studies showing that intramedullary treatments are superior to extramedullary treatments in unstable intertrochanteric femur fractures. It has been demonstrated biomechanically that the proximal femoral nailing system, which is an intramedullary treatment option, can withstand higher axial loads than the extramedullary treatment options due to its short lever arm feature[7]. It has been shown that the risk of mortality is higher in surgeries performed with dynamic hip screws. Due to such reasons, it is seen that intramedullary nailing technique is increasingly preferred over dynamic hip screw in the surgical treatment of intertrochanteric femur fractures every year[8].

Implant-related complications after surgery in the treatment of intertrochanteric femur fractures cause reoperation in patients and increase the risk of mortality in these patients. While the fixation-related complication rate of pertrochanteric fractures is approximately 5%, the reoperation rate is approximately 4.9%.[9] Implant-related complication rates are seen more in unstable intertrochanteric femur fractures than in stable intertrochanteric fracture patterns[10]. The most common complications are cut-out, varus deformity and perimplant fracture formation[11–13].

Cut-out is one of the most common complications in intertrochanteric femur fractures. The average incidence is around 2-3%.[10,12] Inappropriate reduction of the fracture in intertrochanteric femur fractures is one of the biggest reasons that increase the risk of cut ou[14]. As well as reduction of the fracture, central insertion of the blade is very important too in reducing the risk of cut out and implant failure[10,15]. Placing the lag screw anteriorly should be particularly avoide[12]. Another important failure criterion is the tip-apex distance (TAD). It has been shown that the tip-apex distance calculated according to the position of the lag screw on the postoperative radiograph is less than 25mm, which significantly reduces the risk of implant failure[12,16]. It has been observed that the irregularity of the entrance hole of the nail in the anteroposterior axis and the fixation of the proximal part in a posteriorly displaced manner increase the risk of cut-out[17]. In our study, no cut-out was observed in any model in which we applied axial loading. We attribute this to the appropriate fracture reduction, full compliance with the tip-apex distance rule, and the central placement of lag screw.

Varus deformity is one of the other common complications in intertrochanteric femur fractures. Non-union or implant failure may occur as a result of varus deformity[11]. Implant failure mostly develops in patients with osteoporosis or in the patients who have wide canal and thin cortex, when fracture reduction is not fully achieved. After intramedullary nailing of achieved appro-

priate fracture reduction in unstable intertrochanteric femur fractures, varus collapse was observed less often in cases with distal screw locking than in cases without distal screw locking[11]. Although the fractures were not stable in our model, we did not have any bone models with varus collapse after axial loading due to both complete reduction and distal locking.

Periprosthetic femur fracture is one of the other mechanical complications frequently seen in in intertrochanteric femur fractures.[13,18] Peri-implantic fracture rates are seen at variable rates in the literature (1.4% -4.2%)[13,19]. The most common type of implant fracture is seen in the post-operative period.[19] Locking the distal of the femoral nail with a screw reduces the risk of refracture. It was observed that implanted femurs with distal locking screws were fractured more distally than the proximal region of the implan[18]. In all of the bone fracture models that we used, distal screwing was performed, and all fractures after axial loading consisted of distal to the tip of the implant. In this case, our study seems to be compatible with other studies in the literature.

Implant associated bone fracture during the operation is one of the other complications. While some do not require revision surgery, the patient may need to be operated again after some fractures. The insertion position of the nail and the reduction of the fracture are effective in the formation of fractures during surgery[20]. In our study, no new fractures occurred during implant placement. We attribute this to the facts that the nails are suitable for bone anatomy, the appropriate fracture reduction and we can see the entry point of the nail from the most correct point.

In our study, it is important that we use synthetic femoral bone models instead of human femur bone taken from cadavers in terms of giving inaccurate results during biomechanical study. Another important limitation of this study is that only axial loading is applied instead of simulating all the forces applied to the hip in daily life. More multicentral, randomized controlled advanced clinical studies are needed to obtain more accurate results.

Conclusion

Both models of nails can be used safely in unstable intertrochanteric femur fractures. In our study, we did not encounter cut-out and varus collapse complications with correct positioning and complete reduction in proximal femoral nails with lag screws in both models. We think that our biomechanical study is a guide for the application of intramedullary nailing in the treatment of unstable intertrochanteric femur fractures.

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 study's ethical approval was given by the Istanbul Medeniyet University Göztepe Training and Research Hospital Ethics Committee with its decision dated 24.08.2022

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SERUM VITAMIN D CONCENTRATIONS AND COVID-19 IN PREGNANT WOMEN, DOES VITAMIN D SUPPLEMENTATION IMPACT RESULTS? A COMPREHENSIVE STUDY

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Abstract

Aim: Low vitamin D levels were related to an increased risk of upper respiratory tract infection and pneumonia. Vitamin D might therefore protect against symptoms of the Covid 19. The present study aims to evaluate the relationship between the acquisition and course of Covid 19 and serum vitamin D levels and investigate the prophylactic efficacy of vitamin D supplementation in pregnant women.

Methods: This case-control study was conducted on 318 pregnant women admitted to our tertiary clinic to give birth between March 2020 and December 2021. All cases were tested for Covid 19 via nasopharyngeal swab. Fifty-four patients with positive PCR for SARS-CoV-2 (Group 1) were matched with 264 consecutive healthy controls (Group 2). 25 OH D Vitamin levels were measured and compared between the two groups, along with the frequency of vitamin D supplementation.

Results: Group 1 showed significantly low mean 25 OH D levels, compared to Group 2 (10,22 ± 7,10 (3-37) ng/ml vs. 16,63 ± 10,80 (3,40-48,90) ng/ml, p = 0,000). Sixteen point seven % of controls and 3,7% of cases had normal Vitamin D levels (>30 ng/mL); the difference was also statistically significant (p=0,005). The frequency of vitamin D supplementation was also detected higher in controls than those with positive SARS-CoV-2 (35,6% vs. 14,8%, p=0,003).

Conclusions: Sustaining adequate levels of Vitamin D may positively impact protection against Covid 19 during pregnancy. In this context, Vitamin D supplementation should be considered for the pregnant population, particularly in settings where profound vitamin D deficiency is common.

Keywords: *Vitamin D deficiency; COVID-19; pregnancy; vitamin D supplementation*

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Introduction

The World Health Organization declared an acute respiratory syndrome-Coronavirus-2 pandemic in March 2020 as it spreads worldwide[1]. Although most infected individuals are asymptomatic or mildly symptomatic, among elderly patients or those with concomitant comorbid conditions (cardiovascular disease, diabetes, chronic respiratory disease, and hypertension), it tends to be severe[2].On the other hand, physiological changes in the cardiopulmonary system during pregnancy may influence the Covid 19. Increased heart rate reduced pulmonary residual capacity, and hyperventilation during pregnancy facilitate progression and bring the additional risk of a severe form of infection[3].

Growing evidence suggests that maternal Covid 19 increases risks of neonatal morbidities and mortality, preterm delivery, and small for gestational age (SGA) along with maternal morbidity and mortality[4]. Di Mascio et al. also reported a strong relationship between Covid 19 and early pregnancy loss, preterm delivery, preeclampsia, operative labor, and perinatal mortality[5]. The balance between T helper-1 and T helper-2 cells is crucial for a successful pregnancy, and it could be disturbed by a severe form of Covid 19[6].

Low vitamin D levels were related to an increased risk of upper respiratory tract infection and pneumonia[7]. A meta-analysis evaluating 25 randomized controlled trials showed that Vitamin D supplementation avoids acute respiratory tract infections, and people who were very deficient in vitamin D (< 10 ng/mL) experienced particular benefits[8]. Vitamin D induces antimicrobial peptides, defensins, and cathelicidin and plays a pivotal immunomodulatory role[9]. Vitamin D may also protect against symptoms of the Covid 19, primarily by increasing the level of angiotensin-converting enzyme 2 in the lungs[10].

Less is known about Covid 19 prophylaxis. Thus, risk-reducing strategies and preventive measures for the acquisition and course of the disease are warranted. Vitamin D3 supplementation before or during Covid 19 may benefit the results of the recent studies[11]. When considering the increased rate of receive to the intensive care unit and the risk of thromboembolic complications, need for supplemental oxygen, ventilation, and mortality, pregnant women would be a major target population for prophylaxis. Herein, we also investigated the prophylactic efficacy of vitamin D supplementation on the course of infection in pregnant women.

Materials and Methods

This case-control study was carried out between March 2020 and December 2021 at Izmir Katip Celebi University Ataturk Training and Research Hospital, where 1500 deliveries were managed annually. An informed consent form in accordance with the principles of the Declaration of Helsinki was taken from all pregnant women, both for themselves and their newborns. The study protocol was approved by the institutional ethics committee and the Turkish Ministry of Health (0408).

All single pregnant women from the third trimester were tested for SARS CoV 2 infection using quantitative RT PCR (qRT-PCR) from nasopharyngeal and oropharyngeal swabs before admission to give birth in our tertiary clinic and included in the study. Those with maternal systemic diseases (hypertension, diabetes mellitus, systemic lupus erythematosus, chronic kidney failure) and multifetal pregnancies were excluded. Patients were divided into two groups according to PCR positivity; 54 pregnancies with positive PCR were matched with 264 health controls and described as Group 1 and 2, respectively. 25-OH D vitamin (ng/mL) was recorded at the time of approval for delivery. The matched controls matched closely regarding the 25(OH)D concentration measurement date. Patients in Group 1 were evaluated according to WHO Covid-19 guidelines; SARS-CoV-2 seropositive all patients were asymptomatic ex-

cept two patients who had severe disease[12]. Newborns of group 1 were also tested for SARS CoV 2 using quantitative RT PCR (qRT-PCR) from nasopharyngeal and oropharyngeal swabs.

Blood samples of the entire patient's serum 25-OH D vitamin levels were measured using enzyme-linked immunosorbent assay (ELISA) via DxI 800Beckman, Coulter (California) with interassay variation and intraassay variation of 7%. Maternal age; gravidity; parity; disease severity; maternal mortality; mode of delivery; gestational age; obstetric and neonatal outcomes; total hospitalization length; vitamin D supplementation status; and 25-OH D vitamin (ng/mL) at the time of approval for delivery were recorded.

We use Endocrine Society Guidelines criteria for the description of vitamin D deficiency levels such as<10 ng/mL: severe vitamin D deficiency;10-20 ng/mL (50 nmol/L): vitamin D deficiency; 20−29 ng/mL (50−74 nmol/L): vitamin D insufficiency[13].

Table 1. Comparison of demographic features and clinical characteristics according to study groups

Variables	Study Groups		Test Statistics	p-value
	Covid 19 Group (n=54)	Control Group (n=264)		
p-val	27.92 ± 6.17 (17-43)	27.98 ± 5.81 (18-44)	7123.5	0.994
Gravidity				
1	16 (29.6)	76 (28.8)	8.462	0.076
2	19 (35.2)	87 (33.0)		
3	19 (35.2)	38 (14.4)		
4	2 (3.7)	36 (13.6)		
5+	3 (5.6)	27 (10.2)		
Parity				
0	15 (27.8)	81 (30.7)	1.653**	0.899
1	21 (38.9)	94 (35.6)		
2	13 (24.1)	49 (79.0)		
3	3 (11.5)	23 (8.7)		
4	2 (3.7)	14 (5.3)		
5+	0 (0.0)	3 (1.1)		
Birth Weight†	3141.76 ± 668.76 (621.0-4330.0)	3265.76 ± 484.32 (2000.0-4900.0)	6529.0	0.330
1.st minute APGAR				
0-6	6 (11.1)	15 (5.7)	-**	0.142
7-10	48 (88.9)	249 (94.3)		
5.th minute APGAR				
0-6	6 (11.1)	15 (5.7)	-**	0.142
7-10	48 (88.9)	249 (94.3)		
Maternal hospitalization length†	2.37 ± 3.06 (1-20)	2.00 ± 1.52 (1-12)	6319.5	0.147
25-OH D vitamin (ng/mL) †	10.22 ± 7.10 (3-37)	16.63 ± 10.80 (3.40-48.90)	4556.0	0.000*
Vajinal Labor	14 (25.9)	130 (49.2)	26.723	0.000*
Sectio Cesarea	35 (64.8)	126 (47.7)	5.237	0.025*

**p<0.05 and **Fisher's Exact test, †mean ± standard deviation (minimum-maximum).*
Other variables are presented with frequency and percentage based on columns.
APGAR: Appearance, Pulse, Grimace, Activity, Respiration

As the first step of analyzing the data, the conformity to the normal distribution was examined with the Shapiro Wilk test. The Mann-Whitney Y test was used to compare the means of two independent groups that did not have a normal distribution. In cases where the sample size assumption of the relationships between the categorical data is met (n>5), with the Pearson Chi-Square test; In cases where it was not met, it was applied with Fisher's Exact test. Analyzes were performed in IBM SPSS 25 program.

Results

The demographic features and clinical characteristics of the two groups are shown in table 1. The median age of the control group was higher than those with Covid 19, but the difference was not statistically significant (p=0.994). Gravidity, parity, birth weight, APGAR scores, and total hospitalization length were also similar.

Mode of delivery varied significantly different between groups, namely cesarean section rates were 64.8% vs. 47.79% among Group 1 and 2, respectively (p=0.025). The maternal mortality rate was found to be 3.7% (n=2) in the case group, and this rate was statistically significantly higher than the control group (3.7% vs. %0 p= 0.028). Both cases had a severe form of Covid 19 and a history of mitral valve replacement. Gestational ages of the patients at the time of labor were 35 and 25 weeks, while mortality happened at postpartum 20th and 15th days, respectively.

Table 2. Distribution of fetal and maternal mortality rates between the two groups

	Study Groups			
Variables	Covid 19 Group (n=54)	Control Group (n=264)	Test Statistics	p-value
Intrauterine fetal death	2 (3.7)	14 (5.3)	-**	1.000
Maternal mortality	2 (3.7)	0 (0.0)	-**	0.028*

**p<0.05 and **Fisher's Exact test*

†mean ± standard deviation (minimum-maximum). Other variables are presented with frequency and percentage based on columns.

Table 3. Relationship between study groups and vitamin D levels.

	Study Groups			
25-OH D vitamin (ng/mL)	Covid 19 Group (n=54)	Control Group (n=264)	Test Statistic	p-value
Severe vitamin D deficiency	33 (61.1)	110 (41.7)	12.944	0.005*
Vitamin D deficiency	14 (25.9)	54 (20.5)		
Vitamin D insufficiency	5 (9.3)	56 (21.2)		
Normal	2 (3.7)	44 (16.7)		

*p<0.05

Table 4. Relationship between study groups and Vitamin D supplementation.

	Study Groups			
	Covid 19 Group (n=54)	Control Group (n=264)	Test Statistic	p-value
Vitamin D supplementation	8 (14.8)	94 (35.6)	8.895	0.003*

*p<0.05

The first case also had severe vitamin D deficiency with a 25 OH D level of 4 ng/mL. (Table 2). That value could have been lower than before COVID-19 due to COVID-19[14]. Intrauterine fetal death was present at the time of admission in 16 patients. Among them, 2 cases were in controls, and 14 were in the Covid-19 group, while their 25-OH D vitamin levels varied between 5-16 ng/mL. All fetuses had negative PCR test results for SARS-CoV-2. As shown in Table 2, there was no relationship between Covid 19 and fetal death (p =1.000).

The patient with severe vitamin D deficiency (<10 ng/mL) rate in Covid 19 group was significantly lower than in the control group (41.7% vs. 61.1%; p=0.005). Normal vitamin D levels (>30 ng/mL) were detected significantly higher in the control group than those with Covid 19 (16.7 % vs. 3.7%; p=0.005). The categorical distribution of vitamin D levels between groups is shown in table 3. Concerning vitamin D supplementation, we found that it was higher in the control group, and the difference was statistically significant (35.6% vs. 14.8%; p =0.003) (Table 4).

Discussion

In recent years, the effect of vitamin D on the immune system has gained importance, and experimental studies have shown that vitamin D exerts immunologic activities on various components of the native and adaptive immune system, as well as endothelial membrane stability. Some trials demonstrated protective efficacy on infection, especially those of viral origin[15].

Covid-19, which has extended worldwide like a pandemic since March 2020, has led to severe morbidities and even mortality in the immunocompromised and pregnant population. Accordingly, several clinical studies have been conducted to determine vitamin D's effectiveness in preventing and treating disease[15-16]. Thus, our study focused on whether adequate vitamin D level during pregnancy affects the protection against transmission and severity of the disease, and vitamin D supplementation during pregnancy could be an eligible method for this purpose.

Our study found severe vitamin D deficiency (<10 ng/mL) was higher in the Covid-19 + group. This finding suggests that low vitamin D levels may impair local immune system barriers and facilitate the transmission of infection. In their study, Seven et al. also found a relationship between vitamin D status and the severity of Covid 19 in pregnant women. Interestingly, the entire study cohort showed inadequate serum vitamin D concentrations regardless of the severity of the disease. They further reported that a 25(OH)D level under 14.5 ng/ml is associated with severe Covid 19 and/or poor prognostic factors[17]. Similar to our study, In the study of Ferrer-Sánchez et al. [18] in which the vitamin D levels of pregnant women with Covid 19 were compared with the healthy control group, although the levels were low in both groups, 89% of pregnant women with Covid 19 had 25(OH)D deficiency (<20 ng/mL); it was present in 75.30% of Covid 19 negative pregnant women, the results were statistically significant; also they reported that pregnant women with 25(OH)D deficiency was 2.68 times more likely to contract COVID-19.

As a result, adequate vitamin D levels could be protective against both transmission and severity of the disease.

In addition to the relationship between vitamin D levels and the risk of contracting Covid 19, in another study of 159 Turkish patients with Covid 19 and 332 healthy controls, serum 25(OH)D levels were significantly lower in patients with Covid 19[19]. The relationship between vitamin D deficiency and symptomatology of Covid 19 in pregnancy is reported in a recent study[20].

Nonetheless, a cohort study of 447 Turkish pregnant women with positive and negative Covid 19 tests showed no association between vitamin D levels and severity of Covid 19 even when serum 25(OH)D levels

were found to be 37 ± 27 and 31 ± 21 nmol/L in Covid 19 group and control group, respectively (p = 0.001)[21]. This contradictive finding is likely because the entire cohort of the study had normal (>30ng/mL) vitamin D levels; in other words, there were no cases of vitamin D deficiency, and the severity of the disease may be influenced by clinical factors rather than vitamin D levels. In our study, however, the proportion of patients with normal vitamin D levels was significantly higher in the control group (%16.7% (n= 44) vs. 3.7% (n=2)) (p =0.005).

Another study of 50 hospitalized pregnant with Covid 19 showed that the mean serum 25(OH)D level of the study population was 10-59, significantly lower than the accepted cut-off values (p < 0.001). This value was within the limits of severe vitamin deficiency according to the classification in our study, which was found to be higher in the Covid-19 group. The authors concluded that low vitamin D levels might contribute to a deficiency in immune response, and supplementing Vitamin D during the pandemic could be beneficial during pregnancy for prevention[22].

In our study, we found that vitamin D supplementation was significantly higher in the control group compared to the SARS-CoV-2 group, and we found the difference statistically significant (p =0,003). In line with our finding, a case-control study showed that none of the pregnant with severe diseases were supplemented with vitamin D, even though there was no statistically significant difference in taking supplementation between cases and controls19. The major handicap of our study is the relatively low number of Covid 19 + cases because it was conducted in a single center. Another limitation is the retrospective nature of the study. The relationship between vitamin D levels and the severity of Covid-19 couldn't be statistically related due to the limited number of the group with severe disease.

There is a need for other prospective studies to evaluate the relation to vitamin D‘s effect on Covid 19 in pregnancy. Our study will supply additional knowledge to the cumulative data concerning Covid 19 pandemic.

Conclusion

Sustaining adequate levels of Vitamin D may positively impact protection against Covid 19 during pregnancy. Vitamin D supplementation to maintain serum 25(OH)D at a level of at least 30 ng/mL and above may benefit protection or decrease the risk of Covid 19 and its severity. However, there is a need for new studies comparing the severity of the disease with the level of vitamin D to reach a definitive conclusion. In this context, Vitamin D supplementation should be considered for the pregnant population, particularly in settings where profound vitamin D deficiency is common.

Author contributions
All authors read and approved the final manuscript.
M. Sengül: Project development, Data Collection, data analyzing Manuscript writing
H. Sen Selim: Data collection, data analyzing, manuscript writing
S. Sen: Data analyzing, manuscript writing
H.Erbak Yılmaz: Data Collection
K.Kurt: Project development

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
Informed consent was obtained from pregnant women both for herself and the newborn. This study was approved by the ethical committee with date 21.09.2021 and number 408 of Izmir Katip Celebi Univesity, Faculty of Medicine and the Turkish Ministry of Health.

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PHYSICAL ACTIVITY AND URINARY INCONTINENCE IN THE POSTPARTUM PERIOD

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Abstract

Aim: Urinary incontinence (UI) is defined as involuntary urine loss and is more common in women. Postpartum UI is defined for UI seen in the first year after childbirth. Pregnancy and birth are the most important risk factors for UI in women. The complaints of 65% of these patients begin during pregnancy and some of them continue in the postpartum period. The aim of this study is to evaluate the relationship between level of physical activity and UI in postpartum period of physician women.

Methods: This study was an online cross-sectional self-report survey. An online questionnaire was administered to physician mothers via an online social group, "Physician Mothers". The data of 100 participants were analyzed. The questionnaire of this study consisted of three parts, namely, sociodemographic information, the International Physical Activity Questionnaire-Short Form, and the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-SF).

Results: When classified according to physical activity levels; 41 participants (41%) were not active, 57 participants (57%) were moderately active and 2 participants (2%) were very active. Thirty-eight participants (38%) had UI. There was no significant relationship between the physical activity levels and their UI of physician mothers (p =0.278), but moderate physical activity score and ICIQ-SF total score were negatively correlated (p=0.049. r= 0.198).

Conclusions: In this study, it was found that the physical activity levels of physician women in the postpartum period were mostly moderate, and there was an inverse relationship between moderate physical activity levels and the presence of UI symptoms.

Keywords: *Childbirth, exercise, physicians, urinary incontinence*

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Introduction

Urinary incontinence (UI) is defined as all types of urine leak complaints by the International Continence Foundation. Postpartum UI is involuntary loss of urine observed within the first year after birth[1]. Risk factors for UI include pelvic wall diseases, pregnancy, vaginal birth, aging and obesity[2]. UI is an important health problem affecting women of all ages and the prevalence of urine leaks at least one time per year is 35-45%[3]. Prevalence is higher during pregnancy (30-60%). UI present during pregnancy may continue during the postpartum period and the prevalence in this period is 6-35%[4]. A study in Turkey by Ege et al. in 2006 reported the UI incidence in the postpartum period was 19.5%[5]. The quality of life of an individual is negatively affected by UI and it may cause anxiety and social isolation.

Being physically active throughout life carries great importance for remaining healthy and for well-being. Moderate intensity physical activity reduces the incidence of UI in middle-aged and elderly individuals[6,7]. While there are a few studies assessing the correlation between physical activity and UI in the postpartum period in the literature, there is no study performed with Turkish women. The aim of this study was to assess the correlation between physical activity levels with urinary incontinence during the postpartum period among women doctors.

Materials and Methods

This study used an online, cross-sectional, self-report survey. The study was completed based on volunteerism and was designed in accordance with the criteria in the 2008 Helsinki Declaration. The study received permission from the local ethics committee (Approval no: 09, date: 11/11/2020).

The study was applied in the online social group called 'doctor mothers' containing 3787 members who were women doctors. All members with at least one child and with less than one year since their last birth were invited to the study. This group were sent an online survey form and data were collected in this way. Before collecting data in the study, participants were informed in writing and provided informed consent.

During data collection, women with any chronic disease, regular medication use, who were pregnant or with more than one year since birth were removed from the study. A total of 108 people responded, with eight people excluded due to chronic disease and/or regular medication use. Data were analyzed from a total of 100 people participating in the study.

Survey and Outcome Measures

The survey comprised three sections about demographic data, the International Physical Activity Questionnaire-Short Form and the International Consultation on Incontinence Questionnaire-Short Form. The first section questioned sociodemographic data such as participant age, height, weight, place of employment, area of specialization, number of children, type of most recent birth, active working status and chronic diseases. The second and third sections included the standardized surveys explained in detail below.

International Physical Activity Questionnaire-Short Form (IPAQ-SF)

The IPAQ developed by Craig in 2003 was adapted to Turkish with validity-reliability study performed by Sağlam et al. in 2010[8,9]. The IPAQ-SF questions three basic activities performed for at least 10 minutes within the last seven days (walking, moderate intensity activity and high intensity activity) and mean sedentary duration per day. For the three, separate metabolic equivalence scores (metabolic equivalence threshold; MET) are calculated (high intensity activity MET score: 8.0, moderate intensity activity MET score: 4.0, walking

MET score: 3.3). The MET value for the activity is multiplied by the total duration (minutes) of each activity and the frequency (days) to obtain the MET-min/week score. Accordingly, total physical activity score reflects the physical activity levels of participants classified as follows (8):

• Not active at adequate levels
(<600 MET-min/wk)
•Active at moderate levels
(600-3000 MET-min/wk)
• Very active
(>3000 MET-min/wk).

International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF)

The ICIQ was developed by Avery et al. in 2004 to assess UI and the impact of UI on quality of life. The ICIQ was adapted to Turkish by Çetinel et al. in the same year and validity-reliability studies were performed[10,11].

This scale questions the frequency and amount of UI, perceived reasons for IU and impact of UI on quality of life. The scale contains four sections. The first section is about the frequency of UI, the second is about the amount of UI, the third section is about the impact of UI on daily life and the fourth section questions situations causing UI. Assessment adds the points for the first three sections. Responses to the fourth section without points are used to identify the type of UI. Total points on the scale vary from 0-21; low points indicate UI affects quality of life less, while high points indicate high impact[10].

Statistical Analysis

Data were analyzed with the SPSS v.20 program. The Kolmogorov-Smirnov test and Shapiro-Wilk test were used to determine whether the responses given by participants had normal distribution or not. Descriptive data are given as mean ± standard deviation, while nominal variables are given as percentages. The Student t test or Mann-Whitney U test were used according to the distribution of continuous variables. The chi-square test was used for categoric variables. If both variables had normal distribution, correlation coefficient and statistical significance were calculated using the Pearson test; if they did not have normal distribution the Spearman test was used. Statistical significance level was taken as $p<0.05$.

Results

The sociodemographic characteristics of participants are given in Table 1, while employment characteristics are given in Table 2.

When classified according to physical activity levels in the postpartum period, 41 women were not active at adequate levels (41%), 57 women were active at moderate levels (57%) and 2 women were very active (2%). During pregnancy, physical activity frequency was 41%. When doctors were classified according to branch (basic/internal/surgical/dentistry), there was no significant difference between IPAQ-SF total scores ($p = 0.468$). There was no significant difference between the active employment status of participants with IPAQ-SF total scores ($p = 0.825$).

Thirty-eight people had UI (38%). When classified according to UI types, 17 people had stress UI (17%), 9 people had urge UI (9%) and 12 people had mixed UI (12%). The age, BMI, number of children and weight of most recent child of participants were not significantly correlated with the ICIQ-SF ($p = 0.297$, $p = 0.264$, $p = 0.889$, $p = 0.957$, respectively). The type of last birth (vaginal/cesarean) was significantly correlated with ICIQ-SF total score ($p = 0.05$).

The IPAQ-SF total score and ICIQ-SF total score were not significantly correlated ($p = 0.278$); however, there was a low level significant negative correlation between the moderate physical activity MET score with the ICIQ-SF total score ($p = 0.049$, $r = -0.198$).

Table 1. Sociodemographic characteristics of participants

		Mean±SD	Min - Max
Age		32±3.1	26- 42
Height (cm)		164.5±5.6	152 - 178
Weight (kg)		66.1±9.9	49 - 100
BMI (kg/m2)		24.4±3.5	18.6 - 35.4
Birth weight of most recent child (g)		3223±450	1510 - 4335
	Feature		n = 100
Type of birth	Vaginal		32
	Cesarean		68
Number of children	1		73
	2		26
	≥3		2

cm: centimeters, kg: kilogram, SD: Standard Deviation, BMI: body mass index, %: percentage.

Table 2. Employment characteristics of participants

		n = 100
Place of employment	University Hospital	26
	Education and Research Hospital	26
	State Hospital	29
	Public/Family Health Center	13
	Private Hospital	3
	Private Clinic	3
Status	Specialist Doctor	60
	Assistant Doctor	27
	Practitioner Doctor	13
Branch	Basic Sciences	4
	Internal Sciences	61
	Surgical Sciences	18
	Dentistry	17
Active employment	Yes	25
	No	75

In the period before pregnancy, nine participants (9%) had UI symptoms, while 29 participants had UI symptoms (29%) during pregnancy.

Of women with UI during pregnancy, 72.4% (n=21) continued to have UI symptoms. There was no significant difference between the ICIQ-SF total scores of participants with at least moderate levels of activity during pregnancy and those who were not active at sufficient levels (p = 0.886). When participants were classified according to branch and active employment status, there was no significant difference between ICIQ-SF total scores (p =0.418, p = 0.596, respectively).

Discussion

This study was performed with women doctors with at least one child who had given birth within the previous year. The majority of doctors in the postpartum period were active at moderate levels and nearly 40% had UI symptoms. There was no relationship between physical activity levels with UI symptoms; however, there was an inverse relationship between moderate levels of activity and presence of UI symptoms.

There are many studies in the literature assessing UI risk factors; however, there are very few studies assessing the correlation between physical activity and UI. While mild and moderate levels of physical activity reduce the UI development risk, intense levels of activity increase UI frequency, especially stress type[6,12]. Townsend et al. considered that mild and moderate levels of physical activity contributed to reducing UI by preventing weight gain[6]. The UI incidence was 80% for trampoline sportspeople and this result is reported to be the highest UI incidence in the literature[13]. Another study reported high rates of UI with dance

(63%) and mild tempo running (58%). There is very little information about the effect mechanism of physical activity on the anatomy and function of the pelvic wall muscles. It is thought that pelvic wall muscles may affect deep abdominal muscle activity, that performing exercises in positions where the body is vertical may work pelvic wall muscles more and may ensure muscle coordination[12]. In this study, there was no correlation between physical activity with UI; however, there was an inverse correlation between moderate physical activity and UI and this result may be due to the low number of participants.

There are different results from studies assessing the correlation between physical activity during pregnancy with UI in the postpartum period. Some studies found inactivity during pregnancy was correlated with UI, while some studies showed that activity may increase postpartum UI risk[14,15]. A cohort study reported that women performing low intensity physical activity during pregnancy had lower rates of UI[16]. High intensity activities (like running, jumping) during pregnancy appear to be correlated with stress-type UI; however, it was emphasized that this situation may not be the cause of UI[12]. One study observed that UI in the postpartum period was higher in primiparous women with intense levels of activity in the period before pregnancy but did not observe a significant correlation in those with low levels of activity and found 70% of women with UI during pregnancy continued to have UI in the postpartum period[17]. In this study, women with UI during pregnancy were observed to continue symptoms in the postpartum period at similar rates.

There are very few studies assessing the correlation of UI with occupation. A large population-based cohort study performed with Chinese women did not find a correlation between the difficulty level of their work with UI[16]. Two studies with Chinese and Thai women observed more UI in women employed as laborers[18,19]. In India, women who continued with heavy work in the early postpartum period had more UI[20]. In this study, when classified according to those actively employed or not and according to branch, there were no significant differences in terms of UI. This may be due to the low number of participants and/or employed doctors not performing activities that increase intraabdominal pressure like lifting weights.

Studies in the literature found the incidence of UI was 6-33% in the postpartum period and stress UI was observed most frequently[4,17,21]. In our study, the incidence of UI in the postpartum period was 38% for women doctors and the most frequent type was stress UI. A study in Turkey observed that the incidence of UI was 19.5% in the postpartum period, while it was 14.9% for working women and 19.8% for women who were not working and mixed type UI was most frequent[5]. The high incidence of UI in this study may be due to participants answering the questions openly and voluntarily due to surveys not being applied face-to-face and/or doctors accepting UI as a medical status and not avoiding talking about their situation.

Lifelong regular physical activity has important health benefits including reducing chronic disease and mortality risk, in addition to improving physical fitness and psychology. Regular activity in the postpartum period increases quality of life[22,23]. Elliason et al. reported 71% of Norwegian women exercised in the first year postpartum; however, physical activity levels were not measured in the study and exercise was assessed in terms of days on which exercise was performed weekly[17]. In a study in Turkey, Okyay et al. investigated the physical activity levels of women in the postpartum period and assessed physical activity levels with the IPAQ-SF. They reported that nearly 59.7% of participants were active at moderate levels[22]. In our study, the physical activity levels of participants were found to have similar rates to Turkish women.

Limitations

This study cannot be generalized to the whole population or all women as it was performed with women doctors who were in the postpartum period. As women doctors who were not in this group could not be reached, it is not clear whether the doctors participating in the online survey represent all doctors who are mothers in Turkey. As data were collected with the survey method, results are based on self-report and the study results may be assessed as less reliable due to recall or responder bias about information. The participants were asked about physical activity in the week the survey was completed and were not asked about lifelong physical activity.

Conclusion

In this study, the majority of women doctors in the postpartum period had moderate intensity physical activity and an inverse correlation was found between moderate intensity activities and the presence of urinary incontinence symptoms.

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
The study was completed based on volunteerism and was designed in accordance with the criteria in the 2008 Helsinki Declaration. The study received permission from the local ethics committee (İzmir Bozyaka EAH. Approval no: 09, date: 11/11/2020).

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EVALUATION OF CHANGES OVER TIME IN MENSTRUAL PATTERN AFTER POSTPARTUM TUBAL LIGATION

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Abstract

Aim: A wide range of menstrual problems might be seen in women who had undergone bilateral tubal ligation (BTL). There are few studies examining the course of menstrual abnormalities subsequent to BTL with conflicting results. In this study, we aimed to investigate the over-time changes in the severity of menstrual abnormalities experienced by women after to BTL.

Methods: Women who had undergone postpartum BTL at our clinic between January 2018 and October 2021 and had menses for at least 6 months were included in the study. Patients were divided into two groups according to the time since BTL; group 1 included women who had undergone BTL between 1 to 3 years and group 2 included women who had undergone BTL between 3 to 5 years. The severity of menstrual disturbances and premenstrual syndrome (PMS) symptoms were compared between the two groups.

Results: There was no statistically significant difference between groups regarding menstrual regularity (p=0.476). The most commonly experienced menstrual abnormality was delayed menses in group 1 (42.9%) and frequent menses in group 2 (41.2%). There was no significant difference regarding the type of menstrual irregularity between groups (p=0.299). The amount of menstrual blood loss and the severity of dysmenorrhea were also similar between groups (p= 0.880 and, p= 0.473 respectively).

Conclusions: There is no significant change in menstrual disturbances, dysmenorrhea, and PMS symptoms over time among women who had undergone postpartum BTL. Women should not refrain from BTL because of the concern for the long-term occurrence of menstrual problems afterward.

Keywords: *Bilateral tubal ligation, female sterilization, menstrual disorders, post-tubal ligation syndrome, premenstrual syndrome*

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Introduction

Bilateral tubal ligation (BTL) is one of the most commonly preferred contraceptive methods [1]. BTL or female sterilization is a highly effective contraceptive method but suitable only for women who have completed their families [1]. BTL can be performed at the time of cesarean delivery, called postpartum BTL, or separate from pregnancy, called interval BTL [2]. Different techniques can be used for BTL including laparoscopic, hysteroscopic, and laparotomy. Laparoscopy is generally used for interval BTL while postpartum BTL requires laparotomy [2]. Overall, the procedure is safe with very low mortality and complication rates [2].

Although the contraceptive efficacy of BTL is quite high, the method has some drawbacks [1]. Apart from surgical complications, contraceptive failure, and ectopic pregnancy risks, menstrual problems might be seen in women who had undergone BTL [2]. Menstrual disorders following BTL were first described by Williams et al. in the 1950s [3]. A wide range of menstrual disorders including menorrhagia, metrorrhagia, spotting, oligomenorrhea, and psychological disturbances including premenstrual syndrome (PMS) was reported in the studies and the situation was named post-tubal ligation syndrome (PTLS) [2, 4, 5]. It has been suggested that the ligation of the fallopian tubes, and sometimes mesosalpinx results in a reduction of blood flow to the ovaries. This decrease in ovarian blood flow causes impairment of follicular growth and corpus luteum function. In the end, changes in ovarian hormone levels would lead to menstrual irregularities [4]. Furthermore, an increased risk of hysterectomy due to menstrual irregularities was reported in women who had undergone BTL [6, 7].

There are few studies examining the course of menstrual abnormalities subsequent to BTL with conflicting results. A previous study showed that menstrual irregularities were more likely to occur during the fifth year compared to the second year following sterilization [8]. On the other hand, another study found no difference in menstrual abnormalities both at 2 years and 5 years follow-up after BTL [9]. In this study, we aimed to investigate the over-time changes in the severity of menstrual abnormalities experienced by women after BTL. Our further aim was to investigate the long-term risk of hysterectomy following BTL

Materials and Methods

Ethics

This study was approved by the Institutional Review Board of Kocaeli University Faculty of Medicine, Kocaeli, Turkey (approval number: GOKAEK-2022/18.37). All patients gave informed consent to participate in the study.

Study design and participants

This was a retrospective cohort study conducted at Kocaeli University Medical Faculty Department of Obstetrics and Gynecology. Women who had undergone postpartum BTL at our clinic between January 2018 and October 2021 and had menses for at least 6 months were included in the study. We included women who had been using this contraceptive method (postpartum BTL) at least for one year. Because women within the first year of postpartum BTL might be amenorrheic or have irregular periods due to lactation, these women were excluded from the study. Women who are breastfeeding or stopped breastfeeding less than 6 months ago, amenorrheic, have an endocrinologic disease, or are taking medications that might interfere with the menstrual pattern (e.g uncontrolled thyroid disease, prolactinoma, corticosteroid or oral contraceptive use) were also excluded from the study.

A total of 472 women had undergone postpartum BTL at our clinic during the study period. These women were divided into two groups according to the time passed since BTL; group 1 included women who had un-

dergone BTL between 1 to 3 years and group 2 included women who had undergone BTL between 3 to 5 years. The severity of menstrual disturbances, the presence of premenstrual symptoms, and also hysterectomy rate were compared between the two groups.

The data regarding the demographic characteristics of the patients and the date and method of BTL were collected from the hospital records. Data regarding the educational status of the patients, chronic medical conditions, and drug use were collected from the patients during interviews.

BTL technique

Postpartum BTL defines the ligation of tubes at the time of cesarean delivery [2]. The standard method of postpartum BTL at our clinic is the modified Pomeroy technique [10]. The method involves the placement of a suture around a loop of the fallopian tube, and the excision of that portion of the tube. The excised tubal parts were sent for pathological examination to confirm tubal excision.

Menstrual evaluation and PMS scale

Patients were interviewed via phone calls and fulfilled a questionnaire regarding their menstrual patterns and PMS symptoms. All the patients were interviewed by the same interviewer who is an obstetrics and gynecology resident and also a co-author of this manuscript. An average phone call lasted for 10-15 minutes. To evaluate their menstrual pattern; patients were asked how they would define their menstrual regularity: quite regular/regular/seldom irregularities/irregular. The patients who reported their menstrual pattern to be irregular were asked to define their irregularity: intermenstrual bleeding/prolonged menstrual bleeding/frequent menstruation/delayed menstruation. They were also asked about the amount of menstrual bleeding: very heavy/ heavy/ normal/ reduced/ very reduced and the severity of dysmenorrhea: very severe/ severe/ moderate/ mild/ none. A PMS scale developed by Gencdogan et al. was used to evaluate PMS symptoms [11]. The scale is comprised of 44 items. These items measure 9 symptoms of PMS including depressive mood, anxiety, fatigue, irritability, depressive thoughts, pain, appetite changes, sleep disturbances, and edema. Every item is scored from 1 to 5 depending on the severity of the symptom. Therefore, the total score ranges from 44 (no symptoms) to 220 (maximal symptoms).

Statistical analysis

All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Corp, Armonk, NY, USA). The normality of data distribution was tested using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean±standard deviation (SD). Data without normal distribution were expressed as median (25th-75th percentile). Categorical data were expressed as numbers (percentages). Student's t-test was used to compare data with normal distribution. Mann-Whitney U test was used to compare data without normal distribution. Chi-square tests were used to test the categorical variables. A p-value <0.05 was considered statistically significant.

Results

Of 472 women who had undergone BTL during the study period, we were able to contact 249. Of these women, 74 refused to participate in the study. A total of 80 patients were not eligible due to the inclusion criteria or did not answer all the questions. The remaining 95 patients who completed the questionnaire were eligible and included in the analysis. Of these, 47 underwent BTL within 3 years (group 1) and 49 underwent BTL between 3 to 5 years (group 2). The mean age of the groups was 34,5± 3,3 in group 1 and 36,6± 3,3 in group 2 (Table 1). There was a statistically

significant difference between the groups regarding patient age (p=0.003). When body mass index (BMI), gravidity, and the educational status of the two groups were compared, no significant difference was present between the groups (p>0.05).

In group 1, 55.3% of the patients reported that their menses were quite regular or regular while 65.3% reported regular menses in group 2. There was no statistically significant difference between groups (p=0.476). The most commonly experienced menstrual abnormality was delayed menses in group 1 (42.9%) and frequent menses in group 2 (41.2%). Overall, there was no significant difference regarding the type of menstrual irregularity between groups (p=0.299). The amount of menstrual blood loss and the severity of dysmenorrhea were also similar between groups (p= 0.880 and, p= 0.473 respectively).

The median PMS score was 116 (97-154) in group 1 and 123 (95-150) in group 2 (p=0.855). There was no statistically significant difference between groups regarding PMS symptoms. None of the patients in both groups underwent a hysterectomy (Table 2).

Table 1. Baseline characteristics of the patients

Characteristics		Group 1 (n=47)	Group 2 (n=49)	*p*
Age (y)		34.4± 3.3	36.5± 3.3	0.003*
Gravidity		3 (3-4)	3 (2-4)	0.591
BMI (kg/m2)		26.7 (24.3-31.5)	28.3 (24.8-32.4)	0.373
Education	Primary school	21 (44.7%)	17 (34.7%)	0.677
	Secondary school	7 (14.9%)	9 (18.4%)	
	High school	12 (25.5%)	12 (24.5%)	
	University	7 (14.9%)	11 (22.4%)	

Data are presented as mean± standard deviation, median (25th-75th percentile) or n (%).
BMI; body mass index.
**The result is significant at the p level <0.05*

Discussion

Although BTL is a safe and effective method of contraception [1], there is a concern that BTL might lead to menstrual disturbances as a long-term sequela. However, our results have shown that there was no over-time increase in the prevalence of menstrual disorders or PMS symptoms among women who underwent postpartum BTL.

The presence of menstrual abnormalities following BTL was suggested nearly 80 years ago [3]. Since then, millions of women have undergone the procedure [1]. However, the occurrence of menstrual irregularities after BTL is still under debate. There are several studies investigating the long-term course of the menstrual pattern after BTL with conflicting results. A prospective controlled study found that at 1-year follow-up, dysmenorrhea and heavy bleeding were common among women with BTL compared to controls [12]. Another study found higher levels of menstrual pain and heavy menstrual flow five years after BTL. Importantly, menstrual function in the first year of follow-up was similar to pre-sterilization status. The authors concluded that menstrual changes secondary to BTL may take some time to develop [8].In contrast with this study, a prospective study found no

Table 2. Evaluation of menstrual pattern and PMS symptoms

	Parameters	Group 1 (n=47)	Group 2 (n=49)	*p* value
Menstrual regularity	Quite regular	11 (23.4%)	15 (30.6%)	0.476
	Regular	15 (31.9%)	17 (34.7%)	
	Seldom irregularities	7 (14.9%)	9 (18.4%)	
	Irregular	14 (29.8%)	8 (16.3%)	
Type of irregularity	Intermenstrual bleeding	3 (14.3%)	1 (5.9%)	0.556
	Prolonged bleeding	4 (19.0%)	4 (23.5%)	
	Frequent menstruation	5 (23.8%)	7 (41.2%)	
	Delayed menstruation	9 (42.9%)	5 (29.4%)	
Amount of bleeding	Very heavy	9 (19.1%)	8 (16.3%)	0.880
	Heavy	5 (10.6%)	7 (14.3%)	
	Normal	25(53.2%)	23 (46.9%)	
	Reduced	4 (8.5%)	7 (14.3%)	
	Very reduced	4 (8.5%)	4 (8.2%)	
Dysmenorrhea severity	Very severe	7 (14.9%)	7 (14.3%)	0.473
	Severe	4 (8.5%)	5 (10.2%)	
	Moderate	11 (23.4%)	6 (12.2%)	
	Mild	8 (17.0%)	15 (30.6%)	
	None	17 (36.2%)	16 (32.7%)	
PMS Score		116 (97-154)	123 (95-150)	0.855
Hysterectomy		0 (0)	0 (0)	

Data are presented as median (25th-75th percentile) or n (%).
PMS; Premenstrual syndrome

long-term effect of BTL on menstrual indices or pelvic pain. In this study, patients were followed up for 3 to 4.5 years [13]. In line with this study, we found that the prevalence of menstrual disturbances and PMS symptoms were similar among women who had undergone BTL between 1 to 3 years and 3 to 5 years. This data suggests no increase in menstrual disturbances over time.

Several studies found an increased incidence of hysterectomy in women who underwent BTL [14, 15]. These studies suggested that incresed hysterectomy rate in sterilized women is evidence for menstrual abnormalities following BTL [4]. However, most of these studies were uncontrolled for potential confounders such as previous oral contraceptive use. Other studies either found no risk or a slightly increased risk, especially in women who underwent BTL under 30 [4, 13, 16]. In line with these studies, we found no increase in hysterectomy risk in sterilized women over time, suggesting the absence of a serious menstrual irregularity requiring surgery after BTL.

The suggested pathophysiology mechanism for PTLS was that decrease in ovarian blood supply as a result of tubal destruction would lead to follicular dysfunction and subsequent disturbances in ovarian hormone levels [4]. However, studies comparing the hormone levels and ovarian blood flow before and after tubal ligation did not confirm this theory. No difference was found in ovarian artery blood flow or ovarian hormone secretion postoperatively in comparison with

baseline values [17]. In addition, studies failed to show any detrimental effect of BTL on ovarian reserve [18]. Therefore, tubal ligation does not lead to ovarian damage and the underlying mechanism suggested for PTLS is invalid [8]. These results question the existence of PTLS and support the findings of the present study which showed no long-term increase in menstrual abnormalities following BTL.

There are some limitations of the study. The main limitation is the small sample size and the evaluation of self-reported symptoms rather than an evaluation based on an objective scale. Furthermore, the mean age was older in group 2. Group 2 constituted women who had undergone postpartum BTL 3 to 5 years ago. Every population has a mean female age for the last birth and completion of childbearing [19]. Since postpartum BTL is performed during the final childbirth, it is conceivable that more time has passed since the final childbirth in group 2 compared to group 1. Therefore, the mean age of women in group 2 is older. Another limitation is the lack of a control group of women without BTL. The main strength of the study is the long-term follow-up of up to 5 years. Secondly, in addition to menstrual disturbances, we also evaluated PMS symptoms. Finally, the modified-Pomeroy technique was used in all procedures, excluding the effect of different BTL techniques on the outcome [12].

Conclusion

Our results showed that there is not a significant change in menstrual disturbances, dysmenorrhea, PMS symptoms, and hysterectomy rate over time among women who had undergone postpartum BTL. Women should not refrain from BTL because of the concern for the long-term occurrence of menstrual problems afterward.

Author contributions
All authors have made substantial contribution to the design of the study, data collection and analysis, writing of the manuscript and critical analysis. All authors have read and approved the submitted version of the manuscript.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval

This study was approved by the Institutional Review Board of Kocaeli University Faculty of Medicine, Kocaeli, Türkiye (approval number: GOKAEK-2022/18.37). All patients gave informed consent to participate in the study. This study was conducted in accordance with the ethical standards of the Helsinki Declaration and its later amendments

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DETERMINATION OF THE EFFECTS OF INFLAMMATORY MARKERS ON MORTALITY IN INTENSIVE CARE PATIENTS

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Abstract

Aim: Mean platelet volume (MPV), neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), red cell distribution width (RDW) plays important role as effective factors in predicting mortality and morbidity in various diseases. In the present study we aimed to assess and compare MPV, NLR, PLR and RDW of survived and non-survived patients by examining the blood samples taken within the first hour after admission to our intensive care unit.

Methods: This retrospective study included 672 patients who were hospitalized in a mixed 16 bed intensive care unit (ICU) between January 2019 and January 2020. By examining our hospital's computer-based data system, patient data of the survived and non-survived patients who were treated in the ICU were analyzed.

Results: The demographic parameters of the patients (gender), concomitant disease, and laboratory parameters including HTC, PLT, WBC, MPV and PLR were not significantly different between the survived and non-survived patients. RDW, albumin, CRP and NLR were found statistically different between the study groups.

Conclusions: The elevated RDW, NLR and CRP levels were found more significant than the other inflammatory markers for determining mortality of the critically ill patients. In addition, evaluation of albumin level was found important in defining the prognosis of the intensive care unit patients.

Keywords: *Mean platelet volume, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, red cell distribution width, intensive care, mortality*

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Introduction

Critical diseases treated in intensive care unit such as ARDS, pneumonia, exacerbations of chronic lung disease, sepsis, multiorgan failure, cardiovascular disease, cerebrovascular accident etc. cause inflammatory response with high mortality rates in patients. Although Acute Physiological and Chronic Health Evaluation (APACHE) II and the Sequential Organ Failure Assessment (SOFA) are important to predict mortality in critically ill patients, RDW, MPV, NLR and PLR are easily accessible, non-invasive and cost-effective indicators in the ICU.

In this retrospective study, we investigated the association between RDW, MPV, NLR, PLR values and mortality in critically ill patients. Many studies have been conducted to show the effect of these markers in determining mortality but to our knowledge there's no study comparing all of these markers together in ICU patients.

Red cell distribution width (RDW) has been shown to be elevated in various diseases including coronary artery disease, heart failure, atrial fibrillation, stroke and cancer[1]. The association between RDW and mortality can be explained with stressed erythropoiesis and variations in RBC survival[2]. RDW may be an appropriate marker for the differentiation of various diseases.

MPV is an indicator of platelet activation and has been shown to increase with cardiovascular diseases related to atherosclerosis, hypertensive disease and malignant tumors[3,4]. Increased platelet volume and size indicates the presence of a thrombotic and inflammatory activity. For this reason, MPV has been used in various inflammatory disorders such as rheumatoid arthritis and ankylosing spondylarthritis to determine the effectiveness of anti-inflammatory therapy and disease activity[5,6].

The neutrophil to lymphocyte ratio (NLR), is a rapidly accessible marker and has been shown to be useful in determining prognosis in oncological diseases including lung, ovary and breast[7-9]. Also, NLR is a prognostic factor for many conditions such as predicting the mortality of septic patients, outcomes of cardiovascular diseases[10,11].

Jilma et al. reported a 300 % increase in circulating neutrophils 4 to 6 hours after inflammation, while a 96 % reduction in monocytes and 85 % reduction in lymphocytes[12]. Elevated NLR levels indicate an imbalance in the inflammatory response resulting from increased neutrophil and decreased lymphocyte counts. The platelet to lymphocyte ratio (PLR) can also be presented to the clinician as a diagnostic criterion for inflammation in various diseases (pneumonia, bacteremia) and for survival prediction[1].

The target of this study was to analyze RDW, MPV, NLR and PLR values together in the intensive care unit patients and we found that elevated RDW levels were more significant than the other inflammatory markers for determining mortality.

Materials and Methods

Study design

In the present study we investigated whether RDW, MPV, NLR and PLR levels together on admission could predict the mortality of the patients in the intensive care unit. After obtaining Local Ethics Committee approval with the protocol number 2017-KAEK-1892020.07.22.02, we retrospectively analyzed the data of intensive care unit by examining our hospital's computer based data system. Helsinki Declaration guidelines were followed throughout the study.

The patients were divided into two groups; survived patients (patients discharged from ICU) and non-survived (patients who died in the ICU). Demographic data of the patients including age, gender, length of stay in the intensive care unit, comorbidities were collected from the medical records. Hematocrit (HCT), white blood cell counts (WBC), platelet counts (PLT), mean cor-

puscular volume (MCV), red cell distribution width (RDW), neutrophil/lymphocyte count ratio (NLR), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP) and albumin were determined. The laboratory data of the patients consist of blood samples taken when they are admitted to the intensive care unit. NLR was calculated by division of the neutrophil count by the lymphocyte count. PLR value was obtained by division of the platelet count by the lymphocyte count.

Statistical analysis

Number and percentage for classified variable, mean ± standard deviation or median, minimum and maximum values were used for continuous variable data. Conformity of permanent variables to normal distribution was interpret by Kolmogorov-Smirnov test. Chi-square test was used for intergroup comparisons of categorical variables. Student t test or Mann Whitney U test was used for comparison of continuous variables between two groups.

Evaluation of RDW, albumin, CRP and NLR values used to estimate patient's prognosis (survivor / non survivor) were made by ROC analysis. The obtained ''area under the curve'' values and confidence intervals are presented. The P<0.05 value was considered statistically significant.

Results

A total of 672 patients were examined in the study. After admission to the intensive care unit, 169 of these patients were dead and 503 were survived. There was no gender difference between the survived and dead patients (P=0.268). Of the 361 male patients, 264 were survived and 97 were dead. Of the 311 female patients, 239 were survived and 72 were dead. Comorbidities of the deceased and survived patients were found similar (P=0.109). 131 of 169 deceased patients (26.8%) had comorbidities and 358 of 503 survived patients (73.2%) had comorbidities.

Table 1. General characteristics and laboratory data of the study groups

Gender, n (%)		Survived Group	Exitus Group	P
Men		264(73.1%)	97(26.9%)	0.268
Women		239(76.8 %)	72(23.2%)	
Comorbidities (%)		358(73.2%)	131(26.8%)	0.109
Age (years)	Mean (SD)	63.08±20.27	73.25±14.32	<0.001
Hb, g⁄dL		12.54±2.33	11.80±2.35	<0.001
Htc, %		38.11±7.11	36.95±7.62	0.072
WBC, µ⁄mm3		12.63±6.0	14.18±7.4	0.009
RDW		14.60±2.35	16.35± 3.10	<0.001
MPV, fL		10.30±0.98	10.43±1.03	0.184
Duration in ICU (Days)	Median (min-max)	2(1-260)	11(1-270)	<0.001
PLT, µ⁄mm3		228(30-693)	210(40-722)	0.146
NLR		7(1-112)	9(1-63)	0.014
PLR		166(8-1745)	194(9-1208)	0.061
C-reactive protein		17.30(0.60-544)	51.50(0.60-438)	<0.001
Albumin (gr⁄dL)		36.70(15.60-56.20)	32.80(15.40-49)	<0.001

RDW; red cell distribution width, CRP; C reactive protein, HCT; hematocrit, WBC; white blood cell counts, PLT; platelet counts, MCV; mean corpuscular volume, NLR; neutrophil/lymphocyte count ratio, PLR; platelet to lymphocyte ratio, SD; standard deviation

The mean ages of the deceased patients were higher than the survived patients (P<0.001). While the mean age of the deceased patients was found 73.25, the mean age of the survived patients was 63.08. Durations in ICU of the survived and deceased patients were statistically different (P<0.001). The medium length of stay in the ICU of the survived and deceased patients were found 2(1-260) and 11(1-270) days, respectively (Table 1). HTC, PLT and MPV levels were not significantly different between the survived and deceased patients (P>0.05). However, RDW(P<0.001), albumin (P<0.001), CRP(P<0.001), NLR (P=0.014) and WBC (P=0.009) were found statistically different between the study groups. The mean RDW of the survived patients (14.60) were found lower than the deceased patients (16.35) (P<0.001). Serum albumin levels of the survived patients were found higher than the deceased patients (P<0.001). Serum CRP levels of the survivors were found lower than the deceased patients (P<0.001). NLR and PLR of the survived patients were found lower than those of the deceased patients.

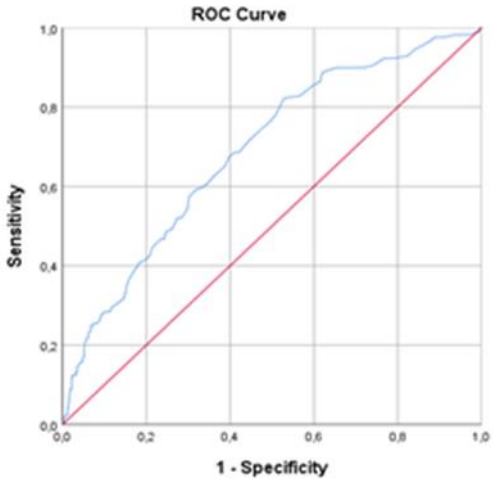

Figure 1. ROC curves analysis for predicting mortality by RDW.

However only the difference in NLR values were found statistically significant between the deceased and survived patients (P=0.014). There was no statistically significant difference in terms of MPV values between the deceased and survived patients (P=0.184). The demographic parameters of the patients (age, gender), comorbidities and laboratory data were shown in Table 1.

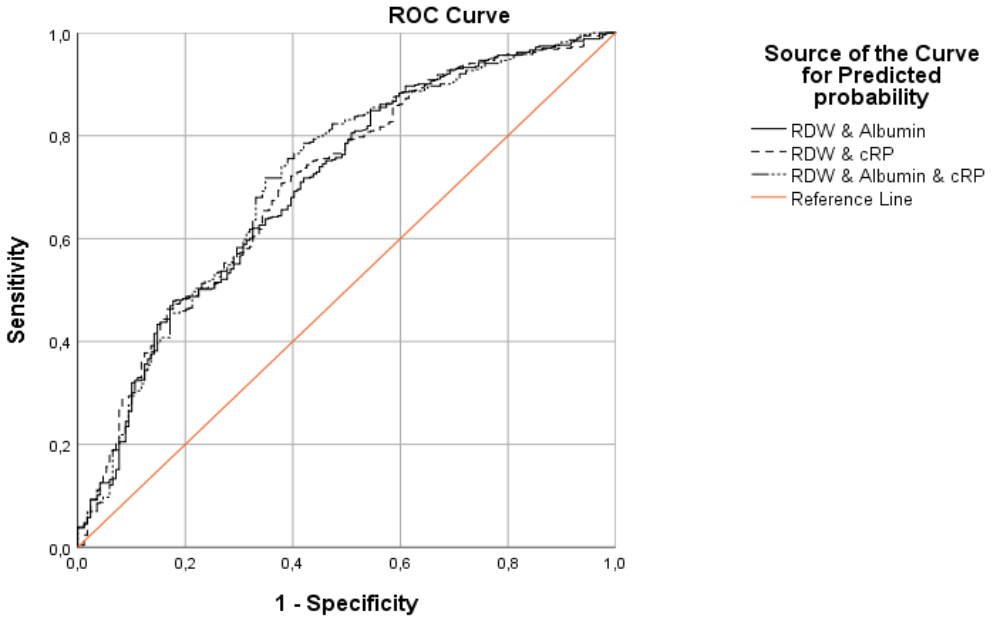

Figure 2. Relationship between inflammation-based markers and survival of the patients in the ICU. RDW, red cell distribution width; CRP, C reactive protein; albumin.

Evaluation of RDW, albumin, CRP and NLR values used to determine patient's prognosis (ex⁄surviving) were made by Roc analysis. RDW was found to be more significant marker than the other markers used to determine the mortality of the patients (Fig.1). The obtained "area under the curve" values and confidence intervals are presented in Fig.2. The area under the curve shows the accuracy-strength of the estimation. While examining albumin and RDW values together has a 70% accuracy in determining mortality of the patients in the ICU, evaluating RDW, albumin and CRP values together provides 71% accuracy.

108 patients admitted to the ICU due to acute respiratory failure, n=22 patients' acute cardiac failure, n= 131 patients cerebrovascular disease, n=28 patients intoxication, n=18 patients infectious reasons, n=54 patients traumatic or non-traumatic brain injury, n=22 patients renal failure, n=279 other reasons (postoperative patient, diabetic ketoacidosis, trauma, gastrointestinal bleeding, tetanus etc.). Also 10 patients had more than one concomitant disease.

Patients' length of stay in the intensive care unit was found longer in the deceased patients (P<0.001). Comorbidities of the survived and deceased patients were found similar. 131(77%) of 169 deceased patients had comorbidities. 358(71.2%) of 503 survived patients had comorbidities.

Discussion

In the present study, we observed that elevated RDW, NLR and CRP levels were more significant than the other inflammatory markers for determining mortality of the critically ill patients. Also, albumin level of the patients was found to be valuable in determining the prognosis of intensive care patients.

Pilling et al. investigated red cell dispersion breadth and common disease onsets in a large population of healthy volunteers and they have stated that increased RDW are important in determining all-cause mortality [2]. It has been shown that high RDW levels are associated with increased incidence of hospital recorded cardiovascular diseases such as HT, heart failure, atrial fibrillation, peripheral vascular disease and stroke[2]. In another study, Lionte et al., showed that, inflammation related indices based on CBC count such as RDW, NLR and MLR (monocyte-lymphocyte ratio) were associated with hospital mortality in acutely poisoned patients[14]. Akcal et al. investigated the impacts of post-operative changes in inflammatory markers such as RDW, MPV, PLR and NLR on mortality rate of the patients operated for hip surgery and found that, only the increase in RDW levels were statistically significant in the non-survivor group in comparison with the survivor group postoperatively[15]. Similar to this study, we found that RDW levels were more significant in determining the mortality of the patients in intensive care unit compared with other markers.

Neutrophil/lymphocyte ratios are accepted as potential markers to classify high risk of death in patients with stage 1 lung cancer, breast cancer or epithelial ovarian cancer [7,8,9]. Ham et al. have found both higher NLR and MPV/platelet ratio in the non-survivor group than in the survivor group and they have declared that MPV/platelet ratio independently associated with an increased mortality at one year in critically ill patients [16]. Zhai et al. conducted a study on cardiac intensive care unit patients to investigate the relationship between PLR and hospital mortality. The patients were grouped according to PLR quartiles. They showed that hospital mortality increased as PLR quartiles increased[17]. In our study, although increased NLR and PLR levels were found in the non-survivor group, only the increase in the NLR levels were statistically significant.

Mean platelet volume (MPV), is an indicator of platelet function and is calculated as the ratio of plateletcrit to platelet count [18]. Zhang et al, investigated the association of platelet volume indices and mortality in intensive care unit patients and found that higher MPV and PDW (platelet distribution width) values are associated with increased

risk of death[19]. In another study, Wang et al showed that MPV and PDW values were decreased in the patients with slight cognitive impairment and Alzheimer's disease[20]. Also confounding factors such as diabetes mellitus, hypertension and many drugs (statins, clopidogrel and angiotensin-converting enzyme inhibitors) may affect MPV levels[21,22]. In our study, MPV of the non-survivor group was found higher than the survivor group but the difference was not found statistically significant. In the present study, the mean age of the deceased patients was higher than the survivor group. Comorbid systemic diseases including slight cognitive spoiling, Alzheimer's disease, medications used by the patients, may have affected their MPV values.

Serum albumin level has been shown to be sensitive marker of protein deficiency malnutrition[23]. Yildiz et al found that geriatric patients with low albumin levels (<3.2 g⁄dL) in the ICU had higher mortality rates, longer hospital stays and microbiologically documented infection than those with normal albumin levels[24]. In the present study, albumin levels were observed lower in the exitus group. Evaluating albumin and RDW values together has been found to have a 70% accuracy in determining mortality of the patients in the ICU.

Previous studies have shown that CRP was a predictor marker in determining prognosis of intensive care patients[25,26]. Similar to these studies, in the present study CRP level of the deceased patients was found higher than the survivor group.

There are several limitations in this study. First of all, this study was retrospective and only one center study. For this reason, the result may not be generalizable to other institutions. Also, all critically ill patients were included for analysis and there were many factors that affected patient admission to the ICU. Our results may be applicable to mixed ICU patients.

Conclusion

RDW was found to be a strong predictor of mortality in ICU patients. While RDW alone is 68 % reliable in determining mortality in intensive care patients, the rate increases to 71% when albumin, CRP and RDW values are evaluated together.

Author contributions
Concept: TH, MH; Design: TH, MH; Supervision: AEŞ, TH; Data Collection and/ or Processing: APÇ, HÖ; Analysis and/ or Interpretation: TH, MH; Literature Search: MH,TH; Writing Manuscript: TH,MH Critical Review: MH,AEŞ,TH

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
This study was reviewed and approved by Yozgat Bozok University institutional review board (Protocol number 2017-KAEK-189_2020.07.22. _02, date: 22.07.2020)

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JoCASS
Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

MULTİPL KABURGA KIRIKLARINDA KABURGA STABİLİZASYONU VE KONSERVATİF TEDAVİNİN ETKİNLİĞİNİN KARŞILAŞTIRILMASI

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Öz

Amaç: Yelken göğüse neden olmayan multipl kaburga kırıkları için cerrahi endikasyonlar konusunda küresel bir kılavuz veya fikir birliği yoktur. Çalışmadaki amacımız, yelken göğüs dışı nedenlerle kaburga stabilizasyonu uygulanan hastalar ile konservatif tedavi uygulanan hastaların sonuçlarını karşılaştırmaktır.

Yöntemler: Ocak 2010 ile Aralık 2021 arasında künt travma sonrası kliniğimize başvuran, multipl kaburga kırığı saptanan 53 hasta çalışmaya dahil edildi. Kaburga stabilizasyonu yapılan hastalar grup 1, konservatif tedavi uygulanan hastalar ise grup 2 olarak kabul edildi. İki grup yaş, cinsiyet, travma nedeni, fraktür sayısı, eşlik eden pulmoner yaralanmalar, eşlik eden toraks dışı yaralanmalar, tüp torakostomi takip süresi, intravenöz analjezik kullanım süresi, kan transfüzyon miktarı, hemoglobin düzeyinde azalma miktarı, yoğun bakım yatış süresi, hastane yatış süresi, pulmoner komplikasyonlar ve mortalite açısından karşılaştırıldı.

Bulgular: Kaburga stabilizasyonu uygulanan 17 hastada cerrahi endikasyonlar: 6 hastada parankim yaralanması ve masif hava kaçağı, 5 hastada clotted hemotoraks ve akciğer ekspansiyon kusuru, 3 hastada deplase segmentin 15 mm'den fazla olduğu multipl kaburga kırığı, 2 hastada intravenöz analjezik tedaviye rağmen şiddetli ağrı ve 1 hastada göğüs kafesinde volüm kaybına neden olan multipl kaburga kırığı idi. Kaburga stabilizasyonu yapılan hastalar ile yapılmayanlar arasında intravenöz analjezik kullanım süresi, yoğun bakım ve hastane yatış süresi açısından anlamlı fark vardı. Ancak tüp torakostomi takip süresi, kan transfüzyon miktarı, hemoglobin düzeyinde düşme miktarı, pulmoner komplikasyon ve mortalite açısından anlamlı fark saptanmadı.

Sonuç: Multipl kaburga kırıklarının cerrahi stabilizasyonu intravenöz analjezik kullanım süresi, yoğun bakım ve hastane yatış süresini azaltan güvenli ve etkili bir prosedürdür.

***Anahtar Kelimeler**: Kaburga kırıkları, kaburga stabilizasyonu, konservatif tedavi*

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Giriş

Kaburga kırığı göğüs duvarını etkileyen kuvvetli bir travma sonucu ortaya çıkar ve toraks travmalarının yaklaşık %40 ile 80'nini oluşturur[1,2]). Travmanın şiddeti, yaş ve hastanın fiziksel durumu kaburga kırığı sayısını belirler. Pnömotoraks, hemotoraks, akciğer kontüzyonu, pnömoni, solunum yetmezliği veya diğer organ yaralanmaları gibi ciddi komplikasyonlar yaralanmaya eşlik edebilir ve posttravmatik mortalite nispeten yüksektir [3,4].

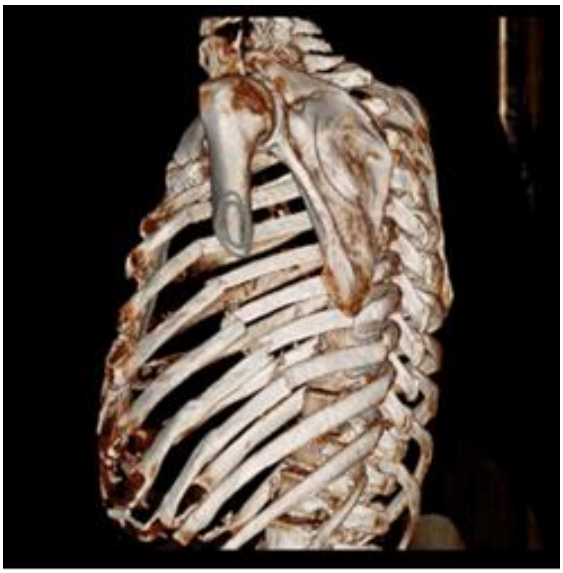
Multipl kaburga kırıklarında cerrahi ve konservatif tedavi olmak üzere iki tedavi seçeneği vardır. Konservatif tedavide ağrı yönetimi, oksijen desteği, mekanik ventilasyon, bronkodilatör ilaçlar ve pulmoner fizyoterapi yer alır. Bu tedavilere rağmen mortalite %34, morbidite ise %35-77 görülmektedir[5-13]. Ayrıca multipl kaburga kırığı sonrası hastaların %29'u travma sonrası 2 yıl tam gün iş hayatına dönememekte iken, %64'ünde göğüs duvarı ağrısı devam etmektedir[3-14]. Multipl kaburga kırığına eşlik eden dayanılmaz ağrılarda epidural analjezi önerilmektedir. İki meta analizde epidural analjezi kullanımının anlamlı oranda ağrıyı azalttığı bildirilmiştir. Ancak epidural analjezinin yoğun bakım ve hastanede kalış süresi, mortalite ve komplikasyon oranlarında anlamlı fayda sağlamadığı bildirilmiştir[15,16]. Cerrahi tedavi olarak kaburga stabilizasyonu özellikle yelken göğüs vakalarında uygulanmaktadır. Multipl kaburga kırıklarında kaburga stabilizasyonu uygulanması ile ilgili çalışma sınırlı sayıdadır.

Çalışmadaki amacımız, yelken göğüs dışı nedenlerle kaburga stabilizasyonu uygulanan hastalar ile konservatif tedavi uygulananlar arasında tüp torakostomi takip süresi, intravenöz analjezik kullanım süresi, kan transfüzyon miktarı, hemoglobin düzeyinde azalma miktarı, yoğun bakım yatış süresi, hastane yatış süresi, pulmoner komplikasyon ve mortalite açısından fark olup olmadığını saptamaktır.

Materyal ve Metot

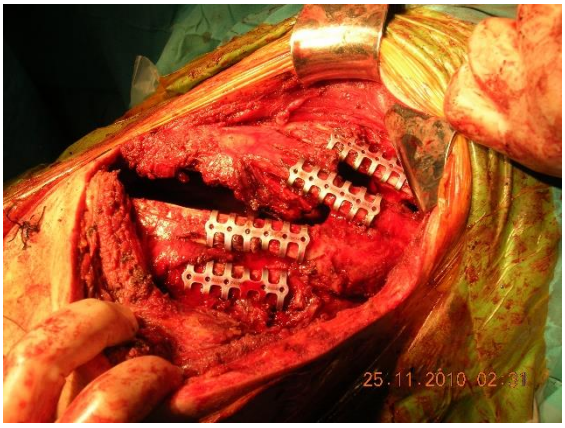
Ocak 2010 ile Aralık 2021 arasında künt travma sonrası kliniğimize başvuran multipl kaburga kırığı saptanan 53 hasta çalışmaya dahil edildi. Çalışmaya dahil etme kriterleri: Yelken göğüs olmaması, 4 veya daha fazla kırık olması, kırıkların tek taraflı olması ve sternal kırık olması. Genel durumu kötü, kafa travması nedeniyle şuuru kapalı, entübe, Glaskow Koma Skalası 8'in altında olan hastalar ve pelvik veya spinal yaralanma nedeniyle lateral dekübit pozisyonu vermenin kontrendike olduğu hastalar çalışmaya dahil edilmedi. Konya İl Sağlık Müdürlüğü Konya Şehir Hastanesi Tıpta Uzmanlık Eğitim Kurulundan 34028083-799 sayılı kararı ile onay alınmıştır.

Tüm hastalarda direkt grafi, klinik ve radyolojik bulguları multipl kaburga kırığını düşündüren hastalarda toraks bilgisayarlı tomografi (BT) çekildi. Toraks BT'deki bulgular ve klinik kaburga stabilizasyonu planlanan hastalarda 3 boyutlu rekonstrüksiyon görüntüleri elde edildi (Resim 1).



Resim 1. Araç içi trafik kazası sonucu deplase multipl kaburga kırığı olan hastanın toraks bilgisayarlı tomografi 3 boyutlu rekonstruksiyon görüntüleri

Torakotomi gerektiren parankim yaralanması, hemotoraks veya uzamış hava kaçağı olan hastalarda, deplase olan segmentin 15 mm'den uzun olduğu multipl kaburga kırıklarında veya intravenöz analjezik tedaviye rağmen şiddetli ağrıları olan hastalarda kaburga stabilizasyonu yapıldı (Resim 2). Ameliyatlar genel anestezi altında tek akciğer ventilasyonu ile yapıldı. Hastalarda kaburga kırıklarına stabilizasyon yapılmaya uygun, kas koruyucu insizyon yapıldı. Kaburgaların stabilizasyonunda osteosentez plakları kullanıldı. Stabilizasyon deplase kırıklara daha az plak kullanmak amacıyla genellikle birer kaburga atlanarak uygulandı. Ancak çok deplase kırıklarda plaklar art arda uygulandı. Stabilizasyon sonrası cilt altına hemovak dren, toraksa 28 F dren yerleştirildi.



Resim 2. Kaburga stabilizasyonu yapılan hastada intraoperatif görüntü.

Hastaların yaş, cinsiyet, travma nedeni, fraktür sayısı, eşlik eden pulmoner yaralanmalar, eşlik eden toraks dışı yaralanmalar, tüp torakostomi takip süresi, intravenöz analjezik kullanım süresi, kan transfüzyon miktarı, hemoglobin düzeyinde azalma miktarı, yoğun bakım yatış süresi, hastane yatış süresi, pulmoner komplikasyon ve mortalite arşiv dosyaları ve otomasyon sisteminde kayıtlı bilgilerden elde edildi. Kaburga stabilizasyonu yapılan hastalar grup 1 (n=17), konservatif tedavi uygulanan hastalar ise grup 2 (n=36) olarak kabul edildi.

Çalışmada elde edilen verilerin analizinde IBM-Statistical Package for Social Sciences (IBM-SPSS Inc., Şikago, IL, ABD) 22.0 programı kullanıldı. Verilerin normal dağılıma uygunluğu 'Kolmogorov-Smirnov testi' ile incelendi. Sürekli değişkenler, dağılım durumlarına göre ortalama ve standart sapma, kategorik değişkenler ise sayı ve yüzde olarak ifade edildi. Kategorik değişkenlerin analizinde Fisher's exact testi, sürekli değişkenlerin analizinde parametrik test varsayımlarının sağlandığı durumlarda bağımsız gruplarda t testi uygulanırken, aksi halde Mann-Whitney U testi uygulandı. İstatistiksel anlamlılık düzeyi $p<0,05$ olarak kabul edildi.

Bulgular

Çalışmaya dahil edilen hastaların 34'ü (%64,1) erkek iken, 19'u (%35,8) bayan idi. Yaş ortalaması 61,2 (42-74) idi. Kaburga kırığı sayısı ortalama 5,3 (4-11) idi. Hastalarda travma nedeni en sık trafik kazası olmak üzere, düşme, darp ve iş kazası idi. Kaburga kırıklarına eşlik eden en sık pulmoner yaralanma akciğer kontüzyonu idi. Toraks dışı yaralanmalar sıklık sırasına göre kraniyal, ekstremite, abdominal ve pelvik yaralanmalar idi. Kaburga stabilizasyonu uygulanan 17 hastada cerrahi endikasyonlar: 6 hastada parankim yaralanması ve masif hava kaçağı, 5 hastada clotted hemotoraks ve akciğer ekspansiyon kusuru, 3 hastada deplase segmentin 15 mm'den fazla olduğu multipl kaburga kırığı, 2 hastada intravenöz analjezik tedaviye rağmen şiddetli ağrı ve 1 hastada göğüs kafesinde volüm kaybına neden olan multipl kaburga kırığı idi. Hastalarda cerrahi stabilizasyon yatıştan ortalama 4 (2-8) gün içinde yapıldı. Kaburga stabilizasyonu 9 hastada 3, 5 hastada 2 ve 3 hastada 4 kaburgaa uygulandı. Toplam 7 hastada pulmoner komplikasyon gelişti. Dört hastada atelektazi, 2 hastada pnömoni ve 1 hastada non invaziv ventilasyonla tedavi edilebilen solunum yetmezliği saptandı.

Tablo 1. Hastaların klinik özellikleri

	Tüm hastalar	Grup 1	Grup 2	p
Yaş (yıl)	61.2 (42-74)	62.4 (47-74)	60.9 (42-72)	0.890
Cinsiyet (Erkek/Bayan)	34/19	11/6	23/13	0.760
Kaburga kırığı sayısı	5.3 (4-11)	5.2 (4-10)	5.3 (4-11)	1.000
Travma nedeni				0.650
Trafik kazası	27 (%50.9)	9 (%16.9)	18 (%33.9)	
Düşme	14 (%26.4)	5 (%9.4)	9 (%16.9)	
Diğer nedenler	12 (%22.6)	4 (%7.5)	8 (%15)	
Eşlik eden pulmoner yaralanma				
Akciğer kontüzyonu	24 (%45.2)	6 (%11.3)	18 (%33.9)	
Pnömotoraks	18 (%33.9)	7 (%13.2)	11 (%20.7)	0.890
Hemotoraks	11 (%20.7)	4 (%7.5)	7 (%13.2)	
Toraks dışı yaralanma				
Kraniyal	5 (%9.4)	2 (%3.7)	3 (%5.6)	
Extremite	4 (%7.5)	1 (%1.8)	3 (%5.6)	0.876
Abdominal	3 (%5.6)	1 (%1.8)	2 (%3.7)	
Pelvik	3 (%5.6)	1 (%1.8)	2 (%3.7)	

Tablo 2. Gruplar arası istatistiksel sonuçlar

	Stabilizasyon uygulanan (n=17)	Stabilizasyon uygulanmayan (n=36)	p
Tüp torakostomi takip süresi	7.4 (5-11)	8.8 (7-12)	0.580
İntravenöz analjezik kullanım süresi	4.8 (4-8)	11.2 (7-15)	0.008*
Kan transfüzyon miktarı (cc)	340 (0-720)	360 (0-810)	0.095
Hemoglobin düzeyinde düşme miktarı (mg/dl)	2.5 (1-4)	2.7 (1-5)	0.678
Yoğun bakım yatış süresi	4.9 (4-7)	9.3 (6-13)	0.001*
Hastane yatış süresi	8.4 (6-11)	12.7 (8-16)	0.001*
Pulmoner komplikasyon	2	5	0.110
Mortalite	0	0	1.000

**: p<0.05*

Yapılan istatistiksel çalışmada, kaburga stabilizasyonu yapılan hastalar ile yapılmayanlar arasında yaş (p=0.890), cinsiyet (p=0.760), kaburga kırığı sayısı (p=1.000), travma nedeni (p=0.650), eşlik eden pulmoner (p=0.890) veya toraks dışı yaralanma (p=0.876) açısından istatistiksel olarak anlamlı fark yoktu (Tablo 1). Kaburga stabilizasyonu yapılan hastalar ile yapılmayanlar arasında intravenöz analjezik kullanım süresi (p=0.008), yoğun bakım (p=0.001) ve hastane yatış süresi (p=0.001) açısından anlamlı fark var iken, tüp torakostomi takip süresi (p=0.580), kan transfüzyon miktarı (p=0.095), hemoglobin düzeyinde düşme miktarı (p=0.678), pulmoner komplikasyon (p=0.110) ve mortalite (p=1.000) açısından anlamlı fark saptanmadı (Tablo 2).

Tartışma

Şu anda multipl kaburga kırıkları için cerrahi endikasyonlar konusunda küresel bir kılavuz veya fikir birliği yoktur. Kaburga kırıkları olan hastalarda farklı çalışmalarda farklı endikasyonlar belirtilmiştir. Bu endikasyonlar: 1. Yelken göğüsü olan hastalar[17]. 2. Peş peşe seri olmayan üç veya daha fazla çift kemik korteksini içine alan deplase kırığı olan hastalar (Bu hastalarda cerrahi tedavi akut ağrının giderilmesi, pulmoner enfeksiyon, hemotoraks, ampiyem, solunum yetmezliği ve trakeotomi süresini azaltarak hastaların prognozunu iyileştirebilir)[13,18,19]. 3. Mekanik ventilasyon gerektiren kaburga kırığı olan hastalar (Bu hastalarda kaburga stabilizasyonu mekanik ventilasyon süresini kısaltabilir ve hasta mortalitesini azal-

tabilir)[20]. 4. Kontrol edilmeyen şiddetli ağrısı olan hastalardır[21,22].

Cerrahi kaburga stabilizasyonunun klinik faydalarını gösteren birkaç çalışma vardır, ancak bu çalışmaların neredeyse tamamı sadece yelken göğüs stabilizasyonuna yöneliktir[22,23]. Multipl kaburga kırıklarının uzun mekanik ventilasyon ve yoğun bakımda kalış sürelerinin, özellikle 65 yaşın üzerindeki yaşlı hastalarda artan mortalite ve morbidite riski ile önemli ölçüde ilişkili olduğu belirtmiştir[9]. Bu hastalarda ağrı narkotik analjezikler ile akut dönemde azalsa bile, yaşam kalitesini etkileyen kronik ağrı uzun dönem devam edebilmektedir[18,24].

Uchida ve arkadaşları, cerrahi kaburga fiksasyonu yapılan hastaların mekanik ventilasyondan derhal ayrılabileceğini ve ameliyattan sonraki 24 saat içinde ekstübe edilebileceğini çalışmalarında göstermişlerdir. Ayrıca, sadece solunum yetmezliği olan hastaların değil, aynı zamanda çoklu kaburga kırığı olan hastaların da solunum fonksiyonlarında önemli ölçüde düzelme olduğunu belirtmişlerdir. Cerrahi kaburga fiksasyonu yapılan hastalarda erken ekstübasyon ve solunum fonksiyonlarında erken düzelme sağlanabildiği için ventilatör ilişkili pnömoni veya aspirasyon pnömonisi gibi sonraki komplikasyonlar önemli ölçüde azaldığını belirtmişlerdir. Ayrıca, cerrahi olarak tedavi edilen tüm hastaların, ameliyattan 48 saat sonra yoğun bakım ünitesinden sorunsuz bir şekilde transfer edildiğini bildirmişlerdir[25]. Çalışmamızda yelken göğüs dışı multipl kaburga kırıklarında stabilizasyonun bu literatürle uyumlu olarak hem yoğun bakım hem de hastanede kalış süresinde azalma olduğunu saptadık.

De Moya ve arkadaşlarının çalışmalarında belirttiği gibi, cerrahi kaburga fiksasyonunun bir diğer önemli faydası da ağrının azalmasıdır[22]. Cerrahi olarak tedavi edilen hastalarda analjezik gereksiniminde önemli bir azalma görüldüğü ve bu ilaçların ameliyattan 48 saat sonra sonlandırıldığı bildirilmiştir[25]. Kaburga kırıklarına bağlı şiddetli ağrı immobilizasyona ve öksürememeye neden olarak, atelektazi, sekresyon birikimi ve pnömoni ile sonuçlanabilmektedir. Erken yapılacak kaburga fiksasyonu bu şiddetli ağrıyı engelleyerek oluşacak morbiditelere engel olabilir. Çalışmamızda kaburga stabilizasyonu uygulanan hastalarda intravenöz analjezik tedavi ortalama 4,8 gün iken, stabilizasyon uygulanmayan hastalarda bu süre 11,4 gün idi ve istatistiksel olarak anlamlı fark vardı. Kaburga stabilizasyonu uygulanan grupta pulmoner komplikasyon daha azdı.

Hemotoraks veya pnömotoraks olan ve cerrahi olarak tedavi edilen tüm hastalarda, ameliyat sırasında pulmoner veya intraplevral yaralanmalar onarılabilmekte ve bunun sonucu olarak tüp torakostomi süresi azalmaktadır[25]. Çalışmamızda tüp torakostomi süresi kaburga stabilizasyonu uygulanan grupta daha kısa olmakla birlikte istatistiksel olarak anlamlı bir fark yoktu.

Sonuç

Sonuç olarak cerrahi kaburga fiksasyonu sadece yelken göğüs için değil, aynı zamanda cerrahi gerektiren pulmoner veya plevral patolojilerde veya dayanılmaz ağrıya neden olan deplase multipl kaburga kırıklarının onarımı için güvenli ve etkili bir prosedür olabileceği sonucuna vardık.

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RECONSTRUCTION WITH SUBMENTAL ISLAND FLAP IN ORAL CAVITY TUMORS: ADVANTAGES AND DISADVANTAGES IN THE CURRENT APPROACH

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Abstract

Aim: Reconstruction of defects emerged after resection of the oral cavity cancers, whose first-line treatment is surgical, is a complex process. The gold standard approach for this is the microvascular free flap. However, the use of pedicle flap remains a valuable option in elderly patients who are not suitable for long-term surgery, have poor nutrition, and have additional comorbid diseases.

Discussion: Submental island flap, is widely used in oral cavity reconstructions. There was no significant difference between free flaps and submental island flaps for swallowing and speech functions, general and local recurrence rates. In addition, submental island flap has important advantages such as shorter operation time, shorter hospital stays, and fewer complications in the donor area.

Conclusion: Submental island flap is a suitable option for the reconstruction of oral cavity defects without compromising oncologic results after tumor resection, especially in patients who are poor candidates for microvascular surgery.

Keywords: *Oral cavity tumor, submental island flap, reconstruction*

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Introduction

Head and neck squamous cell carcinomas are the sixth most common cancer worldwide. Of these, the oral cavity is the most frequently observed region. They are generally observed in middle-aged and elderly individuals[1,2]. These tumors can be seen on the tongue, floor of the mouth, buccal mucosa, inner lip, gingiva, retromolar trigone and hard palate. The most frequently affected subregion is tongue[3]. Reconstruction of oral cavity soft tissue defects is a complex and sophisticated process. In the current approach, gold standard is the microvascular free flap. However, the utilize of free flaps brings with its high cost, need for surgical expertise, and longer hospital stay. Therefore, free flaps are not always an ideal option. Local-regional flaps offer a good alternative option in cases where reconstruction cannot be performed with free flap tissue transfer. In addition, locoregional flaps are a very good option for a salvage procedure due to necrosis in a previously made free flap[4]. Because of these advantages, locoregional flaps must be well-adopted by all surgeons dealing with oral cavity tumors.
Submental island flap (SIF), one of the locoregional flaps, was first described by Martin et al. for the reconstruction of facial defects due to its color, shape and tissue compatibility[5]. Subsequently, Sterne et al. described the utilize of SIF for the reconstruction of the defect emerged after oral cavity tumor resection[6]. Besides the publications claiming that reconstruction of the oral cavity with SIF is a safe oncological option, there also have been some reports to the contrary, due to the potentially compromised neck nodal clearance[7].

Anatomy

The submental island flap is a fasciocutaneous flap that includes a rhomboid skin, subcutaneous tissue, and platysma area located under the lower border of the mandible. The submental artery can supply blood to a skin area as large as 10-16 cm, reaching from one angle of the mandible to the contralateral angle[8]. Although this horizontal dimension includes an area supplied by the bilateral submental artery, the entire flap can be perfused from one side thanks to the anastomoses of the arteries. The anterior-posterior diameter of the flap is determined by leaving enough skin for primary closure, depending on skin flexibility, and usually 6-8 cm of skin can be harvested. The flap is supplied with blood by the submental artery, which is a branch of the facial artery. Venous drainage is from the submental vein, which drains into the facial vein. The submental artery branches from the facial artery in front of the submandibular gland. The submental artery runs anteriorly, between the submandibular gland and the lower edge of the mandible, and then along the lower surface of the mylohyoid muscle[9]. The artery may rarely follow an intraglandular course. While the submental artery runs deep in the anterior belly of the digastric muscle in 70% to 80% of patients, it more rarely courses superficial to this muscle. The submental artery gives off branches to the lower lip, mylohyoid muscle, digastric muscle, mandibular periosteum, platysma, and submental skin. There are perforator vessels connecting the submental artery to the subdermal plexus, and their location and number can be variable. Therefore, it is necessary to include this large area in the flap to ensure that the perforators remain on the harvested flap. For this, the ipsilateral anterior belly of the digastric muscle as well as the part of the mylohyoid muscle that corresponds into this region are included in the flap[10]. This technique does not cause any significant functional deficit. It should be paid attention to the marginal mandibular nerve and the nerve of the mylohyoid muscle, which may be damaged during flap harvesting.

Surgical Technique

The patient is in the supine position with the head slightly extended. To locate the submental artery, it is marked the skin approx-

imately 5.5 cm in front of the angle of the mandible and 7 mm below the lower border of the mandible. The terminal portion of the artery is marked approximately 8 mm below the lower edge of the mandible and 6 mm distance from the midline[6]. The size of the skin island is usually determined by the size of the defect, but will be a maximum of 12 × 6 cm, moreover, it is recommended that the vertical size should not exceed 5 cm to avoid cosmetic and functional problems[11]. The upper border of the skin island should be at least 1 cm inferior to the mandibular arch to hide the scar as much as possible and prevent eversion of the lower lip[12]. To determine the lower border of the skin island, pinch testing is performed to see whether there is enough skin to allow primary closure of the donor area or not[13]. After the borders of the donor area are determined, an incision is made and continued until the platysma. The incision is extended towards the flap pedicle. The marginal mandibular nerve is identified and preserved. The pedicle is determined proximally as the facial artery and vein are easily identifiable. The submental artery will usually be seen by gently pulling down on the submandibular gland. After the vascular structures are found, they are followed towards the lateral border of the anterior belly of the digastric muscle and released from the surrounding tissues (Figure 1). This anterograde approach allows the identification of the location of the submental artery and of "septocutaneous perforators" originating proximal to the anterior belly of the digastric muscle.

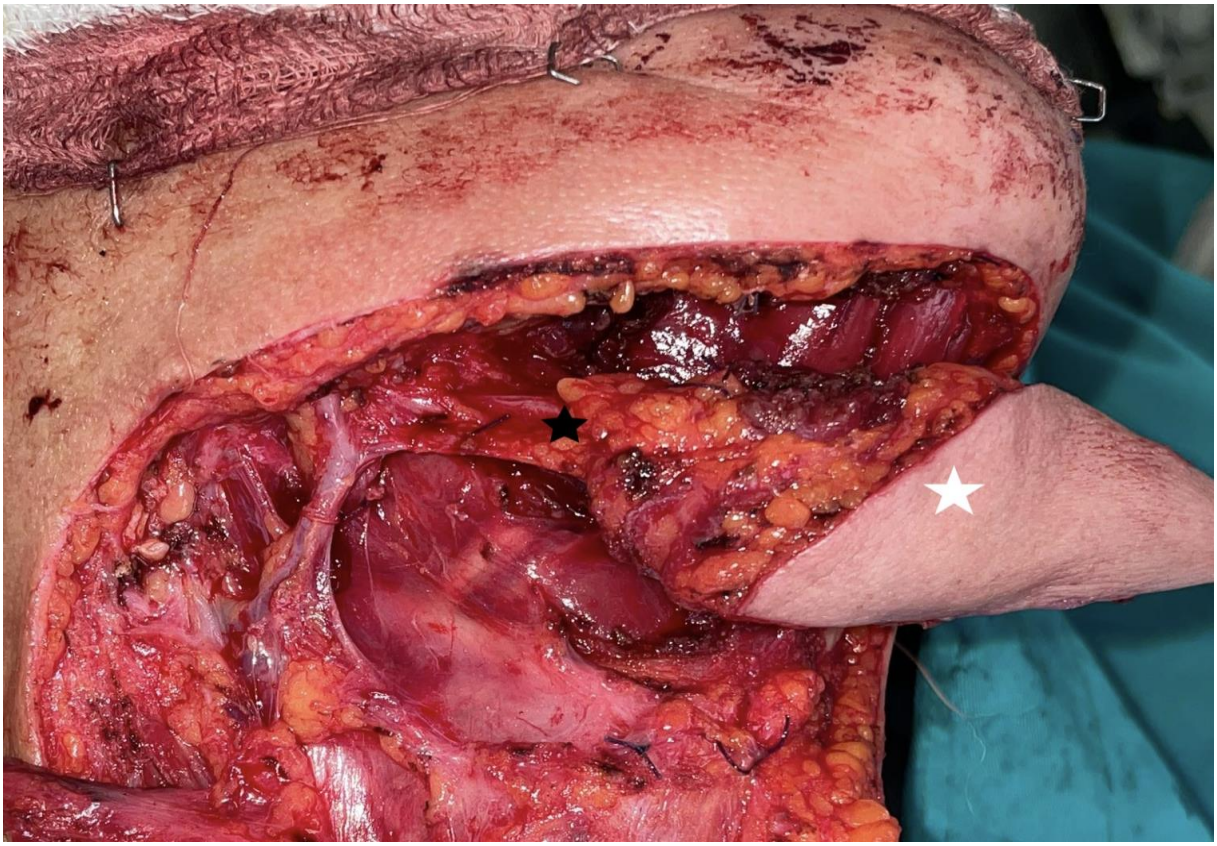

Figure 1. Submental island flap with vascular pedicle on the right side (Black star: Vascular pedicle, white star: Submental skin island)

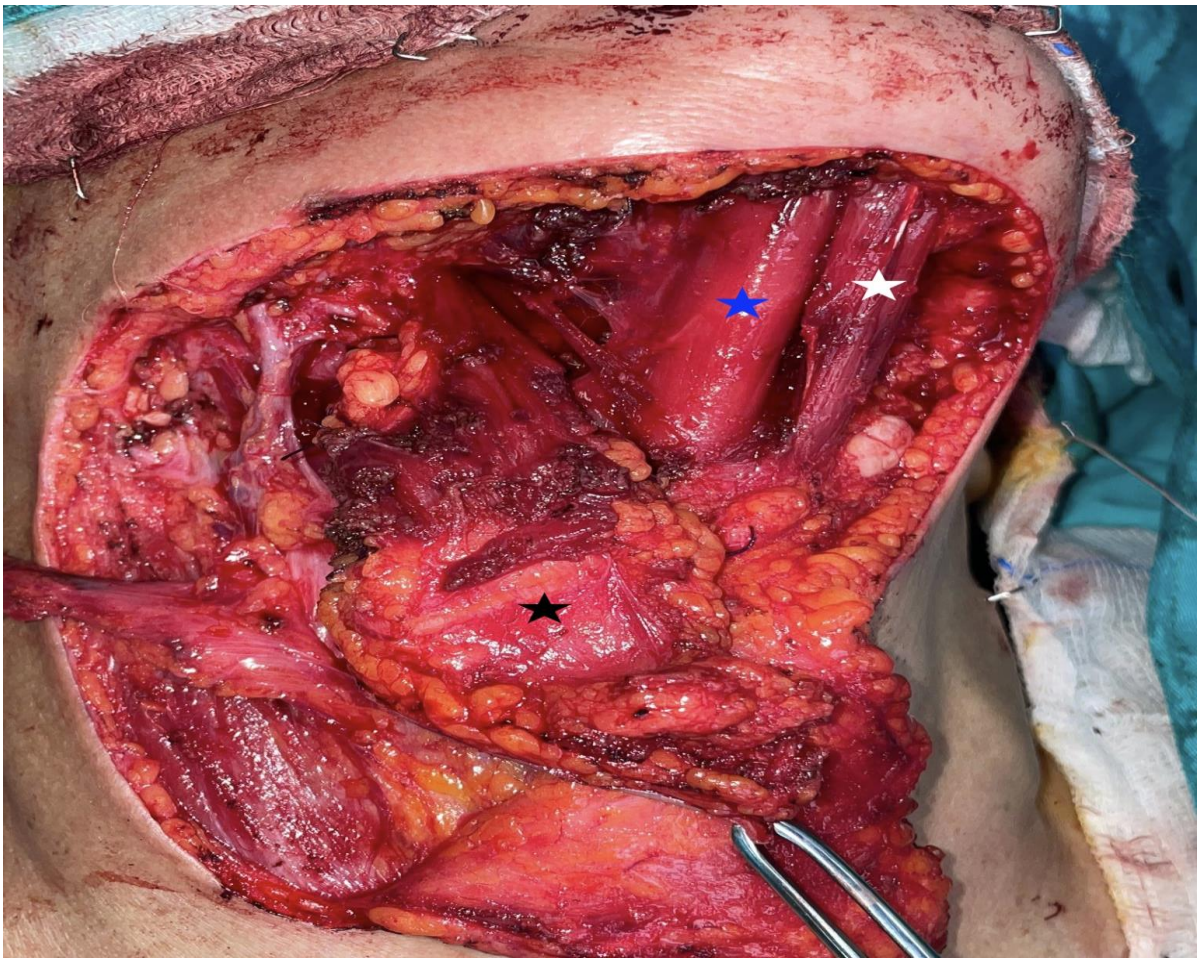

Figure 2. Ventral side of flap and postharvest donor area view (Black star: Right digastric muscle anterior belly and flap with mylohyoid muscle included, white star: Left digastric muscle, blue star: Right geniohyoid muscle)

If these perforators are present, the fasciocutaneous flap can be harvested[11]. If these perforators are not identified, the digastric muscle anterior belly is combined with the flap, and the musculocutaneous flap can be harvested with the perforators to be preserved[11]. Occasionally, a strip of mylohyoid muscle may also be included in the flap to protect the pedicle[10,14] (Figure 2). To increase oncological safety, level I needs to be carefully dissected from the flap to reduce the possibility of lymphatic tissue transfer to the defect site. After full mobilization, a wide tunnel is created to guide the flap into the oral cavity. The defective area in the oral cavity is reconstructed by passing the flap through this tunnel (Figure 3).

Indications and contraindications

Submental island flap has many uses in head and neck surgery, especially in oral cavity tumors. The flap is utilized in oral cavity tumor surgery to reconstruct tongue and/or floor of the mouth defects, buccal mucosal defects, palate defects, and large lip defects. In addition, it can be utilized in the repair of soft tissue defects in the lower, middle and upper parts of the face, in the repair of skin defects in the beard area, in nasal reconstruction, in the repair or reconstruction of the cervical esophagus, in the repair of hemilaryngectomy defects, in the reconstruction of the neopharynx after a total laryngectomy, and in the repair of pharyngocutaneous fistulas.

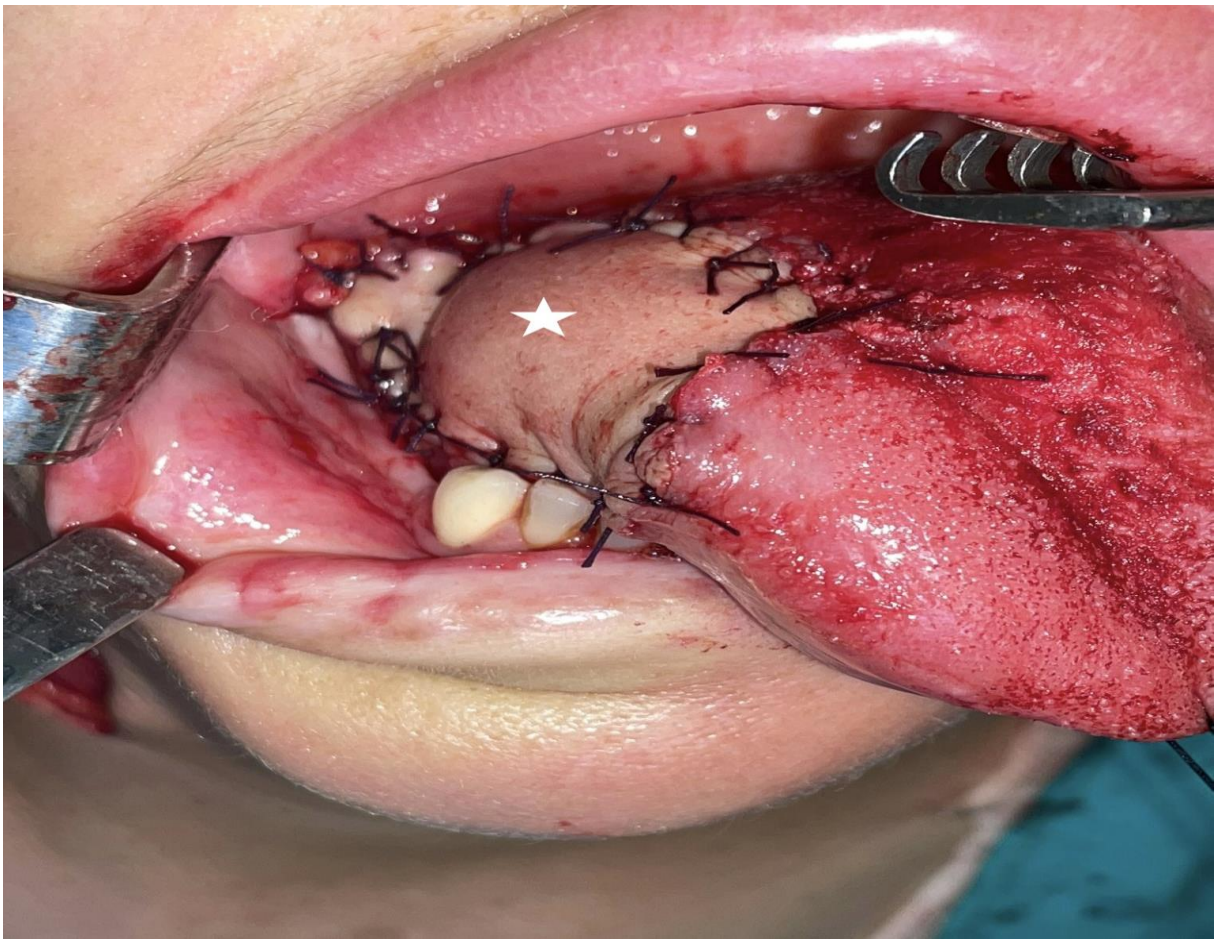

Figure 3: Submental island flap placed on the right-sided tongue defect (White star: Reconstructed flap tissue)

There are few absolute contraindications to the use of a submental island flap for reconstruction in oral cavity tumors. The first is serious medical comorbidities that preclude major surgery. The second is metastatic disease involving ipsilateral Level I lymphatic tissue. This situation will make it extremely difficult to harvest the flap and preserve the pedicle when dissecting an oncologically sound neck.

In addition, in some cases, care should be taken when choosing this flap. Patients with non-Level I neck positivity or deep invasive floor-of-mouth tumor should be meticulously examined. According to the study of Howard et al., they found no tumor recurrence in 50 patients with oral squamous cell carcinoma at Level I who did not have clinical nodal metastases and whose defects were reconstructed with submental island flaps[15]. Nevertheless, since it is not technically possible to completely remove the lymphatic tissue without damaging the flap, an alternative reconstruction method should be considered in case of a high risk of metastasis to this region. In situations that increase the risk of flap failure such as local trauma, especially burns, care should be taken in choosing this flap if the pedicle is adjacent to the trauma area.

Discussion

The use of free flaps has become the first choice for reconstruction after oral cavity tumor resection[2,16]. The most preferred region as a free flap is the radial forearm region. However, the use of pedicle flaps remains a valuable option in elderly patients who are not suitable for long-term surgery,

have poor nutrition, and have additional comorbid diseases[17-19]. There are many studies comparing these two techniques. Both techniques have their own advantages and disadvantages. In Patel's comparison between these two methods in 146 patients, it was found that SIF was advantageous compared to the radial forearm free flap (RFFF) with a shorter operation time, shorter hospital stay, and fewer complications in the donor area. Functional outcomes for swallowing and speech were similar between the two reconstructive techniques and no difference was found between patients who underwent SIF and RFFF in terms of local recurrence rate or overall recurrence. The author advocated that SIF should be the first choice in oral cavity reconstructions, with reduced patient morbidity and lower cost of care[20].

When the SIF compared with traditional pedicle flaps such as pectoral major flap and deltopectoral flap, no difference in survival rate was found and it is quite reliable in terms of survival[15,17,19,21,22]. The fact that the flap can be harvested quickly, the pedicle has a suitable rotation arc, and the flap survival rate is quite high make the SIF a very good option for oral cavity reconstruction. Compared with RFFF, the SIF was associated with a shorter operative time and hospital stay[23]. In the Sittitrai et al.'s study, they found the average operation time to be 3 hours in the SIF group, while it was 7 hours in the RFFF group[17]. Forner et al. compared the cost effectivity between SIF and RFFF used for glossectomy reconstruction. Accordingly, although there was no significant difference in overall hospital stay between the two groups, they indicated a significant reduction in both the operative time and the intensive care unit stay in the SIF group. Thus, they observed a significant cost reduction with SIF compared to RFFF[21].

In the submental flap, donor site morbidity is very minimal. Due to the removal of excess cervical skin, tightening occurs in the anterior cervical region and this creates a positive aesthetic result. Lee et al. confirmed the low morbidity of the SIF in their study[24]. The size of the harvested skin island can be as large as 12 × 6 cm, and the donor site defect can be closed primarily without functional intervention[25]. In the literature, wound dehiscence has been reported rarely (0-7.4%) at the SIF donor site. In contrast, partial skin graft loss and restricted arm function have been identified in a significant number of patients who underwent reconstruction using RFFF[17,23]. SIF is also very suitable for oral cavity reconstruction with its thin and flexible skin structure. When greater volume is required, the flap can be raised as a musculocutaneous flap involving the mylohyoid muscle, or bone tissue can be harvested as an osseomusculocutaneous flap when required[15]. Another advantage is that orocutaneous fistula is rarely seen. The musculofacial component of the flap occludes the dead space resulting from tumor removal and provides watertight closure of the defect[25].

Since the primary lymphatic drainage of oral cavity cancer is to the submental and submandibular lymph nodes, the oncological safety of the use of the SIF has been a concern[15,18,22]. There are differences of opinion among the authors regarding oncological safety. In addition to the authors advocating that SIF is contraindicated in a patient with clinical or radiographic evidence of metastatic disease at level I[15], authors who argue the opposite advocate that SIF can be used without compromising local recurrence in patients who have a cervical lymph node diameter less than 1.5 cm and no clinical evidence of extracapsular invasion and whose sentinel lymph nodes are carefully dissected during the procedure[25]. While using SIF in oral cavity cancer reconstruction, careful patient selection and surgical technique are very important to ensure oncological safety. Each patient should be evaluated meticulously with physical examination and imaging methods before surgery. To ensure adequate treatment of the regional lymphatic area, dissection of these areas should be performed carefully following flap elevation. Howard et al. stated that

they did not experience recurrence due to metastatic disease transfer with SIF technique, which they have applied for 11 years in their studies. Furthermore, according to the results of elective neck dissection in the clinical No neck, the rate of occult metastasis at level I was 10%[15].

The functional outcomes of reconstruction of oral cavity tumors, particularly of the tongue, are determined by the mobility and volume of the reconstructed tongue[26]. While the skin harvested with RFFF, which is preferred as the primary option in oral cavity reconstruction, promises a good function with its thin and flexible structure, SIF is advantageous in terms of providing sufficient bulk tissue. In addition, the more flexible and malleable skin of SIF provides better functional results than traditional regional flaps. In functional evaluation, basically speaking and swallowing functions are evaluated. While objective scales were used for evaluation in some of the studies, a superficial evaluation such as continuous use of the feeding tube and speech intelligibility was made in others. In the study comparing the functional outcomes of RFFF and SIF for oral cavity reconstruction, the authors achieved excellent to good speech results for the majority of patients in both groups, although there was no significant difference between the two groups. While the rate of patients with good or perfect speech was 82.8% in the SIF group, this rate was 92% in the RFFF group. None of these patients needed a permanent feeding tube[17]. Similar results were found in another study[23]. Although there are similar functional results between the two flaps, poor swallowing functions were found in patients who used SIF in anterior floor of mouth reconstruction. Therefore, free flaps should be preferred due to the flexible skin structure in order to minimize the deterioration in tongue movements, especially in defects that may occur due to resection of the anterior part of the tongue and anterior floor of the mouth[20].

Conclusion

Submental island flap offers the advantages of shorter operative time, shorter hospital stay, and avoidance of donor site complications compared to the radial forearm free flap. Functional outcomes for swallowing and speech are similar between the two reconstructive techniques. In patients who underwent submental island flap after resection of malignancy, no significant difference was observed in terms of local recurrence rate or overall recurrence compared to radial forearm free flap. Therefore, this flap is suitable for reconstruction of oral cavity defects without compromising oncologic outcomes after tumor resection, especially in patients who are poor candidates for microvascular surgery.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
Approval was obtained from the patient for this review

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KARDİYOPULMONER BYPASSIN SİTOKİNLER ÜZERİNE ETKİSİ

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Öz

Amaç: Yapılan bu çalışmanın amacı kardiyopulmoner bypass (KPB) eşliğinde yapılan kardiyak cerrahi operasyonlarında KPB'ın sitokinler (VEGF) üzerine etkisini araştırmaktır.

Yöntemler: Çalışmaya KPB eşliğinde kardiyak cerrahi geçirmiş 15 erkek, 15 kadın hasta ve benzer demografik özelliklerde 30 sağlıklı birey kontrol grubu olarak dahil edildi. Hastalardan 5 farklı zamanda ve kontrol grubundan alınan kan numunelerinden "Vasküler endotelyal büyüme faktörü (VEGF)" düzeyleri çalışıldı. Sonuçlar istatistiksel olarak değerlendirildi.

Bulgular: Bu çalışmada; sağlıklı gönüllülerden (Kontrol grubu) ve hastalardan farklı zamanlarda alınan kan numunelerinin VEGF düzeyleri arasında istatistiksel olarak anlamlı fark vardı (p=0,045).

Sonuç: Çalışma sonucunda KPB sırasında ve KPB çıkışında VEGF seviyesinde anlamlı şekilde düşüş olduğu, bunun da cerrahi travma, prime solüsyonu, kardiyopleji ilaçları ve ekstrakorporeal dolaşım ekipmanı gibi nedenlere bağlı olduğunu düşünmekteyiz. Postoperatif servise çıkış dönemde ise normal seviyenin üzerine yükseldiği saptanmıştır. KPB eşliğinde yapılan kardiyak cerrahide ekstrakorporeal dolaşım ekipmanlarının enflamatuvar yanıta neden olabileceğini bunun da postoperatif dönemde VEGF seviyesinde ciddi düzeyde yükselmeye neden olduğunu düşünmekteyiz.

***Anahtar Kelimeler**: Kardiyopulmoner Bypass, Sitokinler, VEGF*

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Giriş

Kardiyopulmoner bypass (KPB) eşliğinde yapılan kardiyak cerrahide kalp ve akciğerlerin fonksiyonlarının devre dışı bırakılması ve kalp içindeki kanın boşaltılması gerekmektedir. Bu işlemler için vücut dışı dolaşımı sağlayan kalp akciğer makinesi kullanılmaktadır. KPB, esas itibari ile akciğerlerin fonksiyonlarını gerçekleştiren bir oksijenatör ve kalbin fonksiyonunu gerçekleştiren bir pompadan oluşmaktadır. Günümüzde teknolojinin gelişimine bağlı olarak, ekstrakorporeal dolaşım (EKD) ekipmanlarında da ciddi anlamda gelişme sağlanmıştır. Günümüzde kullanılmakta olan KPB sistemlerinde, akım hızları, kanın ısısı, akım miktarı, kan gazı parametreleri, bazı biyokimyasal parametreler anlık olarak monitörize edilebilmekte ve takibi, müdahalesi yapılabilmektedir[1].

Kalbin normal fizyolojik çalışma durumu ile ekstrakorporeal dolaşım arasında önemli farklılıklar vardır. Bu farklar ve değişiklikler, kanın nonfizyolojik KPB devre yüzeyleriyle temas etmesi, pulsatil kan akımı yerine laminar akımının varlığı, kardiyopleji ile kalbin soğuk iskemiye maruz kalması, böbrekler, beyin, karaciğer ve akciğerlerin iskemi/reperfüzyonu ve çeşitli derecelerde hipotermi uygulanmasıdır. Bu değişiklikler ve farklar nedeni ile organizmada; lökositler, endotel hücreleri, trombositler, kompleman sisteminin aktivasyonu ve koagülasyon kaskadı'nında içinde yer aldığı yaygın bir enflamatuvar reaksiyon oluşmaktadır. Özellikle bağırsaklardan kaynaklı oluşan bakteriyel translokasyona ikincil gelişen endotoksemi ve cerrahiye bağlı oluşan stres yükü, oluşan enflamatuvar yanıtın nedenleridir[1-6].

KPB'a bağlı sitokinlerin salınımı gerçekleşebilmektedir. Sitokinler hücre yüzeylerindeki reseptörlere etki ederek hücrelerin matürasyonunu, büyümesini ve tamirini düzenleyen, bazen monokin, lenfokin, interferon, interlökin olarak da adlandırılan heterojen bir grup proteindir. Aktive lökositlerden salgılanan sitokinler, özellikle aktive fibroblast, monositler ve endotel hücrelerinden salgılanmaktadırlar. Bu hücrelerin aktivasyonu, doku hasarına karşı en erken hücresel yanıtı oluşturmaktadır. Hücrelerin büyüme ve diferansiyasyonu, organizmaların hücre aracılıklı savunma mekanizmaları ve kronik enflamatuvar hastalıklar gibi durumlara ek olarak enflamatuvar yanıt gibi çeşitli akut etkilerde de sitokinler aracılık etmektedirler. Sitokinler; nötrofil degradasyonu, araşidonik asit metabolitleri, serbest oksijen radikali oluşumu ve kompleman sistemi gibi çeşitli enflamatuvar mediyatörlerin salınımıyla da ilişkilidirler[1,2,4,6]. Sitokinlerin salınımı; endotoksin salınımı, iskemi-reperfüzyon, kompleman sisteminin aktivasyonu ve diğer sitokinler gibi birçok nedene de bağlı olabilmektedir[1,2,5].

"Vasküler endotelyal büyüme faktörü" (VEGF=Vascular endothelial growth factor), çok fonksiyonlu bir sitokin olmakla beraber, aynı zamanda vasküler endotelyal hücre büyümesi, sağ-kalımı ve proliferasyonunu stimüle eden "trombosit kökenli büyüme faktörü" (PDGF=Platelet-derived growth factor) süper ailesinin de bir üyesidir[7-8].

Yapılan bu çalışmanın amacı KPB eşliğinde yapılan kardiyak cerrahi operasyonlarında KPB'ın sitokinler (VEGF) üzerine etkisini araştırmaktır.

Materyal ve Metot

Yapılan bu klinik prospektif çalışmada, çalışma öncesi Harran Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulundan onay alındı (Tarih:13.02.2015, karar no: 15/02/08, sayı no:74059997.050.01.04/032). Bu çalışma Helsinki Deklarasyonunda belirtilen ilkelerine uygun olarak yapıldı. Çalışma öncesi çalışmaya katılacak tüm gönüllülerden bilgilendirilmiş onam alındı.

Kardiyopulmoner Bypass Yöntemi

Yapılan bu çalışmada hastaların ektrakorporeal dolaşım sırasındaki kan akış hızları (Flow) vücut yüzey alanlarına göre (2,4 lt/dk/m^2) belirlendi. Hastanın kilosuna uy-

gun oksijenatör ve tubing set, vücut yüzey alanlarına göre de kanül çapları belirlendi. Tubing set venöz hat çapı 1/2, arteriyel hat çapı 3/8 olarak kullanıldı. Tüm hastalara ekstrakorporeal dolaşım sırasında 32ºC hipotermi uygulandı. Arteriyel hat basınçları KPB sırasında ortalama 150-180mmHg arasında tutuldu. Yeterli antikoagülasyon sağlanarak aktif pıhtılaşma zamanı (Active Clothing Time=ACT) 480 saniye ve üzerinde tutuldu. Prime solüsyon olarak; 1200ml dengeli solüsyon (İsolayte), 150ml %20 mannitol, 5 bin ünite heparin ve 1gr sefazolin® kullanıldı.

Çalışma Grubunun Oluşturulması

Bu çalışmaya; Harran Üniversitesi, Araştırma ve Uygulama Hastanesi, Kalp Damar Cerrahisi kliniğine koroner arter hastalığı, kalp kapak hastalıkları gibi çeşitli kardiyak problemlerle başvuran ve KPB eşliğinde kardiyak cerrahi uygulanan 15 erkek ve 15 kadın toplam 30 hasta dahil edildi. Hasta grubunun yaş ortalaması 49,36; ortalama ağırlıkları 75,42 kg; ortalama boyları ise 170,58 cm idi. Bu hastalardan KPB öncesinde preoperatif anestezi indüksiyonundan önce, anestezi indüksiyonundan sonra, kardiyopulmoner KPB sırasında aortik kross klemp sonrası, kalp-akciğer makinesinden ayrıldıktan hemen sonra ve postoperatif hasta yoğun bakımdan servise çıktıktan sonra toplam 5 farklı zamanda heparinli tüplere 5 cc kan alınarak çalışma grubu oluşturuldu. Benzer demografik özelliklerde 30 (15 erkek, 15 kadın) sağlıklı bireyde kontrol grubu olarak çalışmaya dahil edildi. Kontrol grubunun yaş ortalaması 50,22; ortalama ağırlıkları 71,93 kg; ortalama boyları ise 168,28 cm idi.

Örneklerin Hazırlanması

Hastalardan alınan beş farklı zamandaki kan örnekleri Harran Üniversitesi Araştırma ve Uygulama Hastanesi Biyokimya laboratuvarında 5000 rpm'de 10 dakika süresince santrifüj edildi, daha sonra plazma kısmı ayrılıp Eppendorf tüplerine alınarak -80 ^{0}C'de derin dondurucuda daha sonra çalışılmak üzere saklandı. Yeterli sayıda numune elde edildiğinde biyokimya laboratuvarında numuneler önce çözülerek, daha sonra VEGF Human-Elisa yöntemi ile çalışıldı.

Kullanılan Araç Gereçler

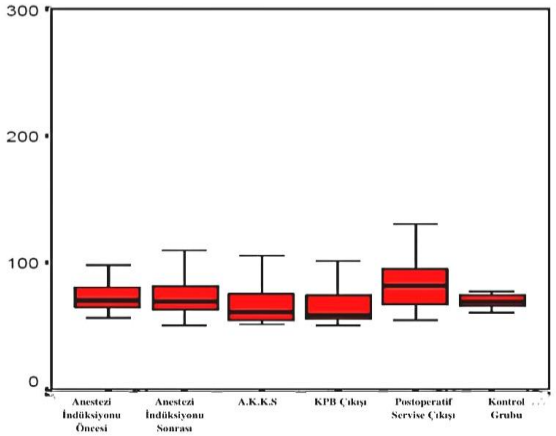
Yapılan bu çalışmada Harran Üniversitesi, Tıp Fakültesi, Araştırma ve Uygulama Hastanesi, Biyokimya laboratuvarında rutin olarak kullanılan cihazlardan yararlanıldı.

VEGF Düzeyinin Ölçülmesi

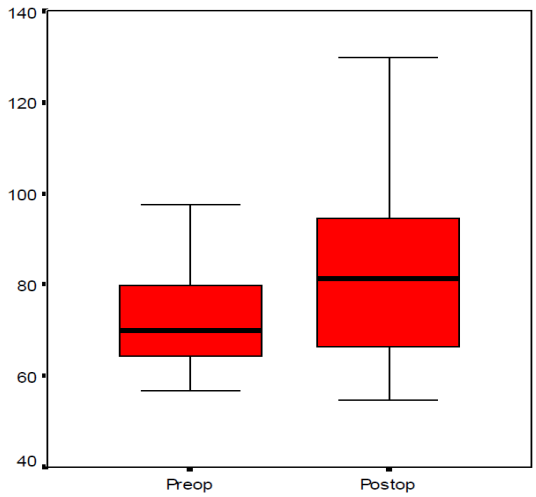
Serum örneklerinin VEGF düzeyleri Human marka ticari Elisa kitlerle ELS 800 Eliza cihazında çalışıldı. Sonuçlar pikogram/ mililitre (pg/ml) olarak ifade edildi.

İstatistiksel Analizler

İstatistiksel analizler SPSS® Versiyon 11.5 (SPSS Inc. Chicago USA) bilgisayar programı kullanılarak gerçekleştirildi. Grupların ortalamaları arasındaki farkın önemi One-Way ANOVA testi ile karşılaştırıldı. Parametreler arasındaki ilişki Pearson korelasyonanalizi ile araştırıldı. İstatistiksel olarak $p<0.05$'ten küçük değerler anlamlı kabul edildi.



Grafik 1. Kardiyopulmoner bypass ameliyatı geçirmiş hastaların ve kontrol grubunun VEGF düzeyleri



Grafik 2. Hastaların preoperatif anestezi indüksiyonu öncesi ile postoperatif servise çıkış VEGF düzeyleri

Bulgular

Tablo 1'de de görüldüğü gibi hasta grubu ile sağlıklı kontrol grubu benzer demografik özelliklere sahipti (p>0,05).

Tablo 2'de de görüldüğü gibi bu çalışmada; sağlıklı gönüllülerden (Kontrol grubu) ve hastalardan farklı zamanlarda alınan kan numunelerinin VEGF düzeyleri arasında istatistiksel olarak anlamlı fark vardı (p=0,045) (Grafik 1-2).

Tablo 3'te de görüldüğü gibi hasta grubunun; koroner (Koroner arter bypass greft replasmanı) ile kalp kapak cerrahisi (Aort ve mitral kalp kapağı replasmanı) uygulanmış hastaları karşılaştırıldığında, VEGF düzeyleri ve KPB süreleri arasında istatistiksel olarak anlamlı fark yoktu (p>0,05).

Tartışma

Açık kalp cerrahisinin ilk yıllarından itibaren, KPB eşliğinde yapılan kardiyak cerrahi hastalarında, diğer cerrahi operasyonlar geçirmiş hastalardan farklı bir takım yan etkilerin ortaya çıktığı görülmüştür. KPB geçiren hastalarda diğer cerrahi hastalarından farklı olarak daha fazla oranda kanama, ödem, enfeksiyon ve solunum problemleri gibi mortalite ve morbiditeyi artıran sorunlar oluşmaktadır[9,10].

Yaptığımız bu çalışmada KPB eşliğinde çeşitli kardiyak cerrrahi operasyonları geçirmiş olan hastalarda KPB'ın sitokinler üzerine etkisini araştırmayı amaçladık. Çalışmamızda elde ettiğimiz en önemli bulgu KPB'ın VEGF düzeyinde ciddi düzeyde değişikliklere neden olduğunun saptanmış olmasıdır. Ekstrakorporeal dolaşım esnasında, kanın endotel kaplı olmayan yüzeyler ile temas etmesi ve sonrasında tekrardan vücut dolaşımına girmesi nedeniyle, kanın bu sentetik yüzeyler ile ve sonrasında farklı dokular ile temas etmesi, vücutta değişik reaksiyonlara yol açmaktadır, yani spesifik (immün) ve non-spesifik (Enflamatuvar) yanıt oluşturur[9].

KPB kullanılarak yapılan kalp cerrahisinde, özellikle hemodilüsyon ve cerrahi strese bağlı olarak ciddi enflamatuvar reaksiyonlar oluşmaktadır[11].

Tablo 1. Çalışmaya ait demografik veriler

		Hasta Grubu (n=30)	Kontrol Grubu (n=30)	p
Cinsiyet (n, %)	Kadın	15, %50	15, %50	p>0,05
	Erkek	15, %50	15, %50	p>0,05
Yaş (Ort±SS)		49,36±13,43	50,22±14,58	p>0,05
Boy (cm)		170.58± 21,16	168.28± 19,25	p>0,05
Ağırlık (Kg)		75.42±6,77	71.93±4,53	p>0,05

Ort±SS:Ortalama±Standart Sapma, n, %:Sayı ve yüzde.

Tablo 2. Çalışma gruplarının VEGF düzeyleri

	Hasta Grubu					Kontrol Grubu	
	Anestezi İndüksiyonu Öncesi Ort±SS	Anestezi İndüksiyonu Sonrası Ort±SS	A.K.K.S Ort±SS	KPB Çıkışı Ort±SS	Postoperatif Servise Çıkışı Ort±SS	Kontrol Ort±SS	P
VEGF, pg/mL	74,23±14,52 (p<0,05)[A]	74,77±21,39 (p<0,05)[B]	66,32±15,87 (p<0,05)[C]	68,75±22,49 (p<0,05)[D]	82,93±20,30	74,82±23,50	0,045 *

Ort±SS:Ortalama±Standart Sapma, A.K.K.S:Aortik Kross Klemp Sonrası, KPB:Kardiyopulmoner Bypass
A. Anestezi indüksiyonu öncesi VEGF düzeyi ile Postoperatif servise çıkış zamanındaki VEGF düzeyi arasında fark vardır (p<0,05).
B. Anestezi İndüksiyonu Sonrası VEGF düzeyi ile Postoperatif servise çıkış zamanındaki VEGF düzeyi arasında fark vardır (p<0,05).
C. Aortik kross klemp sonrası VEGF düzeyi ile Postoperatif servise çıkış zamanındaki VEGF düzeyi arasında fark vardır (p<0,05).
D. KPB çıkışı VEGF düzeyi ile Postoperatif servise çıkış zamanındaki VEGF düzeyi arasında fark vardır (p<0,05).
**. Hasta grubun postoperatif (Postoperatif Servise Çıkışı) VEGF düzeyi ile Kontrol grubunun VEGF düzeyi arasında fark vardır (p<0,05).*

Tablo 3. Hasta grubunun koroner ve kalp kapak cerrahisi olarak VEGF düzeylerinin karşılaştırılması

	KABG (n=15)		KALP KAPAK (n=15)		
Zamana Göre VEGF düzeyleri	3 Greft (n=8)	4 Greft (n=7)	Aort Kapak (n=5)	Mitral Kapak (n=10)	p
Anestezi İndüksiyonu Öncesi (Ort. VEGF)	73,23	75,37	74,12	74,85	p>0,05
Anestezi İndüksiyonu Sonrası (Ort. VEGF)	73,08	76,70	75,19	74,56	p>0,05
A.K.K.S (Ort. VEGF)	65,85	66,85	67,27	65,84	p>0,05
KPB Çıkışı (Ort. VEGF)	68,05	69,55	69,18	68,53	p>0,05
Postoperatif Servise Çıkışı (Ort. VEGF)	82,45	83,47	83,18	82,80	p>0,05
KPB süreleri (Ort±SS)	78,35	91,31	85,83	81,33	p>0,05

Ort. VEGF: Ortalama VEGF düzeyi, Ort:Ortalama, KABG: Koroner arter bypass greft replasmanı uygulanmış hastalar, Aort Kapak: Mekanik aort kalp kapağı uygulanmış hastalar, Mitral Kapak: Mekanik mitral kalp kapağı uygulanmış hastalar

Ayrıca KPB, cerrahi travma ve iskemik perfüzyon hasarı gibi nedenlerle sitokinlerin salınımınıda uyarmaktadır[12]. KPB, tümör nekroz faktör-α (TNF-α), interlökin-1 (IL-1β), interlökin-6 (IL-6) ve interlökin-8 (IL-8) gibi pro-enflamatuvar sitokinlerin salınımı tetiklemektedir[13]. Bu sitokinler sistemik enflamatuvar yanıt sendromu (SIRS=Systemic inflammatory response syndrome) gelişiminde de önemli rol oynamaktadır[12]. TNF-α, makrofaj ve diğer pro-enflamatuvar hücrelerin aktivasyonunu takiben kanda ilk tespit edilen sitokinlerdendir. Endotoksin TNF-α salınımı için güçlü bir uyarandır. Pro-enflamatuvar uyarıyı takiben TNF-α düzeyi hızla yükselmekte ve çok çabuk kaybolmaktadır. KPB esnasında oluşan pro-enflamatuvar si-

tokin seviyesi ile KPB süresi arasında belirgin bir ilişki bulunmaktadır. TNF-α'nın KPB sonrası dönemde miyokardiyal disfonksiyonda ve hemodinamik instabilitede önemli rol oynadığı bilinmektedir[1,2,5]. Kardiyak cerrahi geçirmiş hastalarda, TNF-α'nın ardından IL-1β düzeyide artmaktadır. Bu artış KPB sonrası ilk birkaç saat içerisinde gerçekleşmekte ve pik noktasına ulaşmaktadır. İnterlökin-1β, KPB sonrası vasküler endotel hücrelerinde nitrik oksit sentezini indüklemekte ve sistemik vasküler rezistansı azaltmaktadır[1,2,5,6]. İnterlökin-6, akut faz yanıtının modülasyonunu sağlamaktadır. Hematopoezin düzenlenmesinde ve immün yanıtta görev almaktadır. Vücutta ateşin oluşmasında rol almakta ve adrenokortikotropik hormon'nun (ACTH) salınımını tetikleyebilmektedir. Kardiyak cerrahi dışındaki vakalarda postoperatif iki ve dördüncü saatlerde IL-6 düzeyinde yükselme olmakta, 4 ile 24 saat içerisinde de pik noktaya ulaşmaktadır. Komplikasyon görülmeyen vakalarda IL-6 düzeyleri postoperatif üç ile beş gün sonra preoperatif değerlere dönerler. IL-6, doku hasarının; plazma/serum düzeyleri ile cerrahi travmanın boyutu arasında korelasyonu gösteren duyarlı, erken belirteci olarak gösterilmektedir. İnterlökin-6 değerleri; kan kaybı ve cerrahi süre ile korelasyon göstermektedir. Postoperatif IL-6 değerleri, komplikasyon gelişen hastalarda, komplikasyon gelişmeyen hastalara göre anlamlı olarak yükselmektedir. KPB vakalarında da IL-6 plazma/serum düzeyleri yükselmektedir[1,2,6]. Nötrofiller için güçlü bir kemoatraktan olan interlökin-8, akciğer hasarı ve pulmoner sekestrasyonda da önemli rol oynamaktadır. Çoklu organ yetmezliklerinde de pro-enflamatuvar faktörlerin salınımı önemli bir etken olarak karşımıza çıkmaktadır. Bunların aksine KPB esnasında salınan interlökin-10 (IL-10) gibi anti-enflamatuvar faktörler ise pro-enflamatuvar sitokinleri baskılamaktadırlar. Anti-enflamatuvar faktörler ile pro-enflamatuvar sitokinler arasındaki denge klinikte önemli bir faktördür. Ayrıca, IL-10 konnektif doku hücreleri (Bağ dokusu hücreleri) ve kan mononükler hücreleri üzerinde de düzenleyici etki göstermektedir[9].

Gorjipour ve arkadaşlarının[9] yaptıkları çalışmada KPB sonrası interlökin-6, interlökin-8, interlökin-10 ve tümör nekroz faktör-α gibi sitokinleri araştırmışlardır. Çalışmalarının sonucunda dolaşımdaki yüksek pro-enflamatuvar sitokin düzeyinin; yoğun bakım ünitesinde kalış süresinin uzaması ve mekanik ventilasyon süresinin uzaması gibi olumsuz sonuçlarla ilişkili olduğu, ayrıca böbrek fonksiyonunun olumsuz biyokimyasal parametresi kan üre nitrojeni (BUN) ile de ilişkili olduğunu belirtmişlerdir. Bu olumsuz klinik ve patolojik sonuçların kontrolü için enflamatuvar yanıtın uygun kontrolünün hayati önem taşıdığını belirtmişlerdir[9]. Yaptığımız çalışmada da postoperatif servise çıkış dönemindeki VEGF düzeyindeki yükselişin benzer sebeplerle olabileceği düşünülebilir.

Kankılıç ve arkadaşlarının[14] yaptığı çalışmada KPB sırasında düşük tidal hacimli ventilasyonun enflamatuvar sitokinler üzerindeki etkilerini araştırmışlardır. Çalışmalarında ventilasyonlu ve ventilasyonsuz gruplarda C5a, IL-6, IL-8 ve TNF-α seviyelerini karşılaştırdıklarında benzer sonuçlar bulmuşlar ($P>0.05$). KPB'da düşük tidal hacimli ventilasyonun yararının plevral efüzyon, atelektazi ve pnömoni gibi postoperatif akciğer komplikasyonlarını azalttığı gösterilmiş olmasına rağmen, KPB sırasında karşılaşılan enflamatuvar sitokinlere ilişkin daha kesin ve net kanıtlara sahip olmadıklarını belirtmişlerdir[14]. Yapılan bu çalışmada da, düşük ventilasyonun sonuçlar üzerinde bir etkisinin olmadığı görülmüş, buda bizim çalışmamızı destekler nitelikte olup, KPB cerrahisi geçirmiş hastalarda sitokinlerdeki değişikliklerin daha çok ekstrakorporeal dolaşım ekipmanlarından kaynaklandığını göstermektedir.

Mirhafez ve arkadaşlarının[15] yaptığı çalışmada on-pump ve off-pump olarak gerçekleştirilen kardiyak cerrahi vakalarını serum sitokin seviyelerini karşılaştırmayı amaçlamışlardır. Çalışmalarında iki cerrahi yöntem arasında, IFN-γ, TNF-α, interlökin (IL)-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-

10, VEGF, MCP-1 ve epidermal büyüme faktörünü karşılaştırmışlardır. Cerrahi sonrası on-pump cerrahisi olan hastalarda IL-4, IL-6, IL-10, VEGF, IFN-γ ve MCP-1 serum seviyelerinde, off-pump cerrahisi olanlara kıyasla anlamlı bir artış olduğunu ve iki grup arasında anlamlı fark olduğunu belirtmişlerdir. Ayrıca KPB'ın sistemik inflamasyonu aktive edebileceğini, ancak her iki yönteminde bazı komplikasyonlara yol açabilen enflamatuvar yanıta neden olabileceğini belirtmişlerdir[15]. Yapılan bu çalışmada, sonuçları; çalışmamızdan farklı olarak kontrol grubu yerine ekstrakorporeal dolaşım sisteminin kullanılmadığı (off-pump) kardiyak cerrahisi uygulanmış hasta grubu sonuçlarıyla karşılaştırmışlar ve benzer sonuçlar elde etmişlerdir. KPB'ın sitokinler üzerine etkisi değerlendirildiğinde, bu yönü ile bu çalışma sonuçları çalışmamızı desteklemektedir.

Suzuki ve arkadaşlarının[11] yaptığı çalışmada KPB sırasında modifiye ultrafiltrasyonun (MUF) kullanımının enflamatuvar sitokinler üzerindeki etkilerini araştırmışlardır. Çalışmalarında MUF'dan sonra IL-6 seviyesinin yükseldiğini, IL-8 ve IL-10 seviyelerinin ise önemli ölçüde düştüğü belirtmişlerdir. Sonuç olarak MUF kullanımının sitokinlerin uzaklaştırılması için faydalı olabileceğini belirtmişlerdir[11]. Bai ve arkadaşlarının[16] yaptığı çalışmada ise VEGF'in, KPB ile ilişkili akut böbrek hasarına karşı koruyucu etkisini araştırmışlardır. Deneysel olarak oluşturdukları KPB çalışmalarında deneklere VEGF vermişlerdir. Çalışmalarında VEGF'in renal mikrosirkülasyon perfüzyonunu artırdığını ve VEGF'nin, renal mikroperfüzyonda iyileşme yoluyla böbrekler üzerinde koruyucu bir etki sağladığını belirtmişlerdir[16].

Kardiyak cerrahide koroner cerrahi yapılan ve kapak cerrahisi yapılan hastaların iki farklı grup olarak ayrılması ve birbirleri arasında karşılaştırmalar yapılması daha uygun olacaktır. Bu iki farklı cerrahide VEGF düzeylerinde de farklı sonuçların ortaya çıktığını görmek olası düşünceler arasında olabilir. Acaba kalp odalarının açıldığı ve kapak eksojen bir yüzey olarak sürekli bir inflamatuvar yanıtta artışa neden olmakta mıdır? Koroner cerrahide neticede protez kapak kullanılmadığı için iki farklı cerrahide bu anlamda farklılık bulunabilir. Ancak çalışmamızda VEGF düzeylerinin karşılaştırmasında bu iki cerrahi arasında fark olmadığını gördük.

Yaptığımız çalışmada preoperetif anestezi indüksiyonu öncesi kan seviyelerindeki VEGF normal seviyelerdeyken, hasta uyutulduktan sonra anestezi indüksiyonu sonrası alınan kan değerlerinde ise VEGF seviyelerinde artış olduğu, bunun da heparin ve anestezi ilaçlarının etkisi sonucu olduğu düşünülmektedir. İntraoperatif aortik kross klemp sonrası ve KPB çıkışındaki VEGF seviyelerinin, normal düzeyinden daha düşük ölçülmesinin de KPB sırasında verilen prime solüsyonu, kardiyopleji ilaçları, cerrahi stres/travma ve iskemi reperfüzyonu sonucu olduğunu düşünmekteyiz. Postoperatif dönemdeki VEGF seviyelerinin yükselmesinin de KPB'a bağlı enflamatuvar yanıt sonucu olduğunu düşünmekteyiz.

Yapılan bu çalışmanın sınırlıkları arasında tek merkezli olması ve çalışmaya dahil edilen birey sayısının azlığıdır. Daha çok bireyin çalışmaya dahil edilerek çok merkezli çalışmaların yapılması, ayrıca daha fazla sitokine bakılmasının da sonuçların genellenmesi açısından daha olumlu olacağını düşünmekteyiz.

Sonuç

Yapılan bu çalışma sonucunda KPB sırasında ve KPB çıkışında VEGF seviyesinde anlamlı şekilde düşüş olduğu, bunun da cerrahi travma, prime solüsyonu, kardiyopleji ilaçları ve ekstrakorporeal dolaşım ekipmanı gibi nedenlere bağlı olduğunu düşünmekteyiz. Postoperatif servise çıkış dönemde ise normal seviyenin üzerine yükseldiği saptanmıştır. KPB eşliğinde yapılan kardiyak cerrahide ekstrakorporeal dolaşım ekipmanlarının enflamatuvar yanıta neden olabileceğini bunun da postoperatif dönemde VEGF seviyesinde ciddi düzeyde yükselmeye neden olduğunu düşünmekteyiz.

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THE COMPARISON OF THE PREOPERATIVE AND POSTOPERATIVE NEUTROPHIL TO LYMPHOCYTE RATIO FOR EARLY PREDICTION OF COMPLICATIONS IN TRANSIT BIPARTITION SURGERY

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Abstract

Aim: Metabolic surgery is a newly applied and effective treatment method in type 2 diabetes all over the world. For this reason, blood parameters have come to the fore more frequently in the last decade to predict possible complications early.

Our aim is to evaluate the neutrophil/lymphocyte ratio (NLR), which is a convenient and cheaper parameter for early diagnosis of complications in Transit Bipartition (TB-SG) surgery, which is the last modality in diabetes surgery.

Methods: In our study, we retrospectively evaluated diabetic patients who underwent TB-SG in the metabolic surgery clinic between May 2019 and March 2021 and their surgical results. NLR parameter values of the patients were examined on the 1st and 3rd postoperative days.

Results: 21 female and 19 male participants were included in our study. The mean age of the patients was 42.7 years and their body mass index (BMI) was 46.4 kg/m2. The mean hospital stay of the patients was 3.4 days (2.3−6.7 days) ($p < 0.05$). In the logistic regression study applied, it was shown that the NLR value showed a significant direct ratio with the complications and a correlation was determined.

Conclusions: In the new metabolic surgery method such as TB-SG, NLR was found to be a useful and appropriate parameter in detecting possible complications in the postoperative period.

Keywords: *Diabetes mellitus, metabolic surgery, transit bipartition*

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Introduction

Morbid obesity is widespread disease in all over the world, and the clear solution is bariatric surgery for the patients who have not utilized or profit from any non-surgical treatment methods.
Excess weight earnings led to inflammation and many diseases such as metabolic, cardiovascular, lung diseases, and various malignancies. Elevated levels of inflammatory markers caused to inflammation in the human body, furthermore these mediators are released from adipose tissue particularly in morbid obese patients[1-3]. Obesity leads to systemic inflammation and establish the obesity-associated comorbidities in adipose tissue[4-6].
Many inflammatory markers investigate the inflammation in the body particularly Neutrophil–lymphocyte ratio (NLR) is one of them. NLR is also a forecasting marker for the possible illnesses, such as complications[7-9]. The advantage of NLR outcome has low costing and fastly reachable.
Metabolic surgery not only lead to weight loss but it also decline inflammatory marker activity. Laparoscopic sleeve gastrectomy (LSG) firstly described as a stepwise process for morbid obesity after this procedure it is understood that the patients who have underwent LSG participants blood glucose and insulin necessity decreased and also utilized for diabetic disease surgery[5]. Transit bipartition (TB-SG) was firstly showed and performed by Santoro in 2006 and purposed to join a metabolic constituent to the restrictive efficacy of the sleeve gastrectomy procedure[6,7]. Although more research are suggested, TB-SG has been performed for gaining better results in metabolic components of body physiology compared to conventional sleeve gastrectomy (SG). Furthermore, TB-SG has lead to less complications according to other processes[8,9]. Our purpose was to evaluate the differences in NLR after TB-SG surgery at preoperative and postoperative 1st and 3rd days.

Materials and Methods

We have retrospectively detected 40 patients who underwent Transit bipartition (TB-SG) in metabolic surgery clinic, between the dates of May 2019 and march 2021.Exclusion criteria of this research were being under the age of having any inflammatory illness .
NLR outcomes were identified in the postoperative 1st and 3rd day. Local Ethics Committee has been approved this retrospective research (2020 / 8–decision number 173). The necessary consultations (endocrine, psychiatry, chest, and dietician) were made for the patients who applied before the operation. The BMI values of all patients were > 40 kg / m^2. Bariatric procedures also performed by an experienced bariatric surgeon team.

Interventions

All of the surgical procedures were applied under the anesthesia laparoscopically. low molecular weight heparin and pneumatic compression bands were performed for preventing the thromboembolism, was applied to all the participants. In the TB-SG technique which was described[10]. First, laparoscopic sleeve gastrectomy was performed with the aid of laparoscopic stapler, and then, 80 cm length from the ileocecal valve was prepared for the consociate way and gastro-ileal anastomosis was performed to the antral area which was 150 cm away from the consociate way. At the end, ileo-ileal anastomosis was applied. furthermore, all of the mesenteric gaps were closed by the aid of barbed sutures [11.]

Data collection

All of the outcomes of patients who underwent surgery and also data were investigated from electronic outcomes of hospital data and also analyzed. The NLR were evaluated preoperatively and on the day of postoperative 1 and 3.

Postoperative evaluation

Soluble Contrast agent drinking test is applied to all participants on postoperative day of 2. If there is no detected sign of leakage, water permission begins to the patients. All of the patients are called to the clinic weekly for examination during the postoperative first month. Possible postoperative complications recorded and also showed.

Participants

Of 40 patients who have underwent TB-SG surgery. previous obesity surgery, presence of chronic respiratory disease, alcohol, smoking, and drug dependence were added as exclusion criteria.

Statistical Methods

Data was analyzed using IBM SPSS Statistics 23 (SPSS, Inc., Chicago, IL, USA). The explanation of the marked factors were determined by the ANOVA test. Logistic regression analysis including demographic variables, pre-operative NLR, and PLR values was utilized for detecting the risk factors which can lead. multivariate logistic regression was used to estimate odds ratio (OR) of baseline factors and backward selection was used to select the final model. For all statistical results, P value ≤ 0.05 was accepted as significant for all statistical levels.

Results

Totally 40 participants were identified (21 female and 19 male) in this study. The average age was 42.7 years and body mass index (BMI) was 46.4 kg/m2, however. The clinical characteristics of all participants are showed in Table 1. The length of stay in hospital was 3.4days (range2,3−6,7 days) ($p < 0.05$) (Table 1). WBC outcomes were significantly lower in the Preoperative period than Postoperative period. The widespread complication was hemorrhage of the operation lodge also detected in 3 patients, all of them have observed in ICU and no needed any surgery, none of the patients needed second look. 1 patient with pulmonary embolism and 1 had portal thrombosis. Pulmonary complications showed as initially with dyspnea. Elevated liver enzymes have not lead any negative position. Table 2 shows the analysis of regression of univariate. We have detected the sensitivity of 68% and specificity of 93%. We have determined that positive predictive value of 62-78% for prior complications for post-bariatric applications (Table 3).

Table 1. Demographic and clinical characteristics of study patients.

	Total (n = 40)
Age (mean)	42.7 ± 4.2years
Female	21 (52.5%)
Male	19 (47.5%)
Mean BMI: kg/m2 (range)	46.4 (35−53)
Length of stay in hospital (mean)	3.4 day (2.3−6.7)
Mortality	0
Additional diseases (n = 28)	
DM	40
HT	12
CAD	8
COPD	14
Hepatosteatosis	31
Postoperative complications	
Pulmonary embolism	1
Hemorrhage	3
Elevated liver enzymes	2
Portal vein thrombosis	1
Pulmonary complications	2
Neutrophil to lymphocyte ratio	2.1 (1.5-2.8)

SD: Standard deviation, BMI: Body mass index, NLR: Neutrophil to lymphocyte ratio

Discussion

Metabolic surgery modalities are commonly performed for morbid obese population who have not adequately weight loss after the conservative treatment methods[12]. Bariatric Surgeons need to help for determining the possible complications in the early period and hence the inflammatory markers show their efficacy at this period.

Table 2. Univariate analysis of parameters associated with early post bariatric complications

Parameters	Odds ratio	95%confidence interval	P value
AGE	1.007	0.964-1.026	0.92
BMI	1.054	0.824-3.421	0.26
WBC	1.073	0.984-1.126	0.27
NLR	1.984	1.467-2.737	<0.05
Platelets	1.001	0.962-1.103	0.94
Platelets to lymphocyte ratio	1.017	0.997-1.106	<0.05
Creatinine	1.011	0.977-1.056	0.52
Bun(mg/dl)	1.015	0.866-1.234	0.47
ALT(U/L)	1.004	0.969-1.347	0.23
AST(U/L)	1.007	0.973-1.612	0.71

ALT: alanine aminotransferase,AST: aspartate aminotransferase, BUN:blood urea nitrogen,NLR: neutrophil to lymphocyte ratios, WBC: White blood count,BMI:body mass index

Table 3. Neutrophil to lymphocyte ratios cut off points with their demonstrative statistics

NLR	Sensitivity	Specificity	PPV
3-7.6	10-70	90-100	62-78
2-2.9	75-90	42-75	27-53
1.3-1.98	93-100	12-36	14-32

PPV:positive predictive value, NLR: neutrophil to lymphocyte ratios

Estimator factors such as CRP, NLR can help the surgeons for early detection time, to minimize mortality rate and be beneficial to discharge period. The main purpose of our research was to evaluate the relationship of NLR with post- metabolic process related complications.

Obesity-provoking inflammation is related with elevated adipose tissue volume. These immunological actions lead to increasing in NLR levels[13-16]. NLR is a parameter for forecasting the inflammation process[17]. In addition, NLR levels were determined as a beneficial parameter for identifying the patients who have the risk of morbidities[18].

Santoro et al was firstly demonstrated the technique of TB-SG[19]. TB-SG is plain and easily applicable surgical technique according to other malabsorptive surgical methods. this method does not have any substantial compound and lead to weight loss easily. In this surgical method the digested food went to the ıleum by passing the pass proximal ileum and also malabsorption may not be or less detected according to other malabsorptive methods such as biliopancreatic diversion and Roux N y gastric bypass20.

Carbajo et al. demonstrated that the major complications which are described in the postoperative early phase were uncontrollable such as bleeding, and gastric leakage. In present research, bleeding was showed in two patients, in first patient underwent the second look surgery and in the second stopped by hemodynamic followings. Furthermore, The determined marginal ulcers after the TBSG surgery range among 1% and 7.2%.[21].

On the other hand, Kansou et al. have demonstrated postoperative stenosis rate of 16.9% in this type operations[7]. In this research the follow-up time was 2 years for these group patients and there has been no stenosis detected in patients[22].

NLR marker was utilized for estimating the possible mortality, and morbidity in participants with underwent surgery for malignancy or any inflammatory illness. Furthermore, NLR is a novel studied marker for bariatric surgery types and modalities[23-25]. Da Silva et al found that NLR can estimate

the complications in the early phase of post-operatively bariatric and metabolic procedures[26].In addition, NLR is a very convenient and inexpensive method due to its easily accessible marker and early warning role for surgeons.
The Guclu et al. demonstrated that NLR have a significant role for prognosing the possible infectious illnesses and sepsis[27-31]. Furthermore, NLR play a role in detecting pneumonia and malignancies. Morbid Obese patients are showed as lower inflammatory outcomes than other type patient's, Therefore, as we have shown in our study, the property of NLR, its applicability and efficacy in the setting of bariatric surgeries has been believed and trusted[32].
It is significant to explain that clinical finding are the best idea to detect the possible complications however if there are any lack of symptoms these forecasting biomarker may take an important role for detecting the bariatric surgery complications[33].

The percentage of NLR is more forecasting parameter for the patients who have undergone surgical process[34].

Furthermore Halazun et al. have focused on the efficacy of NLR on participants who have underwent hepatic transplantation due to malignancy and found significantly higher NLR levels[35].In present research, it is detected that NLR has a relationship with complications and utilized as an independent valuable forecasting marker for bariatric surgery modalities.
There are also some limitations of present research. Firstly, its retrospective design, and may hinder the explication of our study outcomes. Secondly the follow up period is short, and patient have not called again in first month control, thirdly the low number of complications such as grade 4 and 5 type according to Clavien–Dindo classification are, the absence, as the fourth study was carried out in a tertiary single bariatric center.

Conclusion

TB-SG is an effective bariatric process for morbid obesity and metabolic surgery. Complications which may have occurred after this process may cause high morbidity and mortality rates. Present research clearly showed that NLR parameter has positive relationship with complications which are associated with bariatric surgery. We suggest utilizing this marker for estimating the bariatric surgery complications earlier. Further prospective research are also needed to approve our outcomes.

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

The study was approved by the University Faculty of Medicine Clinical Research Local Ethics Committee, decision number 2020 / 8 – decision number 173

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2018 Adana

ÇOCUKTA İNTRATORASİK EKSTRAPULMONER DEV LİPOM OLGUSU

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Öz

5 yaşında erkek hasta, 4 yıl önce solunum yolu enfeksiyonu için başvurduğu çocuk acil servisinde çekilen direkt akciğer grafisinde üst mediastende genişleme saptanmış. Başka bir merkezde göğüs cerrahisi kliniği tarafından hasta 4 yıl boyunca takip edilmiş. Lezyonda progresif büyüme olması üzerine hasta kliniğimizde operasyona alındı. Total eksize edilen 10 cm boyutundaki lezyon, literatürde çocuklarda bu boyutta çok nadir görülen intratorasik ekstrapulmoner lipom olgusu olarak sunulmuştur.

***Anahtar Kelimeler**: Dev intratorasik lipom, pediatrik hasta, nadir olgu*

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Giriş

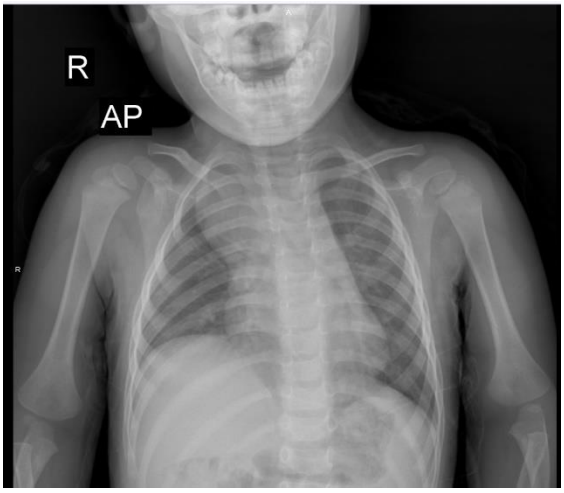
Lipoma, yağ dokusundan ve nadiren fibröz stromadan oluşan, yetişkinlerde sık görülen, benign bir yumuşak doku tümörüdür. İntratorasik yerleşim nadir görülür. Tanı anında hastaların çoğu semptomatik olmadığından, sıklıkla başka endikasyonlar için çekilen akciğer grafilerinde insidental olarak saptanır. Bilgisayarlı tomografi (BT) ve manyetik rezonans görüntüleme (MRG) ile lipoma tanısı koymak mümkündür. Lipomalar yağ atenüasyonunda lezyonlar olduğundan BT'de dansite ölçümleri ile tanınırlar ve MRG lezyonların ileri değerlendirmesi için faydalı olabilir[1].

Olgu Sunumu

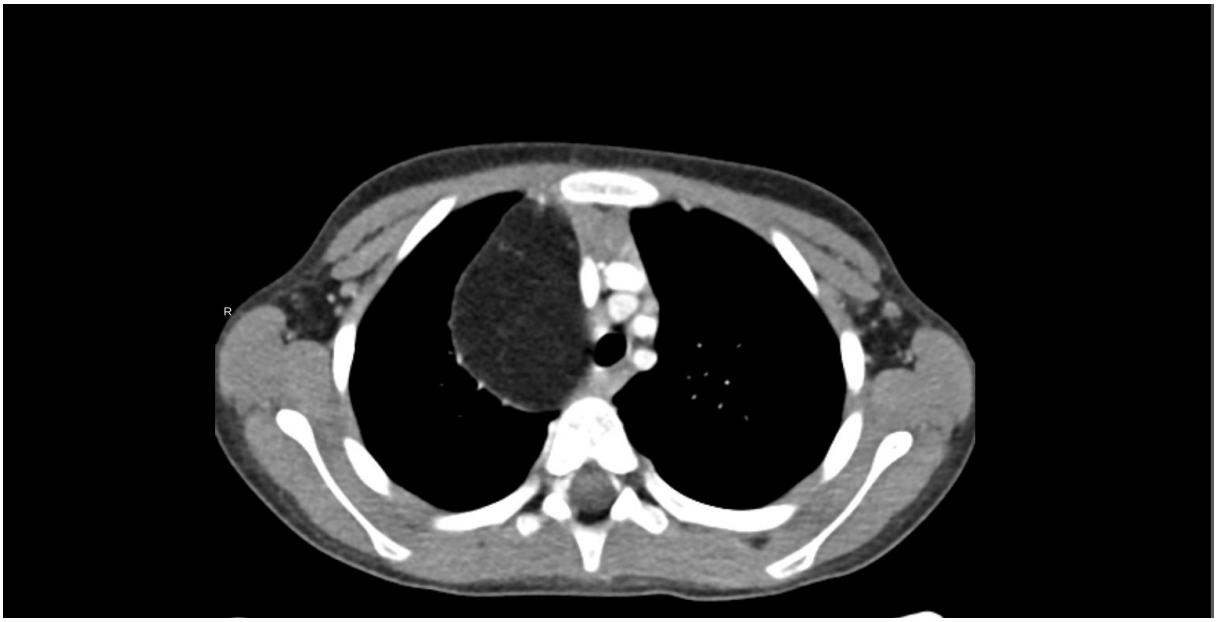
5 yaşındaki erkek hasta, 4 yıl önce solunum yolu enfeksiyonu ile çocuk acil servisine başvurmuş. Çekilen direkt akciğer grafisinde insidental olarak tespit edilen üst mediastende sağ hemitoraksa uzanımı olan lezyon sebebiyle göğüs cerrahisine yönlendirilmiş (Resim 1). Takiplerde lezyonda büyüme olması üzerine hastaya 4. yılda toraks BT çekildi. Toraks BT raporunda "Üst mediastende sağ subklavian arteri ve internal torasik arteri içerisine alan yaklaşık 6x4 cm boyutlarında lipom ile uyumlu lezyon dikkati çekmektedir" denildi (Resim 2). Toraks MR raporu "Sağ akciğer apeks medialinde

yaklaşık 57x46 mm boyutlarında düzgün sınırlı tüm sekanslarda yağ ile izointens sinyal özelliği gösteren lezyon dikkati çekmektedir. Sağ subklavian arter proksimali lezyon içerisinde seyretmektedir. Kitle, vena kava süperiora ekstrinsik bası yapmıştır. Belirgin invazyon bulgusu yoktur. Göğüs duvarı oluşumları normaldir" olarak raporlandı (Resim 3).

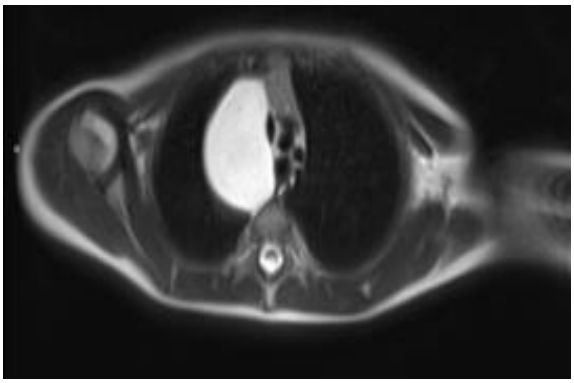
Lezyonun büyümesi, akciğer ekspansiyonuna engel olması, vasküler yapılara basısı ve malignleşme ihtimali göz önüne alınarak operasyona karar verildi. Sağ 4. interkostal aralıktan yapılan torakotomi ile düzgün sınırlı, yumuşak ve kapsüllü intratorasik ekstrapulmoner lezyona ulaşıldı (Resim 4). Lezyon kupulada, sağ subklavian arter ve vena cava superior ile yakın temas halinde idi. Lezyon enerji cihazı kullanılarak künt ve keskin diseksiyon ile enblok ve total olarak eksize edildi (Resim 5 ve 6). Postoperatif 3. gün göğüs tüpü sonlandırılan hasta, postoperatif 4. gün akciğerleri ekspanse olarak taburcu edildi (Resim 7). Patoloji raporu "Makroskopik olarak 9x6x4 cm boyutlarında nodüler görünümde, homojen solid kesit yüzüne sahip kitle, MDM-2 ve CD34 immünohistokimyasal boyaları pozitif, miksolipoma ile uyumludur" olarak raporlandı.



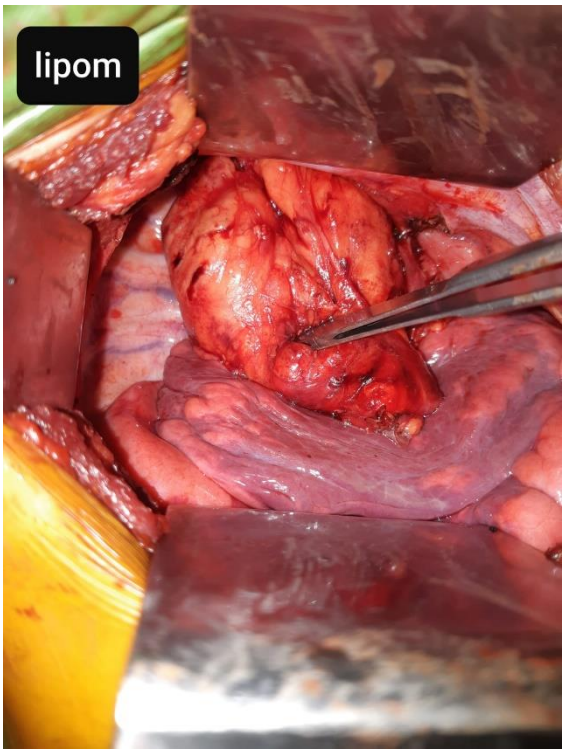
Resim1. Lezyonun Preoperatif Direkt Grafi Görüntüsü



Resim 2. Lezyonun Preoperatif Toraks BT Görüntüsü



Resim 3. Lezyonun Preoperatif Toraks MR Görüntüsü



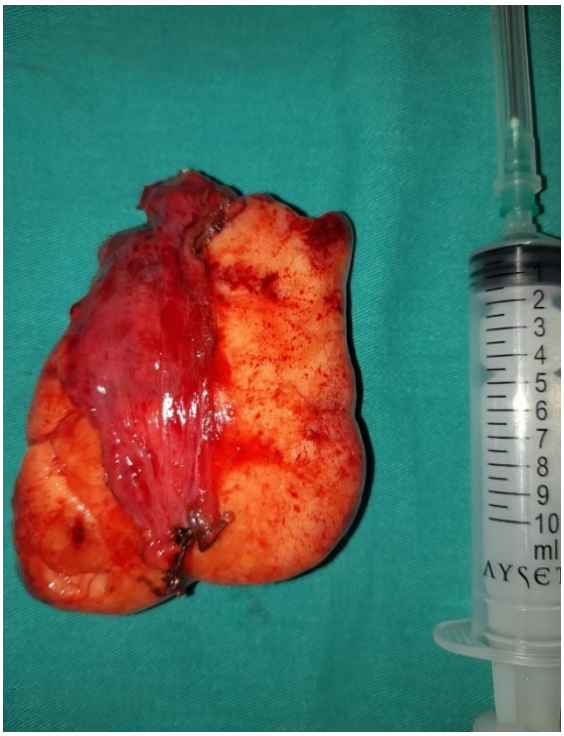
Resim 4. Lezyonun Peroperatif Görünümü

Tartışma ve Sonuç

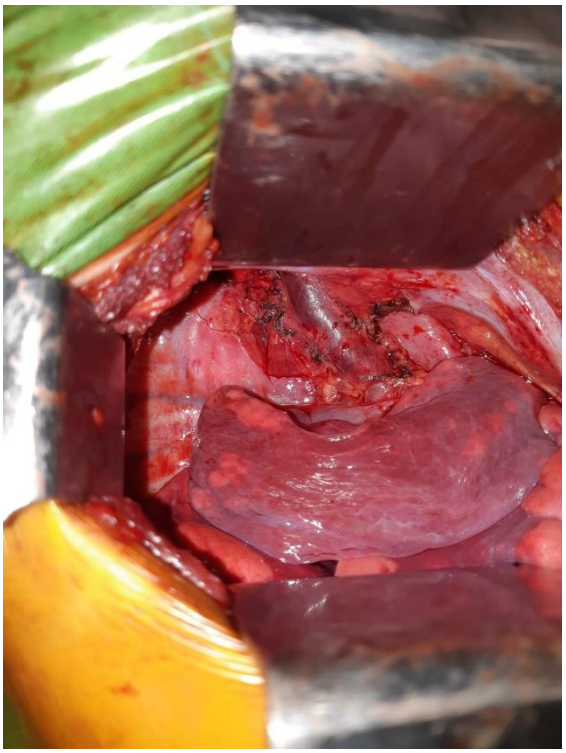
Mediastende görülen ve yağ içeren lezyonların ayırıcı tanısında lipoma, liposarkoma, timolipoma ve germ hücreli tümörler incelenmelidir. Parankimal ve endobronşial yağ içeren lezyonlar hamartom, lipoma ve lipoid pnömonidir. Lipomalar, yağ dokusu içeren fibrolipoma, teratoma gibi diğer tümörlerden yumuşak doku bileşeni içermemesi ile ayrılırlar[2]. Yağ içeren bir lezyon, çevre yapılarda yer değişikliğinden ziyade infiltrasyon oluşturuyorsa, içyapısı heterojen ise ve dansitesi -50 Hounsfield Unit (HU)'den daha fazlaysa liposarkomdan şüphelenilmelidir. Lipomalar ile düşük dereceli liposarkomların radyolojik yöntemlerle ayrımı her zaman yapılamayabilir ve kesin ayrım için biyopsi ile histopatolojik örnekleme gerekir[3]. Lipoblastoma, sıklıkla üç yaş altındaki çocuklarda görülen, immatür yağ hücrelerinden oluşan ve insidental olarak saptanan tümörlerdir[2]. Olgumuzda üst mediastinal alanda kupula bölgesinde büyük bir lezyon mevcuttu. Literatüre göre bizim vakamız çocuklarda tespit edilen üst mediasten yerleşimli en büyük intratorasik lipoma olgusudur.

Lipomalar, matür yağ dokusu ve fibröz stroma içeren benign mezenkimal tümörlerdir. Matür yağ hücreleri ve kollagen septumlara sahiptir ancak mitotik aktiviteleri yoktur. Lipomalar histopatolojik olarak angiolipoma, spindle hücreli lipoma, pleomorfik lipoma, benign lipoblastoma ve angiomyolipoma olarak sınıflandırılabilirler[4].

Torasik lipomalar, intratorasik ve ekstratorasik (transmural) olarak iki grupta incelenir. İntratorasik lipomalar; endobronşiyal, parankimal, mediastinal, kardiyak ve plevral lipomalar olarak sınıflandırılır[5].

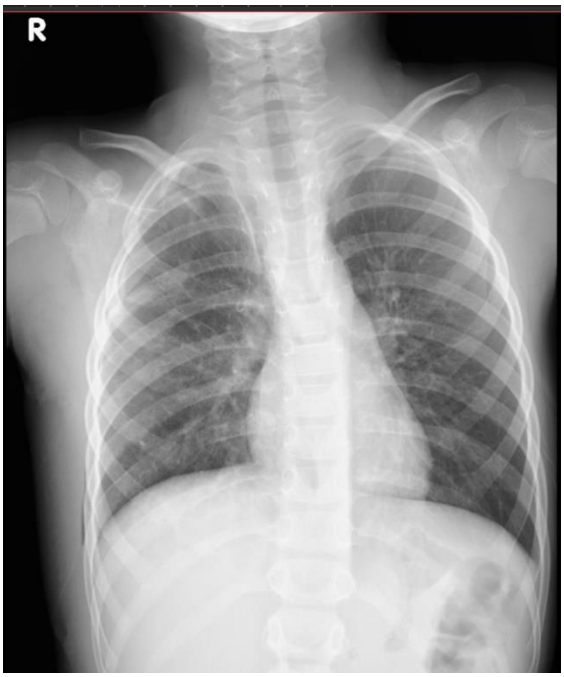


Resim 5. Lezyonun Total Eksize Edilmiş Makroskobik Görünümü



Resim 6. Eksizyon Sonrası Toraksın Görünümü

İntratorasik subplevral lipoma 3-60 yaşlar arasında görülür. Genellikle 2-13 cm çapında değişen boyutlarda ve sıklıkla lateral toraks duvarı yerleşimli lezyonlardır[6-7]. Ekstratorasik lipomalar ise intratorasik ve ekstratorasik komponentler içerirler. İnterkostal alandan ya da sternal bir defektten bu komponentler birleşirler.
Lipomaların kas dokusundan keskin bir sınırla ayrılan düzgün ve belirgin kapsülleri vardır[6]. Yavaş büyüyen intratorasik lipomalarda semptomlar, kitlenin lokalizasyonuna ve büyüklüğüne bağlıdır[8]. Bu semptomlar disfaji, dispne, öksürük, juguler distansiyon ve kardiyak aritmidir[2].
Lipomalar sıklıkla direkt grafilerle saptanırlar; ancak radyografinin lezyonun tam lokalizasyonu ve karakteri hakkında vereceği bilgi sınırlıdır. BT; lezyonun lokalizasyonunu, plevral-parankimal ayrımını, uzanımını ve iç yapısının değerlendirilebilmesini sağlar.
MRG ile yağ baskılama teknikleri kullanılarak lezyonun iç yapısındaki yağ dokusu varlığı, miktarı ve homojenitesini değerlendirmek daha kolaydır.



Resim 7. Postoperatif Direkt Grafi Görüntüsü

Ayrıca, MRG'nin yüksek yumuşak doku çözünürlüğü sayesinde lezyonun uzanımı ve çevre yapılarla ilişkisi saptanabilir.
Plevral lipomalar göğüs duvarı ile geniş açı oluşturan, parankim ve vasküler yapılarda yer değişikliği oluşturan, düzgün konturlu, homojen, yağ dansitesinde lezyonlardır. Dansiteleri ortalama -50 ile -150 (HU) arasında değişim gösterir. Fibröz stroma içeriğine bağlı olarak tamamen homojen olmayabilir[9].
Lipomaların maligniteye dönüşmesi çok nadirdir. Literatürlerde bu konuda birkaç örnek rapor edilmiştir. Rapor edilenlerin bir kısmı pleomorfik lipomalardır; diğerleri ise ilk incelemeler sırasında tümörün malignite karekteri tespit edilememiş olan iyi differansiye liposarkomlardır[4]. Lipomada kitlenin eksizyonu ile lezyonun oluşturduğu bası semptomlarını önlenir ve yeterli cerrahi tedavi ile rekürrensin önüne geçilir[10-11].
Sonuç olarak, mediasten kitleleri ayırıcı tanısısında lipoma da akla gelmeli ve kesin tanısı için cerrahi rezeksiyon yapılmalıdır. Böylece hem tanı konulmuş, hem bası semptomları ortadan kalkmış hem de malignleşme ihtimali olan bir lezyon torakstan uzaklaştırılmış olur.

Etik Komite Onayı:
Bu olgu sunumundaki hasta ebeveyninden yazılı onam alınmıştır.

Çıkar Çatışması:
Yazarlar çıkar çatışması bildirmemişlerdir.

Yazar Katkıları:
Tüm yazarlar çalışma anlayışına ve tasarımına katkıda bulunmuştur. Tüm yazarlar son taslağı okudu ve onayladı.

Hakem Değerlendirmesi:
Dış bağımsız.

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OUR EXPERIENCES AND COMPARISON OF TOTAL EXTRAPERITONEAL (TEP) AND TRANSABDOMINAL PREPERITONEAL (TAPP) TECHNIQUES IN LAPAROSCOPIC INGUINAL HERNIA REPAIR

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Öz

Amaç: Bu çalışmada laparoskopik kasık fıtığı onarımında Total Ekstraperitoneal (TEP) ve Transabdominal Preperitoneal (TAPP) ameliyat yöntemlerinin sonuçlarının karşılaştırılması amaçlanmıştır.
Yöntemler: SBÜ Sultan 2. Abdülhamid Han Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği'nde Ekim 2016 ve Ocak 2021 tarihleri arasında kasık fıtığı teşhisi ile laparoskopik kasık fıtığı onarımı ameliyatı yapılan 317 hastanın verileri retrospektif olarak değerlendirildi. Hastaların yara yeri ayrışması, insizyonda veya skrotumda şişlik, nüks, postoperatif kaçıncı gün işe geri dönüldüğü sorgulandı. TAPP ve TEP yöntemlerinin sonuçları istatistiksel olarak karşılaştırıldı.
Bulgular: Çalışmamızda TEP ve TAPP yöntemi ile ameliyat edilen 317 hastanın yaş ortalaması 50,5 olup, hastaların 27'si kadın ve 290'ı erkek idi. Ameliyat sonrası 21 (%6,6) hastada nüks, 11 (%3,4) hastada yara yeri ayrışması, 44 (%13) hastada insizyonda şişlik ve 30 (%9,4) hastada skrotal şişlik meydana geldiği tespit edildi. TEP prosedürü uygulanan hastaların ortalama 5,09 (1-30) gün sonra, TAPP prosedürü uygulanan hastaların ise ortalama 4,04 (1-14) gün sonra işe dönüş yaptıkları gözlemlendi. İki grup karşılaştırıldığında, postoperatif dönemde işe geri dönüş süresi (p=0,707), nüks (p=0,493), insizyonda şişlik (sırasıyla p=0,479), skrotal şişlik (p=0,356) ve yara yeri ayrışması açısından fark anlamlı bulunmadı (p=0,245).
Sonuç: Kasık fıtığının laparoskopik yöntem ile onarımında günümüzde yaygın olarak kullanılan iki yöntem bulunmaktadır. TEP yönteminde preperitoneal alanda, TAPP yönteminde ise intraperitoneal alanda çalışılmaktadır. Bu çalışmada, TEP ve TAPP yöntemlerinin sonuçları istatistiksel olarak karşılaştırılmış ve postoperatif nüks, işe geri dönüş süresi ile postoperatif komplikasyonlar bakımından iki prosedür arasında anlamlı fark bulunmadığı tespit edilmiştir.

***Anahtar Kelimeler**: İnguinal herni, laparoskopik, TEP, TAPP*

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Giriş

Kasık fıtığı onarımı genel cerrahide en sık yapılan ameliyatlardan biridir. Dünya genelinde her yıl 20 milyon insan kasık fıtığı nedeniyle ameliyat edilmektedir[1]. Düşük nüks ve komplikasyon oranlarıyla birlikte gerilimsiz Lichtenstein tekniği dünyada en sık uygulanan tekniktir[2]. Lichtenstein tekniği ile karşılaştırıldığında minimal invaziv yaklaşımlar, açık yaklaşıma kıyasla yara ile ilgili daha az komplikasyon, daha az postoperatif ağrı, işe/aktiviteye erken dönüş ve daha az kronik ağrı ile ilişkili görünmektedir[3,4]. Klasik açık onarımların yanı sıra, kasık fıtığı onarımını yönetmek için minimal invaziv yaklaşımlar giderek daha fazla tercih edilmektedir[5,6]. 1990'ların başlarındaki ilk tanımlamadan bu yana ve yenilikçi cerrahi platformların ortaya çıkması nedeniyle, cerrahi teknik gelişmiş ve laparoskopik Transabdominal Preperitoneal (TAPP) onarım ve Total Ekstraperitoneal onarım (TEP) ortaya çıkmıştır[7,8]. TEP onarımının avantajı, tamamı preperitoneal boşlukta yapılan işlemle periton boşluğunun ihlal edilmemesidir[9,10]. TAPP onarımında ise intraperitoneal alanda çalışılır ve karşı taraftaki miypoktineal orifisin de muayene imkânı mevcuttur[11,12].

Bu çalışmadaki amacımız, SBÜ Sultan 2. Abdülhamid Han Genel Cerrahi Kliniği'nde yapılan laparoskopik kasık fıtığı onarımı ameliyatlarının verilerini paylaşmak ve TAPP ve TEP ameliyat yöntemlerinin sonuçlarını karşılaştırmaktır.

Materyal ve Metot

SBÜ Sultan 2. Abdülhamid Han Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği'nde Ekim 2016 ve Ocak 2021 tarihleri arasında kasık fıtığı teşhisi ile laparoskopik kasık fıtığı onarımı ameliyatı yapılan hastalar retrospektif olarak değerlendirildi. Hem rektus kası arkasında alt kılıfın önünde, preperitoneal alanda çalışılan Total Ekstraperitoneal (TEP) yöntemi, hem de intraperitoneal alanda çalışılan Transabdominal Preperitoneal (TAPP) yaklaşımı ile ameliyat edilen hastalar çalışmaya dahil edildi. İletişim bilgilerine ulaşılamayan hastalar çalışma dışı bırakıldı. Hastalara telefon ile ulaşılarak ameliyat sonrası yara yeri ayrışması, insizyonda veya skrotumda şişlik olup olmadığı, nüks tanısı alıp almadığı ve ameliyat sonrası kaçıncı gün işe geri dönüldüğü sorgulandı. TAPP ve TEP yöntemlerinin sonuçları istatistiksel olarak değerlendirildi. Hastaların takip süreleri 1 yıl ile 6 yıl arasında olduğundan, nüksler erken ya da geç nüks olarak ayılmadı.

İstatistiksel Analiz

Değişkenlerin tanımlayıcısı olarak ortalama standart sapma, medyan ve aralık değerleri kullanıldı. Parametrik ve parametrik olmayan testler kullanıldı. Grup farklılıklarını karşılaştırmak için Ki Kare ve Mann Whitney U testleri kullanıldı. Farklar istatistiksel olarak %95 güven aralığında değerlendirildi ve p değeri 0,05'ten küçük olduğunda istatistiksel olarak anlamlı kabul edildi. İstatistiksel analiz, SPSS (Statistical Package for Social Sciences) version 25.0 yazılımı (SPSS Inc. , Chicago, ABD) kullanılarak yapıldı.

Bulgular

Ekim 2016 ve Ocak 2021 tarihleri arasında toplam 354 hastaya laparoskopik kasık fıtığı onarımı ameliyatı uygulandı. İletişim bilgileri ile ulaşılamayan 37 hasta çalışma dışı bırakıldı. Geriye kalan 317 hastanın (27 kadın; %8,5 ve 290 erkek; %91,5) 231'ine (%72) TEP yönteminin, 86'sına (%28) TAPP yönteminin uygulandığı görüldü. Hastaların yaş ortalaması 50,5 olarak hesaplandı. Hastalardan 24'ünün (%7,5) nüks fıtık nedeniyle ameliyat edildiği tespit edildi. Hastalardan 83'ünün (%26) bilateral, 143'ünün (%45) sağ ve 91'inin (%29) sol kasık fıtığı olduğu teşhis edildi. Tablo 1'de TAPP ve TEP ameliyatı yapılan hastaların demografik verileri, nüks herni sayıları ve taraf bilgileri yer almaktadır. Ameliyat son-

rası 21 (%6,6) hastada nüks, 11 (%3,4) hastada yara yeri ayrışması, 44 (%13) hastada insizyonda şişlik ve 30 (%9,4) hastada skrotal şişlik meydana geldiği tespit edildi. TEP prosedürü uygulanan hastaların ortalama 5,09 (1-30) gün sonra, TAPP prosedürü uygulanan hastaların ise ortalama 4,04 (1-14) gün sonra işe dönüş sağladıkları tespit edildi. Tablo 2'de hastalarımızın ameliyat sonrası takip verileri gösterilmiştir.

Tablo 1. Demografik veriler, taraf ve nüks bilgileri

Toplam (317 hasta)	TEP (231 hasta)	TAPP (86 hasta)
Yaş	50,7	49,9
Erkek	217 (%93,9)	73 (%84,9)
Kadın	14 (%6,1)	13 (%15,1)
Nüks Herni	13 (%5,6)	11 (%12,7)
Sağ	98 (%42,4)	45 (%52,3)
Sol	65 (%28,1)	26 (%30,2)
Bilateral	68 (%29,5)	15 (%17,5)

TEP ve TAPP grupları arasında postoperatif dönemde işe dönüş günü Mann Whitney U testi ile karşılaştırıldı. İki grup arasında fark izlenmedi. (p=0,707). Postop dönemde nüks gelişen 4 hastanın 2'sinin TEP grubunda, 2'sinin TAPP grubunda olduğu izlendi. Postop nüks açısından iki grup arasında fark görülmedi (p=0,493). İnsizyonda şişliği olan 44 hastanın 34'ünün TEP grubunda olduğu izlendi. İki grup arasında insizyonda şişlik açısından fark izlenmedi (p=0,479). Skrotal şişliği olan 30 hastanın 24'ünün TEP grubunda olduğu izlendi.

Tablo 2. Ameliyat sonrası takip verileri

Toplam (317 hasta)	TEP (231 hasta)	TAPP (86 hasta)
İşe geri dönüş süresi (gün)	5,09 (1-30)	4,04 (1-14)
Nüks	16 (%6,9)	5 (%5,8)
İnsizyonda şişlik	33 (%14,2)	9 (%10,4)
Skrotal şişlik	24 (%10,3)	6 (%6,9)
Yara yeri ayrışması	10 (%4,3)	1 (%1,1)

Skrotal şişlik açısından iki grup arasında fark görülmedi (p=0,356). Yara yeri ayrışması gerçekleşen 11 hastanın 10'unun TEP grubunda olduğu görüldü. İki grup arasında yara yeri ayrışması açısından fark görülmedi (p=0,245).

Tartışma

Kasık fıtığı ameliyatlarının başarısı genellikle nüks oranı dikkate alınarak değerlendirilmektedir[13]. Aiolfi ve ark. 15 randomize kontrollü çalışmayı inceledikleri derlemelerinde TAPP ve TEP yöntemleri arasında nüks açısından anlamlı fark olmadığını ifade etmişlerdir[10]. Nüks oranına ek olarak yaraya bağlı komplikasyonlar ve işe geri dönüş süreleri açısından da iki prosedür arasında anlamlı fark olmadığı bu derlemede ifade edilmiştir. Wake ve ark. da yayınladıkları metaanalizde TAPP ve TEP yöntemleri arasında nüks açısından fark olmadığını ifade etmişlerdir[14]. Başka bir metaanalizde TEP onarımı ile Lichtenstein onarımı karşılaştırılmış ve ameliyat sonrası komplikasyonlar ve tekrar onarım gereksinimi açısından TEP yöntemi daha avantajlı bulunmuştur; ancak aynı avantajın TAPP için geçerli olmadığı gösterilmiştir[15]. TAPP tekniğinde peritoneal kavitenin eksplore edilmesi ve her iki inguinal bölgenin de muayene edilebilmesi avantajı vardır[7,16]. TEP tekniği, karın boşluğuna girmeden miyopektineal orifislerin araştırılmasına, fıtık kesesinin diseksiyon ve redüksiyonuna ve yamanın yerleştirilmesine olanak sağlar[17,18]. Bu çalışmanın sonuçları, TAPP ve TEP yöntemleri arasında nüks açısından anlamlı bir fark bulunmadığı sonucuna ulaşan çalışmalarla uyumlu bulunmuştur.

Sonuç

Bu çalışmada, TEP ve TAPP yöntemlerinin sonuçları karşılaştırıldığında postoperatif nüks, işe geri dönüş süresi ve postoperatif komplikasyonlar bakımından istatistiksel olarak anlamlı fark bulunmadığı tespit edilmiştir. Seçilecek laparoskopik yöntemlerden her birinin bazı avantajları olmasına

rağmen, nüks, komplikasyonlar ve işe dönüş süresi bakımından birbirlerine üstünlükleri yoktur.

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