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AMAÇ

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

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AIM

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

SCOPE

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1. Yazarlar

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

a. Yırtıcı veya Sahte Dergiler

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

2. Dergiler

a. Gizlilik

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

b. Zamanlama

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

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c. Hakem Değerlendirmesi

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

d. Bütünlük

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

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Makaleler / Research Article

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Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

CHOCOLATE OR FETAL DOPPLER SONOGRAPHY FOR NON-REACTIVE NON-STRESS TEST PATTERNS: RANDOMIZED PROSPECTIVE CONTROLLED STUDY

FETAL NON-REAKTİF NON-STRESS TEST PATERNİ TAKİBİNDE FETAL DOPPLER ULTRASON VEYA ÇİKOLATANIN YERİ: PROSPEKTİF RANDOMİZE KONTROLLÜ ÇALIŞMA

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Abstract

Aim: The aim of this study is to compare the effect of 20-second MCA Doppler ultrasonography and bitter chocolate on non-stress test (NST) patterns, fetal movements felt by the mother and cesarean delivery rates.

Methods: Single pregnancies between 36-41 weeks with non-reactive NST pattern were included in the study and prospectively randomized to Doppler ultrasound, bitter chocolate, and non-intervention control groups. NSTs of the patients at the 5th and 30th minutes were examined.

Results: The rate of improvement in the fetal movements felt by the mother did not differ significantly among groups ($p > 0.05$). The 5th minute reactive NST ratio in the Doppler group was significantly higher ($p < 0.05$) than in the follow-up and chocolate group. In the chocolate and non-intervention control group, the 5th minute reactive NST ratio did not differ significantly ($p > 0.05$). In the 30th minute NST, patients with non-reactive results had significantly higher fetal distress rates in the Doppler group compared to the other groups ($p < 0.05$).

Conclusions: We think that with the application of Doppler, the length of hospital stay and accordingly patient's anxiety will reduce. In addition, the patient should be monitored more carefully in terms of fetal distress because it quickly corrects false non-reactivity.

Keywords: Chocolate, Doppler, non-stress test

Öz

Amaç: Bu çalışmanın amacı, 20 saniyelik MCA Doppler ultrasonografi ve bitter çikolatanın, non-stres test (NST) paternleri; anne tarafından hissedilen fetal hareketler ve sezaryen doğum oranlarına etkisini karşılaştırmaktır.

Yöntemler: 36-41 hafta arası reaktif olmayan NST paterni olan tekil gebelikler çalışmaya dahil edildi ve prospektif olarak Doppler ultrason, bitter çikolata ve müdahalesiz kontrol gruplarına randomize edildi. Hastaların 5. ve 30. dakikadaki NST'leri incelendi.

Bulgular: Anne tarafından hissedilen fetal hareketlerdeki iyileşme oranı gruplar arasında anlamlı farklılık göstermedi ($p > 0.05$). Doppler grubunda 5. dakika reaktif NST oranı, takip ve çikolata grubuna göre anlamlı olarak daha yüksekti ($p < 0.05$). Çikolatalı ve müdahalesiz kontrol grubunda 5. dakika reaktif NST oranı anlamlı farklılık göstermedi ($p > 0.05$). 30. dakika NST'de, reaktif olmayan sonuçları olan hastalarda, Doppler grubunda diğer gruplara göre anlamlı derecede daha yüksek fetal distres oranları vardı ($p < 0.05$).

Sonuç: Doppler uygulaması ile hastanede kalış süresinin ve buna bağlı olarak hastanın kaygısının azalacağını düşünüyoruz. Ayrıca yanlış tepkisizliği hızla düzelttiği için hasta fetal distres açısından daha dikkatli izlenmelidir.

Anahtar Kelimeler: Çikolata, Doppler ultrason, non-stres test

Introduction

It is absolutely necessary to evaluate fetal well-being in terms of health of the mother and fetus during pregnancy. The most used method for antepartum fetal evaluation is electronic fetal monitoring method. Non-stress test (NST) is one of the key indices that reflect the biophysical activities of the fetus[1]. NST is a test based on an increase in fetal heart rate in response to fetal movements and reveals two patterns; if it is reactive, it can be said that the fetus is in good condition. If it is non-reactive, it may be associated with poor fetal outcome. According to the NST results, in patients delivered as fetal distress, the specificity is not at the level we want, but then in nearly half of these patients, a poorly affected newborn is obtained[2]. However, the average relative percentage time spent in a silent state is about 26% for the fetus between 30 and 40 weeks[3]. Therefore, if NST monitoring is performed during the quiet period of the fetus, the false non-reactive incidence will be higher; this length varies from 20 to 75 minutes but may also be associated with fetal hypoxemia or acidosis. Other factors associated with non-reactive NST results are maternal race, fetal immaturity, sepsis, maternal cigarette-alcohol intake, and the use of some drugs that can suppress fetal cardiac and neurological activity[4-6].

Many studies have shown that there is a relationship between maternal glucose administration and increased fetal activity[7]. Continuous-wave Doppler ultrasonography close to the fetal ear, which was applied intermittently for a total of 60 seconds within 3 minutes, has been shown to increase fetal movements[8]. It is thought that Doppler ultrasonography does not increase the risk for the fetus, even in the first trimester, unless the duration of exposure is more than 5 minutes[9]. Furthermore, a study of fetuses exposed in utero to vibroacoustic stimulation[10] and a recent study of fetuses exposed to noise generated during an MR exam of the pregnant women[11] showed any deleterious effect on the fetal auditory system.

NST procedures can cause maternal anxiety regarding both the duration of the procedure and the probability of perceived abnormal results[12]. In NST, early reactivation is extremely important both for the patient and her psychology and for the decrease in the hospital stay, beside non-reactivation is very important for the fetus. Therefore, it seems necessary to use strategies to reduce false positive results to identify high-risk fetuses, patient waiting period, medical team and equipment time, and retrench diagnosis and treatment costs.

We aimed to investigate whether Doppler application will provide earlier reactivation in NST and increase fetal movements faster than in patients receiving bitter chocolate or non-intervention.

Materials and Methods

We selected our study group among the patients who came to the outpatient clinic for routine control at Ankara Etlik Zübeyde Hanım Training and Research Hospital and applied to NST between November 2018 and March 2019. The local institutional review board has approved the study (HEK 2018/46, 21/11/2018).

Single pregnancies between 36-41 weeks with non-reactive NST were included in the study. Patients with hypertension, intrauterine growth retardation, oligohydramnios, diabetes (gestational or pregestational), chocolate allergy, fetal anomaly and deceleration in NST were not included in the study.

Fetal heartbeat traces were interpreted by a single physician (HE). The physician (GK) who performed Doppler for all selected Non-reactive NST patients was the same. All traces were recorded by Philips Avalon

FM 30 fetal monitors. Reactive NST was defined as having 2 accelerations of 15 pulses or more, which lasted at least 15 seconds in a 20 minute NST. Patients with non-decelerated nonreactive NST were selected for the study, and consent was obtained as to whether patients would participate in the study.

We divided the selected patients into three groups: Doppler, chocolate and non-intervention control group. 90 patients from each group were written in envelopes by GK, including 1: 1: 1 ratio in three groups. A sample size of 242 was calculated as sufficient for 0.05 error margin and 95% power with G power 3.1.9.2 program. These envelopes were mixed and sealed and delivered to the physician (HE) interpreting NST. The patient with nonreactive NST selected his envelope from HE and brought it to the physician (GK), who would do whatever it takes, without opening the envelope. GK applied the necessary procedure to the patient regardless of which group appeared in the envelope. MCA Doppler was performed by GK in the Doppler group for 20 seconds (Voluson 730 Expert 4D Ultrasound Machine). He gave 50 gr of bitter chocolate to the chocolate group and was allowed to eat next to him (1927 special series nestle bitter chocolate with 60% Cocoa). Nothing was done to the control group. Patients were told not to eat anything else. Then, the patients were connected to NST by HE and the traces were examined in the 5^{th} minute. The procedure was terminated at 20^{th} minute in patients with reactive NST. NST evaluation was repeated at 30^{th} minute in patients with non-reactive NST. Patients were asked whether fetal movements increased. During this process, HE certainly did not know in which group the patients were. NST results were recorded as reactive and non-reactive. The patients whom second NST was non-reactive were hospitalized in the hospital delivery room for a biophysical profile and close follow-up. It was followed whether the hospitalized patients were taken into cesarean section due to fetal distress.

- *Statistical Analysis*

Average, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured by Kolmogorov Simirnov test. In the analysis of quantitative independent data, Kruskal-Wallis and Mann-Whitney U tests were used. Chi-square test was used in the analysis of qualitative independent data. SPSS 22.0 program was used in the analysis.

Results

During this period, a total of 270 patients were randomized and 257 were evaluated for the final analysis. The 5^{th} minute reactive NST rate in the Doppler group was significantly higher than the non-intervention control and chocolate group ($p < 0.05$). In the non-intervention control and chocolate group, the 5^{th} minute reactive NST ratio did not differ significantly ($p > 0.05$). Although fetal movements were improved in the control, chocolate and doppler groups, respectively, there was no statistically significant difference ($p = 0.066$). (Table 1)

In the Doppler group whose NSTs were non-reactive in 30^{th} minute, fetal distress rate was significantly higher compared to the chocolate group and non-intervention controls ($p < 0.05$). (Table 2)

Discussion

NST maintains its importance in fetal monitoring due to its ease of performance and cost effectiveness. Khooshideh et al. showed that the sensitivity and specificity of NST to predict fetal distress are 62 and 42%, respectively, and the negative predictive value is 94%[13]. One of the handicaps of NST application is that it cannot control the incidence of hypoxic-ischemic encephalopathy and increases the

Table 1. Data comparisons among groups

		Non-intervention control group			Bitter Chocolate group			MCA Doppler group			
		Mean±s.d./n-%		Med	Mean±s.d./n-%		Med	Mean±s.d./n-%		Med	p
Gestational age		37.6 ± 1.1		38.0	37.7 ± 1.1		38.0	37.2 ± 1.0		37.0	0.008[K]
NST at 5. min	Reactive	47	55.3%		54	62.8%		79	91.9%		0.000[x2]
	Non-reactive	38	44.7%		32	37.2%		7	8.1%		
	Not perform	47	55.3%		54	62.8%		79	91.9%		
NST at 30. min	Reactive	8	9.4%		7	8.1%		0	0%		0.000[x2]
	Non-reactive	30	35.3%		25	29.1%		7	8.1%		
	Fetal distress	6	7.1%		6	7%		5	5.8%		
Non-reactive	Normal pregnancy follow-up	79	92.9%		80	93%		81	94.2%		0.935[x2]
Improving of fetal moving	Yes	66	77.6%		71	82.6%		78	90.7%		0.066[x2]
	No	19	22.4%		15	17.4%		8	9.3%		

Kruskal-wallis (Mann-whitnes u test)/[x2] Ki-kare test
NST; non-stress test, MCA; middle cerebral artery

Table 2. Fetal distress rates in patients with non-reactive non-stress test in the 30th minute.

		Non-intervention control group		Bitter Chocolate group		MCA Doppler group		P value
		n	%	n	%	n	%	
Non-reactive	Fetal distress	5	16.7%	5	10%	5	71.4	0.008[x2]
	Normal pregnancy	25	83.3%	20	40%	2	28.6	

[x2] Ki-kare test

rate of cesarean section in case of false positivity. One of the most important causes of earlier hospitalization and over-intervention is that false non-reactive NST is very common, and it is very difficult to identify true and false non-reactive[1].

There are many factors that affect reactivity in NST. The most common of these is fetal sleep period. However, fetal distress causes, such as fetal hypoxia, may also cause non-reactive NST in the early period. In this sense, if non-reactive NST is caused by a cause such as fetal hypoxia, it is of great importance to detect it as early as possible. Methods such as maternal glucose intake or mother's change of position are used in clinical practice for many years to increase the activity of the baby[6-7]. Orange juice and chocolate intake is often recommended for maternal glucose uptake[14]. Maternal serum glucose levels have been shown to be associated with NST patterns[15]. Another study showed that high cocoa (70% cocoa) in chocolate provides increased fetal movements and FHR reactivity[16]. McShea and his colleagues have shown that bitter chocolate improves cerebral blood flow[17]. However, there are publications stating that

maternal glucose concentration is not related to fetal activity and FHR patterns[15]. Esin and his colleagues found that orange juice provides more NST reactivation than chocolate[14].

Hasanpour and his colleagues found that acoustic stimulation, another factor other than glucose uptake, improved NST nonreactivity. Based on their findings, it can be concluded that with the feeding of mothers, more NST false cases can be identified than acoustic stimuli. However, when evaluated in terms of time, acoustic stimuli can be a better approach in most false positive cases and can determine test results within a minimum of time[18].

Kisilevsky and his colleagues showed that the maturation of the human fetal response to vibroacoustic stimulation started at the age of about 26 weeks of gestation[19]. In the study of Xi and his colleagues, when NST is applied to pregnant women without stimulation, 29.5% of NST is not reactive; however, when women were given advanced acoustic stimulation with flapping, 92.3% NST were observed to become reactive[1].

In a previous study, listening to music during the NST procedure increased the number of fetal movements, basal heart rate, and large accelerations, but decreased processing time and did not affect the suspected NST number[12].

Fetal ultrasonography has been shown to increase fetal movements[8]. Troyano et al. researched a method for the qualitative and quantitative evaluation of fetal reflex reactivity to external stimuli via the Doppler device. They suggested using this technique as a complementary in determining the moderate response of fetus to hypoxia[20]. Although there is a prominent increase in fetal mobility via Doppler stimuli, there are no prospective studies on the effectiveness of NST in this regard.

In current study, it was observed that Doppler exposure corrected the FHR pattern faster than chocolate. There was no difference between chocolate and non-intervention control groups. As a result, we found that Doppler application corrected the false positive Non-reactive NST of the fetus much more quickly. In addition, the rates of going to cesarean section due to fetal distress were strongly observed in the Doppler group in patients with non-reactivity at 30th minutes NST. Although an increase in fetal movements was observed in Doppler, chocolate and control groups, respectively, this increase did not show a statistically significant difference ($p = 0.066$). This may be secondary to inappropriate reporting of fetal movements due to the mother's lack of information for the concept of fetal movement.

The advantages of this study are its relatively large sample size, prospective and randomized nature. The most important limitation of the study is performing Doppler with a device, even if it is 20 seconds. With the recommendation of the FDA[21], health practitioners should always apply the “reasonably low enough” concept and minimize Doppler ultrasound use during pregnancy while maintaining diagnostic quality. Repetitive vibroacoustic stimulation applications in non-reactive NST cases may pose a risk for fetal safety. In addition, there is a cost created by this application and extra time allocated to the patient by the expert. Future researches’ with more cases with similar pregnancy risks by using more practical Doppler device (such as hand Doppler devices) will yield more practical and better results.

Conclusion

As a result, 20 second Doppler application corrects NST patterns much faster than bitter chocolate and non-intervention control group in the presence of a non-reactive NST. In addition, in patients who underwent Doppler, non-reactive NST ongoing cases are much more likely to go to cesarean section due to fetal distress than bitter chocolate and control group. With this result, we think that with the application of Doppler, the length of hospital stay and accordingly patient’s anxiety will reduce. In

addition, the patient should be monitored more carefully in terms of fetal distress because it quickly corrects false non-reactivity.

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, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
The study was approved by the Ankara Etlik Zübeyde Hanım Training and Research Hospital Ethics Committee (HEK 2018/46, 21/11/2018).

References

1. Xi Q, Du J, Liu X, et al. Clinical study on detecting false non-reactive of non-stress test by improved acoustic stimulation. Arch Gynecol Obstet. 2011; 284 (2): 271-4. doi: 10.1007/s00404-010-1621-z
2. Black RS, Campbell S. Cardiotocography versus Doppler. Ultrasound Obstet Gynecol. 1997; 9 (3):148–51. doi: 10.1046/j.1469-0705.1997.09030148.x.
3. Suwanrath C, Suntharasaj T. Sleep-wake cycles in normal fetuses. Arch Gynecol Obstet. 2010; 281 (3): 449–54. doi: 10.1007/s00404-009-1111-3.
4. Paine LL, Strobino DM, Witter FR, et al. Population differences affect nonstress test reactivity. J Perinatol. 1991; 11 (1): 41–5.
5. Johnson MJ, Paine LL, Mulder HH, et al. Population differences of fetal biophysical and behavioral characteristics. Am J Obstet Gynecol. 1992; 166 (1): 138–42. doi: 10.1016/0002-9378(92)91847-4.
6. Esin S. Factors that increase reactivity during fetal nonstress testing. Curr Opin Obstet Gynecol. 2014; 26 (2): 61-6. doi: 10.1097/GCO.0000000000000050.
7. Miller FC, Skiba H, Klapholz H. The effect of maternal blood sugar levels on fetal activity. Obstet Gynecol. 1978; 52 (6):662–5.
8. Fatemi M, Ogburn PL Jr, Greenleaf JF. Fetal stimulation by pulsed diagnostic ultrasound. J Ultrasound Med. 2001; 20 (8): 883-9. doi: 10.7863/jum.2001.20.8.883.
9. Miller DL, Quddus J. Diagnostic ultrasound activation of contrast agent gas bodies induces capillary rupture in mice. Proc Natl Acad Sci. 2000; 97 (18): 10179-84. doi: 10.1073/pnas.180294397.
10. Nyman M, Barr M, Westgren M. A four-Year follow-up of hearing and develop-ment in children exposed in utero to vibroacoustic stimulation. Br J Obstet Gynaecol. 1992; 99 (8): 685-8. doi: 10.1111/j.1471-0528.1992.tb13856.x.
11. Reeves MJ, Brandreth M, Whitby EH, et al. Neonatal cochlear function: measurement after exposure to acoustic noise during in utero MR imaging. Radiology 2010; 257 (3): 802-9. doi: 10.1148/radiol.10092366.
12. Kafali H, Derbent A, Keskin E, et al. Effect of maternal anxiety and music on fetal movements and fetal heart rate patterns. J Matern Fetal Neonatal Med. 2011; 24 (3): 461-4. doi: 10.3109/14767058.2010.501122.
13. Khooshideh M, Izadi S, Shahriari A, et al. The predictive value of ultrasound assessment of amniotic fluid index, biophysical profile score, nonstress test and foetal movement chart for meconium- stained amniotic fluid in prolonged pregnancies. J Pak Med Assoc. 2009; 59 (7): 471–4.
14. Esin S, Baser E, Cakir C, et al. Chocolate or orange juice for non-reactive non-stress test (NST) patterns: a randomized prospective controlled study. J Matern Fetal Neonatal Med. 2013; 26 (9): 915-9. doi: 10.3109/14767058.2013.766698.
15. Phelan JP, Kester R, Labudovich ML. Nonstress test and maternal serum glucose determinations. Obstet Gynecol. 1982; 60 (4): 437–9.
16. Buscicchio G, Piemontese M, Gentilucci L, et al. The effects of maternal caffeine and chocolate intake on fetal heart rate. J Matern Fetal Neonatal Med. 2012; 25 (5): 528–30. doi: 10.3109/14767058.2011.636104.
17. McShea A, Ramiro-Puig E, Munro SB, et al. Clinical benefit and preservation of flavonols in dark chocolate manufacturing. Nutr Rev. 2008; 66 (11): 630–41. doi: 10.1111/j.1753-4887.2008.00114.x.
18. Hasanpour S, Raouf S, Shamsalizadeh N, et al. Evaluation of the effects of acoustic stimulation and feeding mother stimulation on non-reactive non-stress test: a randomized clinical trial. Arch Gynecol Obstet. 2013; 287 (6): 1105-10. doi: 10.1007/s00404-012-2695-6.
19. Kisilevsky BS, Muir DW, Low JA. Maturation of human fetal responses to vibroacoustic stimulation. Child Dev. 1992; 63 (6): 1497–508.
20. Troyano Luque JM, Maeda K, Kurjak A, et al. Fetal extremity kinetics quantified with Doppler ultrasonography. J Perinat Med. 2008; 36 (1): 82-6.

doi: 10.1515/JPM.2008.008.
21. U.S. Food and Drug Administration (FDA). Information for manufacturers seeking marketing clearance of diagnostic ultrasound systems and transducers. Rockville, MD: FDA; Sept 30, 1997.

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DEPRESSION AND QUALITY OF LIFE RELATED FACTORS IN HEMODIALYSIS PATIENTS

HEMODİYALİZ HASTALARINDA DEPRESYON VE YAŞAM KALİTESİ İLE İLİŞKİLİ FAKTÖRLER

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Abstract

Aim: Depression is the most common psychiatric disorder affecting patients on hemodialysis (HD) and has been associated with impaired Quality of Life (QoL). This study aimed to investigate the prevalence of depression and the relationship between depression, QoL, and demographic factors in HD patients.

Methods: Short form 36 (SF–36) and Beck's depression inventory (BDI) were employed to assess the relationship between depression, QoL and demographics in 50 hemodialysis patients. The relationship between scores of BDI and SF–36, and annual biochemical and demographic data were then evaluated.

Results: Mean age of the patients was 56.4 ±16.4 years and the mean HD duration was 57.11 ±39.09 months. The incidence of depression (BDI>14) was 36%. Age, hemoglobin, ferritin, body mass index (BMI), and Kt/V values were observed to be significantly correlated with the QoL scores ($p<0.05$ for all). These scores, however, were not related to dialysis duration, serum albumin, CRP, calcium, phosphorus, and parathormone values. The target level for hemoglobin, age <45 years, and ideal body weight were associated with high SF–36 social functioning score ($p<0.05$).

Conclusions: The results of this study showed that the depressive symptoms were as high as 36% among the study group linked to poor QoL. Interestingly, annual mean values of Kt/V and the biochemical parameters were not related to BDI scores. Higher levels of ferritin (800) (negatively) and hemoglobin (>11 g/dL) / ideal BMI (18–25 kg/m2) / younger age (18–45 year) (positively) were related to some SF–36 scores. The study emphasizes that hemodialysis patients should also be evaluated for depression and QoL, to optimize clinical outcomes with the help of nephrologists and psychiatrist.

Keywords: Quality of life, depression, hemodialysis

Öz

Amaç: Depresyon hemodiyaliz hastalarını etkileyen en yaygın psikiyatrik bozukluktur ve bozulmuş yaşam kalitesi ile ilişkili olduğu düşünülmektedir. Bu çalışmada hemodiyalize giren hastalarda depresyon ile yaşam kalitesi ve demografik faktörler arasındaki ilişki araştırılmıştır.

Yöntemler: Diyalize girmekte olan elli (n: 50) hemodiyaliz hastasına depresyon, yaşam kalitesi (quality of life, QoL) ve demografik veriler arasındaki ilişkiyi değerlendirmek için kısa form 36 (SF-36) ve Beck depresyon envanteri (BDI) anketleri uygulandı. BDI ve SF-36 skorları ile yıllık biyokimyasal ve demografik veriler arasındaki ilişki değerlendirildi.

Bulgular: Hastaların yaş ortalaması 56,4 ± 16,4 yıl, ortalama HD süresi 57,11 ± 39,09 ay idi. Depresyon insidansı (BDI> 14 olarak belirlendiğinde) %36 idi. Yaş, hemoglobin, ferritin, vücut kitle indeksi (VKİ) ve Kt/v değerleri QoL skorları ile anlamlı olarak korele bulundu (hepsi için $p<0.05$). Ancak QoL skorları diyaliz süresi, serum albümin, C reaktif protein, kalsiyum, fosfor ve parathormon değerleri ile ilişkili değildi. Hemoglobin için hedef seviyede olma, hasta yaşının kırk beşin altında olması, ideal vücut ağırlığında olma hali ise yüksek sosyal fonksiyon skoru (SF-36 alt analizi) ile anlamlı ölçüde ilişkiliydi ($p<0.05$).

Sonuç: Bu çalışmada hemodiyaliz hasta grubunda depresyon sıklığı %36 olarak bulunmuş ve bu durumun kötü yaşam kalitesi skorları ile ilişkili olduğu gösterilmiştir. İlginç olarak iyi diyalizin bir göstergesi olan Kt/v'nin ve hastaların biyokimyasal parametrelerinin QoL ile ilişkisi bulunmamıştır. Ferritinin yüksek olması negatif olarak (>800 mg/dL); hemoglobinin> 11 g/dL'nin üzerinde olması, ideal vücut ağırlığında olmak (VKİ 18-25 kg/m2) ve 18-45 yaş aralığında olmak pozitif olarak bazı SF-36 skorlarıyla ilişkili bulunmuştur. Bu çalışma hemodiyaliz hastalarının iyilik hallerini sağlamak için nefrolog ve psikiyatrların birlikte çalışması gerektiğini vurgulamaktadır.

Anahtar Kelimeler: Yaşam kalitesi, depresyon, hemodiyaliz

Introduction

Depression is the most common psychiatric illness affecting patients with end-stage renal disease (ESRD)[1]. The combination of disturbing physical symptoms and psychological distress results in significantly reduced QoL, thereby leading to the development of depression[2-4].
Despite many studies being carried out in this research area, depression in hemodialysis patients is yet to be completely understood and cured[5]. Beck's Depression Inventory is the standard questionnaire used to monitor depressive symptoms in chronic hemodialysis patients[6]. SF–36 is the most commonly employed instrument that measures health-related quality of life through a well-documented scoring system[7]. Depression and quality of life are intertwined processes. Therefore, they are recommended to be evaluated in combination.
A majority of the previous studies have been conducted by comparing sectional data of the monthly laboratory results of patients with depression, and their QoL scores. In contrast to this mean value of the annual laboratory data of the patients was calculated and its relationship with Beck's and SF-36 scores was examined in the present study.

Materials and Methods

- *Patients*

Fifty hemodialysis patients were included in this cross-sectional and observational study, carried out from January 2017 to December 2017. Patients with malignant diseases, acute infections, acute coronary syndrome, or decompensated heart failure were excluded from the study. Patients over the age of 18 years, with informed consent, participated in this study. Patient history, physical examination, monthly and annual averaged data of the biochemical tests and hemodialysis adequacy were recorded for each patient. BDI and SF–36 QoL questionnaires were both implemented by a single physician.
BDI and SF–36 were translated into Turkish and applied to all the patients. BDI is a questionnaire bearing 21 questions, each one having four possible answers, with scores ranging from 0 to 63. The symptoms of depression during the last week were measured; increased scores indicated the severity of depression. A score of 14 points and above was considered to be the limit for depression[8].
SF–36 evaluates the quality of life in eight sub-titles within two basic components, i.e., the physical components and the mental components. The scales measure Emotional Role Strength, Energy Viability, Vitality, Mental Health, Social Functioning, Physical Function, Physical Role Strength, Pain and General health perception. High scores indicate well-being; well-being increases when the pain rate is low. The results of this questionnaire were also compared with the results of the questionnaire that targeted the general community of Turkey[9]. This study was approved by the local Ethics and Research Committee of the University Hospital.

- *Statistical method*

The mental health score from SF–36 and BDI instruments of the patients were compared and it was observed that the study was consistent. Pearson's *r* correlation test was utilized for this purpose. A comparison between the patients and the results of the Turkish version of SF–36 was made using the chi-square test. The SPSS 20 program was used for the statistical analysis of the data.

Results

Of the 50 patients, 27 were males. The demographic characteristics of the patients are summarized in Table 1. BDI and SF–36 scores in HD patients and in the general community are shown in Table 2. According to BDI, depression frequency was estimated to be 36% (18/50) in the patients; 43.5% in females and 29.6% in males. SF–36 sub-analysis scores (general health perception, pain score) of the seven patients who died within one year after implementation of the instrument were not found to be statistically significant, although their scores were lower than those of the patients alive.

Table 1. Demographic features of hemodialysis patients participating in the study

Variables	
Female(n=23)	58.8±15.8
Male(n=27)	54.4±17
Total(n=50)	56.4±16.4
Tobacco use n (%)	14 (%28)
Cigarette pack-year	31±23.55
Alcohol (%)	6 (%12)
Primary Kidney Disease	
Hypertension	16 (%32)
Diabetes mellitus	12 (%24)
Idiopathic	5 (%10)
Chronic Glomerulonephritis	4 (%8)
Neurogenic	4 (%8)/
Bladder/Stone	2 (%4)
Polycystic kidney disease	2 (%4)
Tubulointerstitial nephritis	1 (%2)
Other	4 (%8)
Arteriovenous fistula/Catheter	36/14 (%72/28)
HBV (+)/HCV (+)	2 (%4)/2 (%4)

The patients were divided into three groups according to their BMIs as: <18, 18–25 (normal), and 25 kg/m2 (overweight). The scores for physical function (p=0.016), energy-vitality (p=0.011) and mental health (p=0.033) were significantly better in patients with normal weight than in those who were overweight. The patients were also divided for age and Kt/V. The scores of BDI and SF–36 in different patient groups are depicted in Table 2. The patients were categorized on the basis of dialysis vintage as <24 months, 24–60 months and >60 months (Table 3). According to the mean annual levels of hemoglobin, albumin, parathormone, CRP, and ferritin of the patients, BDI and SF–36 scores are summarized in Table 4.

Discussion

In addition to the metabolic, cardiovascular, hematologic and bone mineral disorders in patients on chronic dialysis program, poor QoL and depression are common problems. Depression is the most frequent psychological disorder affecting this group[10,11]. At the same time, depression is associated with increased morbidity and mortality in ESRD[12]. According to DOPPS (The Dialysis Outcomes and Practice Patterns Study), the depression frequency in hemodialysis patients has been reported to be about 20% in America and Europe. The relative risk of mortality in patients with depression has been found to be increased by 23%.

Although it has been discussed in the previous studies as to which scoring system would better detect depression in the dialysis patients, most studies have been carried out using BDI as the instrument for detection of depression in these patients[13,14]. Depression frequency was observed to be 36% in the present study, according to BDI. Likewise, depression frequency has been reported by other authors as 33%, 26.7%, 25.3% and, 28%[5,11,15,16].

Table 2. Relationship between gender, weight, age, Kt/v, URR, and survival by SF 36 and Beck's score

	Beck's Depression Analysis	SF36 Physical functioning score	SF36 Physical role functioning Score	SF36 Emotional role functioning Score	SF36 Energy Vitality Score	SF36 Mental Health Score	SF 36 Social Functioning Score	SF36 Pain Score	SF 36 General Health Perception Score
Female (n:23)	14.2±9.6	43.4±31	34.1±23.8	25±25.5	45.4±25.4	68.3±25.9	71.5±37.6	73.7±26.5	39.7±25
Male (n:27)	14±11.8	58.8±30.9	22.2±25.3	18.5±24.6	59.7±28.6	75.6±19.2	75±29.4	74.7±28.6	49.5±30
P	0.944	0.089	0.101	0.372	0.074	0.261	0.723	0.903	0.228
Turkey's Median Female	.	80.6±21.7	82.9±28.6	89.0±22.5	63.4±13.7	70.1±11.4	90.1±12.9	81±20.2	69.1±16.9
Turkey's Median Male	.	87.2±17.1	89.8±19.3	92.8±15.1	65.7±11.9	71±10.6	91.7±12.8	85.1±16.4	73.6±14.9
P*Patient- Turkey's Median Female	.	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P*Patient- Turkey's median Male	.	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Alive (n:43)	12.5±9	54.5±30	29.5±24.8	22.7±25.1	55.4±26.8	73.1±22.9	74.4±31.4	75.1±26.6	48±27.5
Exitus (n:7)	25.1±16.6	29±39.7	10±22.3	10±22.3	35±33.7	65.4±19.4	65±48.7	67±36.4	20±20.3
P	0.55	0.149	0.335	0.264	0.428	0.897	0.259	0.849	0.152
BMI<18 kg/m^2 (n:3)	15.3±11.5	56.6±37.5	16.6±28.8	16.6±28.8	51.6±42.5	53.3±40.4	58.3±52	55.8±43.7	38.3±40.7
BMI 18–25 kg/m^2 (n:27)	12.5±7.1	63±27.7	25±25.4	25±25.4	63.9±22.1	79.6±12.4	77.8±26.5	79.4±23.1	52.8±24.6
BMI>25 kg/m^2 (n:20)	15.9±14.9	36.7±30	17.5±24.4	17.5±24.4	39.7±27.9	65.7±27	70±38.3	70.3±29.8	36.2±29
P	0.573	0.016*	0.298	0.577	0.011*	0.033**	0.528	0.268	0.126
Age 18–45 (n:12)	11.3±7.2	70.8±25.7	25±26.1	25±26.1	69.1±28.3	75.3±24.4	75±36.5	70.6±28.9	55.4±26.9
Age 45–65 (n:18)	12.7±11.3	48.3±33.8	30.5±25	25±25.7	49.8±27.8	68.8±28.3	70.8±34	75.1±27.2	46.7±32
Age>65 (n:20)	17±11.8	43.4±29.2	26.3±25.6	15.7±23.8	46.5±25	73.8±14.5	75±31	75.7±28	37.2±23.3
P	0.29	0.049***	0.814	0.463	0.07***	0.703	0.917	0.871	0.206

*Statistically significant difference in physical functioning, energy vitality, and mental health scores was found between BMI 18–25 kg/m^2 and >25.
** Statistically significant difference in mental health score was found between BMI 18–25 kg/m^2 and <18 kg/m^2
*** Statistically significant difference in physical functioning and energy vitality score was found between the patients with age 18–45 and age >65
Beck's depression inventory and Turkey's median scores do not exist in the literature. BMI: Body mass index, SF–36: Short form 36

Table 3. Relationship between dialysis-associated data by SF 36 and Beck's score

	Beck's Depression Analysis	SF36 Physical functioning score	SF36 Physical role functioning Score	SF36 Emotional role functioning Score	SF36 Energy Vitality Score	SF36 Mental Health Score	SF 36 Social Functioning Score	SF36 Pain Score	SF 36 General Health Perception Score
Monthly Kt/v, <2 median (25)	12.5±11.5	58.4±29.9	26±25.4	20±25	62.6±25.7	79.6±14	84±22.6	82.8±23.2	53.7±26.9
Monthly Kt/v, >2 median (25)	15.6±10	45.2±32.5	29.1±25.1	22.9±25.4	43.6±27.2	64.7±27.2	62.5±38.6	65.4±29	36.2±26.8
P	0.307	0.147	0.664	0.688	0.016	0.02	0.021	0.025	0.028
Yearly Kt/v, <2 median (25)	13.3±10.7	54.8±32.2	21.1±25.1	19.2±24.8	56.6±27.2	76.2±17.3	75.4±29.4	75.3±27.8	48.3±30.8
Yearly Kt/v, >2median (25)	14.8±11	48.6±31.3	34.7±23.5	23.9±25.5	49.5±28.7	67.9±27	71.1±37.2	73±27.6	41.5±24.7
P	0.632	0.506	0.057	0.519	0.38	0.201	0.655	0.769	0.404
Yearly URR, <Median (25)	14.1±11.3	55.3±29.9	23±25.4	21.1±25.1	58±26.9	75.6±17.3	77.4±29.3	75.8±28	48.9±30.4
Yearly URR, Median (n:25)	14±10.4	48±33.7	32.6±24.3	21.7±25.3	48±28.5	68.6±27.2	69±36.9	72.5±27.2	40.9±25.1
P	0.951	0.424	0.188	0.936	0.216	0.283	0.381	0.673	0.324
Duration of dialysis, <24 month (n:13)	13±8	60±30.9	25±26.1	20.8±25.7	57.7±26	76.6±20.9	73.9±31.2	71.8±26.9	48±28
Duration of dialysis, 24–60 month (n:13)	16.3±14.9	54.2±36.8	26.9±25.9	26.9±25.9	49.6±31.3	69.3±20.8	61.5±30.8	73.2±30.6	38.4±29.7
Duration of dialysis >60 month (n:24)	13.5±9.7	46.6±29.2	29.1±25.1	18.7±24.7	53.1±27.6	71.8±24.7	79.6±34.5	76±27	47.3±27.7
P	0.696	0.479	0.895	0.644	0.774	0.722	0.285	0.905	0.611

URR: Urea reduction rate

Table 4. Relationship between yearly median albumin, hemoglobin, parathormone, C-reactive protein, ferritin by SF36 and Beck's score

	Beck's Depression Analysis	SF36 Physical functioning score	SF36 Physical role functioning Score	SF36 Emotional role functioning Score	SF36 Energy Vitality Score	SF36 Mental Health Score	SF 36 Social Functioning Score	SF36 Pain Score	SF 36 General Health Perception Score
Albumin, <3.5 g/dL (n:27)	15.5±11.6	47±32.6	25.9±25.4	16.6±24	47.3±27.1	74±19.2	67.5±36.8	76.1±23.9	43.8±30.5
Albumin, >3.5 g/dL (n:23)	12.3±9.7	57.9±29.9	29.5±25.1	27.2±25.4	60.6±27.6	70.3±26.4	80.6±26.6	72±31.6	46.7±25.2
P	0.307	0.234	0.621	0.141	0.096	0.580	0.17	0.611	0.729
Hb <11 g/dL (n:34)	15.3±11.9	49.5±35.4	25.7±25.3	21.2±25	50.3±30.4	72.4±25.1	65.9±34.5	72.1±27.2	42±29.9
Hb, >11 g/dL (n:16)	11.5±7.5	56.8±22	31.2±25	21.8±25.6	59.3±21.4	72.2±16.8	89±23.6	78.7±28.2	51.5±23.2
P	0.248	0.453	0.479	0.932	0.295	0.980	**0.02**	0.434	0.271
PTH<300 pg/mL (n:22)	17.2±12.2	46.5±30.7	25±25.5	13.6±22.7	46.8±29.2	70±20.7	65.3±37.9	66.2±28.1	38.9±27.1
PTH 300–500, pg/mL (n:10)	7.7±3.8	54.5±30.5	35±24.1	30±25.8	58.3±20.1	81.2±17.7	92.5±12	88.7±15.3	50±24.6
PTH >500, pg/mL (n:18)	13.7±10.4	57.3±34.1	26.4±25.7	26.4±25.7	58.8±29.6	70.1±26.9	72.7±31.3	76.1±29.3	50.3±30.9
P	0.064	0.561	0.576	0.135	0.344	0.390	0.096	0.901	0.384
CRP <0.8 mg/dL (n:23)	12.8±8.9	54.1±33.1	28.2±25.3	26±25	60.4±28.4	74.5±20.3	74.4±31.8	75.2±25	49.6±27.9
CRP >0.8 mg/dL (n:27)	15.1±12.2	50±30.8	26.9±25.4	17.3±24.2	47±26.3	70.4±24.5	72.5±34.6	73.4±29.8	41.1±28
P	0.464	0.653	0.855	0.224	0.094	0.527	0.846	0.826	0.292
Ferritin<100 mg/L (n:3)		70±30	16.6±28.8	33.3±28.8	90±13.2	76±6.9	87.5±21.6	93.3±11.5	71.6±32.1
100–800 mg/L (n:22)		54.5±31.8	25±25.5	18.1±24.6	56±25.7	69.2±25.8	69,.3±35.2	72±28.6	50.1±28.4
>800 mg/L (n:25)		47.2±31.8	31.2±24.7	22.9±25.4	46.2±27.7	74.7±20.7	75.5±32.4	73.9±27.5	37.2±25.1
P		0.449	0.529	0.576	0.028*	0.686	0.622	0.46	0.069

* Statistically significant difference was observed between the patients with ferritin<100 and ferritin >800. Hb: Hemoglobin, PTH: parathormone, CRP: C-reactive protein

In the present study, SF–36 scores were detected to be significantly lower than that observed in community SF–36 study in Turkey[9]. Also, the literature reports another study that estimated a decrease in health-related quality of life in a dialysis patient group[17].

The mental health and energy vitality scores were observed to be statistically better in patients with normal BMI as compared to that in patients who were underweight or overweight. The scores of patients aged 18–45 years were statistically significantly better in terms of mental health and energy vitality than those of patients aged over 65 years. SF–36 QoL scores were more favorable in patients with normal BMI and in those below 45 years of age.

In patients with a monthly median Kt/V value of less than 2, scores for energy vitality, mental health, social functioning, pain, and general health perception were statistically significantly better than in those patients with Kt/V above 2. The fact that Kt/V is insufficient in determining the prognosis of patients with malnutrition and low body surface area, may explain this result. This relationship was established with the monthly median Kt/V values and not by the annual median Kt/V and URR values. Therefore, it can be argued that the monthly Kt/V value is more effective in assessing QoL and BDI scores.

It was observed that the patients with mean annual hemoglobin (Hb) above 11 g/dL had statistically better social functioning scores than patients with Hb levels less than 11 g/dL. The patients with a CRP reference value of less than 0.8 mg/dL were found to have better overall health perception scores than patients with a CRP score above 0.8 mg/dL. It is expected that the target level of hemoglobin and CRP would contribute to the wellbeing of the patients.

When the patients were divided into three groups according to the annual mean ferritin values, the energy vitality score of the patients with low ferritin (<100) was observed to be better than those with higher ferritin levels. Annual hemoglobin level was significantly higher in patients with higher energy vitality score and low ferritin levels (11.09 ±1.62) than in those with high ferritin levels (10.25 ±1.05) (p=0.033). Considering that this difference may be manifested by inflammation and dialysis adequacy, the annual mean CRP, albumin, monthly Kt/V, and annual mean Kt/V values of patients with higher ferritin levels were compared and no statistically significant difference was found between them. The reason for obtaining this result may be the fact that the number of patients with low ferritin level was limited to 3 and also the fact that patients with low energy require continuous intravenous iron or erythropoietin.

One of the limitations of the present study was that the diagnosis of depression was made on the basis of the BDI scale and was not based on DSM 4 criteria. Therefore, it is quite possible that the frequency of depression found in this study could be inaccurately high. At the same time, annual laboratory values of the patients were compared using a single questionnaire. The scientific reliability of the data would have been higher, if the study would have been conducted by implementing the questionnaires at 3 or 6 months interval through a year. The limited number of patients, the use of a single hemodialysis center, and not considering seasonal differences at all are other limitations of the study.

Conclusion

This study employed the BDI instrument for detection of depression in hemodialysis patients. Depression was found to be highly prevalent in these patients with a score of 36%. SF–36 scoring evaluation revealed lower QoL in these patients as compared to that in the general population. Interestingly, yearly or monthly mean values of Kt/V and biochemical parameters, except hemoglobin and ferritin values, were not related to BDI scores. Preventing an increase in the ferritin levels, maintenance

of hemoglobin values at target levels, and ensuring ideal body weight may help improve QoL in these patients. In the HD patient group, it is difficult to clarify whether QoL is decreased by depression or depression is caused by decreased QoL. Therefore, the authors advise that hemodialysis patients should also be evaluated for depression and QoL for optimizing clinical outcomes, by the cooperation of nephrologists and psychiatrists.

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, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
The study was approved by the Ethics Committee Çukurova University (2018/76).

References

1. Kimmel PL, Cukor D, Cohen SD, et al. Depression in end-stage renal disease patients: a critical review. Adv Chronic Kidney Dis. 2007;14 (4):328–34.
   doi: 10.1053/j.ackd.2007.07.007
2. King-Wing MT, Kam-Tao LP. Depression in dialysis patients. Nephrology (Carlton). 2016;21 (8):639–46.
   doi: 10.1111/nep.12742
3. Kimmel PL, Patel SS. Quality of life in patients with chronic kidney disease: focus on end-stage renal disease treated with hemodialysis. Semin Nephrol. 2006;26 (1):68–79.
   doi: 10.1016/j.semnephrol.2005.06.015
4. Kimmel PL, Emont SL, Newmann JM, et al. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. Am J Kidney Dis. 2003;42 (4):713–21.
   doi: 10.1016/S0272-6386(03)00907-7
5. Hedayati SS, Yalamanchili V, Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. Kidney Int. 2012;81 (3):247–55.
   doi: 10.1038/ki.2011.358
6. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561–71.
   doi: 10.1001/archpsyc.1961.01710120031004
7. McHorney CA, Ware JE, Jr., Raczek AE. The MOS 36-Item Short-Form Health Survey (SF–36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care. 1993;31 (3):247–63.
8. Kimmel PL, Peterson RA, Weihs KL, et al. Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis outpatients. Kidney Int. 2000;57 (5):2093–8.
   doi: 10.1046/j.1523-1755.2000.00059.x
9. Demiral Y, Ergor G, Unal B, et al. Normative data and discriminative properties of short form 36 (SF–36) in Turkish urban population. BMC Public Health. 2006;6:247.
   doi: 10.1186/1471-2458-6-247
10. Finkelstein FO, Finkelstein SH. Depression in chronic dialysis patients: assessment and treatment. Nephrol Dial Transplant. 2000;15 (12):1911–3.
    doi: 10.1093/ndt/15.12.1911
11. Kimmel PL, Levy BL. Psychology and rehabilitation. In: Daugirdas JT, Blake PG, Todd SI. eds. Handbook of Dialysis. third ed. Baltimore, MD: LippincottWilliams &Wilkins; 2004:413–9.
12. Lopes AA, Bragg J, Young E, et al. Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. Kidney Int. 2002;62 (1):199–207.
    doi: 10.1046/j.1523-1755.2002.00411.x
13. O'Donnell K, Chung JY. The diagnosis of major depression in end-stage renal disease. Psychother Psychosom. 1997;66 (1):38–43.
    doi: 10.1159/000289104
14. Smith MD, Hong BA, Robson AM. Diagnosis of depression in patients with end-stage renal disease. Comparative analysis. Am J Med. 1985;79 (2):160–6.
    doi: 10.1016/0002-9343(85)90004-X
15. Son YJ, Choi KS, Park YR, et al. Depression, symptoms and the quality of life in patients on hemodialysis for end-stage renal disease. Am J Nephrol. 2009;29 (1):36–42.
    doi: 10.1159/000150599
16. Drayer RA, Piraino B, Reynolds CF, et al. Characteristics of depression in hemodialysis patients: symptoms, quality of life and mortality risk. Gen Hosp Psychiatry. 2006;28 (4):306–12.
    doi: 10.1016/j.genhosppsych.2006.03.008

17. Fukuhara S, Lopes AA, Bragg-Gresham JL, et al. Health-related quality of life among dialysis patients on three continents: the Dialysis Outcomes and Practice Patterns Study. Kidney Int. 2003;64 (5):1903–10.
doi: 10.1046/j.1523-1755.2003.00289.x

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EVALUATION OF CERVICAL SPINAL CORD ATROPHY BY MAGNETIC RESONANCE IMAGING IN PATIENTS WITH MULTIPLE SCLEROSIS

MULTİPL SKLEROZLU HASTALARDA SERVİKAL SPİNAL KORD ATROFİSİNİN MANYETİK REZONANS GÖRÜNTÜLEME İLE DEĞERLENDİRİLMESİ

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Abstract

Aim: Multiple sclerosis (MS) is an inflammatory disease of the brain and spinal cord (SC) that leads to demyelination and neurodegeneration. The relationship between cervical cord atrophy and disability in MS patients was demonstrated.

Methods: The examinations were made with MR-Philips Medical System 1.5 tesla device in sagittal and axial planes with T1-WI and T2-WI. Images were evaluated by two experienced radiologists through the hospital image archive system.

Results: In the sagittal plane measurement from the C3 vertebra level, the mean SC measurement of the patients in the MS group was 7.3 ± 0.7 millimeters (mm), while the mean of the control group was 8.3 ± 0.6. In the sagittal plane measurement from the C6 vertebra level, the mean SC measurement of the patients in the MS group was 6.9 ± 0.7 mm, while the mean of the control group was 7.8 ± 0.5. In the measurements made at all levels, SC thicknesses were lower in MS group patients compared to control group patients, and this decrease was statistically significant.

Conclusions: In daily practice, cervical spinal cord measurements in MS patients can be easily and quickly performed with conventional MRI in two dimensions.

Keywords: MRI, Multiple Sclerosis, Cervical Cord, Spinal Cord

Öz

Amaç: Multipl skleroz (MS), beyin ve spinal kord (SK) demiyelinizasyon ve nörodejenerasyona yol açan inflamatuar bir hastalığıdır. MS hastalarında servikal kord atrofisi ile disabilite arasındaki ilişki gösterilmiştir.

Yöntemler: Muayeneler MR-Philips Medical System 1.5 tesla cihazı ile sagital ve aksiyel planda T1-WI ve T2-WI ile yapıldı. Görüntüler deneyimli iki radyolog tarafından hastane görüntü arşiv sistemi aracılığıyla değerlendirildi.

Bulgular: C3 vertebra seviyesinden sagital düzlem ölçümünde MS grubundaki hastaların ortalama SK ölçümü 7,3 ± 0,7 milimetre (mm), kontrol grubunun ortalaması ise 8,3 ± 0,6 idi. C6 vertebra seviyesinden sagital düzlem ölçümünde MS grubundaki hastaların ortalama SK ölçümü 6.9 ± 0.7 mm, kontrol grubunun ortalaması 7.8 ± 0.5 idi. Tüm seviyelerde yapılan ölçümlerde MS grubu hastalarda kontrol grubuna göre SK kalınlıkları daha düşüktü ve bu azalma istatistiksel olarak anlamlıydı.

Sonuç: Günlük pratikte MS hastalarında servikal omurilik ölçümleri iki boyutlu konvansiyonel MRG ile kolay ve hızlı bir şekilde yapılabilmektedir.

Anahtar Kelimeler: Multiple skleroz, MRG, servikal kord

Introduction

Multiple sclerosis (MS) is an inflammatory disease of the brain and spinal cord (SC) that leads to demyelination and neurodegeneration. Atrophy is considered to be the result of neurodegeneration in MS and can be assessed through magnetic resonance imaging (MRI), the most sensitive technique for detecting changes in tissue integrity in the brain and spinal cord[1-4].
SC abnormalities were observed in 83% of patients with MS, 60% of them in the cervical region[5,6]. SC lesions are of prognostic as well as diagnostic importance in MS[7]. The relationship between cervical cord atrophy and disability in MS patients was demonstrated in a study[8]. SC volume (SCV) or cross-sectional area measurements have been shown to be strongly associated with disability in MS[1,6,9] and SCV loss is more common in progressive forms of the disease[10,11].
Despite the prediction revealed by cross-sectional and volumetric SC studies with short-term follow-up, there is a lack of large-scale, long-term studies on SCV loss in MS for economic, temporal, and technical reasons[12,13]. Accordingly, there is a lack of information about the dynamic changes of SC measurements and their relationship to the patient's clinical picture over time.
In this study, we basically investigated the detectability of atrophy by measuring two-dimensional Cervical Spinal Cord (CSC) diameters and spinal canal diameters. Thus, we aimed to draw attention to the fact that these two-dimensional measurements can be made easily and quickly in routine practice, and that they can be used in the follow-up of MS patients.

Materials and Methods

Our study is retrospective and MS patients who underwent cervical MRI in Malatya Training and Research Hospital between 01.01.2015-30.10.2021 were included in the study. Patients with image artifacts and patients with demyelinating lesions at measurement levels were excluded from the study. MRI sections of 17 MS patients who met the criteria were evaluated. For comparison purposes, a control group consisting of 34 patients who were randomly selected between 01.06.2021 and 30.09.2021, who did not have MS, who were matched with MS patients in terms of age and gender, was formed.
The examinations were made with MR-Philips Medical System 1.5 tesla device in sagittal and axial planes with T1-WI and T2-WI. Images were evaluated by two experienced radiologists through the hospital image archive system.
SC diameters from sagittal to C3 and C6 vertebral levels were measured from the midpoint between the upper and lower end plateaus of the vertebral body and on a line drawn perpendicular to the anterior surface of the SC[14].
SC diameters at the axially C3 and C6 vertebral levels were measured on a line drawn from the midpoint of the vertebral body to the midpoint of the corresponding posterior elements. In addition, axial and sagittal spinal cord diameter measurements were made on the lines defined from these levels (Figures 1 and 2).

- *Statistical Analysis*

SPSS 22 version was used for statistical analysis. Mann-Whitney U test was performed to compare the spinal canal and spinal cord sizes of MS and control group patients. Statistical significance level was taken as $p<0.05$.

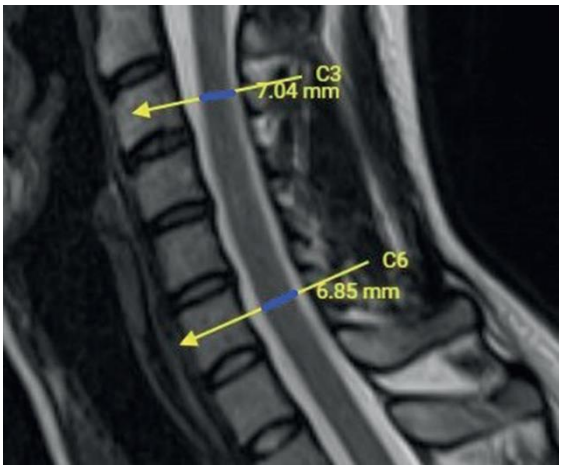

Figure 1. Sagittal diameter measurement of cervical spinal cord from C3 and C6 vertebra levels

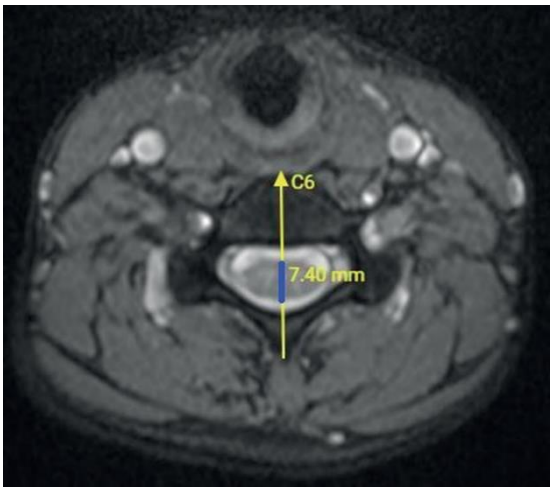

Figure 2. Axial diameter measurement of the cervical spinal cord at the level of the C6 vertebra

Results

27(52.9%) of the patients included in the study were women. The patients were between the ages of 19-62 and the mean age was 39.4 ± 9.9 years.

In the sagittal plane measurement from the C3 vertebra level, the median SC measurement of the patients in the MS group was 7.6 (5.7 - 8.2) millimeters (mm), while the median of the control group was 8.2 (6.8 - 9.1). In the sagittal plane measurement from the C6 vertebra level, the median SC measurement of the patients in the MS group was 7.1 (5.2 - 8.0) mm, while the median of the control group was 7.9 (6.7 – 8.9). In the measurements made at all levels, SC thicknesses were lower in MS group patients compared to control group patients, and this decrease was statistically significant.

There was no significant difference between the control group and MS patients in terms of spinal canal measurements.

The median values of the SC and spinal canal measurements made in the sagittal and axial planes from the C3 and C6 vertebra level and the p values obtained by the Mann-Whitney U test are presented in Table 1.

Table 1. Median (min-max) cord and canal diameters in sagittal and axial planes at C3 and C6 vertebral level

Measurement Location	MS group (n=17)	Control group (n=34)	P
	Median (min-max)		
C3 sagittal cord	7.6 (5.7-8.2)	8.2 (6.8-9.1)	<0.001
C3 axial cord	7.6 (5.4-8.3)	8.2 (7.0-9.4)	0.003
C6 sagittal cord	7.1 (5.2-8.0)	7.9 (6.7-8.9)	<0.001
C6 axial cord	7.3 (5.5-8.0)	7.7 (6.5-8.9)	0.011
C3 sagittal canal	12.7 (10.8-15.9)	13.2 (11.2-14.9)	0.575
C3 axial canal	12.9 (11.2-15.8)	12.9 (11.1-14.2)	0.704
C6 sagittal canal	13.3 (11.1-16.2)	13.5 (11.2-15.0)	0.719
C6 axial canal	13.4 (11.1-16.5)	12.9 (11.0-14.6)	0.826

Discussion

Since most centers do not have workstations or software to perform volumetric analysis in routine practice, most centers do not make any assessment of SC dimensions in the reporting of MS patients. This study is showed that, we can basically assess atrophy by measuring two-dimensional CSC diameters.

The SC is a clinically important region that is affected by pathological changes in most MS patients[13]. Focal spinal cord lesions are commonly seen in patients with MS and are reported in 80-90% of patients on conventional MRI[5,15].

Spinal cord atrophy (SCA) may be due to focal tissue destruction in lesions or pathological changes that damage axons[13]. SCA can be used to determine axon loss, which may be common in patients with MS, and is especially important in the progressive stages of the disease[16,17]. In addition, SCA is a measure that can be used to evaluate the effects of neuroprotective treatments in the management of MS[18]. Recent studies in MS patients with long-term follow-up have shown that SCA measured on MRI is associated with disability independent of brain volume or lesion load[19,20].

Atrophy assessments through qualitative visual assessment are less accurate, resulting in subjective bias. However, it is easy to identify when there is focal atrophy reflecting focal tissue loss in short segments of the SC[5]. Due to the difficulties in the technical detection of gray matter atrophy, which may be clinically significant, current research has aimed to improve the SCA measurement by measuring the spinal cord area[21,22].

Measurement of SC area at the high cervical level has been the most reported MRI measurement of SCA[23]. However, it should not be forgotten that sagittal MRI has a great advantage as it is faster and covers a large SC area[5]. In a recent study, measurement of SCV loss was shown to be a reliable imaging marker for monitoring disease activity and progression in MS[24].

In our current study, we evaluated the diameters of the CSC in the axial and sagittal planes. In our study, as in previous studies, CSC measurements were found to be lower in MS patients. We also examined the axial and sagittal plane measurements of the spinal canal in the MRIs of these patients. Since there was no difference between MS patients and control group patients in terms of cervical spinal canal measurements, it is not meaningful to use it for follow-up in routine practice. We think that it will be sufficient to measure the CSC in the axial and sagittal plane when evaluating cord atrophy in MRI in patients with MS.

The small number of patients can be shown as a limitation of our study, since most of the MS patients are not followed up in public hospitals. However, this study supports that neurology and radiology physicians working under current conditions can take responsibility and follow up patients with the resources available.

Conclusion

In daily practice, cervical spinal cord measurements in MS patients can be easily and quickly performed with conventional MRI in two dimensions. Including these measurements in the reporting will be useful in the follow-up of cord atrophy in MS patients.

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, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
Approval numbered 2021/10 was obtained from Malatya Turgut Özal University Non-Interventional Clinical Research Ethics Committee.

References

1. Rocca MA, Horsfield MA, Sala S, et al. A multicenter assessment of cervical cord atrophy among MS clinical phenotypes. Neurology. 2011;76(24):2096-102. doi:10.1212/WNL.0b013e31821f46b8
2. De Stefano N, Giorgio A, Battaglini M, et al. Assessing brain atrophy rates in a large population of untreated multiple sclerosis subtypes. Neurology. 2010;74(23):1868-76. doi:10.1212/WNL.0b013e3181e24136
3. Abdel-Aziz K, Schneider T, Solanky BS, et al. Evidence for early neurodegeneration in the cervical cord of patients with primary progressive multiple sclerosis. Brain. 2015;138(6):1568-82. doi:10.1093/brain/awv086
4. Bakshi R, Thompson AJ, Rocca MA, et al. MRI in multiple sclerosis: current status and future prospects. The Lancet Neurology. 2008;7(7):615-25. doi:10.1016/S1474-4422(08)70137-6
5. Weier K, Mazraeh J, Naegelin Y, et al. Biplanar MRI for the assessment of the spinal cord in multiple sclerosis. Mult Scler. 2012;18(11):1560-1569. doi:10.1177/1352458512442754
6. Kearney H, Miller DH, Ciccarelli O. Spinal cord MRI in multiple sclerosis—diagnostic, prognostic and clinical value. Nat Rev Neurol. 2015;11(6):327-38. doi:10.1038/nrneurol.2015.80
7. Sombekke MH, Wattjes MP, Balk LJ, et al. Spinal cord lesions in patients with clinically isolated syndrome: A powerful tool in diagnosis and prognosis. Neurology. 2013;80(1):69-75. doi:10.1212/WNL.0b013e31827b1a67
8. Lin X, Tench CR, Evangelou N, Jaspan T, Constantinescu CS. Measurement of Spinal Cord Atrophy in Multiple Sclerosis. Journal of Neuroimaging. 2004; 14:20S-26S. doi:10.1111/j.1552-6569.2004.tb00275.x
9. Lukas C, Sombekke MH, Bellenberg B, et al. Relevance of Spinal Cord Abnormalities to Clinical Disability in Multiple Sclerosis: MR Imaging Findings in a Large Cohort of Patients. Radiology. 2013;269(2):542-52. doi:10.1148/radiol.13122566
10. Lukas C, Knol DL, Sombekke MH, et al. Cervical spinal cord volume loss is related to clinical disability progression in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2015;86(4):410-418. doi:10.1136/jnnp-2014-308021
11. Schlaeger R, Papinutto N, Zhu AH, et al. Association Between Thoracic Spinal Cord Gray Matter Atrophy and Disability in Multiple Sclerosis. JAMA Neurol. 2015;72(8):897. doi:10.1001/jamaneurol.2015.0993
12. Stroman PW, Wheeler-Kingshott C, Bacon M, et al. The current state-of-the-art of spinal cord imaging: Methods. NeuroImage. 2014; 84:1070-1081. doi: 10.1016/j.neuroimage.2013.04.124
13. Gass A, Rocca MA, Agosta F, et al. MRI monitoring of pathological changes in the spinal cord in patients with multiple sclerosis. The Lancet Neurology. 2015;14(4):443-454. doi:10.1016/S1474-4422(14)70294-7
14. Ulbrich EJ, Schraner C, Boesch C, et al. Normative MR Cervical Spinal Canal Dimensions. Radiology. 2014;271(1):172-182. doi:10.1148/radiol.13120370
15. Bot JCJ, Barkhof F, à Nijeholt GL, et al. Differentiation of Multiple Sclerosis from Other Inflammatory Disorders and Cerebrovascular Disease: Value of Spinal MR Imaging. Radiology. 2002;223(1):46-56. doi:10.1148/radiol.2231010707
16. Evangelou N. Pathological study of spinal cord atrophy in multiple sclerosis suggests limited role of local lesions. Brain. 2004;128(1):29-34. doi:10.1093/brain/awh323
17. Bot JCJ, Blezer ELA, Kamphorst W, et al. The Spinal Cord in Multiple Sclerosis: Relationship of High-Spatial-Resolution Quantitative MR Imaging Findings to Histopathologic Results. Radiology. 2004;233(2):531-540. doi:10.1148/radiol.2332031572
18. Kalkers NF, Barkhof F, Bergers E, van Schijndel R, Polman CH. The effect of the neuroprotective agent riluzole on MRI parameters in primary progressive multiple sclerosis: a pilot study. Mult Scler. 2002;8(6):532-3. doi:10.1191/1352458502ms849xx
19. Daams M, Weiler F, Steenwijk MD, et al. Mean upper cervical cord area (MUCCA) measurement in long-standing multiple sclerosis: Relation to brain findings and clinical disability. Mult Scler. 2014;20(14):1860-5. doi:10.1177/1352458514533399
20. Kearney H, Rocca M, Valsasina P, et al. Magnetic resonance imaging correlates of physical disability in relapse onset multiple sclerosis of long disease duration. Mult Scler. 2014;20(1):72-80. doi:10.1177/1352458513492245
21. Kearney H, Yiannakas MC, Abdel-Aziz K, et al. Improved MRI quantification of spinal cord atrophy in multiple sclerosis: Cord Atrophy in MS. J Magn Reson Imaging. 2014;39(3):617-23. doi:10.1002/jmri.24194
22. Horsfield MA, Sala S, Neema M, et al. Rapid semi-automatic segmentation of the spinal cord from magnetic resonance images: Application in multiple sclerosis. NeuroImage. 2010;50(2):446-55. doi: 10.1016/j.neuroimage.2009.12.121
23. Losseff NA, Webb SL, O'Riordan JI, et al. Spinal cord atrophy and disability in multiple

sclerosis: A new reproducible and sensitive MRI method with potential to monitor disease progression. Brain. 1996;119(3):701-708. doi:10.1093/brain/119.3.701
24. Tsagkas C, Magon S, Gaetano L, et al. Spinal cord volume loss: A marker of disease progression in multiple sclerosis. Neurology. 2018;91(4):e349-e358. doi:10.1212/WNL.0000000000005853

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DEMANS HASTALARINDA ÜRİNER İNKONTİNANS VE SARKOPENİ İLİŞKİSİ

THE RELATIONSHIP BETWEEN URINARY INCONTINENCE AND SARCOPENIA IN PATIENTS WITH DEMENTIA

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Abstract

Aim: Dementia, sarcopenia, and urinary incontinence (UI) are common geriatric syndromes. UI is a condition that affects the quality of life, results in social isolation, causes falls and, causes morbidity and mortality due to falls. UI also increases caregiver burnout and the burden of care in dementia patients. Continence requires an intact genito-urinary system, peripheral and central nervous system, and cognitive health. In addition, the importance of the pelvic floor muscles from the striated muscle group and the skeletal system in continence cannot be ignored. In the light of these facts, we aimed to evaluate the relationship between UI and sarcopenia in patients with dementia.

Methods: Dementia patients with sarcopenia who applied to the DEU Geriatrics unit between January 2015 and December 2021 were included. Patients with CDR 3 dementia and those with acute problems were excluded. Patients were grouped according to their UI status and evaluated for sarcopenia using the EWGSOP-2 criteria.

Results: According to the presence of UI, no significant difference was found in demographic and laboratory findings between groups. The frequency of anti-parkinsonian drug usage and depression was more common in the UI group. While, the frequency of probable sarcopenia, severe sarcopenia, slow gait speed, and frailty was higher in the UI group; Barthel's score was lower (p <0.050, for each). After regresion analysis, UI was associated with probable sarcopenia, severe sarcopenia, and slow gait speed (OR: 1.854, 95% CI 1.107-3.106; OR: 2.152, 95% CI 1.193-7.360; OR: 3.065, 95% CI 1.726 –5.443, respectively).

Conclusions: Due to the lack of proven treatment for dementia itself, the treatment and prevention of comorbidities have great importance. Treatment of UI is important in increasing the quality of life and reducing the burden of care. The relationship between sarcopenia and UI should be kept in mind. Moreover, interventions for sarcopenia may be beneficial for UI.

Keywords: Dementia, sarcopenia, urinary incontinence

Öz

Amaç: Demans, sarkopeni ve üriner inkontinans (Üİ) sık görülen geriatrik sendromlardır. Üİ, yaşam kalitesini etkileyen, sosyal izolasyon ile sonuçlanan, düşmeye ve düşmeye bağlı morbidite ve mortaliteye de sebep olan bir durumdur. Ayrıca demans hastalarında bakım yükünü ve bakım veren tükenmişliğini artırır. Kontinans için sağlam bir genito-üriner sistem, periferik ve santral sinir sistemi ve de biliş gerekmektedir. Bunun yanında çizgili kas grubundan pelvik taban kaslarının ve iskelet sisteminin de kontinanstaki önemi göz ardı edilemez. Çalışmamızda demans hastalarında Üİ ile sarkopeni arasındaki ilişkiyi değerlendirmeyi planladık.

Yöntemler: Ocak 2015 ve Aralık 2021 tarihleri arasında Dokuz Eylül Üniversitesi Geriatri birimine başvuran sarkopeni değerlendirmesi olan demans hastaları çalışmaya dahil edilmiştir. Hastalar Üİ durumlarına göre iki gruba ayrılmıştır. Sarkopeni tanısı EWGSOP-2 kriterleri kullanılarak konulmuştur.

Bulgular: Gruplar arasında demografik veriler ve laboratuvar bulgularında anlamlı farklılık saptanmadı. Depresyon ve anti-parkinson ilaç kullanımı Üİ grubunda daha sıktı. Üİ grubunda muhtemel sarkopeni, ciddi sarkopeni, düşük yürüme hızı ve kırılganlık sıklığı daha yüksek; temel günlük yaşam aktivite skoru daha düşük bulundu (p <0,050). Regresyon analizi yapıldığında Üİ; muhtemel sarkopeni, ciddi sarkopeni ve düşük yürüme hızı ile ilişkili bulundu (OR:1,854, %95 CI 1,107-3,106; OR:2,152, %95 CI 1,193-7,360; Or:3,065, %95 CI 1,726 –5,443).

Sonuç: Demansın küratif tedavisinin olmaması nedeniyle eşlik eden komorbid durumların tedavisi ve önlenmesi büyük önem kazanmaktadır. Yaşam kalitesinin artması ve bakım yükünün azaltılmasında Üİ ile mücadele önemlidir. Sarkopeni ve Üİ ilişkisinin akılda tutulması ve buna yönelik girişimler faydalı olabilir.

Anahtar Kelimeler: Demans, sarkopeni, üriner inkontinans

Giriş

Üriner İnkontinans (Üİ) yaşlılarda sık görülmesi ve sonuçları nedeniyle önemli bir geriatrik sendromdur. Bireyde üriner kontinansın sağlanabilmesi için genito-üriner sistemin, nörolojik sistemin ve pelvik anatominin sağlam olması gerekmektedir. Bunlara ek olarak sağlam bir kognisyon ve kas iskelet sistemi kontinansın devamında önemlidir. Yaş ile birlikte genito-üriner sistem değişiklikleri, artan nörolojik hastalık sıklığı, kas iskelet problemleri göz önünde bulundurulduğunda Üİ sıklığındaki artış kaçınılmazdır. Üİ, azalmış yaşam kalitesi, depresyon, sosyal izolasyon, dermatit, tekrarlayan idrar yolu enfeksiyonu gibi olumsuz sonuçlarının yanında bakıcı yükünde artış, bakım evine yerleştirilmede artış, hastaneye yatırılma ve yatış süresinin uzamasına yol açar[1].

Yaşlı erişkinlerde düşük kas gücü ve iskelet kası kütlesinde yaşa bağlı azalma ile karakterize diğer sık görülen geriatrik sendrom ise sarkopenidir[2]. Sarkopeni düşme, kırıklar, günlük yaşam aktivitelerinde kısıtlılık, hastane yatışında artış ve mortalite gibi birçok olumsuz sonuca yol açabilmekte ve yaşlı erişkinlerde sıklığı %9,9 ile %40,4 arasında değişebilmektedir[2,3]. Pelvik tabanı bir grup çizgili kas oluşturur ve somatik sinir sistemi tarafından istemli olarak kontrol edilir. Ayrıca zamanında miksiyon gerçekleştirebilmek için kas iskelet sistemi ve yürüme hızı önemlidir. Bu bilgiler ışığında sarkopeni ve Üİ ilişkisini inceleyen çalışmalar artış göstermektedir[4].

Yaşla birlikte prevalansı artan diğer bir geriatrik sendrom ise demanstır[5]. Kontinansın sağlanmasında bilişsel fonksiyonların da etkili olduğu bilinmektedir. Özellikle frontal loplar olmak üzere bazal ganglionlar, hipotalamus ve limbik bölgenin de dahil olduğu birçok alan miksiyonun uygun zamana kadar ertelenebilmesinde önemli rol oynar[6]. Demans tanılı yaşlı bireylerde ise aşırı aktif mesane gelişimi, ilaç yan etkisi, öz bakım yetersizliği nedeniyle artan idrar yolu enfeksiyonu sıklığı, yaşa bağlı olarak pelvik kas zayıflığı gibi durumlar ve kontinans için gereken koordinasyonun sağlanamaması Üİ gelişimi ile ilişkilidir[7]. Bu bireylerde en sık inkontinans tipi urge inkontinans iken, bunu mikst ve stres tip inkontinans takip etmektedir[8]. Bu bilgilere ek olarak literatürde demans ve sarkopeni ilişkisinin gösterildiği çalışmalar vardır[9,10].

Çağımızın korkulu rüyası olan demansın henüz kesin bir tedavisi yoktur ve semptomatik yaklaşımlar ön plandadır. Bu nedenle demans hastalarında komorbid yönetimi daha da önem kazanmaktadır. Sarkopeni ve Üİ'nin demans hastalarındaki sıklığı ve oluşturdukları morbidite ve artmış bakım yükünden yola çıkarak biz de çalışmamızda demans hastalarındaki sarkopeni ve Üİ ilişkisini değerlendirmeyi amaçladık.

Materyal ve Metot

- *Hasta Seçimi*

Bu çalışmaya Ocak 2015 ve Aralık 2021 tarihleri arasında Dokuz Eylül Üniversitesi Tıp Fakültesi Hastanesi Geriatri Kliniğine başvuran, ayrıntılı geriatrik değerlendirme (AGD), sarkopeni değerlendirmesi, üriner inkontinans sorgusu ve dosyasındaki verileri tam olan 254 demans tanılı hasta dahil edildi.

- *Dışlama kriterleri*

Yürümeye engel olabilecek ciddi osteoartrit veya nöromüsküler hastalığı olanlar, immobil hastalar, akut serebrovasküler olay, gastrointestinal kanama, sepsis, akut böbrek yetersizliği, akut koroner sendrom, akut karaciğer yetersizliği, akut solunum yetmezliği, alkol ve madde kötüye kullanımı olan hastalar, 60 yaşın altındaki hastalar, dosyasında eksik verileri olan hastalar ve CDR evre 3 olan hastalar çalışmadan dışlanmıştır.

- *Ayrıntılı Geriatrik Değerlendirme (AGD) ve Laboratuvar Bulguları*

Hastaların yaş, cinsiyet, eğitim seviyesi, medeni durumu, eşlik eden komorbid durumlar, kullandığı ilaç sayısı kaydedildi. Hastalara AGD amacıyla, nörokognitif değerlendirme için; Mini Mental Durum Muayenesi (MMSE), Montreal Kognitif Değerlendirme (MOCA), günlük yaşam aktiviteleri değerlendirmesi için; Lawton-Brody Enstrümantal Günlük Yaşam Aktivite (EGYA) Skalası, nutrisyonel değerlendirme için; Mini Nütrisyonel Değerlendirme-kısa form (MNA-kf) ölçekleri tarandı[11]. MNA-kf skoru 11 ve altında olanlar malnütrisyon riski ve malnutrisyon var olarak, FRIED ölçeğinden 3 ve üzeri puan alan hastalar ise kırılgan olarak kabul edilmiştir[12].
Hastaların biyokimyasal, metabolik durumlarını değerlendirmek amacıyla hastalara böbrek fonksiyonları, HbA1c, D vitamini, B12 vitamini laboratuvar testleri yapıldı. Bütün bu testler otoanalizer tanısal modüler sistem (Roche E170 and P-800) ile elde edildi. Serum 25-Hidroksi D vitamini [25(OH)D] radioimmünoassay ile ölçüldü.

- *Demans ve Depresyon Değerlendirmesi*

Hastalara demans ve depresyon tanısı; nörokognitif testler, beyin görüntülemesi ile birlikte DSM-V tanı kriterleri ile konuldu[13].

- *Sarkopeni Değerlendirmesi*

Hastaların sarkopeni tanısı European Working Group on Sarcopenia in Older People (EWGSOP-2) kriterleri kullanılarak tanımlandı[2]. Kas gücü değerlendirilmesi için Jamar el dinanometresi kullanılmıştır. Test yapılması sırasında hasta dirseğinin 90 derece fleksiyonda, ön kolu nötral pozisyonda, el bileğinin ise 0 ile 30 derece dorsifleksiyonda olması önerilir. Hasta eli bu pozisyonda iken 5 saniye süre sıkması ve 3 defa tekrarlanması istenir. Tetkik sonuçlarının ortalaması hesaplanır[14]. Dinamometre ölçümlerinde kadınlarda ≤14 kg, erkeklerde ≤28 kg olması düşük el kuvveti, yürüme hızı <0,8 m/sn olması ise düşük yürüme hızı kabul edildi.[15]. Bioimpedans analizi (BİA), belirli bir popülasyonda çift enerjili X-ışını absorpsiyometrisi (DXA) ile ölçülen yağsız kütle referansı ile kalibre edilen bir dönüşüm denklemini ((kg) = (boy(cm)2 / R × 0,401) + (cinsiyet × 3,825) + (yaş ×-0,071) + 5,102) kullanır. İskeletsel kas indeksi (Skeletal muscle mass index (SMI)) ise elde edilen sonucun boyun metre cinsinden karesine bölünmesi ile elde edilir. SMI için eşik değer erkek için 7kg/m2, kadın için 5,5 kg/m2 olarak tanımlandı[15].
Hastalar kas gücünde azalma var ise muhtemel sarkopeni, kas gücünde azalmaya kas kitlesinde azalma eşlik ediyorsa kesin sarkopeni, bu 2 kritere fiziksel performans düşüklüğü de eklenmişse ciddi sarkopeni olarak değerlendirildi[2].

- *Üriner İnkontinans*

Hasta dosyasında herhangi bir sayı, sıklık ve miktarda istemsiz idrar kaçırması ve altta yatan akut-geri dönüştürülebilir bir sebep olmaması durumu Üİ olarak tanımlandı. [16]

- *İstatistiksel analiz*

Verilerin istatistiksel analizinde SPSS 22.0 (SPSS Inc.) paket programı kullanıldı.
Kategorik değişkenler yüzde (%) kullanılarak belirtilirken, sürekli değişkenler ortalama±standart sapma olarak verildi. Öncelikle değişkenler normal dağılım uygunluğu için Kolmogorov-Smirnov testi ile değerlendirildi. Normal dağılan verilerin ortalama değerleri Student's t testi, normal dağılmayan veriler ise Mann Whitney U testi ile karşılaştırılırken, kategorik değişkenlerin yorumu için Ki-kare ve Fischer's Exact testleri kullanıldı. P <0,05 olması anlamlı olarak kabul edildi.
Hastalar Üİ durumlarına göre 2 gruba ayrıldı. Gruplar demografik veriler, komorbid durumlar, ilaç kullanımları,

laboratuvar değerleri, AGD parametreleri, sarkopeni tanısı ve sarkopeni ile ilişkili parametreler açısından kıyaslandı. Üİ ile sarkopeni ilişkisini değerlendirmek için, depresyon ve anti-parkinson ilaç kullanımına göre Binary multivarite lojistik regresyon analizi yapıldı.

- *Örnek Büyüklüğü*

Çalışmamız için Ateş Bulut ve arkadaşlarının yaptığı geriatrik yaş grubundaki komorbid sıklıklarının araştırıldığı çalışmadaki demans sıklığı temel alınmış ve örneklem büyüklüğü hesaplanmıştır[5]. Bu çalışmada yaşlı kişilerde demans sıklığı %21,6 saptanmış olup, %95 güven aralığında minimum örneklem büyüklüğü 214 olarak belirlenmiştir.

- *Etik Kurul Onayı*

Çalışmamız, Dokuz Eylül Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'nun 29.01.2020 tarihli 5227 GOA protokol numaralı kararı (EK - 1) ile uygun bulunmuştur.

Bulgular

Her iki grubun yaş, cinsiyet, eğitim durumu gibi demografik verilerinde ve laboratuvar sonuçlarında anlamlı bir farklılık görülmedi (p>0,05). Eşlik eden komorbid durumlardan sadece depresyonun Üİ olan grupta daha sık olduğu saptandı (p=0,025). Bununla birlikte Üİ olan grupta anti-parkinson ilaç kullanımının daha yaygın olduğu bulundu (p=0,05). Gruplar arasında AGD ölçekleri karşılaştırıldığında Üİ olan grubun kırılganlık sıklığı daha yüksek, TGYA skoru daha düşük idi (<0,001, her biri için).
Sarkopeni ile ilişkili parametrelerde Üİ grubunda muhtemel sarkopeni ve ciddi sarkopeni prevalansı istatistiksel olarak anlamlı yüksekti (p<0,003 ve p<0,005; sırasıyla). Bununla birlikte her iki grubun düşük kas kitlesi sıklığı benzerdi (p>0,05) ve Üİ grubu daha düşük yürüme hızına sahipti (p<0,001). Hastaların özellikleri Tablo-1'de özetlenmiştir.
Depresyon ve anti-parkinson ilaç kullanımına göre regresyon analizi yapıldığında muhtemel sarkopeni, ciddi sarkopeni ve düşük yürüme hızının Üİ ile anlamlı olarak ilişkili olduğu görüldü (OR:1,854, %95 CI 1,107-3,106; OR:2,152, %95 CI 1,193-7,360; OR:3,065, %95 CI 1,726 –5,443; sırasıyla) (Tablo 2).

Tartışma

Demans tanılı yaşlı hastalarda Üİ ile sarkopeni ilişkisini incelediğimiz retrospektif ve kesitsel çalışmamızda Üİ ile muhtemel sarkopeni, ciddi sarkopeni ve yürüme hızını ilişkili bulduk.
Yaşla birlikte sıklığı artan, küratif bir tedavisi henüz bulunmayan demansın yönetimi; hasta, bakım verenler ve klinisyenler için oldukça zordur. Bu sebeple demansa eşlik eden diğer sorunların önlenmesi veya tedavi edilmesi büyük önem taşır.
Üİ demans hastalarında sıkça görülen bir sorundur ve bası yarası, düşme, fraktür, üriner sistem enfeksiyonları, erken dönemde bakım evine yerleştirilme sıklığı, sosyal izolasyon ve depresyon sıklığında artışa neden olmaktadır[7]. Kontinansın sürdürülmesi için hareketlilik, el becerisi, zihinsel kapasite ve motivasyon gereklidir. Demansı olan bireylerde kontinansın sürdürebilmesi, mobilizasyon, el becerisi, kuru kalmaya yönelik motivasyon gibi gerekliliklerde problemler görülür. Demansın, miksiyon refleksi üzerindeki inhibitör etkinin kaybolmasına yol açarak, istemsiz mesane kasılması ve detrusor hiperaktivitesine yol açabileceği bilinmektedir[17]. Demans ve inkontinansı olan hastalarda alt üriner sistem fonksiyonunu inceleyen çalışmalarda, Castleden *ve ark.*, orta-şiddetli bilişsel bozukluğu olan Üİ hastalarının %71'inde detrüsör hiperaktivitesi olduğunu saptamışlardır[18].

Tablo 1. Hastaların karakteristik özellikleri

	Üriner İnkontinans (-) n:127	Üriner İnkontinans (+) n:127	p
Demografik Özellikler (*,%)			
Yaş	75,62±7,43	77,25±7,15	0,076
Cinsiyet (Kadın)	58,30	55,90	0,704
CKİ	5,09±1,76	5,27±1,69	0,404
Eğitim (yıl)	7,45±4,48	6,67±4,63	0,183
Komorbid Durumlar (%)			
HT	51,20	63,00	0,057
SVH	7,10	7,20	0,811
DM	25,20	30,70	0,328
KKY	7,10	3,90	0,271
Depresyon	31,50	45,20	**0,025**
İlaçlar			
Anti-psikotik	17,60	22,00	0,376
Anti-parkinson	7,20	15,00	**0,050**
Diüretik ilaçlar	22,20	33,10	0,055
Laboratuvar (*,%)			
GFH*	73,43±17	72,21±18,08	0,591
Hba1c (%)	6,52±0,98	7,06±1,75	0,704
Vitamin B12*	430,97±353,25	387,89±272,81	0,904
D vitamini*	22,71±16,76	21,71±10,79	0,577
Ayrıntılı Geriatrik Değerlendirme (*,%)			
Kırılganlık (%)	37,40	58,50	**<0,001**
Malnütrisyon ve malnütrisyon riski (%)	32,50	33,60	0,855
MMSE*	17,01±5,38	16,70±5,93	0,685
MOCA*	17,00±4,89	16,03±5,93	0,498
CDR (%) 0 ve 0,5	20,80	12,60	0,081
CDR (%) 1ve üstü	79,20	87,40	
EGYA*	12,79±5,73	11,58±5,75	0,099
TGYA*	92,88±10,75	82,75±14,87	**<0,001**
Sarkopeni ve sarkopeni ilişkili parametreler (%)			
Muhtemel Sarkopeni	41,70	60,60	**0,003**
Kesin Sarkopeni	15,70	12,60	0,472
Ciddi Sarkopeni	21,30	29,10	**0,005**
Düşük kas kitlesi	37,80	41,70	0,522
Düşük Yürüme hızı	20,50	43,30	**<0,001**

CKI: Charlson Komorbidite İndeksi; CDR: Klinik Demans Skalası; DM: Diyabetes Mellitus; EGYA: Enstrümental Günlük Yaşam Aktiviteleri; GFH: Glomerüler Filtrasyon Hızı; HT: hipertansiyon; KKY: Konjestif Kalp Yetmezliği; MMSE: Mental Durum Muayenesi; MoCA: Montreal Kognitif Değerlendirme; SVH: Serebrovasküler Hastalık; TGYA: Temel Günlük Yaşam Aktiviteleri, * ortalama±standart sapma

Tablo 2. Üriner inkontinans ile sarkopeni ilişkisi

Üriner İnkontinans	OR	%95 CI	p
Model 1			
Muhtemel Sarkopeni	**2,033**	1,225-3,375	**0,06**
Ciddi Sarkopeni	**3,312**	1,269-7,730	**0,013**
Düşük Yürüme Hızı	**2,815**	1,605-4,935	**<0,001**
Model 2			
Muhtemel Sarkopeni	**1,854**	1,107-3,106	**0,019**
Ciddi Sarkopeni	**2,152**	1,193-7,360	**0,019**
Düşük Yürüme Hızı	**3,065**	1,726-5,443	**<0.001**

OR: Odds Ratio; CI: Confidence Interval.
Model 1: Depresyon durumuna göre regresyon analizi yapıldı.
Model 2: Depresyon ve anti-parkinson ilaç kullanımına göre regresyon analizi yapıldı.

Bununla birlikte Yu *ve ark.*, 133 inkontinanslı huzurevi sakini arasında, demanslı gruptaki ürodinamik çalışmaların %38'inde detrüsör hiperaktivitesi, %41'inde normal mesane fonksiyonu, %16'sında stres inkontinansı ve %5'inde taşma inkontinansı olduğunu bildirmiştir[19]. Bu grup hastaların çoğunda inkontinansın alt üriner sistem patolojisinden değil, başka nedenlerden kaynaklandığı görülmektedir. Örneğin; Jirovec ve ark. huzurevinde yaşayan demansı olan hastalarda hareketliliğin idrar kontrolünün en iyi göstergesi olduğunu ve bunu kognitif bozukluğun takip ettiğini gösterdiler[20]. Daha önce yapılan birçok çalışma, azalmış mobilite ve günlük yaşam aktivitelerin demanslı bireylerde üriner inkontinansla güçlü ilişkisini tespit etmiştir[21–24].

Sarkopeni demans hastalarında mobilitenin azalmasının sebeplerinden biridir. Yayımlanan bir meta-analizde hastalarda kas kitlesini ve kalitesini değerlendiren çalışma sayısı oldukça azdır[25]. Ancak son zamanlarda bu konuya ilgi artmaktadır. Örneğin bir çalışmada demansı olan kadın ve erkeklerde kalk ve yürü testinin demansı olmayanlara göre daha uzun olduğu ve ortalama el kavrama gücü ölçümlerinin EWGSOP-2'ye göre sarkopenik aralıkta olduğu dikkat çekmiştir[2]. Literatürde azalmış kas gücünün, bilişsel gerileme ve Alzheimer hastalığı (AH) ve Lewy cisimcikli demans ile negatif ilişkisini gösteren çalışmalar bildirilmiştir[9,26,27]. Chong ve ark. yaptıkları çalışmada hafif kognitif bozukluğa kıyasla hafif ve orta evre AH'de daha düşük kas gücü ölçümleri saptamışlardır[28]. Bununla birlikte kas gücünün hipokampal volüm oranlarıyla ilişkili olduğunu ve yağ dışı vücut kitlesinin kaybının AH ilişkili serebral atrofi ile ilişkisini gösteren kanıtlar da mevcuttur.[26,27] Sarkopeninin mobilitenin azalmasına olan katkısı yanında serebral atrofiyle ilişkisinin gösterilmesi demans hastalarındaki Üİ etiyolojisine bakış açısını genişletmiştir. Demanslı bireylerin kontinansın sağlamak

için gerekli bilişsel işlevlerin yetersizliği ile birlikte sarkopeniye bağlı mobilitenin azalması ve tuvalete ulaşımdaki zorluklar düşünüldüğünde bu hasta grubunda üriner inkontinansın kaçınılmaz bir son olduğu görülmektedir. Buna ek olarak kontinansın devamı için olmazsa olmaz olan pelvik tabanın disfonksiyonu sarkopenik hastalarda yüksek prevalansa sahip olup sarkopeni şiddetiyle pozitif ilişkilidir[29]. Bizim çalışmamızda saptadığımız demanslı hastalarda sarkopeni ve Üİ ilişkisi bu bağlamda mevcut çalışmalara katkı sağlamaktadır.

Üİ'nin hastanın duygusal, sosyal ve fiziksel yönlerini etkilediği ve yaşam kalitesi üzerinde olumsuz bir etkisi olduğu iyi bilinmektedir. Üİ yaşayan hastalar sosyal olarak geri çekilir ve bu durum depresyona sebep olabilir. Depresyonun kendisi de psikomotor yavaşlama ile seyredebilen bir hastalıktır[30,31]. Bizim de sonuçlarımızda Üİ grubundaki hastaların hem daha düşük yürüme hızına sahip oldukları hem de depresyon sıklığının yüksek olduğu dikkat çekmektedir. Ayrıca bu grubun daha yüksek oranda anti-parkinson ilacı aldığı da görülmektedir. Biliyoruz ki parkinsonizm bulgularından biri de bradikinezidir[32]. Ancak hem depresyon hem de anti-parkinson ilaç kullanımına göre regresyon analizi yapıldığında düşük yürüme hızının anlamlılığını koruması önemli bir sonuçtur. Yürüme hızının tek başına mortalite ilişkisi zaten bilinmektedir[33]. Demans, sarkopeni ve Üİ her biri ayrı morbidite ve mortalite ile ilişkili olup, bu komorbid durumlarının herhangi birine yapılacak girişim hastalar için çok önemlidir. Üİ özellikle demans hastalarında bakıcı yükünde artış, kognitif düşüşte hızlanma, bakımevine yatırılma sıklığında artış ve ekonomik sorunlara yol açmaktadır.

Çalışmamızın birçok güçlü yönü bulunmaktadır. Öncelikle sarkopeni tanısında en güncel olan EWGSOP-2 tanı kriterlerinin kullanılması ve bu tanı kriterlerinin validasyonu yapılarak bulunan Türk toplumun eşik değerleri kullanıldığı demans hastalarında sarkopeni ve Üİ'nin değerlendirildiği ilk çalışma olmasıdır. Sarkopeni tanısı ile sarkopeni kriterleri de Üİ ilişkisi açısından tek tek incelenmiştir. Çalışmamızın kısıtlılıklarında ise başta retrospektif ve kesitsel oluşu gelmektedir. Ayrıca üriner inkontinans tiplerinin incelenmemiş olması da çalışmamızın bir başka kısıtlılığıdır. Son olarak ise sarkopeni değerlendirmesinde kas kitlesinin altın standart olan DXA yerine indirekt ölçüm olan BİA ile yapılmış olması kısıtlılıklarımız arasında sayılabilir.

Sonuç

Demansın küratif tedavisinin olmadığı düşünüldüğünde, demansa eşlik eden komorbid durumların bilinmesi ve oluşturduğu sorunların giderilmesi önem arz etmektedir. Üİ'nin bu hasta grubunun en önemli sorunlarından biri olması sebebiyle sarkopeni ve Üİ ilişkisini inceleyen özellikle prospektif çalışmaların sayısı arttıkça bu alandaki girişimlerin etkinliğinin artacağı düşüncesindeyiz.

Yazar katkısı

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

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Kaynaklar

1. Melo LS de, Ercole FF, Oliveira DU de, et al. Urinary tract infection: a cohort of older people with urinary incontinence. Rev Bras Enferm. 2017;70(4):838-44. doi:10.1590/0034-7167-2017-0141
2. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on

definition and diagnosis. Age Ageing. 2019;48(4):601-2. doi:10.1093/ageing/afy169
3. Ontan MS, Dokuzlar O, Ates Bulut E, et al. The relationship between osteoporosis and sarcopenia, according to EWGSOP-2 criteria, in outpatient elderly. J Bone Miner Metab. 2021;39(4):684-92. doi:10.1007/s00774-021-01213-6
4. Ida S, Kaneko R, Nagata H, et al. Association between Sarcopenia and Overactive Bladder in Elderly Diabetic Patients. Journal of Nutrition, Health and Aging. 2019;23(6):532-7. doi:10.1007/S12603-019-1190-1
5. Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. Clin Interv Aging. 2018;13:1899-905. doi:10.2147/CIA.S180281
6. Tish MM, Geerling JC. The Brain and the Bladder: Forebrain Control of Urinary (In)Continence. Frontiers in Physiology. 2020;11:658. doi:10.3389/FPHYS.2020.00658
7. Philip Y and Tan D. Urinary incontinence in dementia: a practical approach | Australian Family Physician. 2006: 35(4). https://search.informit.org/doi/abs/10.3316/informit.364281255901965
8. Luber KM, Boero S, Choe JY. The demographics of pelvic floor disorders: current observations and future projections. Am J Obstet Gynecol. 2001;184(7):1496-503. doi:10.1067/MOB.2001.114868
9. Dost FS, Ates Bulut E, Dokuzlar O, et al. Sarcopenia is as common in older patients with dementia with Lewy bodies as it is in those with Alzheimer's disease. Geriatr Gerontol Int. 2022;22(5):418-24. doi:10.1111/ggi.14383
10. Burns JM, Johnson DK, Watts A, et al.. Reduced lean mass in early Alzheimer disease and its association with brain atrophy. Arch Neurol. 2010;67(4):428-33. doi:10.1001/archneurol.2010.38
11. Idil E, Aydin AE, Ates Bulut E, et al. Rationally decreasing the number of drugs seems to be a useful therapeutic approach in older adults: 6-month follow-up study. Arch Gerontol Geriatr. 2021;96:104472. doi:10.1016/j.archger.2021.104472
12. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-156. doi:10.1093/gerona/56.3.m146
13. American Psychiatric Association. DSM-5 Diagnostic Classification. In: Diagnostic and Statistical Manual of Mental Disorders. ; 2013. doi:10.1176/appi.books.9780890425596.x00diagnosticclassification
14. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing. 2011;40(4):423-9. doi:10.1093/ageing/afr051
15. Ates Bulut E, Soysal P, Dokuzlar O, et al. Validation of population-based cutoffs for low muscle mass and strength in a population of Turkish elderly adults. Aging Clin Exp Res. 2020;32(9):1749-55. doi:10.1007/s40520-019-01448-4
16. Resnick N, Medicine SYNEJ. Management of urinary incontinence in the elderly. New England Journal of Medicine. 1985;313(13):800-5. https://www.nejm.org/doi/pdf/10.1056/NEJM198509263131307
17. Staskin DR.Age-related physiologic and pathologic changes affecting lower urinary tract function. Clinics in Geriatric Medicine. 1986; 2(4): 701-10. https://pubmed.ncbi.nlm.nih.gov/3536058/
18. Duffin HM, Asher MJ. Clinical and urodynamic studies in 100 elderly incontinent patients. British Medical Journal (Clinical research ed). 1981;282(6270):1103-5. doi:10.1136/bmj.282.6270.1103
19. Yu LC, Rohner TJ, Kaltreider DL, et al. Profile of Urinary Incontinent Elderly in Long-Term Care Institutions. J Am Geriatr Soc. 1990;38(4):433-9. doi:10.1111/j.1532-5415.1990.tb03542.x
20. Jirovec MM, Wells TJ. Urinary incontinence in nursing home residents with dementia: The mobility-cognition paradigm. Applied Nursing Research. 1990;3(3):112-7. doi:10.1016/S0897-1897(05)80126-0
21. Jewett MAS, Fernıe GR, Hollıday PJ, Pım ME. Urinary Dysfunction in a Geriatric Long-Term Care Population: Prevalence and Patterns. J Am Geriatr Soc. 1981;29(5):211-4. doi:10.1111/j.1532-5415.1981.tb01768.x
22. McLaren SM. Prevalence and severity of incontinence among hospitalised female female psychogeriatric patients." Health Bull 39 (1981): 157-61. https://pubmed.ncbi.nlm.nih.gov/term=Prevalence+and+severity+of+incontinence+among+hospitalised%2C+&filter=datesearch.y_5
23. Borrie MJ, Davidson HA. Incontinence in institutions: Costs and contributing factors. CMAJ. 1992;147(3):322-8.
24. Schnelle JF, MacRae PG, Ouslander JG, Simmons SF, Nitta M. Functional Incidental Training, Mobility Performance, and Incontinence Care with Nursing Home

Residents. J Am Geriatr Soc. 1995;43(12):1356-62. doi:10.1111/j.1532-5415.1995.tb06614.x
25. Waite SJ, Maitland S, Thomas A, et al. Sarcopenia and frailty in individuals with dementia: A systematic review. Archives of Gerontology and Geriatrics. 2021;92. doi:10.1016/j.archger.2020.104268
26. Moon Y, Moon WJ, Kim JO, et al. Muscle Strength Is Independently Related to Brain Atrophy in Patients with Alzheimer's Disease. Dementia and Geriatric Cognitive Disorders. 2019;47:4-6):306-14. doi:10.1159/000500718
27. Burns JM, Johnson DK, Watts A, et al. Reduced lean mass in early Alzheimer disease and its association with brain atrophy. Arch Neurol. 2010;67(4):428-33. doi:10.1001/ARCHNEUROL.2010.38
28. Chong MS, Tay L, Ismail NH, et al. The Case for Stage-Specific Frailty Interventions Spanning Community Aging to Cognitive Impairment. J Am Med Dir Assoc. 2015;16(11):1003.e13-1003.e19. doi:10.1016/J.JAMDA.2015.08.025
29. Silva RRL, Coutinho JFV, Vasconcelos CTM, et al. Prevalence of sarcopenia in older women with pelvic floor dysfunction. Eur J Obstet Gynecol Reprod Biol. 2021;263:159-63. doi:10.1016/J.EJOGRB.2021.06.037
30. Mutlay F, Erken N, Günay FSD, et al. Yaşlılarda Depresyon Düşme Sıklığı ile İlişkilendirilebilir mi? Geriatrik Bilimler Dergisi. 2020; 3(3):103-9. doi:10.47141/geriatrik.826378
31. Heijnen WTCJ, Kamperman AM, Tjokrodipo LD, et al. Influence of age on ECT efficacy in depression and the mediating role of psychomotor retardation and psychotic features. Journal of Psychiatric Research. 2019;109:41-7. doi:10.1016/J.JPSYCHIRES.2018.11.014
32. von Coelln R, Dawe RJ, Leurgans SE, et al. Quantitative mobility metrics from a wearable sensor predict incident parkinsonism in older adults. Parkinsonism & Related Disorders. 2019;65:190-6. doi:10.1016/J.PARKRELDIS.2019.06.012
33. Stanaway FF, Gnjidic D, Blyth FM, et al. How fast does the Grim Reaper walk? Receiver operating characteristics curve analysis in healthy men aged 70 and over. BMJ. 2011;343:d7679. doi:10.1136/bmj.d7679

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REDEFINITION OF BNP AS A PROGNOSTIC BIOMARKER IN INTENSIVE CARE AT COVID-19 INFECTION

COVID-19 ENFEKSİYONUNDA YOĞUN BAKIMDA BNP'NİN PROGNOSTİK BİR BİYOBELİRTEÇ OLARAK YENİDEN TANIMLANMASI

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Abstract

Aim: Coronavirus disease 2019 (COVID-19) has caused a global pandemic and increased mortality has forced researchers to identify prognostic factors to identify patients at higher risk of mortality. In this study, we aimed to investigate the usability of Brain natriuretic peptide (BNP) as a predictor of mortality in critically ill patients hospitalized in the intensive care unit.

Methods: This retrospective study included 50 patients diagnosed with COVID-19 and followed in the intensive care unit. Patients with known heart failure who were found to have heart failure on echocardiography during follow-up were excluded from the study.

Results: The patients were divided into two groups based on their mortality status during hospitalization in the intensive care unit. These groups were found to be statistically similar in terms of chronic disease, gender, and age (p>0.05). Non-survivor group had higher levels of BNP at the admission to intensive care unit when compared to survivor group (93.2 pg/mL (43.5-357.3) vs. 62.9 (25.0-147.1), p=0.004, respectively). Regression analysis revealed that higher BNP levels and lower lymphocyte counts can be used as a predictor of mortality for these patients. ROC curve analysis indicated that best cut-off value for predicting in-hospital death for BNP was 85.6 pg/mL with a sensitivity of 73.1% and a specificity of 70.8%.

Conclusions: High BNP levels at admission to the intensive care unit can be used as an in-hospital mortality indicator in COVID-19 patients followed up in the intensive care unit.

Keywords: Brain natriuretic peptide, COVID-19, prognosis, mortality, intensive care

Öz

Amaç: Coronavirus hastalığı 2019 (COVID-19), küresel bir pandemiye neden olmuş ve artan ölüm oranları, araştırmacıları daha yüksek ölüm riski altındaki hastaları belirlemek için prognostik faktörleri araştırmaya zorlamıştır. Biz bu çalışmada, yoğun bakım ünitesinde yatan kritik hastalarda, beyin natriüretik peptidinin (BNP) mortalitenin bir belirleyicisi olarak kullanılabilirliğini araştırmayı amaçladık.

Yöntemler: Bu retrospektif çalışmaya COVID-19 tanısı konan ve yoğun bakım ünitesinde takip edilen 50 hasta dahil edilmiştir. Bilinen kalp yetmezliği olan ve takiplerinde ekokardiyografide kalp yetmezliği saptanan hastalar çalışma dışı bırakılmıştır.

Bulgular: Hastalar yoğun bakım ünitesinde yatışları sırasındaki mortalite durumlarına göre iki gruba ayrıldı. Bu gruplar kronik hastalık, cinsiyet ve yaş açısından istatistiksel olarak benzerdi (p>0.05). Mortalite ile seyreden grup, hayatta kalan grupla karşılaştırıldığında yoğun bakım ünitesine kabulde daha yüksek BNP seviyelerine sahipti (mortalite ile seyreden grup 93,2 pg/mL (43,5-357,3) ve hayatta kalan grup 62,9 (25,0-147,1), p=0.004). Regresyon analizi, daha yüksek BNP düzeylerinin ve daha düşük lenfosit sayılarının bu hastalarda mortalitenin bir göstergesi olarak kullanılabileceğini ortaya koydu. ROC eğrisi analizi, BNP için hastane içi ölümü öngörmede en iyi eşik değerinin %73,1 duyarlılık ve %70,8 özgüllük ile 85,6 pg/mL olduğunu gösterdi.

Sonuç: Yoğun bakım ünitesinde takip edilen COVID-19 hastalarında yoğun bakıma kabuldeki yüksek BNP seviyeleri hastane içi mortalite göstergesi olarak kullanılabilir.

Anahtar Kelimeler: Beyin natriüretik peptidi, COVID-19, prognoz, mortalite, yoğun bakım

Introduction

Coronavirus disease 2019 (COVID-19) has spread around the world since its emergence from Wuhan province of China in December 2019 and has been declared a global pandemic by the World Health Organization as of March 11, 2020 [1,2]. COVID-19 can cause simple upper respiratory infections, as well as affect the respiratory system in a wide spectrum, ranging from advanced lung diseases and acute respiratory distress syndrome [3–5]. Apart from the respiratory system involvement, COVID-19 may cause cardiac injury, thromboembolic complications, multiorgan failure and other serious complications [6–12]. Knowing which patient will have a worse prognosis and higher risk of death at the first hospitalization will affect our early approach to the patient.

Brain natriuretic peptide (BNP) is a biomarker secreted from the heart due to increased wall tension [13]. It is an established biomarker that is used in the diagnosis of reduced ejection fraction and preserved ejection fraction heart failure and higher levels show poor prognosis in these patients [14,15]. Recent studies showed that N terminal pro BNP might be associated with mortality in patients with COVID-19 [16,17]. BNP also shown to be higher in severe patients compared to mild to moderate patients [18]. With this study we aim to investigate the prognostic value of BNP on mortality among patients who are already at intensive care unit due to severe COVID-19 pneumonia.

Materials and Methods

- *Study design and participants*

For this retrospective study, the patients were recruited at Eskişehir City Hospital intensive care unit from 15.11.2020 to 15.01.2021. All patients were diagnosed as COVID-19 and the diagnosis were confirmed by thorax computerized tomography and polymerase chain reaction for COVID-19. Patients with a history of heart failure, with missing medical data, patients without BNP values at the admission to the intensive care unit and pediatric population were excluded from the study. Transthoracic echocardiography was performed in patients with clinical suspicion of heart failure, and patients with heart failure were excluded.

The patients were treated according to the algorithms in the guidelines prepared by the scientific committee of the Ministry of Health of our country and constantly updated with new literature. The patients we followed in intensive care unit were severe COVID-19 pneumonia, acute respiratory distress syndrome (ARDS) due to COVID-19 infection, sepsis due to COVID-19 and septic shock. Hypoxemic respiratory failure patients were gradually oxygenated (nasal cannula - simple mask - mask with reservoir - high flow nasal cannula- Continious Positive Airway Pressure - invasive mechanical ventilation). Lung protective mechanical ventilator strategies were applied to patients who developed ARDS.

The study was approved by Ministry of Health and local ethics committee.

- *Data collection*

The data set were collected retrospectively and evaluated by two physicians independently to double-check the data. Demographic and clinical information was gained form hospital medical records. The BNP and other laboratory values were obtained from the laboratory results at the admission to the intensive care unit.

The data was summarized at the first three columns of Table 1. Gender, hypertension, diabetes mellitus, respiratory comorbidities, cerebrovascular diseases and chronic renal failure variables are categorical; therefore their percentages in the total data set are reported in parenthesis after the number of patients with the aforementioned characteristic. Our variable of interest

(BNP) and the remaining are all continuous variables. The continuous variables in the data set are reported as "median ± standard deviation" if they are normally distributed, and "median (interquartile range)" if they are non-normally distributed.

- *Comparison of two groups*

The intermediate step in this investigation of BNP and other indicators on the mortality of COVID-19 patients is the comparison of these indicators among the survivor and non-survivor groups. For this purpose three methods are adopted depending on the classification of the variable taken into account [19]. The chi-square test is used to investigate the association among the groups for categorical variables. The independent samples t test is employed to compare the means of the two independent groups for normally distributed continuous variables. Finally, the Mann-Whitney U test is implemented to test whether two groups have the same distribution for non-normally distributed continuous variables.

Although the distinction between categorical and continuous variables are obvious, whether a continuous variable is identically and/or normally distributed is distinguished via Levene and Shapiro-Wilk tests [20]. In other words homogeneity of variances is tested by Levene test and distribution of the variable for normality is tested by Shapiro-Wilk test.

The results used for comparison of the two independent samples are reported in the last column of Table 1. Since there are three different tests employed, only the p-values of the testes are listed. To sum up a p-value of less than 5% (0.05) indicates statistical significance, which in turn means there is a significant difference between survivor and non-survivor groups for whichever variable was under consideration.

- *Logistic regression*

The aforementioned chi-square, independent samples t and Mann Whitney U tests are useful for exploratory investigations and in situations where the number of predictor variables of interest is limited. However they can be cumbersome when multiple explanatory variables are being considered and are not well suited to situations where the explanatory variables may take on a large number of possible values [21]. A popular method when such cases emerge is logistic regression; it has the suppleness and strengths of regression model (it is a multivariate analysis, can take many types of variables such as categorical and continuous, and has predictive ability) as well as the capability to consider a binary dependent variable.

Logistic regression is a modeling approach that can be used to describe the relationship of several explanatory variables to a dichotomous dependent variable [22]. In this study the explanatory variables are listed in the Table 1 as the row names. The dependent variable is mortality or the binary variable that shows whether the patient survived COVID-19 or not. In logistic regression rather than the coefficients of the explanatory variables their odd ratios (OR) are considered. The odds ratio represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure [23]. A simplistic approach to the OR is using it as a tool to determine whether a particular exposure or variable affects a particular outcome, and to compare the magnitude of variables for that outcome:

- ❖ OR=1 Exposure/variable does not affect odds of outcome,
- ❖ OR>1 Exposure/variable associated with higher odds of outcome, and
- ❖ OR<1 Exposure/variable associated with lower odds of outcome.

Although the same approach is suitable for logistic regression, the distance of OR to 1 (where 1 indicates variable has no effect on the outcome, the dependent variable) is a better measure to see how mortality of COVID-19 patient is affected by the change in variable under consideration.

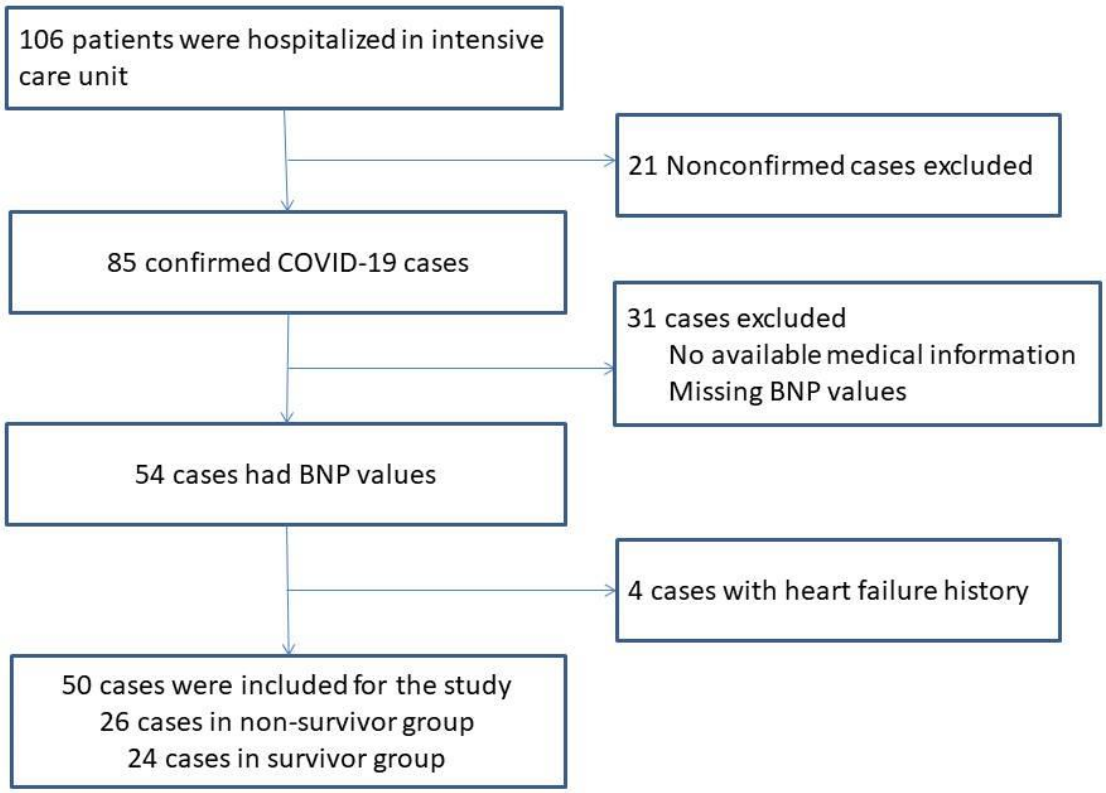

Figure 1. Flowchart of patient recruitment

- *Receiver operating characteristic*

The receiver operating characteristic (ROC) curve constructed by plotting the false positive rate (FPR) which is "1-specificity" against the true positive rate (TPR) which is the "sensitivity" at various threshold settings. It depicts relative tradeoffs between benefits (true positives) and costs (false positives) of a binary prediction or classification[24]. The area under a given ROC curve or AUC measures the performance across the aforementioned threshold settings.
Furthermore ROC curve is a useful tool for finding the optimal threshold setting which also known as best cut-off value. The best cut-off value dichotomizes the values of the explanatory variable in a regression setting; therefore, it provides decision/prediction point regarding which group each observation falls into. Finally, to determine the best cut-off value "Youden's J statistic" as well as "least-distance-to-(0,1)" criteria, which are very well documented in [25], are employed in this study.

Results

- *Patient characteristics*

106 patients were hospitalized at intensive care unit for prediagnosis of COVID-19. According to the results of consecutive 2 negative PCR results, 21 cases were excluded from the study. From the remaining patients, 31 cases were excluded because they do not have BNP values at the admission to the intensive care unit and they do not have sufficient medical information and 4 cases were excluded due to known history of heart failure (Figure 1).
The mean age of the study population was 67.8±13.7 and 54% (n=27) was female.

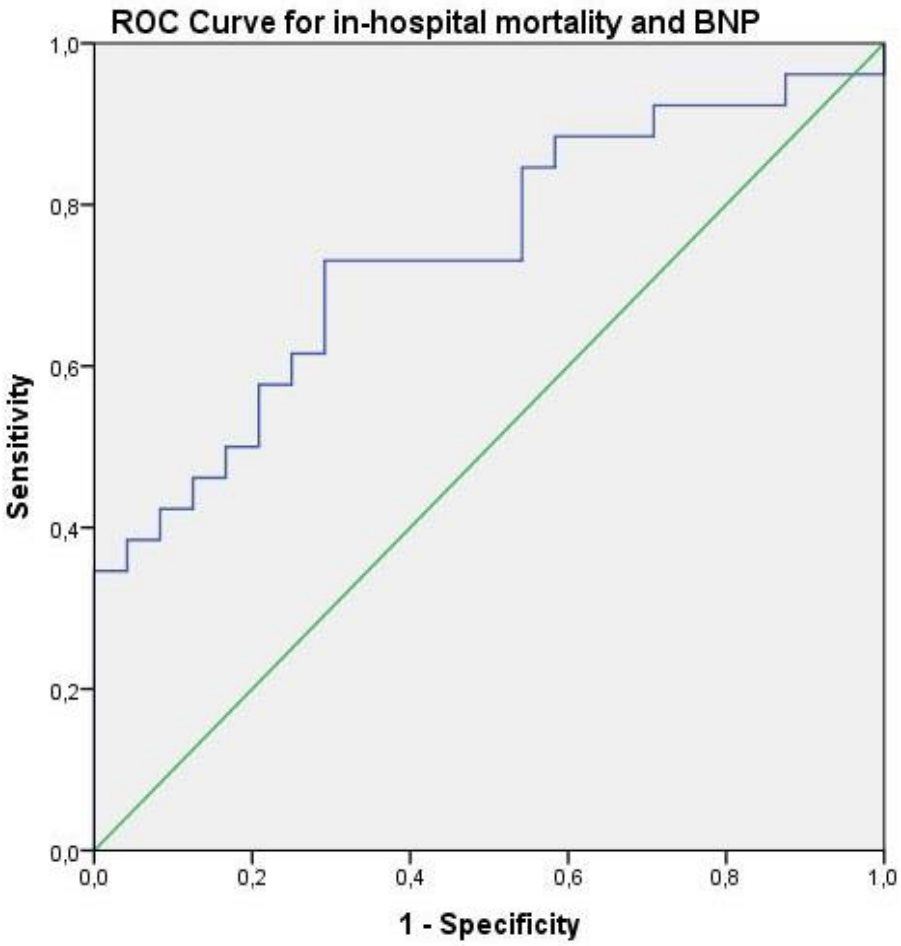

Figure 2. ROC curve of BNP for prediction of in-hospital mortality

The patients were divided into two groups according to the in-hospital mortality status. 52% of the cases who died during intensive care stay are included in the non-survivor group, and the remaining 48% of the patients were discharged from intensive care unit. Non-survivor group and survivor groups were similar in terms of age (71.1±11.1 and 64.1±15.4, p=0.067, respectively), gender (42.3% were female and 66.7 were female, p=0.084, respectively)and with similar comorbidities of hypertension (34.6% (n=9) vs 33.3% (n=8), p=0.924), diabetes mellitus (26.9% (n=7) vs 33.3 (n=8), p=0.621), respiratory diseases (34.6% (n=9) vs 25.0% (n=6), p=0.459), cerebrovascular diseases (0% (n=0) vs 4.1% (n=1), p=0.293) and chronic renal diseases (11.5% (n=3) vs 0% (n=0), p=0.086) (Table 1).

- *Laboratory results*

Median BNP value of the study population was 93.2 (43.5-357.3). Non-survivor group had higher levels of BNP at the admission to intensive care unit when compared to survivor group (93.2 (43.5-357.3) vs 62.9 (25.0-147.1), p=0.004, respectively)
Results of the comparison of the non-survivor and survivor group showed statistically significant difference among troponin-I (26.4 (12.3-81.6) vs. 8.6 (5.4-13.8), p=0.001) values. Other laboratory values showed no significant difference between groups.

Table 1. Baseline characteristics and laboratory results of the patients with COVID-19.

	Patients, no. (%)	Mortality		P value
	All (n=50)	Non-survivor (n=26)	Survivor (n=24)	
Age, mean±SD, y	67.8±13.7	71.1±11.1	64.1±15.4	0.067
Female	27 (54%)	11 (42.3%)	16 (66.7%)	0.084
Hypertension	17 (34%)	9 (34.6%)	8 (33.3%)	0.924
Diabetes Mellitus	15 (30%)	7 (26.9%)	8 (33.3%)	0.621
Cardiovascular diseases	6 (12%)	5 (19.2%)	1 (4.1%)	0.101
Respiratory comorbidities	15 (30%)	9 (34.6%)	6 (25.0%)	0.459
Cerebrovascular diseases	1 (2%)	0 (0%)	1 (4.1%)	0.293
Chronic renal failure	3 (6%)	3 (11.5%)	0 (0%)	0.086
B-type natriuretic peptide, pg/mL	93.2 (43.5-357.3)	194.4 (60.8-958.3)	62.9 (25.0-147.1)	0.004
Hemoglobin, g/dL	12.5±2.1	12.7±2.1	12.2±2.0	0.362
Leukocytes $x10^3/\mu L$	10.9 (7.1-14.8)	11.6 (7.1-15.4)	10.8 (7.0-14.5)	0.846
Neutrophil $x10^3/\mu L$	9.3 (6.0-12.5)	10.1 (6.0-12.9)	8.8 (5.9-12.1)	0.600
Lymphocyte $x10^3/\mu L$	0.82 (0.53-1.19)	0.73 (0.53-1.05)	0.83 (0.51-1.55)	0.290
Platelets $x10^3/\mu L$	246.8±84.4	243.7±91.0	247.6±76.5	0.871
Glucose, mg/dL	146.5 (122.7-255.0)	144.5 (122.5-242.7)	149.0 (122.5-269.2)	0.930
Creatinine, mg/dL	0.84 (0.72-1.13)	0.88 (0.74-1.9)	0.77 (0.69-1.05)	0.090
C-reactive protein, mg/dL	109.4 (57.2-193-2)	122.0 (59.6-191.5)	109.4 (50.8-254.4)	0.764
Troponin I, pg/mL	13.8 (6.6-37.4)	26.4 (12.3-81.6)	8.6 (5.4-13.8)	0.001
D-dimer	1.7 (0.97-5.3)	1.68 (1.12-5.60)	2.26 (0.73-5.12)	0.771

Abb: SD; standard deviation, y; years

The demographic and laboratory values of the patient groups were given at Table 1.

- *Regression analysis*

The association of the variables, especially BNP, to mortality is further investigated by logistic regression. The findings of the regression are reported at Table 2; which depict that BNP and lymphocyte counts are independently associated with mortality. In other words the p-values associated with these two variables are below 5% significance level ($p<0.05$). The odds ratio of lymphocyte count suggests 0.1 unit ($x10^3/\mu L$) increase lowers the odds ratio of mortality by 9% (0.1× (0.104-1)×100=-8.96). A 10 unit (pg/mL) increase in BNP in turn increases the odds of mortality by 8% (10× (1.008-1)×100=8). In this study it is obvious that lymphocyte is associated with lower odds of mortality, while BNP associated with higher odds of mortality.

Finally another logistic regression where the only explanatory variable is BNP, also supports the finding that BNP is significantly ($p=0.0316$ in this case) associated with in-hospital mortality for COVID-19 patients under intensive care.

The other explanatory variables such as chronic diseases (such as hypertension, diabetes mellitus, respiratory comorbidities, and cardiovascular diseases) have no significant impact on the mortality of the COVID-19 patients once the BNP and lymphocyte are controlled for.

Table 2. Binary logistic regression analysis on the risk factors associated with mortality in COVID-19 patients followed at intensive care unit.

Variable	Odds Ratio	95% Confidence Interval	p-value
Age	0.989	0.903-1.083	0.809
Gender	0.278	0.038-2.039	0.208
Hypertension	9.073	0.621-132.515	0.107
Diabetes Mellitus	3.204	0.082-124.566	0.533
Respiratory comorbidities	0.462	0.071-3.019	0.420
Cardiovascular diseases	0.003	0.000-9.457	0.156
B-type natriuretic peptide	1.008	1.001-1.015	0.028
Hemoglobin	1.553	0.956-2.523	0.075
Neutrophil	0.849	0.659-1.095	0.208
Lymphocyte	0.104	0.013-0.826	0.032
Platelets	1.013	0.999-1.026	0.062
Glucose	1.010	0.993-1.028	0.249
Creatinine	1.168	0.038-35.809	0.929
C-reactive protein	0.993	0.982-1.004	0.209
Troponin I	0.989	0.977-1.002	0.097
D-dimer	1.017	0.850-1.217	0.855
Constant	0.114		0.752

Moreover demographic variables such as age and gender are found out to be unassociated with mortality as well. Finally platelets, hemoglobin and troponin-I values have extremely weak ($0.05 \leq p < 0.10$), almost non-existent, association with mortality.

- *Receiver operator characteristic (ROC) curve for prediction in-hospital death*

The previous finding support that BNP is associated with mortality of COVID-19 patients. In this regard, the next question is what values of the BNP predict mortality (with better precision). The answer to this question is easily answered by receiver operation characteristic (ROC) curve. Figure 2 shows the ROC curve of BNP for prediction of in-hospital mortality for intensive care patients. The area under the curve was 0.740 (95% confidence interval 0.603-0.878, p=0.004) which is an acceptable value and indicates that BNP can predict the mortality of the patients. Finally, the best cut-off value for predicting in-hospital death was 85.6 pg/mL with a sensitivity of 73.1% and a specificity of 70.8%. Both "Youden's J statistic" and "least-distance-to-(0,1)" criterion produce the value 85.6 pg/mL for the best cut-off value. In other words optimal choice for predicting which group the COVID-19 patients will fall into is to see whether BNP values are higher or lower than 85.6 pg/mL.

Discussion

This study showed that BNP can use as a reliable biomarker for predicting mortality among severe COVID-19 patients who are followed at intensive care unit. 85.6 pg/mL can be used as a cut-off value for mortality among these patients.

Although COVID-19 originally originated in China, it has now become a global pandemic and has become a common problem of the world that needs to be solved [1,2]. This is not the first pandemic that humanity has faced. For example, the Spanish flu in 1918 also caused a global pandemic, with an estimated 40 to 100 million deaths. The Asian flu, which emerged later in 1957, killed 1.1 million people. The emergence of the vaccine for this virus and the widespread production of the vaccine subsequently prevented the Asian flu pandemic from taking more lives [26]. Likewise, after the spread of COVID-19, scientists shared every finding and every treatment applied with other scientists, allowing the whole world to recognize the disease, globally discuss the reliability and usefulness of the methods tried in terms of diagnosis, prognosis and treatment. One of the issues emphasized was the presence of a biomarker that could predict the course of the disease when the patient applied. In addition to the many biomarkers that have been proposed in this regard, another biomarker that has been emphasized is BNP. When severe/critical patients diagnosed with COVID-19 and mild patients are compared, BNP values are found to be higher in patients with severe prognosis [18]. In another study conducted on COVID-19 patients who were admitted to the hospital and followed up for 7 days, it was found that high BNP levels predict mechanical ventilation need and mortality [27]. Before COVID-19, BNP was already proposed as a prognostic marker for pneumonia [28]. But previous studies mostly aimed to differentiate severe cases and mild cases. Our study aimed to examine the effect of BNP on mortality in critically-ill COVID-19 patients. In other words, our aim was not to identify severe COVID-19 patients, but to aim whether BNP is a predictive factor for mortality in patients who are already in critical condition and followed in intensive care unit. The results of our study suggested that BNP values are higher at admission to the intensive care unit for patients who died compared to survivor group. Also regression analysis showed that BNP can be used as a predictor of mortality at COVID-19 patients. Before our study, many biomarkers other than BNP

have been shown as an indicator of severity for COVID-19 and are used in practice. Examples of these markers are troponin-I, D-dimer, C-reactive ptotein and atherogenic index of plasma. But these biomarkers are indicative of the need for intensive care or mortality in COVID-19 patients [29–31]. Studies conducted generally enable these biomarkers to distinguish severe patients at the first admission to the hospital. The results of our study show that high BNP, troponin-I and low lymphocytes help to differentiate mortality risk in critically ill patients. But regression analysis suggests that only BNP and lymphocyte count may be used as a predictor of mortality for critically-ill patients. Interestingly, D-dimer levels did not differ statistically when the survivor and non-survivor groups were compared. D-dimer was shown to be elevated in patients who required intensive care unit admission, had ARDS during admission or had in-hospital mortality [2,32–34]. Our results showed otherwise most probably due to clinical severity of our patients. The difference in the results of our study may have emerged, as other studies compared all patients who were admitted to the hospital without making separate evaluations of patients in the service or intensive care unit in the study groups.

In individuals with a history of cardiac disease and diagnosed with COVID-19, the BNP was found to be not predictive of death, mechanical ventilation and thromboembolic events [35]. Coexistence of pneumonia and heart failure are factors that increase the risk of mortality. Pneumonia is a predictor of mortality in heart failure patients [36]. Therefore, we chose to exclude heart failure patients from our study. Finding different results from the study of Andreini et al. may be due to this difference in patient selection [35].

High BNP values are indicators of mortality in pneumonia patients [37]. In addition, high BNP levels show poor prognosis in patients with sepsis and septic shock [38,39]. The effect of hypoxia on pulmonary artery pressure in pneumonia patients increases ventricular wall tension, and this may explain the elevation of BNP in pneumonia patients independent of heart failure [16,40]. High pulmonary artery pressure is also seen in COVID-patients, which is an indicator of poor prognosis and mortality [41,42]. This mechanism may explain the elevation of BNP levels in critically ill patients that resulted in mortality in our study.

- *Limitations*

Some limitations exist in our study. First, our study is a single center and single intensive care experience. Secondly, the number of patients is small. A multicentric prospective study with higher number of patients would give more reliable results. Third, we excluded patients with a history of heart failure but we only performed transthoracic echocardiography to whom with a suspicion of heart failure. It would be better to perform all patients transthoracic echocardiography because we may have failed to exclude these patients who are clinically silent without symptoms of heart failure.

Conclusion

Predicting which patients will have a poor prognosis in a disease such as COVID-19 is vital for these patients. With this study, we aim to investigate whether we can predict mortality with simple blood parameters during the admission to the intensive care unit. We found out that BNP tends to be higher in intensive care patients with COVID-19 with in-hospital mortality. Binary logistic regression confirms that BNP has a significant association with the mortality of COVID-19 patients. Additionally, BNP can be used as a predictor of mortality with a cut-off value of 85.6 pg/mL with a sensitivity of 73.1% and a specificity of 70.8% at these patients.

Author contributions

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

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

Authors declared no financial support.

Ethical approval

This study, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
Approval numbered 2021/06-160 was obtained from Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee.

References

1. WHO Western Pacific | World Health Organization. Accessed May 9, 2021. https://www.who.int/westernpacific/emergencies/covid-19
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
3. Ñamendys-Silva SA, Alvarado-Ávila PE, Domínguez-Cherit G, et al. Outcomes of patients with COVID-19 in the intensive care unit in Mexico: A multicenter observational study. Heart & Lung. 2021;50(1):28-32. doi:10.1016/j.hrtlng.2020.10.013
4. Ghasemiyeh P, Mohammadi-Samani S. COVID-19 outbreak: Challenges in pharmacotherapy based on pharmacokinetic and pharmaco-dynamic aspects of drug therapy in patients with moderate to severe infection. Heart & Lung: The Journal of Cardiopulmonary and Acute Care. 2020;49(6):763-73. doi:10.1016/j.hrtlng.2020.08.025
5. Esme H, Kucukosmanoglu I. Ampiyemin eşlik ettiği COVID-19 olgusunda akciğerin histopatolojik bulguları. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2020; 3(3):170-6. doi: 10.36516/jocass.2020.53
6. Zuin M, Rigatelli G, Bilato C, et al. Heart failure as a complication of COVID-19 infection: systematic review and meta-analysis. Acta Cardiologica. 2021;0(0):1-7. doi:10.1080/00015385.2021.1890925
7.. Uslu PU. Pandemi ve İnsomni. Eskisehir Medical Journal. 2020;1(1):5-9. doi:10.48176/esmj.2020.2
8. Yildirim ÖT, Turgay A, Tunay DL. COVID-19 Pandemisi ve Kardiyovasküler Etkileri. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2020;3(3):128-33. doi: 10.36516/jocass.2020.48
9. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507-13. doi:10.1016/S0140-6736(20)30211-7
10. Omar T, Karakayalı M, Perincek G. Assessment of COVID-19 deaths from cardiological perspective. Acta Cardiologica. 2021;0(0):1-8. doi:10.1080/00015385.2021.1903704
11. Duyan M, Kıldan RNO. Evaluatıon Of Mortalıty Rısk Wıth Curb-65 And Psı In Patıents Wıth And Wıthout Gerıatrıc Covıd-19 Pneumonıa. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2022; 5 (1):8-22. doi: 10.36516/jocass.2022.93
12. Yildirim ÖT. COVID-19 Pandemisi, Anjiyotensin dönüştürücü enzim (ACE) inhibitörleri ve Anjiyotensin Resepör Blokörlerinin (ARB) kullanımı. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2020;3(1):47-52. doi: 10.36516/jocass.2020.32
13. Kinnunen P, Vuolteenaho O, Ruskoaho H. Mechanisms of atrial and brain natriuretic peptide release from rat ventricular myocardium: effect of stretching. Endocrinology. 1993;132(5):1961-70. doi:10.1210/endo.132.5.8477647
14. Salah K, Stienen S, Pinto YM, et al. Prognosis and NT-proBNP in heart failure patients with preserved versus reduced ejection fraction. Heart. 2019;105(15):1182-9. doi:10.1136/heartjnl-2018-314173
15. Bay M, Kirk V, Parner J, et al. NT-proBNP: a new diagnostic screening tool to differentiate between patients with normal and reduced left ventricular systolic function. Heart. 2003;89(2):150-4. doi:10.1136/heart.89.2.150
16. Pranata R, Huang I, Lukito AA, Raharjo SB. Elevated N-terminal pro-brain natriuretic peptide is associated with increased mortality in patients with COVID-19: systematic review and meta-analysis. Postgrad Med J. 2020;96(1137):387-91. doi:10.1136/postgradmedj-2020-137884
17. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. Published online March 26, 2020:m1091. doi:10.1136/bmj.m1091
18. Li P, Wu W, Zhang T, et al. Implications of cardiac markers in risk-stratification and

management for COVID-19 patients. Crit Care. 2021;25(1):158. doi:10.1186/s13054-021-03555-z
19. Samuels, Witmer & Schaffner, Statistics for the Life Sciences, Global Edition, 5th Edition | Pearson. Accessed May 18, 2021. https://www.pearson.com/uk/educators/higher-education-educators/program/Samuels-Statistics-for-the-Life-Sciences-Global-Edition-5th-Edition/PGM1097920.html
20. Lawal B. Applied Statistical Methods in Agriculture, Health and Life Sciences. Springer International Publishing; 2014. doi:10.1007/978-3-319-05555-8
21. Vittinghoff E, Glidden DV, Shiboski SC, et al. Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models. 2nd ed. Springer-Verlag; 2012. doi:10.1007/978-1-4614-1353-0
22. Kleinbaum DG, Klein M. Logistic Regression: A Self-Learning Text. 3rd ed. Springer-Verlag; 2010. doi:10.1007/978-1-4419-1742-3
23. Szumilas M. Explaining Odds Ratios. J Can Acad Child Adolesc Psychiatry. 2010;19(3):227-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2938757/pdf/ccap19_3p227.pdf
24. Fawcett T. An introduction to ROC analysis. Pattern Recognition Letters. 2006;27(8):861-74. doi:10.1016/j.patrec.2005.10.010
25. Perkins NJ, Schisterman EF. The inconsistency of "optimal" cutpoints obtained using two criteria based on the receiver operating characteristic curve. Am J Epidemiol. 2006;163(7):670-5. doi:10.1093/aje/kwj063
26. Schwartz RA, Kapila R. Pandemics throughout the centuries. Clinics in Dermatology. 2021;39(1):5-8. doi:10.1016/j.clindermatol.2020.12.006
27. Almeida Junior GLG de, Braga F, Jorge JK, et al. Prognostic Value of Troponin-T and B-Type Natriuretic Peptide in Patients Hospitalized for COVID-19. Arq Bras Cardiol. 2020;115(4):660-6. doi:10.36660/abc.20200385
28. Usuda D, Sangen R, Hashimoto Y, et al. Validation of a B-type natriuretic peptide as a prognostic marker in pneumonia patients: a prospective cohort study. BMJ Open. 2016;6(2):e010440. doi:10.1136/bmjopen-2015-010440
29. Turgay Yıldırım Ö, Kaya Ş. The atherogenic index of plasma as a predictor of mortality in patients with COVID-19. Heart & Lung. 2021;50(2):329-33. doi:10.1016/j.hrtlng.2021.01.016
30. Papageorgiou N, Sohrabi C, Merino DP, et al. High sensitivity troponin and COVID-19 outcomes. Acta Cardiologica. 2021;0(0):1-8. doi:10.1080/00015385.2021.1887586
31. Aladağ N, Atabey RD. The role of concomitant cardiovascular diseases and cardiac biomarkers for predicting mortality in critical COVID-19 patients. Acta Cardiologica. 2021;76(2):132-139. doi:10.1080/00015385.2020.1810914
32. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. doi:10.1001/jama.2020.1585
33. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-7. doi:10.1111/jth.14768
34. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine. 2020;180(7):934-43. doi:10.1001/jamainternmed.2020.0994
35. Andreini D, Conte E, Mushtaq S, et al. Extent of lung involvement over severity of cardiac disease for the prediction of adverse outcome in COVID-19 patients with cardiovascular disease. Int J Cardiol. 2021;323:292-4. doi:10.1016/j.ijcard.2020.10.006
36. Jobs A, Simon R, de Waha S, et al. Pneumonia and inflammation in acute decompensated heart failure: a registry-based analysis of 1939 patients. Eur Heart J Acute Cardiovasc Care. 2018;7(4):362-370. doi:10.1177/2048872617700874
37. Li J, Ye H, Zhao L. B-type natriuretic peptide in predicting the severity of community-acquired pneumonia. World J Emerg Med. 2015;6(2):131-6. doi:10.5847/wjem.j.1920-8642.2015.02.008
38. Falcone M, Corrao S, Venditti M, et al. Performance of PSI, CURB-65, and SCAP scores in predicting the outcome of patients with community-acquired and healthcare-associated pneumonia. Intern Emerg Med. 2011;6(5):431-6. doi:10.1007/s11739-011-0521-y
39. Post F, Weilemann LS, Messow CM, et al. B-type natriuretic peptide as a marker for sepsis-induced myocardial depression in intensive care patients. Crit Care Med. 2008;36(11):3030-7. doi:10.1097/CCM.0b013e31818b9153
40. Yap LB, Mukerjee D, Timms PM, et al. Natriuretic peptides, respiratory disease, and the right heart. Chest. 2004;126(4):1330-6. doi:10.1378/chest.126.4.1330
41. Ceriani E, Marceca A, Lanfranchi A, et al. Early echocardiographic findings in patients

hospitalized for COVID-19 pneumonia: a prospective, single center study. Intern Emerg Med. Published online May 21, 2021. doi:10.1007/s11739-021-02733-9
42. Mishra A, Lal A, Sahu KK, et al. An Update on Pulmonary Hypertension in Coronavirus Disease-19 (COVID-19). Acta Biomed. 2020;91(4):e2020155. doi:10.23750/abm.v91i4.10698

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COMPARISON OF PROCALCITONIN WITH C-REACTIVE PROTEIN IN THE DIAGNOSIS OF INFECTION AFTER CRANIOTOMY

KRANİOTOMİ SONRASI GELİŞEN ENFEKSİYON TANISINDA PROKALSİTONİNİN C-REAKTİF PROTEİNLE KARŞILAŞTIRILMASI

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Abstract

Aim: Classical infection indicators fail to distinguish between the inflammatory reaction induced by neurosurgery and the postoperative infection. In our study, we investigated the sensitivity and specificity of Procalcitonin (PCT) and C-reactive protein (CRP) in differentiating the inflammatory reaction caused by neurosurgery and postoperative infection.

Methods: Our study was carried out in 44 patients with intracranial tumors in Çukurova University Faculty of Medicine Neurosurgery between May 2007 and December 2007. Changes in PCT, white blood cell count, CRP, and fever values during preoperative 1 and postoperative 4 days were examined.

Results: PCT values were found to be above 0.1 ng/ml in all the patients who developed infection in the study. In the light of the results we obtained, we can say that patients with PCT values above 0.1 ng/ml on the postoperative 2nd and 3rd days should be monitored more carefully in terms of postoperative infection. In our study, the majority of patients with CRP infection followed a similar kinetics to that of patients who did not develop infection. CRP values are above normal (CRP>5 ng/ml) in all patients with and without infection. This indicates that CRP will not be used as an important parameter for the follow-up of postoperative infections

Conclusions: Our study demonstrates that PCT is a safe parameter that can be useful in the diagnosis of fever of unknown postoperative etiology in neurosurgery.

Keywords: C-Reactive Protein, infection, procalcitonin, cranitomy

Öz

Amaç: Klasik enfeksiyon göstergeleri, beyin cerrahisinin yaratmış olduğu inflamatuar reaksiyonla, postoperatif gelişen enfeksiyonun ayırt edilmesinde başarısızdır. Biz çalışmamızda beyin cerrahisinin yaratmış olduğu inflamatuar reaksiyonla, postoperatif gelişen enfeksiyonun ayırt etmesinde Prokalsitonin (PKT) ve C-reaktif proteinin (CRP) sensitivite ve spesifisitesini araştırdık.

Yöntemler: Çalışmamız Mayıs 2007-Aralık 2007 tarihleri arasında, Çukurova Üniversitesi Tıp Fakültesi Beyin Cerrahisinde intrakranial tümörü olan 44 hastada yapılmıştır. Preoperatif 1 ve postoperatif 4 gün boyunca PKT, beyaz küre sayısı, CRP ve ateş değerlerindeki değişimler incelenmiştir.

Bulgular: Çalışmaya alınan enfeksiyon gelişen hastaların tümünde PKT değerleri 0,1 ng/ml'nin üzerinde bulunmuştur. Elde ettiğimiz sonuçlar ışığında postoperatif 2. ve 3. günde 0,1 ng/ml üzerinde PKT değeri olan hastaların postoperatif enfeksiyon açısından daha dikkatli monitörize edilmesi gerektiğini söyleyebiliriz. Çalışmamızda CRP enfeksiyon gelişen hastaların büyük kısmında, enfeksiyon gelişmeyen hastalardakine benzer bir kinetik izlemiştir. Enfeksiyon gelişen ve gelişmeyen tüm hastalarda CRP değerleri normalin üstündedir (CRP>5 ng/ml). Bu da CRP'nin postop enfeksiyonları takip açısından önemli bir parametre olarak kullanılmayacağını gösterir.

Sonuç: PKT, beyin cerrahisinde postoperatif etyolojisi bilinmeyen ateşin teşhisinde faydalı olabilen güvenli bir parametre olduğunu düşünmekteyiz.

Anahtar Kelimeler: C-Reaktif Protein, enfeksiyon, prokalsitonin, kraniotomi

Introduction

Despite prophylaxis, postoperative infection is seen between 0.5% and 1.5%. Postoperative infections are diseases with high mortality, morbidity and cost. Surgical site infection is an important socioeconomic problem because it can be resistant to treatment, recur, bring a heavy economic burden and cause mortality[1]. For this reason, early detection of infection and initiation of appropriate treatment are very important for both the patient and the prevention of the economic burden it will bring. For this reason, in addition to the necessity of early diagnosis and treatment, distinguishing whether the emerging picture is an infection, preventing unnecessary antibiotic treatment or making the decision to terminate the started antibiotic early are parameters that are gaining importance in the follow-up of patients[2].

It is known how the inflammatory response, which develops as a response of the host to infections, occurs. Similar inflammatory response may develop after any type of tissue damage such as pancreatitis, major trauma, burns and autoimmune diseases[2-4]. General systemic findings of systemic inflammation (SIRS=Systemic Inflammatory Response Syndrome) such as changes in body temperature, leukocytosis, tachycardia may have infectious or non-infectious etiology. Therefore, old and new indicators are expected to show the presence, source and severity of inflammation. Accordingly, one of the first targets was to determine whether the systemic inflammatory response syndrome (SIYS) [5]. is caused by infection or non-infectious trauma, burn, a process that leads to the formation of an immune complex, or an immunological process such as resection. For this purpose, cytokines such as TNF-α, IL-6, IL-8, C-reactive protein (CRP), β2 microglobulin, acute phase reactants such as erythrocyte sedimentation rate (ESR), ferritin, separately or in combinations of these were used[6].

Postoperative infection is often difficult to diagnose before clinical symptoms become evident. Magnetic resonance imaging can help diagnose soft tissue change, but it is expensive to use as a screening tool and may not be available. Although inflammatory markers such as C-reactive protein (CRP), white blood cell count (WBC), erythrocyte sedimentation rate (ESR) and body temperature (BT) are easily measured, their specificity is not high. Inflammatory response, which develops due to trauma without infection, causes an increase in these parameters[7-9]. For this reason, research and research are continuing an infection indicator that shows infective complications that may develop in the early postoperative period, is not affected by surgical trauma, is specific for bacterial infections, and also responds quickly to treatment after appropriate antibiotic treatment.

Procalcitonin (PCT) is a 116 amino acid glycopeptide produced by the C cells of the thyroid gland under normal conditions and is a precursor of calcitonin[10,11]. The PCT level is undetectable in healthy people. It is known that serum PCT levels increase significantly in cases of sepsis and severe invasive bacterial infection and decrease rapidly with appropriate antibiotic treatment. However, PCT level does not change in severe viral infections and other inflammatory diseases. In our study, we evaluated the CRP and PCT responses of patients with inflammatory reaction and postoperative infection caused by neurosurgery and investigated whether it helps the diagnosis of surgical complications.

Materials and Methods

This study was conducted on 44 patients with intracranial tumors who were treated in the Department of Neurosurgery of Çukurova University Faculty of Medicine between February 2007 and August 2007. All patients who applied to our clinic with the diagnosis of intracranial tumor on the

specified dates were evaluated. Patients with terminal cancer and pathological fractures, patients who received massive blood transfusion, patients with chronic organ failure, multiple trauma, patients who underwent surgery in less than three months, pregnancy, patients with infection at the time of admission or chronic rheumatic disease were excluded from the study.

Demographic data such as age and gender, clinical symptoms and treatments of each patient were recorded at the first admission. The patients were followed up for infection clinically and laboratory for 1 day preoperatively and for 5 days postoperatively. Wound swab samples were taken from patients with blood, urine, CSF, and wound site discharge from patients with fever above 38°C in axillary measurement.

In all of the patients included in the study, mass excision by craniotomy was performed under general anesthesia (total excision with intratumoral debulking or microsurgery).

Antibiotic prophylaxis with cefazolin sodium was administered to all patients 30 minutes before the operation and for 2 days postoperatively.

Blood samples were taken from all patients in the morning for 1 preoperative and 4 days after the operation, and fever was followed up at the same time 4 times a day. The blood samples to be tested for CRP and PCT were placed in dry tubes and centrifuged at 4000 rpm for 10 minutes. Serum was separated from blood samples after centrifugation. Serum samples taken for CRP were studied with the nephelometric method (Dade Behring, Germany BN II device) in the central laboratory of our hospital on the same day.

On the same day, blood samples were taken in the laboratory of our hospital with the Cryptor (BRAHMS Diagnostica-Berlin, Germany) method for PCT and Sysmex XT 2000-i (Roche Diagnostics Gmb H. Mannheim, Germany) device for WBC.

The data were transferred to electronic media and analyzed in SPSS 15.0 Computer Package Program. For group comparisons, an analysis of variance (ANOVA) was performed followed by a Tukey post-hoc test. Statistical significance was accepted at $p<0.05$.

Results

The mean age of 44 patients included in the study was 47 (±19), and the median was 48.5 (Lowest Value=4, Maximum Value=90). Of the patients, 23 (53.3%) were female and 21 (46.7%) were male; the mean age was 46.9 (age range: 4–90 years). Pituitary adenoma in 5 (1 male, 4 female), 5 glioblastoma (4 male, 1 female), 22 grade 1-3 glial mass (12 male, 10 female) and 6 meningiomas (1 male, 5 female) of the patients participating in the study female), 3 PCA (1 male, 2 female), 3 ependymomas (2 males, 1 females) were present.

There was no statistically significant difference between the infected and non-infected groups in terms of age and gender (P=0.983, P=0.587). The distribution and incidence of infections in the patients are shown in Table 1.

Table 1. Distribution of Infections Developing in Patients

Type of Infection	Number of patients	Distribution (%)	Ratio (%)
UTI	1	14,3	2,2
UTI + CCCSI	1	14,3	2,2
UTİ + M	1	14,3	2,2
M	3	42,9	6,7
UTI + LI	1	14,3	2,2
Total	7	100	15,9

UTI: Urinary tract infection, CCCSI: Catheter-connected circulatory system infection, LI: Lung infection, M: Meningitis

No pathological increase was observed in the measured axillary fever of the patients included in the study before the operation. When the preoperative and postoperative

fever values are compared among themselves, it is seen that the fever reaches the highest value on the postoperative 1st day after the operation and then increases in the group with infection, but gradually decreases in the group without infection. When the mean of groups with and without infection were compared, the difference was found to be statistically significant (P<0.001).

An increase in WBC values was observed after the operation (P=0.02). It was observed that the WBC value reached the maximum value on the 2nd postoperative day in all patients and in the infected group. (Fig 1) However, when the means of the two groups are compared, the difference is not statistically significant (P=0.093)

A statistically significant increase in CRP values was observed in all patients after surgery, especially on the postoperative 2nd day (p=0.001). Especially in the infected group, it peaked on the 3rd day and then gradually decreased. (Fig 2) The two curves of the infected and non-infected groups were not parallel to each other (p=0.001). When the means of the two groups are compared, the difference is statistically significant (p=0.006).

A statistically significant increase was found in PCT values from the second postoperative day in the patients included in the study (p=0.002). The daily linear changes of PCT values in groups with and without infection are shown in Figures 3. When the mean scores of the infected and non-infected groups were compared, PCT values were found to be higher in the infected group (p=0.002).

A statistically significant increase was found in the erythrocyte sedimentation rates in the patients included in the study (p=0.001). When the means of the two groups are compared, the difference is statistically significant (p=0.001). An increase was noted on the second and third postoperative days in the infected group.

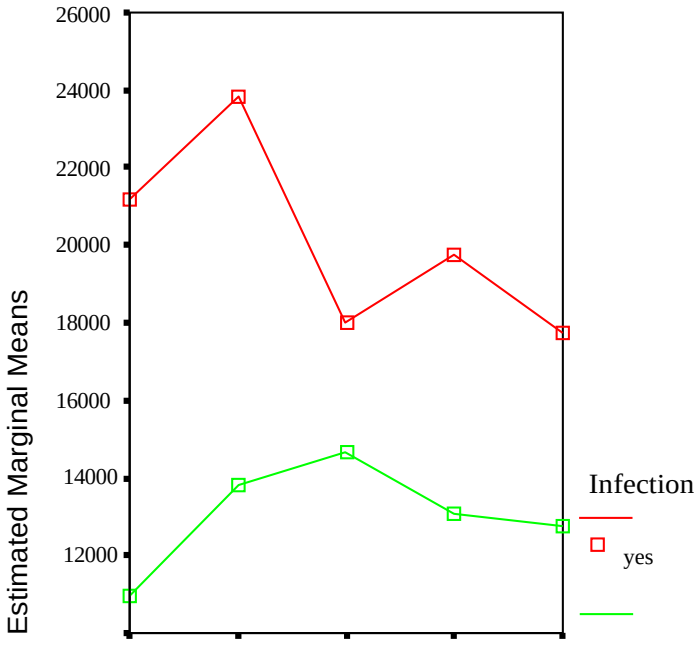

Figure 1. Daily Linear Changes of WBC Values

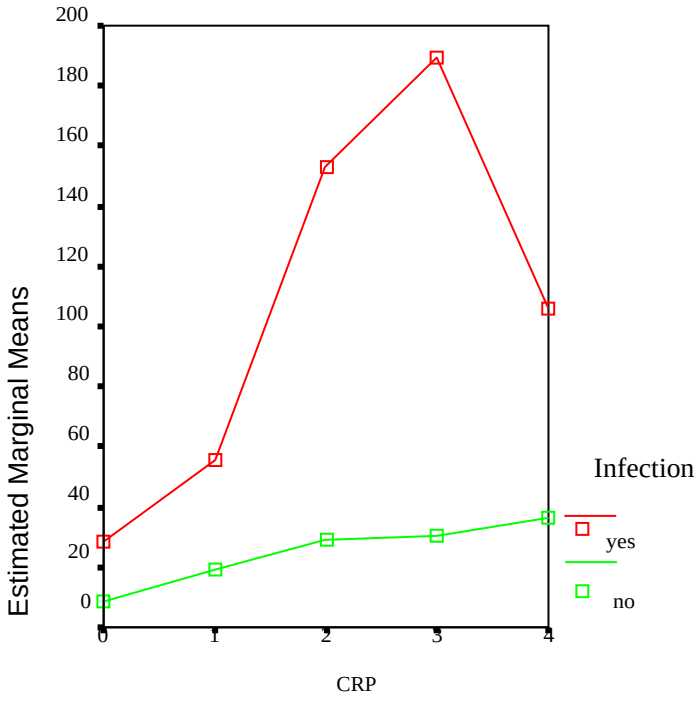

Figure 2. Daily Linear Changes of CRP Values in the Infected and Non-Infected Groups

Discussion

Postoperative fever above 38°C is common in the first few days after surgery. The cause of this fever is usually due to atelectasis due to surgery or to the inflammatory effect of the surgery. But it can be due to fever, embolism or infection. Therefore, it is important to determine the etiology of fever[12]. In the literature, CNS infections after neurosurgery constitute approximately 0.4% to 8% of all hospital infections. Age appears to be an important risk factor. The mortality rate due to meningitis cases developing after craniotomy may reach up to 30%[13].

In their study, Shimetani et al.[14] investigated CRP and PCT levels in serum and CSF in 30 patients with bacterial, viral or mycotic meningitis. They found that serum CRP levels were extremely elevated in 10% of all bacterial and viral meningitis cases, while PCT levels increased only in severe bacterial infections. They showed that there was no significant increase in PCT levels in CSF.

In the study of Mokart et al. on the role of PCT in the diagnosis of sepsis after major surgery, it was found that CRP levels were significantly higher in the group with PCT infection on postoperative 1st day, but CRP levels were similar in both groups[15].

In the study of Meisner' et al.[16], however, it was determined that the PCT value increased above 1 ng/ml in less than 9% of the cases after minor surgeries. The PCT value reached the highest level 24 hours after the operation in most of the patients.

In our study, the PCT levels of 44 patients who underwent surgical treatment were examined, the PCT levels in the non-infected group (n=34) ranged from 0.129 ng/mL to 0.159 ng/mL, the highest value did not exceed 1.15 ng/mL, and this value was reached after the first postoperative day. It has been observed that the mean tends to decrease after the first postoperative day.

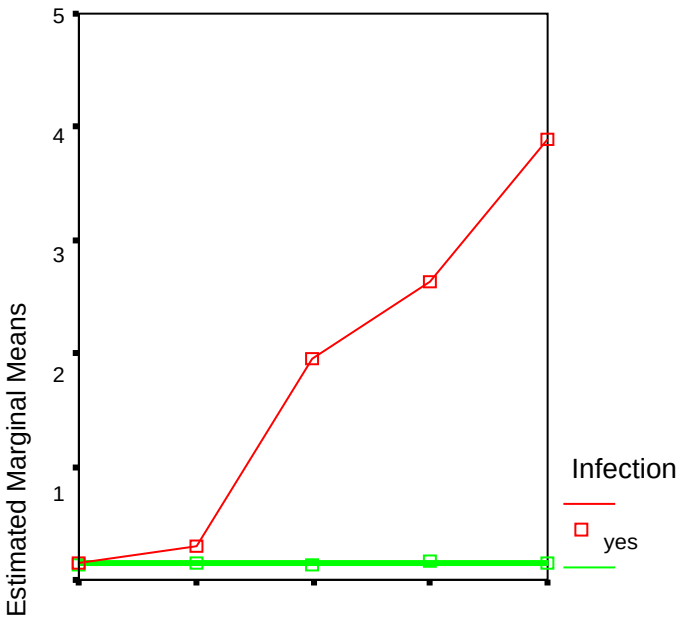

Figure 3. Daily Linear Changes of PCT Values in the Infected and Non-Infected Groups

PCT value above 1 ng/mL was detected in only one of the cases (2.7%). On the contrary, in the group with infection, PCT values increased significantly from the first postoperative day, and the mean value increased above 1.0 ng/ml on the second day. In the light of these results, it can be concluded that the inflammatory reaction caused by surgery does not cause a serious increase in PCT values and that PCT can be used in the early diagnosis of postoperative infections.

The mean preoperative value of CRP, which is one of the other parameters we looked at postoperatively, was found to be 12.0 (3-74.8) mg/L. When we look at the level of CRP after the operation, it was determined that the CRP values of the patients tended to increase after the operation (P=0.001). This increase was observed in both the infected and non-infected groups after craniotomy, and the mean of the infected group was found to be statistically significantly higher than the non-infected group (P=0.006). These results are similar to previous studies. Jensen[17] stated that in 50 patients who underwent lumbar disc surgery, CRP increased rapidly after the operation and reached peak values on the 2nd day. M. Neumaier et al. concluded that the CRP level is affected by the trauma site and, unlike other studies, where it reaches the maximum level on the second postoperative day, may be useful in detecting infection. However, they recommend basal and repetitive CRP measurement rather than a single CRP measurement[18]. Similar to this study, it supports other studies showing the value of CRP in surgical complications, especially deep surgical site infection[19,20].

The other parameter we used in our study was WBC. An increase in WBC values was observed in all cases after the operation (p=0.02). It was observed that WBC values reached the maximum value on the 2nd postoperative day in the non-infected and infected groups. However, when the means of the two groups are compared, the difference is not statistically significant.

Preoperative mean values of fever, which we evaluated in our study, were 36.9 Co. It was affected by the inflammatory response after surgery and started to decrease after peaking on the 1st day.

Postoperative complications occurred in 7 (3.1%) of the patients included in our study. Meningitis developed in 3 of the cases, urinary tract infection in 2, urinary tract infection and concomitant meningitis in 1, urinary tract and lung infection in 1, and lung infection in 1 case. In patients who developed postoperative meningitis, the PCT value increased approximately 100 times (3.12 ng/ml) on the 2nd day and was much higher than normal. CRP is postop. It entered a normal upward trend and started to decrease after reaching the peak value on the 2nd day. Like CRP in the WBC, it peaked on the 2nd day. The fever was found to be high on the 3rd day.

The findings in our study support the findings in the literature. PCT values were found to be above 0.1 ng/ml in all patients with systemic infection. In the light of the results we obtained, we can say that patients with PCT values above 0.1 ng/ml on the postoperative 2nd and 3rd days should be monitored more carefully in terms of postoperative infection.

In our study, the majority of patients who developed complications had CRP movements similar to those of patients who did not develop complications. CRP values are above normal (CRP>5 ng/ml) in all patients with and without complications. This indicates that CRP will not be used as an important parameter for the follow-up of postoperative infections.

In our study, another parameter in the etiology of fever was WBC. WBC does not follow a standard action like PCT and CRP after the operation. Despite this, WBC values were found to be well above the normal limit in patients who developed infections.

PCT is superior to WBC in detecting infections. Looking at the results of our study, we can say that the disadvantage of WBC is that it does not follow a standard kinetics after the operation. This makes WBC a less reliable parameter in determining the infective complications that may develop after the operation.

The results of our study support previous studies. Our study was conducted in a limited patient group (intracranial tumor) in neurosurgery and with a limited number of patients. However, it is a fundamental study in terms of evaluating the kinetics of PCT, a new infection parameter, after craniotomy and its superiority over other routinely used parameters.

Although PCT has been used in many surgical branches in recent years, the fact that our study is the first in the field of craniotomy makes it important for Neurosurgery. In the future, PCT's post-craniotomy system infections are followed-up, whether infection develops, the duration of antibiotic treatment, when it is to be decided, thus avoiding unnecessary and long-term antibiotics, as a result of which secondary infections caused by long-term antibiotic use are prevented and patient costs are reduced. and we think it will be a safe parameter.

Conclusion

Currently, there is no routinely used infection parameter that is specific for bacterial infections and is not affected by the inflammatory reaction caused by surgery. The fact that WBC follows a fluctuating pattern after the operation and is seriously affected by different surgical procedures applied to the same region makes WBC an unsafe parameter in the follow-up of infective complications after neurosurgery. The fact that PCT is not affected by the patient's age, gender, time until the operation, type of anesthesia and surgery shows that PCT can be used safely in neurosurgery in the early postoperative period for infection follow-up.

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, in which patients participated on a voluntary basis, was conducted in accordance with all ethical procedures /standards and the Declaration of Helsinki.
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References

1. Chung YG, Won YS, Kwon YJ, et al. Comparison of serum CRP and procalcitonin in patients after spine surgery. J Korean Neurosurg Soc. 2011;49(1):43-8. doi: 10.3340%2Fjkns.2011.49.1.43.
2. Arslan A, Olguner SK, Vedat AÇ, et al. Comparison of procalcitonin, C-reactive protein, white blood cell and body temperature in the diagnosis of ventriculostomy-associated infection. Cukurova Med J. 2019;44(1):69-76. doi: 10.17826/cumj.551752.
3. Klinger A, Buchfelder M, Schlaffer SM, et al. Infection surveillance in transsphenoidal pituitary surgery-comparison of lipopolysaccharide-binding-protein, interleukin 6, C-reactive protein, white blood cell count, erythrocyte sedimentation rate and body temperature. Acta Neurochir. 2013;155 (11): 2177-82. doi: 10.1007/s00701-013-1875-x.
4. Al-Jabi Y, El-Shawarby A Value of C-reactive protein after neurosurgery: a prospective study. Br J Neurosurg 2010;24(6):653-9. doi: 10.3109/02688697.2010.500408.
5. Boeken U, Feindt P, Gams E, et al. The influence of extracorporeal circulation and inflammatory responses such as SIRS and sepsis on secretion of procalcitonin. J Clin Basic Cardiol 1999;2(2):225-227.
6. Mokart D, Merlin M, Sannini A, et al. Procalcitonin, interleukin 6 and systemic inflammatory response syndrome (SIRS): early markers of postoperative sepsis after major surgery. Br J Anaesth. 2005;94(6):767-73. doi: 10.1093/bja/aei143.
7. Jaye DL, Waites KB. Clinical applications of C-reactive protein in pediatrics. Pediatr Infect Dis J 1997;16(8):735-47. doi: 10.1097/00006454-199708000-00003.
8. Anugu NR, Khan S. Comparing the Diagnostic Accuracy of Procalcitonin and C-Reactive Protein in Neonatal Sepsis: A Systematic Review. Cureus. 2021;13(11). doi: 10.7759/cureus.19485.
9. Covey DC, Albright JA. Clinical significance of the erytrocyte sedimentation rate in orthopaedic surgery. J Bone Joint Surg 1994;76(6):848-53. doi: 10.2106/00004623-199406000-00008.
10. Müler B, Kenneth LB. Procalcitonin: how a hormone became a marker and mediator of sepsis. Swiss Med Wkly 2001;131(41):595-602. doi: 2001/41/smw-09751
11. Meynaar I, Droog W, Batstra M, et al. In Critically Ill Patients, Serum Procalcitonin Is More Useful in Differentiating between Sepsis and SIRS than CRP, Il-6, or LBP. Crit Care Res Pract. 2011;15(1):594-645. doi: 10.1155/2011/594645.
12. Pile JC: Evaluating postoperative fever: a focused approach. Cleve Clin J Med 2006;73(1):62-6. doi: 10.3949/ccjm.73.suppl_1.s62.
13. Berker M, Hazer DB, Yücel T, et al. Complications of endoscopic surgery of the pituitary adeno- mas: analysis of 570 patients and review of the literature. Pituitary. 2012;15(3):288-300. doi: 10.1007/s11102-011-0368-2.
14. Shimetani N, Shimetani K, Mori M. Levels of three inflammation markers, C-reactive protein, serum amyloid A protein and procalcitonin, in the serum and cerebrospinal fluid of patients with meningitis. Scand J Clin Lab Invest. 2001;61(7):567-74. doi: 10.1080/003655101753218337.
15. Mokart D, Merlin M, Sannini A, et al. Procalcitonin, interleukin 6 and systemic inflammatory response syndrome (SIRS): early markers of postoperative sepsis after major surgery. Br J Anaesth. 2005;94(6):767-73. doi: 10.1093/bja/aei143.
16. Meisner M, Tschaikowsky K, Hutzler A, et al. Postoperative plasma concentrations of procalcitonin after different types of surgery. Intens Care Med 1998;24(1):680-4. doi: 10.1007/s001340050644.
17. Jensen CK, Brandslund I, Sogaard I. Lumbar disc surgery and variations in C-reactive protein, erythrocyte sedimentation rate and the complement split product C3d. Acta Neurochir 1988;90(1):42-4. doi: 10.1007/BF01541265.
18. Neumaier M, Scherer MA. C-reactive protein levels for early detection of postoperative

infection after fracture surgery in 787 patients Acta Orthopaedica 2008;79(3):428-32. doi: 10.1080/17453670710015355.
19. Sanzen L, Carlsson A S. The diagnostic value of C-reactive protein in infected total hip arthroplasies. J Bone Joint Surg (Br) 1989;71(1):638-41. doi: 10.1302/0301-620X.71B4.2768312.
20. Foglar C, Lindsey R W. C-reactive protein in orthopedics. Orthopedics 1998;21(1):687-91. doi: 10.3928/0147-7447-19980601-11.

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AN INVESTIGATION ON THE ANTIMICROBIAL ACTIVITY OF HEMP FIBER AND FABRICS AGAINIST COMMON NASOCOMIAL INFECTION AGENTS

KENEVİR LİFİ VE KUMAŞLARININ YAYGIN HASTANE ENFEKSİYON AJANLARINA KARŞI ANTİMİKROBİYAL AKTİVİTESİ ÜZERİNE BİR ARAŞTIRMA

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Abstract

Aim: The aim of this study is to investigate the antibacterial activity of hemp fiber and fabric against common nosocomial infections in intensive care units.

Methods: Raw hemp fiber, hemp fabric in commercial production and cotton fabric with similar properties were used as test material. Antimicrobial activity against 21 common bacterial species in intensive care units was tested using the "disk diffusion method".

Results: Hemp fiber and fabric did not show antibacterial or bacteriostatic effect against any of the 21 hospital infection agents.

Conclusions: The hemp fabric, which seems suitable for use in hospitals with its robust structure, resistance to frequent washing, has not been observed to be superior to cotton fabric in terms of antibacterial properties. However, the genus, species and growing area of the cannabis plant can affect these characteristics. For this reason, more studies on the subject are required.

Keywords: Nosocomial infections, textile materials, hemp, antimicrobial activity, disc diffusion method

Öz

Amaç: Bu çalışmanın amacı yoğun bakımlarda sık karşılaşılan hastane enfeksiyonu etkenlerine karşı kenevir lifi ve kumaşının antibakteriyel etkinliğinin araştırılmasıdır.

Yöntemler: Ham kenevir lifi, ticari üretimde olan kenevir kumaşı ve benzer özellikte pamuklu kumaş test materyali olarak kullanıldı. Yoğun bakımlarda sık karşılaşılan 21 bakteri türüne karşı antimikrobiyal aktivite "disk difüzyon yöntemi" kullanılarak test edildi.

Bulgular: Kenevir lifi ve kumaşı 21 hastane enfeksiyonu etkeninin hiçbirine karşı antibakteriyel ya da bakteriostatik etki göstermedi.

Sonuç: Sağlam yapısı, sık yıkanmaya karşı dayanıklığı ile hastanelerde kullanılmaya uygun görünen kenevir kumaşının antibakteriyel özellikler açısından pamuklu kumaşa göre bir üstünlüğü gözlenmemiştir. Ancak kenevir bitkisinin cinsi, türü ve yetiştirilme alanı bu özellikleri etkileyebilir. Bu sebeple konu ile ilgili daha fazla çalışma yapılması gerekmektedir.

Anahtar Kelimeler: Hastane enfeksiyonları, tekstil malzemeleri, kenevir, antimikrobiyal aktivite, disk difüzyon yöntemi

Introduction

Hospital infections, especially those occur in intensive care units are an important threat to patients' health. These infections that are mostly avoidable lead to longer hospital time, mortality and cost[1]. According to a report published in 2017 by the European Center for Disease Prevention and Control, 3.8 million cases of hospital infections were recorded in Europe annually[2]. In the United States, 100,000 cases of mortality occur due to hospital infections every year. Antibiotics are the most powerful weapons that we possess against infections but the increasing rate of antibiotic resistance is a serious concern[3]. In addition, multiple anti-biotherapies against resistant bacteria can lead to kidney disorders and immune system weaknesses [4]. Early recognition and prevention of infections is still an important step before anti-biotherapy.

The hospital environment plays an important role on the transmission of bacteria. Textile materials, which are widely used in hospitals, are important routes for bacterial transmission and carriage. Bed sheets, pillowcases, clothing of patients and health workers, protective equipment, surgical gowns, napkins, cloths, and other textile materials used in hospitals play an important role on the transmission and spread of infections. Especially health workers can carry infection between patients in this way. A study showed that 4.6 % of health workers are MRSA carriers[5]. Another study found that nurses that had contact with the belongings of MRSA patients have MRSA on their gloves and can carry them to the other patients [6]. The Covid-19 pandemic showed us that the virus can be spread by textiles as well as by aerosols and the practice of changing clothes after being in patients' rooms increased as an adaptation to pandemic conditions [7]. In previous studies, Acinetobacter baumannii, MRSA, VRE, Coagulase-negative staphylococci, Coryne-bacterium spp., Micrococcus spp., Bacillus spp., Non-fermentative gram-negative bacilli, Enterococcus spp., Saprophytic gram-negative bacilli and RNA viruses such as rotavirus have been detected in textile products used on the surgical field[8].

In the hospital environment, blood and tissue remains, food residues and other organic materials create perfect conditions for bacteria growth and transmission if the right textile materials are not used. It was shown that most bacteria can live up to a month on cotton fabrics that are commonly used in hospitals [9]. Antibacterial finishing of textile materials can suppress bacterial growth and transmission [10-12]. There are various methods to achieve antimicrobial activity on textile materials. Metals and metal salts, quaternary ammonium compounds, triclosan, dyes and other materials are commonly used for this purpose. Depending on the type of fibers and textile materials, different application methods of these compounds can be used such as a) coating the fabrics with these substances b) absorption of these materials into the textile structure and fixation by chemical bonding, c) use of antibacterial metal fibers and yarns and d) use of inherently antimicrobial natural fibers such as chitin and chitosan [13]. However, most of the finishing materials can only last a few weeks or months on fabrics due to repeated washing of textile materials [14]. This fact should also be taken into consideration when dealing with the hospital textiles that are subject to intensive washing.

The use of natural fiber materials against pathogenic bacteria has a long tradition. Literature shows some natural fibers possess antimicrobial effectiveness including hemp fiber [14-17]. The use of hemp fiber and textiles dates back to ancient times. However, during the industrial revolution, the improvements in cotton processing and later the invention of synthetic fibers bring about a loss of interest in natural bast fibers such as flax and hemp. The cultivation of industrial hemp was forbidden in many countries due to the psychoactive THC content in some hemp

varieties. However, in recent years, there is an increasing interest in industrial hemp due to its environmentally friendly nature and various other advantages. One of these advantages of hemp plant is its antimicrobial effectiveness shown in various studies[18,19]. Hemp plant contains various chemical ingredients most of which has been shown to be antibacterial such as cannabinoids, nitrogen compounds, amino acids, proteins, glycoproteins, enzymes, sugars, hydrocarbons, alcohols, aldehydes, ketones, acids, esters, lactones, steroids, terpenes, flavonglycosides, vitamins, and pigments [20,21]. Especially a group of cannabinoids extracted from hemp plant showed excellent antibacterial properties [18, 19, 22]. Cannabinoids are found in every part of hemp plant but they are especially abundant in leaf and flowers. Stalk, seed and roots contain much lower amounts of cannabinoids [23,24].

Hemp fibers are more nature-friendly and stronger when compared to cotton fibers and they are mostly referred to as antibacterial and antiallergenic by nature. Hemp fabrics are promising candidates as a potential replacement to the cotton fibers in hospital textiles due to their durability and antibacterial effectiveness. Inprasit et al., [25] showed that Neem extract-applied hemp fabrics are very effective against staphylococcus. Nissen et al., [26] investigated the microbial inhibition properties of extracts from three different hemp varieties. They showed that essential oils extracted from hemp especially those of Futura can effectively inhibit microbial growth. Radu and Sirghie [27] tested hemp fabrics treated with Ag nanoparticles and detected bacteriostatic activity against S. aureus and E. coli. To date, most of the studies dealt with the antimicrobial properties of hemp fabrics treated with antimicrobial agents. There are only a limited number of studies investigating the antimicrobial effectiveness of raw hemp fiber[23,25,27,28].

In this study, the antibacterial effectiveness of raw hemp fibers and two types of hemp fabrics against common hospital infections were investigated and compared with that of cotton which is commonly used in hospital textiles.

Materials and Methods

- *Tested textile materials*

Two types of hemp fabrics such as bleached hemp woven fabric (BHW), bleached hemp woven fabric with sizing (BHW-S) as well as raw hemp fibers (RHF) and cotton woven fabrics (CW) were used. Table 1 lists the characteristics of fibers and fabrics used in this study. Textile materials go through a series of processes from raw fibers to fabrics such as mercerization, bleaching, other preparatory processes, spinning, sizing, weaving, dyeing and finishing. In this study we used raw hemp fibers obtained from retting process without any further chemical treatment to especially keep lignin on the fibers which is known for its antibacterial properties. Besides raw hemp fibers, bleached and bleached/sized hemp fabrics were also used to see if there is any change in antimicrobial properties of raw fibers after these treatments. Commercial cotton fabrics were used as reference materials. Water-retted raw hemp fibers were purchased from a local hemp farmer in Kastamonu, Turkey. Plain-weave bleached hemp woven fabrics (BHW) were produced using a laboratory-type weaving machine located in our Materials Laboratory at Hemp Research Institute, Yozgat, Turkey. Bleached hemp woven fabrics with sizing (BHW-S) were purchased from Maeko Tessuti S.r.l., Milano, Italy. The characteristics of fabrics and raw hemp fibers were shown in Figure 1.

- *Selection of nosocomial infection agents*

Within the scope of this study, 21 microorganisms that were previously isolated and identified in the laboratory and stored at a temperature of -20 °C were tested (3 methicillin-resistant Staphylococcus aureus (MRSA), 3 methicillin-susceptible S. aureus (MSSA), 2 methicillin-resistant S. epidermidis (MRSE), 2 extended-spectrum beta-lactamase (ESBL) positive Escherichia coli, 2 ESBL positive Klebsiella pneumoniae, 4 vancomycin-resistant Enterococcus fecalis (VRE), 2 Carbapenem-resistant Pseudomonas aeruginosa, 2 Carbapenem-resistant Acinetobacter baumannii and 1 Colistin-resistant Acinetobacter baumannii]. Identification of microorganisms and antibiotic susceptibility tests were performed according to the manufacturer's recommendations on the Vitek 2 Compact (Biomerieux, France) device. Colistin susceptibility for A. baunmanii was tested using the liquid microdilution method in accordance with the recommendations of the European Committee on Antimicrobial Susceptibility Testing (Eucast). Standard strains (E. faecalis WDCM 00009, E. coli ATCC 25922, P. aeruginosa ATCC 27853, S. aureus ATCC 25923, S. aureus ATCC 4330) were used for quality control.

- *Antimicrobial activity testing*

The fabrics were cut into 5 mm2 pieces to determine their antibacterial activity, and then sterilized by autoclaving. Hemp plant fiber was used after being cut into 1cm long pieces and sterilized (Figure 2). The presence of the antibacterial effect of fabrics and hemp fiber against selected microorganisms was tested with the “Disc diffusion method” according to the standards of “Clinical and Laboratory Standard Institute (CLSI - M02-A10). Suspensions of 0.5 McFarland (108 microorganisms/ml) were prepared for the microorganisms to be tested. Inoculum taken from the suspensions with sterile swab was spread over the surface of Mueller-Hinton Agar (MHA) plates. 5 mm2 pieces of fabric and 1 cm hemp fibers were placed on agar plates inoculated. Media were evaluated for the presence of an inhibition zone after incubating at 35 ± 1 ° C for 18-24 hours.

Results

For this study, common intensive care infectious agents were tested. Hemp fibers, which are claimed to have antibacterial activity in some studies, were compared with other fabrics and fibers. Figure 2 and Table 2 show the antibacterial activity testing of fibers and fabrics, and various pathogens responsible for nosocomial infections and quality control strains, which were used for study. It was determined that hemp fiber (RHF), hemp fabrics (BHW and BHW-S) and cotton fabric (CW) do not have antibacterial activity against 21 bacteria, the most common cause of nosocomial infections including 3 MRSA, 3 MSSA, 2 MRSE, 2 ESBL-producing E. coli, 2 ESBL-producing K. pneumoniae, 4 VRE, 2 Carbapenem-resistant P. aeruginosa, 2 Carbapenem-resistant A. baumannii and 1 Colistin-resistant A. baumannii. Also, antimicrobial activity was not observed against quality control strains including E. faecalis WDCM00009, E. coli ATCC 25922, P. aeruginosa ATCC 27853, S. aureus ATCC 25923 and S. aureus ATCC 4330. The results obtained showed that hemp fibers and natural fabrics obtained from hemp fibers do not have antibacterial activity and do not have an advantage over cotton fabric in this respect.

Table 1. Characteristics of fibers and fabrics used in the study.

Sample code	Sample description	Fabric type	Yarn count (Nm)	Filling density (yarns/cm)	Warp density (yarns/cm)	Fabric areal weight (g/m^2)
RHF	Raw Hemp Fiber	–	–	–	–	–
BHW	Bleached Hemp Woven Fabric	Plain-weave (1/1)	26	40	10	160
BHW-S	Bleached Hemp Woven Fabric with sizing	Plain-weave (1/1)	24	20	22	170
CW	Cotton Woven Fabric	Plain-weave (1/1)	26	20	22	170

Raw hemp fibers (RHF); bleached hemp woven fabric (BHW); bleached hemp woven fabric with sizing (BHW-S); cotton woven fabric (CW).

Table 2. The common nosocomial infection pathogens selected for the study and the antimicrobial activity testing results of hemp and cotton fabric.

Bacteria; Patient isolates and Quality control strains (n = 26)	Fibers and fabrics used			
	RHF	BHW	BHW-S	CW
Enterococcus faecalis WDCM00009	-	-	-	-
Escherichia coli ATCC 25922	-	-	-	-
Pseudomonas aeruginosa ATCC 27853	-	-	-	-
Staphylococcus aureus ATCC 4330 (methicillin- resistant)				
Staphylococcus aureus ATCC 25923	-	-	-	-
Methicillin-resistant Staphylococcus epidermidis (patient isolate-1)	-	-	-	-
Methicillin-resistant Staphylococcus epidermidis (patient isolate-2)	-	-	-	-
Methicillin-resistant Staphylococcus aureus (patient isolate-1)	-	-	-	-
Methicillin-resistant Staphylococcus aureus (patient isolate-2)	-	-	-	-
Methicillin-resistant Staphylococcus aureus (patient isolate-3)	-	-	-	-
Methicillin- susceptible Staphylococcus aureus (patient isolate-1)	-	-	-	-
Methicillin-susceptible Staphylococcus aureus (patient isolate-2)	-	-	-	-
Methicillin-susceptible Staphylococcus aureus (patient isolate-3)	-	-	-	-
ESBL-producing Escherichia coli (patient isolate-1)	-	-	-	-
ESBL-producing Escherichia coli (patient isolate-2)	-	-	-	-
ESBL-producing Klebsiella pneumoniae (patient isolate-1)	-	-	-	-
ESBL-producing Klebsiella pneumoniae (patient isolate-2)	-	-	-	-
Vancomycin-resistant Enterococcus fecalis (patient isolate-1)	-	-	-	-
Vancomycin-resistant Enterococcus fecalis (patient isolate-2)	-	-	-	-
Vancomycin-resistant Enterococcus fecalis (patient isolate-3)	-	-	-	-
Vancomycin-resistant Enterococcus fecalis (patient isolate-4)	-	-	-	-
Carbapenem-resistant Pseudomonas aeruginosa (patient isolate-1)	-	-	-	-
Carbapenem-resistant Pseudomonas aeruginosa (patient isolate-2)	-	-	-	-
Carbapenem-resistant Acinetobacter baumannii (patient isolate-1)	-	-	-	-
Carbapenem-resistant Acinetobacter baumannii (patient isolate-2)	-	-	-	-
Colistin- resistant Acinetobacter baumannii (patient isolate-1)	-	-	-	-

Raw hemp fibers (RHF); bleached hemp woven fabric (BHW); bleached hemp woven fabric with sizing (BHW-S); cotton woven fabric (CW).

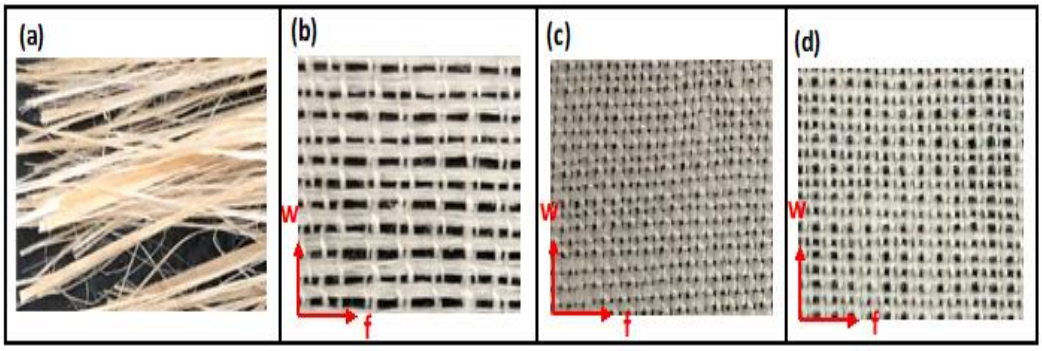

Figure 1. Fibers and fabrics used in the study (w: warp direction, f: filling direction). (a) Raw hemp fibers (RHF); (b) bleached hemp woven fabric (BHW); (c) bleached hemp woven fabric with sizing (BHW-S); (d) cotton woven fabric (CW).

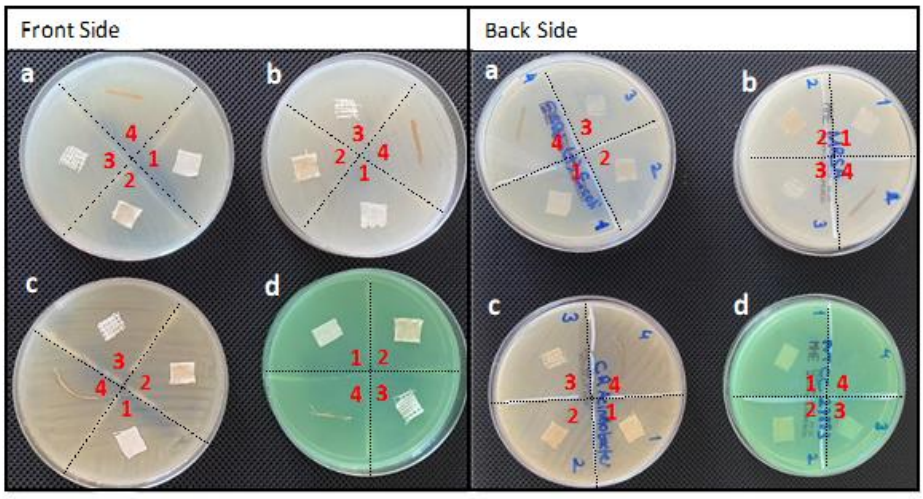

Figure 2. Antibacterial activity of hemp fiber and fabrics and cotton fabric by disc diffusion method against common nosocomial infection agents. (a) ESBL- producing *Escherichia coli*, (b) MRSA, (c) Carbapenem- resistant *Acinetobacter baumannii* (d) *Pseudomonas aeruginosa* ATCC 27853) 1: BHW-S, 2: CW 3: BHW, 4: RHF; MRSA: Methicillin-resistant *Staphylococcus aureus*; ESBL: Extended-spectrum beta-lactamases.

Discussion

The fact that the beds and covers used by the patients in the intensive care units have bactericidal properties or prevent the development of bacteria can make an important contribution to the prevention of hospital infections. Chairs, fabrics and curtains frequently used by patients and their relatives in waiting rooms or wards should be washed frequently. The durability of fabrics that are changed so frequently is

valuable in terms of costs. Hemp fabric, on the other hand, is a promising product in both respects with its durability and potential antibacterial activity[22]. Our study is designed to test this added value. We aimed to test the factors that are seen in intensive care units and constitute an important problem in terms of mortality and morbidity in hospital infections, which are the biggest cost expenses. However, this antibacterial property could not be seen in the hemp fabric in our tests. This situation can be explained by multiple reasons. First, it may have activity against an agent other than the 21 bacterial species we use. Another possible reason is that the raw material from which our hemp fabric is produced can have many sub-types.

The hemp plant is referred to as cannabis sativa (*C. sativa*) in the literature. Today, a total of 545 different compounds were isolated from *C. sativa*. Out of these, more than 100 compounds are phytocannabinoids that are specific to hemp varieties and show cannabinoid activity [29,30].

Phytocannabinoids are produced in leafs, flowers, bracteates and trichomes [31]. Resins secreted form trichomes protects the plant from its natural enemies and acts as a defense mechanism. It also protects the plant from moisture and heat. Cannabinoids are found in every part of a hemp plant but they are mostly present in leafs and flowers. Stalk, seeds and roots contain much lower amounts of cannabinoids [23]. Therefore it is reasonable to think that the antimicrobial effect is higher in leafs and flowers and lower in stalk and fibers. This can be the reason that an antimicrobial effect is not found in this study in any of the hemp fibers and fabrics against the tested bacteria which are common hospital bacteria found in intensive care units. Another reason for the lack of antimicrobial activity may be that we used fibers from a male plant. It is well-known that the male plants usually have fewer amounts of cannabinoids when compared to female ones[32]. A similar study conducted on flax fibers which are similar to hemp in terms of structure and the amount of chemical ingredients showed that there is not an apparent bacteriostatic effect of flax fiber against gram positive and gram-negative bacteria [33]. It was concluded that further study is needed to determine the effectiveness of hemp fiber and fabric against different types of pathogens.

Conclusion

Since hemp fibers are natural and durable products, they attract attention with their potential in hospital textiles. Although previous studies suggested antimicrobial activity of hemp extracts, in the current work, there is not a clear indication of the antimicrobial activity of raw hemp fiber and fabrics against tested infection agents. These findings can be interpreted as the end of a myth. It was concluded that further study is needed to determine comparatively the antimicrobial activity of hemp fiber produced from a female plant containing higher amounts of cannabinoids against nosocomial infection agents by both disc diffusion method and microdilution method.

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

Ethical approval is not required

References

1. Appendino G, Gibbons S, Giana A, et al. Antibacterial cannabinoids from Cannabis sativa: a structure-activity study. J. Nat. Prod., 2008:71, 8.
doi: 10.1021/np8002673

2. Borsa J, in "Handbook of Natural Fibers. Antimicrobial natural fibres", edited by R.M. Kozlowski and M. Mackiewicz-Talarczyk, Elsevier, 2012, Vol. 2, pp. 653-87. doi:10.1016/B978-0-12-818782-1.00020-1
3. Boyce JM. Environmental contamination makes an important contribution to hospital infection. J. Hosp. Infect. 2007;65:50-4. doi: 10.1016/S0195-6701(07)60015-2
4. Chang B, Frendl G, in "Essential Clinical Anesthesia Review Keywords, Questions Answers Boards. Nosocomial infections" edited by L. S. Aglio, R. W. Lekowski, R. D. Urman, Cambridge University Press, 2015, pp. 494-8.
5. Chastre J, Luyt CE, Wolff M. Serious Infections in the ICU: Evolving Concepts in Management and Prevention. Semin Respir Crit Care Med. 2019; 40(04): 417-8. doi: 10.1055/s-0039-1696663
6. Chun DTW, Foulk JA, McAlister DD. Testing for antibacterial properties of cotton/flax denim. Ind Crop Prod. 2009;29(2-3):371-6. doi:10.1016/j.indcrop.2008.07.009
7. Condò C, Messi P, Anacarso I, et al. Antimicrobial activity of silver doped fabrics for the production of hospital uniforms. New Microbiol. 2015;38:551-8.
8. Çalışkan UK, Yıldırım S. Hemp and Its Use in Health. Ankara Ecz Fak Derg. 2020;44(1):112-36. doi: 10.33483/jfpau.559665
9. Direkel Ş, Akpınar ES, Uzunoğlu Karagöz E, et al. Antibacterial Activity of Textile Products Used in Hospital Environment. Van Med. J., 2019;26:268-72. doi: 10.5505/vtd.2019.14238
10. Dayanandan P, Kaufman PB. Trichomes Of Cannabis Sativa L. American Journal of Botany. 1976;65:578-91. doi: 10.1002/j.1537-2197.1976.tb11846.x
11. Dulon M, Peters C, Schablon A, et al. MRSA carriage among healthcare workers in non-outbreak settings in Europe and the United States: a systematic review. BMC Infect Dis. 2014;14:363. doi: 10.1186/1471-2334-14-363
12. El Sohly MA, Slade D. Chemical constituents of marijuana: the complex mixture of natural cannabinoids. Life Sci. 2005;78:5. doi: 10.1016/j.lfs.2005.09.011
13. El Sohly MA, Gul W, in "Handbook of cannabis", edited by R. G. Pertwee, Oxford, London, UK 2014, vol 3, pp. 1093.
14. Eyi S. The Effects of Antimicrobial Medical Textile Products in Reducing Surgical Area Infections. Journal of Education and Research in Nursing, 2019;16:330-8. doi:10.5222/HEAD.2019.330
15. Fairbairn JW. The trichomes and glands of Cannabis sativa L. L Bull Narc. 1972;23:29-33.
16. Ferrer-Vilanova A, Ivanova K, Díaz-González M, et al. Smart Sensing Fabrics for Live Bacteria Detection. Proceedings. 2018;2(13):916. doi: 10.3390/proceedings2130916
17. Hao X, Yang Y, An I, Wang J, Han L. Study on Antibacterial Mechanism of Hemp Fiber. Adv Mat Res. 2014;887-8. doi: 10.4028/www.scientific.net/AMR.887-888.610
18. Husain SA, Husain SA, Khan OU, et al. Review of hygiene adaptations among UK doctors in controlling the spread of SARS-CoV-2 infection. Clin Med. 2021;21:e20. doi: 10.7861/clinmed.2020-0724
19. Inprasit T, Motina K, Pisitsak P, et al. Dyeability and Antibacterial Finishing of Hemp Fabric Using Natural Bioactive Neem Extract. Fiber Polym. 2018;19(10):2121-6. doi: 10.1007/s12221-018-8518-z
20. Khan BA, Warner P, Wang H. Antibacterial Properties of Hemp and Other Natural Fibre Plants: A Review. Bioresources. 2014;9:3642-59.
21. Koca O, Altoparlak U, Ayyildiz et al. Persistence of nosocomial pathogens on various fabrics. Eurasian J Med. 2012;44:28-31. doi: 10.5152/eajm.2012.06
22. Lone TA, Lone RA. Extraction of cannabinoids from cannabis sativa L plant and its potential antimicrobial activity. Universal Journal of Medicine and Dentistry. 2014;1:51-5.
23. López-Gigosos R, Mariscal A, Gutierrez-Bedmar M, et al. How long can nosocomial pathogens survive on textiles? A systematic review. Am J Infect Control. 2014;42:8. doi: 10.1016/j.ajic.2014.04.019
24. Morais DS, Guedes RM, Lopes MA. Antimicrobial Approaches for Textiles: From Research to Market. Materials. 2016;9: 6. doi: 10.3390/ma9060498
25. Neely AN, Maley M. Survival of Enterococci and Staphylococci on Hospital Fabrics and Plastic J Clin Microbiol. 2000;38:2. doi: 10.1128/jcm.38.2.724-726.2000
26. Nissen L, Zatta A, Stefanini I, et al. Characterization and antimicrobial activity of essential oils of industrial hemp varieties (Cannabis sativa L.) Fitoterapia, 2010;81:5. doi: 10.1016/j.fitote.2009.11.010
27. Radwan MM, El Sohly MA, Slade D, et al. Non-cannabinoid constituents from a high potency Cannabis sativa variety. Phytochemistry. 2008;69(14):2627-33. doi: 10.1016/j.phytochem.2008.07.010

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THE ROLE OF THE SYSTEMIC IMMUNE-INFLAMMATION INDEX IN PREDICTING RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY

KARDİYAK RESENKRONİZASYON TEDAVİSİNE YANITIN ÖNGÖRÜLMESİNDE SİSTEMİK BAĞIŞIKLIK-İNFLAMATUVAR İNDEKSİNİN ROLÜ

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Abstract

Aim: Cardiac resynchronization therapy (CRT) is a reliable treatment modality in patients with systolic dysfunction. However, not every patient appears to benefit from CRT. The systemic immune inflammation index (SII) is closely linked to the poor prognosis of various cardiovascular disorders. However, there is no study investigating whether SII has predictive value in determining response to CRT in dilated cardiomyopathy patients. Therefore, we intend to investigate the association between SII and response to CRT.

Methods: A total of 220 patients (mean age 61.2±10.8 years; 120 men) implanted with CRT were involved in this study. Echocardiographic and laboratory measurements were evaluated prior to CRT. Response to CRT was determined as a≥ 15% decrease in left ventricular end-systolic volume at one-year follow-up.

Results: Patients grouped as CRT responders and non-responders. Of these, 143 (64.6%) were considered to be CRT responders, while the remaining 77 (33.4%) were non-responders. Female sex (OR: 3.823, CI: 1.568-9.324 p=0.003), QRS duration (OR: 1.224, CI: 1.158-1.335 p<0.001), and SII (OR: 0.996 CI: 0.995-0.997 p<0.001) were shown to be independent predictors of CRT response in multivariate analysis. A cut-off value of SII >825 estimated no response to CRT with 80% sensitivity and 75% specificity.

Conclusions: SII was associated with unresponsiveness to CRT. Therefore, it may be used to determine optimal patient selection for CRT implantation in routine clinical practice.

Keywords: Cardiac resynchronization therapy, systemic immune-inflammation index, heart failure

Öz

Amaç: Kardiyak resenkronizasyon tedavisi (KRT), sistolik disfonksiyonu olan hastalarda güvenilir bir tedavi yöntemidir. Ancak, KRT'nin faydası belli hasta grupları ile sınırlıdır. Sistemik immün inflamatuvar indeks (SII), çeşitli kardiyovasküler bozuklukların kötü prognozu ile ilişkilidir. Bununla birlikte, dilate kardiyomiyopati hastalarında SII'nin KRT'ye yanıtı belirlemede prediktif değeri olup olmadığını araştıran bir çalışma bulunmamaktadır. Bu nedenle, bu çalışmada SII ile KRT'ye yanıt arasındaki ilişkiyi araştırmak amaçlandı.

Yöntemler: Bu çalışmaya KRT implante edilen toplam 220 hasta (ortalama yaş 61,2±10,8 yıl; 120 erkek) dahil edildi. KRT öncesi ekokardiyografi ve laboratuvar ölçümleri değerlendirildi. KRT'ye yanıt, bir yıllık takipte sol ventrikül sistol sonu hacminde ≥ %15 azalma olarak belirlendi.

Bulgular: Hastalar, KRT'ye yanıt verenler ve yanıt vermeyenler olarak gruplandırıldı. Bunlardan 143'ü (%64,6) KRT'ye yanıt veren olarak kabul edilirken, kalan 77'si (%33,4) yanıt vermeyendi. Kadın cinsiyet (OR: 3.823, CI: 1.568-9.324 p=0.003), QRS süresi (OR: 1.224, CI: 1.158-1.335 p<0.001) ve SII (OR: 0.996 CI: 0.995-0.997 p<0.001) çok değişkenli analizde KRT yanıtının bağımsız öngörücüleri olarak bulundu. SII >825'lik bir sınır değeri, %80 duyarlılık ve %75 özgüllük ile KRT'ye yanıt olmadığını öngördürmüştür.

Sonuç: Bu çalışmada SII'nin KRT'ye yanıtsızlığı öngördüğü gösterilmiştir. Bu nedenle SII rutin klinik uygulamada KRT implantasyonu için optimal hasta seçimini belirlemede kullanılabilir.

Anahtar Kelimeler: Kardiyak resenkronizasyon tedavisi, sistemik immün-inflamatuvar indeks, kalp yetmezliği

Introduction

Myocardial dysfunction is a progressive and complicated clinical disorder associated with ventricular remodeling and changes in intracardiac pressure. Cardiac resynchronization therapy (CRT) is an effective interventional treatment method in dilated cardiomyopathy patients with wide QRS duration[1]. CRT increases patients' symptom-free days and duration of exercise, and reduces hospital admissions and mortality for heart failure[1]. However, not all patients benefit equally from CRT[2].

Previous studies have reported that female gender, non-ischemic cardiomyopathy, left bundle branch block (LBBB), longer QRS duration, and sinus rhythm is associated with a positive response to CRT[3]. However, limited data are still available to determine which patients will benefit from CRT. Overall, one-third of patients are unresponsive to CRT[2,4].

Several inflammatory mediators and immune system cells [lymphocytes (L), neutrophils (N), platelets (P), etc.] play a significant role in pathogenesis of myocardial dysfunction[5]. However, the pathophysiological basis of the interaction among leukocyte subsets, inflammatory markers, and heart failure is complex[6]. Although there have been some studies using inflammatory biomarkers or immune system cells to determine the patient's response to CRT, none have been able to evaluate previously identified pathophysiological mechanisms as a whole in the similar patient group[7,8,9,10]. Therefore, there is still a need to identify different predictors that reveal different aspects of cardiomyopathy.

The systemic immune-inflammation index (SII) is a new inflammatory biomarker that incorporates lymphocyte (L), neutrophil (N), and platelet (P) counts[11]. So far, it has been affirmed that SII is closely linked to the poor prognosis of various cardiovascular disorders, such as myocardial infarction, infective endocarditis, aortic valve disease, and heart failure, and showed good application prospects[12,13,14,15]. However, there are no studies investigating whether SII has predictive value in determining response to CRT.

In light of this, our study sought to elucidate the role of SII as a potential predictor of response to CRT in heart failure patients.

Materials and Methods

- *Study population*

This retrospective study involved 220 consecutive patients with systolic dysfunction (mean age: 61.2±10.8 years; male: 120), who were implanted with CRT at a tertiary hospital between March 2014, and April 2021. Ethical approval was taken from the Kosuyolu Training and Research Hospital local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.2022/10/606). Written and oral informed permission was taken from each patient. Patients with (1) symptomatic chronic congestive dilated cardiomyopathy despite optimal medical therapy [New York Heart Association (NYHA) functional class II, III or ambulatory class IV)], (2) left ventricular ejection fraction (LVEF) ≤ 35% and wide QRS duration (> 130 ms) were included in the study. QRS duration was evaluated from all possible leads in the 12-lead electrocardiogram (ECG) recorded 1 month prior to CRT implantation and the longest QRS duration was analyzed.

Patients with atrial fibrillation (AF), bundle branch blocks other than LBBB, decompensated heart failure, history of coronary artery revascularization within six months, acute or chronic all inflammatory or infectious diseases, hematologic diseases, malignancies, renal or hepatic diseases, left ventricular lead placed in branches other than the lateral or postero-lateral branches of the coronary sinus were excluded from the study. Moreover, patients without close follow-up (follow-up interval of fewer than 12 months) and detailed clinical information were also not included in the study.

Figure 1 shows patient selection and exclusion criteria.

The study participants were categorized into two groups based on their response to CRT. A ≥ 15% reduction in left ventricular end-systolic volume (LVESV) (compared to baseline) at 12 months follow-up was classified as CRT responders[16].

Baseline clinical and demographic characteristics were recorded for each patient, including age, gender, hypertension (HT), diabetes mellitus (DM), heart failure etiology, and other comorbidities. Patients with significant coronary artery disease and/or a previous history of the acute coronary syndrome were classified as ischemic. Patients without a history of the acute coronary syndrome and ≥50% evidence of coronary atherosclerotic lesions were classified as non-ischemic.

We have followed up the patients for 1 year after CRT implantation and clinical examinations, routine laboratory tests, and echocardiographic measurements (at baseline and 12 months after CRT implantation) were performed. Heart failure functional assessment was assessed during routine clinical examinations with the NYHA classification.

All patients received the maximum tolerated doses [beta blockers, angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA), and diuretics] before and after CRT implantation.

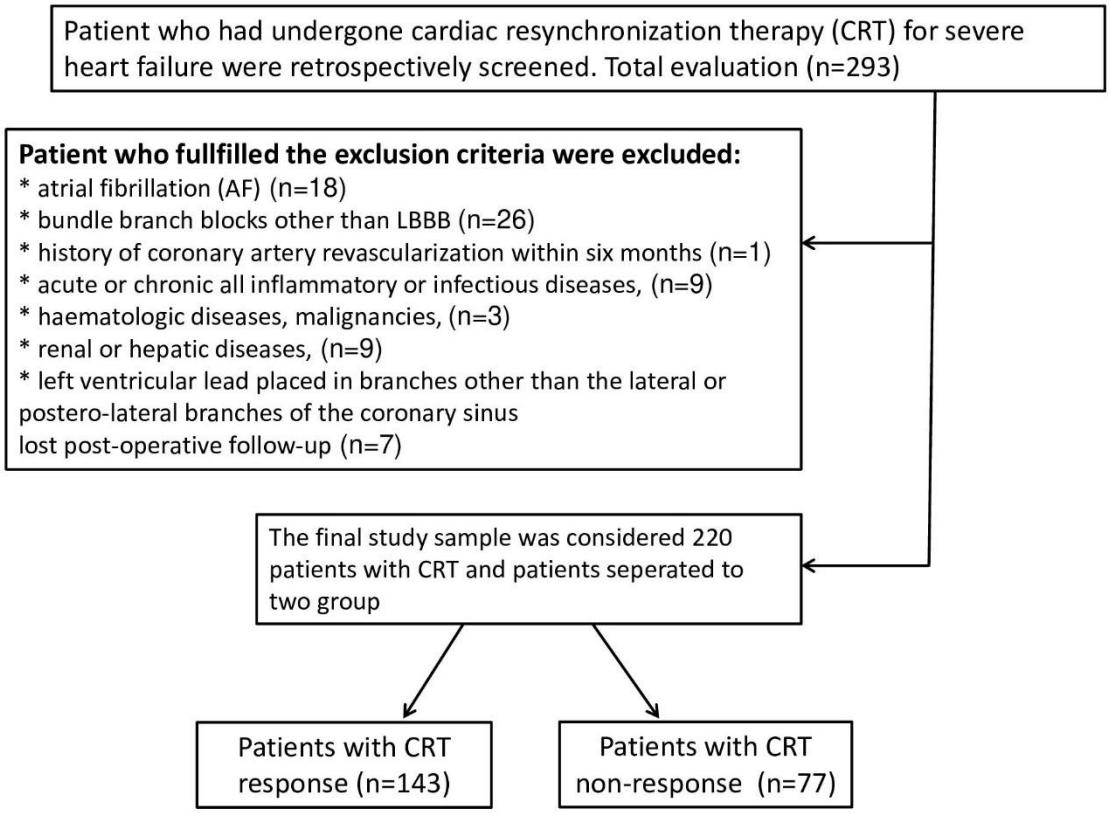

Figure 1. Patient inclusion and exclusion flow chart

- *Echocardiography*

Transthoracic echocardiography (TTE) (VIVID 7) was performed in all patients both before and 12 months after the CRT procedure. After CRT implantation, all echocardiographic measurements were evaluated while the CRT was in active pacing mode. Left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) were measured from standard view. Teicholz formula was used to calculate left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV). To calculate the LVEF the modified biplane Simpson method was used[17].

- *Blood samples*

Laboratory parameters were measure prior to CRT implantation as part of the routine clinical evaluation. Complete blood count (CBC), including neutrophils (N (, lymphocytes (L) and platelets (P), was analyzed without delay. The analyzer automatically calculated the absolute numbers of white blood cell (WBC) subgroups (neutrophils N, lymphocytes L, etc.). All other laboratory parameters were measured using commercially available kits. The SII was calculated as neutrophil-to-lymphocyte ratio (N/L) X total platelet count (P) [SII= (N/L ratio) X P][11].

- *CRT device implantation*

CRT devices were implanted transvenously, targeting the lateral or posterolateral coronary sinus branch for left ventricular lead position in the vast majority of patients[1]. Epicardial lead was placed in the posterolateral region by a minimally invasive method by the cardiothoracic surgeon in 16 cases where transvenous lead could not be placed due to procedural difficulties.
The CRT device mode was set to DDD or DDDR mode to maximize biventricular pacing with 100 ms atrioventricular sensing delay and 130 ms paced delay, optimized according to our clinic's standard protocols. During follow-up, lead positions and pacing mode were analyzed at regular intervals. Biventricular stimulation rate was over 90% in all patients (96.2% ± 1.8%).

- *Statistical analysis*

SPSS version 21 (SPSS, Inc., Chicago, Illinois) was used to carry out statistical evaluation. After determining the CRT response group by the given formula initially, patients were divided into two groups as response (+) and non-response (-). Continuous and normally distributed variables were compared through the two-tailed Student t-test which were presented as mean values, and non-normally distributed continuous variables were tested by Mann Whitney u test which were presented as interquartile ranges.
In addition, a percentage scheme was used to present categorical variables which were analyzed by a chi-square test. The second categorization was made before and after the CRT implantation group. Related parameters were compared by paired sample t-test between these groups. The unadjusted $p<0.1$ value was considered to be clinically significant. At the last stage, parameters that were clinically associated with CRT response were included in univariate and multivariate regression analyses respectively. In addition, the predictive value of SII was estimated by the areas under the receiver operating characteristic (ROC) curve analysis.

Results

A total of 220 patients (mean age 61.2±10.8 years, 120 men) with LBBB and heart failure underwent successful CRT implantation. Drug treatment included ACEI or ARB in 92%, beta-blockers in 95%, MRA in 85%, diuretics in 88%. All medications were continued after CRT implantation. The medication was similar in both groups.

Patients were categorized into two groups based on response to CRT. Of these, 143 (64.6%) were considered to be CRT responders, while the remaining 77 (33.4%) were non-responders. Baseline clinical, hematological, electrocardiographic and echocardiographic parameters are displayed in Table 1.

Age, HT, DM, alcohol consumption and smoking were similar between responders and non-responders. There was also no significant difference in biventricular stimulation rate between the two groups (96.4% vs. 94.6%, respectively (p=0.530).

Mean NYHA functional class before CRT implantation in responders and non-responders were 2.79±0.5 and 2.69±0.6, respectively (p=0.083). Also, preprocedural LVEF, LVEDD, and LVEDV were similar in both groups. However, pre-procedure LVESD, and LVESV were significantly lower in patients who responded to CRT. Responders to CRT were more often female, had non-ischemic cardiomyopathy, and had a wider QRS duration on the 12-lead ECG (Table 1).

Table 1. Baseline demographic, echocardiographic and hematological parameters of responder and non-responder patients

Variables	All (n=220)	CRT response (n=143)	CRT non-response (n=77)	p
Female (n,%)	100 (45.5)	80 (55.9)	20 (26)	0.002*
Age (years)	61.2±10.8	60.7±11.2	62.2±10	0.335
HT (n,%)	98 (44.5)	64 (44.8)	34 (44.2)	0.523
DM (n,%)	52 (23.6)	34 (23.8)	18 (23.4)	0.543
Alcohol (n,%)	33 (15.0)	21 (14.6)	12 (15.5)	0.243
Smoking (n,%)	78 (35.4)	51 (35.6)	27 (35.0)	0.546
Ischemic (n,%)	54 (24.5)	24 (16.8)	30 (39)	<0.001*
Nonischemic (n,%)	166 (75.5)	119 (83.2)	47 (61)	<0.001*
LVEF (%)	26±5.2	26.9±4.9	26.2±5.8	0.310
LVEDD (mm)	6.9±0.7	6.9±0.7	7±0.9	0.573
LVESD (mm)	5.9±0.7	5.8±0.7	6.1±0.8	0.003*
LVEDV (ml)	256±64	253±58	260±74	0.433
LVESV (ml)	181±52	173±48	196±57	0.002*
NLR	2.9 (2.2-3.9)	2.5 (1.9-3.3)	3.7 (3-4.7)	<0.001*
PLR	121 (94-169)	107 (91-136)	194 (150-258)	<0.001*
SII	617 (443-958)	481 (391-706)	1007 (866-1060)	<0.001*
CRP (mg/L)	3 (1-3.6)	3.1 (0.9-3.8)	1.9 (1.2-3.1)	0.511
WBC ($x10^9$/L)	8.1±1.6	8.2±1.6	8±1.7	0.336
QRS duration (ms)	151±9.1	155.5±8.6	144.9±5.3	<0.001*
NYHA class (mean)	2.75±0.5	2.79±0.5	2.69±0.6	0.083

CRT: cardiac resynchronization therapy, DM: diabetes mellitus, HT: hypertension, LVEDD: left ventricular end-diastolic diameter, LVEF: left ventricular ejection fraction, LVEDV: left ventricular end diastolic volume, LVESD: left ventricular end-systolic diameter, LVESV: left ventricular end systolic volume, NLR: neutrophil/lymphocyte ratio, NYHA: New York Heart Association, PLR: platelet/lymphocyte ratio, SII: systemic immune inflammation index. Numerical variables were presented as median with range or mean ±SD, and categorical variables as number and percentages. *P<0.05

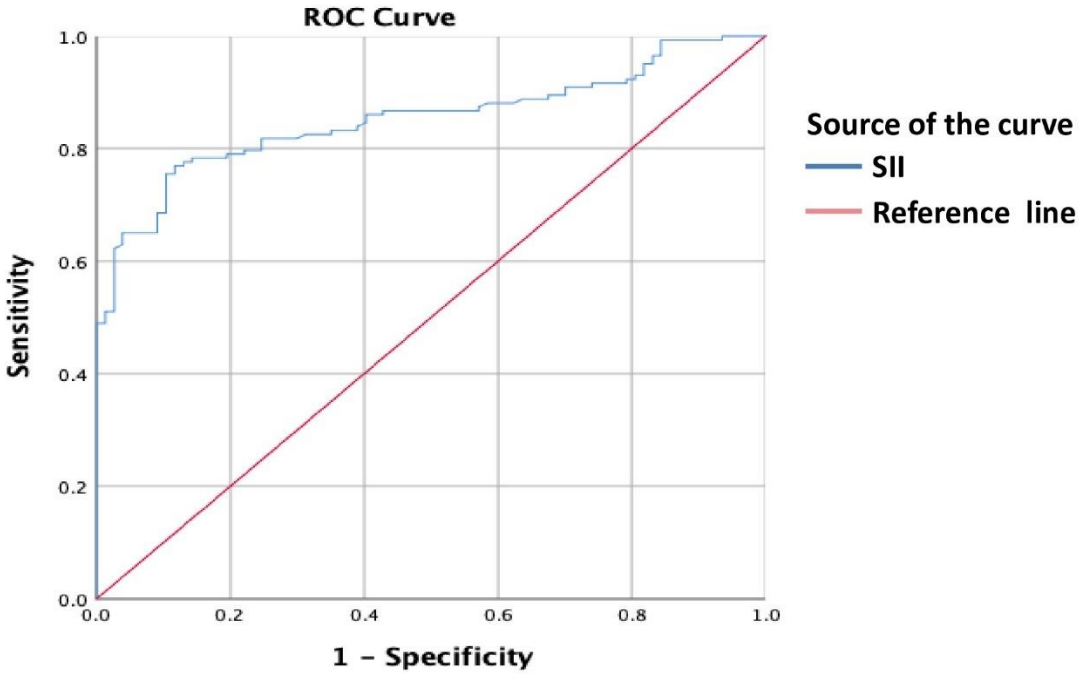

Figure 2: Receiver operating characteristic curve analysis of SII for prediction of response to CRT

Table 2. Comparison of baseline and 1 year of echocardiographic parameters in responder and non-responder patients

Variables	CRT response		p	CRT non-response		p
	Baseline	1 year		Baseline	1 year	
LVEF (%)	26.9±4.9	38.4±7.5	<0.001*	26.2±5.8	21±5.2	<0.001*
LVEDD(mm)	6.9±0.7	6.2±0.5	<0.001*	6.9±0.3	7±0.5	<0.001*
LVESD(mm)	5.8±0.7	4.9±0.7	<0.001*	5.8±0.3	5.9±0.2	<0.001*
LVEDV(ml)	253±58	195±38	<0.001*	248.6±27.3	259.6±44	<0.001*
LVESV(ml)	173±48	121±41	<0.001*	172.3±20.4	175.6±14	<0.001*

LVEDD: left ventricular end-diastolic diameter, LVEF: left ventricular ejection fraction, LVEDV: left ventricular end diastolic volume, LVESD: left ventricular end-systolic diameter, LVESV: left ventricular end systolic volume.
Numerical variables were presented as mean ±SD., *P<0.05

Table 3. Independent predictors of CRT response in multivariate analysis

Variables	Univariable OR (95% CI)	p	Multivariable OR (95% CI)	p
Age	0.988 (0.962-1.014)	0.353		
Female	2.473 (1.338-4.570)	0.004*	3.823 (1.568-9.324)	0.003*
Nonischemic	3.165 (1.679-5.967)	<0.001*	1.741 (0.787-3.859)	0.171
Pre-QRS	1.207 (1.146-1.271)	<0.001*	1.224 (1.158-1.335)	<0.001*
Pre-LVEF	1.028 (0.975-1.083)	0.309		
Pre-LVESD	0.569 (0.389-0.832)	0.004*	5.124(0.065-10.642)	0.330
Pre-LVESV	0.992 (0.986-0.997)	0.003*	0.958 (0.884-1.037)	0.288
Pre-SII	0.996 (0.995-0.997)	<0.001*	0.996 (0.995-0.997)	<0.001*
Pre-NLR	0.431 (0.323-0.574)	<0.001*	1.493 (0.862-2.586)	0.152
Pre-PLR	0.977 (0.970-0.984)	<0.001*	0.995 (0.980-1.009)	0.455

LVEF: left ventricular ejection fraction, LVESD: left ventricular end-systolic diameter, LVESV: left ventricular end systolic volume, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, Pre: pre- procedural, SII: systemic immune inflammation index. *P<0.05

Before CRT implantation, median neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and SII were significantly higher in the CRT non-responder group than in the responder group. However, WBC and CRP levels were similar in both groups before CRT implantation (Table 1).

Echocardiographic parameters before and 12 months after CRT implantation are presented in Table 2. At 1 year after CRT implantation, LVEF had significantly improved from 26.9±4.9% to 38.4±7.5% in responders. Also, LVEDD, LVESD, LVEDV, LVESV had significantly decreased in responders. However, no significant improvement in left ventricular size, volume, and function was detected in those who did not respond to CRT (Table 2).

We performed regression analysis to determine predictors associated with CRT response. Female sex (OR: 3.823, CI: 1.568-9.324 p=0.003), QRS duration (OR: 1.224, CI: 1.158-1.335 p<0.001), and SII (OR: 0.996 CI: 0.995-0.997 p<0.001) were found to be independent predictors of CRT response in multivariate analysis. (Figure 2)

The ROC curve analysis was performed to identify the relationship between SII and response to CRT. A cut-off value of SII in predicting non-response to CRT was 825 with 80% sensitivity and 75% specificity (area under the curve (AUC): 0.853 (95% confidence interval (CI): 0.803–0.902, p< 0.001).

Discussion

In the present study, we evaluated several aspects, including clinical, biochemical, echocardiographic, and electrocardiographic determinants of CRT responsiveness at 1 year following CRT implantation. The main finding of this study is that high level of SII was associated with non-response to CRT. In addition, female gender and longer QRS duration were revealed to be significant determinants of response to CRT.

Several prognostic parameters have already been introduced to predict the CRT response in patients undergoing CRT implantation for heart failure. These parameters are primarily based on demographic and clinical parameters including age, gender, heart failure etiology, LBBB morphology

and QRS duration[3]. Additionally, serum levels of inflammatory markers, lymphocyte count, NLR, and PLR are key prognostic inflammatory parameters that support the predictive value of these indices[7,8,9,10]. However, no data exist on the association between SII and CRT response, which was evaluated in patients with dilated cardiomiyopathy in this study. And the results confirmed that high level of SII could be an independent predictor for CRT unresponsiveness. A cut-off value of SII >825 predicted inconclusive CRT response with 80% sensitivity and 75% specificity. As we know, the relationship between SII and response to CRT was firstly evaluated by the current study. Recently, Tang et al. investigated the potential predictive value of SII in 4606 patients with decompansated heart failure to assess poor prognosis, which showed that the SII value was divided into three parts as <1144.28, ≥1144.28, <2730.11 and ≥2730.11, and the third tertile of the SII group was significantly associated with short term mortalities, as well as the high risk of major adverse cardiac events (MACEs) occurence[15]. Also, Hayiroglu et al. investigated the effect of SII on long-term mortality and true ICD shock during 10 years follow-up in patients with ICD. They found that, in patients with an SII ≥1119, mortality and appropriate ICD shock rates were significantly higher at long-term follow-up[18].

The SII may be considered a modified but reliable version of NLR and PLR[11,19]. In a study by Agacdiken et al. NLR was significantly higher in the CRT non-responder group, and a higher baseline NLR was associated with CRT unresponsiveness[7]. Similarly, Balcı et al. showed that higher PLR and NLR values were related with inconclusive CRT response[8]. However, in our study, although NLR and PLR were elevated in the CRT non-responder group and were associated with CRT non-responsiveness in univariate analysis, multivariate analysis eliminated their significance. Indeed, our study highlighted the independent efficacy of SII for CRT non-responsiveness independent of NLR and PLR. As the combined effect of NLR and PLR was assessed at SII, it may have better predicted CRT non-response independent of other variables.

In the same line with previous large randomised clinical trials, female gender and longer QRS duration were revealed to be independent predictors of CRT response. Unlike other major studies, the non-ischemic etiology was not associated with CRT response in multivariate analysis. This consequnces may arise from that the majority of the patients in the current study had non-ischemic etiology and therefore the effect of ischemic etiology was not adequately evaluated.

Conclusion

SII, an inexpensive and readily available test calculated from a complete blood count, was found to be associated with unresponsiveness to CRT. Therefore, it may be used to determine optimal patient selection for CRT implantation in routine clinical practice.

- *Limitations*

The current study has a few limitations. First of all, as well as being retrospective study, it was also a single-center experience. Secondly, the follow-up period after CRT implantation was relatively short. It would be important to identify additional changes in left ventricular volume and function after a longer follow-up period. Finally, well established inflammatory markers were not evaluated and compared with SII as they are expensive and not readily available in daily practice.

Author contributions

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

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

Authors declared no financial support.

Ethical approval

Ethical approval was taken from the Kosuyolu Training and Research Hospital local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.2022/10/606).

References

1. Bristow MR, Saxon LA, Boehmer J, et al. Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350(21):2140-50. doi: 10.1056/NEJMoa032423
2. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the MUltisite STimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol. 2002;40(1):111-8. doi: 10.1016/S0735-1097(02)01932-0
3. Goldenberg I, Moss AJ, Hall WJ, et al. Predictors of response to cardiac resynchronization therapy in the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT). Circulation. 2011;124(14):1527-36. doi: 10.1161/CIRCULATIONAHA.110.014324
4. Abraham WT, Fisher WG, Smith AL, et al. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346(24):1845-53. doi: 10.1056/NEJMoa013168
5. Vasan RS, Sullivan LM, Roubenoff R, et al. Inflammatory markers and risk of heart failure in elderly subjects without prior myocardial infarction: the Framingham Heart Study. Circulation. 2003;107(11):1486-91. doi: 10.1161/01.CIR.0000057810.48709.F6
6. Dick SA, Epelman S. Chronic Heart Failure and Inflammation: What Do We Really Know? Circ Res. 2016;119(1):159-76. doi: 10.1161/CIRCRESAHA.116.308030
7. Agacdiken A, Celikyurt U, Sahin T, et al. Neutrophil-to-lymphocyte ratio predicts response to cardiac resynchronization therapy. Med Sci Monit. 2013;19:373-7. doi: 10.12659/MSM.883915
8. Balci KG, Balci MM, Sen F, et al. The role of baseline indirect inflammatory markers in prediction of response to cardiac resynchronisation therapy. Kardiol Pol. 2016;74(2):119-26. doi: 10.5603/KP.a2015.0142
9. Boros AM, Széplaki G, Perge P, et al. The ratio of the neutrophil leucocytes to the lymphocytes predicts the outcome after cardiac resynchronization therapy. Europace. 2016;18(5):747-54. doi: 10.1093/europace/euv100
10. Liquori ME, Christenson RH, Collinson PO, et al. Cardiac biomarkers in heart failure. Clin Biochem. 2014;47(6):327-37. doi: 10.1016/j.clinbiochem.2014.01.032
11. Wang BL, Tian L, Gao XH, et al. Dynamic change of the systemic immune inflammation index predicts the prognosis of patients with hepatocellular carcinoma after curative resection. Clin Chem Lab Med. 2016;54(12):1963-69. doi: 10.1515/cclm-2015-1191
12. Yang YL, Wu CH, Hsu PF, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. Eur J Clin Invest. 2020;50(5):e13230. doi: 10.1111/eci.13230
13. Agus HZ, Kahraman S, Arslan C, et al. Systemic immune-inflammation index predicts mortality in infective endocarditis. JSaudi Heart Assoc. 2020;32(1):58-64. doi: 10.37616/2212-5043.1010
14. Tosu AR, Kalyoncuoglu M, Biter Hİ, et al. Prognostic Value of Systemic Immune-Inflammation Index for Major Adverse Cardiac Events and Mortality in Severe Aortic Stenosis Patients after TAVI. Medicina (Kaunas). 2021;57(6):588. doi: 10.3390/medicina57060588
15. Tang Y, Zeng X, Feng Y, et al. Association of Systemic Immune-Inflammation Index with Short-Term Mortality of Congestive Heart Failure: A Retrospective Cohort Study. Front Cardiovasc Med. 2021;8:753133. doi: 10.3389/fcvm.2021.753133
16. Verdonschot JAJ, Merken JJ, van Stipdonk AMW, et al. Cardiac Inflammation Impedes Response to Cardiac Resynchronization Therapy in Patients with Idiopathic Dilated Cardiomyopathy. Circ Arrhythm Electrophysiol. 2020;13(11):e008727. doi: 10.1161/CIRCEP.120.008727
17. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of

Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39.e14. doi: 10.1093/ehjci/jev014
18. Hayıroğlu Mİ, Çınar T, Çinier G, et al. Evaluating systemic immune-inflammation index in patients with implantable cardioverter defibrillator for heart failure with reduced ejection fraction. Pacing Clin Electrophysiol. 2022 Feb;45(2):188-95. doi: 10.1111/pace.14436
19. Sert ZS, Bulbul R. A. Predictive value of systemic immune-inflammation index in patients with preterm labor. Cukurova Med J 2022;47(2):697-703.

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EFFECTS OF THE COVID-19 PANDEMIC ON SURGICAL CLINICS

COVID-19 PANDEMİSİNİN CERRAHİ KLİNİKLERE ETKİLERİ

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Abstract

Aim: This study aimed to reveal how surgical clinics were affected by the COVID-19 pandemic based on concrete data.

Methods: In this study, the outpatient clinics of surgical branches were examined in terms of the number of presenting patients, number of visits, patient age, number of patient revisits, number of appointments made, patients' time of arrival for their appointments, patient throughput times, number of patients that underwent surgery, and number of surgical operations performed during the COVID-19 pandemic.

Results: During the first year of the pandemic, concerning the number of presenting patients and number of visits, the most affected outpatient clinic was otorhinolaryngology and the least affected was gynecology and obstetrics. It was determined that the highest decrease in the mean age of patients presenting to outpatient clinics was in urology, and the lowest decrease in pediatric surgery. The patients who were the earliest to arrive for their appointments to undergo examinations were those that presented to the cardiovascular surgery clinic, while pediatric surgery patients arrived at the hospital closest to their appointment times. In the first year of the COVID-19 pandemic, the number of patients that underwent surgery decreased by 53% and the operations performed by 55% compared to the previous year.

Conclusions: With the effect of the pandemic, there was a decrease in the number of patients that presented to the outpatient clinics of surgical branches, number of visits to these clinics, appointments made, repeated visits, patients that underwent surgery, number of operations performed, and mean age of patients.

Keywords: COVID-19 Pandemic, outpatient clinics, surgical branches, surgery

Öz

Amaç: Bu çalışmada cerrahi kliniklerinin COVİD-19 pandemisinden nasıl etkilendiği somut verilerle ortaya konulmak istenmiştir.

Yöntemler: Bu çalışmada COVİD-19 pandemisi sürecinde polikliniğe başvuran hasta sayıları, polikliniğe yapılan başvuru sayıları, polikliniğe başvuran hastaların yaşları, polikliniğe yapılan mükerrer başvurular, polikliniğe alınan randevu sayıları, polikliniğe alınan randevuya geliş zamanları, poliklinik işlem süreleri, ameliyat olan hasta sayıları, yapılan ameliyat sayıları analiz edilmiştir.

Bulgular: Pandemi döneminde; polikliniklerine başvuran hasta sayıları ile bu polikliniklere yapılan başvuru sayıları açısından Kulak Burun Boğazın en fazla, Kadın Hastalıkları ve Doğumun en az etkilendiği görülmektedir. Polikliniklere başvuran hastaların yaş ortalamasındaki en fazla düşüşün üroloji hastalarında, en az düşüşün ise çocuk cerrahisinde olduğu görülmektedir. Poliklinik randevusuna en erken gelip muayene olan hastaların Kardiyovasküler Cerrahiye başvuranlar olduğu, randevu saatine en yakın muayene olanların ise Çocuk Cerrahisine başvuranların olduğu izlenmiştir. Pandeminin etkili olduğu yılda, önceki yıla göre, ameliyat olan hastaların sayısında %53, gerçekleştirilen cerrahilerde ise %55 düşüş izlenmiştir.

Sonuç: Pandeminin etkisiyle: cerrahi branş polikliniklerine başvuran hasta, bu polikliniklere başvuru, polikliniklere alınabilen randevu, mükerrer başvuru, cerrahi branşlara ameliyat olan hasta, gerçekleşen ameliyat sayıları ile polikliniklere başvuran hastaların yaş ortalaması azalmıştır. Polikliniklerindeki işlem süreleri genel olarak artmıştır.

Anahtar Kelimeler: COVID-19 Pandemisi, poliklinikler, cerrahi branşlar, cerrahi

Introduction

Due to the COVID-19 pandemic, all surgical specialties had to limit their surgical practices and regulate operations performed[1]. Increasing demands for ventilators, hospital areas, and staff during the pandemic reduced the surgical capacity and made it difficult to perform surgical operations[2,3]. The decreased number of patient presentations due to the cancellation of elective operations, reduction in the capacity of clinics providing patient care, and minimization of surgical teams to reduce their exposure to the virus and create labor force for other departments also led to a decline in surgical capacity[4]. In particular, the cancellation of elective surgery is expected to have cumulative devastating consequences for health systems around the world[2]. In a statement dated November 23, 2020, the American College of Surgeons stated the critical importance of providing basic surgical procedures, and in another statement dated October 27, 2020, it emphasized that delaying 'non-essential' surgical procedures resulted in significant delays[5,6].

Recommendations for reducing elective operations have been reported in many parts of the world during the COVID-19 pandemic[7,8]. In Turkey, the first case infected with COVID-19 was announced on March 11, 2021, through a press release. Subsequently, with the letter of the Turkish Ministry of Health entitled "Infection Control Precautions to be Taken in Operating Rooms during the Pandemic Period", it was recommended to postpone elective surgical and endoscopic procedures[9,10]. However, despite the normalization circular published on June 1, 2020, no statement was made concerning whether elective operations could continue to be performed throughout the country. In the normalization process, in addition to guidelines published by professional organizations and associations, hospitals also took their own decisions regarding the need for elective operations to be performed with certain precautions[11-13].

Health Sciences University Bursa Yuksek Ihtisas Training and Research Hospital is the largest and most equipped hospital with a capacity of 1,520 beds in the South Marmara Region of Turkey and accepts patients not only from Bursa where the hospital is located but also from many provinces nearby. As the effects of the pandemic became more serious, the hospital allocated certain staff (especially anesthesiologists and nurses) to COVID-19 units, which were created by converting existing clinics. Emergency measures were taken to reduce the use of inpatient beds, outpatient clinic rooms, and operating rooms in almost every department. The hospital's 32 operating rooms did not operate at full capacity even in the first year of the pandemic compared to the pre-pandemic period.

This study aimed to obtain concrete data to reveal how surgical clinics in a tertiary training and research hospital were affected by the pandemic. We consider that the analysis of these retrospectively obtained data will provide an insight into possible future pandemic waves or new pandemics.

Materials and Methods

The study was conducted after receiving approval from the Clinical Research Ethics Committee of Health Sciences University Bursa Yuksek Ihtisas Training and Research Hospital, with the protocol number 2011-KAEK-25 2021/02-04. The data used for the study were retrospectively obtained from the hospital information management system following the first anniversary of the first reported COVID-19 case in Turkey.

Within the scope of the study, the outpatient clinics of the surgical branches were evaluated in terms of the number of presenting patients, number of presentations, patient age, number of patient revisits, number of appointments made, patients' time of arrival for their appointments, patient throughput times, number of patients that underwent

surgery, and number of operations performed. The patient throughput time was calculated based on the time elapsed from the patients' arrival at the outpatient clinic to the completion of patient care when there was no other action left to be taken. Thus, this period did not only cover patient examination; it started with the patients' entrance into the outpatient clinic, included their registration with the hospital information management system in the outpatient room and necessary notes being taken or examinations being requested, and all the subsequent procedures undertaken until they left the clinic (laboratory and imaging tests, etc.).

The data were analyzed in three groups according to the evaluation period: Group A covering the one-year period starting from the first reported COVID-19 case in Turkey (March 11, 2020-March 10, 2021), Group B covering the year before the first reported case in Turkey (March 11, 2019-March 10, 2020), and Group C covering the year two years before the first reported case in Turkey (March 11, 2018-March 10, 2019).

- *Statistical analysis*

The data were analyzed using the Shapiro-Wilk test to determine whether they showed a normal distribution. The results were presented as mean ± standard deviation or frequency and percentage values. Normally distributed data were compared with the independent-samples t-test or one-way analysis of variance. The Bonferroni test was used as a multiple comparison test. Categorical variables were compared between the groups using Pearson's chi-square test and the Fisher-Freeman-Halton test. The significance level was accepted as $p < 0.05$. Statistical analyses were performed using IBM SPSS ver. 23.0 (IBM Corp. Release 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

Results

The retrospective analysis of the data performed following the first anniversary of the first reported COVID-19 case in Turkey revealed that a total of 903,072 patients had presented to the surgical outpatient clinics over the three-year study period. The distribution of these patients according to Groups A, B, and C was 149,534, 374,730, and 378,808, respectively. Table 1 summarizes the differences between the surgical branch groups. Examining the ratios of the number of patients presenting to the outpatient clinics of surgical branches over the total number of patients in each group, there was a significant increase in the number of those presenting to the urology, orthopedics, gynecology and obstetrics, and ophthalmology outpatient clinics in Group A compared to Groups B and C. In contrast, this number significantly decreased for the neurosurgery, general surgery, otorhinolaryngology, and plastic, reconstructive and esthetic surgery outpatient clinics ($p < 0.05$). Concerning the number of patients presenting to the outpatient clinics, the otorhinolaryngology clinic was most affected and the gynecology and obstetrics clinic was least affected (Table 1).

The distribution of the total 1,804,481 presentations to the outpatient clinics of surgical branches was as follows: 288,567 for Group A, 758,736, for Group B, and 757,179 for Group C. The ratio of the number of presentations to the outpatient clinics over the total number of presentations in each group significantly increased for the urology, orthopedics, gynecology and obstetrics, and ophthalmology clinics in Group A compared to Groups B and C. On the other hand, there was a significant decrease in the ratio of patients presenting to the neurosurgery, general surgery, cardiovascular surgery, otorhinolaryngology, and plastic, reconstructive and esthetic surgery clinics during the pandemic period ($p < 0.05$).

Table 1. Distribution of the number of patients presenting to the outpatient clinics of surgical branches according to the groups (repeated presentations not included)

Surgical branch	Group A		Group B		Group C		Total		p
	n	(%)	n	(%)	n	(%)	n	(%)	
Urology	19,250	(12.9)[a]	44,094	(11.8)[b]	43,302	(11.4)[c]	106,646	(11.8)	**<0.001**
Orthopedics	25,788	(17.2)[a]	53,702	(14.3)[b]	53,427	(14.1)[c]	132,917	(14.7)	
Brain surgery	11,524	(7.7)[a]	31,139	(8.3)[b]	31,905	(8.4)[c]	74,568	(8.3)	
General surgery	13,695	(9.2)[a]	38,053	(10.2)[b]	37,497	(9.9)[c]	89,245	(9.9)	
Cardiovascular surgery	8,608	(5.8)[a]	20,529	(5.5)[b]	22,094	(5.8)[a]	51,231	(5.7)	
Thoracic surgery	1,360	(0.9)[a]	2,909	(0.8)[b]	3,280	(0.9)[a]	7,549	(0.8)	
Otorhinolaryngology	16,225	(10.9)[a]	64,411	(17.2)[b]	66,900	(17.7)[c]	147,536	(16.3)	
Pediatric surgery	4,291	(2.9)[a]	6,519	(1.7)[b]	10,545	(2.8)[a]	21,355	(2.4)	
Obstetrics and gynecology	29,470	(19.7)[a]	63,829	(17.0)[b]	59,201	(15.6)[c]	152,500	(16.9)	
Plastic, reconstructive and esthetic surgery	2,346	(1.6)[a]	9,952	(2.7)[b]	13,759	(3.6)[c]	26,057	(2.9)	
Ophthalmology	16,977	(11.4)[a]	39,219	(10.5)[b]	36,887	(9.7)[c]	93,083	(10.3)	
Pediatric urology	-	-	374	(0.1)[b]	11	(0.0)[a]	385	(0.0)	
Total	149,534	(100.0)	374,730	(100.0)	378,808	(100.0)	903,072	(100.0)	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 2. Distribution of the number of presentations to the outpatient clinics of surgical branches according to the groups (repeated presentations included)

Surgical branch	Group A		Group B		Group C		Total		p
	n	(%)	n	(%)	n	(%)	n	(%)	
Urology	37,471	(13.0)[a]	93,582	(12.3)[b]	89,031	(11.8)[c]	220,084	(12.2)	**<0.001**
Orthopedics	48,113	(16.7)[a]	102,173	(13.5)[b]	105,163	(13.9)[c]	255,449	(14.2)	
Brain surgery	19,769	(6.9)[a]	53,934	(7.1)[b]	57,703	(7.6)[c]	131,406	(7.3)	
General surgery	21,728	(7.5)[a]	70,488	(9.3)[b]	70,488	(9.3)[b]	162,704	(9.0)	
Cardiovascular surgery	13,596	(4.7)[a]	37,945	(5.0)[b]	39,736	(5.2)[b]	91,277	(5.1)	
Thoracic surgery	1,935	(0.7)[a]	4,984	(0.7)[a]	5,409	(0.7)[b]	12,328	(0.7)	
Otorhinolaryngology	20,535	(7.1)[a]	109,578	(14.4)[b]	114,836	(15.2)[c]	244,949	(13.6)	
Pediatric surgery	6,338	(2.2)[a]	10,783	(1.4)[b]	17,922	(2.4)[c]	35,043	(1.9)	
Obstetrics and gynecology	82,337	(28.5)[a]	179,122	(23.6)[b]	163,881	(21.6)[c]	425,340	(23.6)	
Plastic, reconstructive and esthetic surgery	4,028	(1.4)[a]	19,729	(2.6)[b]	28,076	(3.7)[c]	51,833	(2.9)	
Ophthalmology	32,717	(11.3)[a]	75,422	(9.9)[b]	64,921	(8.6)[c]	173,060	(9.6)	
Pediatric urology	-	-	996	(0.1)[b]	13	(0.0)[a]	1,009	(0.1)	
Total	288,567	(100.0)	758,736	(100.0)	757,179	(100.0)	1,804,481	(100.0)	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 3. Age distribution of patients presenting to the outpatient clinics of surgical branches by groups

Surgical branch	Group A (mean ± SD)	Group B (mean ± SD)	Group C (mean ± SD)	Total (mean ± SD)	p
Urology	46.83 ± 17.86[a]	50.08 ± 19.00[b]	50.02 ± 19.27[b]	49.47 ± 18.95	**<0.001**
Orthopedics	38.82 ± 20.22[a]	40.85 ± 21.56[b]	41.18 ± 21.29[c]	40.59 ± 21.21	**<0.001**
Brain surgery	44.36 ± 17.35[a]	47.15 ± 17.55[b]	46.97 ± 17.48[b]	46.64 ± 17.52	**<0.001**
General surgery	45.26 ± 15.99[a]	46.85 ± 16.07[b]	47.15 ± 16.05[c]	46.73 ± 16.07	**<0.001**
Cardiovascular surgery	53.30 ± 15.39[a]	55.23 ± 15.53[b]	55.45 ± 15.80[b]	55.00 ± 15.64	**<0.001**
Thoracic surgery	47.00 ± 16.89[a]	50.55 ± 17.82[b]	48.85 ± 16.89[c]	49.17 ± 17.39	**<0.001**
Otorhinolaryngology	33.70 ± 22.92[a]	35.62 ± 23.11[b]	34.78 ± 23.13[c]	35.03 ± 23.10	**<0.001**
Pediatric surgery	7.82 ± 6.59[a]	8.21 ± 5.70[b]	8.91 ± 5.46[c]	8.48 ± 5.79	**<0.001**
Obstetrics and gynecology	33.74 ± 11.33[a]	36.24 ± 12.29[b]	36.65 ± 12.10[c]	35.92 ± 12.08	**<0.001**
Plastic, reconstructive and esthetic surgery	36.22 ± 19.17[a]	38.00 ± 20.13[b]	37.35 ± 19.21[c]	37.50 ± 19.57	**<0.001**
Ophthalmology	40.79 ± 21.61[a]	42.06 ± 23.73[b]	41.95 ± 23.55[b]	41.78 ± 23.29	**<0.001**
Pediatric urology	-	9.09 ± 4.69	8.64 ± 3.80	9.07 ± 4.66	0.242
Total	39.51 ± 19.48[a]	41.70 ± 20.52[b]	41.37 ± 20.69[c]	41.20 ± 20.43	**<0.001**

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 4. Distribution of repeated visits to the outpatient clinics of surgical branches according to the groups (only patients that presented to the outpatient clinic more than once in each period were included in the evaluation)

Surgical branch	Group A		Group B		Group C		p
	Mean ± SD	(min-max)	Mean ± SD	(min-max)	Mean ± SD	(min-max)	
Urology	3.10 ± 2.23	(2-35)[a]	3.26 ± 2.24	(2-34)[b]	3.21 ± 2.21	(2-33)[c]	**<0.001**
Orthopedics	3.36 ± 2.39	(2-40)[a]	3.24 ± 2.18	(2-39)[b]	3.37 ± 2.32	(2-45)[a]	**<0.001**
Brain surgery	2.65 ± 1.33	(2-18)	2.64 ± 1.36	(2-24)	2.67 ± 1.42	(2-22)	0.366
General surgery	2.94 ± 1.60	(2-18)[a]	3.12 ± 1.71	(2-26)[b]	3.19 ± 1.81	(2-29)[c]	**<0.001**
Cardiovascular surgery	3.08 ± 2.20	(2-29)	3.10 ± 1.87	(2-22)	3.14 ± 2.18	(2-36)	0.234
Thoracic surgery	2.70 ± 1.32	(2-11)[a]	3.14 ± 1.91	(2-18)[b]	2.90 ± 1.74	(2-18)[a]	**<0.001**
Otorhinolaryngology	2.34 ± 0.83	(2-13)[a]	2.80 ± 1.63	(2-28)[b]	2.81 ± 1.69	(2-30)[b]	**<0.001**
Pediatric surgery	2.96 ± 1.51	(2-14)[a]	2.90 ± 1.5	(2-16)[a,b]	3.01 ± 1.52	(2-23)[a,c]	**0.040**
Obstetrics and gynecology	3.75 ± 2.45	(2-26)[a]	3.81 ± 2.57	(2-26)[b]	3.94 ± 2.70	(2-30)[c]	**<0.001**
Plastic, reconstructive and esthetic surgery	3.03 ± 2.02	(2-21)[a]	3.26 ± 2.04	(2-26)[b]	3.43 ± 2.01	(2-28)[c]	**<0.001**
Ophthalmology	4.49 ± 4.45	(2-36)[a]	4.48 ± 4.12	(2-36)[a]	4.10 ± 3.49	(2-33)[b]	**<0.001**
Pediatric urology	-	-	3.79 ± 2.31	(2-13)	-	-	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **SD:** standard deviation, **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 5. Distribution of the number of appointments made for the outpatient clinics of surgical branches according to the groups

Surgical branch	Group A		Group B		Group C		Total		p
	n	(%)	n	(%)	n	(%)	n	(%)	
Urology	16,772	(14.6)[a]	56,796	(14.7)[a]	57,654	(14.3)[b]	131,222	(14.5)	**<0.001**
Orthopedics	19,532	(17.0)[a]	48,629	(12.6)[b]	48,764	(12.1)[c]	116,925	(12.9)	
Brain surgery	9,935	(8.6)[a]	34,185	(8.8)[a]	35,430	(8.8)[a]	79,550	(8.8)	
General surgery	10,504	(9.1)[a]	42,873	(11.1)[b]	45,409	(11.2)[b]	98,786	(10.9)	
Cardiovascular surgery	6,036	(5.3)[a]	19,138	(4.9)[b]	23,372	(5.8)[c]	48,546	(5.4)	
Thoracic surgery	1,414	(1.2)[a]	3,919	(1.0)[b]	3,956	(1.0)[b]	9,289	(1.0)	
Otorhinolaryngology	10,576	(9.2)[a]	61,438	(15.9)[b]	55,932	(13.8)[c]	127,946	(14.1)	
Pediatric surgery	4,268	(3.7)[a]	5,948	(1.5)[b]	11,921	(3.0)[c]	22,137	(2.4)	
Obstetrics and gynecology	28,206	(24.5)[a]	82,040	(21.2)[b]	82,895	(20.5)[c]	193,142	(21.3)	
Plastic, reconstructive and esthetic surgery	1,946	(1.7)[a]	9,548	(2.5)[b]	18,040	(4.5)[c]	29,534	(3.3)	
Ophthalmology	5,745	(5.0)[a]	21,768	(5.6)[b]	20,511	(5.1)[a]	48,024	(5.3)	
Pediatric urology	0	(0.0)[a]	574	(0.1)[b]	8	(0.0)[a]	582	(0.1)	
Total	114,934	(100.0)	386,856	(100.0)	403,893	(100.0)	905,683	(100.0)	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 6. Distribution of patient arrival times at the outpatient clinics of surgical branches according to the groups

Surgical branch	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	p
Urology	-0:11:47 ± 1:03:30[a]	-0:20:14 ± 1:24:43[b]	-0:15:39 ± 1:29:19[c]	**<0.001**
Orthopedics	-0:10:22 ± 1:08:40[a]	-0:10:03 ± 1:08:37[a]	-0:08:14 ± 1:12:15[b]	**<0.001**
Brain surgery	-0:10:09 ± 1:15:56[a]	-0:03:24 ± 1:05:09[b]	0:02:42 ± 1:11:40[c]	**<0.001**
General surgery	-0:01:12 ± 0:58:38[a]	-0:02:36 ± 1:02:06[a]	0:02:26 ± 1:00:17[b]	**<0.001**
Cardiovascular surgery	-0:18:08 ± 1:14:13[a]	-0:12:40 ± 1:10:03[b]	-0:07:21 ± 1:08:57[c]	**<0.001**
Thoracic surgery	-0:06:06 ± 0:55:45[a]	-0:16:28 ± 0:59:06[b]	-0:19:19 ± 1:25:16[b]	**<0.001**
Otorhinolaryngology	-0:05:51 ± 1:02:55[a]	-0:04:37 ± 0:52:23[a]	-0:03:31 ± 0:54:41[b]	**<0.001**
Pediatric surgery	0:00:15 ± 1:03:42[a]	-0:14:04 ± 1:30:35[b]	-0:00:39 ± 1:06:15[a]	**<0.001**
Obstetrics and gynecology	-0:04:27 ± 0:58:35[a]	-0:09:04 ± 1:10:28[b]	-0:02:07 ± 1:04:00[c]	**<0.001**
Plastic, reconstructive and esthetic surgery	-0:07:02 ± 1:00:44[a]	0:04:16 ± 0:52:07[b]	-0:00:00 ± 0:53:13[c]	**<0.001**
Ophthalmology	-0:12:10 ± 1:00:01[a]	-0:14:25 ± 1:30:49[a]	0:02:12 ± 1:01:32[b]	**<0.001**
Pediatric urology		0:02:51 ± 0:33:37	0:06:15 ± 0:21:01	0.775

'-' indicates arrival at the clinic before the appointment time (data given in 'hours:minutes:seconds'), **[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **SD:** standard deviation, **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 7. Distribution of patient throughput times of the outpatient clinics of surgical branches according to the groups

Surgical branch	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	Total Mean ± SD	p
Urology	0:20 ± 0:55[a]	0:18 ± 1:11[b]	0:13 ± 0:47[c]	0:16 ± 1:00	**<0.001**
Orthopedics	0:38 ± 1:07[a]	0:18 ± 0:47[b]	0:15 ± 0:39[c]	0:21 ± 0:49	**<0.001**
Brain surgery	0:25 ± 0:53[a]	0:21 ± 0:55[b]	0:18 ± 0:45[c]	0:21 ± 0:51	**<0.001**
General surgery	0:20 ± 0:47[a]	0:21 ± 1:08[b]	0:12 ± 0:36[c]	0:17 ± 0:53	**<0.001**
Cardiovascular surgery	0:09 ± 0:25[a]	0:14 ± 1:11[b]	0:07 ± 0:28[c]	0:10 ± 0:50	**<0.001**
Thoracic surgery	0:25 ± 0:43[a]	0:40 ± 1:06[b]	0:42 ± 1:07[b]	0:39 ± 1:04	**<0.001**
Otorhinolaryngology	0:34 ± 0:58[a]	0:18 ± 0:45[b]	0:15 ± 0:37[c]	0:18 ± 0:43	**<0.001**
Pediatric surgery	0:09 ± 0:30[a]	0:14 ± 0:54[b]	0:08 ± 0:31[a]	0:10 ± 0:40	**<0.001**
Obstetrics and gynecology	0:33 ± 0:52[a]	0:34 ± 1:11[a]	0:29 ± 1:03[b]	0:32 ± 1:04	**<0.001**
Plastic, reconstructive and esthetic surgery	0:10 ± 0:27[a]	0:11 ± 0:35[a]	0:08 ± 0:24[b]	0:09 ± 0:29	**<0.001**
Ophthalmology	0:43 ± 1:05[a]	0:35 ± 1:01[b]	0:40 ± 1:07[c]	0:39 ± 1:04	**<0.001**
Pediatric urology	-	0:07 ± 0:21	0:07 ± 0:06	0:07 ± 0:21	0.996
Total	0:30 ± 0:56[a]	0:24 ± 1:02[b]	0:19 ± 0:49[c]	0:23 ± 0:56	**<0.001**

Data given in 'hours:minutes', [a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **SD:** standard deviation, **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 8. Distribution of operated patients according to the groups

Surgical branch	Group A		Group B		Group C		Total		p
	n	(%)	n	(%)	n	(%)	n	(%)	
Urology	998	(6.6)[a]	3,030	(9.3)[b]	2,965	(9.6)[b]	6,993	(8.9)	**<0.001**
Orthopedics	1,619	(10.7)[a]	2,788	(8.6)[b]	2,589	(8.4)[b]	6,996	(8.9)	
Brain surgery	1,189	(7.8)[a]	2,125	(6.5)[b]	2,250	(7.3)[a]	5,564	(7.1)	
General surgery	1,253	(8.3)[a]	3,991	(12.3)[b]	4,453	(14.5)[c]	9,697	(12.4)	
Cardiovascular surgery	797	(5.2)[a]	2,044	(6.3)[b]	2,118	(6.9)[c]	4,959	(6.3)	
Thoracic surgery	129	(0.8)[a]	370	(1.1)[b]	362	(1.2)[b]	861	(1.1)	
Otorhinolaryngology	86	(0.6)[a]	1,500	(4.6)[b]	1,596	(5.2)[c]	3,182	(4.1)	
Pediatric surgery	992	(6.5)[a]	1,825	(5.6)[b]	2,477	(8.0)[c]	5,294	(6.7)	
Obstetrics and gynecology	4,828	(31.8)[a]	6,410	(19.7)[b]	6,247	(20.3)[b]	17,485	(22.3)	
Plastic, reconstructive and esthetic surgery	304	(2.0)[a]	2,457	(7.6)[b]	3,626	(11.8)[c]	6,387	(8.1)	
Ophthalmology	2,986	(19.7)[a]	5,934	(18.3)[b]	2,114	(6.9)[c]	11,034	(14.1)	
Pediatric urology	0	(0.0)[a]	26	(0.1)[b]	1	(0.0)[a]	27	(0.0)	
Total	15,181	(100.0)	32,500	(100.0)	30,798	(100.0)	78,479	(100.0)	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Table 9. Distribution of the number of operations according to the groups

Surgical branch	Group A		Group B		Group C		Total		p
	n	(%)	n	(%)	n	(%)	n	(%)	
Urology	2,136	(9.8)[a]	5,987	(12.3)[b]	6,008	(12.7)[b]	14,131	(12.0)	
Orthopedics	2,283	(10.5)[a]	3,840	(7.9)[b]	3,564	(7.5)[b]	9,687	(8.2)	
Brain surgery	2,130	(9.8)[a]	3,757	(7.7)[b]	3,914	(8.3)[c]	9,801	(8.3)	
General surgery	1,627	(7.5)[a]	5,017	(10.3)[b]	5,640	(11.9)[c]	12,284	(10.4)	
Cardiovascular surgery	1,719	(7.9)[a]	4,801	(9.9)[b]	4,839	(10.2)[b]	11,359	(9.7)	
Thoracic surgery	180	(0.8)[a]	481	(1.0)[a,b]	517	(1.1)[b]	1,178	(1.0)	**<0.001**
Otorhinolaryngology	129	(0.6)[a]	2,856	(5.9)[b]	2,899	(6.1)[b]	5,884	(5.0)	
Pediatric surgery	1,493	(6.9)[a]	2,427	(5.0)[b]	3,440	(7.3)[a]	7,360	(6.3)	
Obstetrics and gynecology	6,261	(28.8)[a]	8,994	(18.5)[b]	8,586	(18.1)[b]	23,841	(20.3)	
Plastic, reconstructive and esthetic surgery	424	(2.0)[a]	3,880	(8.0)[b]	5,318	(11.2)[c]	9,622	(8.2)	
Ophthalmology	3,334	(15.4)[a]	6,568	(13.5)[b]	2,599	(5.5)[c]	12,501	(10.6)	
Pediatric urology	0	(0.0)[a]	32	(0.1)[b]	1	(0.0)[a]	33	(0.0)	
Total	21,716	(100.0)	48,640	(100.0)	47,325	(100.0)	117,681	(100.0)	

[a, b, c]: same letters indicate no statistically significant difference between the groups for the given surgical branch; i.e., different letters indicate that the difference between the groups is statistically significant ($p < 0.05$), **Group A:** March 11, 2020-March 10, 2021 (one-year period starting from the first reported COVID-19 case in Turkey), **Group B:** March 11, 2019-March 10, 2020 (the year before the first reported case in Turkey), **Group C:** March 11, 2018-March 10, 2019 (two years before the first reported case in Turkey).

Concerning the number of presentations made to the outpatient clinics, the otorhinolaryngology clinic was most affected, and the gynecology and obstetrics clinic was least affected (Table 2).

The mean ages of the patients presenting to the outpatient clinics of surgical branches were found to be 39.51, 41.70, and 41.37 years for Groups A, B, and C, respectively. It was observed that the mean age of the patients significantly decreased during the pandemic period compared to the previous years ($p < 0.05$). The highest decrease in the mean patient age was determined for the urology clinic and the lowest decrease for the pediatric surgery clinic (Table 3).

When repeated (more than one) patient visits were evaluated, the mean number of repeated visits for Groups A, B, and C was 3.36, 3.32, and 3.32, respectively. In Group A, the number of repeated visits increased, and this difference was statistically significant compared to Groups B and C ($p \leq 0.001$). The highest decrease in the number of repeated visits was seen in the otorhinolaryngology clinic and the highest increase in the ophthalmology clinic (Table 4).

The number of appointments made to the outpatient clinics of surgical branches decreased by approximately 70% during the pandemic period. The evaluation of their ratio over the total number of appointments within each group revealed that the highest increase was in the orthopedics clinic and the highest decrease was in the otorhinolaryngology clinic (Table 5).

The patients generally arrived at the hospital within 15 min before their appointment times. When these data were further examined according to the outpatient clinics, it was determined that the patients that arrived for their appointments earliest to undergo examination were those that presented to the cardiovascular surgery clinic, while those that made appointments with the pediatric surgery clinic arrived at the hospital closest to their appointment times (Table 6).

The mean patient throughput times of the outpatient clinics of surgical branches was found to be 30 min, 24 min, and 19 min for Groups A, B, and C, respectively, indicating a statistically significant difference between the groups ($p \leq 0.001$). With the effect of the pandemic, the patient throughput times of the outpatient clinics generally increased. During the pandemic period, the patient throughput time increased most in the orthopedics clinic and decreased most in the thoracic surgery clinic (Table 7).

The number of patients undergoing surgery was determined as 15,181 for Group A, 32,500 for Group B, and 30,798 for Group C. The ratio of the number of patients that underwent surgery in each outpatient clinic over the total number of operated patients in each group significantly differed between Group A and Group B for all the outpatient clinics of surgical branches. The highest decrease in this ratio was observed in the plastic, reconstructive and esthetic surgery clinic and the highest increase in the obstetrics and gynecology clinic (Table 8).

The number of operations performed was 21,716, 48,640, and 47,325 for Groups A, B, and C, respectively. With the effect of the pandemic, the number of operations decreased by more than half compared to the pre-pandemic period. The ratio of the number of operations performed in each clinic over the total number of operations undertaken in each group statistically significantly differed between Group A and Group B for all clinics except thoracic surgery. The highest decrease in this ratio was seen in the otorhinolaryngology clinic and the highest increase in the obstetrics and gynecology clinic (Table 9).

Discussion

With the beginning of the COVID-19 pandemic, a series of measures were taken in hospitals in Turkey, as in many countries across the world. In our hospital located in Bursa, which is among the top five big cities in Turkey, the following measures were taken during this period: The bed capacities of clinics were reduced to provide potential inpatient beds for patients with COVID-19. For all patients that visited the emergency

department with the suspicion of COVID-19 disease, symptoms were questioned, and evaluations were made in a separate unit reserved for COVID-19 cases within this department. All clinical and preclinical physicians in the COVID-19 unit of the emergency department contributed to the management of the pandemic process. Following the increasing exposure of the anesthesia team and growing number of personnel infected with the virus, the number of operating rooms was reduced. Due to the insufficiency of intensive care units reserved for patients with COVID-19, the emergency observation areas were converted to areas providing intensive care. Lastly, as of January 14, 2021, with the start of the vaccination process in our hospital, an inpatient clinic was reserved for vaccination.

In a study evaluating data obtained from the urology clinics of six large hospitals in Istanbul over the first three months of the pandemic, it was determined that the number of operations performed, and outpatient clinic presentations decreased by approximately 75% compared to the same period of the previous year[14]. In a study including the data of orthopedics clinics in Hong Kong comparing the two-month period in the first quarter of 2020 with the previous four years, it was observed that the operations of this branch decreased by 44.2% and those of outpatients by 29.4%[15]. In another study conducted by the neurosurgery department of Washington University, the number of outpatients decreased by up to 75%[16]. In the current study, similar to previous studies, during the pandemic, there was a 60% decrease in the number of patients that presented to the outpatient clinics of our hospital and a 62% decrease in the number of presentations made, regardless of the surgical branch, compared to one and two years before the pandemic. This is an important finding since it implies that patients who required surgery may have postponed their visits to the hospital, which may have led to the progression of their diseases.

In our study, the mean age of the patients who presented to the outpatient clinics of surgical branches was 41.7 years in the pre-pandemic period and 39.5 years in the first year of the pandemic. The reason for the younger age of the patients visiting outpatient clinics during the pandemic period may be the curfews implemented for citizens aged 65 years and over, representing one of the populations that was most affected by strict isolation methods that entered our lives with the effect of the pandemic. This is further supported by the decrease in the mean age of the patients who presented to the urology outpatient clinic compared to the other surgical branches.

Another important finding of this study is that when the surgical branches were separately examined, the repeated visits of the patients to the same branch were observed to have generally decreased during the pandemic, with the highest decrease being observed in the otorhinolaryngology clinic. While this finding can be positively interpreted, possibly indicating that patients did not need to revisit their doctors, it may also be unsettling considering the generally low health literacy rate of individuals in Turkey. As a result, some patients may have presented to the hospital only when they felt pain or their condition was unbearable, avoiding hospital visits other times despite the need for follow-up.

In the first year of the pandemic, through the efforts of all physicians, the treatment of patients diagnosed with COVID-19 was provided. Physicians working in surgical branches were on duty in many COVID-19 services and intensive care units that were newly opened for these patients. This additional workload adversely affected the capacity of outpatient appointments, which is part of the routine operations of surgical branches. Concerning the number of appointments made to the outpatient clinics, there was a 70% decrease in the first year of the pandemic compared to the previous year. This finding raises concerns that some patients may not have been able to find an

appointment to visit the hospital although they needed to, and this may have delayed their diagnosis and treatment. In this study, it was observed that among the surgical branches, the otorhinolaryngology clinic was most negatively affected in terms of outpatient appointment services. Due to this dramatic difference, after the normalization process, the need for outpatient applications is likely to increase in all surgical clinics, but mostly in this branch.

During the pandemic, some surgical clinics asked patients to arrive at the hospital close to the scheduled appointment time and stated that if they arrived early, they would not be allowed into the waiting area[17]. In our study, it was observed that during the pandemic, the arrival times of the patients at the hospital differed between the surgical branches. Among the patients who made an appointment for the surgical branches in our hospital, those that most strictly followed their appointment times were those that presented to the pediatric surgery clinic. We consider that in future pandemics, when patients need to go to hospital appointments, the time they spend in the hospital should be minimized. They should have a scheduled appointment time and be advised not to arrive early.

Another important finding of this study is that the patient throughput times increased in the outpatient clinics of surgical branches during the first year of the pandemic. This increase was mostly observed in the orthopedic clinic. In order to evaluate the reason for this situation, further comprehensive studies should examine the outpatients of surgical branches in more detail.

Researchers suggested that surgical care that was not essential or time-critical could be delayed and postponed to a later date when the pandemic subsided[18,19]. In our study, there was a 53% decrease in the number of patients that underwent surgery, and a 55% decrease in the number of operations performed during the first year of the pandemic compared to the previous year. It was determined that among the surgical branches, gynecology and obstetrics was the clinic that was least affected in terms of the number of operated patients and number of operations performed. One of the most important reasons for this finding may be that this clinic mostly serves obstetric cases whose care and treatment cannot be postponed.

The most important limitation of our study is its single center and retrospective design. Another limitation is that since our hospital was a COVID-19 reference center in Bursa, some patients may have preferred to visit hospitals in the province due to the fear of contracting the virus. Despite these limitations, this is a large-scale study that examined the effects of the COVID-19 period on all surgical branches, included a very large number of patients, and covered a long period of time. In addition, it contributes to the literature in terms of offering an idea about the situation in surgical branches after the normalization process and in future COVID-19 waves or other possible pandemics.

Conclusion

In the first year of the COVID-19 pandemic, there was a decrease in the number of patients that presented to the outpatient clinics of surgical branches, number of presentations to these clinics, number of appointments made, mean age of patients, number of repeated visits, number of operated patients, and number of operations performed, while the patient throughput times of surgical branches generally increased. This study provided data on the extent to which surgical branches were affected by the COVID-19 pandemic at the level of outpatient clinics and surgical operations. The findings of the study should be supported by future multicenter and comprehensive studies evaluating surgical branches separately.

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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

Permission was obtained from the Bursa Yüksek Ihtisas Training and Research Hospital Clinical Research Ethics Committee for this study, and Helsinki Declaration rules were followed to conduct this study. (17.02.2021, 2011-KAEK-25 2021/02-04)

References

1. Al-Jabir A, Kerwan A, Nicola M, et al. Impact of the Coronavirus (COVID-19) pandemic on surgical practice - Part 2 (surgical prioritisation). 2020 Jul;79:233-48. doi: 10.1016/j.ijsu.2020.05.002
2. Søreide K, Hallet J, Matthews JB, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. Br J Surg. 2020 Sep;107(10):1250-61. doi: 10.1002/bjs.11670
3. Fowler AJ, Dobbs TD, Wan YI, et al. Resource requirements for reintroducing elective surgery during the COVID-19 pandemic: modelling study. Br J Surg. 2021 Jan 27;108(1):97-103. doi: 10.1093/bjs/znaa012
4. Effect of COVID-19 on Surgical Training Across the United States: A National Survey of General Surgery Residents. Aziz H, James T, Remulla D, et al. J Surg Educ. 2021 Mar-Apr;78(2):431-439. doi: 10.1016/j.jsurg.2020.07.037
5. American College of Surgeons. Joint Statement: Roadmap for Maintaining Essential Surgery during COVID-19 Pandemic, Updated on August 10, 2020. Available from: https://www.facs.org/covid-19/clinical-guidance/roadmap-maintain-essential-surgery Date of access: 15.11.2021
6. American College of Surgeons. American College of Surgeons Recommendations Concerning Surgery Amid the COVID-19 Pandemic Resurgence, Released October 27, 2020. Available from: https://www.facs.org/-/media/files/covid19/acs_recommendations_concerning_surgery_amid_covid19_resurgence.ashx Date of access: 15.11.2021
7. American Collage of Surgeons. COVID-19: Elective Case Triage Guidelines for Surgical Care, Online March 24, 2020. Available from: https://www.facs.org/covid-19/clinical-guidance/elective-case Date of access: 15.11.2021
8. Bhangu A, Lawani I, Ng-Kamstra JS, et al. Global guidance for surgical care during the COVID-19 pandemic. COVID Surg Collaborative. Br J Surg. 2020 Aug;107(9):1097-103. doi: 10.1002/bjs.11646
9. T.C. Sağlık Bakanlığı. COVID-19 Pandemi Döneminde Ameliyathanelerde Alınacak Enfeksiyon Kontrol Önlemleri, Güncellenme Tarihi: 27.04.2020. Available from: https://dosyahastane.saglik.gov.tr/Eklenti/165645,covid19-pandemi-doneminde-ameliyathanelerdepdf.pdf?0 Date of access: 15.11.2021
10. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü. COVID-19 (SARS-CoV-2 Enfeksiyonu) Rehberi, 7 Aralık 2020, Ankara. Available from: https://covid19.saglik.gov.tr/Eklenti/39551/0/covid-19rehberigenelbilgilerepidemi-yolojivetanipdf.pdf Date of access: 15.11.2021
11. TTB - COVID-19 Pandemisinde Yeniden Açılma Sürecinde Elektif Cerrahiler, 01.06.2020, Ankara. Available from: https://www.ttb.org.tr/haber_goster.php?Guid=702965ce-a438-11ea-bd3c-ba8d943d7595 Date of access: 15.11.2021
12. Türk Anestezi ve Reanimasyon Derneği. Anesteziyoloji ve Reanimasyon Uzmanları için COVID-19 Pandemisi Normalleşme Döneminde Elektif Cerrahilere Başlama Önerileri, 21 Mayıs 2020. Available from: http://www.tard.org.tr/assets/pdf/COVID-Elektif-Cerrahilere-Basslama-Kilavuzu-2.1.pdf Date of access: 15.11.2021
13. İstanbul Tıp Fakültesi Hastanesi Başhekimliği İnfeksiyon Kontrol Komitesi "Normalleşme Sürecinde Ameliyathanelerdeki Değişiklikler" konulu yazısı, 14.06.2020. Sayı:95747, İstanbul. https://cdn.istanbul.edu.tr/FileHandler2.ashx?f=normalles%CC%A7me-su%CC%88recinde-ameliyathanelerdeki-o%CC%88nlemler.pdf Date of access: 15.11.2021

14. Çakıcı MÇ, Temiz MZ, İplikçi A, et al. The clinical impact of the COVID-19 pandemic on daily urological practice: first 3-month multicenter results from Istanbul. Turk J Med Sci. 2021 Jun 28;51(3):962-71. doi: 10.3906/sag-2009-184
15. Wong JSH, Cheung KMC. Impact of COVID-19 on Orthopaedic and Trauma Service: An Epidemiological Study. J Bone Joint Surg Am. 2020 Jul 15;102(14):e80. doi: 10.2106/JBJS.20.00775
16. Sivakanthan S, Pan J, Kim L, et al. Economic Impact of COVID-19 on a High-Volume Academic Neurosurgical Practice. World Neurosurg. 2020 Nov;143:e561-e566. doi: 10.1016/j.wneu.2020.08.028
17. Pearlman AN, Tabaee A, Sclafani AP, et al. Establishing an Office-Based Framework for Resuming Otolaryngology Care in Academic Practice During the COVID-19 Pandemic. Otolaryngol Head Neck Surg. 2021 Mar;164(3):528-41. doi: 10.1177/0194599820955178
18. What's Important: What Is Our Role in the COVID-19 Pandemic? Lockey SD. J Bone Joint Surg Am. 2020 Jun 3;102(11):931-2. doi: 10.2106/JBJS.20.00444
19. Managing COVID-19 in Surgical Systems. Brindle ME, Gawande A. Ann Surg. 2020 Jul;272(1):e1-e2. doi: 10.1097/SLA.0000000000003923

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EVALUATION OF THE QUALITY AND RELIABILITY OF YOUTUBE VIDEOS ON DRY NEEDLING PROCEDURE

KURU İĞNELEME İLE İLGİLİ YOUTUBE VİDEOLARININ KALİTESİNİN VE GEÇERLİLİĞİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: With the popularization of the Internet, social media platforms are used frequently as an information source. Patients can watch YouTube videos and gather information on dry needling especially before the procedure. This cross-sectional study aimed to assess the reliability and quality of videos on dry needling.

Methods: A search was conducted on YouTube using the keyword "dry needling". Features of videos, such as the number of views and duration of the videos, were noted. The reliability and quality of videos were assessed with the DISCERN and the Journal of the American Medical Association (JAMA).

Results: A total of 150 videos were screened and 50 videos were excluded: 30 were duplicates, 10 were off-topic, 5 were in a language other than English, and 5 had no audio. Most of the videos were uploaded by non-physician health personnel (42%) and physicians (27%). The most common video content was demonstration (53%) of dry needling. The mean scores of the JAMA and DISCERN tools were 1.9 and 35.3, respectively. Thirty-four percent of videos were very poor, 31% were poor, 18% were fair, 11% were good, and only 6% were excellent.

Conclusions: YouTube is a platform where medical information is freely shared and widespread. In this study, we found that most of the YouTube videos on dry needling were of low quality. Future efforts by healthcare professionals and academic institutions are necessary to improve the reliability and quality of medical information on dry needling.

Keywords: Dry needling, YouTube videos, quality, reliability

Öz

Amaç: İnternetin yaygınlaşmasıyla birlikte sosyal medya platformları bilgi kaynağı olarak sıklıkla kullanılmaktadır. Hastalar özellikle işlem öncesi YouTube videolarını izleyebilir ve kuru iğneleme hakkında bilgi toplayabilir. Bu kesitsel çalışma, kuru iğneleme ile ilgili videoların güvenilirliğini ve kalitesini değerlendirmeyi amaçlamıştır.

Yöntemler: "Kuru iğneleme" anahtar kelimesi kullanılarak YouTube'da arama yapıldı. Videoların izlenme sayıları ve süreleri gibi özellikleri not edildi. Videoların güvenilirliği ve kalitesi DISCERN ve Journal of the American Medical Association (JAMA) skalaları ile değerlendirildi.

Bulgular: Toplam 150 video tarandı ve 50 video çalışmadan hariç tutuldu. Dışlanan videoların 30'u yinelenen, 10'u konu dışı, 5'i İngilizce dışında bir dildeydi ve 5'inde ses yoktu. Videoların çoğu hekim olmayan sağlık personeli (%42) ve doktorlar (%27) tarafından yüklenmişti. En yaygın video içeriği kuru iğneleme işleminin uygulama yöntemiyle ilgiliydi (%53). JAMA ve DISCERN araçlarının ortalama puanları sırasıyla 1.9 ve 35.3 idi. Videoların yüzde %34'ü çok zayıf, %31'i zayıf, %18'i orta, %11'i iyi ve sadece %6'sı mükemmeldi.

Sonuç: YouTube, tıbbi bilgilerin özgürce paylaşıldığı ve yaygınlaştırıldığı bir platformdur. Bu çalışmada, kuru iğneleme ile ilgili YouTube videolarının çoğunun düşük kalitede olduğunu bulduk. Kuru iğneleme ile ilgili tıbbi bilgilerin güvenilirliğini ve kalitesini artırmak için sağlık uzmanları ve akademik kurumların gelecekteki çabaları gereklidir.

Anahtar Kelimeler: Kuru iğneleme, YouTube videoları, kalite, güvenilirlik

Introduction

Local injection therapies or wet needling involves hollow-bore needle injections using corticosteroids, local anesthetics, botulinum toxins, and so forth [1]. However, dry needling is performed without using any medication or solution. It only involves insertion of thin monofilament needles [2]. Dry needling is usually used to treat musculoskeletal problems such as back or neck pain [3, 4]. The needle penetrates the skin and stimulates underlying myofascial trigger points, muscles, ligaments, tendons, and subcutaneous fascia for the management of a variety of neuromusculoskeletal problems [4]. Some professional organizations state that dry needling is a procedure that involves needles only inserted into the trigger points [1]. However, several studies showed that dry needling targets not only trigger points, but also neural, muscular and connective tissues [1]. Although this method of treatment is quite safe, some complications such as bleeding, pain, sympathetic symptoms (nausea, vertigo) and pneumothorax can occur [5].
Patients can use the Internet and social media to obtain information on dry needling and also perform it in their clinical practice by using these videos [6]. In recent years, YouTube has become a popular source of health information; it has been shown that 80% of Internet users access health information online [7]. The fact that YouTube videos are easily accessible and free of charge is one of the most important reasons for its popularity [8]. On the other hand, there are not enough control mechanisms for video quality analysis [6]. As a result, the quality and reliability of videos varies, so healthcare professionals should be alert and guide their patients on the way to obtain accurate and reliable information [9]. There is a potential risk of spreading inaccurate information, which can cause significant problems in healthcare [10]. Moreover, the results of a YouTube search are based on an algorithm that uses the relevancy and popularity of videos [10]. Therefore, patients can watch popular videos that may contain misleading information. In outpatient clinics, patients can confuse dry needling with acupuncture and some patients do not have any idea about the procedure and think that hollow bore needles are used instead of monofilament needles. It can be difficult to change patients' attitude and prejudice when they believe what they watched. Since the quality of dry needling videos has not been evaluated before, this study was conducted to analyze the quality of videos giving information about dry needling to patients.

Materials and Methods

YouTube was searched using the keyword "dry needling". Two-hundred videos were screened and listed by relevance on 15 February 2022. One hundred videos met the inclusion criteria and were analyzed further. Videos in English and that contained information about the introduction, demonstration, indications, and complications of dry needling were evaluated. All videos were watched and analyzed by two reviewers independently and a consensus meeting was held when any discrepancy arose. Videos without sound, videos that were not in English, and duplicated or overlapping videos were excluded. This is a cross-sectional study that included no human or animal participants, so ethical approval was not required and consent was waived.

- *Characteristics of videos*

The number of views, view ratio (number of views/day), total video duration, total number of "likes" and "dislikes", total number of comments, comments ratio (number of comments/day), time since upload, number of subscribers and source of upload were noted. All videos were categorized by source into four groups: physician, non-physician healthcare professional, academic institutions/professional organizations and health-related websites. The content of vid-

eos was categorized as introduction, demonstration, indications and complications of dry needling. Moreover, like ratio and video power index (VPI) were used to evaluate the popularity of the videos. The like ratio was found by using the following formula: [number of likes/(number of dislikes +number of likes)]*100. VPI was calculated as like ratio*view ratio/100 [11].

- *Assessment of quality of videos*

The DISCERN instrument was developed to analyze the quality of information. It consists of 15 questions plus an overall quality rating [12]. It is composed of three sections evaluating reliability (section 1 with 8 questions), quality of information about treatment options (section 2 with 7 questions), and the overall quality of the information (section 3). Each question was scored on a five-point (1-5) scale. If the quality criterion was completely fulfilled, it was scored as 5, and if not fulfilled at all, it was scored as 1. If it met the criterion to some extent, it was scored as 2 to 4 according to the assessors' judgment [13]. The total DISCERN score was calculated by adding up the first 15 questions. It can be categorized as excellent (63-75), good (51-62), fair (39-50), poor (27-38), and very poor (<27) [12, 13].
The Journal of the American Medical Association (JAMA) benchmark criteria were published in order to evaluate the quality of internet information on health care. It assesses four criteria: authorship, attribution, disclosure, and currency. Each criterion scored as 1. The maximum possible score is 4, which represents the maximum score [14]. All of the scales that were used are shown in Table 1.

- *Statistical Analysis of Data*

The Shapiro-Wilk test was performed to test the normality of data. Descriptive measures such as mean, standard deviation, frequency, percentage, and minimum-maximum values were noted. The Kruskal-Wallis test was performed to compare two or more independent variables. The Dunn-Bonferroni post-hoc method was used following a significant Kruskal-Wallis test for pairwise comparison. The Spearman test was performed for correlation analysis. The inter-rater agreement was assessed with the kappa coefficient. The results were evaluated at a 95% confidence interval and a significance level of $P < .05$. The Statistical Package for the Social Sciences 22 (IBM, Armonk, NY, USA) was used for analysis.

Results

A total of 150 videos were screened and 50 videos were excluded: 30 were duplicates, 10 were off-topic, 5 were in a language other than English, and 5 had no audio. The characteristics of the 100 analyzed videos are summarized in Table 2. Most of the videos were uploaded by non-physician health personnel (42%) and physicians (27%). The most common video content was demonstration (53%) of dry needling. The mean scores of the JAMA and DISCERN tools were 1.9 and 35.3, respectively. Thirty-four percent of videos were very poor, 31% were poor, 18% were fair, 11% were good, and only 6% were excellent. The Cohen kappa score was calculated as 0.87 for the JAMA score and 0.85 for the DISCERN total score. DISCERN reliability, DISCERN quality, DISCERN total and JAMA scores were significantly higher in videos that were uploaded by physicians (Table 3). When Bonferroni adjustment was performed, videos uploaded by physicians had higher scores of DISCERN reliability, DISCERN quality, and DISCERN total compared to non-physician health personnel ($p<0.05$). Videos uploaded by physicians also had significantly higher JAMA scores compared to non-physician health personnel ($p=0.04$) and health-related websites ($p=0.003$).

Table 1. Scales used for assessment of quality of videos on dry needling

		Question		Score (1-5)
DISCERN	**Section 1**	1	Are the aims clear?	
		2	Does it achieve its aims?	
		3	Is it relevant?	
		4	Is it clear what sources of information were used to compile the publication (other than the author or producer)?	
		5	Is it clear when the information used or reported in the publication was produced?	
		6	Is it balanced and unbiased?	
		7	Does it provide details of additional sources of support and information?	
		8	Does it refer to areas of uncertainty?	
	Section 2	9	Does it describe how each treatment works?	
		10	Does it describe the benefits of each treatment?	
		11	Does it describe the risks of each treatment?	
		12	Does it describe what would happen if no treatment is used?	
		13	Does it describe how the treatment choices affect overall quality of life?	
		14	Is it clear that there may be more than one possible treatment choice?	
		15	Does it provide support for shared decision making?	
	Section 3	16	Based on the answers to all of these questions, rate the overall quality of the publication as a source of information about treatment choices	
		Question		1 point per question
JAMA		1	Authorship (authors, contributors, affiliations, and credentials)	
		2	Attribution (references and sources used for the content and copyright information)	
		3	Disclosures (ownership, sponsorship, advertising, commercial funding and potential conflicts of interests)	
		4	Currency (dates of posted and updated information)	

Table 2. Baseline descriptive statistics of videos on dry needling (n=100)

		Number (%)
Source of upload	Physician	27 (27)
	Nphp	42 (42)
	Academic institution/professional organizations	10 (10)
	Health related websites	21 (21)
		Number (%)
Content of video*	Introduction	10 (10)
	Demonstration	53 (53)
	Indications	20 (20)
	Mentioning introduction, demonstration, indications and complications	17 (17)
		Mean (SD), min-max
Detailed features of videos	Video duration (min)	8.5 (18.5), 0.65-122.3
	Time since upload (days)	1312.1 (818.8), 26-3150
	Number of views	85339 (238752), 85-1717649
	View ratio	59.2 (158.1), 0.11-973
	Number of comments	18.2 (31.4), 0-217
	Number of likes	405.6 (1484.1), 0-11000
	Number of dislikes	21.9 (49.8), 0-376
	Like ratio	92.9 (5.5), 75-100
	VPI	56.1 (151.9), 0.11-965.7
	DISCERN	35.3 (15.4), 15-75
	JAMA score	1.9 (0.8), 0-4

N: number, nphp: non-physician health personnel, VPI: Video Power Index, JAMA: Journal of American Medical Association, SD: standard deviation, min-max: minimum-maximum, *Each video may contain more than one subject.

Table 3. Assessment of video quality according to the source of upload [results are presented as median (min-max)]

	Physician	Nphp	Academic institution/ professional organizations	Health related websites	P-value
DISCERN reliability	23 (11-40)	16 (8-40)	19.5 (11-40)	19 (9-27)	0.040
DISCERN treatment	14 (7-35)	10 (7-35)	13 (7-35)	13 (7-24)	0.077
DISCERN quality	3 (1-5)	2 (1-5)	2 (1-5)	2 (1-4)	0.023
DISCERN total	39 (19-75)	26 (15-75)	31.5 (20-75)	32 (16-51)	0.037
JAMA score	2 (1-4)	2 (0-4)	2 (1-4)	1.5 (1-2)	0.002

Min-max: minimum-maximum; JAMA: Journal of the American Medical Association; Nphp: non-physician health personnel, Values in bold were significant.

There was a strong correlation between total score of DISCERN and reliability subgroup of DISCERN (rho=0.97, p<0.0001), treatment subgroup of DISCERN (rho=0.94, p<0.0001), quality subgroup of DISCERN (0.93, p<0.0001), and JAMA (rho=0.57, p<0.0001). There was no statistically significant correlation between DISCERN scores and audience interaction parameters, such as number of views, number of subscribers, view ratio, number of comments, number of likes/dislikes, and VPI. The duration of videos had a significant moderate correlation with DISCERN reliability (rho=0.43, p<0.0001), DISCERN treatment (rho=0.42, p<0.0001), DISCERN quality (rho=0.49, p<0.0001), DISCERN total score (rho=0.45, p<0001), and JAMA score (rho=0.40, p<0.0001).

Discussion

This study aimed to evaluate the content and quality of YouTube videos on dry needling. Demonstration and indications of dry needling were the most popular content uploaded. The mean DISCERN and JAMA scores were 35.3 and 1.9, respectively. The majority of videos were very low and low quality. Most of the videos were uploaded by non-physician health personnel, mainly physiotherapists, and physicians. The videos uploaded by physicians had higher quality scores compared to non-physician health personnel. As the duration of videos increase, DISCERN and JAMA scores increase; in other words, the quality of the videos increases.

The Internet is an important and popular source of health-related information. Dry-needling is an invasive procedure that causes a tendency for patients to seek online information before or after the procedure. Since the quality of online information is variable and unchecked, this may lead patients to obtain misleading information and can impact the patient-healthcare provider relationship. Watching videos related to the procedure could increase or decrease patient anxiety, according to previous studies [15, 16]. On the other hand, patients can take an active role in the decision about the treatment if they obtain accurate and reliable information [17]. Health-care providers should be aware of the content of YouTube videos on dry needling in order to guide their patients properly.

In the literature, there were studies evaluating the quality and reliability of YouTube videos as a source of information for patients [11, 18-20]. In our study, most of the videos were uploaded by physicians and non-physician health personnel. Non-

physician health personnel were composed mainly of physiotherapists, because dry needling is performed by physicians and other non-physician health personnel like physiotherapists and osteopaths. Similarly, Bagcier et al., who evaluated the quality of YouTube videos on knee osteoarthritis exercises found that the vast majority of the videos were uploaded by non-physician health personnel [18]. As dry needling is an invasive procedure, it is not surprising that the content of most of the videos were about the demonstration of dry needling. More than 50% of the videos were of low quality according to the DISCERN tool. Previous studies also showed that YouTube videos on several topics such as fibromyalgia, kyphosis and rotator cuff tears were of low quality, in line with the current study [11, 19, 20]. It is more difficult to accurately inform and guide patients who have acquired misleading information. The patients can have a preconception, especially about invasive procedures in clinics. Therefore, it is sometimes challenging to break these prejudices.

DISCERN reliability, DISCERN quality, DISCERN total, and JAMA scores were significantly higher in videos that were uploaded by physicians compared to non-physician health personnel. In the literature, several studies showed that videos uploaded by physicians and academic institutions were of high quality [11, 21, 22]. We also found that as the duration of videos increases, their quality increases, similar to the study by Ozsoy-Unubol et al. [11]. As expected, the subject can be explained clearly and extensively with longer videos. On the other hand, viewers can lose interest while watching videos of longer duration [11].

Like previous YouTube studies, we had similar limitations. Only English-language videos were analyzed, meaning that we could not analyze videos in other languages that may represent the entire population of YouTube videos. The analysis was performed as a snapshot; that is, we performed the analysis at a single time point. YouTube is constantly updated, and its content is changing. Also, YouTube lists videos by relevance, which may also affect the results. On the other hand, all videos were analyzed by two independent physical medicine and rehabilitation specialists, who showed almost perfect agreement.

Conclusion

Before or after an invasive procedure like dry needling patients tend to gather information by using the Internet, especially YouTube. As the quality of YouTube videos is variable, it can be challenging to convince patients by countering misleading information. Physicians, non-physician health personnel, and academic institutions should be aware of this issue, and they should upload high-quality, reliable videos with relevant references and state their conflict of interest to prevent patients from obtaining misleading information.

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 is a cross-sectional study that included no human or animal participants, so ethical approval was not required and consent was waived.

References

1. Dunning J, Butts R, Mourad F, et al. Dry needling: a literature review with implications for clinical practice guidelines. Phys Ther Rev : PTR. Aug 2014;19(4):252-65. doi:10.1179/108331913x13844245102034
2. Casanueva B, Rivas P, Rodero B, et al. Short-term improvement following dry needle stimulation of tender points in fibromyalgia. Rheumatol Int. Jun 2014;34(6):861-6. doi:10.1007/s00296-013-2759-3

3. Berger AA, Liu Y, Mosel L, et al. Efficacy of Dry Needling and Acupuncture in the Treatment of Neck Pain. Anesth Pain Med. Apr 2021;11(2):e113627. doi:10.5812/aapm.113627
4. Funk MF, Frisina-Deyo AJ. Dry needling for spine related disorders: a scoping review. Chiropr Man Therap. May 11 2020;28(1):23. doi:10.1186/s12998-020-00310-z
5. Boyce D, Wempe H, Campbell C, et al. Adverse Events Associated with Therapeutic Dry Needling. Int J Sports Phys Ther. Feb 2020;15(1):103-13.
6. Zengin O, Onder ME. Educational quality of YouTube videos on musculoskeletal ultrasound. Clin Rheumatol. Oct 2021;40(10):4243-51. doi:10.1007/s10067-021-05793-6
7. Onder ME, Zengin O. YouTube as a source of information on gout: a quality analysis. Rheumatol Int. Jul 2021;41(7):1321-8. doi:10.1007/s00296-021-04813-7
8. Nason K, Donnelly A, Duncan HF. YouTube as a patient-information source for root canal treatment. Int Endod J. Dec 2016;49(12):1194-1200. doi:10.1111/iej.12575
9. Chang MC, Park D. YouTube as a Source of Information on Epidural Steroid Injection. J Pain Res. 2021;14:1353-7. doi:10.2147/jpr.s307506
10. Derakhshan A, Lee L, Bhama P, et al. Assessing the educational quality of 'YouTube' videos for facelifts. Am J Otolaryngol. Mar-Apr 2019;40(2):156-9. doi:10.1016/j.amjoto.2019.01.001
11. Ozsoy-Unubol T, Alanbay-Yagci E. YouTube as a source of information on fibromyalgia. Int J Rheum Dis. Feb 2021;24(2):197-202. doi:10.1111/1756-185x.14043
12. Charnock D, Shepperd S, Needham G, et al. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. J Epidemiol Community Health. 1999;53(2):105-11. doi:10.1136/jech.53.2.105
13. Kaicker J, Borg Debono V, Dang W, et al. Assessment of the quality and variability of health information on chronic pain websites using the DISCERN instrument. BMC medicine. Oct 12 2010;8:59. doi:10.1186/1741-7015-8-59
14. Silberg WM, Lundberg GD, Musacchio RA. Assessing, controlling, and assuring the quality of medical information on the Internet: Caveant lector et viewor--Let the reader and viewer beware. Jama. Apr 16 1997;277(15):1244-5.
15. Kazancioglu HO, Tek M, Ezirganli S, et al. Does watching a video on third molar surgery increase patients' anxiety level? Oral Surg Oral Med Oral Pathol Oral Radiol. Mar 2015;119(3):272-7. doi:10.1016/j.oooo.2014.10.012
16. Ahmed KJ, Pilling JD, Ahmed K, et al. Effect of a patient-information video on the preoperative anxiety levels of cataract surgery patients. J Cataract Refract Surg. Apr 2019;45(4):475-9. doi:10.1016/j.jcrs.2018.11.011
17. Longtin Y, Sax H, Leape LL, et al. Patient participation: current knowledge and applicability to patient safety. Mayo Clin Proc. Jan 2010;85(1):53-62. doi:10.4065/mcp.2009.0248
18. Bagcier F, Yorulmaz E, Temel MH. YouTube as a Source of Patient Information for Knee Osteoarthritis Exercises. Turk J Osteoporos. 2021;27(3)
19. Erdem MN, Karaca S. Evaluating the Accuracy and Quality of the Information in Kyphosis Videos Shared on YouTube. Spine (Phila Pa 1976). Nov 15 2018;43(22):E1334-e1339. doi:10.1097/brs.0000000000002691
20. Kuru T, Erken HY. Evaluation of the Quality and Reliability of YouTube Videos on Rotator Cuff Tears. Cureus. Feb 3 2020;12(2):e6852. doi:10.7759/cureus.6852
21. Delli K, Livas C, Vissink A, et al. Is YouTube useful as a source of information for Sjögren's syndrome? Oral Dis. Apr 2016;22(3):196-201. doi:10.1111/odi.12404
22. Koller U, Waldstein W, Schatz KD, et al. YouTube provides irrelevant information for the diagnosis and treatment of hip arthritis. Int Orthop. Oct 2016;40(10):1995-2002. doi:10.1007/s00264-016-3174-7

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A SINGLE CENTER EXPERIENCE OF ATRIAL FIBRILLATION ABLATION WITH CRYOBALLOON

KRİYOBALON İLE TEK MERKEZDE ATRİYAL FİBRİLASYON ABLASYONU DENEYİMİ

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Abstract

Aim: Electrical isolation of the pulmonary veins is known as the fundamental of for atrial fibrillation (AF) treatment invasively, and thus, has been suggested as the first-line therapy in AF curation. In this study, we presented our single center pulmonary vein isolation (PVI) experience and long-term clinical outcome.

Methods: One hundred and six symptomatic AF patients resistant to medical therapy underwent cryoablation of the pulmonary veins. Participants were divided into two groups regarding AF categorization as persistent or paroxysmal. Recurrence and peri-procedural complications were evaluated after the treatment.

Results: A 106 patients, 67 males (63.2%), with mean age of 51.8 ±13.1 years, underwent cryoablation. While the paroxysmal AF group was composed of 90 patients (84.9%); the persistent AF group consisted of 16 patients (15.1%). The procedure mean time was 115,9±9,1 minute while the fluoroscopy mean time was 29,2±5,6 minutes. A total of 8 (7.5%) non-fatal complications were experienced. A total of 18 recurrences (17%) were observed during mean duration of 25.2 months follow-up period. The survival rates without AF were 85.6% and 61.8 % in in the paroxysmal and persistent groups, respectively.

Conclusions: The cryoballoon PVI seems to be a successful and reliable method of treating AF and may be preferred as a primary procedure even in patients with persistent AF.

Keywords: Atrial fibrillation, cryoballoon, phrenic nerve palsy

Öz

Amaç: Pulmoner venlerin elektriksel izolasyonu, atriyal fibrilasyonun (AF) invaziv tedavisinin temel taşı olarak bilinir ve bu nedenle, AF ablasyonunda ilk adım olarak önerilmiştir. Bu çalışmada, persistant ve paroksismal AF tanısı koyulan hastalarda pulmoner ven izolasyonu (PVI) deneyimimizi ve klinik sonuçlarımızı analiz ettik.

Yöntemler: Antiaritmik tedaviye dirençli semptomatik AF'si olan ardışık yüz altı hastaya pulmoner venlerin izolasyonu için kriyoablasyon uygulandı. Hastalar AF sınıflamasına göre persistant veya paroksismal olmak üzere iki gruba ayrıldı. Rekürrens ve peri-prosedürel komplikasyonlar sırasıyla birincil ve ikincil sonuçlar olarak analiz edildi.

Bulgular: Yaş ortalaması 51,8 ±13,1 yıl, 67'si erkek (%63,2) olan 106 hastaya kriyoablasyon tedavisi uygulandı. 90 hastada paroksismal AF (%84,9) ve 16 hastada persistant AF (%15,1) vardı. Ortalama işlem süresi 115,9±9,1 dakika ve ortalama floroskopi süresi 29,2±5,6 dakikaydı. Ölümcül olmayan 8 (%7,5) komplikasyon gözlendi. İşlem sonrası 3 aylık dönem çıkarıldığında ortalama 25,2 aylık takip süresinde 18 nüks (%17) gözlendi. Paroksismal ve persistan gruplarda AF'nin nükssüz oranları sırasıyla %85,6 ve %61,8'idi.

Sonuç: Kriyobalon ile pulmoner ven izolasyonu AF tedavisinde başarılı ve güvenilir bir yöntem olarak görünmektedir. Sonuçlarımız, kriyoablasyonun persistant AF'si olan hastalarda bile başlangıç tekniği olarak kullanılabileceğini gösteren önceki çalışmalarla uyumludur.

Anahtar Kelimeler: Atriyal fibrilasyon, kriyobalon, frenik sinir paralizisi

Introduction

Clinical atrial fibrillation (AF) is described as the detection of an AF episode by 12-lead electrocardiography (ECG) or any documentation of an AF episode longer than 30 seconds in 24 hours ECG Holter. AF is an important disease that is of great interest for clinicians both clinically, economically and in terms of mortality and morbidity, and which can be avoided by different management modalities. The incidence of AF in the adult population is 2-4%[1].

In recent guidelines, in addition to medical treatment in AF, AF ablation seems to be one step ahead of medical treatment that the increased data on the provision of cure with ablation. After the detection and classification of clinical AF, evaluation of the patient for complications of AF and ensuring sinus rhythm as soon as possible is the primary goal in accordance with the new modalities[1]. The main target aimed at AF ablation is the electrical inaccessibility of pulmonary veins. In the current studies, a success rate of over 80% was reported in long-term follow-up after successful AF ablation procedure[2]. In the recent guidelines, pulmonary vein isolation (PVI) is the primary suggested non-drug cure option for both persistent and paroxysmal symptomatic AF patients who are resistant to medication[3-5].

In this study, we aimed to show our clinic's (a referral arrhythmia center) experience of electrical isolation through cryoballoon of pulmonary veins in AF patients.

Materials and Methods

- *Study population*

The individuals treated by cryoablation because of AF between May 2016-December 2018 were retrospectively examined in this study. In all procedures, the second-generation cryo energy balloons were used (Arctic Front Advance Cardiac Cryoablation Catheter System, Medtronic, Inc Minneapolis, MN). AF episodes shorter than 7 days (conversion to sinus rhythm with spontaneous or medical treatment) were defined as paroxysmal and AF episodes longer than seven days were described as persistent AF[3]. The patient's anamnesis and examinations' notes (ECG, echocardiography, 24 hours ECG Holter and blood parameters) were obtained from the visit notes and the hospital records.

Exclusion criteria were intermediate-advanced valve pathologies (stenosis and insufficiency), congenital heart diseases, bleeding diathesis, contraindications for any anticoagulants, detection of thrombus in transesophageal echocardiography, advanced-stage heart failure, and left atrial diameter bigger than 5.5 centimeters. All patients were given detailed information about the procedure, success rate, and risks, and the consent forms were signed. Kosuyolu Research and Education Hospital of Medicine Clinical Research Ethics Committee approved this study with number and date of 06.10.2020/9/356. The study was conducted in keeping with all ethical procedures/standards and the Declaration of Helsinki.

- *Preprocedural management*

Hemogram, kidney and thyroid functions, liver enzymes, and prothrombin time parameters were examined in all patients before the procedure. Before ablation, patients were evaluated for ejection fraction (EF), valve pathologies, and left atrium diameter by transthoracic and transesophageal echocardiography[6]. It was shown that there were no intracardiac thrombi for all patients. Anticoagulation therapy was started at least 3 weeks prior to the procedure and anticoagulation was continued without interruption during ablation. The International Normalized Ratio (INR) value was ensured the level of between 2 and 3 before the procedure in warfarin user patients. The patients taking a new generation of oral anticoagulants

(NOACS), took their last doses 12-24 hours prior to the ablation depending on NOAC type.

- *Ablation procedure*

Ablation was performed with local anesthesia (lidocaine) and sedation (midazolam, fentanyl) for all patients. 2 pieces of 6 French vascular sheaths were positioned in the left femoral vein and another 8 French vascular sheath was positioned in the right femoral vein access. Coronary sinus and quadripolar diagnostic catheters were engaged into the coronary sinus and his area from the left femoral vein access. The septostomy procedure was performed using fluoroscopic anatomy. The vascular sheath in the right femoral vein was replaced with a SL-1 septostomy sheath (Abbott, Chicago, IL, USA) with the help of a 0.32 wire and SL-1 was positioned into the superior vena cava. After insertion of the Brockenbrough needle (BRK-1, Abbott) into the SL-1 catheter, the catheter was withdrawn and when it reached the patent foramen ovale (PFO) region, the needle was removed from the catheter tip and the septostomy procedure was performed. After confirming with a contrast agent and 0.014 floppy wire that the needle tip was in the left atrium, the SL1 catheter was advanced into the left atrium (Figure 1). A 0.35 guidewire was sent into the SL1 catheter, and the catheter was replaced with a (FlexCath Advance) steerable sheath (Medtronic). A 20- or 25-mm circular (Achieve™) mapping catheter (Medtronic) and a 28mm cryoballoon catheter were advanced from the steerable sheath.

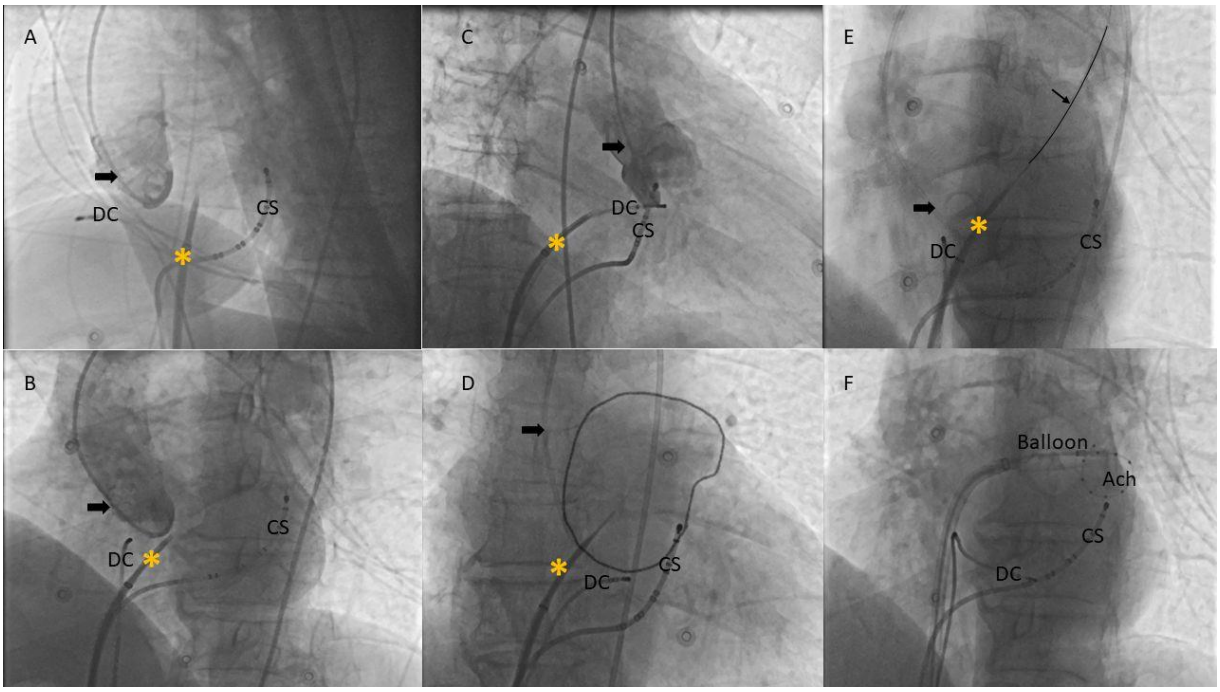

Figure 1: Transseptal puncture guided by fluoroscopic anatomy.
Figure 1 shows transseptal puntruce of a patient by fluoroscopy guidance.
A: Left lateral (90^0) fluoroscopic view shows the position of the septostomy sheath posterior to the aorta.
B: Left anterior oblique (30^0) fluoroscopic view shows the position of the septostomy sheath.
C: Right anterior oblique (30^0) fluoroscopic view shows the position of the septostomy sheath.
D: Contrast enhancement of the left atrium with opaque administation after septostomy.
E: Wiring of left upper pulmonary vein with floppy after septostomy to prevent injury of the left atrium.
F: Achieve and cryo-ballon catheter positioned towards to the left inferior pulmonary vein.
*: septostomy sheath, DC: diagnostic catheter, CS: coranary sinus, Ach: achieve circular mapping catheter, Thick arrow: pigtail positioned in non-coranary cuspis, Thin arrow: 0.014 wire positioned in the left upper pulmonary vein, Straight line: Left atrium border

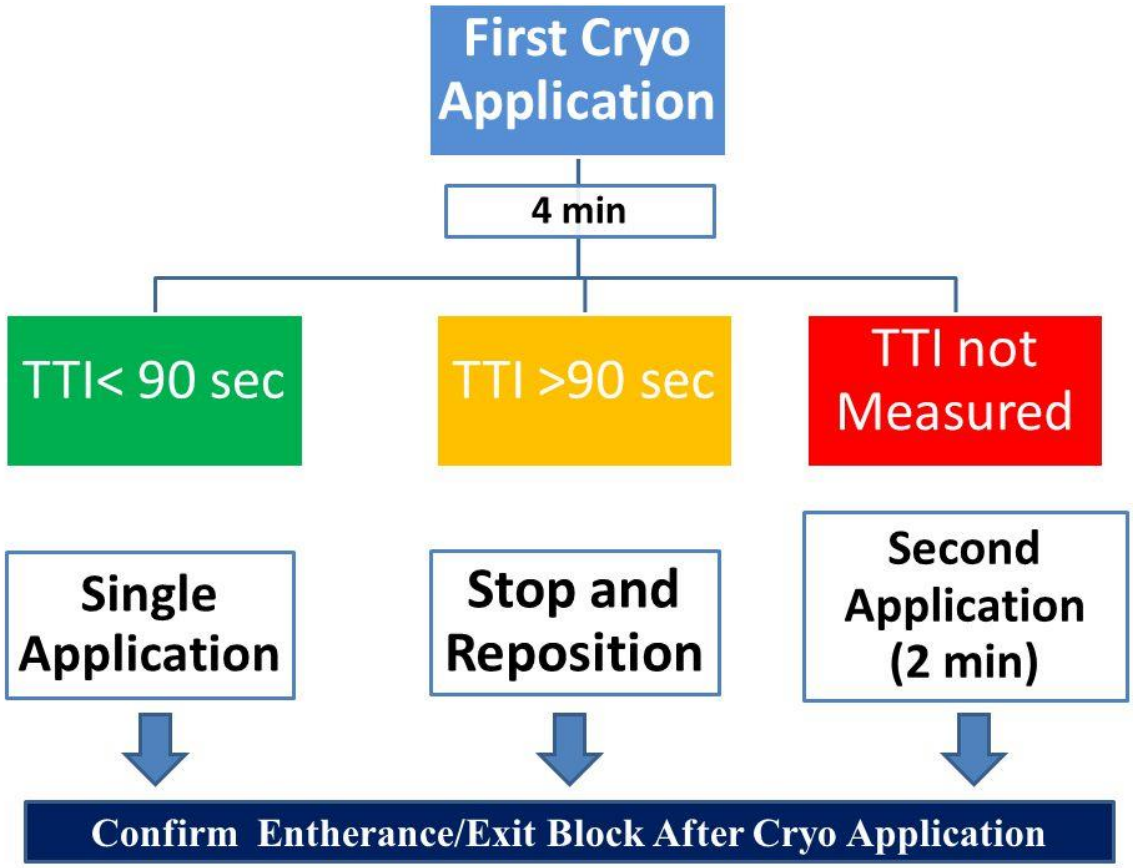

Figure 2. Freezing Protocol (Figure 2 shows the number and time of cryoenergy applications in each pulmonary vein varied as a function of the time necessary to achieve electrical isolation of the vein.)
TTI: time to isolation.

After taking the electrical potentials of the pulmonary vein with a circular catheter from the pulmonary vein ostium, the cryoballoon catheter was inflated and advanced to the pulmonary vein ostium (Figure 1). Cryoablation was started after the selective stop-flow or slow-flow pulmonary contrast imaging. The dissociation or disappearance of pulmonary vein potentials (time-to-isolation) was followed up with the circular mapping catheter. If the pulmonary vein isolation was achieved within 90 seconds, only a single ablation of 240 seconds was performed. If it was not isolated for over 90 seconds, the balloon was deflated, repositioned and the ablation was performed again. If the insulation phase could not be quantified upon the need to advance the balloon to a better position with the aim of PV occlusion, distinct two application as 240 and 120 seconds was used (Figure 2). In order to prevent phrenic nerve paralysis while cryoenergy was applied to the right pulmonary veins, the decapolar catheter was placed in the superior vena cava (SVC) region and stimulation of phrenic nerve was performed with electrical stimulus (2500 msec cycle). Tactile feedback of diaphragmatic contraction method was used to assess the phrenic nerve function loss.

After ablation, if the rhythm was AF, electrical cardioversion was executed for achieving sinus rhythm, then pulmonary veins were shown, via exit and entrance blocks, to be electrically isolated.

Transthoracic echocardiography was executed immediately after ablation to evaluate possible pericardial effusion.

- *Postprocedural management*

Patients were followed up in the in-patient department with an ECG and non-invasive blood pressure monitoring if no complications were observed after the procedure. After the bleeding control was achieved, the patient was given anticoagulation therapy (if NOACs were used, the NOACs dose was given to the patients, and if warfarin was used, the warfarin dose determined for that day was given to the patients). The morning after the ablation, the patients were examined, and their treatment was reconsidered and discharged.

- *Follow-up period*

Ablation success was described by way of the nonappearance of atrial arrhythmia (atrial tachycardia, fibrillation or flutter) over 30 seconds after a blanking period of 3 months from the ablation procedure[5]. The follow-up was performed with 1st and 12th-month echocardiography; 1st, 3rd, 6th, and 12th month ECG; 12th-month 24-hours ECG Holter. Long-term follow-up (>1-year post-intervention) was completed once a year. Patients were also followed up by phone calls. It was suggested to the patients that if they felt any palpitations within any period of time, they should take ECG.

- *Statistical analysis*

While categorical variables were stated by ratios scheme and compared with chi-square test, continuous data were expressed with mean±SD scheme and assessed with student-T and paired T-tests. The Kolmogorov-Smirnov test was applied to check the normally distribution. In the following process AF recurrence was assessed with the Kaplan–Meier method. Event-free time was considered from the procedure day to the recurrence day or the last day of the patient's hospital visit.

Patients who had no recurrence of AF by the last follow-up were assumed as the event-free patient. The Kaplan–Meier curve for event-free analysis was drawn to assess the recurrence between groups, divided recurrence, and non-recurrence group. Univariate regression analysis was executed to define the crucial parameter on AF recurrence. In addition, parameters that showed the recurrence well were evaluated by the multivariate COX regression analyses. Statistical analyses were executed through the SPSS Statistics software (Windows v. 20, IBM) and statistically significance was defined as the p values of under the 0.05.

Results

106 patients were included in this study. While 90 patients had paroxysmal AF, 16 patients diagnosed with persistent AF. There was a male predominance (63.2%) with mean age of 51±13 years. The mean time of procedure and fluoroscopy were 115.9±9.1 and 29.2±5.6 minutes, respectively. The patients were followed averagely 25.2±15.5 months. The baseline characteristics and procedural characteristics are summarized in Table 1.

During the follow-up (25.2 months) AF recurrence was observed in 18 patients (17%). A statistically significant lower recurrence rate was observed in the paroxysmal AF group than in the persistent AF group (p=0.05). Recurrence was observed for 13 patients (14.4%) in the paroxysmal AF group and 5 patients (31.2%) in the persistent AF group (p=0.0032) (Figure 3).

The AF recurrence predictors were ejection fraction (p=0.004), left ventricular end-diastolic diameter (p=0.005), left atrium (LA) diameter(p<0.001), and persistent AF (p=0.05). LA diameter was determined as an independent predictor in multivariate regression analysis (p=0.05).(Table 2)

Table 1. Demographic and clinical variables

	AF Recurrence (-) 88 (83%)	AF Recurrence (+) 18 (17%)	Total 106	P
Gender Female n %	34 (38.6 %)	5 (27.8 %)	39 (36.8%)	0.547
Male n %	54 (61.4%)	13 (72.2 %)	67 (63.2%)	
Age (years) ±SD	52.1 ±12.5	50.1 ±15.8	51.8 ±13.1	0.554
BMI (kg/m^2) ±SD	26.9 ±2.8	27.2 ±2.7	26.9 ±2.8	0.685
CAD n %	7 (8%)	1 (5.6%)	8 (7.5%)	1.000
Hypertension n %	36 (40.9%)	6 (33.3%)	42 (39.6%)	0.738
Diabetes Mellitus n %	14 (19.3%)	4 (22.2%)	21 (19.8%)	1.000
Hyperlipidemia n %	15 (17%)	5 (27.8%)	20 (19.8%)	0.466
CKD n %	5 (5.7%)	2 (11.1%)	7 (6.6%)	0.746
CHA_2DS_2VASc Score ±SD	1.2 (±1.4)	1.3 (±1.1)	1.3 (±1.3)	0.936
Persistant AF n %	11 (12.5%)	5 (27.7%)	16 (15.1%)	0.05
EF % ±SD	61.5 (±6.3)	56.4(8.7%)	60.7(7%)	0.004
LVEDD (cm) ±SD	4.7 (±0.3)	4.9 (±0.4)	4.7 (±0.3)	0.005
LVESD (cm) ±SD	2.9 (±0.4)	3.2 (±0.7)	2.9 (0.4)	0.005
LA Diameter (cm) ±SD	3,7 (±0.4)	4,2 (±0.4)	3.8 (±0.5)	<0.001
AF Diagnosed Time (month) ±SD	31.9 (±18.7)	36 (±14.4)	32.6 (±18.1)	0.379
Time of the Procedure (minute) ±SD	115.8 (±9)	116.8(±9.6)	95.9(±9.1)	0.649
Fluoroscopy time (minute) ±SD	29.2(±5.5)	26.4(±6.2)	29.2(±5.6)	0.856

AF: atrial fibrillation, BMI: body mass index, CAD: coranary artery disease, CHA2DS2-VASc: Congestive heart failure, Hypertension, Age >_75 years, Diabetes mellitus, Stroke, Vascular disease, Age 6574 years, Sex category (female), CKD: chronic kidney disease, EF: ejection fraction, LA: left atrium, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter.

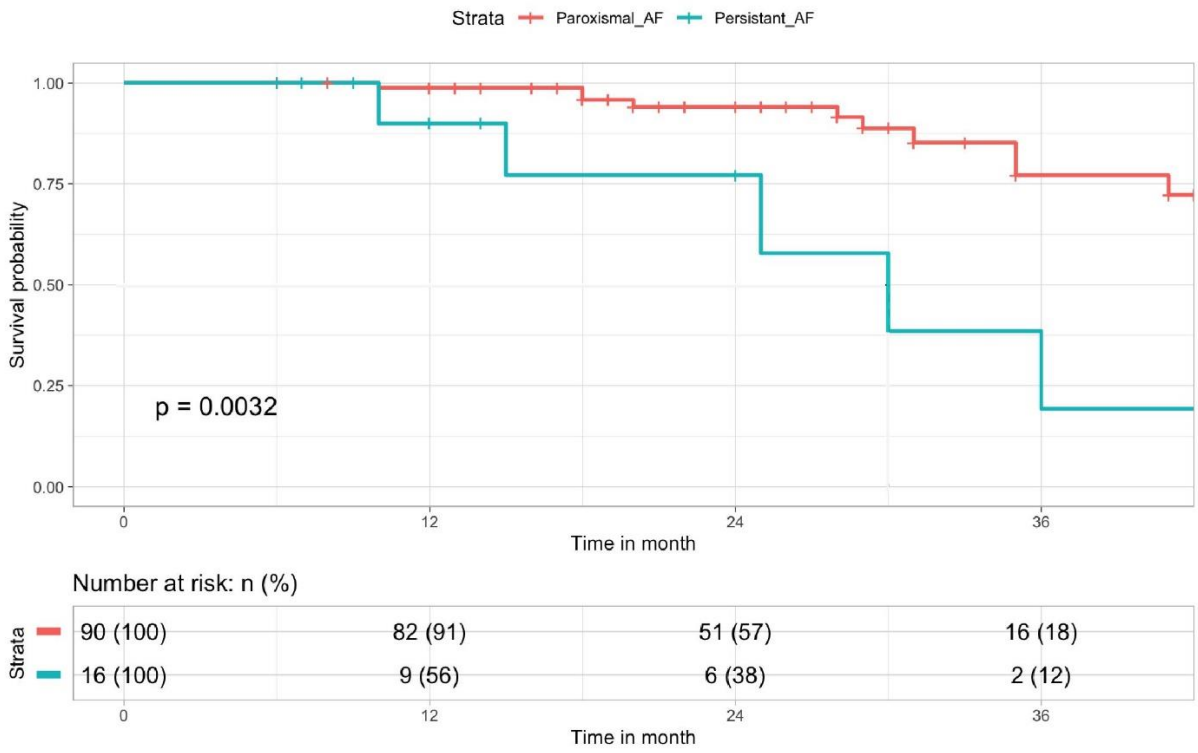

Figure 3. Atrial Fibrillation Free Survival by the Kaplan-Meier Curve (Kaplan Meier curve shows that the reccurence of AF was much more common in patients with persistent AF compared to the patients with paroxysmal AF.)

In this study, there were 416 (8 patients were observed to have common left pulmonary veins) pulmonary veins totally and 412 showed electrical isolation during the procedure (99%). The patients who had non-isolated pulmonary veins during the procedure (4 patients) had early period AF recurrence.

Complications were observed in 8 patients. 3 patients had temporary phrenic nerve paralysis lasting less than 15 minutes, one patient had permanent phrenic nerve paralysis at discharge (It was observed that phrenic nerve paralysis disappeared during the 1st-month control), one patient had minor pericardial effusion, one patient had hematoma that did not require intervention in the femoral region and, one patient had a cerebrovascular event 48 hours after the procedure. The patient who had cerebrovascular event was intervened with percutaneously at an early stage and any

Table 2. Multivariate COX Regression Analyses for Predicting Recurrence of AF

	Univariable HR 95% CI	p	Multivariable HR 95% CI	p
CHA_2DS_2VASc (increase from 0 to 2)	1.18 (0.53-2.65)	0.67	0.72 (0.31-1.68)	0.45
LA diameter (increase from 3.6 to 4.1)	3.38 (1.16-9.87)	0.007	3.63 (1.21-10.84)	0.05*

LA: left atrium.

sequelae were not observed. After the ablation procedure, there was no major bleeding, no major pericardial effusion requiring pericardiocentesis, and no death was observed.

Discussion

This study revealed that after a cryoballoon ablation procedure, 83% of patients were had no AF recurrence in the long-term follow-up. Although AF recurrence was more frequent in patients with persistent AF, our study showed that cryoballoon ablation for atrial fibrillation was effective and reliable in the treatment of paroxysmal AF similar to the results of previous studies[7-10].

AF is the most common atrial arrhythmia and one of the important causes of morbidity and mortality. The EARLY-AF study showed the preference of rhythm control over rate control by catheter ablation in terms of preventing both AF progression and pathophysiological changes in AF patients[11].

In addition, Jais P et al. showed that rhythm control is a more preferable method compared to rate control, and especially the AF catheter ablation may be initially selected in patients with paroxysmal and short-term persistent AF patients[12]. Randomized controlled trials and meta-analyses stated that AF catheter ablation is superior to rate control with antiarrhythmic drugs in the scores of the quality of life.

In addition to these data, there are not enough randomized controlled trials related to stroke, which is a serious cause of mortality and morbidity in the AF ablation patient group[13-17]. The complete pulmonary veins isolation is the main target for AF ablation irrespective of the technique used.

In the literature, no significant dissimilarities were found between cryoballoon ablation and radiofrequency ablation (RFA) in terms of successful PVI. In addition, approaches such as substrate modification and posterior wall isolation that can be applied with RFA are not recommended, especially in patients who underwent AF ablation for the first time[1,18-23]. As known before, in persistent AF, triggers may come from non-pulmonary vein foci (posterior wall, SVC, LAA, CS ostium, etc.) and only pulmonary vein isolation is not sufficient however, in paroxysmal AF, the triggers mostly come from PVI[3,10]. PVI is still the main goal in AF ablation, and wider areas of ablation techniques are not praised in the first-line intervention according to current guidelines. In our study, the majority of patients (84.9%) had paroxysmal AF and only pulmonary vein isolation was determined as a target at the first stage of treatment. The causes of recurrence after AF ablation may be considered as the development of reconnection in the pulmonary veins, another AF triggers out of pulmonary veins, or the extensive scarring of the atrial tissue[24]. AF-free survival was 85.6% for the paroxysmal AF group and 68.8% for the permanent AF group during the follow-up period. Similarly, Boghossian et al. found a recurrence rate of 10.8% for paroxysmal AF and 32.6% for persistent AF in the single-center experience[25].

In contrast to our result, in the CIRCA-DOSE study, in which recurrence was evaluated by implantable monitors, the recurrence rate in proximal AF patients was 36%. We can explain this discrepancy by the fact that, in our study, no implantable loop recorder (ILR) was used in the post-procedural follow-up period (only ECG-Holter and ECG monitoring were performed at certain intervals)[26].

AF type and duration, EF, LA diameter, presence of structural heart disease, hypertension (HT), diabetes mellitus (DM), age, etc. were found as parameters related with AF recurrence after AF ablation[24]. Similarly in our study, in univariate analysis, AF recurrence was found to be associated with EF, ventricle diameters, LA diameter, and the presence of persistent AF. However, in multivariate analysis, only the LA diameter was found to be an independent predictor of AF recurrence. In our study, HT, DM, age, and gender were

not associated with AF recurrence and may be associated with a small number of patients enrolled in the study.

The most common cause of recurrence after cryoablation is the inability to isolate the pulmonary veins during the procedure or reconnection of the pulmonary veins[27,28]. Similarly, in our study, in 4 out of 13 PAF patients who developed AF recurrence, the pulmonary veins could not be electrically isolated during the procedure.

In our study, there was a similar rate of complications (7.5%) with the literature[29,30]. The most common complication was transient phrenic nerve damage that was shown in 4 patients. In addition, one patient developed cerebrovascular disease, one developed pericardial effusion that did not require intervention, and one had vascular complications after the procedure. No death related to the procedure or permanent sequelae were observed in any patient.

Our clinical experience has similar success and complication rates as the other studies in the literature[10,30-34]. As a result, cryoablation, which is less dependent on operator experience and has a shorter processing time can be considered as first-line therapy in PAF patients when the pulmonary veins are considered to be a trigger of AF.

Conclusion

Isolation of PV with cryoballoon seems to be a successful and reliable method of treating AF. In addition to the fact that the chances of success in paroxysmal AF are quite high, it also may be selected to be the first choice of method in persistent AF.

- *Limitations*

The current study has several limitations. First of all, this is a single-center observational study without a control group. Therefore, there might be a bias in patient selection. Secondly, although patients were checked regularly during outpatient clinic visits with ECG, and symptomatic patients were followed with holter monitoring. However, routine holter monitoring was performed only after 1 year of ablation. Therefore, the incidence of AF recurrence may have been underestimated. Lastly, although the median follow-up was 25.2 months, higher AF recurrence may occur after a longer follow-up period.

Author contributions

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Design: Ayhan Kup, Mehmet Celik, Taylan Akgun
Data Collection and Processing: Ayhan Kup, Kamil Gulsen
Analysis or Interpretation: Ayhan Kup, Mehmet Celik, Abdulkadir Uslu
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Writing: Ayhan Kup, Abdulkadir Uslu

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

Ethical approval was taken from the Kosuyolu Training and Research Hospital local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.2020/9/356).

References

1. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb 1;42(5):373-498. doi: 10.1093/eurheartj/ehaa612
2. European Heart Rhythm Association (EHRA), European Cardiac Arrhythmia Scoiety (ECAS), American College of Cardiology (ACC), American Heart Association (AHA), Society of Thoracic Surgeons (STS), Calkins H, et al.

HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures an follow-up. A report of the Heart Rhythm Society (HRS) Tasck Force on catheter and surgical ablation of atrial fibrillation. Heart Rhythm. 2007;4(6):816-61. doi:10.1016/j.hrthm.2007.04.005
3. Kirchhof P, Benussi S, Kotecha D, et al. 2016 Esc Guidelines for the management of atrial fibrilation developed in collaboration with EACTS. Europace. 2016;18(11):1609-78.
4. Wong KC, Paisey JR, Sopher M, et al. No benefit of complex fractionated atrial electrogram ablation in addition to circunferential pulmonary vein ablation and linear ablation: benefit of complex ablation study. Circ Arrhythm Electrophysiol. 2015;8(6):1316-24.
5. Fink T, Schlüter M, Heeger CH, et al. Stand-alone pulmonary vein isolation versus pulmonary vein isolation with additional substrate modification as index ablation procedures in patients with persistent and long standing persistent atrial fibrillation: the Randomized Alster-Lost-AF Trial (Ablation at St Georg Hospital for long standing persistent atrial fibrillation). Circ Arrhythm Electrophysiol. 2017;10(7):pii:e005114.
6. Franceschi F, Koutbi L, Mancini J, et al. Novel electromyographic monitoring technique for prevention of right phrenic nerve palsy during cryoballoon ablation. Circ Arrhythm Electrophysiol. 2013; 6:1109-14. doi:10.1161/CIRCEP.113.000517
7. Chierchia GB, Di Giovanni G, Ciconte G, et al. Second-generation cryoballoon ablation for paroxysmal atrial fibrillation: 1-year follow-up. Europace. 2014 May;16(5):639-44. doi: 10.1093/europace/eut417.
8. Fürnkranz A, Bordignon S, Dugo D, et al. Improved 1-year clinical success rate of pulmonary vein isolation with the second-generation cryoballoon in patients with paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2014 Aug;25(8):840-4. doi: 10.1111/jce.12417.
9. Ciconte G, Ottaviano L, de Asmundis C, et al. Pulmonary vein isolation as index procedure for persistent atrial fibrillation: One-year clinical outcome after ablation using the second-generation cryoballoon. Heart Rhythm. 2015 Jan;12(1):60-6. doi: 10.1016/j.hrthm.2014.09.063.
10. Lemes C, Wissner E, Lin T, et al. One-year clinical outcome after pulmonary vein isolation in persistent atrial fibrillation using the second-generation 28 mm cryoballoon: a retrospective analysis. Europace. 2016 Feb;18(2):201-5. doi:10.1093/europace/euv092.
11. Andrade JG, Champagne J, Deyell MW, et al. A randomized clinical trial of early invasive intervention for atrial fibrillation (EARLY-AF) methods and rationale. Am Heart J 2018;206:94-104. doi: 10.1016/j.ahj.2018.05.020.
12. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. Circulation 2008;118:2498-2505. doi: 10.1161/CIRCULATIONAHA.108.772582.
13. Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. JAMA 2010;303:333-40. doi: 10.1001/jama.2009.2029.
14. Cosedis Nielsen J, Johannessen A, Raatikainen P, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. N Engl J Med 2012;367:15871595. doi:10.1056/NEJMoa1113566.
15. Blomstrom-Lundqvist C, Gizurarson S, Schwieler J, et al. Effect of catheter ablation vs antiarrhythmic medication on quality of life in patients with atrial fibrillation: the CAPTAF randomized clinical trial. JAMA 2019;321(11):1059-68. doi:10.1001/jama.2019.0335.
16. Mark DB, Anstrom KJ, Sheng S, et al. Effect of catheter ablation vs medical therapy on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial. JAMA 2019;321(13):1275-85. doi:10.1001/jama.2019.0692.
17. Shi LZ, Heng R, Liu SM, et al. Effect of catheter ablation versus antiarrhythmic drugs on atrial fibrillation: a meta-analysis of randomized controlled trials. Exp Ther Med 2015;10:816-22. doi: 10.3892/etm.2015.2545.
18. Kuck K-H, Brugada J, Fürnkranz A, et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. N Engl J Med. 2016;9;374(23):2235-45. doi: 10.1056/NEJMoa1602014.
19. Tamborero D, Mont L, Berruezo A, et al. Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study. Circ Arrhythm Electrophysiol 2009;2:35-40. doi:10.1161/CIRCEP.108.797944.
20. Verma A, Jiang CY, Betts TR, et al. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med 2015;372:1812-1822. doi: 10.1056/NEJMoa1408288.
21. Arbelo E, Guiu E, Ramos P, et al. Benefit of left atrial roof linear ablation in paroxysmal atrial fibrillation: a prospective, randomized study. J Am Heart Assoc 2014;3:e000877.

doi:10.1161/JAHA.114.000877.
22. Da Costa A, Levallois M, Romeyer-Bouchard C, et al. Remote-controlled magnetic pulmonary vein isolation combined with superior vena cava isolation for paroxysmal atrial fibrillation: a prospective randomized study. Arch Cardiovasc Dis 2015;108:163-71. doi: 10.1016/j.acvd.2014.10.005.
23. Hu X, Jiang J, Ma Y, et al. Is there still a role for additional linear ablation in addition to pulmonary vein isolation in patients with paroxysmal atrial fibrillation? An updated meta analysis of randomized controlled trials. Int J Cardiol 2016;209:266-274. doi:10.1016/j.ijcard.2016.02.076.
24. Vizzardi E, Curnis A, Latini MG, et al. Risk factors for atrial fibrillation recurrence: a literature review. J Cardiovasc Med (Hagerstown). 2014 Mar;15(3):235-53. doi: 10.2459/JCM.0b013e328358554b.
25. Boghossian SHC, Barbosa EC, Boghossian E, et al. Experience in a Brazilian Center with Cryoablation for Electric Isolation of the Pulmonary Veins in Paroxysmal and Persistent Atrial Fibrillation - Preliminary Results in Brazil. Arq Bras Cardiol. 2020 Sep;115(3):528-35. doi: 10.36660/abc.20200320
26. Andrade JG, Champagne J, Dubuc M, et al. Cryoballoon or Radiofrequency Ablation for Atrial Fibrillation Assessed by Continuous Monitoring: A Randomized Clinical Trial. Circulation. 2019 Nov 26;140(22):1779-88. doi:10.1161/CIRCULATIONAHA.119.042622
27. Heeger CH, Wissner E, Mathew S, et al. Once Isolated, Always Isolated? Incidence and Characteristics of Pulmonary Vein Reconduction After Second-Generation Cryoballoon-Based Pulmonary Vein Isolation. Circ Arrhythm Electrophysiol. 2015 Oct;8(5):1088-94. doi: 10.1161/CIRCEP.115.003007.
28. Reddy VY, Sediva L, Petru J, et al. Durability of Pulmonary Vein Isolation with Cryoballoon Ablation: Results from the Sustained PV Isolation with Arctic Front Advance (SUPIR) Study. J Cardiovasc Electrophysiol. 2015 May;26(5):493-500. doi: 10.1111/jce.12626.
29. Kuck KH, Brugada J, Fürnkranz A, et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. N Engl J Med. 2016 Jun 9;374(23):2235-45. doi: 10.1056/NEJMoa1602014.
30. Tondo C, Iacopino S, Pieragnoli P, et al. Pulmonary vein isolation cryoablation for patients with persistent and long-standing persistent atrial fibrillation: Clinical outcomes from the real-world multicenter observational project. Heart Rhythm. 2018 Mar;15(3):363-8. doi:10.1016/j.hrthm.2017.10.038.
31. Kuck KH, Fürnkranz A, Chun KR, et al. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. Eur Heart J. 2016 Oct 7;37(38):2858-65. doi: 10.1093/eurheartj/ehw285.
32. Mörtsell D, Arbelo E, Dagres N, et al. Cryoballoon vs. radiofrequency ablation for atrial fibrillation: a study of outcome and safety based on the ESC-EHRA atrial fibrillation ablation long-term registry and the Swedish catheter ablation registry. Europace. 2019 Apr 1;21(4):581-9. doi: 10.1093/europace/euy239.
33. Boveda S, Metzner A, Nguyen DQ, et al. Single-Procedure Outcomes and Quality-of-Life Improvement 12 Months Post-Cryoballoon Ablation in Persistent Atrial Fibrillation: Results From the Multicenter CRYO4PERSISTENT AF Trial. JACC Clin Electrophysiol. 2018 Nov;4(11):1440-1447. doi: 10.1016/j.jacep.2018.07.007.
34. Providencia R, Defaye P, Lambiase PD, et al. Results from a multicentre comparison of cryoballoon vs. radiofrequency ablation for paroxysmal atrial fibrillation: is cryoablation more reproducible? Europace. 2017 Jan;19(1):48-57. doi: 10.1093/europace/euw080.

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CLINICAL OUTCOMES OF NON-OPERATIVE TREATMENT OF SUSPECTED UNCOMPLICATED APPENDICITIS IN CHILDREN

KOMPLİKE OLMAYAN APANDİSİT ÖN TANILI ÇOCUKLARDA AMELİYATSIZ TEDAVİNİN KLİNİK SONUÇLARI

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Abstract

Aim: Non-operative treatment approach is another method used in the treatment of uncomplicated appendicitis, in which the infection in the appendix is suppressed and treated with antibiotics. Our study aims to investigate the clinical outcomes and the risk factors for recurrence in our pediatric patients with suspected uncomplicated appendicitis, who underwent non-operative treatment.

Methods: The medical data of the patients who underwent non-operative treatment with the diagnosis of suspected uncomplicated appendicitis between January 2016 and January 2021 in a tertiary pediatric surgery center were analyzed. Demographic data, treatment process, and clinical results of the patients were recorded. Statistical evaluation was made by comparing the two groups with and without recurrence after non-operative treatment.

Results: The median age of 41 patients whose data were evaluated was 13 (6-17) years. Eight patients (19.5%) had appendicolith. The median duration of IV antibiotic treatment was 4 (3-7) days, and the patients' abdominal tenderness disappeared in a median of 2 (1-4) days. Recurrence developed in 8 (19.5%) patients after a median of 7 (1-14) months after non-operative treatment. It was found that the time to the disappearance of abdominal tenderness was statistically longer in the group that developed recurrence than that in the group that did not (p=0.01).

Conclusions: Our study revealed that appendicolith was not a risk factor for the development of recurrence. The time to the disappearance of abdominal tenderness may be useful for detecting patients at a higher risk of recurrence.

Keywords: appendicitis, non-operative treatment, antibiotic, children

Öz

Amaç: Ameliyatsız tedavi yaklaşımı, apendiksteki enfeksiyonun baskılandığı ve antibiyotiklerle tedavi edildiği komplike olmayan apandisit tedavisinde kullanılan diğer bir yöntemdir. Çalışmamızın amaçları komplike olmayan apandisit ön tanılı çocuk hastalarda ameliyatsız tedavinin klinik sonuçlarının ve rekürrens gelişmesi için risk faktörlerinin araştırılmasıdır.

Yöntemler: Ocak 2016 ve Ocak 2021 tarihleri arasında üçüncü basamak bir çocuk cerrrahisi merkezinde komplike olmayan apandisit ön tanılı ve ameliyatsız tedavi uygulanmış hastaların tıbbi verileri değerlendirildi. Hastaların tanımlayıcı bilgileri, tedavi süreci ve klinik sonuçları kaydedildi. Ameliyatsız tedavi sonrası rekürrens gelişen ve gelişmeyen iki hasta grubunun verileri istatistiksel olarak karşılaştırıldı.

Bulgular: Ortanca yaşı 13 (6-17) yıl olan 41 hastanın verileri değerlendirildi. Sekiz (%19,5) hastada apendikolit vardı. Ortanca IV antibiyotik tedavi süresi 4 (3-7) gün ve hastaların ortanca abdominal hassasiyetlerinin kaybolma süresi 2 (1-4) gündü. Ameliyatsız tedaviden ortanca 7 (1-14) ay sonra 8 (%19,5) hastada rekürrens gelişti. Rekürrens gelişen grupta abdominal hassasiyetin kaybolma süresi diğer gruba göre istatistiksel anlamlı olarak daha uzundu (p=0.01).

Sonuç: Çalışmamız apendikolitin rekürrens gelişimi için risk faktörü oluşturmadığını ortaya koydu. Abdominal hassasiyetin kaybolması için geçen zaman rekürrens gelişimi için yüksek riskli hastaların tespitinde faydalı olabilir.

Anahtar Kelimeler: Apandisit, ameliyatsız tedavi, antibiyotik, çocuk

Introduction

Appendicitis is the most common cause of emergency surgeries of the abdomen in children[1,2]. The risk of having appendicitis in children up to the age of 18 is 2.5%, and one out of every six cases is complicated appendicitis[1,2]. Appendicitis is most common in the second decade of childhood and is more common in males[2]. It is divided into two groups, complicated and uncomplicated, according to the perforation of the appendix[3,4]. The basic approach in the treatment of appendicitis is the surgical excision of the appendix[4]. Another treatment method for uncomplicated appendicitis is the non-operative treatment (NOT) with antibiotics approach, which does not have a standardized protocol yet. While the first clinical results regarding the NOT approach for treating appendicitis in adult patients were published in 1959, the results in children began to be published in the second half of the 90s[5,6]. The positive aspects of the NOT approach in uncomplicated appendicitis are the avoidance of unnecessary surgery and anesthesia and the lower costs compared to the surgical approach. The most frequently criticized aspects are the recurrence rates of 5-37%, the lack of a standard treatment algorithm, and the fact that it is unknown how many of the patients who underwent NOT had appendicitis, since appendicitis is a histopathological diagnosis[7-13].

Our study aims to evaluate the clinical results of the uncomplicated appendicitis cases treated with NOT in our clinic and determine the factors that increase the risk of recurrence.

Materials and Methods

The medical data of the pediatric patients under the age of eighteen who applied to our clinic between January 2016 and January 2021, who were diagnosed with uncomplicated appendicitis and underwent the NOT approach, were retrospectively analyzed. The descriptive information of the patients, the treatment protocol applied, the clinical course in the treatment process, the follow-up period after discharge, the recurrence information, and the histopathological evaluations were examined.

Information about the latest clinical status of the patients was obtained by contacting them by phone. The term suspected uncomplicated appendicitis (SUA) was used as the patients' diagnoses, since the diagnosis of uncomplicated appendicitis was not made after a histopathological evaluation. After evaluations from two experienced pediatric surgeons, the patients were diagnosed with SUA, and NOT was applied. The inclusion and exclusion criteria and the patients' discharge criteria after NOT are shown in Table 1. During NOT, cefazolin (50 mg/kg/day, divided into three doses) or cefazolin and metronidazole (30 mg/kg/day, divided into three doses) were used together as intravenous (IV) antibiotics. After discharge, amoxicillin-clavulanic acid was perorally used for seven days at age-appropriate doses. The definition of recurrent appendicitis in the study is the diagnosis of appendicitis after the relapse of abdominal pain in SUA patients who underwent NOT.

For the study, approval was obtained from the Ethics Committee of Non-Interventional Clinical Studies, dated 5.03.2021 and numbered 109. Informed consent was obtained from the parents of the patients participating in the study.

- *Statistical analysis*

Statistical evaluation was done with IBM® SPSS® Statistics 20.0. We presented categorical variables as frequency (percentage) and continuous variables as median with minimum and maximum values. We used Chi-square test to compare categorical variables between groups and Mann-Whitney U test to compare continuous variables. If the p-value was less than 0.05, the result was considered statistically significant.

Table 1. Inclusion and exclusion criteria for the study and the discharge criteria of the patients

Research Inclusion Criteria
❖ No fever at admission ❖ Localized abdominal tenderness ❖ Appendix MOD ≥ 6 mm ❖ NOT was applied and discharged
Research Exclusion Criteria
❖ Fever at admission ❖ Widespread abdominal tenderness at admission (perforation, diffuse peritonitis, abscess) ❖ Development of fever during NOT ❖ Development of widespread abdominal tenderness during NOT ❖ History of previous abdominal surgery ❖ Administration of antibiotics before NOT ❖ Undergoing an appendectomy during hospitalization during NOT ❖ Use of oral antibiotics for less or more than 7 days after discharge ❖ Re-implementation of NOT
Discharge Criteria of Patients
❖ Ability to tolerate a normal diet ❖ The disappearance of abdominal tenderness on clinical examination

MOD: Maximum Outer Diameter, NOT: Non-Operative Treatment, SUA: Suspected Uncomplicated Appendicitis

Results

Fifty-three patients met the study criteria. Twelve patients were excluded from the study due to insufficient data, treatment incompatibility, and the lack of follow-up information. There was additional disease in four patients (asthma n=3, type 2 diabetes mellitus n=1). Two groups were formed in the study; group A included 33 patients who underwent NOT and did not develop recurrence in the follow-up, and the group B comprised 8 patients who developed recurrence and underwent appendectomy. All patients had right lower quadrant tenderness (McBurney's sing) in the first physical examination. The median age of the study group was 13 (6-17) years, and the percentages of males and females were close to each other. Patients age, gender, weight, time to start antibiotic treatment, white blood cell, diameter of appendix on ultrasound, type of IV antibiotic used, duration of IV antibiotic treatment, time of disappearence of abdominal tenderness, initiation to feeding and duration of hospitalization were evaluated as descriptive features. The descriptive features and the clinical findings of all the patients are presented in Table 2. No statistically significant difference was found between the two groups in terms of descriptive features. When the clinical results between the two groups were compared, it was found that the time of disappearance of abdominal tenderness on physical examination during the application of NOT was statistically significantly longer in the group B than that in the other group ($p = 0.01$). A comparison of descriptive features and clinical results between the two groups is presented in Table 3.

Table 2. Descriptive characteristics and clinical outcomes of the study group

	All patients **n = 41**
Age (years)	13 (6-17)
Gender	
❖ Male	20 (48.7%)
❖ Female	21 (51.3%)
Weight (kilograms)	45 (17-109)
White Blood Cell (cells/microliter)	13700 (2000-22600)
Diameter of appendicitis on ultrasound (millimeters)	7 (6-12)
Fecalitis on ultrasound	
❖ Yes	8 (19.5%)
❖ No	33 (80.5%)
Time to start antibiotic treatment (days) *	2 (1-7)
Duration of IV antibiotic treatment (days)	4 (3-7)
Disappearance of abdominal tenderness (days)	2 (1-4)
Initiation to feeding (days)	2 (1-2)
Duration of hospitalization (days)	5 (3-7)
Type of IV antibiotic used	
❖ Cefazolin	10 (24.3%)
❖ Cefazolin + Metronidazole	31 (75.7%)
Recurrence	
❖ Yes	8 (19.5%)
❖ No	33 (80.5%)
Duration between **NOT and recurrence (months)	7 (1-14)
Follow up period (months) (non-recurrent group)	21 (11-65)
Follow up period (months) (patients with appendicolith)	26 (21-89)

Values are median (minimum-maximum) or n (%).
*Time between the onset of abdominal pain and the initiation of treatment
**Non-Operative Treatment

Table 3. Comparison of descriptive characteristics and clinical outcomes between the two groups

	Non recurrent group n = 33	Recurrent group n = 8	P value
Age (years)	13 (6-17)	11.5 (8-16)	0.5
Gender			
Male	16	4	0.6
Female	17	4	
Weight (kilograms)	45 (17-109)	36.5 (25-54)	0.4
Time to start antibiotic treatment (days) *	2 (1-7)	1.5 (1-3)	0.6
White Blood Cells (cells/microliter)	13000 (2000-22600)	14450 (8100-19600)	0.6
Diameter of appendix on ultrasound (millimeters)	7 (6-12)	8 (6-10)	0.6
Type of IV antibiotic used			
❖ Cefazolin	9	1	0.7
❖ Cefazolin + Metronidazole	24	7	
Duration of IV antibiotic treatment (days)	4 (3-7)	4 (3-7)	0.7
Disappearance of abdominal tenderness (days)	2 (1-4)	3 (2-4)	**0.01**
Initiation to feeding (days)	2 (1-2)	2 (1-2)	0.9
Duration of hospitalization (days)	5 (3-7)	4.5 (3-7)	0.6

Values are median (minimum-maximum)
*Time between the onset of abdominal pain and the initiation of treatment

Discussion

In SUA patients, NOT was performed on 41 patients, and recurrence developed in 8 (19.5%). Recurrence developed a median of 7 (1-14) months after NOT. The time required for the disappearance of abdominal tenderness after the initiation of IV antibiotic therapy during hospitalization was found to be statistically significantly longer in the group with recurrence (p = 0.01).

The median age of the study group was 13 (6-17) years, consistent with the age range where appendicitis is most common in the literature, and the percentage of males in the study group was found to be less (48.7%) than in the literature[2]. The median body weight of the patients was 45 (17-109) kilograms, and Body Mass Index could not be calculated due to the lack of height data. It was found that the patients had applied to our clinic a median of 2 (1-7) days after the onset of abdominal pain. There was no sta-

tistically significant difference between the two groups in terms of the time between the onset of abdominal pain and the initiation of IV antibiotic therapy (p = 0.6). All the patients experienced pain in the right lower quadrant of the abdomen and tenderness at the first examination, but there was no sign of diffuse peritonitis and fever.

White Blood Cell (WBC) elevation has been defined in pediatric patients with appendicitis, and its sensitivity for the diagnosis of appendicitis has been reported as 67-88% and specificity as 53-80%[14,15]. Grönroos stated in his study that 7% of the children with acute appendicitis had normal leukocyte levels[15]. In our study, the median WBC value of the patients at the beginning of the hospitalization was 13700 (2000-22000) cell/mcL, and the WBC value of 20 (48.7%) patients was within normal limits. WBC value was found below the normal limits in one patient at 2000 cell/mcL, and this patient's platelet value was 39000 cell/mcL. This patient was followed up for further hematological examination, and no recurrence developed in this patient.

One of the imaging methods frequently used in the diagnosis of appendicitis in children is ultrasonographic evaluation of the abdomen. It has been published that the sensitivity and the specificity of the ultrasound in the diagnosis of appendicitis are 88% and 94%, respectively[16]. Findings of mesenteric fat stranding, fluid collection, non-compressible appendix, and an appendix diameter over six millimeters in the abdominal ultrasound performed for abdominal pain were defined as compatible with appendicitis[17]. In our study, since only the maximum outer diameter (MOD) of the appendix was regularly reported among the findings supporting appendicitis in the abdominal ultrasound reports, the MOD of the appendix was evaluated in the study. Tanaka et al. found in their study that the mean appendix MOD was 8.5 ± 2.1 mm in the group without recurrence and 9.5 ± 2.3 mm in the group with recurrence, and no statistically significant difference was found between them[8]. In our study group, the median appendix MOD was 7 (6-12) mm, and there was no statistically significant difference between the two groups when the appendix MOD was compared (p = 0.6).

Appendicolith is defined as fecal concentration and is more common in children than in adults[18]. Singh et al. reported that 29.9% of the pediatric patients with acute appendicitis, and 56.1% of those with perforated appendicitis had appendicolith in the appendix. In a prospective non-randomized study examining the feasibility of NOT in children with acute appendicitis in whom appendicolith was detected, 60% of the patients developed recurrence within five months after the application of NOT, and the study was stopped[19]. In another study, the recurrence rate was 47% in the patients with appendicolith, while the recurrence rate was reported as 23.7% in the patients who did not (p = 0.049)[8]. In our study, appendicolith was detected in the appendix by ultrasound in 8 (19.5%) patients, but recurrence did not develop in any of them. The median and range of the follow-up period of these patients were 26 (21-89) months. The reason for this result, which is inconsistent with the literature, may be the duration of the antibiotic use, which was longer in our study than in both of the other studies[8,19].

The published studies state that different antibiotic protocols and durations of use were applied during the NOT. Tanaka et al. used different IV antibiotic protocols, such as sulbactam/ampicillin and ceftazidime or meropenem or imipenem/cilastatin and gentamicin, to increase the probability of success when the success rate after cefmetazole, the first antibiotic used, was 85.7% when applying NOT. They stated that the success rate after the modified antibiotic protocol was 98.7%. However, it has been reported that different antibiotic regimens, such as IV piperacillin/tazobactam and ciprofloxacin/metronidazole, were used in the first treatment[8,11,20]. In some study protocols, IV antibiotics were discontinued after 1-2 doses, depending on the improvement in the clinical condition after hospitalization, while oral antibiotic treatment was

started afterwards[11,20,21]. The pediatric literature has studies in which oral antibiotics are not given after discharge and studies in which oral amoxicillin-clavulanic acid or ciprofloxacin/metronidazole are used[9,11,22].
In our study, 10 (24.3%) patients were given IV cefazolin and 31 (75.7%) patients were given IV cefazolin and metronidazole for a median of 4 (3-7) days while NOT was applied. No statistical difference was found between the groups in the study in terms of the duration and the types of IV antibiotic administration (p = 0.7, p = 0.7). Oral amoxicillin-clavulanic acid treatment was administered to all patients in the study group for seven days after discharge.
In the literature, there is no standardization in the discharge criteria of patients. Tanaka et al. determined CRP < 0.5 mg/dl, absence of fever, and absence of abdominal pain as discharge criteria. However, the absence of fever, decrease or disappearance of pain, and the ability to tolerate feeding were generally used as discharge criteria[8,9,21,23]. The discharge criteria of our study were loss of abdominal tenderness and tolerance to oral feeding. The median duration of loss of abdominal tenderness in our patients was 2 (1-4) days, and the median time to start oral feeding was 2 (1-2) days. The disappearance of abdominal tenderness after starting IV antibiotics was found to be statistically significantly longer in the group B (p = 0.01), while there was no statistically significant difference between the initiation of oral feeding in both groups (p = 0.9). We think that the statistically longer duration of the disappearance of abdominal tenderness on physical examination after IV treatment in the group B may be important data for the early detection of patients who may develop recurrence.
Although few studies in the literature discuss the economic impact of NOT in children with SUA, Mosuka and Wu emphasized that NOT is cost-effective[12,24]. In our study, however, the economic dimension of the treatment was not evaluated.
The hospitalization time of the patients in our study was 5 (3-7) days, and no statistically significant difference was found between the two groups in terms of hospitalization time (p = 0.6).
Abdominal pain may develop in patients discharged after NOT administration. If this abdominal pain is diagnosed as recurrent appendicitis, there are options, such as a new course of NOT treatment or an appendectomy. It is observed that the recurrence rates increase with the prolongation of the follow-up period of the patients. While the one-year success rates are 71-95%, overall success rates have been reported as 62-76%[7,8,21]. In the meta-analysis of Georgiou et al., in which 413 patients were evaluated, the recurrence rate was reported as 14%[10]. When comparing success rates, it should be kept in mind that there is serious heterogeneity between the patients' characteristics, treatment protocols, and follow-up periods in the studies.
In our study, 8 (19.5%) patients who were treated with NOT developed recurrence after a median of 7 (1-14) months, and appendectomy was performed on them. In three patients, NOT was performed for the second time after recurrence, and they were discharged. These patients did not develop recurrence and were not included in the study group. Three patients who developed recurrence and underwent appendectomy were operated on outside of our clinic. The histopathological results of the five patients whose results we reached were reported as acute appendicitis. The median follow-up period of the group A was 21 (11-65) months.
The most important limitations of our study are that it is a retrospective study, it does not include a large cohort, and there is no research on the economic cost of NOT.

Conclusion

In our study, our recurrence rate was 19.5% in SUA patients who underwent NOT. The presence of appendicolith in the appendix on ultrasound was not found to be a risk factor for the development of recurrence. The time between the initiation of IV antibiotics

and the disappearance of abdominal tenderness in the group with recurrence was found to be statistically significantly longer than that in the group without recurrence. We think that this result can be useful in detecting patients who may develop recurrence after NOT. However, the reliability of this data needs to be checked in larger series.

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

Ethical approval was taken from the Cukurova University local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.05.03.2021/109).

References

1. Omling E, Salö M, Saluja S, et al. Nationwide study of appendicitis in children. Br J Surg. 2019;106(12):1623-31. doi: 10.1002/bjs.11298
2. Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990;132(5):910-25. doi: 10.1093/oxfordjournals.aje.a115734
3. Mariage M, Sabbagh C, Grelpois G, et al. Surgeon's Definition of Complicated Appendicitis: A Prospective Video Survey Study. Euroasian J Hepatogastroenterol. 2019;9(1):1-4. doi: 10.5005/jp-journals-10018-1286
4. López JJ, Deans KJ, Minneci PC. Nonoperative management of appendicitis in children. Curr Opin Pediatr. 2017;29(3):358-62. doi: 10.1097/MOP.0000000000000487
5. Coldrey E. Five years of conservative treatment of acute appendicitis. J Int Coll Surg. 1959;32:255–61.
6. Weiner DJ, Katz A, Hirschl RB, et al. Interval appendectomy in perforated appendicitis. Pediatr Surg Int. 1995;10:82–5. doi: 10.1007/BF00171160
7. Svensson JF, Patkova B, Almström M, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. Ann Surg. 2015;261(1):67-71. doi: 10.1097/SLA.0000000000000835
8. Tanaka Y, Uchida H, Kawashima H, et al. Long-term outcomes of operative versus nonoperative treatment for uncomplicated appendicitis. J Pediatr Surg. 2015;50(11):1893-7. doi: 10.1016/j.jpedsurg.2015.07.008
9. Svensson JF, Hall NJ, Eaton S, et al. A review of conservative treatment of acute appendicitis. Eur J Pediatr Surg. 2012;22(3):185-94. doi: 10.1055/s-0032-1320014
10. Georgiou R, Eaton S, Stanton MP, et al. Efficacy and Safety of Nonoperative Treatment for Acute Appendicitis: A Meta-analysis. Pediatrics. 2017;139(3):e20163003. doi: 10.1542/peds.2016-3003
11. Minneci PC, Mahida JB, Lodwick DL, et al. Effectiveness of Patient Choice in Nonoperative vs Surgical Management of Pediatric Uncomplicated Acute Appendicitis. JAMA Surg. 2016;151(5):408-15. doi: 10.1001/jamasurg.2015.4534
12. Wu JX, Sacks GD, Dawes AJ, et al. The cost-effectiveness of nonoperative management versus laparoscopic appendectomy for the treatment of acute, uncomplicated appendicitis in children. J Pediatr Surg. 2017;52(7):1135-40. doi: 10.1016/j.jpedsurg.2016.10.009
13. Zampieri N, Camoglio FS. Are we doing right suggesting a non-operative management for suspected appendicitis in children? J Pediatr Surg. 2017;52(10):1702-3. doi: 10.1016/j.jpedsurg.2017.05.019
14. Wang LT, Prentiss KA, Simon J, et al. The use of white blood cell count and left shift in the diagnosis of appendicitis in children. Pediatr Emerg Care. 2007 Feb;23(2):69-76. doi: 10.1097/PEC.0b013e31802d1716
15. Grönroos JM. Do normal leucocyte count and C-reactive protein value exclude acute appendicitis in children? Acta Paediatr. 2001 Jun;90(6):649-51.
16. Doria AS, Moineddin R, Kellenberger CJ, et al. US or CT for Diagnosis of Appendicitis in Children and Adults? A Meta-Analysis. Radiology. 2006;241(1):83-94. doi: 10.1148/radiol.2411050913
17. Chicaiza HP, Malia L, Mulvey CH, et al. Revisiting the Appendiceal Diameter via Ultrasound for the Diagnosis of Acute Appendicitis. Pediatr Emerg Care. 2018 Nov;34(11):757-60. doi: 10.1097/PEC.0000000000001278
18. Singh JP, Mariadason JG. Role of the faecolith in modern-day appendicitis. Ann R Coll Surg Engl. 2013 Jan;95(1):48-51. doi: 10.1308/003588413X13511609954851
19. Mahida JB, Lodwick DL, Nacion KM, et al. High failure rate of nonoperative management of acute

appendicitis with an appendicolith in children. J Pediatr Surg. 2016 Jun;51(6):908-11. doi: 10.1016/j.jpedsurg.2016.02.056
20. Mudri M, Coriolano K, Bütter A. Cost analysis of nonoperative management of acute appendicitis in children. J Pediatr Surg. 2017;52(5):791-4. doi: 10.1016/j.jpedsurg.2017.01.050
21. Hartwich J, Luks FI, Watson-Smith D, et al. Nonoperative treatment of acute appendicitis in children: A feasibility study. J Pediatr Surg. 2016;51(1):111-6. doi: 10.1016/j.jpedsurg.2015.10.024
22. Knaapen M, van der Lee JH, Heij HA, et al. Clinical recovery in children with uncomplicated appendicitis undergoing non-operative treatment: secondary analysis of a prospective cohort study. Eur J Pediatr. 2019;178(2):235-42. doi: 10.1007/s00431-018-3277-9
23. Knaapen M, van der Lee JH, Bakx R, et al. APAC collaborative study group. Initial non-operative management of uncomplicated appendicitis in children: a protocol for a multicentre randomised controlled trial (APAC trial). BMJ Open. 2017 Nov 15;7(11):e018145. doi: 10.1136/bmjopen-2017-018145
24. Mosuka EM, Thilakarathne KN, Mansuri NM, et al. A Systematic Review Comparing Nonoperative Management to Appendectomy for Uncomplicated Appendicitis in Children. Cureus. 2021;13(10):e18901. Published 2021 Oct 19. doi: 10.7759/cureus.18901

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IMAGING METHODS USED IN THE DIAGNOSIS OF GASTROINTESTINAL PERFORATION AND IMAGING FINDINGS

GASTROİNTESTİNAL PERFORASYON TANISINDA KULLANILAN GÖRÜNTÜLEME YÖNTEMLERİ VE GÖRÜNTÜLEME BULGULARI

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Abstract

Aim: To evaluate the imaging methods used in patients diagnosed with gastrointestinal perforation (GIP) and the contribution of these methods to the diagnosis.

Methods: Preoperative radiological examinations of 73 patients 18 years old or older whose surgical results indicated GIP were retrospectively evaluated. The perforation sites were divided into 4 groups, namely the first segment of the gastroduodenum, part of the small intestine beginning with the second segment of the duodenum, the colorectum, and the appendix. Esophageal perforations were considered as a separate group and excluded from the study.

Results: Fifty-two (71.2%) of the patients were male. The mean age of the patients was 45.1±18.2 years with a range of 18-87 years. Forty (54.8%) patients had perforations of the appendix and 25 (34.2%) patients had perforations of the gastroduodenum. Computed tomography (CT) was performed in 56 (76.7%) of the patients, ultrasonography (USG) in 55 (75.3%), and radiography (RG) in 48 (65.8%). The evaluation of RG images of the patients for the presence of subdiaphragmatic free air showed that 50% of the patients with non-appendix perforations had subdiaphragmatic free air. The most common findings in the USG results of the patients with appendix perforations were an increase in the diameter and heterogeneity of mesenteric fatty tissue, while the most common USG finding in the patients with the other perforations was free fluid. The site of perforation was accurately determined in 83.9% of the patients diagnosed with non-appendix perforations by CT.

Conclusions: CT is the most preferred imaging modality and has the most diagnostic value in the diagnosis of GIP. It is also useful in determining the perforation site.

Keywords: Gastrointestinal tract, perforation, imaging

Öz

Amaç: Bu çalışmanın amacı gastrointestinal perforasyon (GIP) tanısı konulan hastalarda kullanılan görüntüleme yöntemlerini ve bu yöntemlerin tanıya katkısını değerlendirmektir.

Yöntemler: Çalışmamızda operasyon sonuçları GIP olarak belirtilen 18 yaş ve üzeri 73 hastanın operasyon öncesi radyolojik tetkikleri retrospektif olarak değerlendirildi. Perforasyon bölgeleri mide-duodenum birinci kesimi, duodenum ikinci kesimi başlangıcından itibaren ince barsak, kolorektal ve apendiks olarak 4 gruba ayrıldı. Özofagus perforasyonları ayrı bir grup olarak düşünülüp çalışma dışı bırakıldı.

Bulgular: Hastaların 52 (%71,2) si erkekti. Yaşları 18 ile 87 arasında olup ortalama yaşları 45,1±18.2 bulundu. 40(%54,8) hastada apendiks perforasyonu, 25(%34,2) hastada mide-duodenum perforasyonu vardı. 56 (%76,7) hastaya bilgisayarlı tomografi (CT), 55 (%75,3) hastaya ultrasonografi (USG) ve 48(%65,8) hastaya radyografi (RG) tetkiki yapılmıştı. Hastaların RG'leri subdiyafragmatik serbest hava varlığı açısından değerlendirildiğinde apendiks dışı perforasyonu olan hastaların %50 sinde subdiyafragmatik serbest hava görüldü. Apendiks perforasyonu olan hastaların USG'lerinde en sık tanımlanan bulgular çap artışı ve mezenterik yağlı dokuda heterojenite iken diğer perforasyonlarda en sık USG bulgusu serbest sıvıydı. CT ile apendiks dışı perforasyonu olan hastaların %83,9'unda perforasyon yeri doğru olarak belirlendi.

Sonuç: Çalışmamızda GIP tanısı konulurken en fazla tercih edilen ve tanısal değeri en yüksek olan görüntüleme modalitesinin CT olduğunu saptadık. Ek olarak CT perforasyon yerini belirlemede de faydalıydı.

Anahtar Kelimeler: Gastrointestinal sistem, perforasyon, görüntüleme

Introduction

Gastrointestinal perforation (GIP) is a surgical emergency. It can occur due to peptic ulcer, blunt or penetrating trauma, inflammatory bowel disease, iatrogenic factors, neoplasm, or foreign bodies[1]. Currently, laparoscopic methods are used instead of conventional laparotomy in appropriate cases depending on the site and cause of perforation[2-3]. Therefore, along with the diagnosis of perforation, it is important to determine the site and cause of the perforation and other accompanying findings.

The most preferred imaging method for diagnosing suspected GIP is radiography (RG). Along with abdominal RG, standing lung RG may also be performed for this purpose. Extraluminal air may be seen in these radiographs. However, if the perforation is too small or closes spontaneously, extraluminal air may not be seen. The sensitivity of RG regarding detection of extraluminal air varies from 50% to 70%[4-5]. Ultrasonography (USG) does not play a major role in the diagnosis of GIP. However, in patients with localized abdominal symptoms, USG can be used for differential diagnosis[6.] USG may help show the presence of pneumoperitoneum and pneumoretroperitoneum as direct findings and free fluid and thickened bowel segments as indirect findings[7]. Currently, the preferred imaging method used in patients with suspected GIP is computed tomography (CT). CT is also useful for determining the site and cause of perforations[8-11].

The aim of the present study was to evaluate the imaging methods used in patients diagnosed with GIP and the contribution of these methods to the diagnosis.

Materials and Methods

In this retrospective study, patients 18 years old or older whose surgical results indicated GIP between 01.01.2021 and 03.31.2022 were listed using the hospital information processing system and all patients (73 patients) were included in the study. The perforation sites were divided into 4 groups, namely the first segment of the gastroduodenum, part of the small intestine beginning with the second segment of the duodenum, the colorectum, and the appendix. Esophageal perforations were considered as a separate group and excluded from the study. The radiological images of the patients were evaluated by a radiologist via the hospital imaging archive system. Since appendix perforations may have some specific signs, the radiologist was informed about patients suffering from these. However, the cause and site of the other perforations were not known by the radiologist. RG images were evaluated for presence of extraluminal air. Figure 1 shows an RG image of subdiaphragmatic free air.

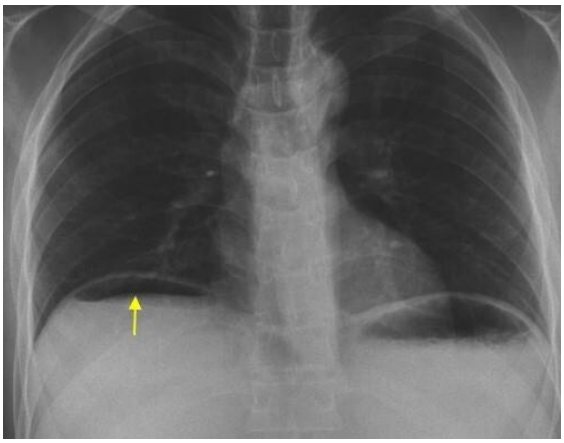

Figure 1. The radiography of a patient with gastroduodenal perforation; the arrow shows subdiaphragmatic free air.

CT images were evaluated for findings of free air, free fluid, mural thickening, mural contrast, mural discontinuity and fat stranding in the non-appendix perforations. Figure 2 shows a CT image of free air and mural discontinuity. Diameters, mucosal hyperenhancement, mucosal defect, periappendiceal air, periappendiceal fluid, fat stranding, appendicoliths, and abscess

findings in appendix perforation were evaluated. Figure 3 shows a CT image of an appendicolith and fat stranding.

- *Statistical analysis*

The statistical analysis was performed using SPSS v.22 (SPSS Inc. Chicago, IL, USA). The means and standard deviations of the continuous variables and the number and percentage values of the categorical data were calculated. In order to compare the groups, the chi-square test was performed. The level of statistical significance was set at $p<0.05$.

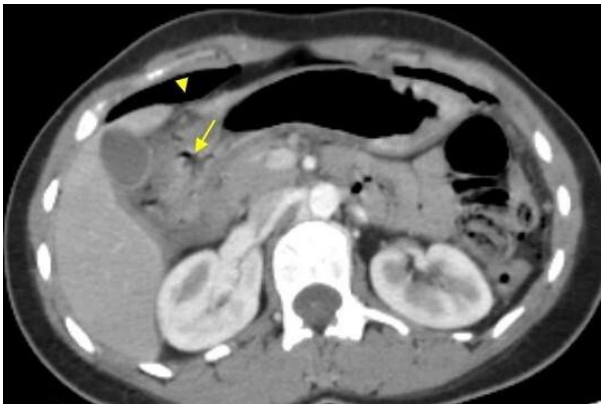

Figure 2. The axial CT image of a patient with gastroduodenal perforation; the arrowhead shows free air and the arrow shows mural discontinuity.

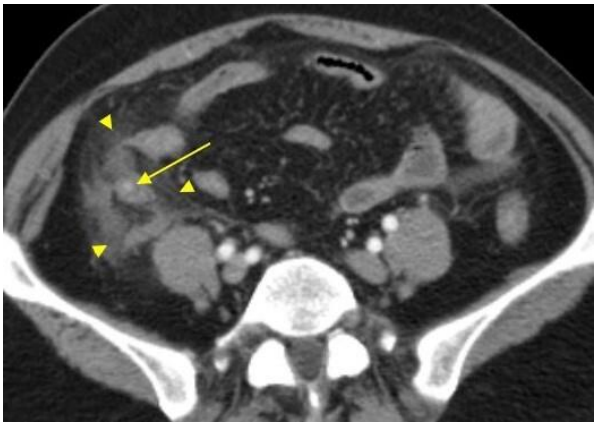

Figure 3. The axial CT image of a patient with appendix perforation; the arrow shows the appendicolith and the arrowheads show fat stranding

Results

Fifty-two (71.2%) of the patients were male and 21 (28.8%) were female. The mean age of the patients was 45.1±18.2 years with a range of 18-87. Forty (54.8%) patients had perforations of the appendix and 25 (34.2%) had gastroduodenal perforations. The demographic characteristics and perforation sites of the patients are presented in Table 1.

Table 1. Demographic characteristics and perforation sites of the patients

	n(%)
Age	45.1±18.2
Male	52 (71.2)
Female	21 (28.8)
Gastroduodenum	25 (34.2)
Small intestine	3 (4.1)
Colorectum	5 (6.9)
Appendix	40 (54.8)

n: Number of patients

Fifty-six (76.7%) patients were screened with CT, 55 (75.3%) with USG, and 48 (65.8%) with RG. The RG was primarily performed for gastroduodenal perforations, CT was primarily performed for small intestine and colorectal perforations and USG for appendix perforations. There was a significant difference in terms of the presence or absence of RG, USG, and CT examinations according to the site of perforation. The p values of these differences are $p=0.040$, $p<0.01$, and $p<0.01$, respectively (Table 2). Only one of these examinations was performed in 12 (16.4%) of the patients, while 25 (34.2%) patients underwent RG, USG, and CT examinations. The examinations performed in the patients before surgery are presented in Table 3.

Table 2. Use of radiography, ultrasonography, and computed tomography examination according to the site of perforation

Site of perforation	RG was used n(%)	USG was used n(%)	CT was used n(%)
Gastroduodenum (n=25)	20 (80.0)	17 (68.0)	23 (92.0)
Small intestine (n=3)	1 (33.3)	0 (0)	3 (100)
Colorectum (n=5)	1 (20)	0 (0)	5 (100)
Appendix (n=40)	26 (65.0)	38 (95.0)	25 (62.5)
All patients (n=73)	48 (65.8)	55 (75.3)	56 (76.7)
p value	0.040	<0.001	0.017

n: Number of patients; RG: direct radiography; USG: ultrasonography; CT: computed tomography

Table 3. Co-use and percentage distribution of examinations performed in patients

Examination	Appendix perforation n(%)	Non-appendix perforation n(%)	All n(%)
Only RG	0 (0)	1 (3.0)	1 (1.4)
Only USG	2 (5.0)	0 (0)	2 (2.7)
Only CT	1 (2.5)	8 (24.2)	9 (12.3)
RG and USG	13 (32.5)	1(3.0)	14 (19.2)
RG and CT	1 (2.5)	7 (21.2)	8 (11.0)
USG and CT	11 (27.5)	3 (9.1)	14 (19.2)
RG, USG, and CT	12 (30.0)	13 (39.4)	25 (34.2)
Total	40 (100)	33 (100)	73 (100)

RG: direct radiography; USG: ultrasonography; CT: computed tomography

The evaluation of RG images of patients for the presence of subdiaphragmatic free air showed that 50% of the patients with non-appendix perforations had subdiaphragmatic free air. None of the RG images of patients suffering from perforations of the appendix showed free air.

The most common findings in the USG images of patients suffering from appendix perforations were increased diameter and heterogeneity of mesenteric fatty tissue, while the most common finding in other perforations was free fluid.

The most common CT finding in patients suffering from perforations of the appendix was an increase in diameter (100%), while the least common finding was periappendiceal air (20%) (Table 4). In the other perforations, free air was the most common CT finding (96.8%) (Table 5).

The perforation site was correctly determined in 26 (83.9%) of the 31 patients diagnosed with non-appendix perforations who underwent CT examinations.

Discussion

In our study, at least one out of RG, USG, and CT was used for the diagnosis of patients with GIP. Among these, the least used diagnostic modality was RG. RG is a fast and inexpensive diagnostic modality and is useful in the diagnosis of GIP and for differential diagnosis. However, the site of perforation cannot be determined with RG, and its sensitivity is too low in cases in which the amount of air is small. In addition, false positive results may occur with the spread of air from other injury sites, such as the lungs, mediastinum, and

genitourinary system[12]. The incidence of free air observed in RG has been reported to be 50%-70% in the literature[4-5]. In our study, this incidence rate was 50%. A study that only evaluated patients with gastroduodenal perforations reported an incidence rate of 86%[13]. In our study, this incidence rate was also 50%. There is little or no free air involved in perforations of the appendix[14]. In our study, no free air was observed in RG images of any of the patients with appendix perforations.

Table 4. CT findings of patients with appendix perforations

CT Finding	n(%) Total n=25
Increase in diameter	25 (100)
Mucosal hyperenhancement	15 (60.0)
Mucosal defect	17 (68.0)
Periappendiceal air	5 (20.0)
Periappendiceal fluid	15 (60.0)
Moderate or advanced fat stranding	23 (92.0)
Appendicolith	10 (40.0)
Abscess	7 (28.0)

CT: Computed tomography; n: number of patients

In non-appendix perforations, signs such as pneumoperitoneum, intestinal wall thickening, increased echogenicity in mesenteric fatty tissue, and free fluid may be observed on USG. In our study, the most common USG finding was free fluid, and USG images of 13 (72.2%) of the 18 patients showed free fluid. The perforation sites of patients were not indicated in any USG images. USG does not play a major role in the diagnosis of non-appendix perforations, but it is reliable and widely used in the diagnosis of appendicitis[15]. Findings such as increased appendix diameter, periappendiceal fat inflammation, and the presence of appendicoliths can help determine whether the appendix is perforated in a patient diagnosed with appendicitis by USG[16]. The sensitivity of ultrasound imaging for appendicitis perforations in the diagnosis of appendix perforation was reported to be between 29% and 84% in the literature[17]. Since our study only included patients with perforations, this sensitivity could not be calculated.

Table 5. CT findings of patients with perforation of the gastroduodenum, small intestine, and colorectum

CT Finding	n(%) Total n=31
Mural discontinuity	14 (45.2)
Mural thickening	16 (51.6)
Free air	30 (96.8)
Free fluid	25 (80.6)
Mural contrast	15 (48.4)
Fat stranding	17 (54.8)

CT: Computed tomography; n: number of patients

The use of CT in the diagnosis of perforations has increased significantly in recent years due to its diagnostic accuracy[18]. In our study, 93.9% of the patients with non-appendix perforations underwent CT examinations. CT was the most commonly performed examination in these patients. CT is the most reliable imaging method for determining the presence of GIP and its site, cause, and complications. One of the most important findings used to determine the site of perforations by CT is mural discontinuity. This finding can directly indicate the site of the perforation, but its incidence rate is low. In the study by Imuta et al.[19], the perforation site of 52% of their patients was directly imaged with mural discontinuity. The rate of this occurrence was 45.2% in our study. The site of perforation can be determined by CT using all CT findings with 80%-95% success [3,9,10,20,21]. In our study, the site of perforation was accurately determined in 83.9% of patients. We did not include appendix perforations in our study when determining the site of perforation because

appendix perforation is a complication of appendicitis and it is easy to recognize appendicitis with CT. However, there is no single specific CT finding to distinguish between perforated appendicitis and non-perforated appendicitis[22]. For this reason, the role of scoring systems using CT findings is being investigated[23]. In our study, we evaluated CT findings that may be useful in the differential diagnosis of perforated appendicitis. An increase in diameter (100%) and periappendiceal moderate or advanced fat stranding (92%) were the most common findings.

Magnetic resonance imaging (MRI) may be applied in children and pregnant women since it does not utilize radiation. Rapid diagnosis can be achieved in acute intestinal pathologies with high-speed sequences[5]. In our study, MRI was not performed in any patient.

Limitations of the Study: This study was retrospective and the number of patients was low.

Conclusion

RG, USG, and CT examinations were used in the diagnosis of GIP. Of these, CT was the method used most and it had the highest diagnostic value. CT was also useful in determining the site of perforation. Using CT findings, we determined the perforation site with a success rate of 83.9%.

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 retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Malatya Turgut Özal University Clinic Ethics Committee (Date: 2022, Decision no: 95).

References

1. Romano S, Somma C, Sciuto A, et al. MDCT Findings in Gastrointestinal Perforations and the Predictive Value according to the Site of Perforation. Tomography. 2022;8:667-87. doi: 10.3390/tomography8020056
2. Siu WT, Chau CH, Law BK, et al. Routine use of laparoscopic repair for perforated peptic ulcer. Br J Surg. 2004;91:481-4. doi: 10.1002/bjs.4452
3. Hainaux B, Agneessens E, Bertinotti R, et al. Accuracy of MDCT in predicting site of gastrointestinal tract perforation. AJR Am J Roentgenol. 2006;187:1179-83. doi: 10.2214/AJR.05.1179
4. Singh JP, Steward MJ, Booth TC, et al. Evolution of imaging for abdominal perforation. Ann R Coll Surg Engl. 2010;92:182–8. doi: 10.1308/003588410X12664192075251
5. Faggian A, Berritto D, Iacobellis F, et al. Imaging Patients with Alimentary Tract Perforation: Literature Review. Semin Ultrasound, CT MR. 2016; 37(1): 66-9. doi: 10.1053/j.sult.2015.09.006
6. Kuzmich S, Burke CJ, Harvey CJ, Kuzmich T, Fascia DTM. Sonography of Small Bowel Perforation. AJR. 2013; 201:283–91. doi: 10.2214/AJR.12.9882
7. Coppolino FF, Gatta G, Di Grezia G, et al. Gastrointestinal perforation: ultrasonographic diagnosis. Critical Ultrasound Journal. 2013; 5(Suppl 1): S4 doi: 10.1186/2036-7902-5-S1-S4
8. Furukawa A, Sakoda M, Yamasaki M, et al. Gastrointestinal tract perforation: CT diagnosis

of presence, site, and cause. Abdom Imaging. 2005; 30: 524–34.
doi: 10.1007/s00261-004-0289-x
9. Ilgar M, Elmalı M, Nural MS. The role of abdominal computed tomography in determining perforation findings and site in patients with gastrointestinal tract perforation. Turkish Journal of Trauma & Emergency Surgery. 2013; 19(1): 33-40.
doi: 10.5505/tjtes.2013.44538
10. Maniatis V, Chryssikopoulos H, Roussakis A, et al. Perforation of the alimentary tract: evaluation with computed tomography. Abdom Imaging. 2000;25:373–9.
doi: 10.1007/s002610000022
11. Pouli S, Kozana A, Papakitsou I, et al. Gastrointestinal perforation: clinical and MDCT clues for identification of aetiology. Insights into Imaging. 2020; 11:31.
doi: 10.1186/s13244-019-0823-6
12. Shin D, Rahimi H, Haroon S, et al. Imaging of Gastrointestinal Tract Perforation. Radiol Clin N Am. 2020;58:19–44.
doi: 10.1016/j.rcl.2019.08.004
13. Nouri D, Soleimanian N, Ataei F, et al. Effects of sex, age, size and site of perforation on the sensitivity of erect chest X-ray for gastroduodenal perforation. Radiography. 2021;27(4):1158-61.
doi: 10.1016/j.radi.2021.06.006
14. Shaffer HA (1992) Perforation and obstruction of the gastrointestinal tract. Assessment by conventional radiology. Radiol Clin North Am. 30:405–26.
15. Şahin T. Contribution of ethical approach and effective communication to the correct diagnosis of acute appendicitis – a single center experience from a pragmatic perspective. Eur Rev Med Pharmacol Sci 2022; 26 (11): 3911-8.
16. Rawolle T, Reismann M, Minderjahn M, et al. Sonographic differentiation of complicated from uncomplicated appendicitis. BJR. 2019; 92(1099): 20190102.
doi: 10.1259/bjr.20190102
17. Leeuwenburgh MMN, Wiezer MJ, Wiarda BM, et al. Accuracy of MRI compared with ultrasound imaging and selective use of CT to discriminate simple from perforated appendicitis. BJS. 2014;101(1):147-55.
doi: 10.1002/bjs.9350
18. Park JM, Yoon YH, Horeczko T, et al. Changes of Clinical Practice in Gastrointestinal Perforation with the Increasing Use of Computed Tomography. Journal of Trauma and Injury. 2017;30(2):25-32.
doi: 10.20408/jti.2017.30.2.25
19. Imuta M, Awai K, Nakayama Y, et al. Multidetector CT findings suggesting a perforation site in the gastrointestinal tract: analysis in surgically confirmed 155 patients. Radiat Med. 2007;25:113-8.
doi: 10.1007/s11604-006-0112-4
20. Rodriguez LC, de Gracia MM, Galan NS, et al. Use of multidetector computed tomography for locating the site of gastrointestinal tract perforations. Cir Esp. 2013;91(5):316-23.
doi: 10.1016/j.cireng.2013.10.013
21. Lee D, Park M, Shin BS, Jeon GS. Multidetector CT diagnosis of non-traumatic gastroduodenal perforation. Journal of Medical Imaging and Radiation Oncology. 2016;60:182-6.
doi: 10.1111/1754-9485.12408
22. Kim HY, Park JH, Lee YJ, et al. Systematic Review and Meta-Analysis of CT Features for Differentiating Complicated and Uncomplicated Appendicitis. Radiology. 2018;287(1):104-15.
doi: 10.1148/radiol.2017171260
23. Avanesov M, Wiese NJ, Karul M, et al. Diagnostic prediction of complicated appendicitis by combined clinical and radiological appendicitis severity index (APSI). Eur Radiol. 2018;28(9):3601-10.
doi: 10.1007/s00330-018-5339-9

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EVALUATION OF THE SAFETY AND EFFICACY OF TRANSCATHETER CYANOACRYLATE GLUE EMBOLIZATION IN ACUTE ARTERIAL BLEEDING

AKUT ARTERİYEL KANAMALARDA TRANSKATATER SİYANOAKRİLAT GLUE EMBOLİZASYONUN GÜVENLİĞİNİN VE ETKİNLİĞİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: To demonstrate the safety and efficacy of endovascular embolization with N-butyl cyanoacrylate glue in acute bleeding.

Methods: The data of 31 patients who underwent endovascular embolization using N-butyl cyanoacrylate glue due to acute visceral hemorrhage were retrospectively evaluated. In order to detect the bleeding focus before the procedure, computed tomography with contrast-enhanced and non-contrast phases was routinely performed on the suspected bleeding site. Technical success was accepted as the closure of the targeted artery in control angiography, and clinical success was defined as the absence of bleeding that would require reoperation within one month postoperatively.

Results: Eleven patients with gastrointestinal tract or vaginal bleeding or hematuria due to malignancy, nine with hemoptysis due to infection sequelae or bronchiectasis, four with bleeding secondary to percutaneous medical procedures, three with trauma-related hemorrhage, and four with hemorrhage due to peptic ulcers were treated with endovascular embolization. Embolization was undertaken using a glue-lipiodol mixture of 5% in 17 patients and 10% in 14 patients. The targeted artery was closed in all patients, and the technical success rate was 100%. No technical and clinical complications developed during and after the procedure.

Conclusions: N-butyl cyanoacrylate is a safe embolizing material with high technical and clinical success in patients with active bleeding.

Keywords: N-butyl cyanoacrylate glue, embolization, hemorrhage, endovascular treatment

Öz

Amaç: Akut kanamalarda N-butyl cyanoacrylate glue ile yapılan endovasküler embolizasyonun güvenliğini ve etkinliğini göstermek.

Yöntemler: Akut visseral kanama nedeni ile tarafımızca glue ile endovasküler embolizasyon uygulanan toplam 31 hastanın verileri retrospektif olarak değerlendirildi. Hastalara işlem öncesi kanama odağını saptama amacıyla rutin olarak kontrastsız ve kontrastlı fazlardan oluşan şüphe edilen kanama bölgesine yönelik bilgisayarlı tomografi çekildi. Teknik başarı kontrol anjiografide hedeflenen damarın kapatılması, klinik başarı ise post-op 1 aylık sürede tekrar işlem gerektirecek kanama olmaması şeklinde kabul edildi.

Bulgular: Maligniteye bağlı gastrointestinal sistem (GİS), vajinal kanama ya da hematürisi olan 11 hasta, enfeksiyon sekeli ya da bronşektaziye bağlı hemoptizisi olan 9 hasta, perkütan tıbbi işlemler sonrası kanaması olan 4 hasta, travmaya bağlı kanaması olan 3 hasta, peptik ülser nedeni ile kanaması olan 4 hasta endovasküler embolizasyon ile tedavi edildi. 17 hastada %5'lik, 14 hastada ise %10'luk glue-lipiodol karışımı embolizasyon için kullanıldı. Hedeflenen arter tüm hastalarda kapatıldı ve teknik başarı oranı %100 idi. İşlem sırasında ve sonrasında herhangi bir teknik ve klinik komplikasyon gelişmedi.

Sonuç: N-butil siyanoakrilat aktif kanaması olan hastalarda teknik ve klinik başarısı yüksek güvenilir bir embolizan materyaldir.

Anahtar Kelimeler: N-butil siyanoakrilat glue, embolizasyon, hemoraji, endovasküler tedavi

Introduction

Acute bleeding has high mortality and morbidity, therefore it is an emergency that requires rapid and effective treatment[1]. Transcatheter arterial embolization using gelatin sponge, coils, polyvinyl alcohol (PVA), N-butyl cyanoacrylate (NBCA) glue, or a combination of these agents is widely used in the treatment of acute visceral hemorrhage or tumor hemorrhage[2,3]. Although these methods are successful in most cases, adequate hemostasis may not be achieved in some patients due to reasons such as insufficient access to the bleeding site, formation of collateral circulation after embolization, and recanalization of embolized arteries[3,4]. NBCA glue is an embolizing liquid material that undergoes rapid polymerization upon contact with blood and also causes rapid and permanent embolization. NBCA glue can also provide the simultaneous embolization of collateral arteries connected to the bleeding focus, which can prevent reverse bleeding from retrograde collateral flow. However, complications such as catheter sticking and reflux scare the operators and are seen as the main obstacle to the widespread use of NBCA glue. The current study aimed to evaluate the safety, efficacy and complication rates of NBCA glue in acute arterial bleeding.

Materials and Methods

This retrospective study was approved by the Ethical Committee and conducted in full accordance with the guidelines of the Declaration of Helsinki. The Ethics Committee approval was obtained from Clinical Research Ethics Committee. Informed consent was obtained from both patients and their relatives before the embolization procedure. The data of 31 patients, who presented to our center with acute visceral hemorrhage between September 2019 and February 2022, continued to have persistent hemorrhage despite attempts with endoscopy or bronchoscopy, and therefore, patients who underwent endovascular embolization using a mixture of 5% or 10% N-butyl cyanoacrylate glue and lipiodol were evaluated retrospectively. Embolization was performed on the patients included in the study by 3 operators. This study is single-center. Before the procedure, the patients routinely underwent hemogram and biochemistry tests, and computed tomography (CT) comprising non-contrast and contrast-enhanced phases was performed for the suspected bleeding site to detect the bleeding focus. In addition, cone beam CT was used to map and clarify the bleeding focus during the procedure and to confirm whether intraoperative bleeding persists after embolization of the targeted focus. Technical success was accepted as the closure of the targeted artery in follow-up angiography, and clinical success was defined as the absence of bleeding that would require reoperation within one month postoperatively. Embolization results were evaluated separately in terms of technical and clinical success.

- *Technique*

Lipiodol (iodophendylate oil) was mixed with 5% (distal embolization) or 10% (proximal embolization) to increase the visibility of the glue under angiography and dilute it. The preferred microcatheter diameter for embolization was selected in the range of 1.9 F- 2.4 F according to the lumen width of the artery to be catheterized (Fig 1). Artery with signs of bleeding was mapped with cone beam CT at every step of the embolization procedure. The mixture was prepared in a small sterile ceramic cup immediately before embolization. Care was taken in the preparation of the glue mix to avoid contamination with ionic solutions that could cause polymerization, such as blood and normal saline. The microcatheter was washed with 5% dextrose solution before injection. During this procedure, the most common technical problem is that the glue polymerizes proximally before penetrating to the desired depth. 5%

dextrose was attached to the guide catheter and continuous flushing of the periphery of the microcatheter aimed to avoid this problem. It was thought that this technique could prevent complications, which are thought to be more common, while embolizing the distal artery, which is difficult to reach, especially with current generation micro-catheters.

The mixture was drawn into a 5 ml syringe and connected directly to the superselective catheterized microcatheter. Injection was performed in a slow controlled manner to prevent the reflux and adherence of the catheter. After the injection was completed, the microcatheter was quickly withdrawn.

Results

There were 25 male and 6 female patients, with a mean age of 58.1 (34-75) years. Eleven patients had malignancy-related hemorrhage (Fig 2,3), including five patients with gastrointestinal bleeding, three with cervical cancer causing vaginal bleeding, three with causing hematuria; nine patients had hemoptysis due to infection sequelae or bronchiectasis (Fig 1) ; four patients had iatrogenic hemorrhage following percutaneous procedures; three had trauma-related hemorrhage; and four had hemorrhage due to peptic ulcers (Table 1). For the embolization procedure, a glue-lipiodol mixture of 5% was used in 17 patients and 10% in 14 patients. The targeted artery was closed in all patients, and the technical success rate was 100%.

No technical and clinical complications developed during and after the procedure. However, clinical success was not achieved in eight patients (25.8%). In seven (87.5%) of these eight patients, the cause of hemorrhage was mass bleeding due to malignancy. The mean duration of admission with re-hemorrhage was 22 (15-30) days. Nineteen patients had at least one of the angiography findings indicating the bleeding site (active extravasation, pseudoaneurysm, or hypervascularity), and the technical and clinical success rate of treatment was 100% in these patients.

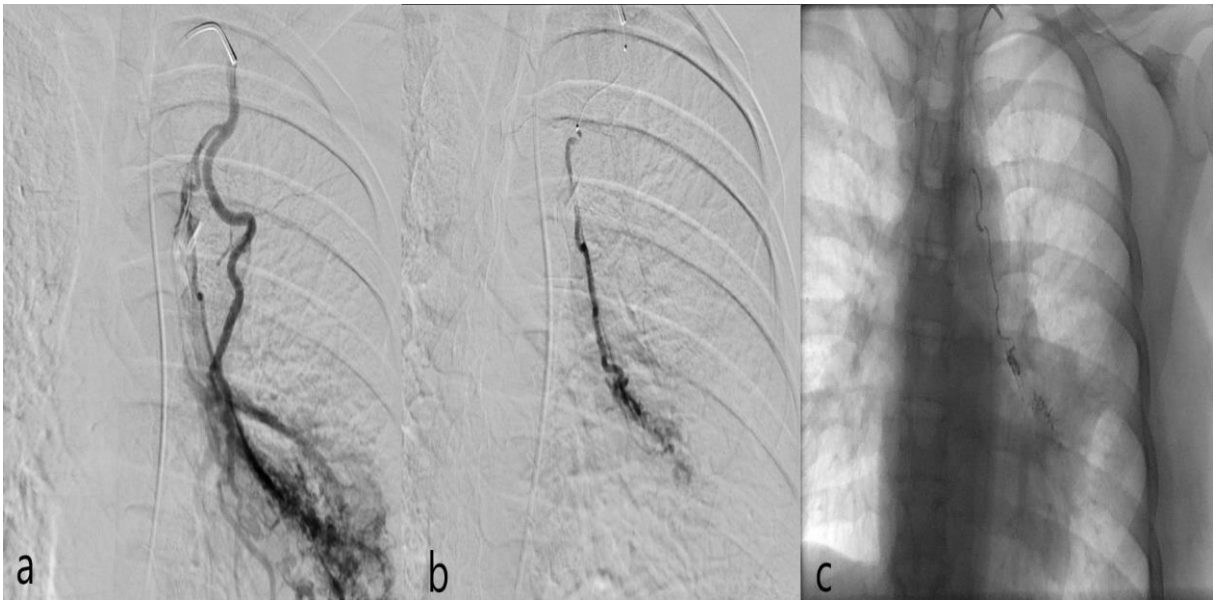

Figure 1. After left bronchial artery catheterization, DSA examination with microcatheter superselective catheterization reveals prominent tortuous arteries and hypervascularity. (a) After the injection of glue-lipiodol, the absence of contrast filling (b) and the mixture of glue-lipiodol (c) are confirmed in the control imaging.

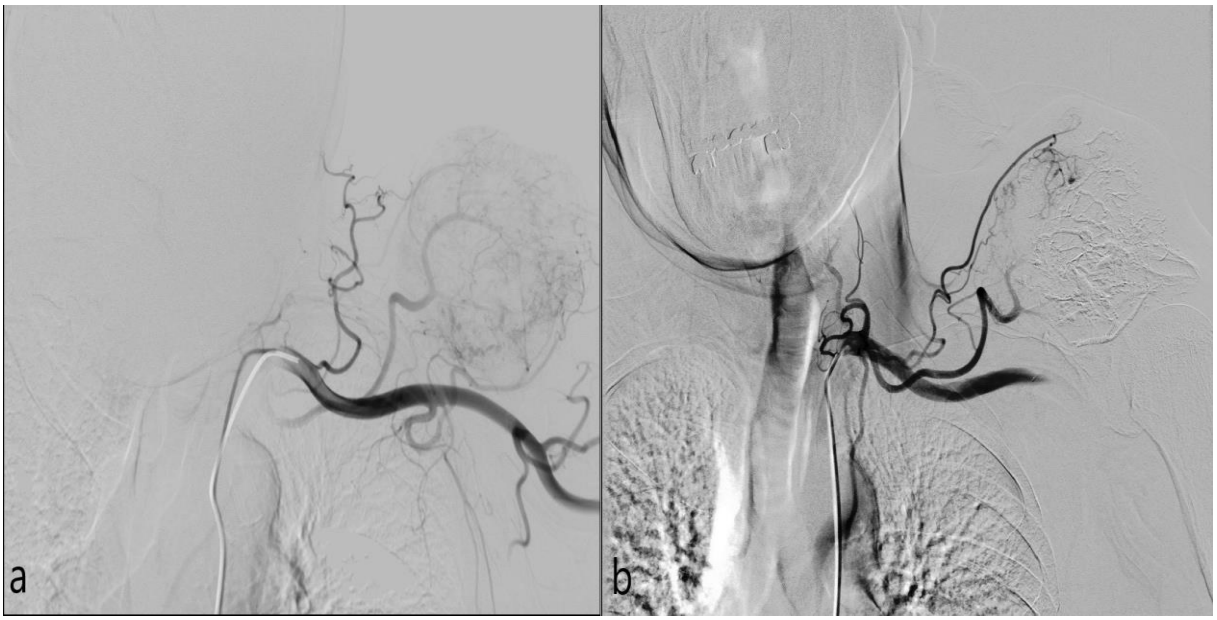

Figure 2. Hepatocellular carcinoma metastasis in the posterior left shoulder. After left subclavian artery catheterization, arteries responsible for mass feeding are observed in DSA. (a) In the control DSA taken after the glue injection, it is seen that the mass does not show contrast filling and the glue completely occludes the arteries. (b)

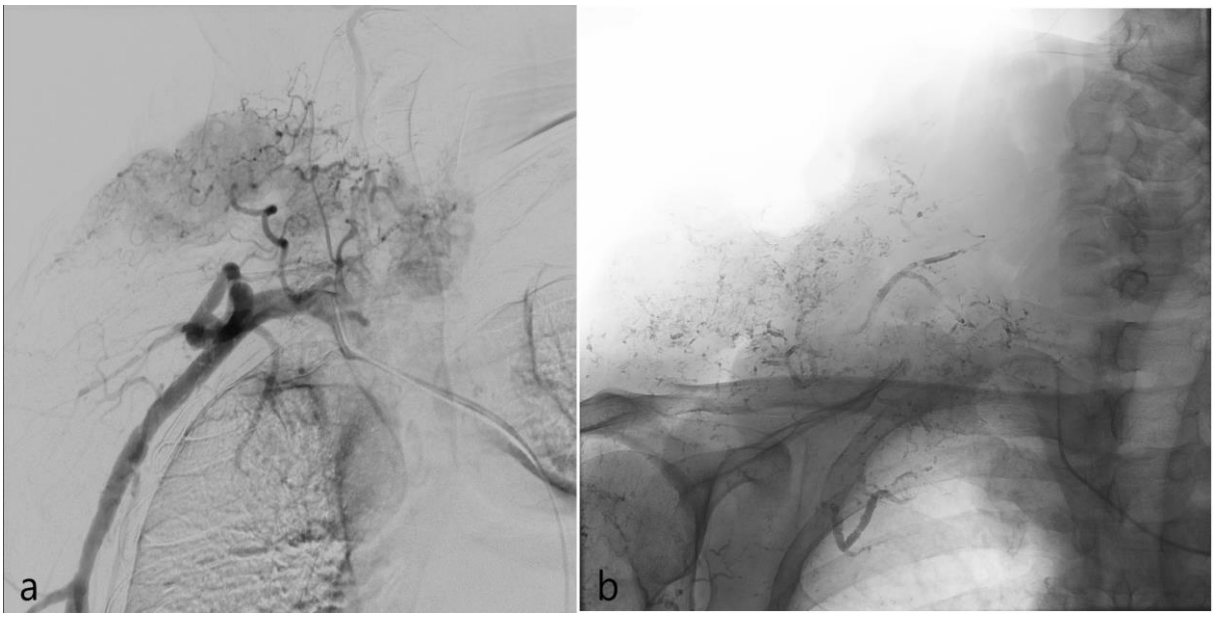

Figure 3. Giant RCC metastasis located adjacent to the right scapula. In DSA images taken after subclavian artery catheterization, it is seen that the mass is significantly enhanced. (a) After the glue-lipiodol injection, it was observed that the mass did not enhance and the glue-lipiodol mixture was distributed up to the distal part of the mass. (b)

Table 1. Explaining the causes of bleeding in patients undergoing embolization

	Total
Arterial bleeding due to malignancy	11
GI bleeding	0
Stomach adeno cancer	2
Gastric non-Hodgkin lymphoma (NHL)	1
Plasmocytoma with duodenal invasion	1
Hepatocellular cancer with gastric invasion (HCC)	1
Vaginal bleeding (cervical cancer)	3
Hematuria	
Renal cell cancer (RCC)	2
Bladder cancer	1
Hemoptysis due to infection sequela or bronchiectasis	9
Iatrogenic bleeding after percutaneous procedures	0
Lithotripsy	2
Percutaneous kidney parenchyma biopsy	1
After percutaneous transhepatic cholangiography (PTC)	1
Bleeding after trauma	3
Bleeding due to peptic ulcer	4

Discussion

Although endoscopic treatment methods are the first choice in the treatment of arterial bleeding, they are often insufficient[5]. Endovascular embolization is a suitable option for patients with surgical risk, especially in cases of acute bleeding or where endoscopy has failed[5,6]. In coil or PVA particle embolization, the occlusion of arteries or pseudoaneurysms is due to thrombosis rather than the embolic material itself, and the patient's coagulation function is critical for the final success of the embolization procedure for hemorrhage[7]. Considering the speed and efficiency of hemostasis, liquid embolic materials, such as NBCA should be used more frequently, especially in the presence of coagulation disorders[1,6,8].

Several factors affect the depth of glue penetration, with the most important being the velocity of the flow passing through the catheter tip, the ratio of NBCA to lipiodol, and the injection technique[1,8]. Therefore, in cases where proximal embolization is desired, more diluted mixtures should be preferred if more intense and distal embolization is desired. When the literature is reviewed, 50%-70% dense mixtures have been preferred for proximal embolization and 25-50% mixtures for distal embolization[2,8,9]. Complications such as catheter adhesion at certain rates, glue reflux, and non-target embolization have been described in these cases[10,11]. Due to these glue-related complications, operators avoid the use of this material[12,13]. However, in our study, a 10% mixture was preferred when proximal embolization was to be performed, and a 5% mixture for distal embolization. The technical success rate of 100% and the absence of complications in our case series suggest that these mixing ratios can be used safely.

In addition, the use of cone-beam computed tomography during the use of NBCA, as in all endovascular procedures, increases both technical and clinical success[14,15]. Conical CT is known to be superior to DSA in providing microcatheter-guided navigation in order to embolize the correct vessel and showing the presence of other vessels causing bleeding. Cone beam CT was used during all embolization procedures included in this study.

Major complication rates in the use of NBCA have been defined as 3-5%. The primary concerns regarding the use of glue-lipiodol mixture are reflux and catheter adhesion [15,16]. Other common complications include non-target embolization and ischemia-necrosis after over-embolization [17]. Arterial embolization in the upper gastrointestinal tract above the ligament of Treitz is

generally considered safe due to the rich collateral supply. It is considered that the risk of ischemic complications is higher in the lower gastrointestinal tract [18,19]. These major complications are seen more frequently in patients with vascular malformation, tortuosity, and previous surgery or radiotherapy [20,21]. However, when careful attention is paid to the technique, the probability of these complications is very low. In our study, no complication was encountered in any of the patients that underwent embolization. In recent studies, the frequency of NBCA use in gastrointestinal bleeding is increasing. In our study, we achieved complete technical and clinical success in patients with hemorrhage caused by peptic ulcer.

Technical success was confirmed by a follow-up angiography examination in all patients embolized with Glue-lipiodol mixture. Re-hemorrhage was detected in a total of eight patients, who were accepted to be clinically unsuccessful cases. Seven of these eight patients with re-hemorrhage had undergone embolization due to malignant mass bleeding. This suggests that the reason for recurrence was not due to the inadequacy of our technique or glue, but it was associated with the nature of malignant bleeding. When the literature is reviewed, the number of studies on the effect of glue-lipiodol mixture on malignant mass bleeding is limited, and there is a need for large case series on this subject. There may be several reasons for recurrent hemorrhage. As the main reason, we hypothesize that the malignant mass forms new feeding vessels or collaterals during the follow-up period. Another possible reason is that the glue-lipiodol mixture may not have provided sufficient distal embolization. Further studies with larger case series are needed to clarify this.

- *Limitations*

There were major limitations of our study, the main ones being; the reasons were that the study was retrospective and single-centered, the number of cases was low, unknown comorbidities, the anatomical localizations embolized, that is, the vessels were different, and therefore the diameters of the catheters used were not standard.

Conclusion

NBCA is a highly effective and safe liquid embolizing material in patients with active bleeding, who are planned to undergo endovascular embolization. A mixture of 5% and 10% NBCA-lipiodol can be safely used in acute bleeding.

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

Ethical approval was taken from the Cukurova University School of Medicine local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.2022/08/04-121).

References

1. Kim PH, Tsauo J, Shin JH, et al. Transcatheter arterial embolization of gastrointestinal bleeding with N-Butyl cyanoacrylate: a systematic review and metaanalysis of safety and efficacy. J Vasc Interv Radiol. 2017;28:522-31. doi: 10.1016/j.jvir.2016.12.1220
2. Loffroy R, Mouillot T, Bardou M, et al. Current role of cyanoacrylate glue transcatheter embolization in the treatment of acute nonvariceal gastrointestinal bleeding. Expert Rev Gastroenterol Hepatol. 2020 Oct;14(10):975-84.
3. Kodani M, Yata S, Ohuchi Y, et al. Safety and risk of superselective transcatheter arterial embolization for acute lower gastrointestinal hemorrhage with N-Butyl cyanoacrylate: angiographic and colonoscopic evaluation. J Vasc Interv Radiol. 2016;27:824-30. doi: 10.1080/17474124.2020.1790355

4. Okada T, Yamaguchi M, Takahashi T, et al. Is embolization of the pancreas safe? Pancreatic histological changes after selective transcatheter arterial embolization with N-butyl cyanoacrylate in a swine model. Cardiovasc Intervent Radiol. 2012;35:161-7.
doi: 10.1007/s00270-011-0130-1
5. Abdulmalak G, Chevallier O, Falvo N, et al. Safety and efficacy of transcatheter embolization with Glubran®2 cyanoacrylate glue for acute arterial bleeding: a single-center experience with 104 patients. Abdom Radiol (NY). 2018;43:723-33.
doi: 10.1007/s00261-017-1267-4
6. Jawhari R, Chevallier O, Falvo N, et al. Outcomes of transcatheter arterial embolization with a modified N-Butyl cyanoacrylate glue for spontaneous Iliopsoas and rectus sheath hematomas in anticoagulated patients. J Vasc Interv Radiol. 2018;29:210-17.
doi: 10.1016/j.jvir.2017.08.006
7. Kawai N, Sato M, Minamiguchi H, Ikoma A, Sanda H, Nakata K, et al. Basic study of a mixture of N-butyl cyanoacrylate, ethanol, and lipiodol as a new embolic material. J Vasc Interv Radiol. 2012;23:1516-21.
doi: 10.1016/j.jvir.2012.08.017
8. Tanaka F, Kawai N, Sato M, et al. Effect of transcatheter arterial embolization with a mixture of n-butyl cyanoacrylate, lipiodol, and ethanol on the vascular wall: macroscopic and microscopic studies. Jpn J Radiol. 2015;33:404-49.
doi: 10.1007/s11604-015-0432-3
9. Chewning RH, Monroe EJ, Lindberg A, et al. Combined glue embolization and excision for the treatment of venous malformations. CVIR Endovasc. 2018;1:22.
doi: 10.1186/s42155-018-0028-y
10. Chevallier O, Comby PO, Guillen K, et al. Efficacy, safety and outcomes of transcatheter arterial embolization with N-butyl cyanoacrylate glue for non-variceal gastrointestinal bleeding: A systematic review and meta-analysis. Diagn Interv Imaging. 2021;102:479-87.
doi: 10.1016/j.diii.2021.03.004
11. Chevallier O, Fauque P, Poncelet C, et al. Relevant Biological Effects of Varicocele Embolization with N-Butyl Cyanoacrylate Glue on Semen Parameters in Infertile Men. Biomedicines. 2021;9:1423.
doi: 10.3390/biomedicines9101423
12. Doniselli FM, Paolucci A, Conte G, et al. Glue embolization of a pial arteriovenous fistula of the spinal artery. Acta Biomed. 2020;91(10-S):e2020004.
doi: 10.23750/abm.v91i10-S.10282
13. Soga S, Suyama Y, Shinmoto H. Balloon-occluded retrograde glue embolization for intractable lymphorrhea from bilateral iliac lymphatics following surgery for rectal cancer. Radiol Case Rep. 2020;15:371-74.
doi: 10.1016/j.radcr.2020.01.017
14. Cho Y, Park, W, Kang JM, et al. Newly Developed *N*-butyl Cyanoacrylate (EG glue) for Arterial Embolization: A Preclinical Study in Rabbit Renal Artery. Macromol Res. 2021**;**178–84.
doi: 10.1016/j.diii.2016.05.013
15. Yip SWY, Li YL, Chu YLE, et al. Adrenal and renal abscesses following glue embolization of gastric varices: a case description. Quant Imaging Med Surg. 2020;1566-9.
doi: 10.21037/qims-19-1026
16. Hargis PA, Henslee B, Pokala N, et al. Percutaneous Lymphatic Maceration and Glue Embolization for High-output Chylous Ascites after Robot-assisted Laparoscopic Nephrectomy and Lymphadenectomy. J Clin Imaging Sci. 2021;11:56.
doi: 10.25259%2FJCIS_100_2021
17. Toyoda H, Kumada T, Sone Y, et al. Late-onset colonic occlusion after emergent selective embolization of sigmoid artery with N-butyl cyanoacrylate for lifethreatening traumatic bleeding. J Vasc Interv Radiol. 2009;20:1376–79.
doi: 10.25259/JCIS_100_2021
18. Gordhan AD, Newey CR, Wong G, et al. N-butyl cyanoacrylate embolization of small bowel arteriovenous malformation presenting with acute massive lower gastrointestinal hemorrhage. J Vasc Interv Radiol. 2008;19: 1669–70.
doi: 10.1016/j.jvir.2008.08.017
19. Kodani M, Yata S, Ohuchi Y, et al. Safety and risk of superselective transcatheter arterial embolization for acute lower gastrointestinal hemorrhage with N-butyl cyanoacrylate: angiographic and colonoscopic evaluation. J Vasc Interv Radiol. 2016;27:824–30.
doi: 10.1016/j.jvir.2016.01.140
20. Morishita H, Yamagami T, Matsumoto T, et al. Transcatheter arterial embolization with N-butyl cyanoacrylate for acute life-threatening gastroduodenal bleeding uncontrolled by endoscopic hemostasis. J Vasc Interv Radiol. 2013;24:432–38.
doi: 10.1016/j.jvir.2012.12.017
21. Lee CW, Liu KL, Wang HP, et al. Transcatheter arterial embolization of acute upper gastrointestinal tract bleeding with N-butyl-2-cyanoacrylate. J Vasc Interv Radiol. 2007;18:209–16.
doi: 10.1186/s12957-016-0803-y

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EVALUATION OF THE EFFECTS OF ULTRASOUND-GUIDED TRANSVERSUS ABDOMINAL PLANE BLOCK FOR POSTOPERATIVE ANALGESIA ON RECOVERY AND POSTOPERATIVE HEMODYNAMIC PARAMETERS IN LAPAROSCOPIC CHOLECYSTECTOMY

POSTOPERATİF ANALJEZİ İÇİN ULTRASON KILAVUZLUĞUNDA TRANSVERSUS ABDOMİNAL PLAN BLOĞUNUN LAPAROSKOPİK KOLESİSTEKTOMİDE DERLENME VE POSTOPERATİF HEMODİNAMİK PARAMETRELER ÜZERİNE ETKİLERİNİN DEĞERLENDİRİLMESİ

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Abstract
Aim: Laparoscopic cholecystectomy has become quite common all over the world. Severe pain may also develop after laparoscopic procedures. Postoperative pain can cause changes in many systems and increase the risk of complications. In this study, we aimed to evaluate the effect of ultrasound-guided Transversus Abdominis plane block on recovery and postoperative hemodynamic parameters in laparoscopic cholecystectomy.
Methods: The patients were divided into 2 groups as those who received paracetamol for postoperative analgesia and those who received paracetamol and TAP block. Postoperative hemodynamic parameters, peripheral oxygen saturations, VAS scores and Aldrete Scores of the patients were recorded from the patient files and compared.
Results: VAS scores and systolic-diastolic arterial pressures were statistically significantly lower and Modified Aldrete scores and oxygen saturations were statistically significantly higher in patients with TAP block.
Conclusions: We showed that in addition to conventional analgesia methods in patients who underwent laparoscopic cholecystectomy, TAP block applied with USG facilitates postoperative pain control, provides a more stable hemodynamics and both better and earlier recovery. It will provide an advantage in terms of both recovery and complication risk, especially in patients with cardiovascular system disorders.

Keywords: TAP Block, Regional anesthesia, Transversus Abdominis Plan Block, Laparoscopic cholecystectomy, Postoperative analgesia

Öz
Amaç: Laparoskopik kolesistektomi tüm dünyada oldukça yaygın hale gelmiştir. Laparoskopik işlemlerden sonra da şiddetli ağrı gelişebilir. Ameliyat sonrası ağrı birçok sistemde değişikliğe neden olabilir ve komplikasyon riskini artırabilir. Bu çalışmada, laparoskopik kolesistektomide ultrason eşliğinde yapılan Transversus Abdominis plan bloğunun derlenme ve postoperatif hemodinamik parametrelere etkisini değerlendirmeyi amaçladık.
Yöntemler: Hastalar postoperatif analjezi için parasetamol alanlar ve parasetamol ve TAP blok alanlar olarak 2 gruba ayrıldı. Hastaların postoperatif hemodinamik parametreleri, periferik oksijen satürasyonları, VAS skorları ve Aldrete Skorları hasta dosyalarından kaydedilerek karşılaştırıldı.
Bulgular: TAP bloklu hastalarda VAS skorları ve sistolik-diyastolik arter basınçları istatistiksel olarak anlamlı düşüktü ve Modifiye Aldrete skorları ve oksijen satürasyonları istatistiksel olarak anlamlı derecede yüksekti.
Sonuç: Laparoskopik kolesistektomi yapılan hastalarda konvansiyonel analjezi yöntemlerine ek olarak USG ile uygulanan TAP bloğun postoperatif ağrı kontrolünü kolaylaştırdığını, daha stabil bir hemodinami sağladığını ve hem daha iyi hem de daha erken derlenme sağladığını gösterdik. Özellikle kardiyovasküler sistem bozukluğu olan hastalarda hem iyileşme hem de komplikasyon riski açısından avantaj sağlayacaktır.

Anahtar Kelimeler: TAP blok, rejyonel anestezi, transversus abdominis plan bloğu, laparoskopik kolesistektomi, postoperatif analjezi

Introduction

Laparoscopic cholecystectomy has become very common all over the world and has become the first preferred method in the treatment of cholelithiasis by both physicians and patients. Despite the decrease in postoperative pain, which is one of the biggest advantages compared to laparotomy, most of the patients can still talk about severe pain after laparoscopic cholecystectomy[1].
Postoperative pain is acute pain that begins with surgical incision and ends with wound healing. Post-operative pain can cause changes in many systems. It may cause hypoxemia, atelectasis and pneumonia in the respiratory system[2-4]. In the cardiovascular system, it can cause hypertension, tachycardia, arrhythmia, increased stroke volume, and increased myocardial oxygen consumption. It may increase the risk of myocardial ischemia and infarction[5,6]. Consequently, the risk of postoperative morbidity and mortality increases. With an effective analgesia, both the development of complications can be prevented and the cost of hospital stay can be shortened.
Alternatively, the transverse abdominis plane block (TAP block), first described by Rafi, can also be used for analgesia. In TAP block, a local anesthetic is injected into the neurofascial plane of the abdominal muscle, thereby blocking the sensory nerves and providing pain control[7]. TAP block is performed by advancing the needle in the so-called "Petit triangle", which is bounded by the lattisimus dorsi muscle posteriorly, the external oblique muscle (EOM) anteriorly, and the iliac crest below[8]. Considering the risk of complications during the procedure, ultrasound-guided application is generally preferred instead of the blind technique.
In this study, we aimed to investigate the effects of ultrasound-guided TAP block for postoperative analgesia on recovery and postoperative hemodynamics in patients who underwent laparoscopic cholecystectomy.

Materials and Methods

In our study, 825 patients who underwent laparoscopic cholecystectomy were selected from 7868 patients who were operated for various reasons in Kastamonu Training and Research Hospital between January 2019 and 2020, and their files were reviewed retrospectively.

As inclusion criteria;

- To be operated under general anesthesia (propofol, fentanyl, rocuronium bromide)
- >18 years old, ≤65 years old
- American Society of Anesthesia (ASA) 1-2
- Premedication has been applied
- Staying in the post anesthesia care unit (PACU) for at least 30 minutes
- Systolic arterial pressure <150 mmHg, diastolic arterial pressure <90 mmHg
- TAP block with paracetamol or paracetamol for postoperative analgesia
- Heart rate <100/minute, >60/minute

Also, as exclusion criteria;

- History of cardiovascular diseases (hypertension, arrhythmia, heart failure, etc.)
- Having additional diseases such as malignancies, stroke, visual and hearing impairment
- Conversion from laparoscopic surgery to open
- Having developed postoperative nausea and vomiting (due to the possibility of affecting hemodynamics)
- Having applied additional postoperative analgesia
- Performing more than one surgical procedure or developing surgical or hemodynamic complications (cholecystectomy and umbilical hernia repair, etc.)
- Pregnancy status

- *Recording Data Section*

Age, gender, comorbidity, ASA scores, preoperative, post-extubation, 5th, 10th, 15th, 20th and 30th minute heart rates, systolic and diastolic blood pressures, mean arterial pressures, and saturation values were scanned in patient files was recorded. 5th minute, 10th minute, 15th minute, 20th minute and 30th minute modified aldrete scores and visual analog scale (VAS) scores were recorded in the PACU from the patient files[9].

- *Statistical Analysis*

Statistical analyzes were performed using the SPSS 26.0 software program (SPSS Inc., Chicago, IL, USA). After Kolmogorov - Smirnov test was applied to all data, Student t test was used for data with normal distribution in the evaluation between groups, and Mann Whitney U test was used for data with skewed distribution. Chi-square test was used for comparison of nominal values between groups. $p<0.05$ was considered significant.

Results

The study included 110 patients who met the criteria. Patients who underwent bilateral TAP block with ultrasound after the end of the surgical procedure with paracetamol for postoperative analgesia were divided into Group I (n=49), and patients who received only paracetamol were divided into Group II (n=61).
No statistically significant difference was observed between the two groups included in the study in terms of demographic data. Demographic data are presented in table 1.
There was no additional disease in 37 patients in group I and 48 patients in group 2. The most common comorbid disease in both groups was diabetes mellitus (DM). The ASA classification of 38 patients in group 1 was ASA 1, and the ASA classification of 48 patients in group 2 was ASA 1.

Table 1. Demographic characteristics of patients

		Group I (n=49)	Group II (n=61)	P
Age		48,84±12,77	46,97±11,82	,420
Gender	Female	10	18	,273
	Male	39	43	
Comorbidities	None	37	48	,216
	Diabetes Mellitus	10	12	
	Respiratory system	0	1	
	Neurological	2	0	
ASA	I	38	48	,886
	II	11	13	

ASA; American Soceity of Anesthesia

Table 2. Hemodynamic parameters and $Sp0_2$ values of the patients

		preop Mean ±SD	0.minute Mean ±SD	5. minute Mean ±SD	10. minute Mean±SD	15. minute Mean±SD	20. minute Mean±SD	30. minute Mean±SD
Heart Rate	Group 1	84,41±13,17	87,04±14,06	73,51±12,15	68,04±11,15	67,88±11,36	66,59±10,75	67,86±10,67
	Group 2	81,90±10,87	107,82±10,53	104,31±18,81	104,54±15,42	102,89±15,39	102,28±14,55	100,79±13,73
	P	,277	,000	,000	,000	,000	,000	,000
Systolic Arterial Pressure	Group 1	133,57±14,74	133,37 ±18,62	132,59±20,08	131,27±20,38	130,55±20,15	132,65±20,34	131,82±19,10
	Group 2	132,28 ±15,11	163,54±16,64	160,02±25,11	159,89±17,45	158,18±14,79	156,18±17,92	154,89±16,60
	P	,653	,000	,000	,000	,000	,000	,000
Diastolic Arteial Pressure	Group 1	77,02±10,62	81,24±11,55	77,02±12,75	76,22±13,10	76,18±11,66	76,80±12,12	77,27±10,10
	Group 2	79,64±9,28	95,46±11,77	93,36±13,69	94,26±14,52	93,90±13,03	91,41±12,19	91,99±11,05
	P	,171	,000	,000	,000	,000	,000	,000
Mean Arterial Pressure	Group 1	96,69±17,70	99,04±13,93	93,90±12,95	92,37±12,67	92,22±11,47	92,20±13,20	92,31±13,72
	Group 2	100,80±13,45	117,66±14,85	113,13±15,29	115,43±15,90	113,77±15,25	109,82±19,74	110,85±13,83
	P	,169	,000	,000	,000	,000	,000	,000
Saturation	Group 1	97,84±2,65	98,35±1,60	97,86±2,29	98,00±1,86	98,20±1,93	98,31±1,79	98,31±1,66
	Group2	98,59±1,33	93,44±1,85	93,48±1,58	94,16±1,25	94,92±1,23	95,59±1,11	95,92±0,98
	P	,075	,000	,000	,000	,000	,000	,000

preop; preoperative, SD; standard deviation.

Table 3. Comparison of Modified Aldrete Score and Visual Analogue Scale

		5. minute Mean ±SD	10. minute Mean±SD	15. minute Mean±SD	20. minute Mean±SD	30. minute Mean±SD
Modified Aldrete Score	Group 1	10,14±1,06	10,78±0,94	11,02±0 ,87	11,37±0,75	11,43±0,67
	Group 2	7,46±0,84	7,92±0,73	8,26±0,68	8,64±0,68	9,07±0,25
	P	,000	,000	,000	,000	,000
Visual Analogue Scale	Group 1	2,16±1,90	1,96±1,70	2,12±1,70	2,16±1,72	2,04±1,49
	Group 2	7,80±1,66	7,64±1,61	7,64±1,61	7,64±1,61	7,64±1,61
	P	,000	,000	,000	,000	,000

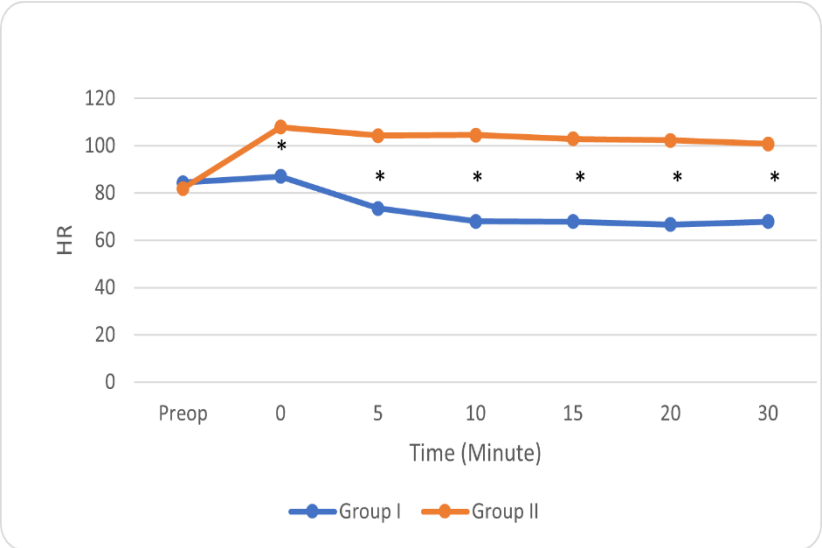
SD; standard deviation.

When the preoperative period heart rates of the groups were compared, no statistically significant difference was found. When the 0 (post-extubation), 5th, 10th, 15th, 20th and 30th minutes values were compared, it was found to be statistically significantly higher in Group II ($p<0.05$, table 2, graph 1). When the systolic arterial pressures were compared, there was no statistically significant difference between the two groups for the preoperative period, while the 0th, 5th, 10th, 15th, 20th and 30th minute values were found to be statistically significantly higher in Group II ($p< 0.05$, Table 2, Graph 2).

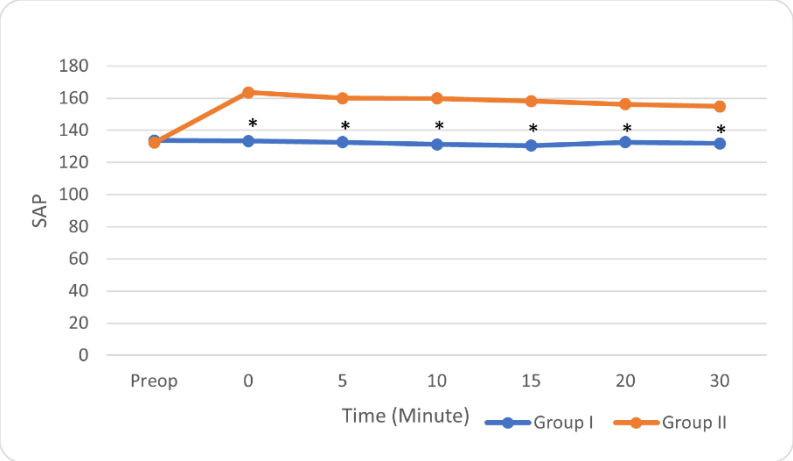
When the diastolic arterial pressures were compared, there was no statistically significant difference between the two groups for the preoperative period, while the 0th, 5th, 10th, 15th, 20th and 30th minute values were found to be statistically significantly higher in Group II ($p< 0.05$, Table 2, Graph 3).

Graphic 1. Heart rate (HR) changes between groups.

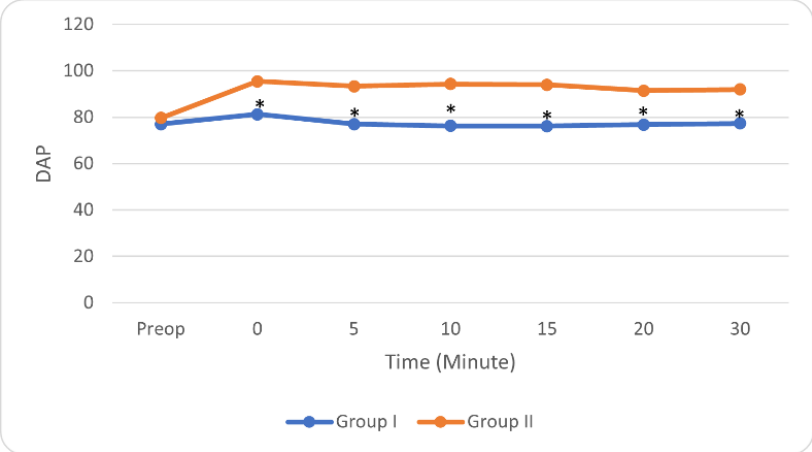
* Stastically significant change according to former value in the group. ($p<0.05$), HR: Heart rate)



Graphic 2. Sistolic arter pressure changes between groups.
* Stastically significant change according former value in the group. (p<0.05), SAP: Systolic arterial pressure.



Graphic 3. Diastolic arter pressure changes between groups.
* Stastically significant change according former value in the group. (p<0.05), DAP: Diastolic arterial pressure.



When the mean arterial pressures were compared, no statistical difference was found for the preoperative period, while the 0th, 5th, 10th, 15th, 20th and 30th minute values were statistically significantly higher in Group II (p<0.05, Table 2). There was no difference between the preoperative period saturation values of the groups. 0., 5., 10., 15., 20. and 30. minutes values were found to be statistically significantly higher in Group I (p<0.05, Table 2).
When the visual analog scale values of the groups were compared, the 5th, 10th, 15th, 20th and 30th minute values were found to be statistically significantly lower in Group I (p<0.05, table 3). When the scores of the groups were compared according to the Modified Aldrete Scoring system, the 5th, 10th, 15th, 20th and 30th minute values were statistically significantly higher in Group I (p<0.05, table 3).

Discussion

As a result of this study, heart rate and systolic-diastolic arterial pressures were more stable, saturation values were higher, visual analog scale scores were lower in patients who received TAP block in addition to the analgesic agent. The modified alderete score was found to be higher in patients who received TAP block in addition to the analgesic agent compared to the patients who received a single analgesic agent. It is seen that TAP block applied in addition to the analgesic agent for postoperative pain has positive effects on postoperative hemodynamics and respiration, as well as providing early and better recovery.
With laparoscopic surgery, the sympathetic system is stimulated, resulting in a metabolic and endocrine response. There are studies reporting that surgical trauma and stress response are directly proportional[10]. Pain is the result of many factors such as tissue trauma, abdominal distension, trauma secondary to gallbladder removal, chemical irritation of the peritoneum, and pneumoperitoneum[11-14]. Visceral, parietal, and shoulder pain components should be effectively reduced for postoperative analgesia after laparoscopic cholecystectomy[13]. For pain control after laparoscopic cholecystectomy, intravenous patient-controlled analgesia, pa-

tient-controlled thoracic epidural analgesia, intraperitoneal local anesthetic injection, low-pressure pneumoperitoneum and heated air supply were used[15,16]. Alternatively, the transverse abdominis plane block (TAP block), first described by Rafi, can also be used for analgesia.

Cholecystectomy, laparoscopic procedures, cesarean section, and retropubic prostatectomy have proven effective for postoperative analgesia[17-19]. It has been reported that pain increases myocardial workload, oxygen demand and, consequently, the risk of coronary vasoconstriction and myocardial ischemia and infarction[5,6]. Alsadek et al., in their study called ultrasound-guided TAP block for the relief of pain in children who had undergone lower abdominal surgery, stated that the heart rate and mean arterial pressure were lower in patients who applied TAP block for postoperative analgesia, although not statistically significant, and that hemodynamics was more stable compared to the patients who did not undergo the block[20]. In our study, no difference was found for preoperative heart rate, systolic arterial pressure, diastolic arterial pressure and mean arterial pressure, while heart rate, systolic-diastolic and mean arterial pressures in all other measurements were significantly higher in the non-blocked patient group. It was seen that TAP block provided a more stable hemodynamics for the patients.

In their study, Jain et al. proved that TAP and caudal block provide additional benefits to multimodal analgesia in children undergoing lower abdominal surgery, require a low rate of additional postoperative analgesia, and provide lower pain scores[20]. Similarly, in our study, we observed that the VAS score was lower in all measurements in patients who underwent TAP block for multimodal analgesia.

Pulmonary dysfunction is one of the most important causes of mortality and morbidity after surgery and anesthesia. This situation can be prevented by providing postoperative analgesia[21]. Conacher reported in a study that an effective analgesia can prevent the decrease in pulmonary functions that cause hypoxemia and hypercarbia[22]. In our study, peripheral oxygen saturations were significantly higher in patients who underwent TAP block.

Perioperative and postoperative pain management is an important factor in postoperative recovery. In this way, autonomic, somatic and endocrine reflexes are suppressed, thereby reducing perioperative morbidity[23]. Aytaç et al. reported the effect of pain management on recovery parameters in laparoscopic cholecystectomy in their study, and it was emphasized that Aldrete scores were low in patients who did not receive intraoperative analgesia[24]. In our study, Modified Aldrete was also used in patients who underwent TAP block. We observed that their scores were higher in all measures and recovery was earlier.

There are some limitations in our study. These are the number of patients included in the study, the anesthetic agents used in TAP block application and their volumes may be different, the max values of inhaler anesthetics are not known, and the duration of the surgical operation is different.

We know that the intraoperative analgesia approach is important in the development of postoperative pain and complications in patients who underwent laparoscopic cholecystectomy. In this study, we showed that in addition to traditional analgesia methods, TAP block with USG facilitates postoperative pain control, provides more stable hemodynamics, and provides both better and earlier recovery in patients who underwent laparoscopic cholecystectomy. It will provide an advantage in terms of both recovery and complication risk, especially in patients with cardiovascular system disorders. Since it is a simple method under USG guidance and the risk of complications is low, it can be easily applied in clinics.

Author contributions

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

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

Authors declared no financial support.

Ethical approval

The ethics committee of Kastamonu Training and Research Hospital approved this study, which was written according to the principles of the Declaration of Helsinki. (1964) (ethical consent: 12.01.2022, 2020-KAEK-143-147).

References

1. Kaloo P, Armstrong S, Kaloo C, et al. Interventions to reduce shoulder pain following gynaecological laparoscopic procedures. Cochrane Database Syst Rev. 2019;1(1): CD011101. doi:10.1002/14651858.CD011101.pub2
2. Reisli R, Akkaya ÖT, Arıcan Ş, et al. Akut postoperatif ağrının farmakolojik tedavisi: Türk Algoloji-Ağrı Derneği klinik uygulama kılavuzu Agri. 2021;33(Suppl 1):1-51. doi: 10.14744/agri.2021.60243
3. Ferguson MK. Preoperative assessment of pulmonary risk. Chest. 1999;115(5 Suppl):58S-63S. doi: 10.1378/chest.115.suppl_2.58s
4. Hall JC, Tarala R, Harris J, et al. Incentive spirometry versus routine chest physiotherapy for prevention of pulmonary complications after abdominal surgery. Lancet. 1991;337(8747):953-6. doi:10.1016/0140-6736(91)91580-n
5. Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: time for a reconsideration?. J Clin Anesth. 1996;8(6):441-5. doi:10.1016/0952-8180(96)00131-6
6. Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. Anesth Analg. 2001;93(4):853-8. doi:10.1097/00000539-200110000-00010
7. Akyol Beyoğlu Ç, Özdilek A, Erbabacan E, et al. Evaluation of the effects of subcostal transversus abdominis plane block on acute and subacute pain development following inguinal herniography: Randomized clinical study. Agri. 2018;30(3):123-9. doi:10.5505/agri.2018.49344
8. Netter FH. Abdomen Posterolateral Abdominal Wall. In: Netter FH, Editor. Atlas Of Human Anatomy Summit. New Jersey: The Ciba-Geigy Corporation; 1989. Pp. 231–40.
9. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7(1):89-91. doi:10.1016/0952-8180(94)00001-k
10. Foster MA, Taylor AE, Hill NE, et al. Mapping the Steroid Response to Major Trauma from Injury to Recovery: A Prospective Cohort Study. J Clin Endocrinol Metab. 2020;105(3):925-37. doi:10.1210/clinem/dgz302
11. Kim HY, Choi JB, Min SK, et al. A randomized clinical trial on the effect of a lidocaine patch on shoulder pain relief in laparoscopic cholecystectomy. Sci Rep. 2021;11(1):1052. doi:10.1038/s41598-020-80289-y
12. Chung JW, Kang KS, Park SH, et al. İntraperitonal CO etkisi 2 laparoskopik kolesistektomide ameliyat sonrası ağrı ile ilgili konsantrasyon. Ann Surg Tedavi Arş. 2017;93(4):181-5. doi:10.4174/astr.2017.93.4.181
13. Altıparmak B, Korkmaz Toker M, Uysal AI, et al. Ultrasound-guided erector spinae plane block versus oblique subcostal transversus abdominis plane block for postoperative analgesia of adult patients undergoing laparoscopic cholecystectomy: Randomized, controlled trial. J Clin Anesth. 2019;57:31-6. doi:10.1016/j.jclinane.2019.03.012
14. Barazanchi AWH, MacFater WS, Rahiri JL, et al. Evidence-based management of pain after laparoscopic cholecystectomy: a PROSPECT review update. Br J Anaesth. 2018;121(4):787-803. doi:10.1016/j.bja.2018.06.023
15. Barczyński M, Herman RM. A prospective randomized trial on comparison of low-pressure (LP) and standard-pressure (SP) pneumoperitoneum for laparoscopic cholecystectomy. Surg Endosc. 2003;17(4):533-8. doi:10.1007/s00464-002-9121-2
16. Mouton WG, Bessell JR, Millard SH, et al. A randomized controlled trial assessing the benefit of humidified insufflation gas during laparoscopic surgery. Surg Endosc. 1999;13(2):106-8. doi:10.1007/s004649900915
17. Faiz SHR, Alebouyeh MR, Derakhshan P, et al. Comparison of ultrasound-guided posterior transversus abdominis plane block and lateral transversus abdominis plane block for postoperative pain management in patients undergoing cesarean section: a randomized double-blind clinical trial study. J Pain Res. 2017;11:5-9. Published 2017 Dec 19. doi:10.2147/JPR.S146970
18. Khan KK, Khan RI. Analgesic Effect of Bilateral Subcostal Tap Block After Laparoscopic Cholecystectomy. J Ayub Med Coll Abbottabad. 2018;30(1):12-5.
19. Shahait M, Lee DI. Application of TAP Block in Laparoscopic Urological Surgery: Current Status and Future Directions. Curr Urol Rep. 2019;20(5):20. doi:10.1007/s11934-019-0883-7
20. Alsadek WM, Al-Gohari MM, Elsonbaty MI, et al. Ultrasound guided TAP block versus ultra-

sound guided caudal block for pain relief in children undergoing lower abdominal surgeries. Egyptian Journal of Anaesthesia. 2015;31(2): 155-60.
doi: 10.1016/j.egja.2015.03.001
21. Jain S, Kalra S, Sharma B, et al. Evaluation of Ultrasound-Guided Transversus Abdominis Plane Block for Postoperative Analgesia in Patients Undergoing Intraperitoneal Onlay Mesh Repair. Anesth Essays Res. 2019;13(1):126-31.
doi:10.4103/aer.AER_176_18
22. Conacher ID. Pain relief after thoracotomy. Br J Anaesth. 1990;65(6):806-12.
doi:10.1093/bja/65.6.806
23. Kara H, Sahin N, Ulusan V, et al. Magnesium infusion reduces perioperative pain. Eur J Anaesthesiol. 2002;19(1):52-6.
doi:10.1017/s026502150200008x
24. Güven Aytac B, Aytaç İ, Lafçı A, et al. The effect of pain management in laparoscopic cholecystectomy on recovery parameters. TJCL. 2018; 9(3): 216-20.
doi: 10.18663/tjcl.445926

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EFFICACY AND SAFETY OF PERCUTANEOUS NEPHROLITHOTOMY IN ELDERLY PATIENTS: EXPERIENCE OF 128 CASES

YAŞLI HASTALARDA PERKÜTAN NEFROLİTOTOMİNİN ETKİNLİĞİ VE GÜVENİLİRLİĞİ: 128 VAKA DENEYİMİ

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Abstract

Aim: This study aimed to evaluate the efficacy and safety of percutaneous nephrolithotomy in elderly patients (≥65 years) with kidney stones > 2 cm in size.

Methods: Patients aged ≥65 years who underwent percutaneous nephrolithotomy for kidney stones between January 2015 and January 2022 were included in this study. Patient profiles, preoperative stone data, operative information, and postoperative complications were reviewed. We applied the Guys Stone score to predict the net results of percutaneous nephrolithotomy.

Results: Percutaneous nephrolithotomy was performed on 128 geriatric patients. Of these patients, 68 (53.1%) were male and 60 (46.9%) were female. The mean age was 69.87 ± 7.06 (65–80) years. The mean stone size was 28.7 ± 6.5 mm (22–46 mm). The mean operative time was 90.33 ± 40.56 min and fluoroscopy time was 5.16 ± 2.81 min. The reentry catheter was removed after an average of 3.21 ± 1.82 days. The mean duration of hospital stay was 3.17 ± 2.19 days. The stone-free survival rate was 90.6%. Transfusion was performed in four (3.1%) patients due to hemorrhage, and urine extravasation from the re-entry tract occurred in eight (6.2%) patients, and this required Double j-stent placement. When the four Guys stone score groups were compared, there was a statistically significant difference in stone-free rates (p = 0.001).

Conclusions: According to our results, percutaneous nephrolithotomy is a safe and effective treatment option for nephrolithiasis in the elderly, with high stone-free and acceptable complication rates.

Keywords: Elderly patients, percutaneous nephrolithotomy, nephrolithiasis, Guys stone score

Öz

Amaç: Bu çalışmada böbrek taşı> 2 cm olan yaşlı hastalarda (≥65 yaş) perkütan nefrolitotominin etkinlik ve güvenilirliğinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Ocak 2015 ile Ocak 2022 tarihleri arasında böbrek taşı nedeniyle perkütan nefrolitotomi uygulanan 65 yaş ve üzeri hastalar bu çalışmaya dahil edildi. Hasta profilleri, ameliyat öncesi taş verileri, ameliyat bilgileri ve ameliyat sonrası komplikasyonlar gözden geçirildi. Perkütan nefrolitotominin net sonuçlarını tahmin etmek için Guys Stone skorunu uyguladık.

Bulgular: 128 geriatrik hastaya perkütan nefrolitotomi uygulandı. Bu hastaların 68'i (%53,1) erkek, 60'ı (%46,9) kadındı. Ortalama yaş 69.87 ± 7.06 (65-80) yıldı. Ortalama taş boyutu 28.7 ± 6.5 mm (22-46 mm) idi. Ortalama ameliyat süresi 90.33 ± 40.56 dk ve floroskopi süresi 5.16 ± 2.81 dk idi. Yeniden giriş kateteri ortalama 3.21 ± 1,82 gün sonra çıkarıldı. Ortalama hastanede kalış süresi 3.17 ± 2.19 gündü. Taşsız sağkalım oranı %90,6 idi. Dört hastada (%3,1) kanama nedeniyle transfüzyon yapıldı ve sekiz hastada (%6,2) yeniden giriş yolundan idrar ekstravazasyonu meydana geldi ve bu, Double j-stent yerleştirilmesini gerektirdi. Dört Guys taş skor grubu karşılaştırıldığında, taşsızlık oranlarında istatistiksel olarak anlamlı bir fark vardı (p = 0.001).

Sonuç: Sonuçlarımıza göre, perkütan nefrolitotomi, yaşlılarda nefrolitiazis için yüksek taşsızlık ve kabul edilebilir komplikasyon oranları ile güvenli ve etkili bir tedavi seçeneğidir.

Anahtar Kelimeler: Yaşlı hastalar, perkütan nefrolitotomi, nefrolitiazis, Guys taş skoru

Introduction

The elderly constitutes 10–12% of all patients with stones; the burden of stone disease in elderly patients is expected to increase significantly because of the significant increase in the population of the elderly and metabolic changes due to aging in recent years[1]. Some recent population-based studies have shown that the number of elderly patients who receive treatment for kidney stones and the proportion in the general population are increasing daily[2,3]. Aging is the most important risk factor for perioperative complications and all possible adverse outcomes. Additionally, comorbid diseases are more common in the elderly, which may affect treatment decisions[4]. Therefore, it is important to manage stones more effectively and safely in elderly populations and to pay attention to this issue. Owing to recent developments in endoscopic instruments and surgical techniques, the success rates of percutaneous nephrolithotomy (PCNL) have increased and complication rates have decreased. However, data on kidney stones in the elderly population are lacking and have been reported by very few centers worldwide[5-7]. This study aimed to evaluate the efficacy and safety of this procedure in elderly patients (aged ≥65 years) who underwent PCNL for kidney stones > 2 cm.

Materials and Methods

This study was approved by the local ethics committee of our tertiary education and research hospital. The operative data of 128 elderly patients who underwent PCNL for kidney stones > 2 cm between January 2015 and January 2022 were retrospectively analyzed. Our study complied with the principles of the Declaration of Helsinki, and informed consent was obtained from each patient. Patients who were > 65 years of age, had normal renal function, had kidney stones > 2 cm, and underwent PCNL were included in the study. Preoperative history was obtained from all patients, and a physical examination was performed. Preoperative urinalysis, urine culture, serum urea and creatinine levels, complete blood cell count, and coagulation tests were performed for all patients. Ultrasound (USG), kidney-ureter-bladder radiography (KUB), and noncontrast abdominopelvic computed tomography (NCCT) were used as imaging modalities. Patients with positive urine cultures were treated with appropriate antibiotics before surgery and underwent surgery after the culture was negative. Stone size was calculated by measuring the longest axis of the stone on preoperative imaging; in those with multiple stones, stone size was determined as the longest axis of the largest stone. The operation time, bleeding requiring transfusion, number of percutaneous accesses, and complication rates were evaluated intraoperatively, and the mean hospital stay and nephrostomy time, urinary tract infection rate, leakage rate from the nephrostomy tract, fever rate, and complication development rate were evaluated postoperatively. KUB radiography was taken on the 1st postoperative day. Clavien degree of complication was used to assess complications. The stone-free rate (SFR) was evaluated using KUB radiography for opaque stones and CT for non-opaque stones. Kidney ultrasonography was performed 1 month after the operation. CT scans were not considered, except for patients with non-opaque stones who were in between owing to excessive radiation concerns. To estimate the net results of PCNL, we applied the Guys stone score (GSS), a 4 categorical rating according to the complexity of the stones, as described by Thomas et al[8].

- *Surgical Technique*

Standard PCNL was applied to all patients using a one-stage procedure in the prone position under general anesthesia. In the lithotomy position, a 6 Fr multi-hole ureteral catheter was inserted into the pelvicalyceal system using a cystoscope and fixed to the urethral Foley catheter. The patient was then placed in the prone position, and the

pelvicalyceal system was visualized with fluoroscopic guidance through an opaque 6 Fr ureteral catheter. Renal access was achieved by entering the appropriate calyx with an 18-gauge needle, and a guidewire was placed and fixed. After a 0.5-cm skin incision was made, a Renax tube was inserted through the guide wire by serial dilation up to 24–28 Fr with an Amplatz dilator. After detecting the stone using nephroscopy (Wolf), lithotripsy was performed using a pneumatic lithoclast, and the stone particles were removed with forceps. A nephrotomy tube was routinely placed in all patients at the end of the surgery. A double-J stent was inserted antegrade only in patients with suspected stenosis or injury at the ureteropelvic junction or in patients with severe edema. Usually, the nephrostomy tube is removed on the third postoperative day. The stents were removed with sedation or short-term general anesthesia in the 1st postoperative month in patients who had a double-J stent implanted.

- *Statistical Analysis*

Continuous variables are expressed as means and standard deviations. Categorical variables are presented as numbers and percentages. All statistical analyses were performed using Statistical Package for the Social Sciences (SSPS) software version 13.0 (IBM, SPSS Inc., Chicago, USA). One-way ANOVA was used to compare continuous variables. The chi-square test was used to compare categorical values in the different Guy stone score subgroups. P-values < 0.05 indicated statistical significance.

Results

The mean age of the patients was 69.87 ± 7.06 (65–80) years. Overall, 68 (53.1%) patients were male and 60 (46.9%) were female. The mean stone size was 28.7 ± 6.5 mm (22–46 mm). Many stones (57.8%) were located in the pelvis and were opaque (84.3%).

Table 1. Demographic characteristics of 128 elderly patients who underwent percutaneous nephrolithotomy (PNL).

Gender	Male	68 (%53.1)
	Female	60 (%46.9)
Age (years)[Y]		69,87 ± 7,06 (65-80)
Comorbidities	DM	48 (37.5%)
	HT	62 (48.4%)
	IHD	10 (7.8%)
	UTI	17 (15.17%)
Stone size (mm)[Y]		28.7 ± 6.5, 22–46
Stone location[X]	Renal pelvis	74 (57.8%)
	Renal pelvis /Lower pole	22 (17.1%)
	Staghorn	16 (12.5%)
	Multiple	16 (12.5)
Stone laterality[X]	Right	58 (45.3%)
	Left	70 (54.7%)
Radiopacity of stone[X]	Opaque	108 (84.3%)
	Lucent	20 (15.6%)
Hydronephrosis[X]	Mild	77 (60.1%)
	Moderate	36 (28.1%)
	Severe	15 (11.7%)
Preoperative HB (g/dl)[Y]		13.4 ± 2.6, 11–15.6
Preoperative BUN (mg/dl)[Y]		15 ± 3.2, 12–23
Preoperative creatinine (mg/dl)[Y]		1.4± 0.56, 0.8–2.5

[x]Data were presented as n (%). [y]Data were presented as mean ± SD, range.ESWL, extracorporeal shock wave lithotripsy; HB, hemoglobin; mm, millimeter; UTI, urinary tract infection; BUN, blood urea nitrogen; DM (Diabetes Mellitus); HT (Hypertension); IHD (ischemic heart disease)

Table 2. Outcome and complications of PNL surgery of 128 elderly patients.

Stone clearance status[x]		Early stone free	112 (87.5%)
		Final stone free	116 (90.6%)
Puncture site [X]		Upper calyx	26 (20.3%)
		Middle calyx	36 (28.1%)
		Lower calyx	55 (42.9%)
		Multiple calyx	11 (8.5%)
Operation time (min)[Y]			90.33 ± 40.56
Fluoroscopy screening time (min)[Y]			5.16 ± 2,81
Nephrostomy duration (day)[X]			3,21 ± 1,82
Postoperative hospitalization (day)[Y]			3,17± 2,19
Complications	Grade 1[X]	Fever	5 (3.9%)
		Blood transfusion	4 (3.1%)
	Grade 2[X]	Urine leakage	8 (6.2%)
		Infection (UTI)	5 (3.9%)
	Grade 3[Y]	DJ placement for urine leakage	8 (6.2%)
		Residual	8 (6.2%)
	Grade 4[X]	Urosepsis	2 (1.5%)
		Visceral injury	0 (0.00%)
	Grade 5[X]	Death	0 (0.00%)

[x]Data were presented as n (%). [y]Data were presented as mean ± SD, range.
DJ, double J; UTI, urinary tract infection.

The most frequent preoperative complication was grade 1 hydronephrosis (84.3%). In 55 (42.9%) patients, the lower calyx was affected, the middle calyx was affected in 36 (28.1%) patients, the upper calyx in 26 (20.3%) patients, and 11 (8.5%) patients had stones in multiple calyces. The mean operative time was 90.33 ± 40.56 min, and fluoroscopy time was 5.16 ± 2.81 min (Table I). The reentry catheter was removed after an average of 3.21 ± 1.82 days. The mean hospital stay was 3.17±2.19 days. The early stone-free rate was 87.5%, and the final stone-free rate was 90.6%. While transfusion was performed in four (3.1%) patients due to bleeding, urine extravasation occurred in eight (6.2%) patients from the re-entry tract, which required DJ stent placement. Angioembolization was performed in two (1.5%) patients after severe hematuria using interventional radiology.

Table 3. Results according to Guys stone score (GSS) categorization

Variables	GSS-1	GSS-2	GSS-3	GSS-4	*p*-value
Stone free	81/86 (94.1%)	22/26 (84.6%)	7/10 (70%)	4/6 (66.6%)	0.001*
Hospital stays	3±1.3	3±1.1	3±0.8	3.2±1.4	0.7
Complications	9 (16.6%)	3 (27.2%)	2 (33.3%)	2 (25%)	0.9

Data were presented as n (%) and mean ± SD, range. $p \leq 0.05$

Five (3.9%) patients were treated with 7 days of IV antibiotic therapy because of postoperative fever and urinary tract infection (UTI). Urosepsis was seen as a clavian grade 4 complication in only two patients (Table II). When the four Guys stone score (GSS) groups were compared, there were statistically significant differences in stone-free rates (Table III). However, no significant difference was observed in the length of hospital stay and complications among the four GSS category patients (Table III).

Discussion

Surgery in elderly patients is associated with many challenges. In this population, various complications and undesirable results may occur as a result of age-related changes in the cardiovascular, pulmonary, nervous, metabolic, and locomotive systems[9,10]. However, owing to advances in endoscopic technologies and expertise, percutaneous nephrolithotomy (PCNL) has become easier to perform, even in advanced age, and appears to be as effective and safe as in the standard adult population[5].

The main indicator of success in PCNL can be defined as the patient getting rid of the stone with minimal damage. Anagnostou et al[11] In their study, in which they evaluated 779 patients in two groups comprising individuals who were over 70 years old and those less than 70 years old. However, they found no difference between the two groups in terms of complications, complete stone-free rates, and clinical success rates. Similar to this study, a study by Nakamon et al[12] showed that there was no significant difference between the two groups in terms of operation time, complete stone-free rate, hospital stay, and complications. Stoller et al[5] reported that the complete stone-free rate was 82% at the third-month follow-up in 33 elderly patients who underwent PCNL. Although there was no young control group in our study, stone-free (90.6%) and complication rates were similar to those reported in the literature.

Although some studies[13] have shown that critical complications after PCNL are rare and death is not observed in elderly patients, studies have reported the need for a relatively higher blood transfusion rate in this age group. While blood transfusion was administered to only four patients (3.1%) in our study, high blood transfusion rates of up to 12% have been reported in some studies[14]. Sepsis is an important complication of PCNL. Nakamon et al[12] reported that the incidence of sepsis in the elderly group was 6% versus 13%; however, high urine culture positivity in elderly patients in the preoperatively led to an increase in the incidence of sepsis, but the difference was not statistically significant. In our study, no difference was observed in sepsis rates between the different GSS category groups (Table III). After the PCNL procedure, only two patients (1.5%) had sepsis. We believe that this success is due to the specific patient selection and extra care given to the patients preoperatively (for example, no patient was treated without culture-negative, nephrostomy catheter, or double-J stent placement in patients with infected kidneys before PCNL).

One of the common complications of PCNL is fever. Seitz et al[15] İn a systemic review that evaluated PCNL complications, reported that fever is a common complication after PCNL, and the overall incidence is as high as 10.8%. However, as can be seen in Table II, the complications in our study were minor, and the rates of fever and sepsis were low (3.9–1.5%).

Studies on the safety of PCNL in the elderly have recently been published. Okeke et al[16] compared PCNL in elderly and young patients and reported that the hospital stay was longer in elderly patients than in younger patients (approximately 5 days vs. 3 days). Ozturk et al[17] in their study which had a small sample size, reported that the tubeless PCNL procedure can be safely applied in the elderly population. However, in these studies, complications or stone complexity in elderly patients undergoing PCNL was not studied. The most important strength of

our study is that we divided elderly patients into Guys stone score groups to rank complications, and to examine the differences in the results based on these categories.
The present study has some limitations. First, the study has a retrospective study design that reflects single-center results. Although the incidence of stones in this age group was lower than that in the younger group, we believe that the number of patients was sufficient, thus increasing the reliability of the statistical analysis. Second, biochemical analyses of the stones could not be performed.

Conclusion

The results of our study showed that PCNL is a safe and effective treatment option for elderly patients with nephrolithiasis due to its high stone-free and acceptable complication rates. Elderly patients with a low Guys stone score were found to have a higher stone-free rates than those with a high score.

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

In accordance with the 1964 Helsinki Declaration, our study was approved by the clinical research ethics committee of the Health Sciences University, Adana City Training and Research Hospital (Date: 21.04.2022, number: 1907). Informed written consent was obtained from all individual participants included in the study.

References

1. McCarthy JP, Skinner TA, Norman RW. Urolithiasis in the elderly. Can J Urol. 2011;18(3):5717–20.
2. Ordon M, Urbach D, Mamdani M, et al. A population-based study of the changing demographics of patients undergoing definitive treatment for kidney stone disease. J Urol. 2015;193(3):869–74. doi: 10.1016/j.juro.2014.09.096
3. Ghani KR, Sammon JD, Karakiewicz PI, et al. Trends in surgery for upper urinary tract calculi in the USA using the nationwide inpatient sample: 1999–2009. BJU Int. 2013;112(2):224–30. doi: 10.1111/bju.12059
4. Sahin A, Atsu N, Erdem E, et al. Percutaneous nephrolithotomy in patients aged 60 years or older. J Endourol. 2001;15(5): 489–91. doi: 10.1089/089277901750299276
5. Stoller MS, Bolton DB, Lezin M, et al. Percutaneous nephrolithotomy in the elderly. Urology. 1994;44:651–54. doi: 10.1016/s0090-4295(94)80198-3
6. Shohab D, Iqbal N, Alam MU, et al. Comparison of Outcome of Percutaneous Nephrolithotomy in Adult Versus Paediatric Patients. J Coll Physicians Surg Pak. 2016;26(5):371–73.
7. Sighinolfi MC, Micali S, Grande M, et al. Extracorporeal shock wave lithotripsy in an elderly population: How to prevent complications and make the treatment safe and effective. J Endourol. 2008;22(10):2223–26. doi: 10.1089/end.2008.9704
8. Thomas K, Smith NC, Hegarty N, et al. The Guy's stone score--grading the complexity of percutaneous nephrolithotomy procedures. Urology. 2011;78(2):277–81. doi: 10.1016/j.urology.2010.12.026
9. Tonner PH, Kampen J, Scholz J. Pathophysiological changes in the elderly. Best Pract Res Clin Anaesthesiol. 2003;17:163–77. doi: 10.1016/s1521-6896(03)00010-7
10. Sieber FE. Postoperative delirium in the elderly surgical patient. Anesthesiol Clin. 2009;27:451–64. doi: 10.1016/j.anclin.2009.07.009
11. Anagnostou T, Thompson T, Ng CF, et al. Safety and outcome of percutaneous nephrolithotomy in the elderly: retrospective comparison to a younger patient group. J Endourol. 2008;22:2139–46. doi: 10.1089/end.2007.0432
12. Nakamon T, Kitirattrakarn P, Lojanapiwat B. Outcomes of percutaneous nephrolithotomy: comparison of elderly and younger patients. Int Braz J Urol. 2013;39: 692–1. doi: 10.1590/S1677-5538.IBJU.2013.05.12
13. Romero V, Akpinar H, Assimos DG. Kidney stones: A global picture of prevalence, incidence, and associated risk factors. Rev Urol. 2010;12(2-3):e86–96. doi: 10.3909/riu0459
14. Resorlu B, Diri A, Atmaca A et al. Can we avoid percutaneous nephrolithotomy in high-risk el-

derly patients using the charlson comorbidity index? Urology. 2012;79(5):1042–47.
doi: 10.1016/j.urology.2011.10.060
15. Seitz C, Desai M, Häcker A, et al. Incidence, prevention, and management of complications following percutaneous nephrolitholapaxy. Eur Urol. 2012;61(1):146–58.
doi: 10.1016/j.eururo.2011.09.016
16. Okeke Z, Smith AD, Labate G, et al., on behalf of the CROES PCNL Study Group, JJ. Prospective comparison of outcomes of percutaneous nephrolithotomy in elderly patients versus younger patients. J Endourol. 2012;26(8): 996–1.
doi: 10.1089/end.2012.0046
17. Ozturk H. Tubeless versus standard PCNL in geriatric population. Actas Urol Esp. 2015;39(8):494–1.
doi: 10.1016/j.acuro.2015.02.010

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FACTORS AFFECTING LENGTH OF STAY IN LAPAROSCOPIC NEPHRECTOMY: SINGLE CENTER 330 CASE EXPERIENCE

LAPAROSKOPİK NEFREKTOMİDE YATIŞ SÜRESİNİ ETKİLEYEN FAKTÖRLER: TEK MERKEZ 330 VAKA DENEYİMİ

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Abstract

Aim: In this study, we aimed to investigate the factors affecting the length of stay in patients who underwent laparoscopic nephrectomy.

Methods: The data of 330 patients who underwent laparoscopic nephrectomy in our clinic between January 2013 and December 2021 were analyzed retrospectively. Demographic data, preoperative, peroperative and postoperative characteristics of the patients were recorded. The patients included in the study were divided into two groups as hospital stay ≤4 days (group A) and >4 days (group B). Potential risk factors for prolonged hospitalization were evaluated by comparing demographic characteristics, operation data, and perioperative and postoperative complications between the groups.

Results: There were 330 patients who underwent laparoscopic nephrectomy in our study. The mean age of the patients in group A was 49.1 ± 11.45 years, while it was 50.61 ± 11.60 years in group B. Body weight (kg), BMI (Body mass index) (kg/m2) and comorbidities were statistically significantly higher in group B (p=0.003, p=0.016, p<0.001, respectively). While the operation time was 125 minutes in group A, it was 155 minutes in group B, and this difference was statistically significant (p<0.001). It was observed that 220 (66.7%) of the patients were hospitalized for ≤4 days and 110 (33.3%) were hospitalized longer than 4 days. While the duration of hospitalization was found to be longer in patients with a long operation time (p<0.001), the hospitalization period was found to be longer in patients who developed perioperative and postoperative complications (respectively: p=0.017, p=0.002).

Conclusions: In our study, the length of hospital stay was significantly longer in patients who had a long operation time and developed perioperative and postoperative complications. Reducing operation times and complication rates as much as possible may be beneficial in reducing the length of stay.

Keywords: Laparoscopic surgery, nephrectomy, complication, length of stay

Öz

Amaç: Bu çalışmamızda laparoskopik nefrektomi yapılan hastalarda yatış süresini etkileyen faktörleri araştırmayı amaçladık.

Yöntemler: Ocak 2013-Aralık 2021 tarihleri arasında kliniğimizde laparoskopik nefrektomi yapılan 330 hastanın verileri retrospektif olarak incelendi. Hastaların demografik verileri, preoperatif, peroperatif ve postoperatif özellikleri kaydedildi. Çalışmaya dahil edilen hastalar yatış süresi ≤4 gün (grup A) ve >4 gün (grup B) olarak iki gruba ayrıldı. Gruplar arasında demografik özellikler, operasyon verileri, peroperatif ve postoperatif komplikasyon durumu karşılaştırılarak yatış süresinin uzaması açısından olası risk faktörleri değerlendirildi.

Bulgular: Çalışmamızda laparoskopik nefrektomi yapılan 330 hasta vardı. Grup A'daki hastaların yaş ortalaması 49,1 ± 11,45 yıl iken, grup B'de ise 50,61 ± 11,60 yıl idi. Vücut ağırlığı (kg), VKİ (Vücut kitle indeksi) (kg/m2) ve komorbiditeler istatistiksel anlamlı olarak grup B'de daha yüksekti (sırasıyla p=0,003, p=0.016, p<0,001). Operasyon süresi grup A'da 125 dk iken grup B'de 155 dk idi ve bu fark istatistiksel olarak anlamlıydı (p<0,001). Hastaların 220'sinin (%66,7) ≤4 gün, 110'unun (%33,3) ise 4 günden uzun yattığı görüldü. Operasyon süresinin uzun olduğu hastalarda yatış süresinin daha uzun olduğu saptanırken (p<0,001), benzer şekilde peroperatif ve postoperatif komplikasyon gelişen hastalarda da yatış süresi uzun saptandı (sırasıyla: p=0,017, p=0,002).

Sonuç: Çalışmamızda, operasyon süresi uzun olan, peroperatif ve postoperatif komplikasyonlar gelişen hastalarda yatış süresi belirgin uzundu. Operasyon sürelerinin ve komplikasyon oranlarının olabildiğince düşürülmesi yatış süresini azaltmada faydalı olabilir.

Anahtar Kelimeler: Laparoskopik cerrahi, nefrektomi, komplikasyon, yatış süresi

Giriş

İlk laparoskopik nefrektomi, 1990 yılında Clayman ve ark.[1] tarafından 3 cm böbrek kitlesi olan yaşlı bir hastanın operasyonu ile başlamıştır. O zamandan beri laparoskopik nefrektomiye ürologlar yoğun ilgi göstermektedir ve günümüzde ürolojide yapılan en yaygın laparoskopik cerrahi haline gelmiştir[2]. Her ne kadar onkolojik sonuçlarda farklılık olmasa da, postoperatif analjezi ihtiyacının az olması, normal aktivitelere daha hızlı dönüş, daha kısa hastane yatışı, daha düşük morbidite oranı ve potansiyel olarak daha düşük maliyetler nedeniyle laparoskopik nefrektomi açık nefrektomiden daha üstündür[3-6]. Özellikle laparoskopi lehine olan kısa hastane yatışı ve düşük maliyet oranı, günümüzde sağlık hizmetlerinin artan maliyetini dizginleme çabaları açısından tüm ülkeler için kritik önem arz etmektedir. Bu bakımdan hastanede kalış süresi kaliteyi değerlendirme ve iyileştirme için önemli bir göstergedir[7,8]. Ancak hastanede kalış süresinin tahmin edicileri ürolojide iyi çalışılmamıştır. Çalışmamızda demografik özellikler, operasyon verileri, peroperatif ve postoperatif komplikasyon durumu gibi değişkenlere odaklanarak, laparoskopik nefrektomi sonrası yatış süresini etkileyen faktörleri değerlendirilmeyi amaçladık.

Materyal ve Metot

Çalışmamız 3. basamak eğitim ve araştırma hastanemiz yerel etik kurulu tarafından onaylandıktan sonra (Tarih: 21/04/2022, Karar no: 1908), Ocak 2013 – Aralık 2021 tarihleri arasında laparoskopik nefrektomi uygulanan 360 hastanın operasyon verilerinin retrospektif olarak incelenmesi ile oluşturuldu. Çalışmamıza laparoskopik radikal ve simple (basit) nefrektomi yapılan hastalar dahil edildi. Laparoskopik nefrektomi sırasında çeşitli nedenlerle açığa dönülen vakalar çalışma dışı bırakıldı. Dışlama kriteri sonrası çalışmamıza 330 hasta ile devam edildi. Çalışmamız Helsinki deklarasyonu ilkelerine uygun şekilde yürütülmüştür. Çalışmaya dahil edilen hastalar yatış süresi ≤4 gün (grup A) ve >4 gün (grup B) olarak iki gruba ayrıldı. Hastaların, yaş, cinsiyet, vücut kitle indeksi (VKİ), ek hastalıklar, serum üre ve kreatinin, tam kan sayımı sonuçları, böbrek boyutu, operasyon yönü, ameliyat endikasyonu, ameliyat süresi, peroperatif ve postoperatif komplikasyonları, ameliyat sonrası analjezi ihtiyacı, kan kaybı, hastanede kalış süresi ve kan transfüzyonu ihtiyacı kaydedildi. Komplikasyonlar için Clavien komplikasyon derecesi kullanıldı. İstatistiksel analiz için SPSS 25.0 paket programı (IBM, Armonk, NY, ABD) kullanıldı. Kategorik ölçümler sayı ve yüzde olarak, sürekli ölçümler ise ortalama, standart sapma ve minimum-maksimum olarak gösterildi. Normal dağılım gösteren parametreler için bağımsız Student t testi, normal dağılım göstermeyen parametreler için Mann Whitney U testi kullanıldı. Kategorik değişkenlerin karşılaştırılması Ki-kare testi ile yapıldı. Tüm testler için istatistiksel anlamlılık düzeyi 0,05 olarak alındı.

- *Cerrahi Prosedür*

Laparoskopik nefrektomide hemen hemen tüm vakalarda transperitoneal yaklaşım kullanıldı. Hasta flank pozisyonuna alındı. İşlem için genellikle üç trokar kullanıldı ancak lüzum halinde dördüncü trokar da yerleştirildi. İlk trokar (10 mm) göbek hizasında rektus kılıfının lateraline yerleştirildi. Açık Hasson veya veres iğne giriş teknikleri kullanılarak pnömoperitoneum sağlandı. İkinci ve üçüncü trokarlar (5 mm) ön aksiller hatta üçgen olacak şekilde yerleştirildi. Gerota yağı ve psoas kası belirlenene kadar kolon medialize edildi. Psoas kası boyunca üreter tespit edilerek babcock klemp ile askıya alındı. Üreter böbreğe kadar serbestlenip pediküle gidildi. Renal arter ve veni ayırmadan önce tutturmak için metal klipsler veya stapler kullanıldı. Üreter, böbreği arka taraftan mobilize etmeye yardımcı olmak için önce klipslendi ve kesildi. Daha sonra örnek, bir organ toplama torbası yardımıyla dışarıya alındı.

Tablo 1. Yatış süresine göre demografik hasta verileri

	Grup A (n = 220)	Grup B (n =110)	P
Yaş (Ort±SS)	49,1 ± 11,45	50,61 ± 11,60	0,480
Cinsiyet (K/E)	60 (%27) 160 (%73)	70 (%63,6) 40 (%36,4)	0,001*
Vücut ağırlığı (kg)	72,5 (34–130)	79 (49–120)	0,003*
VKİ (kg/m^2)	26,6 (14,2–46,9)	27.6 (17–41,5)	0,016*
Komorbidite	77 (%35)	59 (%62,7)	<0,001*
Diabetes mellitus	15 (%6,8)	42 (%38,1)	
Hipertansiyon	82 (%37,2)	73 (%66,3)	
Koroner arter hastalığı	24 (%10,9)	30 (%45,4)	
KOAH	15 (%6,8)	12 (%10,9)	
Serebrovasküler hastalık	1 (%0,45)	1 (%1,8)	
Kronik böbrek yetmezliği	3 (%0,13)	5 (%4,5)	
ASA skor			
• I	152 (%69)	40 (%36,3)	
• II	60 (%27,2)	30 (%27,2)	<0,001*
• III	7 (%3,1)	30 (%27,2)	
• IV	1 (%0,45)	10 (%9,9)	

Dağılımın normalliğine göre sürekli değişkenler için ortalama ± standart sapma veya medyan (minimum-maksimum) olarak ve kategorik değişkenler için frekans (yüzde) olarak verilen veriler.
ASA: Amerikan Anestezi Uzmanları Derneği, VKİ: Vücut kitle indeksi, KOAH: Kronik obstrüktif akciğer hastalığı. *P ≤ 0,05

Bulgular

Çalışmamızda laparoskopik nefrektomi yapılan 330 hastanın 130'u (%39,3) kadın, 200'ü (%60,7) erkek idi. Grup A'daki hastaların yaş ortalaması 49,1 ± 11,45 yıl iken, grup B'de ise 50,61 ± 11,60 yıl idi. Vücut ağırlığı (kg), VKİ (Vücut kitle indeksi) (kg/m2) ve komorbiditeler istatistiksel anlamlı olarak grup B'de daha yüksekti (sırasıyla p=0,003, p=0,016, p<0,001). Her iki grupta da en sık görülen komorbidite hipertansiyondu. Her iki grupta ASA (Amerikan Anestezi Uzmanları Derneği) skor I en sık görülürken, yüksek ASA skoru Grup B'de anlamlı şekilde daha fazlaydı. Operasyon Süresi grup A'da 125 dk iken grup B'de 155 dk idi ve bu fark istatistiksel olarak anlamlıydı (p<0,001). Kanama miktarı (cc), kan transfüzyonu, radyolojik boyut (mm), hemoglobin (g/dl), hematokriti değerleri açısından iki grup arasında anlamlı fark yok iken, preoperatif ve postoperatif kreatinin (mg/dl) değerleri arasında hem her iki grup arasında hem de grup içi istatiksel anlamlı farklılık vardı (p<0,001). Peroperatif ve postoperatif komplikasyon gelişen hastaların yatış süresi komplikasyon gelişmeyenlere göre daha uzundu (sırasıyla: p=0,017, p=0,002)

Tartışma

Çalışmamız, VKİ yüksekliğinin, komorbidite varlığının ve sayısının fazla olmasının, operasyon süresinin uzun olmasının ve peroperatif ve postoperatif komplikasyon gelişmesinin, laparoskopik nefrektomi sonrası yatış süresinin uzamasına neden olabileceğini göstermiştir.
Preoperatif risk faktörleri yatış süresini tahmin etmede önemli rol oynar[9,10]. Literatürdeki bazı çalışmalar çeşitli cerrahi işlemler için uzamış yatış süresi ile ilişkili preoperatif risk faktörlerini içeren değişkenleri araştırmıştır[11-15]. Ürolojik en sık yapılan kanser cerrahilerinden olan nefrektomi, prostatektomi, sistektomi gibi ürolojik vakalarda, ileri hasta yaşı, bağımlı fonksiyonel durum, serum albümin ve hematokrit seviyelerinin düşük ve kreatinin seviyesinin yüksek olmasının yatış süresini arttıran önemli faktörler olduğu belirtilmiştir[12,15].

Tablo 2. Yatış süresine göre iki grup arasındaki peroperatif ve postoperatif verilerin karşılaştırılması

	Grup A (n =220)	Grup B (n =110)	P
Operasyon Süresi (dk)	125 (40–420)	155 (90–240)	<0,001*
Kanama miktarı (cc)	50 (0–3200)	75 (0–250)	0,120
Kan transfüzyonu	6 (%4,08)	2 (%2,70)	0,114
Postopeatif komplikasyon (var/yok)	10 (%4,5) 210 (%95,4)	15 (%13,6) 95 (%86,3)	0,002*
Peroperatif komplikasyon (var/yok)	5 (%2,2) 115 (%97,8)	10 (%9,9) 100 (%90,1)	0,017*
Radyolojik boyut (mm)	38 (10-130)	47 (5-120)	0,394
Hemoglobin (g/dl)			
• Preop	13,73 ± 1,98	14,08 ± 1,78	0,768
• Postop	12,38 ± 1,74	12,91 ± 1,82	
Hematokrit			
• Preop	40,33 ± 5,58	43,76 ± 4,80	0,895
• Postop	38,21 ± 4,06	39,70 ± 5,48	
Kreatinin (mg/dl)			
• Preop	0,95 (0,55–5,10)	0,75 (0,39–1,06)	<0,001*
• Postop	1,03 (0,57–16,00)	0,98 (0,54–1,94)	
P (gruplar arası)	<0,001*	<0,001*	<0,001*

Dağılımın normalliğine göre sürekli değişkenler için ortalama ± standart sapma veya medyan (minimum-maksimum) olarak ve kategorik değişkenler için frekans (yüzde) olarak verilen veriler. *P ≤ 0,05

Bizim çalışmamız ise, eşlik eden komorbitelerin, obezite varlığının ve yüksek ASA skorunun preoperatif risk faktörü olarak yatış süresini arttırdığını göstermiştir.

Hastane hacmide, çeşitli maligniteler için yatış süresinin belirleyicisi olabilir[16-20]. Bazı literatür çalışmaları, yüksek hacimli hastanelerde operasyonda ölüm oranlarının daha düşük olduğunu göstermiştir[21]. Aslında bu durumu oluşturan yüksek hacimli hastanelerin daha geniş, ileri tıbbi teknoloji ve hizmet yelpazesinin olması ve aynı zamanda ilgili cerrahi prosedürler konusunda yüksek deneyime sahip cerrahlar ve ekiplere sahip olmasından kaynaklıdır[22]. Böylece yüksek hastane hacmine göre, bu hastanelerin ameliyat sonrası daha iyi sonuçları yani daha kısa hastane kalış süresini yakalaması olağandır. Nefrektomi bağlamında ise hastane hacmi ile cerrahi sonuçlar arasındaki ilişki açısından değerlendirmeler büyük farklılıklar göstermektedir. Örneğin, Birkmeyer ve ark.[21] 1994 ve 1999 yılları arasında nefrektomi geçiren hastaların Medicare verilerini incelemiş ve yüksek hacimli bir hastanede tedavi edilenlerin düşük hacimli hastanelerdeki emsallerine kıyasla ameliyat sonrası ölüm olasılığının %20 daha az olduğunu bulmuşlardır. Ancak, Konety ve ark.[23] yüksek hacimli bir hastane tecrübesinin nefrektomi sonrası hastane içi ölüm oranlarının azalmasını garanti etmediğini gösterdiler. Benzer şekilde Finlayson ve ark.[24] Ülke çağında yapılan nefrektomileri baz alarak yaptıkları çalışmada (örneklem büyüklüğü 200.000), hastane hacmine göre hastane içi mortalite açısından farklılık olmadığını gösterdiler. Literatürdeki karşıt görüşler ışığında, kliniğimizde 330 laparoskopik nefrektomi vakası gerçekleştirerek yüksek hacimli hastane kategorisine girmektedir. Bu yüksek volüm ve cerrahi tecrübe sonucu olarak yatış süresi ≤4 olan hasta sayısı tüm hastaların büyük kısmını oluşturmaktadır. Dolayısıyla bizde hastane hacminin nefrektomi sonrası yatış süresini azalttığını düşünmekteyiz.

Laparoskopik nefrektomi sonrası hastanede kalış süresi literatürdeki çalışmalarda farlılık gösterse de ortalama 2-4 gündür[25,26]. Ancak Azawi ve ark.[27] Danimarka tabanlı 6790 hastayı içeren nefrektomi serilerinde yatış süresinin 9,1 güne kadar uzayabileceğini göstermişlerdir. Bizim çalışmamızda

da hastaların büyük çoğunluğunda yatış süresi 4 günün altında kalmıştır ancak 4 günün üstündeki hasta sayısı da azımsanmayacak sayıdadır.

Yukardaki bilgiler ışığında çalışmamızda belirttiğimiz gibi yatış süresini etkileyen çeşitli preoperatif, peroperatif ve postoperatif çoklu değişkenlerin olduğunu görmekteyiz. Çalışmamız sonuçlarına göre yatış süresini uzatan temel değişkenlerin başında uzamış operasyon süresi gelmektedir. Yine benzer şekilde peroperatif ve postoperatif komplikasyon varlığının yatış süresini direkt etkilediği ve komplikasyon varlığında hastaların 4 günden fazla yattığı görülmüştür. Ayrıca preoperatif değişkenler bağlamında, hastaların ileri yaşta olması, eşlik eden komorbitelerinin olması, VKİ ve preoperatif kreatinin seviyelerinin yüksek olmasının cerrahi süresini ve dolayısıyla yatış süresini artırdığı görülmüştür.

Mevcut çalışmamızın bazı kısıtlılıkları vardır. Çalışmamız retrospektif bir çalışmadır ve tek merkez sonuçlarını yansıtmaktadır. İkinci olarak, çalışmamızda böbrek tümör tipi ve özellikleri belirtilmemiştir. Ayrıca çalışmamız veri eksikliğinden dolayı patolojik bilgileri içermemektedir.

Sonuç

Bu çalışma, preoperatif yüksek VKİ'nin, yüksek serum kreatinin seviyesinin, komorbidite varlığının ve ASA skor yüksekliğinin, peroperatif operasyon süresinin uzun olmasının, ayrıca peroperatif ve postoperatif komplikasyon gelişmesinin, laparoskopik nefrektomi sonrası yatış süresinin uzamasına neden olabileceğini göstermiştir.

Yazar katkısı

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

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Kaynaklar

1. Clayman RV, Kavoussi LR, Soper NJ, et al. Laparoscopic nephrectomy: initial case report. J Urol. 1991;146:278-82. doi: 10.1016/s0022-5347(17)37770-4
2. Siqueira JR TM, Kuo RL, Gardner TA, et al. Major complications in 213 laparoscopic nephrectomy cases: the Indianapolis experience. J Urol. 2002;168:1361-5. doi: 10.1097/01.ju.0000023288.55478.42
3. Kerbl K, Clayman RV, McDougall EM, et al. Transperitoneal nephrectomy for benign disease of the kidney: a comparison of laparoscopic and open surgical techniques. Urology. 1994;43:607-13. doi: 10.1016/0090-4295(94)90171-6
4. Wilson BG, Deans GT, Kelly J, et al. Laparoscopic nephrectomy: initial experience and cost implications. Br J Urol. 1995;75:276-80. doi: 10.1111/j.1464-410x.1995.tb07337.x
5. Fornara P, Doehn C, Friedrich HJ, et al. Nonrandomized comparison of open flank versus laparoscopic nephrectomy in 249 patients with benign renal disease. Eur Urol. 2001;40:24-31. doi: 10.1159/000049745
6. Gill IS, Clayman RV, McDougall EM. Advances in urological laparoscopy. J Urol. 1995;154:1275-94.
7. Rotter T, Kinsman L, James E, et al. Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs. Cochrane Database Syst Rev. 2010;3:CD006632. doi: 10.1002/14651858.CD006632.pub2
8. Clark DE and Ryan LM. Concurrent prediction of hospital mortality and length of stay from risk factors on admission. Health Serv Res. 2002;37(3):631-45. doi: 10.1111/1475-6773.00041
9. Ingraham AM, Cohen ME, Bilimoria KY, et al. Association of surgical care improvement Pro-

ject infection-related process measure compliance with risk-adjusted outcomes: implications for quality measurement. J Am Coll Surg. 2010;211(6):705-14.
doi: 10.1016/j.jamcollsurg.2010.09.006
10. Davenport DL, Henderson WG, Khuri SF, et al. Preoperative risk factors and surgical complexity are more predictive of costs than postoperative complications: a case study using the National Surgical Quality Improvement Program (NSQIP) database. Ann Surg. 2005;242(4):463.
doi: 10.1097/01.sla.0000183348.15117.ab
11. Polverejan E, Gardiner JC, Bradley CJ, et al. Estimating mean hospital cost as a function of length of stay and patient characteristics. Health Econ. 2003;12(11):93547.
doi: 10.1002/hec.774
12. Hollenbeck BK, Miller DC, Taub D, et al. Risk factors for adverse outcomes after transurethral resection of bladder tumors. Cancer. 2006;106(7):1527-35.
doi: 10.1002/cncr.21765
13. Aronow HD, Peyser PA, Eagle KA, et al. Predictors of length of stay after coronary stenting. Am Heart J. 2001;142(5):799-5.
doi: 10.1067/mhj.2001.119371
14. Ghali WA, Hall RE, Ash AS, et al. Identifying preand postoperative predictors of cost and length of stay for coronary artery bypass surgery. Am J Med Qual. 1999;14(6):248-54.
doi: 10.1177/106286069901400604
15. Wallner LP, Dunn RL, Sarma AV, et al. Risk factors for prolonged length of stay after urologic surgery: the National Surgical Quality Improvement Program. J Am Coll Surg. 2008;207(6):904-13.
doi: 10.1016/j.jamcollsurg.2008.08.015
16. Dimick JB, Cowan JA, Colletti LM et al: Hospital teaching status and outcomes of complex surgical procedures in the United States. Arch Surg 2004; 139(2):137-41.
doi: 10.1001/archsurg.139.2.137
17. Jeldres C, Suardi N, Capitanio U, et al. High surgical volume is associated with a lower rate of secondary therapy after radical prostatectomy for localized prostate cancer. BJU Int. 2008; 102(4):463-67.
doi: 10.1111/j.1464-410X.2008.07705.x
18. Begg CB, Cramer LD, Hoskins WJ, et al. Impact of hospital volume on operative mortality for major cancer surgery. JAMA. 1998; 280(20):1747-51.
doi: 10.1001/jama.280.20.1747
19. Khuri SF and Henderson WG. The case against volume as a measure of quality of surgical care. World J Surg. 2005; 29(10):1222-29.
doi: 10.1007/s00268-005-7987-6
20. Keeler EB, Rubenstein LV, Kahn KL, et al. Hospital characteristics and quality of care. JAMA. 1992;268(13):1709-14.
doi:10.1001/jama.1992.03490130097037
21. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. N Engl J Med. 2002;346(15):1128-37.
doi: 10.1056/NEJMsa012337
22. Miller DC, Daignault S, Wolf JS Jr, et al. Hospital characteristics and use of innovative surgical therapies among patients with kidney cancer. Med Care. 2008;46:372-79.
doi: 10.1097/MLR.0b013e31816099a7
23. Konety BR, Allareddy V, Modak S, et al. Mortality after major surgery for urologic cancers in specialized urology hospitals: are they any better? J Clin Oncol. 2006;24(13):2006-12.
doi: 10.1200/JCO.2005.04.2622
24. Finlayson E, Goodney P and Birkmeyer JD. Hospital volume and operative mortality in cancer surgery: a national study. Arch Surg. 2003;138(7):721-25.
doi:10.1001/archsurg.138.7.721
25. Cheema IA, Manecksha RP, Murphy M, et al. Laparoscopic nephrectomy: initial experience with 120 cases. Ir Med J. 2010;103:49-51.
26. Dunn MD, Portis AJ, Shalhav AL, et al. Laparoscopic versus open nephrectomy: a 9-year experience. J Urol 2000;164:1153-9.
27. Azawi NH, Christensen T, Petri AL, et al. Prolonged length of hospital stay in Denmark after nephrectomy. Dan Med J. 2012;59(6):A4446.

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ERİŞKİN DÖNEMİN NADİR GÖRÜLEN BEYİN TÜMÖRÜ: MEDULLOBLASTOM TANILI 28 HASTANIN DEMOGRAFİK ÖZELLİKLERİ

RARE ADULT BRAIN TUMOR: DEMOGRAPHIC CHARACTERISTICS OF 28 PATIENTS DIAGNOSED WITH MEDULLOBLASTOM

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Abstract

Aim: Medulloblastom is one of the most common brain tumor which is seen pediatric population. It is rarely seen in adults. In the present study, we aimed share of the clinical and pathological features of patients that got diagnosed medulloblastom.

Methods: Between November 2010 and April 2020, twenty-eight patients with medulloblastom were included to this study. Age, gender, date of diagnosis, date of death, date of progression, tumor localization, tumor histopathological subtype, surgical type data were recorded from the patient files. The 5-year median survival and progression-free survival rates of the patients were calculated.

Results: Mean age of the patients was 32. 16 patients were male, and 12 patients were female. Histopathological features of the patients were classic variant in 17 patients and desmoplastic variant in 11 patients, respectively. Disease recurrence was detected in 15 patients, and recurrence was not seen in 13 patients. 16 patients died and 12 patients were alive. Five-year overall survival and progression free survival rate were 59.4 % and 42.3 %, respectively.

Conclusions: As medulloblastom was rarely seen in adults there is not enough data about this subject. Complete resection is very important in these patients population for survival.

Keywords: Medulloblastom, adult patient, overall survival

Öz

Amaç: Medulloblastom çocukluk çağında sık görülen beyin tümörlerinden biridir. Erişkin yaşta ise çok nadir olarak görülmektedir. Bu çalışmamızda medulloblastom tanılı hastalarımızın klinik ve patolojik özelliklerini paylaşmayı amaçladık

Yöntemler: 2010 Kasım ile 2020 Nisan ayı arasında medulloblastom tanısı alan 28 hasta çalışmaya dahil edilmiştir. Hasta dosya sisteminden yaş, cinsiyet, tanı tarihi, ex tarihi, progresyon tarihi, tümör lokalizasyonu, tümör histopatolojik alt tipi, cerrahi şekli verileri kaydedildi. Hastaların 5 yıllık ortalama sağkalım ve progresyonsuz sağkalım oranları hesaplandı.

Bulgular: Hastaların ortalama yaşı 32 idi. 16 hasta erkek 12 si ise kadındı. Histopatolojik özelliklerine bakıldığında 17 hasta klasik varyant, 11 hasta ise desmoplastik histopatolojiye sahipti. 15 hastada nüks saptanırken 13 hasta nüks bulgusuna rastlanılmadı. 28 hastanın 16'sı yaşıyor 12 hasta ise ex olmuştu. Hastaların 5 yıllık OS %59,4, 5 yıllık PFS ise %42,3 idi

Sonuç: Medulloblastom erişkin dönemde çok nadir olarak görüldüğü için bu hastalık ile ilgili yeterli veri bulunmamaktadır. Komplet rezeksiyon bu hastalarda sağkalım açısından büyük önem içermektedir.

Anahtar Kelimeler: Medulloblastom, erişkin hasta, ortalama sağkalım

Giriş

Medulloblastom çocukluk çağında en sık olarak görülen beyin tümörüdür. Oldukça agresif bir tümör olup tanı anında metastaz yapma eğilimindedir. Ortalama tanı yaşı 5'tir. Erişkin çağda görülen tümörlerin ise yaklaşık olarak %1 ini oluşturmaktadır[1,2]. Erişkin medulloblastom tanı yaşı ortalama 30 olup 40 yaş üzerinde çok daha nadir olarak görülmektedir. Cinsiyete göre dağılımına bakıldığında erkeklerde daha sık olarak görülmekte olup erkek kadın oranı 1,5'tur[3]. 5 yıllık sağkalım oranları %40-90 arasında değişkenlik gösterebilmektedir[4].
Erişkin çağı medulloblastom vakaları çoğunlukla lateral lokalizasyonda yerleşim gösterme eğiliminde iken bu oran çocukluk çağında ise %10 civarındadır[5-7]. Bundan dolayıda erişkin çağı medulloblastom vakaları çoğunlukla rezektabledır. Histopatolojik varyantlarda da erişkin ve çocukluk çağı vakalarında farklılıklar görülebilmektedir. Desmoplastik variant çocukluk çağında %15 oranında görülürken, erişkin çağda yaklaşık %50 ye varan oranlarda görülmektedir[8,9]. Erişkin çağının medulloblastom vakaları sıklıkla pediatrik dönemdeki uygulanan tedavi protokolleri ile tedavi edilmektedirler. Çocukluk çağı ve erişkin dönemde görülen medulloblastom vakalarının survival sonuçları birbirine benzerlik göstermekle birlikte aralarında farklılıklar bulunabilmektedir[10].
Erişkin çağı medulloblastom vakaları ile sınırlı düzeyde veri bulunmakta olup bizde medulloblastom nedeniyle takip ettiğimiz hastaların özelliklerini literatürle paylaşmayı amaçladık.

Materyal ve Metot

2010 Kasım ile 2020 Nisan ayı arasında medulloblastom tanısı alan 28 hasta çalışmaya dahil edilmiştir. ≥ 18 yaş üzeri hastalar çalışmaya dahil edildi. Hasta dosya sisteminden yaş, cinsiyet, tanı tarihi, ex tarihi, progresyon tarihi, tümör lokalizasyonu, tümör histopatolojik alt tipi, cerrahi şekli verileri kaydedildi. Hastaların 5 yıllık ortalama sağkalım ve progresyonsuz sağkalım oranları hesaplandı.
İstatiksel analizde; hasta özellikleri için tanımlayıcı istatistiksel yöntem uygulandı. Kategorik değişkenlerin karşılaştırılması için Pearson-ki kare testi yapıldı. Numerik değişkenlerin normal dağılıp dağılmadığını değerlendirmek için Shapiro Wilk testi kullanıldı. Normal dağılım gösteren değerler için Independent sample t testi uygulandı. Ortalama sağkalım tanı anından ölüme kadar geçen süre olarak, progresyonsuz sağkalım ise tanı anından progresyon ya da ölüme kadar geçen süre olarak hesaplandı. Sağkalım analizi için Kaplan Meier analizi ve log rank yöntemi kullanıldı. $p < 0,05$ istatiksel anlamlılık için cut-off olarak kabul edildi.
Çalışma için Adana Şehir Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan onam alınmıştır (Karar no: 1777, Tarih:10.02.2022)

Bulgular

Hastaların ortalama yaşı 32 idi (18-66). 16 hasta (%57,2) erkek, 12'si ise (%42,8) kadın idi. Hastalardan 11 (%39,2) inin histopatolojik özelliği desmoplastik iken 17 hasta (%60,8) ise klasik varyant idi. 15 hastada (%53,5) tümör sağ hemisferde yerleşim gösterirken, 8 hastada (%28,5) ise sol hemisferde lokalizasyon göstermekte idi. 21 (%75,0) hastaya total rezeksiyon yapılırken ,7 (%25,0) hastada ise subtotal rezeksiyon yapılabildi. Cerrahi sonrası tüm hastalara radyoterapi tedavisi uygulandı. Hastaların takibinde 12 hasta ex olurken, 15 hastada progresyon gözlendi. Tablo 1'de hasta demografik özellikleri özetlenmiştir.
Hastaların ex durumuna göre cinsiyet, yaş, tümör lokalizasyonu, tümör histopatolojisi ve cerrahi durumuna göre karşılaştırması yapıldı. Exitus olan hastaların yaş ortalaması 37,2 saptanırken, yaşayan hastaların yaş ortalaması 28,1 saptandı ve aradaki fark istatiksel olarak anlamlıydı (p=0,05). 12 hastada ex görülürken 16 hastada ise görülmedi.

Tablo 1. Hastaların demografik özellikleri

	n=28
Yaş(ort)	32,0
Cinsiyet (n, %)	
• Erkek	16 (57,2)
• Kadın	12 (42,8)
Tümör histolojisi	
• Desmoplastik	11 (39,2)
• Klasik	17 (60,8)
Tümör lokalizasyonu (n, %)	
• Sağ hemisfer	15 (53,5)
• Sol hemisfer	8 (28,5)
• Diğer	5 (18,0)
Cerrahi tipi (n, %)	
• Total	21 (75,0)
• Subtotal	7 (25,0)
Sağkalım (n, %)	
• Yaşıyor	16 (57,2)
• Ex	12 (42,8)
Progresyon durumu (n, %)	
• Var	15 (53,6)
• Yok	13 (46,4)
5 yıllık OS (%)	59,4
5 yıllık PFS (%)	42,3

OS: Ortalama sağkalım, PFS: Progresyonsuz sağkalım

Yaşayan hastaların 9'unda tümör sağ hemisferde 4'ünde ise sol hemisferde yerleşim gösterirken, 3 hastada diğer bölgelerde yerleşim göstermekte idi.

Exitus olan hastalarda ise 6 hastada sağ hemisferde 4 hastada sol hemisferde ve 2 hastada ise diğer bölgelerde yerleşim göstermekte idi iki grup arasındaki fark anlamlı değildi (p=0,88). Yaşayan hastaların tümör histopatolojisinde 7 hastada desmoplastik, 9 hastada ise klasik varyant tespit edildi. Exitus olan hastalarda ise 8 hastada klasik, 4 hastada desmoplastik varyant tespit edilmişti (p=0,70). Yaşayan hastaların 14'inde total rezeksiyon 2'sinde subtotal rezeksiyon yapılırken, exitus olan hastalarda ise 7 hastada total 5 hastada ise subtotal rezeksiyon yapılmıştı (p=0,37). Hastaların sağkalım durumuna göre yapılan iki grup karşılaştırması özellikleri tablo 2 de özetlenmiştir.

Hastaların sağkalım özelliklerine bakıldığında, 12 hasta ex olurken 16 hasta yaşamaktaydı. Hastaların 5 yıllık ortalama sağkalım oranları %59,0, progresyonsuz sağkalım oranları ise %42,3 idi.

Tablo 2. Hastaların sağkalım durumuna göre özelliklerinin karşılaştırılması

	Sağkalım		
	Sağ n:16 (%)	Ex n:12 (%)	p
Yaş	28,1±11.,3	37,2±11,9	0,05
Tümör lokalizasyonu			
• Sağ hemisfer	9(56,2)	6 (50,0)	
• Sol hemisfer	4(25,0	4 (33.3)	0,88
• Diğer	3(18,8)	2(16,7)	
Tümör histopatolojisi			
• Desmoplastik	7 (43,8)	4 (25,0)	0,70
• Klasik	9(56,2)	8(75,0)	
Cerrahi			
• Total	14(87,5)	7(58,3)	0,10
• Subtotal	2(12,5)	5(41,7)	
Cinsiyet			
• Erkek	8(50,0)	8(75,0)	0,37
• Kadın	8(50,0)	4(25,0)	

Histopatolojik özelliklerine göre karşılaştırıldığında ise desmoplastik hasta grubunda 5 yıllık ortalama sağkalım oranı %62,3, klasik tipte ise %57,4 idi (p=0,70). 5 yıllık progresyonsuz sağkalım oranları ise desmoplastik grupta %50, klasik grupta ise %36 idi (p=0,58). Cinsiyete göre 5 yıllık sağkalım oranlarına bakıldığında erkeklerde 5 yıllık ortalama ve progresyonsuz sağkalım oranları sırasıyla %52,5 ve %20,0 idi Kadınlarda ise 5 yıllık ortalama ve progresyonsuz sağkalım oranları her ikisi içinde %66,7 olarak saptandı.

Tartışma

Medulloblastom serebellumdan köken alan nadir görülen bir tümördür. Adolesan ve erişkin dönemde nadir olarak karşımıza çıkmaktadır. Sıklıkla serebellar vermisten köken almaktadır. Erişkin çağı beyin tümörlerinin %1 ini oluşturmaktadır[11,12]. Menon ve arkadaşlarının yaptığı çalışmada hastaların yaş ortalaması 31,5 iken bizim çalışmamızda ise hastaların yaş ortalaması 32,0 olarak saptandı[13].

Tablo 3. Hastaların 5 yıllık sağkalım oranlarının karşılaştırılması

	n (%)	5 yıllık OS (%)	p	5 yıllık PFS (%)	p
Tümör histolojisi					
• Desmoplastik	11 (39,2)	62,3	0,70	50,0	0,58
• Klasik	17 (60,8)	57,4		36,0	
Cinsiyet					
• Erkek	16 (57,2)	52,5	0,38	20,0	0,67
• Kadın	12 (42,8)	66,7		66,7	

OS: Ortalama sağkalım, PFS: Progresyonsuz sağkalım

Medulloblastom erkeklerde daha fazla görülmekle birlikte, moleküler alt gruplarına göre görülme sıklığı değişkenlik gösterebilmektedir[14]. Bizim çalışmamızda da hastaların büyük çoğunluğu erkekti.

Medulloblastom genetik özellikleri ve histopatolojik özelliklerine göre sınıflandırması yapılmıştır. Genetik sınıflamasına göre 4 gruba ayrılmaktadır. Bunlar sırası ile WNT sinyal yolağı aktive, SHH aktive- p53 wild tip, SHH aktive-p53 mutant ve WNT ve SHH olmayan olmak üzere 4 gruba ayrılmaktadır[15,16]. Erişkinde en sık olarak görülen SHH aktive-p53 wild tiptir. Vakaların yaklaşık olarak %50 sini oluşturmaktadır. P53 mutasyon varlığının olması ise kötü prognoza işarettir. Ayrıca erişkinde en iyi prognoza sahip olan alt tipte SHH aktive alt tiptir[17]. Erişkin WNT aktive medulloblastom vakaların yaklaşık olarak %15 ini oluştururken, non WNT/non SHH ise yaklaşık olarak %25 ini oluştumaktadır[10,18]. Medulloblastomun birkaç histopatolojik alt tipi bulunmaktadır. Bunlar arasında klasik tip, desmoplastik/nodular, ekstantif nodülaritenin eşlik ettiği medulloblastom ve large cell/anaplastik medulloblastom yer almaktadır. Bunlar içerisinde en agresif seyir gösteren large cell/anaplastik medulloblastomdur[19]. Histopatolojik alt tipler baktığımızda vakaların yaklaşık olarak %40-45 klasik formda, %30-35'i desmoplastik, %10 ekstantif nodülaritenin eşlik ettiği medulloblastom, %15-20 ise anaplastik/large cell histolojide yer almaktadır[20]. Yapılan farklı çalışmalarda da klasik varyant alt tipi daha sık olarak görülmüştür[21]. Bizim çalışmamızda da vakaların büyük çoğunluğu klasik varyantta yer almaktaydı. Ayrıca yapılan çalışmalarda desmoplastik medulloblastomlu hastalarda hastalıksız sağkalım ve ortalama sağkalım sürelerinin klasik form medulloblastomlu hastalara göre daha iyi olduğu gösterilmiştir[22]. Bizim çalışmamızda ise hastaların histopatolojisine göre bakıldığında 5 yıllık sağkalım oranları desmoplastik grupta klasik gruba göre oran daha fazla idi ancak aradaki fark istatiksel olarak anlamlı değildi.

Medulloblastom biyolojisi farklı yaş gruplarında farklılıklar gösterebilmektedir. Erişkin medulloblastom hastalarının yönetimi daha çok çocukluk çağında uygulanan tedavi yöntemlerine istinaden şekillenmektedir. Hastalığın standart tedavisinde primer kitlenin total eksizyon yer almaktadır. Çünkü subtotal rezeksiyon yapılan hastalarda sağkalımın daha kötü olduğu gösterilmiştir[23,24]. Bizim çalışmamızda hastaların çoğuna total rezeksiyon yapılmıştı ve bu hastalarda ki 5 yıllık sağkalım oranları subtotal rezeksiyon yapılanlara göre daha iyiydi. Cerrahi sonrasında hastalara radyoterapi tedavisi uygulanmaktadır. Radyoterapi ile kemoterapi tedavisinde sıklıkla sisplatin, karboplatin, vinkristin, siklofosfamid ve lomustin gibi ajanlar kullanılmaktadır. Radyoterapi ile kemoterapi uygulaması çocuk hastalarda daha sık uygulanırken erişkin hastalarda bununla ilgili veriler hala tam olarak net değildir[23,25].

Sonuç

Sonuç olarak; medulloblastom erişkinlerde nadir olarak görülen primer beyin tümörüdür. Çalışmamızdaki hastaların büyük çoğunluğu klasik varyant histolojiye sahipti ve çoğunluğu erkekti. Farklı çalışmalarda sağkalım oranları ile değişik oranlar belirtilmiş olmakla beraber bizim çalışmamızdaki sağkalım oranları bu çalışmalara benzerlik göstermekte idi. Daha fazla hasta sayısı, birden fazla merkez katılımı ile gerçekleştirilecek çalışmalara ihtiyaç bulunmaktadır.

Yazar katkısı

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

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Kaynaklar

1. Herrlinger U, Steinbrecher A, Rieger J. Adult medulloblastoma. Prognostic factors and response to therapy at diagnosis and at relapse. J Neurol 2005;252:291–9. doi: 10.1007/s00415-005-0560-2
2. Tabori U, Sung L, Hukin J, et al. Distinctive clinical course and pattern of relapse in adolescents with medulloblastoma. Int J Radiat Oncol Biol Phys. 2005;64:402–7. doi: 10.1016/j.ijrobp.2005.07.962
3. Kann BH, Lester-Coll NH, Park HS, et al. Adjuvant chemotherapy and overall survival in adult medulloblastoma. Neuro-Oncology. 2017;19:259–69. doi: 10.1093/neuonc/now150
4. Lai R. Survival of patients with adult medulloblastoma: a population-based study. Cancer. 2008;112(7):1568–74. doi: 10.1002/cncr.23329
5. Haie C, Schlienger M, Constans JP, et al. Results of radiation treatment of medulloblastoma in adults. Int J Radiat Oncol Biol Phys. 1985; 11:2051–56. doi: 10.1016/0360-3016(85)90083-5
6. Park TS, Hoffman HJ, Hendrick EB, et al. Medulloblastoma: Clinical presentation and management—Experience at the Hospital for Sick Children, J Neurosurg. 1983; 58:543–52. doi: 10.3171/jns.1983.58.4.0543
7. Prados MD, Warnick RE, Wara WM, et al. Medulloblastoma in adults Int J Radiat Oncol Biol Phys. 1995; 32:1145–52. doi : 10.1016/0360-3016(94)00476-2
8. Chatty EM, Earle KM: Medulloblastoma: A report of 201 cases with emphasis on the relationship of histologic variants to survival Cancer. 1971; 28:977–83. doi: 10.1002/1097-0142(1971)28:4<977::aid-cncr2820280422>3.0.co;2-7
9. Kretschmar CS, Tarbell NJ, Kupsky W et al. Preirradiation chemotherapy for infants and children with medulloblastoma: A preliminary report. J Neurosurg 1989; 71:820–25. doi: 10.3171/jns.1989.71.6.0820
10. Remke M, al Hielscher T, Northcott PA et. Adult medulloblastoma comprises three major molecular variants. J Clin Oncol 2011;29 (19):2717–23. doi: 10.1200/JCO.2011.34.9373
11. Smoll NR, Drummond KJ. The incidence of medulloblastomas and primitive neurectodermal tumours in adults and children. J Clin Neurosci. 2012; 19:1541–44. doi: 10.1016/j.jocn.2012.04.009
12. Franceschi E, Hofer S, Brandes AA, et al. EANO-EURACAN clinical practice guideline for diagnosis, treatment, and follow-up of postpubertal and adult patients with medulloblastoma. Lancet Oncol 2019; 20:e715–28. doi: 10.1016/S1470-2045(19)30669-2
13. Girish Menon, K. Krishnakumar, S. Nair Adult medulloblastoma: Clinical profile and treatment results of 18 patients. Journal of Clinical Neuroscience. 2008; 122–26. doi: 10.1016/j.jocn.2007.06.007
14. Giordana MT, Schiffer P, Lanotte M, et al. Epidemiology of adult medulloblastoma. Int. J. Cancer 1999; 80:689–92. doi: 10.1002/(sici)1097-0215(19990301)80:5<689::aid-ijc10>3.0.co;2-g
15. Kool M, Korshunov A, Remke M, et al. Molecular subgroups of medulloblastoma: an international meta-analysis of transcriptome, genetic aberrations, and clinical data of WNT, SHH, Group 3, and Group 4 medulloblastomas. Acta Neuropathol. 2012;123(4): 473–84. doi: 10.1007/s00401-012-0958-8
16. Northcott PA, Korshunov A, Witt H, et al. Medulloblastoma comprises four distinct molecular

variants. J Clin Oncol. 2011; 29(11):1408–14. doi: 10.1200/JCO.2009.27.4324
17. Zhukova N, Ramaswamy V, Remke M, et al. Subgroup-specific prognostic implications of TP53 mutation in medulloblastoma. J Clin Oncol. 2013; 31:2927–35. doi: 10.1200/JCO.2012.48.5052
18. Remke M, Hielscher T, Northcott PA, Witt H, Ryzhova M, Wittmann A. Adult medulloblastoma comprises three major molecular variants. J Clin Oncol. (2011) 29:2717–23.
19. Leonard JR, Cai DX, Rivet DJ, et al. Large cell/anaplastic medulloblastomas and medullomyoblastomas: clinicopathological and genetic features. J Neurosurg. 2001;95(1):82. doi: 10.3171/jns.2001.95.1.0082
20. Rausch T, David TW , Marc Z, et al. Genome sequencing of pediatric medulloblastoma links catastrophic DNA rearrangements with TP53 mutations. Cell. 2012; 148: 59–71. doi: 10.1016/j.cell.2011.12.013
21. Annie W. Chan, M.D., Nancy J. et al : Prognostic Factors and Patterns of Relapse Neurosurgery 2000;47(3):623-31. doi: 10.1097/00006123-200009000-00018
22. Rutkowski S, von Hoff K, Emser A et al. Survival and prognostic factors of early childhood medulloblastoma: an international meta-analysis J Clin Oncol. 2010;28(33):4961-68. doi: 10.1200/JCO.2010.30.2299
23. Albright AL, Wisoff JH, Zeltzer PM, et al. Effects of medulloblastoma resections on outcome in children: a report from the Children's Cancer Group. Neurosurgery 1996; 38:265–71. doi: 10.1097/00006123-199602000-00007
24. Thompson EM, Hielscher T, Bouffet E . Prognostic value of medulloblastoma extent of resection after accounting for molecular subgroup: a retrospective integrated clinical and molecular analysis. Lancet Oncol. 2016; 17: 484–95. doi: 10.1016/S1470-2045(15)00581-1
25. Gajjar A, Chintagumpala M, Ashley D, et al. Risk-adapted craniospinal radiotherapy followed by high-dose chemotherapy and stem-cell rescue in children with newly diagnosed medulloblastoma (St Jude Medulloblastoma-96): long-term results from a prospective, multicentre trial. Lancet Oncol. 2006;7(10):813–20. doi: 10.1016/S1470-2045(06)70867-1

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VERTEBRAL KOMPRESYON KIRIKLARININ PERKÜTAN KİFOPLASTİ İLE TEDAVİSİNDE ANESTEZİ YÖNTEMLERİNİN ETKİNLİĞİNİN KARŞILAŞTIRILMASI

COMPARISON OF THE EFFICIENCY OF ANESTHESIA METHODS IN THE TREATMENT OF VERTEBRAL COMPRESSION FRACTURES WITH PERCUTANEOUS KYPHOPLASTY

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Abstract

Aim: Kyphoplasty is a percutaneous interventional procedure that can help strengthen structural integrity and reduce pain in vertebral compression fractures. This study aimed to investigate the ideal anesthesia technique for percutaneous kyphoplasty.

Methods: This prospective and nonrandomized controlled study was conducted between January 2022 to June 2022. The patients were divided into three groups as general anesthesia, local anesthesia, and epidural anesthesia. Perioperative pain and occurred complications were evaluated.

Results: Forty patients who underwent percutaneous kyphoplasty due to vertebral compression fracture in our center were included in the study. Since the number of patients who underwent surgery under general anesthesia was very small, the relevant patient group was only shown in descriptive statistics and not evaluated in comparative statistics. While bearable pain was experienced at all timing points in the local anesthesia group, 25% experienced serious complications. 4 patients needed intensive care follow-up after surgery. While the pain was experienced during trocar insertion in the epidural anesthesia group, no pain was experienced at other times. The complication rate was lower than the local anesthesia group and there was no need for intensive care follow-up.

Conclusions: Epidural anesthesia is a safe anesthetic technique for percutaneous kyphoplasty. Postoperative analgesia is advantageous over local anesthesia in terms of low complication rate and the need for a postoperative intensive care unit. However, epidural anesthesia is disadvantageous in terms of application time and cost.

Keywords: Vertebral compression fracture, percutaneous kyphoplasty, epidural anesthesia, local anesthesia

Öz

Amaç: Kifoplasti vertebral kompresyon kırıklarında ağrıyı hafifletmeye ve vertebranın yapısal bütünlüğünü korumaya yardımcı olan, perkütan minimal invazif bir prosedürdür. Bu işlem için farklı anestezi teknikleri kullanılmaktadır. Bu çalışmada; perkütan kifoplasti için ideal anestezi tekniğinin araştırılması amaçlanmıştır.

Yöntemler: Prospektif, randomize olmayan çalışmamız Ocak 2022-Haziran 2022 arasında gerçekleştirildi. Hastalar üç gruba ayrıldı: Genel anestezi, lokal anestezi, epidural anestezi grubu. Perioperatif ağrı ve komplikasyonlar değerlendirildi.

Bulgular: Vertebral kompresyon kırığı nedeniyle kliniğimizde perkütan kifoplasti uygulanan 40 hasta çalışmaya alındı. Genel anestezi altında operasyon geçiren hasta sayısı çok az olduğu için, bu grup sadece tanımlayıcı istatistiklerde gösterilip, karşılaştırma istatistiklerinde değerlendirmeye alınmadı. Lokal anestezi grubunda; tüm zamanlama noktalarında katlanılabilir ağrı yaşanırken, %25 oranında ciddi komplikasyon yaşandı ve 4 hastanın ameliyat sonrası yoğun bakım takibi ihtiyacı oldu. Epidural anestezi grubunda; trokar girişi sırasında ağrı yaşanırken, diğer zamanlamalarda ağrı yaşanmadı. Komplikasyon oranı ise lokal anestezi grubundan düşüktü, yoğun bakım takip ihtiyacı yoktu.

Sonuç: Epidural anestezi, perkütan kifoplasti için güvenli bir anestezi tekniğidir. Postoperatif analjezi, düşük komplikasyon oranı ve ameliyat sonrası yoğun bakım ünitesi ihtiyacı ile ilgili olarak lokal anesteziden avantajlıdır. Fakat epidural anestezi uygulama süresi ve maliyet açısından dezavantajlıdır.

Anahtar Kelimeler: Vertebral kompresyon kırığı, perkütan kifoplasti, epidural anestezi, lokal anestezi

Giriş

Omurga kırıkları, fiziksel işlevde psikososyal performansta bozulmaya neden olan şiddetli ağrıya neden olur[1]. Ağrı ve deformitenin, yaşam kalitesi üzerine olumsuz etkileri vardır[2]. Perkütan kifoplasti (PKP); vertebral kompresyon kırıkları (VKK)[3] ve travmatik burst kırıkları[4] için güvenli ve etkili, minimal invaziv cerrahi bir tedavidir. Perkütan kifoplasti, hasta yaşam beklentisini önemli ölçüde artırır. Vertebral kompresyon kırıklarında konservatif tedavinin neden olduğu komplikasyonları büyük ölçüde azaltır. Perkütan kifoplasti, spinal dizinin rekonstrüksiyonunu kolaylaştırır ve omurgayı yeniden dikleştirir[5,6].
Bu prosedürlerin uygulandığı hastalarda genellikle önemli yandaş hastalıklar vardır. Bu nedenle intraoperatif anestezi yöntemini belirlemek zor olabilir[7]. Lokal anestezi[8], epidural anestezi[9], subaraknoid anestezi[10,11], erektör spina plan bloğu[12] ve genel anestezi[13] bu prosedür için uygulanabilen anestezi seçenekleridir. Perkütan kifoplasti için hangi anestezi yönteminin ideal olduğu hala belirsizliğini korumaktadır.
Bu çalışmada, vertebral kompresyon kırığı olan ve perkütan kifoplasti uygulanan hastalarda genel, lokal ve epidural anestezinin etkinliklerinin değerlendirilmesi amaçlanmıştır.

Materyal ve Metot

1 Ocak 2022- 15 Haziran 2022 tarihleri arasında prospektif, randomize olmayan kontrollü çalışma olarak planlanmıştır. Çalışmaya Sağlık Bilimleri Üniversitesi Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu tarafından onay alındıktan sonra başlanmıştır (2011-KAEK-25-2021/12-09). Çalışma, Helsinki Deklarasyonu'na uygun olarak yürütülmüştür. Tüm hastalardan yazılı bilgilendirilmiş onam alındıktan sonra anestezi yöntemleri anlatılarak anestezi yöntemi seçimi hastalara bırakılmıştır. Hastanın seçtiği yöntem için kontrendikasyon yoksa, anestezi yönetimine seçilen yöntem ile devam edilmiştir. 18 yaş üstü, elektif koşullarda, manyetik rezonans görüntüleme ile tek seviyeli VKK teşhisi konulmuş, operasyon öncesi analjezik ilaca yanıt vermeyen sırt ağrısı ve vertebrada ≥ %15 yükseklik kaybı olan, ASA I-III grubu, bilinç açık, kooperasyon kurulabilen hastalar çalışmaya dahil edilmiştir.
Semptomatik nörolojik hasarı olan, kooperasyon kurulamayan, metastatik kanser veya osteomiyelit nedeniyle patolojik vertebra kırığı olan, ASA IV-V grubu hastalar ile koagülasyon bozukluğu olan ya da antikoagülan kullanan, ameliyat bölgesinde lokalize enfeksiyonu olan hastalar çalışmaya dahil edilmemiştir.
Hastalar lokal anestezi (LA), genel anestezi (GA) ve epidural anestezi (EA) grubu olarak üçe ayrılmıştır.

I. Lokal Anestezi (LA) grubu

Trokar giriş bölgesindeki deri ve deri altı dokuya 10 mL %0.25 bupivakain uygulandı. Midazolam, propofol ve fentanil kombinasyonları ile sedasyon sağlandı.

II. Epidural Anestezi (EA) grubu

Hasta oturur pozisyondayken, cilt dezenfeksiyonu yapılıp 2 mL %2 lidokain ile lokal anestezi uygulandı. Kırık seviyesinin bir üst intervertebral aralığından 18 G Tuohy iğnesiyle epidural aralığa girilerek kateter yerleştirildi. Negatif aspirasyon sonrası kateterden 3 mL izobarik lidokain (%2) ve epinefrin (1:200.000) içeren test dozu uygulandı. Beş dakika sonra hasta sorgulandı. Bacakta uyuşma, karıncalanma, uyuşukluk gibi belirtiler veya intravasküler enjeksiyon bulguları yoksa, 10 mL %0.25' lik izobarik bupivakain epidural aralığa verildi.

III. Genel Anestezi (GA) grubu

2 µg/kg intravenöz fentanil, 2 mg/kg intravenöz propofol ve 0,6-1 mg/kg intravenöz rokuronyum ile indüksiyon yapıldı, ardından minimal alveolar konsantrasyon 1 ola-

cak şekilde sevofluran inhalasyonu ile anesteziye devam edildi.
Hastaların yaş, cinsiyet, yandaş hastalıkları, kırık seviyeleri, yaralanma mekanizmaları, operasyon ve anestezi süreleri, komplikasyon varlığı, ameliyat sonrası çıkış yeri (anestezi sonrası yoğun bakım-PABU, servis), hastanede kalış süreleri kayıt altına alındı. Komplikasyonlar; kusma, motor blok, hipotansiyon (OAB <60mmHg), hipertansiyon (sistolik arter basıncında %25 artış), bradikardi (kalp atım hızı <60/dk), hipoksemi (periferik oksijen saturasyonu %90'ın altında) olarak tanımlandı.
LA ve EA grubunda VAS (visüel analog skoru), beş farklı zaman noktasında değerlendirildi[8].

T1. Hasta operasyon odasına alındığında (Zaman noktası 1)
T2. Vertebra gövdesine trokar uygulandığında (Zaman noktası 2)
T3. Omur gövdesine kemik çimentosu enjeksiyonu sırasında (Zaman noktası 3)
T4. Ayılma odası (Zaman noktası 4)
T5. Ameliyattan 24 saat sonra (Zaman noktası 5)

Genel anestezi grubunda ise VAS T1, T4, T5 zaman noktalarında üç kez değerlendirildi. Bütün hastaların ameliyat sonrası ilk ağrı şikayetleri olduğu zamanlar kaydedildi. LA ve EA grubuna geleneksel maske ile 3 L/dk oksijen verildi ve elektrokardiyografi, periferik oksijen satürasyonu, solunum hızı, kalp atım hızı ve noninvaziv arteriyel kan basıncı izlendi.

- *Cerrahi prosedür*

Floroskopi görüntüleme ile tek taraflı transpediküler (lomber vertebra) veya ekstrapediküler (torasik vertebra) ponksiyon yapıldı. Omur gövdesinin arka kenarına ulaştıktan sonra, kemik iğnesi çalışan bir kanül ile değiştirildi. Yeterli yükseklik restorasyonu ve kifoz düzeltmesi sağlanana kadar hasarlı vertebra gövdesini eski haline getirmek için kırık vertebra gövdesinin üzerine radyoopak bir ortam içeren bir balon yerleştirildi. Balon daha sonra söndürüldü ve geri çekildi ve elde edilen intravertebral boşluk polimetil metakrilat çimento ile dolduruldu[14].
LA ve EA grubunda hasta ile kooperasyon kurularak sinir hasarı varlığı sorgulandı, genel anestezi grubunda intraoperatif sinir hasarı değerlendirilemedi.

- *İstatistiksel Yöntem*

Power analizi PASS (NCSS Corp. Released 2011. Power Analyzes Sample Size for Windows, Version 11.0. Utah, USA) paket programı ile yapıldı. Çalışma sonucunda gruplarındaki skorlar 3,7 ve 0 olarak bulunmuştur. Lokal anestezi grubuna 20 ve epidural anestezi grubuna 15 hasta ile alfa anlamlılık düzeyi %5 alındığında çalışmadaki testin gücü %100 olarak bulunmuştur.
Çalışma kapsamında toplanan hasta verileri IBM Statistical Package for the Social Sciences (SPSS) for Windows 23.0 (IBM Corp., Armonk, NY) paket programı ile analiz edildi. Kategorik veriler için sıklık ve yüzde, sürekli veriler için medyan, minimum ve maksimum tanımlayıcı değer olarak verildi. Gruplar arası karşılaştırmalarda "Mann Whitney U Testi", kategorik değişkenlerin karşılaştırılmasında "Ki-kare veya Fisher'sExact Testi" kullanıldı. Sonuçlar, p değerinin 0,05'ten küçük olduğu durumlarda istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışma tarihleri arasında PKP yapılan, dahil edilme kriterlerine uyan 40 hasta değerlendirilmeye alındı. 5 hastaya genel anestezi (GA), 20 hastaya lokal anestezi (LA), 15 hastaya epidural anestezi (EA) uygulandı.

Tablo 1. Hastaların Demografik ve Klinik Özelliklerinin Dağılımı

Karakteristikler	Toplam (n=40)	LA (n=20)	EA (n=15)	GA (n=5)
	n (%) veya Medyan (Min-Maks)			
Yaş, yıl	69 (46-87)	69 (58-86)	67 (46-87)	76 (54-83)
Cinsiyet				
• Erkek	11 (27,5)	5 (25)	4 (26,7)	2 (40)
• Kadın	29 (72,5)	15 (75)	11 (73,3)	3 (60)
ASA				
• I	5	2	2	0
• II	30	16	10	4
• III	6	2	3	1
Komorbidite	32 (80)	16 (80)	11 (73,3)	5 (100)
Hipertansiyon	26 (65)	12 (60)	11 (73,3)	3 (60)
Koroner arter hastalığı	16 (40)	9 (45)	5 (33,3)	2 (40)
Diabetes Mellitus	9 (22,5)	5 (25)	2 (13,3)	2 (40)
Kronik akciğer hastalığı	1 (2,5)	1 (5)	0 (0)	0 (0)
Diğer	4 (10)	3 (15)	0 (0)	1 (20)
Kırık seviyesi, vertebra				
• Lomber1	9 (22,5)	3 (15)	4 (26,7)	2 (40)
• Lomber2	5 (12,5)	0 (0)	4 (26,7)	1 (20)
• Lomber3	5 (12,5)	4 (20)	1 (6,7)	0 (0)
• Lomber5	3 (7,5)	2 (10)	0 (0)	1 (20)
• Torakal1	1 (2,5)	1 (5)	0 (0)	0 (0)
• Torakal10	1 (2,5)	1 (5)	0 (0)	0 (0)
• Torakal11	2 (5)	2 (10)	0 (0)	0 (0)
• Torakal12	14 (35)	7 (35)	6 (40)	1 (20)
Yaralanma Mekanizması				
• Düşme	37 (92,5)	18 (90)	14 (93,3)	5 (100)
• Osteoporoz	2 (5)	2 (10)	0 (0)	0 (0)
• Kaza	1 (2,5)	0 (0)	1 (6,7)	0 (0)
T1 VAS	6 (1-8)	6 (4-7)	5 (1-8)	6 (5-7)
T 2 VAS	2 (0-4)	2 (1-3)	2 (0-4)	
T 3 VAS	3 (0-5)	3 (2-5)	0 (0-3)	
T4 VAS	2 (0-4)	2 (1-4)	0 (0-0)	3 (2-4)
T 5 VAS	1 (0-4)	2 (1-4)	0 (0-0)	3 (2-3)
Operasyon süresi (dk)	40 (20-120)	42,5 (20-120)	35 (25-75)	50 (30-120)
Anestezi süresi (dk)	60 (40-180)	60 (40-180)	60 (45-90)	60 (45-140)
Peroperatif Komplikasyon varlığı	11 (27,5)	5 (25)	3 (20)	3 (60)
Hipertansiyon	2 (5)	1 (5)	0 (0)	1 (20)
Hipotansiyon	4 (10)	1 (5)	3 (20)	0 (0)
Solunum sıkıntısı	3 (7,5)	2 (10)	0 (0)	1 (20)
Psikoz	2 (5)	2 (10)	0 (0)	0 (0)
Bulantı/Kusma	3 (7,5)	1 (5)	1 (6,7)	1 (20)
Ameliyat sonrası ilk ağrı zamanı, saat	1 (1-12)	1 (1-1)	6 (2-12)	1 (1-1)
Taburculuk zamanı, gün	1 (1-5)	1 (1-2)	1 (1-1)	2 (1-5)
Ameliyat sonrası takip yeri				
• PABU	5 (12,5)	4 (20)	0 (0)	1 (20)
• Servis	35 (87,5)	16 (80)	15 (100)	4 (80)

PABU: anestezi sonrası bakım ünitesi; T1: Hasta operasyon odasına alındığındaki zaman noktası T2: Vertebra gövdesine trokar uygulandığındaki zaman noktası T3: Omur gövdesine kemik çimentosu enjeksiyonu sırasındaki zaman noktası T4: Ayılma odasındaki zaman noktası T5. Ameliyattan 24 saat sonra; VAS: Visüel analog skala

Tablo 2. Lokal Anestezi ve Epidural Anestezi gruplarının Demografik ve Klinik Özelliklerinin Dağılımı

Karakteristikler	Toplam (n=35)	LA (n=20)	EA (n=15)	p
	n (%) veya medyan (Min-Maks)			
T 1 VAS	6 (1-8)	6 (4-7)	5 (1-8)	0,717
T 2 VAS	2 (0-4)	2 (1-3)	2 (0-4)	0,945
T3 VAS	3 (0-5)	3 (2-5)	0 (0-3)	<0,001
T 4 VAS	2 (0-4)	2 (1-4)	0 (0-0)	<0,001
T 5 VAS	1 (0-4)	2 (1-4)	0 (0-0)	<0,001
Komplikasyon varlığı	8 (22,9)	5 (25)	3 (20)	1,000
Hipertansiyon	1 (2,9)	1 (5)	0 (0)	1,000
Hipotansiyon	4 (11,4)	1 (5)	3 (20)	0,292
Solunum sıkıntısı	2 (5,7)	2 (10)	0 (0)	0,496
Psikoz	2 (5,7)	2 (10)	0 (0)	0,496
Bulantı/Kusma	2 (5,7)	1 (5)	1 (6,7)	1,000
Ameliyat sonrası ilk ağrı zamanı, saat	1 (1-12)	1 (1-1)	6 (2-12)	<0,001
Taburculuk zamanı, gün	1 (1-2)	1 (1-2)	1 (1-1)	0,214
Ameliyat sonrası takip yeri				
PABU	4 (11,4)	4 (20)	0 (0)	0,119
Servis	31 (88,6)	16 (80)	15 (100)	

PABU: anestezi sonrası bakım ünitesi; T1: Hasta operasyon odasına alındığındaki zaman noktası T2: Vertebra gövdesine trokar uygulandığındaki zaman noktası T3: Omur gövdesine kemik çimentosu enjeksiyonu sırasındaki zaman noktası T4: Ayılma odasındaki zaman noktası T5. Ameliyattan 24 saat sonra; VAS: Visüel analog skala

Lokal anestezi grubunda tüm hastalara midazolam, fentanil, propofol ile sedasyon uygulanırken, EA grubunda 5 hastaya sedasyon uygulaması gerekmedi. 10 hastaya sadece trokar girişi sırasında midazolam ve fentanil uygulandı.

Genel anestezi altında operasyon geçiren hasta sayısı yeterli sayıda olmadığından ilgili hasta grubu sadece tanımlayıcı istatistiklerde gösterilip karşılaştırma istatistiklerinde değerlendirmeye alınmamıştır. Hastaların %27,5'i (11 kişi) erkek, %72,5'i (29 kişi) kadınlardan oluşmaktaydı ve hastaların medyan yaşı 69 (Minimum:46, Maksimum:87) idi. Hastaların ASA skorları açısından fark bulunmamıştır. Anestezi türlerine göre hastaların demografik ve klinik bulgularının dağılımı Tablo 1'de yer almaktadır.

LA ve EA gruplarının demografik ve klinik bulgularının dağılımı Tablo 2'de yer almaktadır. İki grup arasında yaş ve cinsiyet bakımından istatistiksel açıdan anlamlı bir farklılık yoktu (p>0,05). T3 ve T4 noktasında VAS değerleri, ameliyat sonrası ilk ağrı zamanı ve T5 noktasındaki VAS değerlerindeki fark anlamlıydı (p<0,05). İstatistiksel olarak anlamlı olmamakla birlikte, komplikasyon oranı LA grubunda %25 iken, EA grubunda %20 idi.

Lokal anestezi grubu ile epidural anestezi grubu arasında komorbiditeler ve komplikasyon gelişmesi bakımından istatistiksel açıdan anlamlı ilişki görülmemiştir. (Tablo 2) Lokal anestezi grubunun komplikasyon oranını etkileyebilecek komorbiditelerin varlığını belirlemek için ayrıca lojistik regresyon analizi yapılmış olup tüm komorbiditeler için istatistiksel açıdan anlamlı bir farklılık gözlenmemiştir. Benzer şekilde Epidural anestezi grubunda da bir farklılık görülmemiş olup komplikasyon gelişmesinde komorbidite varlığının etkisi yoktur.

LA grubunda 4/16 hastada PABU izlemi gerekli görülürken, EA grubunda bütün hastalar servis takibine verilmiştir. Lokal anestezi grubunda 4 hastanın peroperatif hemodinamik ve solunumsal parametreleri unsta-

bil seyrettiği için PABU'da takip edilmiş ve sonrasında komplikasyonsuz olarak taburcu edilmişlerdir.

Tartışma

Vertebral kompresyon kırıklarının kifoplasti ile tedavisinde ideal anestezi yöntemi, ağrı giderilmesinde etkin ve güvenli olmalıdır. Bu çalışmada perioperatif süreçte epidural anestezinin lokal anesteziden daha etkili bir analjezi sağladığı, komplikasyon oranının daha düşük olduğu görülmüştür.

Hızlı başlangıç, kesinlik ve maliyet etkinliği nedeniyle[12], PKP sırasında lokal anestezi yaygın olarak kullanılmaktadır. Bununla birlikte, vertebra gövdesine lokal anestezik enjekte edilememesi nedeniyle hastalar PKP sırasında dayanılmaz olabilecek şiddetli ağrı yaşarlar[15]. Kifoplasti yapılan hasta popülasyonunun genelde yaşlı olması, komorbiditelerin varlığı, cerrahinin pron pozisyonda yapılması sedasyon düzeyinin bilinçli düzeyde kalmasını zorlaştırmaktadır. LA grubunda, tüm zamanlama noktalarında katlanılabilir düzeyde de olsa ağrı yaşanmış ve intravenöz sedasyon ve analjezik uygulaması gerekli olmuştur. Bu da pron pozisyondaki hastada solunum depresyonu gelişmesi endişesini arttırmaktadır. Sedasyon için midazolam ile birlikte fentanil önerilmektedir[16]. Ohara et al.[17] propofolün sedasyonda kullanımının solunum depresyonu ile ilişkili olabileceğini bildirmiştir. Çalışmamızda 2 hastada gelişen solunum sıkıntısına hava yolu açma manevraları ile müdahale edilmiştir. Aynı zamanda bilinç düzeyinin bozulması ameliyat sırasında kooperasyonu ve nörolojik motor muayeneyi zorlaştırmıştır.

Genel anestezi hem hastalar hem de hekimler için konforlu bir cerrahi durum sağlamak amacıyla PKP sırasında kullanılabilmektedir. Ancak genel anestezinin bu hasta grubundaki riskleri; yoğun bakım ihtiyacının, hastanede kalış süresi ve maliyetin artmasıdır[17]. Bizim merkezimizde cerrahi prosedürde deneyimin artışıyla beraber genel anestezi uygulamaları azalmıştır. Çalışma aralığımızda 5/40 hastada genel anestezi uygulanmış, %20 si PABU'ya çıkmıştır. Operasyon sırasında hastanın sinir yaralanması ancak motor uyarılmış potansiyeller (MEP) ile anlaşılabilir. Bunun da uygulamalarda maliyeti arttırıcı etkisi olacaktır. Bu çalışmadaki genel anestezi grubunda motor uyarılmış potansiyeller (MEP) kullanılamamıştır. Bazı çalışmalar MEP monitörizasyonu olmaksızın PKP'nin daha deneyimli cerrahlar tarafından genel anestezi altında yapılabileceğini bildirmekle beraber[15,19] güvenlik hala büyük bir endişedir.

Guay ve ark.[20]'nın sistematik değerlendirme yaptıkları çalışmalarında yaşlı, kardiyak ve solunumsal komorbiditesi olan hastalarda mümkünse GA yerine nöroaksiyel anestezi tercih edilmesinin mortaliteyi azaltacağı bildirilmiştir. Nöroaksiyel bloklardan spinal anestezide lokal anestezik dağılımı ve blokaj süresi tahmin edilemeyeceği belirtilirken[11], bir analizde lomberdisk hernisi cerrahisi sırasında epidural anestezi kullanımının lokal anestezik ajanın etkilerinden daha fazla yarar sağladığı belirtilmiştir[21].Çalışmamızda, epidural aralığa verilen düşük konsantrasyonlarda bupivakainin ameliyat sırasındaki ağrıyı etkili bir şekilde önleyebildiği belirlenmiştir. Alt ekstremitelerin motor işlevini sürdürerek cerrahın hastadan geri bildirim almaya devam edebilmesi sinir monitorizasyonu gerektirmeksizin güvenli operasyon ortamı sağlamıştır.

Apan ve ark.[19], kifoplasti için segmental epidural anestezi uygulamasını GA ile karşılaştırmışlar ve sonuçlarına göre, epidural anestezi sadece daha iyi ağrı kontrolü sağlamakla kalmamış, aynı zamanda PABU'da daha kısa kalış süresi ve postoperatif bulantı insidansının azalması ile de ilişkilendirilmiştir.

Çalışmamızda Albayrak ve ark.[22] gibi cerrahi yapılacak seviyenin bir üst seviyesinden girişim yaparak kateter yerleştirilmesi tercih edildi. Cerrahi ekip tarafından yeri doğrulandıktan sonra düşük konsantrasyonda bupivakain verildi. Kırık seviyesinin 2 seviye üstü ve 2 seviye altında analjezi sağlandığı tespit edildi. Kateterin yerinde bırakılması, optimal analjezi için segmental

blok ve aralıklı titrasyon yapılabilmesine olanak sağladığı için avantaj olarak değerlendirildi. Apan ve ark.[19] kırık seviyesinin bir alt seviyesinden single-shut epidural anestezi yaptıkları çalışmalarında, bir hastada yetersiz blok olduğunu genel anesteziye döndüklerini belirtmişlerdir. Çalışmamızda yetersiz blok gözlenmedi. Hastalarımızın 12/15'inde trokar girişi sırasında katlanılabilir düzeyde ağrı olduğu ifade edildi. Ağrının cerrahiye erken başlanması ile ilişkili olduğu düşünüldü. Özellikle çimento enjeksiyonu sırasında hastalarda ağrı şikayetinin olmaması bu düşüncemizi desteklemektedir. Operasyon sonrası 3 hasta dışında (ort. 6 saat içinde) hiçbir hastanın 24 saatte ağrısı olmadı. Epidural girişimi, üst seviyeden uygulamamıza rağmen 3 hastamızda bir kez ortalama arter basıncının 60 mmHg'nın altına düştüğü görüldü. Bir kez intravenöz 10 mg efedrin verilerek tedavi edildi.

Ge ve ark.[8], epidural anestezi uygulaması sırasında hastaların lateral ve fleksiyon pozisyonunda kalmalarının, vertebra kırığını şiddetlendirebileceğini, ayrıca anestezik-lerin subaraknoid boşluğa sızarak ve total spinal blok ile solunum inhibisyonuna neden olabileceğini belirtmişlerdir. Çalışmamızda epidural anestezi uygulaması oturur pozisyonda yapıldığı için hastalarda pozisyon verme sırasında ağrı artışı ya da vertebral kırığını şiddetlendirmesi gibi bir sorunla karşılaşılmadı. Ek olarak spinal aralığa sızma komplikasyonu yaşanmadı. Bir hastada ameliyat sonrası 1. saatte idrar yapmada zorluk olduğu belirtildi, ancak motor blok olmayışı ve hastanın şikayetinin 30 dakika gibi bir sürede sonlandığı görüldü. İleri yaş, erkek hasta olduğu göz önünde bulundurularak ürolojik problemlere ikincil olabileceği düşünüldü.

Luginbühl[15], VKK'nın kifoplasti ile tedavisinde balon şişirme ile distraksiyonun çok ağrılı olduğunu ve genel anestezi gerektirdiğini düşünmektedir. Oysa çalışmamızda epidural anestezi uygulanan hastalarımızda bu zamanlama noktasında hiç ağrı gözlenmemiştir. Bu da epidural anestezi uygulanmasının peroperatif ağrıyı önlemede yeterli olduğunu düşündürmüştür.

Literatürde genel anestezi ile lokal anesteziyi[13,14], genel anestezi ile epidural anesteziyi[21] karşılaştıran çalışmalar mevcuttur. Çalışmalarda komplikasyon oranlarının genel anestezi grubunda daha fazla olduğu belirtilmiştir. Bu çalışmada genel anestezi alan hasta sayısının azlığı bizim bu komplikasyon sayılarına yükselmemize engel olmuştur.

Çalışmamızda, epidural anestezi grubunun daha düşük ve ciddi olmayan komplikasyon oranına sahip olduğu görülmüştür. Lokal anestezi grubunda 4/20 (%20) hastanın operasyon sonrası PABU da izlem ihtiyacı olmuştur. Epidural anestezi grubundaki hastaların hiçbirinde PABU takibi gerekmemiştir. Ancak anestezi uygulama prosedürü ve yeterli analjezinin sağlanması için gereken bekleme süresinin uzun oluşu ve maliyetinin LA'ya göre biraz daha yüksek olması epidural anestezinin dezavantajı olarak belirlenmiştir.

Çalışmamızda anestezi yöntemleri hastalara anlatılmış ve seçim hastalara bırakılmıştır. Rastgele olmayan çalışma dizaynı, seçim yanlılığına sebep olmuş olabilir. Hastaların ve cerrahın kör olmaması nedeniyle performans yanlılığına yol açabilme olasılığı çalışmamızın sınırlılığıdır.

Sonuç

Perkutan kifoplasti osteoporotik, travmatik vertebra kırıkları olan hastalarda uygulanan minimal invaziv bir prosedürdür. Komorbidite varlığı, hastaya müdahaleyi zorlaştıran pron pozisyonu, solunum depresyonu riski, hemodinamik bulguların değişkenliği anestezi güvenliği için endişe kaynağıdır. Epidural anestezi; etki başlangıcının geç olması dışında perioperatif dönemde uygulanacak etkili bir anestezi seçeneği olarak değerlendirilmelidir. Epidural anestezi, perkütan kifoplasti uygulanan yüksek riskli hastaların anestezi yönetiminde, lokal anestezi veya genel anesteziye alternatif olarak düşünülebilir.

Yazar katkısı

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

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Kaynaklar

1. Chandra RV, Maingard J, Asadi H, et al. Vertebroplasty and kyphoplasty for osteoporotic vertebral fractures: what are the latest data? American Journal of Neuroradiology. 2020;39(5):798-806. doi: 10.3174/ajnr.A5458
2. Cook DJ, Guyatt GH, Adachi JD, et al. Quality of life issues in women with vertebral fractures due to osteoporosis. Arthritis Rheum. 1993;36(6):750-6. doi: 10.1002/art.1780360603
3. Denaro V, Longo UG, Maffulli N, et al. Vertebroplasty and kyphoplasty. Clinical Cases in Mineral and Bone Metabolism. 2009;6(2):125-30. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2781232/
4. Fuentes S, Metellus P, Fondop J, et al. Percutaneous pedicle screw fixation and kyphoplasty for management of thoracolumbar burst fractures. Neuro-chirurgie. 2007;53(4): 272-6. doi: 10.1016/j.neuchi.2007.04.006
5. Wardlaw D, Cummings SR, Van Meirhaeghe J, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. The Lancet. 2009;373(9668):1016-24. doi: 10.1016/S0140-6736(09)60010-6
6. Ma XL, Xing D, MaJX, et al. Balloon kyphoplasty versus percutaneous vertebroplasty in treating osteoporotic vertebral compression fracture: grading the evidence through a systematic review and meta-analysis. European Spine Journal. 2012;21(9):1844-59. doi: 10.1007/s00586-012-2441-6
7. Wiles MD, Nowicki RW, Hancock SM, et al. Anaesthesia for vertebroplasty and kyphoplasty. Current Anaesthesia and Critical Care. 2009;20(1): 38-41. doi: 10.1016/j.cacc.2008.07.006
8. Ge C, Wu X, Gao Z, et al. Comparison of different anesthesia modalities during percutaneous kyphoplasty of osteoporotic vertebral compression fractures. Scientific Reports. 2021;11(1): 1-7. doi: 10.1038/s41598-021-90621-9
9. Alfahel WS, Dabbous AS, Thompson ME. Epidural analgesia for percutaneous kyphoplasty in a patient with multiple medical comorbidities. Avicenna Journal of Medicine. 2019;9(02):75-7. doi: 10.4103%2Fajm.AJM_73_18
10. Souvatzis X, Katonis PG, Licoudis SA, et al. Subarachnoid anesthesia for kyphoplasty: is anesthesia adequate? Anesthesia and Analgesia. 2010;111(1):238-40. doi: 10.1213/ANE.0b013e3181e0574c
11. Hannallah M, Gibby E, Watson V. Fluoroscopy-guided, small-dose spinal anesthesia for kyphoplasty: A collaborative effort between the anesthesiologist and interventional radiologist. Anesthesia and Analgesia. 2008;106:1329–30. doi: 10.1213/ANE.0b013e3181e0574c
12. Ergün MO, Güvenç Y. Comparison of the Effectiveness of Anesthesia Methods on Percutaneous Kyphoplasty: Erector Spinae Plane Block Versus Local Anesthesia. Istanbul Medical Journal. 2022; 23(2):149-53. doi: 10.4274/imj.galenos.2022.13911
13. Liu J, Wan L, Chai M, et al. Analysis of anesthesia methods in percutaneous kyphoplasty for treatment of vertebral compression fractures. Journal of Healthcare Engineering. 2020;(1) 9;2020:3965961 doi: 10.1155/2020/3965961
14. Zhang LG, Gu X, Zhang HL, et al. Unilateral or bilateral percutaneous vertebroplasty for acute osteoporotic vertebral fracture: a prospectivestudy. Clinical Spine Surgery. 2015;28(2):85-8. doi: 10.1097/bsd.0000000000000147
15. Luginbühl M. Percutaneous vertebroplasty, kyphoplasty and lordoplasty: implications for the anesthesiologist. Current Opinion in Anesthesiology. 2008;21(4): 504-13. doi: 10.1097/ACO.0b013e328303be62
16. Vasconcelos C, Gailloud P, Beauchamp NJ, et al. Is percutaneous vertebroplasty without pretreatment venography safe? Evaluation of 205 consecutive procedures. American Journal of Neuroradiology.2002; 23(6):913-7.
17. Ohara T, Takahashi M, Yamamoto Y, et al. Use of propofol for painful procedures in cancer pain management. Masui. The Japanese Journal of Anesthesiology. 2003;52(7):740-3. https://europepmc.org/article/med/12910974
18. Civelek E, Cansever T, Yilmaz C, et al. The retrospective analysis of the effect of balloon kyphoplasty to the adjacent-segment fracture in 171

patients. Clinical Spine Surgery. 2014;27(2):98-104.
doi: 10.1097/BSD.0b013e31824e9b98
19. Apan A, Apan ÖC, Köse EA. Segmental epidural anesthesia for percutaneous kyphoplasty: Comparison with general anesthesia. Turkish Journal of Medical Sciences. 2016;46(6):1801-7.
doi: 10.3906/sag-1507-90
20. Guay J, Choi PT, Suresh S, et al. Neuraxial anesthesia for the prevention of postoperative mortality and major morbidity: an overview of cochrane systematic reviews. Anesth Analg. 2014; 119(3):716-725.
doi: 10.1213/ANE.0000000000000339
21. Wang W, Ni BB, Shen H, et al. Comparison of surgical outcomes of lumbar disc herniation using local anesthesia and epidural anesthesia: A meta-analysis. Medicine. 2020;99(33):18958.
doi: 10.1097%2FMD.0000000000018958
22. Albayrak S, Demırel I, Ayden O, et al. Lumbar disc surgery with epidural anesthesia: review of 700 cases. Turkish Neurosurgery. 2016;26(3):399-403.
doi: 10.5137/1019-5149.JTN.8715-13.1

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PROTECTIVE EFFICACY OF ROSMARINIC ACID ON ACUTE PANCREATITIS IN RATS

RATLARDA ROSMARİNİK ASİT'İN AKUT PANKREATİT ÜZERİNDEKİ KORUYUCU ETKİNLİĞİNİN İNCELENMESİ

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Abstract

Aim: Acute pancreatitis is a serious disease, with an incidence of 5 - 35 in 100,000 individuals. New studies are constantly planned for the treatment of pancreatitis. Many studies have shown that Rosmarinic acid has antioxidant properties. In this study, we examined the protective effect of Rosmarinic acid on acute pancreatitis.

Methods: A total of 28 animals were used during the experiment, and 4 groups were formed with 7 animals in each group. Group 1 is the control group and no drugs were used during the experiment. The rats in Group 2 were administered 75 µg/kg Cerulein every hour intraperitoneally at one-hour intervals, a total of four times. Group 3 experimental animals were given 50 mg/kg Rosmarinic acid by per oral gavage. The rats in group 4 were given 50 mg/kg Rosmarinic acid per oral gavage after 75 µg/kg Cerulein was injected intraperitoneally every hour for a total of four times. Afterwards, all animals were sacrificed by exsanguination, blood samples and pancreatic tissue were taken for examination.

Results: Examination of pancreatic tissues revealed necrosis, edema and inflammation in the acute pancreatitis group. Both histopathological and serum values of the rosmarinic acid group were close to the control group. The use of Rosmarinic acid after acute pancreatitis had a positive effect on the pacreatic tissues and blood values, but still did not cause complete recovery.

Conclusions: In the case of acute pancreatitis, it was concluded that rosmarinic acid has a partial curative effect, but still does not provide a full recovery.

Keywords: Acute pancreatitis, Cerulein, Rosmarinic Acid.

Öz

Amaç: Akut pankreatit her yüz bin kişide 5-35 kişi arasında görülen ciddi bir hastane yatış sebebidir. Pankreatit durumunun tedavisi konusunda sürekli yeni çalışmalar planlanmaktır. Rozmarinik asit'in yapılan birçok çalışmada antioksidan özelliğe sahip olduğu gösterilmiştir. Bizde yaptığımız bu çalışmada Rosmarinik asit'in akut pankreatit üzerinde koruyucu etkinliğini incelemeyi amaçladık.

Yöntemler: Deney süresince toplam 28 hayvan kullanılmış olup, her grupta 7 hayvan olacak şekilde 4 grup oluşturuldu. Grup 1 kontrol grubu olup deney süresince hiçbir ilaç kullanılmadı. Grup 2'deki ratlara saatte bir 75 µg/kg Cerulein birer saat arayla intraperitoneal olarak, toplam dört defa enjekte edildi. Grup 3 deney hayvanlarına peroral gavaj yoluyla 50 mg/kg dozda Rosmarinik asit verildi. Grup 4'teki ratlara ise saatte bir 75 µg/kg Cerulein intraperitoneal olarak toplam dört defa olmak üzere enjekte edildikten sonra, Rosmarinik asit peroral gavaj yoluyla 50 mg/kg verildi. Sonrasında çalışma gruplarındaki tüm hayvanlar ekzanguinasyon ile sakrifiye edildi, kalpten alınan kan örnekleri ve pankreas dokusu inceleme amacıyla alındı.

Bulgular: Pankreas dokularının ışık mikroskobik incelemelerinde akut pankreatit grubunda dokularda nekroz, ödem ve inflamasyon görüldü. Rosmarinik asit grubunun hem histopatolojik hem de serum değerlerinin kontrol grubuna yakın olduğu görüldü. Akut pankreatit sonrası Rosmarinik asit kullanımının pankreas dokularda ve kan değerlerinde pozitif etkili olduğu, fakat yine de tamamen iyileşmeye neden olmadığı tespit edildi.

Sonuç: Akut pankreatit durumunda Rosmarinik asit'in kısmen iyileştirici özelliğinin olduğu fakat yine de tam bir iyileşme sağlamadığı kanaatine varıldı.

Anahtar Kelimeler: Akut pankreatit, Cerulein, Rosmarinik Asit

Introduction

Acute pancreatitis is an inflammatory disease with mild to severe symptoms. In general, it is thought that in the beginning of acute pancreatitis, digestive zymogens lead to early intraacinar cell activation and once these enzymes are activated, they cause acinar cell damage[1]. Early acinar cell damage in acute pancreatitis leads to local inflammatory reactions. Then, a systemic inflammatory response syndrome (SIRS) occurs[2]. It is known that acute pancreatitis occurs in two stages as early and late stages. The severity of the disease is classified as mild, moderate or severe. The most common form is mild acute pancreatitis and it can cause organ failure, local or systemic complications, which usually resolves within the first week. Moderate acute pancreatitis results in transient organ failure and local complications. If severe acute pancreatitis lasts longer than 48 hours, permanent organ failure develops[3].
Rosmarinic acid (RA) is a polyphenolic antioxidant that is widely found in many plants[4-6].
In many studies, antioxidant, anticarcinogenic, anti-inflammatory, antidepressant and antimicrobial effects of RA has been revealed[7,8]. RA increases the expression of cytoprotective genes and affects several enzymes of the antioxidant system, and as a result it acts as an antioxidant [9].
In this study we examined whether RA can be an effective treatment for acute pancreatitis by utilizing its antioxidant, anti-inflammatory and other therapeutic properties and to add new findings to science on the treatment of such a serious and fatal disease.

Materials and Methods

- *Formation of Experimental Groups*

In this study, 28 Wistar Albino male rats were used, which were 8-10 weeks old and weighing 250-300 g. Rats were divided into 4 groups in groups of 7 in cages in an environment with a ventilation system.

Group 1 (n=7):
(Control Group)
Intraperitoneal (i.p.) saline was administered to the rats during the experiment.

Group 2 (n=7):
(Acute Pancreatitis Group)
Seventy-five µg/kg Cerulein was administered to the rats every hour at one-hour intervals, a total of four times.

Group 3 (n=7):
(Rosmarinic acid group)
Peroral (p.o.) Rosmarinic acid was administered at a dose of 50 mg/kg via gavage.

Group 4 (n=7):
(Acute pancreatitis + Rosmarinic acid group)
50 mg/kg Rosmarinic acid per oral gavage after 75 µg/kg Cerulein was injected intraperitoneally every hour for a total of four times.

We obtained Cerulein from Sigma-Aldrich, (St. Louis, MO, USA) to initiate acute pancreatitis.
At the end of the experiment Ketamine HCl (90 mg/kg, Pfizer Inc, USA) + Xylazine HCl (10 mg/kg, Bayer HealthCare AG, Germany) i.p. was administered to the rats and the rats were sacrificed by exsanguination under general anesthesia and the study was terminated. The collected pancreatic tissues were fixed in containers containing 10% buffered formol (Sigma #SZBE2450V).

- *Histopathological Analysis*

Pancreatic tissue samples washed in tap water for 12 hours after fixation were passed through increasing alcohol series for dehydration. Sections taken after routine histological tissue follow-up were stained with Hematoxylin & Eosin (H&E) for histological evaluation.
Paraffin depolymerization was provided in an oven at 58°C for 1 hour before staining

on tissue samples taken on positively charged slides. Hematoxylin-Eosin (H&E) staining protocol was applied to the sections taken from the oven for histological evaluation. Edema, acinar cell necrosis, and inflammation in the pancreatic tissue were evaluated using Schoenberg's Pancreatic Injury Scoring System, which ranges from 0 to 4[10].

- *Biochemical Analysis*

The blood samples taken were centrifuged at 3000/min for 10 minutes and the serum samples were separated and sent to the Biochemistry Laboratory. Serum amylase level, serum OSI, pancreatic OSI, TNF-α, IL-1β, IL-6 values were measured.

- *Measurement of total antioxidant status (TAS)*

It is a method that measures the body's total antioxidant capacity against strong free radicals. In this study, venous blood samples taken from rats in all groups were taken into EDTA tubes and centrifuged at 900 g at 4°C for 10 minutes. For evaluating the total antioxidant status (TAS) level from blood samples, we purchased the kits from Rel Assay Diagnostics (Gaziantep, Turkey). An automated measurement method which was improved by Erel[11] was used to analyze the TAS of the supernatantphase. “mmol/L” was used as the measurement unit of TAS.

- *Measurement of total oxidant status (TOS)*

In this study, venous blood samples taken from rats in all groups were taken into EDTA tubes and centrifuged at 900 g at 4°C for 10 minutes. For evaluating the total oxidant status (TOS) level from blood samples, we purchased the kits from Rel Assay Diagnostics (Gaziantep, Turkey). An automated measurement method which was improved by Erel[12] was used to analyze the TOS levels of the supernatant fragments. “μmol/L” was used as the measurement unit of TOS.

- *Measurement oxidative stress index (OSI)*

OSI indicates the degree of oxidative stress and is calculated using following formula[13]: OSI: (TOS/TAS) × 100.

- *Statistical Analysis*

Statistical analyzes of the data were done with SPSS for Windows version 20 (SPSS Inc., Chicago, IL, USA). The compatibility of the data with the assumption of normal distribution was examined by applying the Shapiro Wilk test. The Kruskal Wallis test, which is one of the non-parametric tests, was applied to the values that did not show normal distribution, and the Mann Whitney U test was performed between the two groups for the differences between the variables that were found to be significant. Significance level was accepted as significant in case of $p<0.05$ value.

Results

- *Histopathological Findings*

In the histopathological analysis of pancreatic tissue, when all study groups were evaluated in terms of edema, hemorrhage, inflammation and necrosis, no pathological findings were found in the pancreatic tissues of the control group (Figure 1). Similarly, no pathological findings were found in the pancreatic tissue of the Rosmarinic acid group (Figure 1). Numerous cell necrosis and cytoplasmic vacuoles were found in the pancreatic tissues of the group receiving cerulein (Figure 1). When the pancreatic tissues of the Cerulein+ Rosmarinic acid group were examined, it was observed that the severity of the findings decreased compared to the group that received Cerulein, but it was not as normal as the control or Rosmarinic acid group (Figure 1).

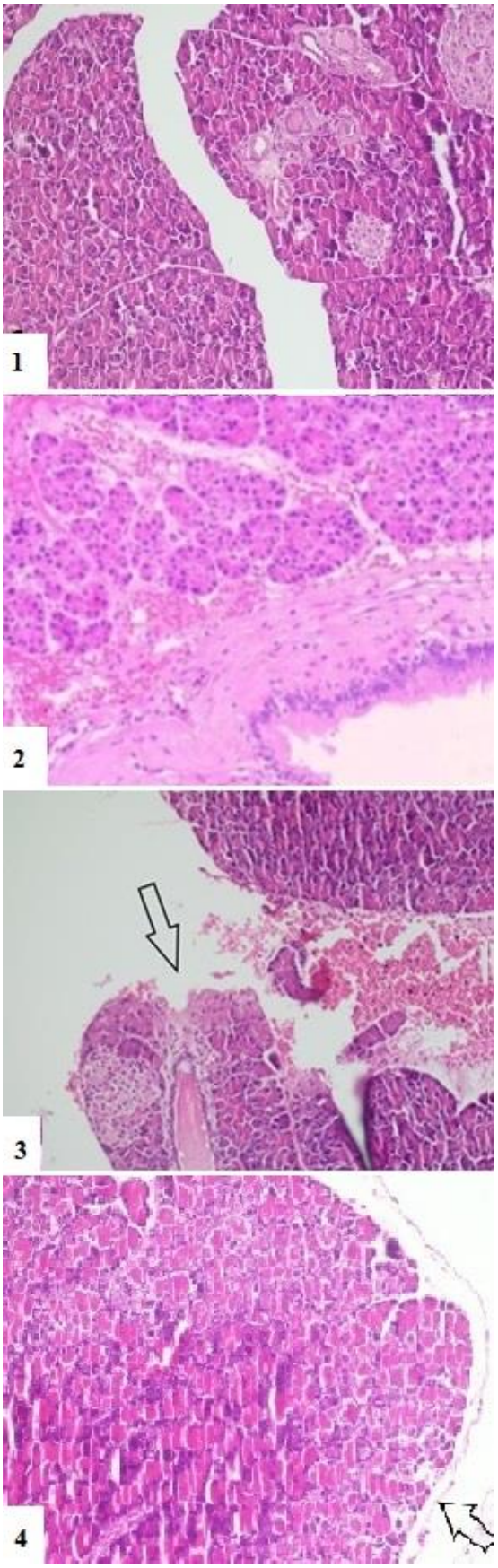

Figure 1.H&E Staining of the pancreas of the groups (H&E:Hematoxylin and Eosin)

According to the statistical analyzes made between the groups.

When examined in terms of edema, it was seen that the Acute pancreatitis + Rosmarinic acid group had the highest score compared to the other groups, while no difference was observed between the other groups ($p<0.05$).

In the evaluation of necrosis, Acute pancreatitis group had the highest scoring, while no necrosis was found in the Control and Rosmarinic acid groups. Acute pancreatitis Rosmarinic acid group had a lower score compared to the acute pancreatitis group ($p<0.05$).

In the hemorrhage evaluation, no hemorrhagic changes were found in the study groups except the acute pancreatitis group ($p<0.05$).

In inflammatory changes, it was observed that the acute pancreatitis+ Rosmarinic acid group had lower inflammation compared to the acute pancreatitis group ($p<0.05$).

The mean±standard deviation and p values of the histopathological (edema, inflammation, hemorrhage and necrosis) changes that were statistically analyzed are summarized in Table 1.

- *TAS and TOS Analysis*

As a result of the evaluation of TAS levels in both tissue and serum, it was found that there was no statistically significant difference between the groups ($p>0.05$).

As a result of the evaluation of TOS levels in tissue and serum, it was found that it was significantly higher in the acute pancreatitis group compared to all other groups ($p<0.05$). It was found that it was lower in the Acute pancreatitis+ Rosmarinic acid group compared to the Acute pancreatitis group, but it was significantly higher compared to the control and Rosmarinic acid groups ($p<0.05$).

In the OSI calculations made in line with these data.

The OSI level in pancreatic tissue was found to be the highest in the Acute pancreatitis group compared to the other groups

Table 1: The mean±standard deviation and p values of the histopathological analyzes (edema, necrosis, hemorrhage and inflammation), biochemical analyzes (serum Amylase, TNF-α, IL-1β, IL-6), TAS (in serum and tissue), TOS (in serum and tissue), Serum OSI, Pancreatic OSI.

Parameters	Control group	Rosmarinic Acid (RA) group	Acute Pancreatitis (AP) group	AP + RA group	P
TAS (nmoltroloxequiv/mg protein) –pancreas	0.32 ±0.29	0.39±0.33	0.35±0.14	0.55±0.29	N.S.
TAS- Serum	0.78±0.06	0.84±0.05	0.87±0.26	0.83±0.16	N.S.
TOS (nmol H2O2 equiv/mg protein)– pancreas	326.29±109.9	320.95±103.1	1561.10±647.89[a,b]	1202.03±344.50[a,b]	<0.001
TOS - Serum	565.58±223.95	553.29±87.64	1638.01±910.11 [a,b]	908.01±247.22 [a,b]	0,003
OSI-Pancreas	186823.29±196128.44	257782.26±322786.03	507711.84±293901.92[a]	297670.46±202272.78	N.S.
OSI-serum	66172.92±22672.39	70628.2±8369.91	183723.88±60828.14[a,b]	115854.27±52963.21[a,b]	0.005
Serum- TNF-α(pg/mL)	44.45±2.13	47.26±3.74	133.71±25.75[a,b]	46.19±2.42[c]	0,001
Serum- IL 1β(pg/mL)	421.3±24.21	442.45±44.54	793.92±307.89[a,b]	452.16±32.70[c]	0,012
Serum IL-6(pg/mL)	25.93±3.64	26.55±1.75	54.17±30.78[a,b]	28.59±3.87[c]	0,004
Serum Amilase (IU/L)	760.85±96.88	674.85±46.84	2042.42±593.21[a,b]	1473.71±339.31[a,b]	<0.001
Pancreatic Tissue Edema Formation	0.0±0.0	0.0±0.0	0.0±0.0	1.00±0.57	<0.001
Development of Pancreatic Tissue Necrosis	0.0±0.0	0.0±0.0	1.14±0.69	0.14±0.37	0.001
Pancreatic Tissue Hemorrhagic Changes	0.0±0.0	0.0±0.0	0.42±0.53	0.0±0.0	0.018
Pancreatic Tissue Inflammatory Changes	0.0±0.0	0.0±0.0	1.28±1.11	0.42±0.53	0.01

Acute Pancreatitis group (AP), Acute Pancreatitis+ Rosmarinic Acid group (AP+RA), Not significant (N.S.).

a: Different from the control group, b: Different from the RA group, c: Different from the AP group, d: Different from the AP+RA group

($p<0.05$), but there was no significant difference between the other groups ($p>0.05$).
OSI level in the serum was found to be higher in the Acute pancreatitis group compared to all other groups ($p<0.05$). It was found that it was lower in the acute pancreatitis and rosmarinic acid group compared to the acute pancreatitis group, but higher than the control and rosmarinic acid groups ($p<0.05$). It was found that it was lower in the acute pancreatitis + rosmarinic acid group compared to the acute pancreatitis group, but higher than the control and rosmarinic acid groups ($p<0.05$).
TAS and TOS values, mean±standard deviation and p values of pancreatic OSI and serum OSI levels are summarized in Table-1.

- *Biochemical Analysis*

According to the results of serum amylase, serum Oxidative Stress Index (OSI), pancreatic OSI, IL-1β, IL-6 and TNF-α levels that we have checked as a result of the blood samples we have taken.
Serum amylase levels were found to be significantly higher in the acute pancreatitis group compared to all other groups ($p<0.05$). It was found to be lower in the acute pancreatitis + Rosmarinic acid groups compared to the acute pancreatitis group ($p<0.05$).
TNF-α levels were found to be significantly higher in the Acute pancreatitis group compared to all other groups ($p<0.05$), while it was lower in the Acute pancreatitis+ Rosmarinic acid group ($p<0.05$).
While IL-1β levels were found to be similarly low in the control group and Rosmarinic acid groups ($p<0.05$), they were higher in the acute pancreatitis+ Rosmarinic acid group compared to these two groups ($p<0.05$).
IL-6 levels were found to be lower in the Acute pancreatitis+ Rosmarinic acid group compared to the Acute pancreatitis group ($p<0.05$).
The mean±standard deviation and p values of serum Amylase, TNF-α, IL-1β, IL-6 levels are summarized in Table-1.

Discussion

Acute pancreatitis is an inflammatory disease that can result in acute inflammation or necrosis of the pancreatic gland parenchyma[14]. The prognosis of acute pancreatitis generally depends on the presence of accompanying complications such as organ failure and infected pancreatic necrosis. Although the incidence of this disease is increasing, unfortunately we have no specific treatment methods to diminish the symptoms and course of the disease yet[15]. In our study, we examined the protective effects of Rosmarinic acid, which is an alternative treatment for pancreatitis.
Fan et al found in their study that acute pancreatitis is characterized by the onset of necrosis and peripancreatic tissue inflammation. These findings are similar to severe acute pancreatitis in humans[16]. Luo et al showed in their study that rosmarinic acid pretreatment significantly improved the pathological change in the pancreas. They also found that it caused a decrease in serum amylase and lipase activity[17]. Similarly, Mccue et al showed in their study that Rosmarinic acid reduces serum amylase level[18,19]. In our study, we observed that necrotic changes and inflammation had a very high score in the acute pancreatitis group, in terms of histopathological evaluation. In addition, we found that administration of Rosmarinic acid after acute pancreatitis caused decreases in serum amylase values.
IL-1β and TNF-α are major proinflammatory mediators and are responsible for all other systemic complications[20]. Seyed Abbas Metal showed that it was highest in the acute pancreatitis group in their studies[21].In our study, we observed that serum TNF-α values were lower in the group treated with Rosmarinic acid after acute pancreatitis. In other studies, it has been confirmed that Rosmarinic acid has positive results thanks to its anti-inflammatory and antioxidant effects[22-25]. In our study, we observed that rosmarinic acid decreased serum amylase, serum TNF-α, IL-1β and IL-6 values positively.

Ilhan et al showed in their study that there was a significant increase in TAS levels of the group receiving rosmarinic acid[26-27]. However, in this study, we found that there was no statistically significant difference as a result of the evaluation of TAS levels in both tissue and serum. Our study was not compatible with this study in this context.

Conclusion

As a result of the evaluation of biochemical parameters and histopathological findings; It was observed that rosmarinic acid had a partial healing effect on pancreatic tissue and blood values in acute pancreatitis, but still did not cause complete recovery. In line with this information, we came to the conclusion that more comprehensive studies with different doses and durations are required in order to fully understand the curative effect of rosmarinic acid in acute pancreatitis, by which mechanisms it occurs at the cellular level.

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 experiment was approved by Experiments of the Dicle University Local Ethics Committee2021/23 with protocol number approved.

References

1. Saluja AK, Steer ML. Pathophysiology of pancreatitis. Digestion. 1999;60:27–33. doi: 10.1159/000051450.
2. Bhatia M, Wong FL, Cao Y, et al. Pathophysiology of Acute Pancreatitis. Pancreatology. 2005;5:132–44. doi: 10.1159/000085265
3. Banks PA, Bollen TL, Dervenis C, et al. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013 ;62(1):102-111. doi: 10.1136/gutjnl-2012-302779.
4. Han S, Yang S, Cai Z, et al. Anti-Warburg effect of rosmarinic acid via miR-155 in gastric cancer cells.Drug Des Devel Ther. 2015; 9: 2695–703. doi: 10.2147/DDDT.S82342
5. Miranda LE, Capellini VK, Reis GS, et al. Effects of partial liver ischemia followed by global liver reperfusion on the remote tissue expression of nitric oxide synthase: lungs and kidneys. Transplant Proc. 2010; 42(5): 1557–62. doi: 10.1016/j.transproceed.2010.02.097.
6. Xu Y, Jiang Z, Ji G, et al. Inhibition of bone metastasis from breast carcinoma by rosmarinic acid. Planta Med. 2010; 76(10): 956–62. doi: 10.1055/s-0029-1240893
7. Chu X, Ci X, He J, et al. Effects of a natural prolyl oligopeptidase inhibitor, rosmarinic acid, on lipopolysaccharide-induced acute lung injury in mice. Molecules. 2012; 17(3): 3586–98. doi: 10.3390/molecules17033586
8. Xu Y, Xu G, Liu Li, et al. Anti-invasion effect of rosmarinic acid via the extracellular signal regulated kinase and oxidation- reduction pathway in Ls174-T cells. J Cell Biochem. 2010; 111(2): 370–379. doi: 10.1002/jcb.22708
9. Moon DO, Kim MO, Lee JD, et al. Rosmarinic acid sensitizes cell death through suppression of TNF-alpha-induced NF-kappaB activation and ROS generation in human leukemia U937 cells. Cancer Lett. 2010; 288(2): 183–191. doi: 10.1016/j.canlet.2009.06.033
10. Schoenberg M H, Büchler M, Gaspar M, et al. Oxygen free radicals in acute pancreatits of the rat. Gut 1990; 31: 1138-43. doi: 10.1136/gut.31.10.1138
11. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem, 2004; 37: 112–19. doi: 10.1016/j.clinbiochem.2003.10.014
12. Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem, 2005; 38: 1103–11. doi: 10.1016/j.clinbiochem.2005.08.008
13. Tüfek A, Tokgöz O, Aliosmanoglu I, et al. The protective effects of dexmedetomidine on the liver and remote organs against hepatic ischemia reperfusion injury in rats. Int J Surg. 2013;11(1):96–100.

doi: 10.1016/j.ijsu.2012.12.003.
14. Irrera N, Bitto A, Interdonato M, et al. Evidence for a role of mitogen-activated protein kinases in the treatment of experimental acute pancreatitis. World J. Gastroenterol. 2014; 20 (44): 16535–43.
doi: 10.3748/wjg.v20.i44.16535
15. Kambhampati S, Park W, Habtezion A. Pharmacologic therapy for acute pancreatitis. World J. Gastroenterol. 2014;20 (45): 16868–80.
doi: 10.3748/wjg.v20.i45.16868
16. Fan YT, Yin GJ, Xiao WQ, et al. Rosmarinic acid attenuates sodium taurocholate-induced acute pancreatitis in rats by inhibiting nuclear factor-kappa B activation. Am. J. Chin. Med. 2015; 43 (6): 1117–35.
doi: 10.1142/S0192415X15500640
17. Luo C, Zou L, Sun H, et al. A Review of the Anti-Inflammatory Effects of Rosmarinic Acid on Inflammatory Diseases. Front Pharmacol. 2020; 28 (11):153.
doi: 10.3389/fphar.2020.00153
18. McCue PP, Shetty K. Inhibitory effects of rosmarinic acid extracts on porcine pancreatic amylase in vitro. Asia Pacific Journal of Clinical Nutrition. 2004;13: 101-6.
19. Alagawany M, Abd El-Hack ME, Farag MR, et al. Rosmarinic acid: modes of action, medicinal values and health benefits. Animal Health Research Reviews, 2017;18(2): 167-76.
doi: 10.1017/S1466252317000081.
20. J Norman, "The role of cytokines in the pathogenesis of acute pancreatitis," The American Journal of Surgery. 1998; 175 (1):76–83.
doi: 10.1016/S0002-9610(97)00240-7
21. Mirmalek SA, Boushehrinejad AG, Hassan Yet al. Antioxidant and Anti-Inflammatory Effects of Coenzyme Q10 on L-Arginine-Induced Acute Pancreatitis in Rat. Hindawi Publishing Corporation Oxidative Medicine and Cellular Longevity. 2016; 2016: 8.
doi: 10.1155/2016/5818479
22. Ramalho LNZ, Pasta ÂAC, Terra VA, et al. Rosmarinic acid attenuates hepatic ischemia and reperfusion injury in rats. Food and chemical toxicology. 2014; 74: 270-8.
doi: 10.1016/j.fct.2014.10.004.
23. Ahmed MM. Rosmarinic acid attenuates the hepatotoxicity induced by ethanol in rats. American Journal of Biochemistry. 2016; 6(3): 82-90.
doi: 10.5923/j.ajb.20160603.03
24. Oğuz A, Böyük A, Ekinci A, et al. Investigation of antioxidant effects of rosmarinic acid on liver, lung and kidney in rats: a biochemical and histopathological study. Folia morphologica. 2020; 79 (2): 288-95.
doi: 10.5603/FM.a2019.0087
25. Sadeghi A, Bastin AR, Ghahremani H, et al. The effects of rosmarinic acid on oxidative stress parameters and inflammatory cytokines in lipopolysaccharide-induced peripheral blood mononuclear cells. Molecular biology reports. 2020; 47(5): 3557-66.
doi: 10.1007/s11033-020-05447-x.
26. Ilhan N, Bektas I, Susam S, et al. Protective effects of rosmarinic acid against azoxymethane-induced colorectal cancer in rats. J Biochem Mol Toxicol. 2021;12:e22961.
doi: 10.1002/jbt.22961.
27. Mohammed FS, Karakas M, Akgul H, et al. Medicinal Properties of Allium Calocephalum Collected from Gara Mountain (Iraq). Fresenius Environmental Bulletin. 2019; 28 (10): 7419-26.

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MITIGATING THE SEVERITY OF BINGE EATING EPISODES IN OBESE INDIVIDUALS

OBEZ KİŞİLERDE TIKINIRCASINA YEME ATAKLARININ ŞİDDETİNİN AZALTILMASI

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Abstract

Aim: The study aimed to analyze the change in the severity of binge eating disorder in obese individuals registered to the Adana City Training and Research Hospital Obesity Center training program.

Methods: The study was a single-arm, prospective, quasi-experimental study with an interrupted time-series design. Inclusion criteria were having registered to the center for training, age between 18 to 65 years, a body mass index (BMI) equal to or over 30 and having binge eating disorder. Binge eating disorder evaluation (BEDE) was a structured form exclusively using DSM-5 binge eating disorder (BED) diagnosis and the severity criteria. The progress record included a weekly curriculum that a physician, dietitian, psychologist administered, and the physiotherapist and the monthly individual meetings data.

Results: The BEDE reports showed a significant improvement, with 65 of the patients scoring below the BED diagnosis at the final evaluation. There was no difference between the genders regarding improvement in episodes. The current study showed that after twenty weeks of training that lasted for approximately 80 hours, the patients reported fewer episodes.

Conclusions The training could be considered efficacious for reducing the severity of binge eating episodes in obese patients seeking treatment.

Keywords: Obesity, binge eating disorder, weight loss

Öz

Amaç: Çalışma, Adana Şehir Eğitim ve Araştırma Hastanesi Obezite Merkezi Eğitim Programına kayıtlı Obez kişilerde tıkınırcasına yeme bozukluğunun şiddetindeki değişimi analiz etmeyi amaçlamıştır.

Yöntemler: Çalışma, kesintili bir zaman serisi tasarımına sahip, tek kollu, prospektif, yarı deneysel bir çalışmaydı. Dahil edilme kriterleri, eğitim için merkeze kayıtlı olmak, 18-65 yaş arasında olmak, vücut kitle indeksi (VKİ) 30'a eşit veya üzerinde olmak ve tıkınırcasına yeme bozukluğuna sahip olmaktı. Tıkınırcasına yeme bozukluğu değerlendirme (BEDE) formu, yalnızca DSM-5 Tıkınırcasına yeme bozukluğu (BED) tanısı ve şiddet kriterleri kullanılarak yapılandırılmış bir formdu. İlerleme kaydı, bir doktor, diyetisyen, psikolog ve fizyoterapistin uyguladığı haftalık bir müfredatı ve aylık bireysel toplantı verilerini içeriyordu.

Bulgular: BEDE raporları, son değerlendirmede 65 hastanın BED tanısının altında puan almasıyla önemli bir gelişme gösterdi. Epizotlardaki iyileşme açısından cinsiyetler arasında fark yoktu. Mevcut çalışma, yaklaşık 80 saat süren yirmi haftalık eğitimden sonra hastaların daha az atak bildirdiğini gösterdi.

Sonuç: Tedavi arayan obez hastalarda tıkınırcasına yeme ataklarının şiddetini azaltmak için eğitimin etkili olduğu düşünülebilir.

Anahtar Kelimeler: Obezite, tıkınırcasına yeme bozukluğu, kilo verme

Introduction

In the recent Diagnostic and Statistical Manual of Mental Disorders (DSM-5), binge eating disorder (BED) is classified as a specific disorder with recurrent episodes of binge eating in a discrete period, an amount of food that is larger than most people would eat in a similar period under similar circumstances with the sense of lack of control overeating during the episode. Individuals with BED have impulsive, recurrent binge eating episodes in the absence of inappropriate compensatory weight control methods[1]. BED has been reported to have the highest lifetime and 12-month prevalence among eating disorders with 2.22% and 0.87%, respectively[2]. It is also considered as a heritable condition that is influenced by both genetic and environmental factors[3]. The disorder has significant medical complications related to excess body weight and impaired psychosocial functioning[4].

In the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5), a new severity indicator was added based on the episodes' frequency. Four severity groups were defined for BED based on the weekly episodes: mild, moderate, severe, and extreme with episode frequencies 1-3, 4-7, 8-13, and over 14 per week, respectively[1].

Outcomes of treatments for binge eating spectrum disorders are yet to yield desirable results, reporting up to 60–70% of patients remaining symptomatic at post-treatment[5].

- *Obesity Center Training Program*

Adana City Training and Research Hospital Obesity Center is designed to provide multidisciplinary health care services and training for groups of obese patients seeking professional help. The center includes a physician, dietitian, physiotherapist, psychologist, public relations officer, and a nurse acting as a life coach. The program is planned to carry out initial assessments, health screening, necessary medical attention related to obesity, cognitive change, behavioral change, and sustainability activities. The assessment part consists of one-on-one interviews with the physician, psychologist, dietitian, physiotherapist, and nurse. (Table 1) Patients with severe or mismanaged medical conditions, including chronic diseases, neurological diseases, significant affective and psychotic disorders, and substance abuse or addiction disorders are directed to relevant clinics before registration. The patients who complete the assessment are arranged into groups. In two group meetings, basic medical knowledge and frequently asked questions are discussed. The center staff and the patients get acquainted. In the following twenty weeks, the physician, dietitian, psychologist, and physiotherapist conducted group training sets. The subjects of the meetings are as follows; medical information about obesity, using the technology to aid weight loss, self-questioning what, when, how, and why to eat, nutrition groups, ration management, water consumption, self-awareness, stress management, obesity and the association between the psychological processes, warming up and mobilization, correct stance and posture, and adequate physical activity. In addition to group meetings, in monthly individual sessions, the progress is evaluated.

The study aimed to analyze the change in the severity of binge eating disorder in patients registered to the program. The study expected to show a decrease in the frequency of the BED episodes.

Materials and Methods

The study was a single-arm, prospective, quasi-experimental study with an interrupted time-series design. There were no sampling methods; all patients registered to the program with binge eating disorder were asked to be included. Inclusion criteria were having registered to the center for training, passed the first three steps, age between 18 to 65 years, a body mass index (BMI) equal to or over 30, and having binge eating disorder.

Table 1. Trainers and the topics discussed in weekly group meetings

Sets	Week	*Physician*	*Dietitian*	*Psychologist*	*Physiotherapist*
1	1	What is obesity	Water Consumption	Communication skills	How to warm-up
	2	Obesity and the musculoskeletal system	Portion control	Imagination	Knee exercises
	3	Obesity, chronic diseases, and cancer	Food types	Role-play	Spine exercises
	4	Parameters used in weight evaluation	Calories of Fats	Personality theories	Upper extremity
2	5	Daily requirements and expenditure of the body	The Calories of the Sugars	Role-play	Lower Extremity
	6	Vegetarians and vegans	Calories of meat-rich foods	Stress management	Lower body (lying)
	7	Fitness, weight tracking, and technology	Calories of the dairies	Role-play	Lower body (standing)
	8	Conditions related to overweight	Calories of fruits	Self-perception	Upper body exercises
3	9	Insulin resistance and glycemic index	Calories of vegetables	Role-play	Back exercises
	10	How does my body work?	Calories of grains	Psychological traumas	Abdominal exercises
	11	What do I think about eating?	Healthy nutrition	Role-play	Stretching exercises
	12	What I feel about eating?	Distribution of daily energy intake	Childhood and adolescent traumas	Relaxation exercises
4	13	What exactly do I eat?	Meal-time planning	Role-play	Aerobic exercises
	14	How much do I eat?	Meal enrichment	Anxiety disorders	Routine activity
	15	When do I eat?	Nutrients that complicate weight loss	Role-play	Correct posture
	16	How do I eat?	Label reading	Avoidance behavior and affirmation	Effects of exercises on basal metabolic rate
5	17	Why do I eat?	Consumption of packaged products	Personal motivation	Alternative exercises
	18	5W3H Summary	Healthy meal preparation	Imagination	Yoga and Pilates
	19	Local key opinion leadership (KOL) on health and nutrition	Portion control	Coping with Stress	Summary of exercises
	20	Summary	Healthy Food Cooking and Storage	Role-play applications in social network	Summary of exercises

Table 2. Summary of the demographics and the clinical characteristics

		%	Initial evaluation Weight	BMI	p weight	p bmi
Gender	Female	97(%82,2)	99,34±15,89	38,66±6,10	0,02	0,53
	Male	21(%17,8)	112,77±23,99	37,69±7,75		
	Total	118	101,73±18,23	38,49±6,40		
Marital status	Married	94(%79,7)	100,50±18,13	38,03±6,28	0,14	0,12
	Single	24(20,3)	106,53±18,18	40,28±6,70		
Age	Female	47,15±10,84				
	Male	49,38±11,26				
	Total	47,5±10,90				
Educational	None	2(1,7)	93,00±26,30	39,93±10,94	0,23	0,12
	Elementary	49(41,5)	104,98±22,12	40,12±6,96		
	Middle	40(33,9)	97,52±15,75	37,27±6,14		
	High	27(22,9)	102,72±11,75	38,49±4,97		
Socioeconomic status	Low	41(34,7)	103,89±16,27	39,14±6,22		
	Medium	66(55,9)	100,51±20,05	38,13±6,60	0,64	0,72
	High	11(9,3)	100,97±18,23	38,49±6,40		
Occupation	Employee	5(4,2)	112,44±15,36	38,91±6,46		
	Others	8(6,8)	111,86±16,44	38,96±7,28	0,14	0,99
	Retired	21(17,8)	103,46±24,85	38,39±7,32		
	Unemployed	84(71,2)	99,70±16,23	38,44±6,19		
Beck Score	Beginning of the training	11,96±3,72			0,000	
	The end of the 20th week	10,06±3,98				

Table 3. BEDE severity by variables

	Weight	BMI	Binge Eating Episodes	Severity score			
				Mild	Moderate	Severe	Extreme
Initial evaluation	101,73±18,23	38,49±0,59	5,33±4,17	50(%42,4)	44(%37,3)	18(%15,3)	6(%5,1)
Beginning of the training	100,45±17,90	38,00±0,57	5,17±3,59	50(%42,4)	45(%38,1)	16(%13,6)	7(%5,9)
Fourth week	98,11±17,58	37,12±0,56	3,88±3,66	70(%59,3)	34(%28,8)	11(%9,3)	3(%2,5)
Eighth week	95,68±17,42	36,21±0,57	3,14±3,72	74(%62,7)	33(%28,0)	7(%5,9)	4(%3,4)
Twelfth week	93,64±17,40	35,44±0,57	3,00±3,55	76(%64,4)	32(%27,1)	6(%5,1)	2(%3,4)
Twentieth week	92,21±6,871	34,91±0,56	2,95±3,56	77(%65,3)	29(%24,6)	7(%5,9)	5(%4,2)
p	0,00	0,00	0,00	0,00			

Patients who failed to attend more than four pieces of training and complete a binge eating evaluation were excluded from the study.

The training materials were developed by the trainers and edited by the director of the obesity center (author) for the final version before training.

The data collection was performed via socio-demographic information form, binge eating disorder evaluation (BEDE) form, and progress record forms. The socio-demographic information form included age, gender, marital status, education level, employment, financial self-appraisal, physical activity, smoking, and alcohol consumption. BEDE was a structured form exclusively using DSM-5 BED diagnosis and the severity criteria[1]. The progress record included a weekly curriculum that a physician, dietitian, psychologist administered, and the physiotherapist and the monthly individual meetings data.

The patients were planned to receive 80 hours of training in the group meetings by the physician, dietitian, psychologist, and physiotherapist. The total of 80 hours was divided into five sets, at the end of which BEDE forms were completed. Including the initial evaluation, patients were planned to report six BEDE forms. At the beginning of the training, at the end of the 4^{th}, 8^{th}, $12^{th,}$ and 20^{th} training. The depression scores of the cases were also assessed by using the Beck Depression Inventory in the beginning and at the end of the study.

- *Statistical Analysis*

Statistical Package for the Social Sciences (SPSS 23) software was used in data analysis. In the data obtained by counting, frequency was accepted as descriptive measures, and in variables obtained by measurement, mean, standard deviation, were accepted as descriptive measures. $p<0.05$ was considered statistically significant. Anova test and repeated measure analyzed tests was used for comparison between groups.

Results

The number of subjects participated in the study was 118. In table 2, the demographics and the clinical characteristics of the group, the means, and the standard deviations for

the variables at pre and post-treatment were presented.
During the training lasted for 20 weeks, including the initial evaluation, patients reported six BEDE forms, at the beginning of the training, at the end of the 4th, 8th, 12th, and 20th training.
The BEDE reports showed a significant improvement, with 65 of the patients scoring below the BED diagnosis at the final evaluation.
Scores from the Beck depression scale decreased statistically between the first and last evaluation. (Table 2)
Participants had lower body weights in the later weeks of the training program. (Table 3) Binge eating attacks also decreased statistically significantly. The severity scores formed according to the weekly eating attacks also decreased statistically significantly. (Table 3)

Discussion

The nonattendance rate was low compared to other studies indicating that approximately a third of patients referred to treatments do not use the services [6]. The low adherence rates were related to many reasons since for individuals with an eating disorder recovery expectations fluctuate[7]. A person may be in denial or having negative anticipations of the treatment results. Moreover, patients trapped in this disorder adapt to a condition of using it as a tool in coping with daily challenges. Although the burden of BED is agonizing, the patients perceive the episodes as a vital part of their presence. They often internalize the disorder, forming an unalterable circle, an almost untreatable condition[8].
Reports are indicating that pretreatment BE frequency rates have significant value in prediction and are strongly associated with BED treatment outcome[9]
In this study, 9.3% weight loss and a decrease in binge eating frequency were achieved within a 20-week program. Eldredge et al.[10] in their study, found that prolonging the duration of CBT up to 12 weeks in BED patients who did not respond to the first treatment increased its effectiveness of the treatment. In our study, the program was continued for 20 weeks, which showed increased effects similar to the literature. Brownley et al.[11] in a review of 26 studies found that individual or group behavioral therapies reduced binge eating and improved abstinence rates for up to 4 months following treatment which did not result in weight loss. They also stated that the effectiveness of drug therapy was higher. Fluoxetine, fluvoxamine, sertraline, citalopram, imipramine, topiramate, and sibutramine were used in drug-treated studies, and it was emphasized that binge eating attacks decreased in these drug-treated groups and weight loss was achieved in some groups.
Grilo et al.[12] studied comparing the groups given fluoxetine and behavior change with placebo, they stated that the CBT + fluoxetine group was more effective in weight loss and reducing the frequency of attacks compared to the other groups. Gorin et al.[13] in a study, showed a decrease in BMI, frequency of eating attacks, and depression scores in the Bed group, which received cognitive behavioral therapy and had a 12-week follow-up period. Wilfley et al.[14] comparing BED patients who underwent CBT with the group who received interpersonal psychotherapy (IPT), BMI decreased, while Binge eating increased slightly through follow-up but remained significantly below pretreatment levels.
Tunay et al.[15] conducted a targeted study of group interviews and healthy lifestyle changes in a group of obese women. In this study, successful weight loss was achieved in obese patients in primary care with similar training programs. Emphasis was placed on the continuity of the participants. Our study and similar ones have provided motivating results in terms of conducting similar interventional studies in a multidisciplinary manner by family physicians in our country. Undoubtedly, obesity remains as an important health problem for our country. In the MONICA[16] (monitoring trends and determinants in cardiovascular disease) study

conducted by the World Health Organization, which lasted 12 years, it was reported that there was an increase of 10-30% in the prevalence of obesity in 10 years.
Family physicians have a unique opportunity with their holistic approach and continuity of care in the treatment and prevention of obesity.
There were too many subjects showing no change. Aware of the limitations of the single-arm study, which restricts the possibility of observing a control group, it is not entirely correct to suggest that the training did not help the participants show little or no change. Considering the possibility that their condition would have worsened in time if untreated, there may be an opportunity to detect an additional positive effect of the training[17].

- *Limitations*

The study had several significant limitations. First, since there were no control groups, we could not show the difference between the effect of the treatment, a placebo effect, and the effect of natural history. The social events, regression to the mean, and spontaneous remission in the elapsed time were other significant limitations that should be addressed. Based on regression to the mean, it was known that patients who scored exceptionally on a variable on one evaluation would tend to score less exceptionally on the next one. Moreover, spontaneous remission is closely related and extremely important to psychological research and must be kept in mind in evaluating the outcome of such studies[18]. Besides, the Hawthorne effect should always be kept in mind, as it is generally defined as a change in the behavior of the participants in experimental or observational studies[19]. Finally, only the patients registered to a single center were studied, and therefore the sample size was relatively small. Therefore, the analyses might have been underpowered.

Conclusion

The current study showed that after twenty weeks of training the patients reported fewer episodes. The program could be considered efficacious for reducing the severity of binge eating episodes in obese patients seeking treatment. Additional research with more participants is required to verify our results and evaluate whether similar training programs could be appropriate for other related disorders.

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 Adana City Training and Research Hospital Ethical Committee on June 19, 2019, with reference number 483. The study is registered at (ClinicalTrials.gov-Identifier:NCT04127136).
http://www.clinicaltrials.gov
Informed consent was obtained from the parents or legal guardians.

References

1. American Psychiatric Association, American Psychiatric Association, editors. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Washington, D.C: American Psychiatric Association; 2013. 947 p. doi: 10.1176/appi.books.9780890425596
2. Qian J, Hu Q, Wan Y, et al. Prevalence of eating disorders in the general population: a systematic review. Shanghai Arch Psychiatry. 2013;25:212-23.
3. Bulik CM, Kleiman SC, Yilmaz Z. Genetic epidemiology of eating disorders: Curr Opin Psychiatry. 2016;29:383-8. doi: 10.1097/YCO.0000000000000275
4. Dakanalis A, Riva G, Serino S, et al. Classifying Adults with Binge Eating Disorder Based on Se-

verity Levels: Severity of Binge Eating Disorder. Eur Eat Disord Rev. 2017;25:268-74.
doi: 10.1002/erv.2518
5. Linardon J. Meta-analysis of the effects of cognitive-behavioral therapy on the core eating disorder maintaining mechanisms: implications for mechanisms of therapeutic change. Cogn Behav Ther. 2018;47:107-25.
doi: 10.1080/16506073.2018.1427785
6. Waller G, Schmidt U, Treasure J, et al. Problems across care pathways in specialist adult eating disorder services. Psychiatr Bull. 2009;33:26-9.
doi: 10.1192/pb.bp.107.018325
7. Leavey G, Vallianatou C, Johnson-Sabine E, et al. Psychosocial barriers to engagement with an eating disorder service: a qualitative analysis of failure to attend. Eat Disord. 2011;19:425-40.
doi: 10.1080/10640266.2011.609096
8. Eaton CM. Eating Disorder Recovery: A Metaethnography. J Am Psychiatr Nurses Assoc. 2019;107839031984910.
doi: 10.1177/1078390319849106
9. Vall E, Wade TD. Predictors of treatment outcome in individuals with eating disorders: A systematic review and meta-analysis: Erratum. Int J Eat Disord. 2016;49:432-3.
doi: 10.1002/eat.22518
10. Eldredge KL, Agras SW, Arnow B, et al. The effects of extending cognitive-behavioral therapy for binge eating disorder among initial treatment nonresponders. International Journal of Eating Disorders. 1997;21(4):347-52.
doi: 10.1002/(SICI)1098-108X(1997)21:4<-347::AID-EAT7>3.0.CO;2-O
11. Brownley KA, Berkman ND, Sedway JA, et al. Binge eating disorder treatment: a systematic review of randomized controlled trials. International Journal of Eating Disorders. 2007;40(4):337-48.
doi: 10.1002/eat.20370
12. Grilo CM, Masheb RM, Wilson GT. Efficacy of cognitive behavioral therapy and fluoxetine for the treatment of binge eating disorder: A randomized double-blind placebo-controlled comparison. Biol Psychiatry 2005;57:301-309.
doi: 10.1016/j.biopsych.2004.11.002
13. Gorin A, Le Grange D, Stone A. Effectiveness of spouse involvement in cognitive behavioral therapy for binge eating disorder. Int J Eat Disord 2003;33:421-433.
doi: 10.1002/eat.10152
14. Wilfley DE, Welch RR, Stein RI, et al. A randomized comparison of group cognitive-behavioral therapy and group interpersonal psychotherapy for the treatment of overweight individuals with binge-eating disorder. Arch Gen Psychiatry. 2002;59:713-21.
doi: 10.1001/archpsyc.59.8.713
15. Tunay M, Kurdak H, Özcan S, et al. Family physician-led group visits for lifestyle modification in women with weight problems: a pilot intervention and follow-up study. Obesity Facts, 2018;11:1-14.
doi: 10.1159/000486133
16. Silventoinen K, Sans S, Tolonen H,et al. Trends in obesity and energy supply in the WHO MONICA Project. International journal of obesity.2004;28(5):710-8.
doi: 10.1038/sj.ijo.0802614
17. Evans SR. Clinical trial structures. J Exp Stroke Transl Med. 2010;3:8-18.
doi: 10.6030/1939-067X-3.1.8
18. Price P, Jhangiani R, Chiang I. Research Methods in Psychology. 2nd ed. BCCampus; 2015.

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HİDATİTORAKSIN CERRAHİ TEDAVİSİ: 24 HASTAYI KAPSAYAN RETROSPEKTİF BİR ÇALIŞMA

SURGICAL TREATMENT OF HYDATITHORAX: A RETROSPECTIVE STUDY OF 24 PATIENTS

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Abstract

Aim: Intrapleural perforation of a hydatid cyst can lead to serious complications such as pleural effusion, pneumothorax, empyema, secondary pleural hydatid disease, acute respiratory failure, and anaphylactic shock. Our aim in this study is to present the clinical features of the patients we operated for hydatid cyst perforated into the pleural space and to share our surgical experience.

Methods: Between January 2010 and December 2020, 24 patients who applied to our clinic and were operated on due to perforation of the pulmonary hydatid cyst into the pleural space were retrospectively analyzed. Age, gender, symptoms, size and location of the hydatid cyst, surgical procedure, postoperative complications, chest tube length of stay and hospitalization duration were reviewed and noted in the patient files.

Results: The mean age of the patients was 36.4 (18-67) years. Of the patients, 14 (58%) were male and 10 (41%) were female. There was 7.4 (0-19) days between the onset of symptoms and admission to the hospital. While 19 (79%) patients had pleural effusion, 5 (20%) had hydropneumothorax. Cystotomy and capitonnage were performed in 23 (95%) patients, segmentectomy in 1 (4.1%) and decortication in 10 (41%) patients. Postoperative complications were seen in 4 (16%) patients.

Conclusions: Perforated hydatid cyst should not be forgotten in the differential diagnosis of pleural effusion, pneumothorax and empyema. Preoperative medical treatment should be performed in patients with pneumonia due to perforated hydatid cyst, and in patients with massive pleural effusion, significant pneumothorax or empyema, after adequate chest tube drainage, the operation should be performed without delay.

Keywords: Hydatid cyst, intrapleural perforation, surgery

Öz

Amaç: Hidatik kistin plevral aralığa perforasyonu plevral efüzyon, pnömotoraks, ampiyem, sekonder plevral hidatik hastalık, akut solunum yetmezliği ve anaflaktik şok gibi ciddi komplikasyonlara yol açabilir. Bu çalışmadaki amacımız plevral aralığa perfore olan hidatik kist nedeniyle opere ettiğimiz hastaların klinik özelliklerini sunmak ve cerrahi deneyimlerimizi paylaşmaktır.

Yöntemler: 2010 Ocak- 2020 Aralık tarihleri arasında akciğer hidatik kistinin plevral aralığa perfore olması sonucu kliniğimize başvuran ve opere edilen 24 hasta geriye dönük olarak incelendi. Hastaların yaş, cinsiyet, semptom, hidatik kistin büyüklüğü ve yeri, uygulanan cerrahi işlem, postoperatif komplikasyonlar, göğüs tüpü kalış süresi ve hastane yatış süresi hasta dosyaları incelenerek not edildi.

Bulgular: Hastaların ortalama yaşları 36,4 (18-67) idi. Hastaların 14'u (%58) erkek, 10'u (%41) ise bayan idi. Semptomların başlaması ile hastaneye başvuru arasında 7,4 (0-19) gün vardı. Hastaların 19'unda (%79) plevral efüzyon var iken, 5'inde (%20) hidropnömotoraks var idi. Hastaların 23'ünde (%95) kistotomi ve kapitonaj, 1'inde (%4,1) segmentektomi, 10'unde (%41) ampiyem nedeniyle dekortikasyon uygulandı. Postoperatif komplikasyon 4 (%16) hastada görüldü.

Sonuç: Plevral efüzyon, pnömotoraks ve ampiyemin ayırıcı tanısında perfore hidatik kist unutulmamalıdır. Perfore hidatik kiste bağlı pnömoni olan hastalarda preoperatif medikal tedavi, masif plevral efüzyon, belirgin pnömotoraks veya ampiyem olan hastalarda ise yeterli göğüs tüpü drenajı sonrası operasyon geciktirilmeden yapılmalıdır.

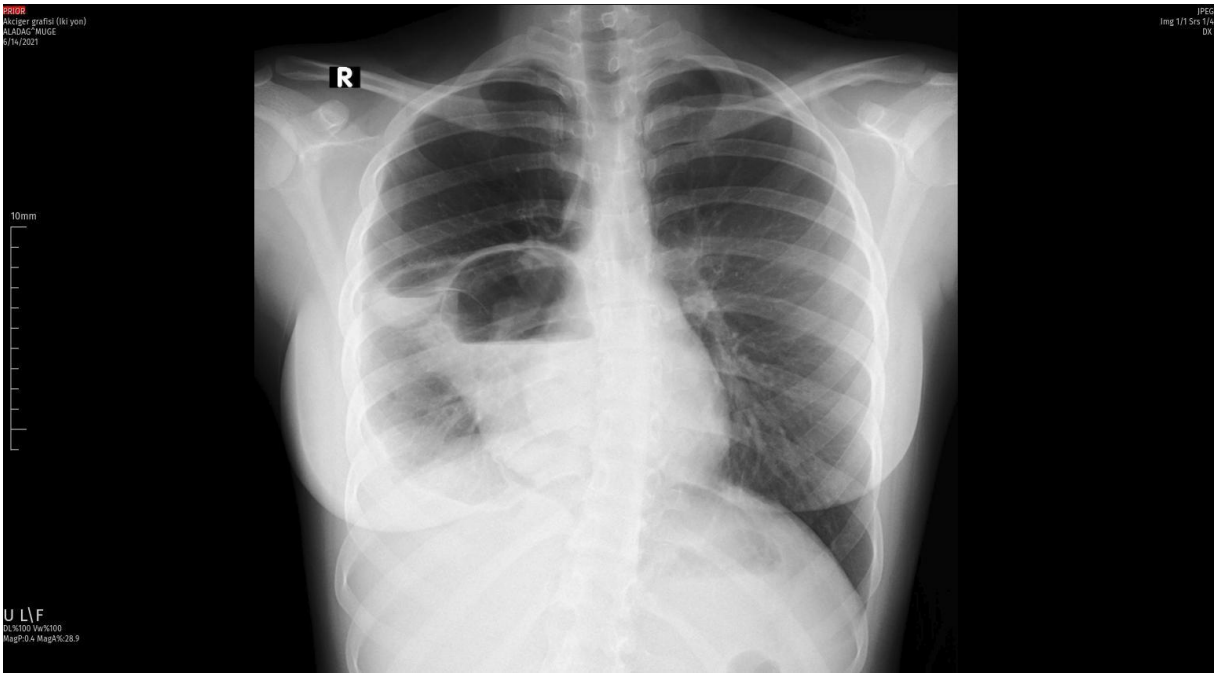
Anahtar Kelimeler: Hidatik kist, intraplevral perforasyon, cerrahi

Giriş

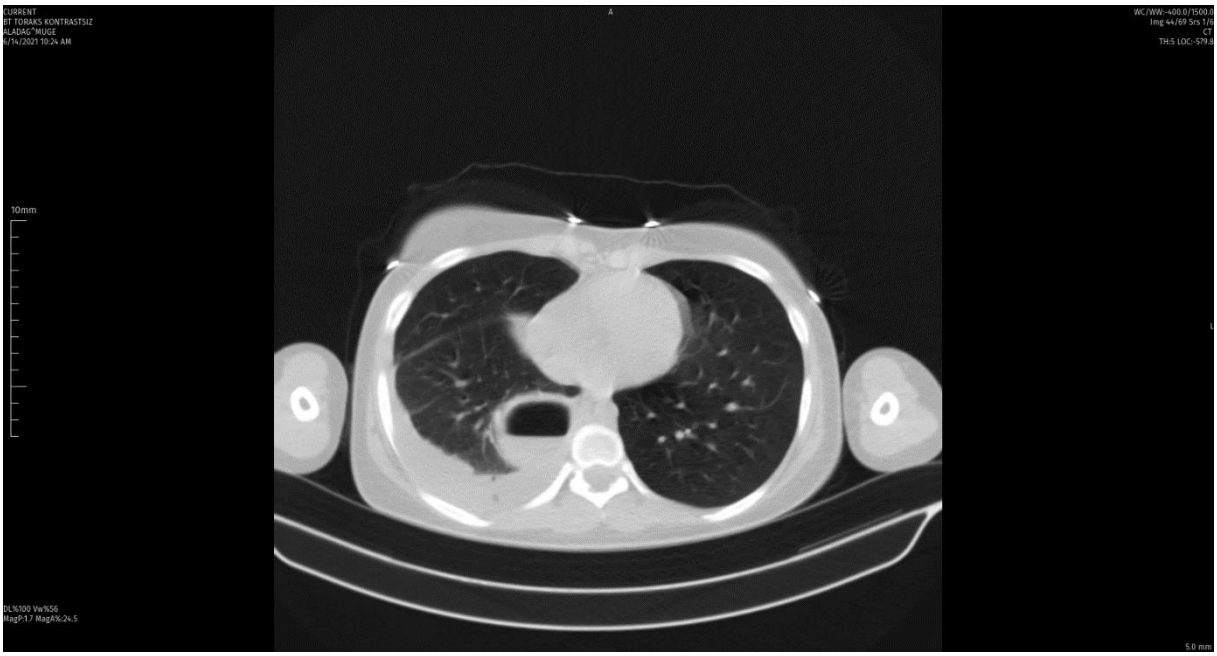
Akciğer hidatik kistleri çevre parankimde enfeksiyon, mediastinal yapılara bası, bronşial ağaca veya plevral aralığa perforasyon gibi komplikasyonlara yol açabilir[1,2]. Plevral aralığa perforasyon plevral efüzyon, pnömotoraks, ampiyem, sekonder plevral hidatik hastalık, akut solunum yetmezliği ve anaflaktik şok gibi ciddi komplikasyonlara yol açabilir. Akciğer hidatik kisti olan hastada ani başlayan göğüs yan ağrısı, öksürük, nefes darlığı ve ateş kistin plevral aralığa perfore olduğunun belirtisi olabilir. Rüptüre olan hidatik kistlerde postoperatif morbidite ve mortalite oranları intakt olan hidatik kistlere oranla daha yüksektir[3,4]. Bu çalışmadaki amacımız plevral aralığa perfore olan hidatik kist nedeniyle opere ettiğimiz hastaların klinik özelliklerini sunmak ve cerrahi deneyimlerimizi paylaşmaktır.

Materyal ve Metot

2010 Ocak- 2020 Aralık tarihleri arasında akciğer hidatik kistinin plevral aralığa perfore olması sonucu kliniğimize başvuran ve opere edilen 24 hasta geriye dönük olarak incelendi. Hidatik kistin perfore olduğunu düşündüren radyolojik bulguların ve hidrotoraks veya hidropnömotoraksın eşlik ettiği 18 yaşından büyük hastalar çalışmaya dahil edildi. Hasta bilgileri; arşiv dosyaları ve otomasyon sistemindeki toraks bilgisayarlı tomografi (BT) raporları, ameliyat notları ve patoloji raporlarından elde edildi. Hastaların yaş, cinsiyet, semptom, hidatik kistin büyüklüğü ve yeri, uygulanan cerrahi işlem, postoperatif komplikasyonlar, göğüs tüpü kalış süresi ve hastane yatış süresi hasta dosyaları incelenerek not edildi.



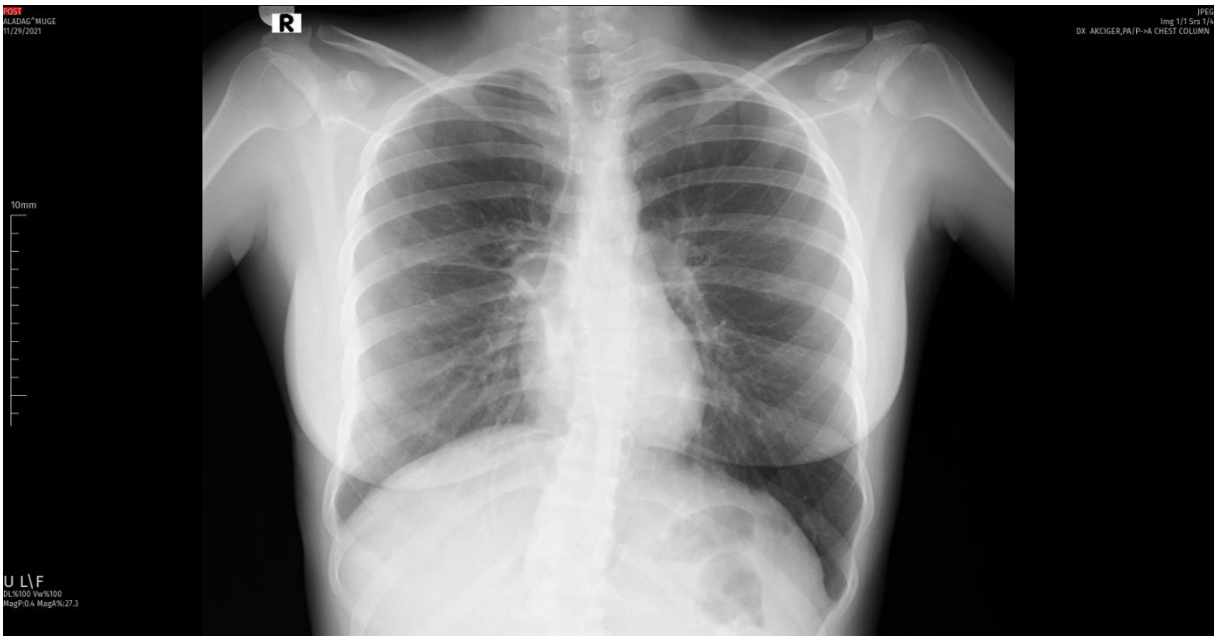
Resim 1. PA akciğer grafisinde hidatik kistin intraplevral perfore olması sonucu plevral efüzyon



Resim 2. Toraks bilgisayarlı tomografide perfore hidatik kist ve plevral efüzyon

Tüm hastalar direk PA akciğer grafisi ve toraks BT'ye sahipti. Tüm hastaların radyolojik incelemelerinde plevral efüzyon vardı. Hidatitoraks; kistin radyolojik olarak perfore olduğunu gösteren radyolojik bulguların varlığıyla birlikte hidrotoraks veya hidropnömotoraks varlığı olarak kabul edildi (Resim 1, 2 ve 3).

Kas koruyucu torakotomi ile kistotomi ve kapitonajı içeren parankim koruyucu cerrahi yöntem tercih edildi. Tüm hastalarda cerrahi işlem sonunda en az 3 defa toraks kavitesi betadinli izotonik solüsyon ile yıkandı. Tüm hastalarda yatış gününde Albendazol (10 mg/kg/gün) başlandı ve postoperatif 3 ay devam edildi. Tedavi sırasında hastaların karaciğer fonksiyon testleri yakından takip edildi.



Resim 3. Kistotomi, kapitonaj ve dekortikasyon sonrası PA akciğer grafisi

Tablo 1. Klinik ve radyolojik bulgular

Yaş (yıl)	36,4 (18-67)
Cinsiyet (Erkek/Kadın)	14 (%58) / 10 (%42)
Hastaneye başvuru süresi (gün)	7,4 (0-19)
<5	10 (%42)
>5	14 (%58)
Semptom	
Göğüs Ağrısı	19 (%79)
Öksürük	17 (%70)
Nefes darlığı	13 (%54)
Hemoptizi	3 (%12)
Ateş	2 (%8)
Kistin büyüklüğü (cm)	7.2 (4-12)
Kistin Bulunduğu lob	
Sağ alt lob	9 (%37)
Sol alt lob	6 (%25)
Sağ üst lob	4 (%16)
Sol üst lob	3 (%12)
Sağ orta lob	2 (%8)
Postoperatif komplikasyon	
Uzamış hava kaçağı	2 (%8)
Rezidü kavite	1 (%4)
Yara yeri enfeksiyonu	1 (%4)
Göğüs tüpü drenaj süresi (gün)	5.9 (4-12)
Hastane yatış süresi (gün)	7.8 (5-16)
Taburculuk sonrası takip süresi (ay)	21 (9-42)

Bulgular

Hastaların ortalama yaşları 36,4 (18-67) idi. Hastaların 14'u (%58) erkek, 10'u (%41) ise kadındı. Semptomların başlaması ile hastaneye başvuru arasında 7,4 (0-19) gün vardı. Beş günden az sürede başvuran hastaların sayısı 10 (%41) iken, 5 gün ve daha fazla sürede başvuran hastaların sayısı 14 (%58) gün idi. Hastaların 19'unda (%79) göğüs ağrısı, 17'sinde (%70) öksürük, 13'ünde (%54) nefes darlığı, 3'ünde (%12) hemoptizi ve 2'sinde (%8,3) ateş şikâyeti mevcut idi. Asemptomatik hasta yok idi (Tablo 1). Hidatik kistlerin büyüklüğü ortalama 7,2 (4-12) cm idi. Hidatik kistlerin 16'sı (%66) sağ tarafta iken, 8'i (%33) sol tarafta idi. Dokuzu (%37) sağ alt lopda, 6'sı (%25) sol alt lobda, 4'ü (%16) sağ üst lobda, 3'ü (%12) sol üst lobda, 2'si (%8,3) ise sağ orta lobda idi. Hastaların 19'unda (%79) plevral efüzyon var iken, 5'inde (%20) hidropnömotoraks var idi. Hastaların 23'ünde (%95) kistotomi ve kapitonaj, 1'inde (%4,1) segmentektomi, 10'unda (%41) dekortikasyon uygulandı.

Postoperatif komplikasyon 4 (%16) hastada görüldü. Uzamış hava kaçağı 2 hastada görülürken, 1 hastada rezidü kaviter lezyon saptandı. Ampiyeme sahip ve dekortikasyon uygulanan 1 hastada yara yeri enfeksiyonu gelişti. Uzamış hava kaçağı olan hastalarda medikal tedavi, gomko ile intermittan negatif basınç uygulanması ve pulmoner fizyoterapi ile 8. ve 12. günde hava kaçağı tedavi edildi. Rezidü kaviter lezyonu olan hasta taburcu olduktan sonraki takiplerinde kavitede küçülme olduğundan cerrahi bir işlem uygulanmadı. Yara yeri enfeksiyonu pansuman ve antibiyoterapi ile tedavi edildi. Postoperatif mortalite görülmedi. Göğüs tüpü drenaj süresi ortalama 5,9 (4-12) gün idi. Ortalama hastanede yatış süresi 7,8 (5-16) gün idi. Ortalama takip süresi 21 (9-42) ay idi. Takip sırasında hiçbir hastada intraplevral nüks saptanmadı.

Tartışma

Pulmoner hidatik kistlerin intraplevral rüptürü nispeten nadirdir, tüm akciğer hidatik kistlerinin %1,5 ile %6'sında görülür (1,5-7). Kistin plevral boşluğa perforasyonu spontan pnömotoraks, hidropnömotoraks, tansiyon pnömotoraks, ampiyem, plevral kalınlaşma, sekonder plevral hidatik hastalık ve hepatoplevral veya hepatobronşiyal fistüllere neden olabilir[4,8-10]. Ayrıca intraplevral rüptür sonucu ortaya çıkan plevral efüzyon, hidatik kistin tüberküloz, akciğer kanseri ve akciğer enfeksiyonları gibi hastalıklarla karışmasına neden olmakta, ayırıcı tanıda zorluklara neden olabilmektedir. Rüptür çoğunlukla yüzeyel ve büyük çaplı hidatik kistlerde görülürken, bazen travmaya veya tanı amaçlı yapılan ince iğne aspirasyonuna bağlı da görülebilir[1,11,12]. Bazı klinisyenler cerrahiye bağlı travmadan kaçınmak için tıbbi tedaviyi alternatif bir tedavi olarak görebilmektedir[13,15]. Tıbbi tedavinin kendisi özellikle büyük kistlerde kütiküler membranın gerilme gücünü azaltarak perforasyona yol açabilmektedir[16]. Perfore hidatik kistin postoperatif morbidite ve

mortalitesi intakt kistlere göre çok daha fazla olduğundan, cerrahi ile çıkarılabilecek bir hidatik kist için medikal tedavi verilmesinin ciddi komplikasyonlara yol açabileceği unutulmamalıdır.

Toraks BT, akciğer hidatik kist hastalığının tanısını koymada ve kistin yerini belirlemede genellikle başarılıdır. Akciğerdeki perfore hidatik kist ile ilgili tanısal BT bulguları, perikistik tabakadan ayrılmış veya kollabe olmuş bir endokist membranı ve buna eşlik eden hidrotoraks veya hidropnömotorakstır. Plevral boşlukta yapışıklıklar yoksa, perforasyonu takiben pnömotoraks veya hidropnömotoraks gelişebilir ve hidatik kist içeriği tüm plevral boşluğa yayılabilir. Plevral boşlukta yapışıklıklar varsa, perforasyonu takiben yayılma daha az olacaktır, yapışıklıkların koruyucu etkisi ile sınırlı miktarda plevral efüzyon ortaya çıkabilir. Hastalarımızın sadece %20'sinde pnömotoraks var iken, tümünde perforasyona plevral efüzyon eşlik etti. Geç tanı konan hastalarda plevral efüzyon enfekte olarak ampiyem poşuna ve akciğerde atelektaziye neden olacaktır[7,17]. Geç başvuran 14 hastamızdan 10'unda ampiyem vardı ve bunlarda cerrahi sırasında dekortikasyon uygulandı.

Plevral aralığa perforasyon sonrası belirgin pnömotoraks, masif plevral efüzyon veya ciddi plevral ampiyemi olan hastalarda, göğüs tüpü takılarak tıbbi tedavi uygulanılması ve ardından hasta stabil hale gelir gelmez torakotominin yapılması önerilmektedir[11,18]. Hastalarımızda operasyon öncesi 4 hastada masif plevral efüzyon ve 3 hastada belirgin pnömotoraks nedeniyle göğüs tüpü uygulandı. Masif plevral efüzyon nedeniyle göğüs tüpü uygulanan hastalardan 3'ü ampiyem ile uyumlu idi. Göğüs tüpü drenajı ve medikal tedavi sonrası klinik olarak stabil hale gelen hastalar opere edildi. Pnömotoraks nedeniyle göğüs tüpü uygulanan hastaların 1'inde radyolojik olarak perfore hidatik kist düşünülerek 3 gün sonra opere edildi. Pnömotoraks nedeniyle göğüs tüpü uygulanan 2 hasta ise radyolojik olarak hidatik kist düşünmediğimizden 7 gün sonunda göğüs tüpünde hava kaçağının devam etmesi üzerine uzamış hava kaçağı olarak kabul edilerek opere edildi. Operasyon sırasında perfore hidatik kist nedeniyle pnömotoraks geliştiği anlaşıldı.

Perfore hidatik kistlerde çevre dokunun kist sıvısına bağlı olarak kimyasal irritasyonu veya çevre dokunun enfeksiyonu sonucu konsolide veya atelektatik alanlar olabilmektedir. Kliniğimizde perfore veya komplike olan hidatik kistlerde operasyon öncesi 5 gün albendazol ve antibiyotik tedavisi vermekteyiz. Bu tedavinin hem paraziter hastalığın yayılmasını engellemede hem de çevre parankim dokusunun iyileşmesine ve akciğerin postoperatif daha kolay ekspanse olmasına yardımcı olacağını düşünüyoruz. Bununla birlikte perfore hidatik kistlerde ameliyatın 10 gün veya daha fazla gecikmesi, postoperatif bronkoplevral fistül ve/veya ampiyemin gelişmesinde bir risk faktörü olduğu bildirilmiştir[19]. Bu nedenle klinik olarak stabil hale gelen hastaların çok bekletilmeden opere edilmesinin doğru bir yaklaşım olacağını düşünmekteyiz.

Perfore hidatik kistlerde postoperatif Albendazol tedavisi rutin olarak verilmesi önerilmekte ancak ne kadar süre verilmesi hakkında fikir birliği yoktur. Yaygın görüş antihelmintik tedavinin 3 ay süreyle verilmesidir[8,19-22]. Kabiri ve arkadaşları özellikle plevral aralıkta kız veziküllerinin görüldüğü yaygın yayılımın olabileceği hastalarda antihelmintik tedavinin 6 ay süreyle verilmesini önermişlerdir[23]. Biz hastalarımızda 3 ay süreyle antihelmintik tedavi verdik, takiplerde hiçbir hastamızda plevral aralıkta nüks saptamadık. Ayrıca cerrahi işlem sonunda en az 3 defa toraks kavitesinin betadinli izotonik solüsyon ile yıkanmasının nüks gelişimini engellemede önemli bir role sahip olduğunu düşünüyoruz.

Sonuç

Sonuç olarak plevral efüzyon, pnömotoraks ve ampiyemin ayırıcı tanısında perfore hidatik kist unutulmamalıdır. Perfore hidatik kiste bağlı pnömoni olan hastalarda preoperatif medikal tedavi, masif plevral efüzyon, belirgin pnömotoraks veya ampiyem olan hastalarda ise yeterli göğüs tüpü drenajı

sonrası operasyon geciktirilmeden yapılmalıdır. Plevral aralığa perfore olan hidatik kistlerde postoperatif 3 ay antihelmintik tedavi nüksü önlemede önemli role sahiptir.

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Kaynaklar

1. Thameur H, Chenik S, Abdelmoulah S, Bey M, et al. Thoracic hydatidosis: Areview of 1619 cases. Rev Pneumol Clin, 2000; 56: 7-15.
2. Aarons BJ. Thoracic surgery of hydatid disease. World J Surg, 1999; 23: 1105-9. doi:10.1007/s002689900631
3. Balci AE, Eren N, Eren S, et al. Ruptured hydatid cysts of the lung in children: clinical review and results of surgery. Ann Thorac Surg. 2002; 74: 889-92. doi:10.1016/S0003-4975(02)03785-2
4. Fındık G, Aydogdu K, Hazer S, et al. The management of postoperative complications in childhood pulmonary hydatid cysts. Turk J Thorac Cardiovasc Surg. 2012; 20(4): 850-6. doi:10.5606/tgkdc.dergisi.2012.165
5. Kilani T, Ben Safta Z, Jamoussi M, et al. Pleural complications of hydatid cyst of the lung. Apropos of 16 cases. Ann Chir, 1988; 42: 145-8.
6. Islambekov E, Tishchukov AA, Ismailov DA. Treatment of rupture of pulmonary echinococcosis to the pleural cavity. Grud Serdechnososudistia Khir, 1990; 3: 34-7
7. Solak H, Ceran S, Ozpinar C, et al. Lung hydatid cyst rupture and its surgery. Indian J Med Sci, 1994; 48: 155-7.
8. Sayır F, Cobanoglu U, Sehitogulları A. Surgical treatment of pulmonary hydatid cysts, which perforated to pleura. Eurasian J Med. 2012; 44(2):79-83. doi:10.5152/eajm.2012.19
9. Kiral H, Evman S, Tezel C, et al. Pulmonary resection in the treatment of life-threatening hemoptysis. Ann Thorac Cardiovasc Surg. 2015; 21(2): 125-31. doi:10.5761/atcs.oa.14-00164
10. Demirhan R, Onan B, Kıral H, Yalcınkaya I. Surgical treatment of giant hydatid cysts in childhood. Turk J Thorac Cardiovasc Surg. 2010; 18(2): 121-5.
11. Ramos G, Duque JL, Yustem M, et al. Intrapleural rupture of the pulmonary hytatid cyst: A propos de 15 observation. Ann Chir, 1983; 37: 114-6.
12. Ozer Z, Cetin M, Kahraman C. Pleural involvement by hydatid cysts of the lung. Thorac Cardiovasc Surg, 1985; 33: 103-5. doi:10.1055/s-2007-1014097
13. Aydogdu B, Sander S, Demirali O, et al. Treatment of spontaneous rupture of lung hydatid cysts into a bronchus in children. J Pediatr Surg. 2015; 50: 1481-3. doi:10.1016/j.jpedsurg.2015.01.010
14. Simon D, Koegelenberg CFN, Sinha Roy S, Allwood BW, Irusen EM. Can large hydatid cysts resolve with medical treatment alone? Respiration. 2016; 92: 428-31. doi:10.1159/000451032
15. Keshmiri M, Baharvahdat H, Fattahi SH, et al. A placebo controlled study of albendazole in the treatment of pulmonary echinococcosis. Eur Respir J. 1999; 14(3): 503-7. doi:10.1034/j.1399-3003.1999.14c05.x
16. Usluer O, Kaya SO, Samancilar O, Ceylan KC, Gursoy S. The effect of preoperative albendazole treatment on the cuticular membranes of the pulmonary hydatid cysts. Should it be administered preoperatively? Kardiochirurgia Torakochirurgia Pol. 2014; 11(1): 26-9. doi:10.5114/kitp.2014.41926
17. Oto O, Silistreli E, Erturk M, Maltepe F. Thoracoscopic guided minimally invasive surgery for giant hydatic cyst. Eur J Cardiothorac Surg, 1999; 16 : 494-5.
18. Aggrarwal P, Wali JP. Albendazole in the treatment of pulmonary echinococcosis. Thorax, 1991; 46: 599-600. doi:10.1136/thx.46.8.599
19. Cernay J, Bensenouci A, Boukhelal H, Zaouchea A, Grangaud JP. The rupture of the pleura: a serious complication of hydatid cyst of the lung in children. Rev Fr Mal Resp, 1979; 7: 45-7.
20. Hasdıraz L, Onal O, Oguzkaya F. Bilateral staged thoracotomy for multiple lung hydatidosis. J Cardiothorac Surg 2013; 8: 121. doi:10.1186/1749-8090-8-121
21. Topçu S, Kurul IC, Tastepe I, et al. Surgical treatment of pulmonary hydatid cysts in children. J Thorac Cardiovasc Surg 2000; 120: 1097-101. doi:10.1067/mtc.2000.110181
22. Cangir AK, Sahin E, Enön S, et al. Surgical treatment of pulmonary hydatid cysts in children. J Pediatr Surg 2001; 36: 917-20. doi:10.1053/jpsu.2001.23974

23. Kabiri el-H, Caidi M, Al Aziz S, El Maslout A, Benosman A. Surgical Treatment of Hydatidothorax Series of 79 Cases. Acta chir belg, 2003; 103: 401-4.
doi:10.1080/00015458.2003.11679452

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Çukurova Anestezi ve Cerrahi Bilimler Dergisi
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ASSESSMENT OF GLEASON SCORE CONCORDANCE BETWEEN PROSTATE BIOPSY AND RADICAL PROSTATECTOMY

PROSTAT BİYOPSİ VE RADİKAL PROSTATEKTOMİDE GLEASON SKOR KONKORDANSININ DEĞERLENDİRİLMESİ

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Abstract

Aim: Prostate cancer is being diagnosed and graded by examining needle biopsies. As needle biopsies may represent the low percentage of general tumor histology, downgrading or upgrading can cause problems in radical prostatectomy (RP) specimens. Our aim in this study was to put forth the concordance between needle biopsy and RP Gleason scores.

Methods: The biopsy pathology results, and post-RP pathology results of 112 patients diagnosed as prostate cancer and underwent RP were revised and the concordance of the biopsy and RP Gleason score was analyzed by kappa statistics in addition to percentages of downgrading or upgrading rates.

Results: The mean age, and PSA values of the patients were 64,4 (±6,2) years, and 11,7 (±9,2) ng/mL, respectively. There was a moderate agreement between biopsy and prostatectomy gleason scores(κ=0,452) and between Gleason groups

Conclusions It is important for the urologists to be aware of the variety of Gleason score between biopsy results and prostatectomy specimens as needle biopsies represent small areas of tumors.

Keywords: Radical prostatectomy, Gleason score, prostate cancer.

Öz

Amaç: Prostat kanseri, iğne biyopsileri incelenerek teşhis edilmekte ve derecelendirilmektedir. İğne biyopsileri, genel tümör histolojisinin düşük yüzdelik bir alanını temsil edebileceğinden, Gleason derecesinin düşüşü veya artışı radikal prostatektomi (RP) numunelerinde sorunlara neden olabilir. Bu çalışmadaki amacımız iğne biyopsisi ile RP Gleason skorları arasındaki uyumu ortaya koymaktır.

Yöntemler: Prostat kanseri tanısı konan ve RP uygulanan 112 hastanın biyopsi patoloji sonuçları ve RP sonrası patoloji sonuçları revize edildi ve biyopsi ve RP Gleason skorunun uyumu, derece düşüş veya artış oranlarının yüzdelerine ek olarak kappa istatistikleri ile analiz edildi.

Bulgular: Hastaların yaş ortalaması ve PSA değerleri sırasıyla 64,4 (±6,2) yıl ve 11,7 (±9,2) ng/mL idi. Biyopsi ve prostatektomi gleason skorları arasında (κ=0,452) ve Gleason grupları arasında orta derecede bir uyum vardı

Sonuç: İğne biyopsileri küçük tümör alanlarını temsil ettiğinden, ürologların biyopsi sonuçları ile prostatektomi örnekleri arasındaki Gleason skorunun çeşitliliğinin farkında olmaları önemlidir.

Anahtar Kelimeler: Radikal prostatektomi, Gleason skoru, prostat kanseri

Introduction

Prostate cancer is the most common cancer in men and also the second most common reason of cancer related deaths[1]. PSA level is most commonly used for determining patients to whom needle biopsy should be performed. Although the cut-off values of PSA may change between different centers the general approach is to biopsy patients with a minimum PSA level of 4 ng/ml[2].
Gleason grading is the most used grading system for prostate cancer which is revised by WHO in 2016 (3,4). Gleason grading system which was recently modified by WHO is a grading system used for prostate cancer. Gleason score is based on the sum of the most common primary and secondary histological patterns however the new grading system has 5 groups indicating score 3+3 as grade group1, 3+4 as grade group2, 4+3 as grade group 3, 4+4 as grade group 4, and score >8 as grade group 5[3].
As needle biopsies may represent the low percentage of general tumor histology, downgrading or upgrading can cause problems in radical prostatectomy (RP) specimens. The concordance of biopsy and RP Gleason scores (GS) has been researched by different studies with results of 41.3-63% (5-8). GS upgrading is more commonly observed than downgrading. The change of GS after RP, especially upgrading of GS, effect the treatment option, since some patients should have been avoided from surgical procedures if patients found to have high-risk adenocarcinoma at biopsy
GS is one of the most important factors in determining optimal treatment and predicting prognosis for prostate cancer. Our aim in this study was to put forth the concordance between needle biopsy and RP Gleason scores.

Materials and Methods

A total of 112 patients with a diagnosis of prostate cancer by needle biopsy and underwent RP between 2013 and 2017 in our clinic were included in the study. The demographic, pre-biopsy PSA values, biopsy pathology results, and post-RP pathology results were noted from hospital records.
The patients with elevated PSA levels over 2,5 ng/mL, and/or suspicious digital rectal examination were recommended to undergone transrectal ultrasound guided prostate biopsy. All the prostate biopsies were performed in the lateral decubitus position under local anesthesia with peri-prostatic nerve block using 1% or 2% lidocaine, and 18-gauge, 200 mm biopsy needles were used to take tissue samples. The biopsy and RP specimens were evaluated and examined by the same uropathologist. All the specimens were scored according to the 2005 and 2014 ISUP Gleason grading system.
We divided the patients according to the biopsy gleason scores in three groups: low, intermediate, and high-risk groups consisted of the patients with gleason score 6, 7, and >7, respectively.
Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) for windows (Version 18.0; SPSS Inc., Chicago, IL) software. The concordance between the biopsy and prostatectomy results was analyzed with weighted kappa method, and the chi-square test and Fisher's exact tests were used for categorical variables.

Results

A total of 112 patients were included in the study. The mean age, and PSA values of the patients were 64.4 (±6.2) years, and 11.7 (±9.2) ng/mL, respectively.
Based on the biopsy results; gleason score was <7 for 57 (50.9%) of the patients, 7 for 44 (39.3%) patients, and >7 for 11 (9.8%) of the patients. On the other hand, gleason score was <7 for 42(37.5%) patients, 7 for 60 (53.8%) patients, and >7 for 10(8.9%) of the patients according to prostatectomy reports. (Table 1).

Table 1. Biopsy/Radical prostatectomy total Gleason score

Gleason score	Number of cases (n)	Percentage (%)
6	57 / 42	50,9 / 37,5
7	44 / 60	39,3 / 53,6
8	6 / 4	5,4 / 3,6
9	5 / 6	4,5 / 5,4
Total	112/112	100,0 /100,0

Table 2. Biopsy/Radical prostatectomy Gleason Grade Groups

Gleason grade group	Number of cases (n)	Percentage (%)
1	57 /42	50,9 / 37,5
2	34 /46	30,4 / 41,1
3	9 /14	8,0 / 12,5
4	7 /4	6,3 / 3,6
5	5 /6	4,5 / 5,4
Total	112/112	100,0/100,0

Gleason score 3+3 was the most common result with 50.9%, and 3+4 was the second most common with 30.5% according to biopsy. In contrast, gleason score 4+3 was the most common result with 41.1%, and 3+3 was the second most common with 37.5% in the prostatectomy reports. (Table 2)

While 13 (11.6%) patients' score were downgraded, 70 (62.5%) of the patients remained within the same gleason score, and 29 (25.9%) of them were upgraded.

We divided the patients according to the biopsy gleason scores in to three groups: low, intermediate, and high-risk groups consisted of the patients with gleason score 6. 7, and >7, respectively. 32(72.7%) of the patients within the intermediate group stayed in the same group, and that ratio was the highest amongst the three groups (Table 3). The difference between the groups were statistically significant (p=0.00). Also, there was a moderate agreement between biopsy and prostatectomy gleason scores(κ=0.452) and between Gleason groups (κ=0.437).

Discussion

The most used grading system for prostate cancer is the Gleason scoring system, which was recently revised to grade grouping[3,4]. GS is also one of the most important prognostic indicators of prognosis. However, GS may vary between needle biopsy and RP specimens. Various researches focused on the possibility of discordance of GS after RP compared with biopsy[9,10].

The discordance between GS of biopsies and RP specimens has been the focus of numerous studies with different results in the literature. San Francisco et al reported a concordance rate of 67% with a downgrading and upgrading percentages of 11% and 22%, respectively[11]. However, the discordance rate changes study to study. Cookson et al found concordance rate as 31% in their study and upgrading rate was 54% whilst downgrading rate was 15%[12].

Upgrading was more common than downgrading according to many studies. Tilki et al., reported that GS upgrades in approximately one third of patients at RP than at biopsy[13]. Kuroiwa et al. and Reis et al. reported upgrading and downgrading rates as 21.9 and 47.4%; 5-20.7%, respectively[6,7]. In one of the most recent studies, Öztürk et al. has reported the concordance, upgrading and downgrading rates as 64.2%, 26.9% and 8.8% respectively[14]. We found our rates were similar with the literature. The agreement rate was lower and upgrading rate was 94.2% in patients with low Gleason scores[15]. In the study of D'elia et al. the agreement rate between biopsy and RP scores was 58% in patients with high GS (GS 9 and 10)[18]. In the study of Öztürk et al. nearly half of the patients with high biopsy GS (>7) were downgraded whereas the other half had compatible results[14]. Many reasons and potential predictors were blamed for upgrading phenomenon such as age, intraabdominal obesity, serum PSA level, number or percentage of positive cores, maximum percentage of cancer per

Table 3. Gleason score difference between biopsy and RP

			Biopsy Gleason D'amico Group			
			Low	Intermediate	High	Total
Gleason score difference between biopsy and RP	Same	Count	33	32	5	70
		% Within biopsy Gleason D'amico Grubu	57,9%	72,7%	45,5%	62,5%
	Downgrade	Count	0	8	5	13
		% Within biopsy Gleason D'amico Grubu	0,0%	18,2%	45,5%	11,6%
	Upgrade	Count	24	4	1	29
		% Within biopsy Gleason D'amico Grubu	42,1%	9,1%	9,1%	25,9%
Total		Count	57	44	11	112
		% Within biopsy Gleason D'amicoGrubu	100,0%	100,0%	100,0%	100,0%

core and prostate weight[17,18].

For these possible reasons, in the last decade new monograms targeting to predict the possibility of upgrading have been designed by many authors[18,19]. By designing monogram using preoperative PSA level, digital rectal examination abnormality and biopsy GS; Xu et al. reported a lower upgrading rate of 26.16% in their study when compared with conventional methods[18].

In addition to these reasons the subjective microscopic examination when biopsy and RP specimen were evaluated by different pathologists can be one of the major reasons of the discordant GS between biopsy and RP specimens. Öztürk et al. also reported this phenomenon as one of the limitations of their study[14].

Another possible factor for especially studies published before Gleason grade grouping system which was offered by Pierorazio et al. and Epstein et al. and accepted by WHO in 2016 was the subjective evaluation of different histopathological patterns[3,4,20]. It was thought that discordance rates will decrease by using grade grouping. For example, as all patients with pattern 5 were accepted in the same grade group or all patients with low GS (<7) were added in the grade group 1, downgrading and upgrading rates were expected to be lower in centers using grade grouping[4].

The strengths of our study is that most of our patients were evaluated by the same pathologist which avoids the interobserver variability as well as biopsied and operated by the same urologists. The weakness of our study is the lowest number of high Gleason grade group (Grade group 5) cases as they have generally treated with radiotherapy or systemic chemotherapy.

Conclusion

In conclusion, it is important to remember that Gleason grade may vary between biopsy results and prostatectomy specimens as needle biopsies represent small areas of tumors. New monograms targeting to predict the possibility of upgrading have been studied worldwide and saturation biopsies are being used for detailed sampling. In addition to this, Grade

grouping also may lower the upgrading and downgrading rates especially in tumors with pattern 5.

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 experiment was approved by Experiments of the Muğla Sıtkı Koçman University Faculty of Medicine Local Ethics Committee 2021/29-210029 with protocol number approved.

References

1. Greenlee RT, Hill-Harmon MB, Murray T, Thun M: Cancer statistics, 2001. CA Cancer J Clin 2001, 51(1):15-36. doi: 10.3322/canjclin.51.1.15
2. Cooperberg MR, Pasta DJ, Elkin EP, Litwin MS, Latini DM, Du Chane J, Carroll PR. The University of California, San Francisco Cancer of the prostate risk assessment score: a straightforward and reliable preoperative indicator of disease recurrence after radical prostatectomy. J Urol 2005; 173 (6):1938-42. doi: 10.1097/01.ju.0000158155.33890.e7
3. PA, Egevad L, Netto G, Amin MB, Epstein JI, Rubin MA. Acinar adenocarcinoma, Chapter 3: Tumors of the prostate in WHO Classification of Tumours of the Urinary System and Male Genital Organs. 4th edition, 2016; pp:152-4.
4. Epstein JI, EgevadL,Amin MB, Delahunt B, Srigley JR, Humprey PA, the grading commitee. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma Definition of Grading Patterns and Proposal for a New Grading System. Am J of Surg Pathol. 2016; 40(2):244-52. https://doi.org/10.1097/PAS.0000000000000530
5. Cohen MS, Hanley RS, Kurteva T, et al. Comparing the Gleason prostate biopsy and Gleason prostatectomy grading system: the Lahey Clinic Medical Center experience and an international metaanalysis. Eur Urol. 2008;54:371-81. doi: 10.1016/j.eururo.2008.03.049
6. Kuroiwa K, Shiraishi T, Naito S. Gleason score correlation between biopsy and prostatectomy specimens and prediction of high-grade Gleason patterns: significance of central pathologic review. Urology. 2011;77:407-11. doi: 10.1016/j.urology.2010.05.030
7. Reis LO, Zani EL, Freitas LL, et al. Higher prostate weight is inversely associated with Gleason score upgrading in radical prostatectomy specimens. Adv Urol. 2013;710421. doi: 10.1155/2013/710421
8. Van Praet C, Libbrecht L, D'Hondt F, et al. Agreement of Gleason score on prostate biopsy and radical prostatectomy specimen: is there improvement with increased number of biopsy cylinders and the 2005 revised Gleason scoring? Clin Genitourin Cancer. 2014;12:160-6. doi: 10.1016/j.clgc.2013.11.008
9. Garnett JE, Oyasu R, Grayhack JT. The accuracy of diagnostic biopsy specimens in predicting tumor grades by Gleason's classification of radical prostatectomy specimens. J Urol. 1984;131:690-3. doi: 10.1016/S0022-5347(17)50583-2
10. Bostwick DG. Gleason grading of prostatic needle biopsies. Correlation with grade in 316 matched prostatectomies. Am J Surg Pathol. 1994;18:796-803. doi: 10.1097/00000478-199408000-00006
11. San Francisco IF, DeWolf WC, Rosen S, et al. Extended prostate needle biopsy improves concordance of Gleason grading between prostate needle biopsy and radical prostatectomy. J Urol. 2003;169:136-40. doi: 10.1016/S0022-5347(05)64053-0
12. Cookson MS, Fleshner NE, Soloway SM, et al. Correlation between Gleason score of needle biopsy and radical prostatectomy specimen: accuracy and clinical implications. J Urol. 1997;157:559-62. doi: 10.1016/S0022-5347(01)65201-7
13. Tilki D, Schlenker B, John M, Buchner A, Stanislaus P, Gratzke C, et al. Clinical and pathologic predictors of Gleason sum upgrading in patients after radical prostatectomy: results from a single institution series. Urol Oncol. 2011;29:508-14. doi: 10.1016/j.urolonc.2009.07.003
14. Öztürk E, Yıkılmaz TN. Gleason Score Correlation Between Prostate Biopsy and Radical Prostatectomy Specimens. Bulletin of Urooncology, 2018;17:1-4 doi: 10.4274/uob.921
15. Stav K, Judith S, Merald H, et al. Does prostate biopsy Gleason score accurately express the biologic features of prostate cancer? Urol Oncol. 2007;25:383-6. doi: 10.1016/j.urolonc.2006.12.013

16. D'elia C, Cerruto MA, Cioffi A, et al. Upgrading and upstaging in prostate cancer: From prostate biopsy to radical prostatectomy. Mol Clin Oncol. 2014;86:284-7.
doi: 10.3892/mco.2014.370
17. Sahin A, Urkmez A, Yuksel OH, Verit A. Influence of Obesity on Gleason Score Inconsistencies between Biopsy and Radical Prostatectomy Specimens.J Coll Physicians Surg Pak. 2018;28(7):541-5.
doi: 10.29271/jcpsp.2018.07.541
18. Xu H, Bai PD, Hu MB, Mao SH, Zhu WH, Hu JM, et al. Infragradación de la biopsia de próstatarespecto a la pieza de prostatectomía la población China: nomogramasactualizados. ActasUrol Esp. 2017;41:162-71.
doi: 10.1016/j.acuro.2016.04.015
19. Payton S. Prostate cancer: new nomogram predicts risk of Gleason upgrading. Nature Rev Urol. 2013;10:553.
doi: 10.1038/nrurol.2013.218
20. Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. BJU Int. 2013;111:753-60.
doi: 10.1111/j.1464-410X.2012.11611.x