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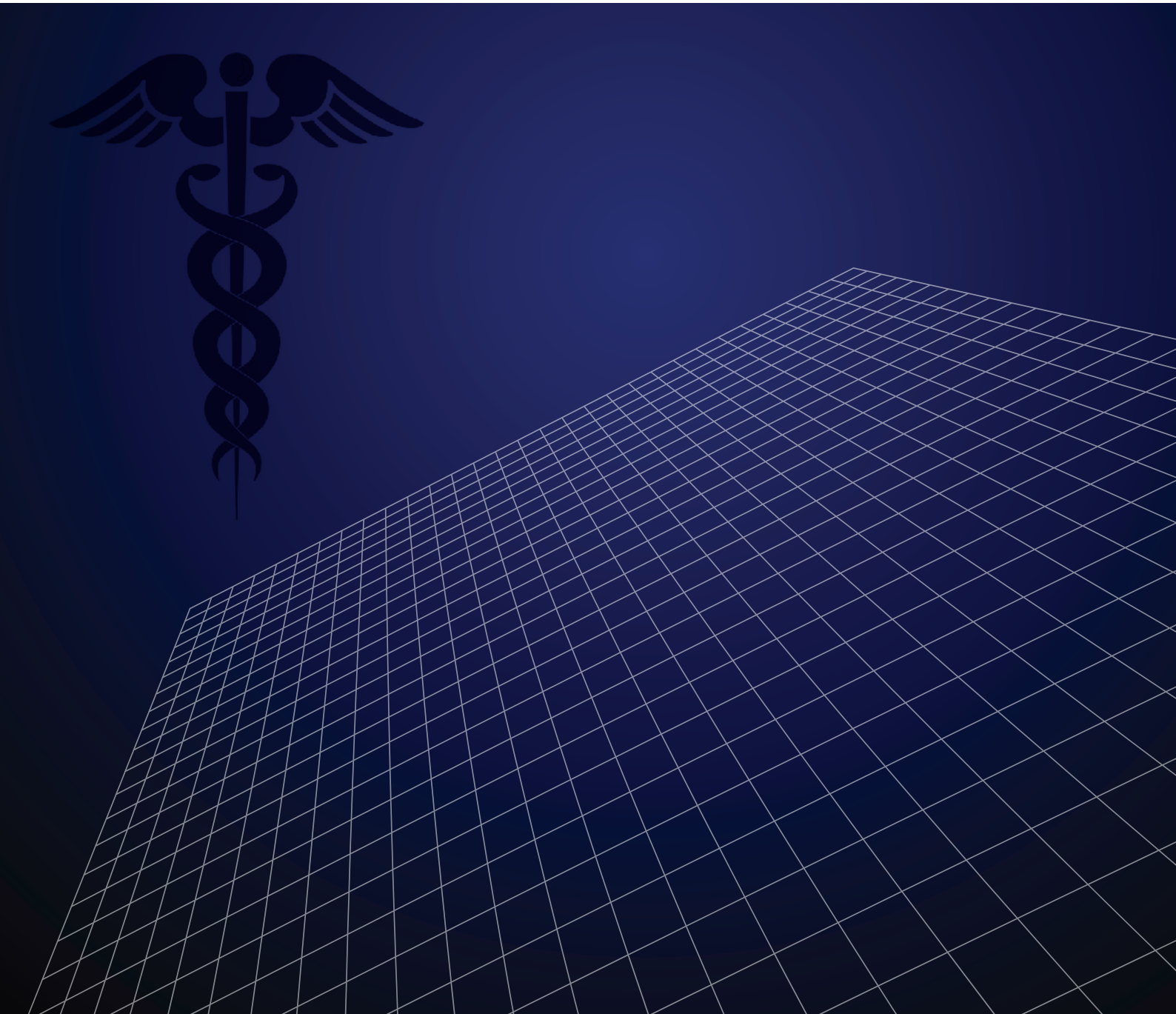

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To cite this article: Altunal C, Sahiner İT. Relationship of deaths caused by malignant neoplasm of stomach with healthy life expectancy (HALE) and health expenditures: a time-based longitudinal analysis on the ICD-10 mortality list. Turk J Clin Lab 2023; 1: 1-6

Original Article

Relationship of deaths caused by malignant neoplasm of stomach with healthy life expectancy (HALE) and health expenditures: a time-based longitudinal analysis on the ICD-10 mortality list

Mide malign neoplazmının neden olduğu ölümlerin sağlıklı yaşam beklentisi (HALE) ve sağlık harcamaları ile ilişkisi: ICD-10 ölüm listesinde zamana dayalı bir analiz

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ABSTRACT

Aim: In this research, it was aimed to evaluate the relationship of deaths caused by malignant neoplasm of the stomach with healthy life expectancy (HALE) and health expenditures: a time-based longitudinal analysis on the ICD-10 mortality list.

Material and Methods: World Health Organization (WHO) ICD-10 mortality data and WHO-HALE at birth and HALE at 60 ages for 14 countries between 1996-2017 were used. Spearman's rho, year controlled partial correlation analysis and Logit model were used for the analysis of research parameters.

Results: Minimum total death was 1, and the maximum was 25.898 for all years and countries. The mean death was 3.030.50±6.307.23. HALE at birth mean was 62.75±4.52, and HALE at 60 age mean was 13.93±1.90. Both Spearman's rho correlation analysis and yea- controlled partial correlation analysis results showed that malignant neoplasm of stomach death is negatively correlated with HALE at birth and HALE at 60 ages ($p<0.01$). Year-controlled correlation coefficients showed that these correlations have been in decreasing trend in a time period. Both HALE at birth and HALE at 60 ages have been significantly affected from malignant neoplasm of stomach deaths, gender, and country. Year has a positive and significant effect on HALE at 60 ages ($p<0.01$), whereas its effect was insignificant for HALE at birth ($p>0.05$). Model R2 values showed that HALE at 60 age model has a higher explanation value than the model for HALE at birth.

Conclusion: Deaths due to malignant neoplasms of the stomach still emerge as an important public health problem in certain parts of the world. In addition, the fact that the HALE at birth and HALE at 60 age indicators do not have a certain order in these countries and there is no progress in time shows that there are still important deficiencies in public health. With such studies, it is important to examine public health variables in the global sense in terms of reaching all segments of health services and providing health services to each individual.

Keywords: Malignant neoplasm, stomach, ICD-10, mortality, HALE.

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ÖZ

Amaç: Bu araştırmada, midenin malign neoplazmına bağlı ölümlerin sağlıklı yaşam beklentisi (SYB) ile ilişkisinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: 1996-2017 yılları arasında 14 ülke için Dünya Sağlık Örgütü (DSÖ) tarafından yayınlanan ICD-10 ölüm verileri ile yine DSÖ tarafından yayınlanan SYB-doğum ve SYB-60 yaş parametreleri kullanıldı. Araştırma parametrelerinin analizinde Spearman'ın rho yıl kontrollü kısmi korelasyon analizi ve Logit modeli kullanıldı.

Bulgular: Tüm yıllar ve ülkeler için minimum toplam ölüm 1, maksimum ölüm 25.898 idi. Ortalama ölüm 3.030.50±6.307.23 idi. SYB-doğum ortalaması 62.75±4.52, SYB-60 yaş ortalaması 13.93±1.90 idi. Hem Spearman'ın rho korelasyon analizi hem de yıl kontrollü kısmi korelasyon analizi sonuçları, mide malign neoplazmına bağlı ölümün SYB-doğum ve SYB-60 yaş ile negatif korelasyon gösterdiğini gösterdi ($p<0.01$). Yıl kontrollü korelasyon katsayıları, bu korelasyonların zaman diliminde azalma eğiliminde olduğunu gösterdi. Hem SYB-doğum hem de SYB-60 yaş midenin malign neoplazmından, cinsiyet ve ülkeden önemli ölçüde etkilenmiştir. Yıl, SYB-60 yaş üzerinde pozitif ve anlamlı bir etkiye sahipken ($p<0.01$), SYB-doğum için etkisi önemsizdi ($p>0.05$). Model R2 değerleri, SYB-60 yaş modelinin SYB-doğum modeline göre daha yüksek anlama sahip olduğunu göstermiştir.

Sonuç: Midenin malign neoplazmına bağlı ölümler dünyanın bazı bölgelerinde hala önemli bir halk sağlığı sorunu olarak karşımıza çıkmaktadır. Ayrıca SYB-doğum ve SYB-60 yaş göstergelerinin bu ülkelerde belirli bir düzene uymaması ve zamanla bu süreçte gelişme olmaması halk sağlığı konusunda halen önemli eksikliklerin olduğunu göstermektedir. Bu tür çalışmalarla halk sağlığı değişkenlerinin küresel anlamda incelenmesi, sağlık hizmetlerinin tüm kesimlerine ulaşması ve her bireye sağlık hizmeti sunulması açısından önemlidir.

Anahtar kelimeler: Malign neoplazm, Mide, ICD-10, Mortalite, HALE

Introduction

Malignant neoplasm of the stomach is still among the cancer types that cause death today and is one of the important public health problems, especially in undeveloped countries. In the literature, many studies have been conducted on deaths caused by malignant neoplasms of stomach [1-8]. However, it can be stated that these studies do not adequately address the disease in the context of public health at a global level.

Healthy life expectancy (HALE) at birth and HALE at 60 ages are important health indicators developed and used by World Health Organization (WHO). Health indicators have an important role in showing health inequalities between countries, especially in the global context. In this respect, HALE is an important public health indicator in terms of revealing the healthy life expectancy of individuals [9-12].

Although HALE and malignant neoplasm of stomach issues are the subjects of various studies in the literature, there are not enough studies that address the relationship between malignant neoplasm of the stomach and HALE a global context. In this research, it was aimed to evaluate the relationship of deaths caused by malignant neoplasm of the stomach with healthy life expectancy (HALE) and health expenditures: a time-based longitudinal analysis on the ICD-10 mortality list.

Material and Methods

In the research, WHO ICD-10 mortality data and WHO-HALE at birth and HALE at 60 ages were used. ICD-11 has been recently published, but its mortality parameters were not confirmed yet. In the ICD-10 mortality list, a total of 14 countries were listed for malignant neoplasm of stomach mortality (Seychelles, Brunei Darussalam, Cyprus, Oman, Sri Lanka, Syrian Arab Republic, Andorra, Azerbaijan, Belarus, Kazakhstan, Russian Federation, San Marino, Turkmenistan, Ukraine). According to years, 1996-2017 years were reported as malignant neoplasm of stomach deaths.

Nominal parameters were described with frequency analysis, whereas scale parameters were described with means and standard deviations. Kolmogorov Smirnov Test was used for normality of parameters. Spearman's rho correlation was used for correlation analysis, and partial correlation analysis was used for year-controlled longitudinal analysis. Since parameters were not normally distributed, logistic transformation was used for HALE at 60 age and total death parameters. Logit model was used for multivariate analysis with cofounders. All analysis was performed at SPSS 17.0 for windows at a 95% confidence interval.

Ethics: This study is observational research. No human/animal participant is avaiable so no ethics approval is mandatory. All study is done under Helsinki declarations.

Results

Turkmenistan had the highest malignant neoplasm of stomach death rate (13.7%) followed by the Russian Federation (12.9%), Brunei Darussalam (12.0%), Seychelles (9.6%) and Syrian Arab Republic (9.6%) (Table 1).

Table 1. Gender and country distributions of malignant neoplasm of stomach deaths for all years

	Gender		Total
	Male	Female	
Seychelles	13 (54,2)	11 (45,8)	24 (9.6)
Brunei Darussalam	15 (50,0)	15 (50,0)	30 (12.0)
Cyprus	2 (50,0)	2 (50,0)	4 (1.6)
Oman	1 (50,0)	1 (50,0)	2 (0.8)
Sri Lanka	7 (50,0)	7 (50,0)	14 (5.6)
Syrian Arab Republic	12 (50,0)	12 (50,0)	24 (9.6)
Andorra	5 (55,6)	4 (44,4)	9 (3.6)
Azerbaijan	4 (50,0)	4 (50,0)	8 (3.2)
Belarus	9 (50,0)	9 (50,0)	18 (7.2)
Kazakhstan	9 (50,0)	9 (50,0)	18 (7.2)
Russian Federation	16 (50,0)	16 (50,0)	32 (12.9)
San Marino	5 (50,0)	5 (50,0)	10 (4.0)
Turkmenistan	17 (50,0)	17 (50,0)	34 (13.7)
Ukraine	11 (50,0)	11 (50,0)	22 (8.8)
Total	126 (50,6)	123 (49,4)	249 (100.0)

In 1996, 1997, 1998, and 2015, total malignant neoplasm of stomach death rates was lower, compared to other years. In 1999, the death rate was the highest (Figure 1).

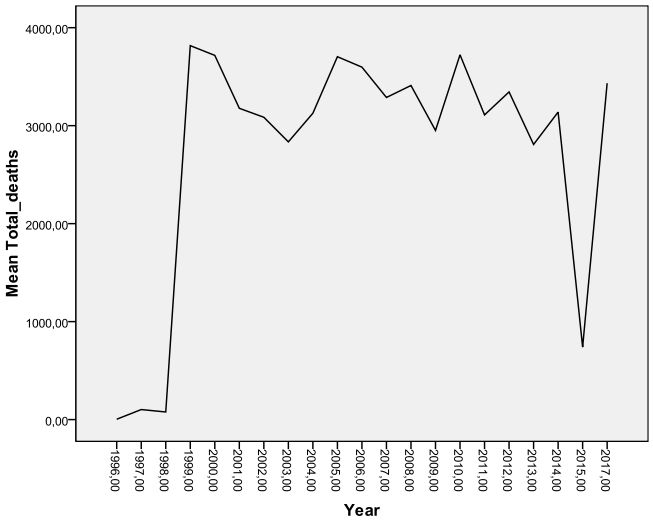

Figure 1. Total deaths for all countries according to years

HALE at birth and HALE at 60 ages were the highest in Oman. HALE at birth was the lowest in Turkmenistan, and HALE at 60 ages was the lowest in Kazakhstan (Figure 2).

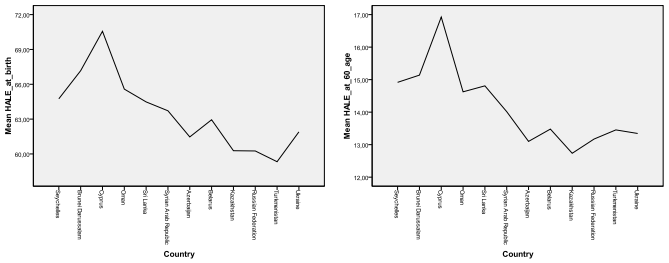

Figure 2. HALE at birth and 60 ages changes of countries for all years

In 1996, HALE at birth was the highest, whereas the lowest in 2005. HALE at 60 age was also the lowest in 2005. The highest rate of HALE at 60 ages was seen in 2014. According to change trends, both HALE at birth, and 60 ages did not have a trend and randomly changed within time periods (Figure 3).

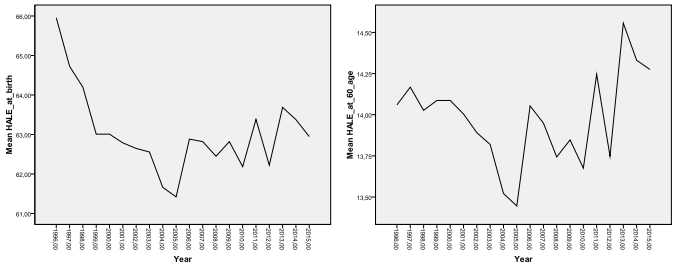

Figure 3. HALE at birth and 60 ages changes according to years for all countries

Minimum total death was 1, and the maximum was 25.898 for all years and countries. The mean death was 3.030.50±6.307.23. HALE at birth mean was 62.75±4.52, and HALE at 60 age mean was 13.93±1.90. According to Kolmogorov Smirnov Test, HALE at birth distribution was not significantly different from standard normal distribution ($p>0.05$). However, total death and HALE at 60 age parameter distributions were significantly different from the standard normal distribution ($p<0.05$) (Table 2). Thus, logarithmic transformations were applied for total deaths and HALE at 60 ages for the logit model.

Both Spearman's rho correlation analysis and year controlled partial correlation analysis results showed that malignant neoplasm of stomach death is negatively correlated with HALE at birth and HALE at 60 ages ($p<0.01$). Year controlled correlation coefficients showed that these correlations have been in decreasing trend in time period (Table 3).

Logit model results showed that both HALE at birth and HALE at 60 ages have been significantly affected from malignant neoplasm of stomach deaths, gender and country. Year has a positive and significant effect on HALE at 60 ages ($p<0.01$), whereas its effect was insignificant for the HALE at birth ($p>0.05$). Model R2 values showed that HALE at 60 age model has a higher explanation value than the model for HALE at birth (Table 4).

Table 2. Descriptive values and normality tests of research parameters

	Minimum	Maximum	Mean	Std. Deviation	Kolmogorov Smirnov-Z	p
Total deaths	1.00	25898.00	3030.50	6307.23	5.799	0.000
HALE at birth	52.46	71.91	62.75	4.52	1.270	0.079
HALE at 60 ages	10.10	18.06	13.93	1.90	1.504	0.022

Table 3. Spearman's rho correlation and year controlled correlation analysis results for total deaths

	Spearman's rho		Year controlled	
	r	p	r	p
HALE at birth	-0.451	0.000	-0.347	0.000
HALE at 60 ages	-0.399	0.000	-0.302	0.000

Table 4. Logit Model for time dependent regression for HALE at birth and 60 ages

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
HALE at birth					
(Constant)	-66.814	75.163		-0.889	0.375
Log Total deaths	-0.397	0.105	-0.257	-3.797	0.000
Year	0.063	0.037	0.068	1.691	0.092
Gender	5.948	0.356	0.659	16.719	0.000
Country	-0.001	0.000	-0.236	-3.539	0.000
R2: 0.654; F: 108.142; p<0.01					
HALE at 60 ages					
(Constant)	-3.673	2.031		-1.809	0.072
Log Total deaths	-0.016	0.003	-0.326	-5.556	0.000
Year	0.003	0.001	0.105	3.022	0.003
Gender	0.208	0.010	0.738	21.602	0.000
Country	-1.863E-5	0.000	-0.118	-2.040	0.042
R2: 0.740; F: 162.302; p<0.01					

Discussion

Although malignant neoplasm of the stomach is still among the important types of cancer today, it has lower mortality rates compared to other cancer types on the WHO ICD-10 list for all countries. However, it still causes deaths in undeveloped countries. Studies on malignant neoplasm of the stomach in the literature report that important new diagnoses and treatment possibilities regarding the disease are being developed day by day [13-21]. Although there have been significant improvements in diagnosis and treatment opportunities, malignant neoplasm of stomach deaths is still a serious public health problem, especially in for some countries. In our study, Turkmenistan had the highest mortality rates, followed by Russia and Brunei Darussalam, respectively. In all these countries, rates of over 10% of all deaths were seen.

According to deaths due to malignant neoplasm of stomach, it was not observed that the effect of time was limited, or that there was no decrease or increase in the mortality rate among the countries studied over time. This situation shows that there is not enough struggle with deaths due to malignant neoplasm of stomach.

When the studies on HALE at birth and HALE at 60 ages are examined, it is seen that these indicators are affected by many different public health indicators. Among these, mortality rates have an important place [22-25]. In our study, the average values of both indicators were relatively low in countries where deaths due to malignant neoplasm of stomach were reported.

According to the results of correlation analysis, although it is seen that the studies on HALE at birth and HALE at 60 ages have an effect on mortality over time, the logit model results show that this effect is only valid for HALE at 60 ages, for HALE at birth the year or It shows that the time variable has no significant contribution.

Conclusion

Although health is seen as a global public good today, deaths due to malignant neoplasms of stomach still emerge as an

important public health problem in certain parts of the world. In addition, the fact that the HALE at birth and HALE at 60 age indicators do not have a certain order in these countries and there is no progress in time shows that there are still important deficiencies in public health. With such studies, it is important to examine public health variables in the global sense in terms of reaching all segments of health services and providing health services to everyone.

Ethics

This study is observational research. No human/animal participant is avaible so no ethics approve is mandatory. All study is done under Helsinki declarations.

Conflict of interest

There is no any conflict of interest for this study. There is not any funding/sponsor for this study.

Ethics Committee Approval

This study is retrospective observational research. No human/animal participant is available, so no ethics approve is mandatory. All study is done under Helsinki declarations.

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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Orijinal Makale

Kutanöz Malign Melanom Nedeniyle Takip Ettiğimiz Hastaların Klinikopatolojik Özellikleri

Clinicopathological Characteristics of Patients that We Followed for Cutaneous Malignant Melanoma

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Öz

Amaç: Bu çalışmada, merkezimizde kutanöz malign melanom tanısı alan hastaların demografik özelliklerini, aldıkları tedavileri ve yanıtlarını incelemeyi amaçladık.

Gereç ve Yöntemler: Temmuz 2012- Haziran 2022 arasında onkoloji kliniğimizde malign melanom tanısı alan 45 hasta retrospektif olarak taranarak toplam 32 hasta çalışmaya dahil edildi. Klinik ve demografik veriler deskriptif analizlerle sunuldu. Kategorik ve numerik değişkenler sayı ve yüzde olarak verildi(n,%). Progresyonsuz sağkalım(PS) ve genel sağkalım(GS) Kaplan-meier yöntemi ile hesaplandı.

Bulgular: Çalışmaya dahil edilen hastaların 19'u(%59.4) erkek, 13'ü kadın(%40.6) idi. Hastaların median yaşı 65 (38-86) idi. Primer tümör sırasıyla 13(%40.6) hastada extremitede, 6(%18.8) hastada gövdede ve 13(% 40.6) hastada baş-boyunda yerleşimli idi. 8(%25) hastada BRAF mutasyonu mevcuttu. Hastaların 22(%68.7)'si metastatik evrede idi. Metastatik evredeki hastalarda progresyonsuz sağkalım) 5.2 ay (std. err:1.21, %95CI:2.86-7.59) iken, median genel sağkalım 23.9 (std. err:3.65, %95CI:16.8-31.11) ay idi.

Sonuç: Sonuç olarak kutanöz malign melanom en sık görülen onbeşinci kanser türüdür. İleri evrede mortalite oranları çok yüksektir ve multidisipliner takip gerekmektedir.

Anahtar kelimeler: Melanom; Kütanöz malign; BRAF

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Abstract

Aim: In this study, we aimed that examine the demographic characteristics, treatments and responses of patients diagnosed with cutaneous malignant melanoma in our center.

Material and Methods: Between July 2012 and June 2022, 45 patients that diagnosed with malignant melanoma in our medical oncology clinic were retrospectively screened and a total of 32 patients were included in the study. Clinical and demographic data were presented with descriptive analyses. Categorical and numerical variables were given as numbers and percentages (n,%). Progression-free survival(PFS) and overall survival(OS) were calculated by Kaplan-Meier method.

Results: Patients that included in the study, 19 (59.4%) were male and 13 (40.6%) were female. The median age of the patients was 65 (38-86). The primary tumor was located in the extremities in 13 (40.6%) patients, on the trunk in 6 (18.8%) patients, and in the head and neck in 13 (40.6%) patients. 8 (25%) patients had BRAF mutations. 22 (68.7%) of the patients were in the advanced stage. PFS was 5.2 months (std. err:1.21, 95%CI:2.86-7.59) and median OS was 23.9 (std. err:3.65, 95%CI:16.8-31.11) months in patients in the metastatic stage.

Conclusions: In conclusion, cutaneous malignant melanoma is the fifteen most common cancer. Mortality rates are very high in the advanced stage and multidisciplinary follow-up is required.

Keywords: Melanoma; Cutaneous malignant; BRAF.

Giriş

Melanositler, cilde rengini veren melanin adlı pigmentin üretimini sağlayan epidermisin bazal tabakasında bulunan deri hücreleridir [1]. Kutanöz melanom bu melanositlerden köken alır, bazal ve skuamoz hücreli kanserlerden sonra cilt kanserleri içinde üçüncü sıra yer alır ve sıklığı % 5'ten azdır [2]. Agresif seyri nedeniyle cilt kanserine bağlı ölümlerin %65'inden soruludur [3, 4].

Dünya genelinde kutanöz melanom oranı son yıllarda artmaktadır ve bu artış hızı diğer malignitelere oranla fazladır [5]. Son verilere göre yaşamları boyunca kadınlarda kutanöz melanom gelişme riski 34'te 1 iken erkeklerde bu oran 53'te 1'dir. [6] Median tanı yaşı 59'dur. Risk faktörleri içinde açık ten rengi, atipik veya displastik nevüsler, daha önce geçirilmiş melanom öyküsü, ailede melanom öyküsü ve genetik mutasyonlar yer alır [7]. Bunlara ek olarak aşırı güneş mazuriyeti ve UV (Ultra viole) bazlı suni bronzlaşma gibi çevresel faktörlerde kutanöz melanom gelişimine katkıda bulunur [8, 9].

Kutanöz melanomlar yüksek somatik mutasyon yüküne sahip kanserlerden biridir [10]. BRAF mutasyonu en sık görülen somatik mutasyondur ve melanomların yaşlaşık %50'sinde güneş mazuriyetinin hasarına bağlı olarak BRAF mutasyonu görülür [11,12]. En sık V600E(%80) ve V600K(%5-12) mutasyonları görülür. Bu mutasyonlar mitogen-activated protein kinaz(MAPK) ve phosphoinositol-3-kinaz(PI3K) yolaklarında işlev bozukluğuna yol açarlar [13]. Bu yolaklardaki bozukluklar melanom onkogenezinde rol alır.

Kutanöz melanomların yaklaşık %85'i lokal hastalık olarak görülürken, %10'u lokal ileri %5'i metastatik evrede tanı alır [14]. Lokalize hastalıkta prognoz çok iyidir ve 5 yıllık sağkalım %90'ın üzerindedir. İleri evrede sağkalım oranları azalmaktadır ve metastatik evrede %10'unun altına düşmektedir [15]. Erkeklerde hastalık progresyon ve mortalite oranları kadınlara göre daha yüksektir [16].

Bu çalışmamızda merkezimizde malign melanom tanısı alan hastaların demografik özelliklerini, aldıkları tedavileri ve yanıtlarını inceledik.

Gereç ve Yöntemler

Temmuz 2012-Haziran 2022 arasında onkoloji kliniğimizde malign melanom tanısı alan 45 hasta retrospektif olarak tarandı. Tanı anında hastane bilgisayar kayıtlarında ve hasta dosyasında bilgilerine ulaşılamayan hastalar çalışma dışı bırakılarak toplam 32 hasta çalışmaya dahil edildi. Hastaların tıbbi dosya kayıtları, laboratuar sonuçları, patoloji raporları incelendi. Demografik ve klinikopatolojik özellikleri aldıkları tedaviler ve yanıtları, son kontrol tarihleri kaydedildi. Çalışma Helsinki Deklerasyon ilkelerine göre yapıldı ve Ankara Etlik Şehir hastanesi etik kurulundan onay alındı.

İstatistik Analizi

İstatistiksel analizler IBM SPSS yazılımı (IBM SPSS Statistics version 22.0,) kullanılarak yapıldı. Klinik ve demografik veriler deskriptif analizlerle sunuldu. Kategorik ve numerik değişkenler sayı ve yüzde olarak verildi(n,%). PFS ve OS Kaplan-Meier metoduyla hesaplandı. Hazard ratio (HR) ve 95% Confidence Interval (CI) değerleri Cox-regression modeliyle hesaplandı. Gruplar arasındaki farklılıklar log-rank testi ile hesaplandı. P değeri < 0.05 tüm analizler için istatistiksel olarak anlamlı kabul edildi.

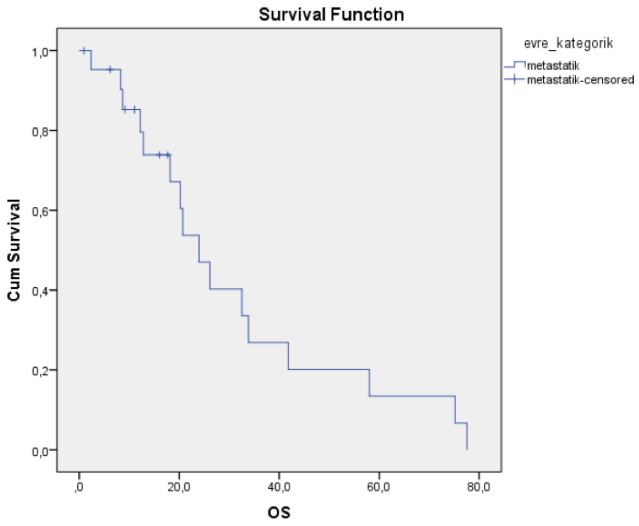
Bulgular

Çalışmaya dahil edilen hastaların 19'u(%59.4) erkek, 13'ü kadın(%40.6) idi. Hastaların median yaşı 65 (38-86) idi. 17 (%53.1) hastanın en az bir komorbid hastalığı mevcuttu. Primer tümör sırasıyla 13(% 40.6) hastada extremite (% 40.6), 6(%18.8) hastada gövde 6 ve 13(% 40.6) hastada baş-boyun yerleşimli idi. 7 (%21.9) hastada V600E ve 1 (% 3.1) hastada V600K mutasyonu olmak üzere toplam 8 (%25) hastada BRAF mutasyonu mevcuttu. Hastaların 22'si(%68.7) metastatik evrede idi. Bu hastalardan 18'i (% 56.3) tanı anında metastatik iken, 4 (%12.5) hasta takipte metastatik hale gelmişti. 10(%31.3) hastada akciğer, 5 (%15.6) hastada karaciğer, 10(%31.3) hastada lenf nodu, 5 (%15.6) hastada ve 4(%12.5) hastada kemik metastazı mevcuttu. 15(%46.9) hasta metastatik birinci basamak tedavide temozolamid, 7(%21.9) hasta ise darafenib+trametinib tedavisi almıştı. İkinci basamakta 1(%3.1) hasta dabrafenib+trametinib, 2(%6.2) hasta ipilimumab, 1(%3.1) hasta nivolumab+ipilimumab ve 6(%18.8) hasta tek ajan Nivolumab almıştı (Tablo1).

Tablo 1. hasta karakteristik özellikleri

variables		n	Yüzde (%)
Cinsiyet	Kadın	13	40,6
	Erkek	19	59,4
Komorbidite	Var	15	46,9
	Yok	17	53,1
Tümör Yeri	Ekstremite	13	40,6
	Gövde	6	18,8
	Baş-boyun	13	40,6
Sentinal Lap	Yapıldı	10	31,2
	Yapılmadı	22	68,8
BRAF mut	YOK	24	75
	V600E	7	21,9
	V600K	1	3,1
Evre	1	3	9,4
	2	5	15,6
	3	2	6,2
	4	22	68,8
Operasyon	var	7	21,9
	yok	15	46,9
Metastaz	Yok	10	31,3
	Denova	18	56,3
	Metakron	4	12,4
Ac met	var	10	31,2
	yok	22	68,8
Kc met	var	5	15,6
	yok	27	84,4
LAP met	var	10	31,2
	yok	22	68,8
Kemik met	var	4	12,5
	yok	28	87,5
Parotis met	var	5	15,6
	yok	27	84,4
Metastatik 1. basamak tedavi	Dabrafenib+trametinib	7	21,9
	Temodal	15	46,9
Metastatik 2. basamak tedavi	Dabrafenib+trametinib	1	3,1
	Nivolumab	6	18,8
	İpilumab	2	6,3
	Nivolumab+İpilumab	1	3,1

Metastatik evredeki hastalarda progresyonsuz sağkalıma (PFS) bakıldığında median PFS 5.2 (std. err:1.21, %95CI:2.86-7.59) ay idi. Median PFS birinci basamakta temozolamid alanlarda 3.4 (std. err:0.50, %95CI:2.47-4.43) ay, dabrafenib+trametinib alanlarda 15.4 (std. err:7.28, %95CI:1.21-29.74) ay olarak bulundu. Genel sağkalıma (GS) bakıldığında metastatik hasta grubunda median sağkalım 23.9 (std. err:3.65, %95CI:16.8-31.11) ay idi. Metastatik hastalarda ekstremite gövde ve başboyun yerleşimli tümörü olanlarda median sağkalım sırayla 20,2 ve 41 ay idi (Figür 1).



Figür 1. Evre 4 hastaların kaplan-meier sağkalım eğrisi

Tartışma

Melanom her iki cinstede de en sık görülen kanserler arasında beşinci sıradadır ve en çok ölüme neden olan cilt kanseri türüdür [17]. Kadınlarda erkeklere göre daha sık görülmektedir ancak erkeklerde prognoz ve mortalite kadınlardan daha kötüdür [16, 18]. Bizim verilerimize göre ise erkek hasta sıklığı kadınladan fazla idi. Bunun sebebi hasta sayımızın az olması olabilir. Daha önce yapılan çalışmalara göre ortalama tanı yaşı 59 iken bizim hasta yaş ortalamamız 65 idi ve hastalarımızın 46,9'u en az bir komorbiditeye sahipti.

Melanom hastaları TNM evreleme sistemine göre sınıflanırlar. Tümör kalınlığı (T evresi), lenf nodu tutulumu (N evresi) ve metastaz varlığı (M evresi) ile evre belirlenir [15, 19, 20]. Hastalar genelde evre 2 (lokal) ve evre 3 (lokal ileri) evrede tanı alırlar. Breslow'a göre, bu evrelerde hastanın prognognozunu belirleyen en önemli faktörler tümör kanlığı (breslow), cerrahi sınır durumu ve sentinal lenf nodu pozitifliğidir [19]. Verilerimize göre 3 hasta evre 1, 5 hasta evre 2 ve 6 hasta evre 3 olarak tanı almıştı. Bu hastaların hepsine lenf nodu örneklemesi yapılmış ve 6 hastada lenf nodu pozitifliği saptanmıştı. Bunun

aksine hastaların 18'i (% 56.3) tanı anında metastatik idi, 4 hastada ise takipte metastaz gelişmişti. Hastalarımızın büyük bir kısmının tanı anında metastatik olmasının sebebi erken evre ve rezeksiyon yapılan hastaların onkoloji başvurularının az olması, birçok hastanın başvuru sonrası takibe gelmemesi nedeniyle çalışmaya alınamasıdır.

Prognozu etkileyen bir diğer faktör ise tümörün yerleşim yeridir ve gövde yerleşimli melanomların ekstremite yerleşimli olanlara göre daha kötü prognoza sahip olduğu belirtilmiştir [21-25]. Bizim hastalarımızın 13'ünde tümör ekstremitelerde 6'sında ise gövdede yerleşimli idi. Ekstemite yerleşimli tümörlerin 6'sı (%46,1) tanı anında metastatik iken, gövde yerleşimli olanların ise 3'ü (%50) tanıda metastatik idi. Metastatik hastaların yerleşim yerine göre sırasıyla median sağkalımları ekstremite gövde ve baş-boyun yerleşimli tümörü olanlarda 20, 23 ve 41 ay idi. Bizim bulgularımızda göre de gövde yerleşimli tümör ekstremite yerleşimli olana göre tanıda daha fazla metastatik evrede idi ve sağ kalım sonuçları daha kötü idi.

Hastalar TNM evreleme sisteminde lenf nodu, akciğer ve diğer metastaz bölgeleri olarak ayrı kategoride sınıflandırılırlar. [15] Verilerimize göre 10 hastamızda akciğer, 10 hastamızda da sentinal dışı diğer lenf nodlarında metastaz saptanmıştı. Diğer metastaz bölgeleri sıklık sırasına göre karaciğer, parotis ve kemik idi. 2 hastamızda ise beyin metastazı görülmüştü. Parotis metastazı literatürde sık görülmemesine rağmen hastalarımızın 5 tanesinde saptanmıştı.

Kutanöz melanomlarda BRAF mutasyonu sıktır ve yaklaşık %50 hastada saptanmaktadır. En sık olarak V600E(%80) ve V600K(%5-12) mutasyonları görülür [11, 12]. Bizimde 7 (%21.9) hastamızda V600E ve 1 (% 3.1) hastamızda V600K mutasyonu olmak üzere toplam 8 (%25) hastamızda BRAF mutasyonu mevcuttu. Literatüre göre daha düşük oranda BRAF mutasyonu saptamasının nedeni erken evre tüm hastalara BRAF mutasyonu bakılamamış olması idi. Hastalarda metastatik evrede tedavi kararı BRAF mutasyon durumuna göre verilmektedir. BRAF mutasyonuna sahip hastalar tedavide BRAF/MEK inhibitöründen fayda görmektedirler [26-29]. Aynı zamanda metastatik evrede hastalar immünoterapi ajanlarından da fayda görmektedirler [30, 31]. Çalışmalara göre BRAF/MEK inhibitöründen ortalama PFS oranı 18 ay iken bizim metastatk birinci basamakta bir BRAF/MEK inhibitörü kombinasyonu olan dabrafenib+trametinib alan hastalarımızın ortalama PFS'i 15,4 ay idi [29, 32]. Ülkemizdeki geri ödeme şartları nedeniyle çoğu hastada metastatik birinci basamakta hastalarda immünoterapi ajanlarını kullanamamaktayız. Ancak ikinci basamak tedavide 9 hastamız immünoterapi ajanlarını kullandı. Tüm metastatik hasta grubunda median genel sağkalım 23.9 ay idi.

Sonuç olarak kutanöz malign melanom her iki cinste en sık görülen onbeşinci kanserdir ve en çok ölüme neden olan cilt kanseri tipidir. Erken evrede teşhisi ile yüksek sağkalım ile seyrederken, metastatik evrede mortalite oranları çok yüksektir. Erken evrede tanı alan hastaların cildiye, plastik cerrahi ve onkoloji tarafından multidisipliner takibi gerekmektedir.

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Original Article

The evaluation of breast biopsy results before and after the inception of COVID-19 pandemic: Single center retrospective study

COVID-19 pandemisi başlangıcından önce ve sonra yapılan meme biyopsilerinin değerlendirilmesi: Tek merkezli retrospektif çalışma

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Abstract

Aim: This study aimed to evaluate breast biopsy procedures performed in radiology unit before and after COVID-19 pandemic initiation, and compare breast cancer diagnosis.

Material and Methods: Breast biopsies performed two years before and after March 2020 were retrospectively analyzed. Patient demographics, referral reason (screening/diagnostic), biopsy type and region, tumor size, BI-RADS category and pathology were evaluated. Statistical analysis was made using chi-square test, independent samples t-test and Mann-Whitney U test.

Results: Among 903 biopsies, the mean age was 51 (range 15 to 88 years). Biopsy volume decreased in the early six months of the pandemic, but accelerated soon after, with numbers even more than the pre-pandemic era. Screening intention on patient referral decreased significantly in the pandemic period, where diagnostic purposes arised ($p<0.05$). The prominent imaging modality used for diagnosis was mammography before pandemic and ultrasonography after pandemic ($p<0.05$). There was no statistical difference regarding biopsy type, biopsy region, tumor size, axillary lymph node invasion and pathology results by period.

Conclusion: Despite the sudden decrease of breast biopsy volume in the early pandemic, demand of screening reduced and diagnostic referrals increased dramatically afterwards . Therefore, the interruption of cancer screening programmes should be avoided to prevent cancer burden.

Keywords: Imaging aided breast biopsy, COVID-19, breast cancer

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Öz

Amaç: Bu çalışma ile COVID-19 pandemisi öncesi ve pandemi sırasında radyoloji biriminde yapılan meme biyopsilerini değerlendirmek ve bu dönemlerdeki meme kanseri teşhislerini karşılaştırmak amaçlanmıştır.

Gereç ve Yöntemler: Mart 2020 öncesi ve sonrasındaki 2 yıl boyunca yapılan meme biyopsileri retrospektif olarak incelendi. Hastaların demografi bilgileri, başvuru sebebi (tarama/tanısal), biyopsi tipi ve bölgesi, kitle boyutu, BI-RADS kategorisi ve patolojisi değerlendirildi. İstatistiksel analiz için ki-kare testi, bağımsız örneklem t-testi ve Mann-Whitney U testi kullanıldı.

Bulgular: Toplam 903 biyopsi hastasında ortalama yaş 51 (15-88) bulundu. Biyopsi sayısının pandeminin erken ilk 6 ayında düşüp hemen sonrasında, pre-pandemi döneminden de fazla olmak suretiyle, yükselmeye başladığı izlendi. Pandemi döneminde tarama başvuruları ile ilişkili biyopsi sayıları anlamlı olarak düşerken tanısal başvurularla gelen biyopsi sayılarının arttığı görüldü ($p<0.05$). Tanısal amaçlı en sık kullanılan görüntüleme yöntemi pandemi öncesi mamografi iken pandemi sonrası ultrason olmuştur ($p<0.05$). Biyopsi tipi, bölgesi, kitle boyutu, aksiller lenf nodu tutulumu ve patoloji sonuçlarında dönemsel olarak anlamlı farklılık saptanmadı.

Sonuçlar: Erken pandemi döneminde meme biyopsisi sayısında izlenen ani düşüşe rağmen, hemen izleyen dönemde tarama ilişkili biyopsi sayısında azalma ve tanısal başvurulara bağlı yapılan biyopsi sayısında belirgin artış saptandı. Bu sebeple, olası kanser kanser yoğunluğunun önüne geçebilmek amacıyla kanser tarama programlarının sekteye uğramaması için gerekli önlemler alınmalıdır.

Anahtar kelimeler: Görüntüleme eşliğinde biyopsi, COVID-19, meme kanseri

Introduction

In the spring of 2020, the coronavirus disease 2019 (COVID-19) disrupted daily life, including preventive health care services worldwide. Cancer screening programmes were interrupted yielding to a temporary decrease in cancer diagnoses (1, 2). Many professional organizations and cancer societies recommended asymptomatic individuals to postpone their routine cancer screening appointments (3). This health issue brought out the consequences of its own, where an abrupt increment of newly diagnosed cancers arised due to extended delays, with additional burden on the health care system (4).

It has been reported that during the initial pandemic outbreak and lockdowns, many hospitals closed outpatient clinics and postponed or cancelled elective surgeries as precaution against COVID-19 spread (5). In parallel with the reduction of hospital visits of patients, radiological imaging utilization also markedly decreased (6, 7). Screening mammography programmes were paused internationally in the spring of 2020, due to the governmental advisory about avoiding nonurgent demand of health care (1, 8). This sharp decrease in monthly screening volumes returned to normal when recalls were started by the following summer (3, 8).

It is predicted that these delays in cancer screening programmes will impact the outcomes of breast cancer (9-11). With regard to breast cancer, during the lockdowns, the number of diagnosed malignancy rates decreased in certain countries (9, 12). On the other hand, in Finland, oncological surgery rates were not affected from postponed elective surgeries (11). In this context, we aimed to evaluate breast biopsies performed in out breast imaging unit of radiology department and compare their results before and after the initiation of COVID-19 pandemic.

Material and Methods

This retrospective study was conducted between March 2018 and March 2022, after being approved by the Research and Ethics Committee of a private University School of Medicine. All breast biopsy procedures recorded in the breast imaging unit of the radiology department between the indicated dates were scanned. The total sum was divided into two groups, where referrals before March 2020 were noted as the pre-pandemic group and after March 2020 were defined as the pandemic group.

The imaging modality used to diagnose, breast imaging reporting and data systems (BI-RADS) category of the lesion, biopsy procedure features, pathology results and the demographics of the patient population were noted. Imaging modalities used to guide biopsies consisted of breast ultrasound (US) and mammography. All patient data at the time of the referrals were scanned through the database system of the hospital and the cases were categorized upon intention of the imaging; rather screening or diagnostic

purpose. Screening group was defined as annual or biannual examinations with no symptoms or already known breast cancer patients attending to their scheduled oncologic examination. Diagnostic group was related to patients visiting the hospital for a new breast symptom. The radiologic type of the breast intervention for tissue sampling was noted, including US-guided fine needle biopsy, core-needle biopsy, wire localization or stereotactic biopsy. Ultrasound-guided core-needle biopsies were performed with 9 cm 16-gauge biopsy device (Argon medical devices SuperCore Biopsy Instrument, TX, USA) and stereotactic biopsies were performed with 10 cm long 20-gauge guide wire (Argon medical devices, Accura BLN, TX, USA). Patients who had more than one type of biopsy procedure for the same lesion were not repeatedly included in the study. Only one biopsy data was accounted for such patients: either excisional biopsy or the procedure finalized in malignancy, if present.

Data analysis was performed with statistical software (SPSS, version 20.0, IBM Company, Chicago, IL). Descriptive statistics were computed for all demographic data. Group differences were calculated by using chi-square test, independent samples t-test and Mann-Whitney U test. Statistical significance was accepted for $p < 0.05$.

Results

In total, 903 biopsy procedures were conducted in four years. The mean age was 51 (range 15 to 88 years) and women with age below 40 made 15% of the patient population. The demographics of the patients are shown in Table 1. Thirteen men were evaluated during pre-pandemic period and eight in the pandemic period, all of whom were all sampled of axillary lymph node. About 38% (n=344) of all biopsies were diagnosed malignant, where the rest 62% (n=559) was concluded in benign pathology. Seventeen lesions were reported ductal carcinoma in situ (DCIS) in the pre-pandemic group, against twenty preinvasive malignant lesions in the pandemic group (Table 2). We observed an increase in the number and ratio of malignant breast lesions during COVID-19 pandemic. However, this difference in biopsy results among two periods was not statistically significant.

The mean dimension of the breast lesions was 18 mm in the pre-pandemic period and 23 mm in the pandemic period. Biopsies scheduled due to screening referrals was 307 in the pre-pandemic period, and 261 in the pandemic period, whereas diagnostic referrals was 130 and 205, respectively. The number of ultrasound procedures used as the first step diagnosis tool was significantly higher that mammography in the pandemic period. In 12 patients US-guided fine-needle biopsy and 379 patients core-needle biopsy was performed, where the remaining had excisional biopsy including 419 patients with US-guided wire localization and 93 cases with stereotactic biopsy. The biopsy and tumor related features of the breast lesions are summarized in Table 2.

The maximum reduction in the number of biopsies during the pandemic period was observed in April 2020 (n=3), followed by May 2020 (n=15). Despite the number of reduced breast biopsies, the ratio of malignancy did not decrease (Table 3). In the first 6 months of the pandemic period, the malignancy rate was 39% and it had tendency to increase in the following intervals. When compared to the pre-pandemic era, the total number of malignant breast biopsies increased, and the malignancy rate was higher (34% vs. 39%).

Table 1. Comparison of patient demographics, referrals and imaging modalities by period

	Period		P Value
	Pre-pandemic (n=437)	**Pandemic (n=466)**	
Age (years) (mean ± SD)	52.1 ± 10.9	50.6 ± 10.1	0.528
Gender (n) (%)			
Female	424 (97%)	458 (98%)	0.072
Male	13 (3%)	8 (2%)	
Patient referral (n) (%)			
Screening	307 (70%)	261 (56%)	<0.05
Annual/biannual examination	197 (44%)	162 (35%)	
Oncological follow-up	110 (26%)	99 (21%)	
Diagnostic	130 (30%)	205 (44%)	
Imaging modality that first diagnosed the breast lesion (n) (%)			
Mammography			
Ultrasound (US	184 (38%)	131 (28%)	<0.05
	253 (57%)	335 (66%)	

Table 2. Comparison of biopsy and tumor related data by period

	Period		P Value
	Pre-pandemic (n=437) (48%)	**Pandemic (n=466) (52%)**	
Biopsy type (n) (%)			0.380
US-guided			
Fine needle aspiration	10 (2%)	2 (0.5%)	
Core-needle biopsy	179 (41%)	200 (43%)	
Wire localization	207 (47.5%)	212 (45.5%)	
Stereotactic biopsy	41 (9.5%)	52 (11%)	
Biopsy localization			
Breast tissue	412 (94%)	428 (92%)	0.151
Axilla	25 (6%)	38 (8%)	
BI-RADS category			
BI-RADS 4A	161 (37%)	98 (21%)	
BI-RADS 4B	52 (12%)	49 (10.5%)	
BI-RADS 4C	114 (26%)	135 (29%)	<0.05
BI-RADS 5	66 (15%)	119 (25.5%)	
BI-RADS 6	44 (10%)	65 (14%)	
Tumor size (mean ± SD)	18 mm (± SD)	23 mm (± SD)	0.217
Axillary lymph node invasion (n) (%)	106 (24%)	137 (29%)	0.082
Pathology (n) (%)			0.634
Benign	274 (63%)	285 (61%)	
Malignant	163 (37%)	181 (39%)	
DCIS	17 (10%)	20 (11%)	

Table 3. Biopsy volume by 6 months period in pre-pandemic and pandemic era

	Period					
	Pre-pandemic (n=437, 48%)			**Pandemic (n=466, 52%)**		
	Total	**Malignant (34%)**	**DCIS**	**Total**	**Malignant (39%)**	**DCIS**
1st 6M	94	30 (32%)	3			
2nd 6M	108	42 (38%)	5			
3rd 6M	114	44 (38%)	7			
4th 6M	121	38 (31%)	3			
5th 6M				81	32 (39%)	2
March 2020				17	5 (29%)	0
April 2020				3	1 (33%)	0
May 2020				15	7 (46%)	0
June 2020				19	7 (37%)	0
July 2020				10	4 (40%)	2
August 2020				17	6 (35%)	0
6th 6M				91	37 (40%)	4
7th 6M				144	56 (38%)	6
8th 6M				150	63 (42%)	8

* 6M: six months period

Discussion

The COVID-19 pandemic related breast cancer mortality is unknown yet and will be unclear for at least a decade. However, collateral outcomes, including pandemic-related diagnostical delays regarding breast cancer, are being reported up to date and providing insight of a probable picture of future results. In this analysis of data collected from a single center breast imaging unit of a university hospital, diagnosis of breast cancer is observed to reduce initially with the onset of COVID-19 pandemic outbreak, when compered to two years' registries prior to the pandemic and took a rapid increase after the two months of the early pandemic era.

In our study, the number of breast biopsies and diagnosed breast cancers increased soon after the spring of 2020 and got even higher than the pre-pandemic era. This finding was in line with similar published studies concerning the volume of breast cancer (3, 9). Nyante et al. reported that the reduction of biopsy volume in the pandemic period was associated with the decline in screening mammography numbers (3). We did not retrospectively evaluate the mammography size of both era before and after the pandemic initiation. However, we analyzed the medical history of patients at the time of referral and found that diagnostic intention was significantly higher in the early pandemic era compared to screening purposes.

Previous studies have shown that the impact of pandemic on delayed breast cancer diagnosis is predominantly due to interrupted screening rather than diagnostic imaging (3, 13). This would be the reason of a probable decline in the volume of early-stage breast cancer (14, 15). Our results are in opposite with the literature regarding the diagnosed early breast cancer volume, which decreased only in the early months of the COVID-19 pandemic and increased in overall 2 years' period of pandemic, compared to the pre-pandemic era. This might be the consequence of imbalance between diagnostic and screening imaging, that could have elevated the number of more advanced tumors, which presents with marked clinical symptoms, in the early pandemic and the total volume of breast cancer which showed a rapid increase right after the first summer of the pandemic. However, this is another subject to analyze that should be focused on in future studies.

Nyante et al. reported in their study that the decrease in the number of breast biopsies lagged behind the decrease in screening and diagnostic mammography (3). This might be the reason that the biopsy volume of our study in the pandemic period is higher than we expected. In the early period of the pandemic era, especially in the first 6 months, the number of breast biopsies reduced. However, in the following months an abrupt rise is observed in the biopsy volume, and the increase continued with an acceleration. Therefore, we think that the decrease of biopsies in the initial pandemic period will have consequences concerning advanced breast cancer and cancer related deaths. We don't have data to evaluate this subject, which would be a new topic of future studies.

The biopsy procedures in our breast screening unit also included axillary lymph node sampling. Axillary lump is an important referral reason of advanced breast cancer or metastasis, apart from benign etiology. Advanced disease in the pandemic period, including axillary lymph node invasion or greater tumor size, had a higher ratio in the present study. Reported delayed diagnoses in literature were not only due to postponed screening appointments or surgeries, but also pandemic related anxiety and concerns of women to undergo any procedure at the hospital, even though they had obvious clinical symptoms (9, 16). However, our results do not represent the whole patient population biopsied for axillary lymphadenopathy, because a part of this biopsy group is evaluated in our interventional radiology department. This split might be the reason of insignificant axillary lymph node related results in our study . Also, unilateral axillary lymphadenopathy reported after COVID-19 vaccination during pandemic (17) would be another reason of our insignificant but relatively higher number of axillary lymph node biopsy in the pandemic group.

We hypothesized that the total breast biopsy volume would not decrease dramatically in our hospital compared to the pre-pandemic period. The reason of this assumption was that our hospital was not declared as one of the "COVID-19 pandemic hospitals" by the national ministry of health and was assigned as one of the few "non-pandemic hospitals" in the whole city, where health services can be maintained for non-COVID patients. But our results of early pandemic period demonstrated an abrupt decrease in the number of breast biopsies. We thought that this is related to the national lockdowns, recommendations of different cancer societies and community organizations to stay home together with the fear and anxiety of hospital visits during the initiation of the pandemic.

The impact of lockdowns was prominent on the reduced rates of patient referrals to hospitals, especially for elective surgeries, non-oncological procedures and follow-up programmes. Postponing elective surgeries due to the pandemic had an effect on the relative decrease of oncological surgery rates in many countries (11). The ratio of BI-RADS 4C, BI-RADS 5 and 6 diagnoses in overall breast imaging modalities of our study presented a significant increase in the pandemic period, compared to the pre-pandemic period. This might be attributed to the decrease in screening referrals due to the will of patients to postpone their screening programmes until after the pandemic, and the increase of diagnostic presentations instead. Together with insignificant but greater size of tumor presented in the pandemic period and increased rate of axillary lymph node invasion, the number of significantly elevated BI-RADS category could be the early signs of upcoming advanced disease. Besides, the rate of oncological patients' attendance to their scheduled hospital visit had a minimal reduction in the pandemic, but with no significant difference between the two periods. We thought that this would be owing to the fact that our hospital was declared as a non-pandemic center, so that the oncology patients were encouraged to attend their follow-ups accordingly.

Major limitation of our study was the fact that the COVID-19 pandemic is still ongoing and its longterm outcomes on breast cancer cannot yet fulfilly be discussed. Future studies, especially focused on COVID-19 pandemic associated advanced breast cancer and breast cancer related deaths, should be the topics in agenda. Another limitation was the inhomogenity of the two compared groups, pre-pandemic and pandemic periods, due to the diversity of patient volume in the pandemic group that has changed with the unstable course of the disease.

Conclusion

In conclusion, this study shows that the COVID-19 pandemic had an obvious effect on the breast biopsy numbers, both in the early pandemic and later on, conversely. The implementation of our center to become a non-pandemic hospital provided some advantages, but still the breast biopsy volume decreased, especially in the lockdown period, and dramatically increased afterwards. Therefore, complete shutdown of healthcare services should be avoided in case of any future pandemic disease for routine cancer screening programmes to be maintained.

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Original Article

Hypomagnesemia and the risk of contrast-induced nephropathy in patients undergoing elective coronary angiography

Elektif koroner anjiyografi yapılan hastalarda hipomagnezemi ve kontrast ilişkili nefropati riski ilişkisi

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Abstract

Aim: The present study aimed to assess the influence of hypomagnesemia (hypoMg) on the risk of developing contrast-induced nephropathy (CIN) after coronary angiography.

Material and Methods: This is a single-center prospective, observational study conducted at a tertiary referral hospital between December 31, 2016, and February 28, 2021. 223 patients who had undergone coronary angiography procedures and had preprocedural baseline Mg levels were enrolled in this study. CIN was defined as an increase of >0.5 mg/dl or >25 % in serum creatinine concentration over baseline within 48-72 h after administration. HypoMg was defined as Mg< 1.60 mg/dL.

Results: Of 223 patients enrolled, CIN occurred in 28 patients (12.6%). CIN occurred in 53.3 % of the patients with hypoMg and 8.9 % of those with non-hypoMg (P<0.01). Multivariate logistic regression analysis found that baseline Mg levels were independent predictors of CIN.

Conclusion: HypoMg was associated with an increased risk for CIN. These results suggest magnesium replacement in hypomagnesemia may be beneficially indicated before diagnostic/interventional studies using contrast media.

Keywords: Hypomagnesemia, Coronary Angiography, Contrast-Induced Nephropathy

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Öz

Amaç: Bu çalışma, hipomagnezeminin (hipoMg) elektif koroner anjiyografi sonrası kontrast kaynaklı nefropati (KKN) geliştirme riski üzerindeki etkisini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Bu çalışma, üçüncü basamak bir eğitim ve araştırma hastanesinde yürütülen tek merkezli ileriye dönük, gözlemsel bir çalışmadır. 31 Aralık 2018 ve 28 Şubat 2022 tarihleri arasında koroner anjiyografi işlemi geçirmiş ve işlem öncesi başlangıç Mg seviyeleri olan 223 tane hasta bu çalışmaya dahil edilmiştir. CIN, uygulamadan sonra 48-72 saat içinde başlangıca göre serum kreatinin konsantrasyonunda >0.5 mg/dl veya > %25 artış olarak tanımlanmıştır. HipoMg, Mg< 1.60 mg/dL olarak tanımlanmıştır.

Bulgular: Kaydedilen 223 hastanın 28'inde (%12.6) KKN meydana geldi. KKN, hipoMg'si olan hastaların %36.4'ünde ve hipoMg'si olmayanların %11,3'ünde meydana gelmiştir. (P=0,002). Çok değişkenli lojistik regresyon analizi, başlangıç Mg düzeylerinin KKN' nin bağımsız öngörücüleri olduğunu bulunmuştur.

Sonuç: HipoMg, artan KKN riski ile ilişkili olarak bulunmuştur. Bu sonuçlar, hipoMG'de magnezyum replasmanı yapılmasının, kontrast madde kullanılan tanısal/girişimsel işlemlerden önce fayda sağlayabileceğini düşündürmektedir.

Anahtar kelimeler: Hipomagnezemi, Koroner Anjiyografi, Kontrast Kaynaklı Nefropati

Introduction

Contrast-induced nephropathy (CIN) is a disorder from exposure to contrast media. The CIN implicates impairment of renal function (the elevation of serum creatinine by >0.5 mg/dl or >25 %) occurring within three days following the intravascular administration of contrast media, not attributable to other causes(1, 2). CIN is associated with increased morbidity and mortality, particularly in high-risk patients undergoing coronary angiography or percutaneous coronary intervention (PCI).

Animal studies have shown that apoptotic processes are faster in animals with low magnesium levels; therefore, cell death is more common in animals with low magnesium levels(3, 4). Cell damage due to oxygen radicals is also observed less in individuals with normal magnesium levels(5). The conclusion to be drawn from this is that it will be more challenging to repair and recycle any cell damage in individuals who already have low magnesium levels. Studies have also shown that magnesium has a nephroprotective effect in using many nephrotoxic drugs, and deterioration in renal functions is reversed more quickly in patients with adequate magnesium levels(6, 7). It achieves this effect by increasing renal blood supply both with the above-mentioned cellular activity and renal vasodilation(8).

The nephrotoxic efficacy of iodine-based contrast agents routinely used in coronary angiography procedures has been known for a long. Magnesium (Mg) has been shown to protect the kidney from contrast media-produced oxygen free radicals (9). In addition, it has been demonstrated that the prophylactic use of intravenous Mg significantly reduces CIN in primary PCI patients(5, 10). However, there is no report in the literature disclosing that hypoMg was a risk factor for CIN after coronary angiography. Thus, the current study aimed to assess the role of hypoMg in the development of CIN after elective coronary angiography.

Material And Methods

Study population

Between December 31, 2016, and February 28, 2018, a total of 223 patients who had undergone coronary angiography procedures and had preprocedural baseline Mg levels were enrolled in this study. HypoMg was defined as Mg< 1.60 mg/dL according to the reference values of the hospital biochemistry device. Among them, 137 were men and 86 women; the median age was 64 (34–89 years). Patients with chronic kidney disease (CKD) stage 5, end-stage kidney disease, active infection, allergic reaction to contrast material, incomplete patient data, those who have used nephrotoxic drugs in the last seven days (NSAID, etc.), contrast agent exposure in the past seven days, and unstable cardiac conditions were excluded. Patients with reduced renal function were hydrated with 0.9 % saline at 1 ml/kg/h for 12 h before and after catheterization. A nonionic, low-osmolality contrast agent (iohexol (300 mg iodine/ml; 672 mosml/kg of water; Kopaq; KOÇSEL İLAÇ SAN. VE TİC. A.Ş.; Türkiye and Omnipaque; GE Healthcare İnc. The USA) was used almost exclusively in our

laboratory.

Study variables

Serum creatinine concentrations were measured before and within 72 h of administration of contrast media in every patient, and further measurements were performed in all patients developing CIN. The serum Mg levels were collected before the coronary angiography. Renal function was assessed by the estimated glomerular filtration rate (eGFR) using the MDRD formula.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD), and categorical data are presented as absolute values and percentages. T-tests were used for parametric comparison. Chi-square tests were used for the comparison of categorical variables as required. A two-sided 95 % confidence interval (CI) was constructed around the odds ratio (OR) point estimate. Logistic regression analysis evaluated the independent association between Mg level, HypoMg, and CIN. All hypothesis testing was two-tailed. A p-value <.05 was considered statistically significant. Analysis was performed by using SPSS 23.0 statistical software.

Results

The baseline clinical characteristics of patients with CIN and non-CIN are summarized in Table 1. Of the 233 patients in this study, hypoMg was present in 15(%6.7) at baseline. Twenty-eight patients (12.6 %) experienced CIN after the procedure. These patients had a significantly higher incidence of hypoMg(%28.6).

Patients who developed CIN had a lower eGFR (Table 1). Compared to patients with or without CIN, patients with CIN also had lower Mg levels. As shown in Fig. 1, compared to patients without CIN, patients with CIN also had lower Mg levels (1.96± 0.15 vs. 1.73±0.08 P<.001).

Table 1. Baselines clinical characteristics.

	Non-CIN (n = 195)	CIN (n =28)	P value
Demographics			
Age(years)	63.6 ± 10.6	65.5 ± 10.0	.382
Male	118(60.5%)	19(67.9%)	.451
Hypertension (HTN)	122(62.6%)	17 (60.7%)	.856
Hyperlipidemia (HL)	70(35.9%)	11(39.3%)	.734
Diabetes mellitus (DM)	50(25.6%)	18(64.3%)	<.001
Congestive Heart Failure (CHF)	61(31.3%)	14(50%)	.044
Coronary artery disease (CAD)	41 (21%)	12(42.9%)	.026
Anemia	45(23.1%)	16(57.1%)	<.001
CKD(<60mL/min/1.73m2)	39(20%)	12(41.7%)	.027
Drugs			
Statın used	75(38.5%)	9(32.1%)	.590
Dıuretıc used	42 (21.5%)	9(32.9%)	.218
ACE/ARB used	106(54.4%)	12(42.9%)	.267
Amount of contrast agent ml	102.43±42.04	104.52±37.68	.534
Laboratory data			
Hgb(g/dl)	13.1±1.8	12.6±2.5	<.001
WBC (10^3 /µl)	9.41±3.16	9.43±3.38	.682
Platelets, mm3	270.25±78.04	273.59±92.84	.135
Creatinine (mg/dl)	1.02±0.91	1.36±1.17	.039
GFR(mL/min/1.73m2)	74.8±17.2	64.4±14.7	<.001
Glucose (mg/dl)	119.34±52.86	153.46±67.29	.019
LDL-C (mg/dl)	124.82±51.22	126.51±48.25	.890
LVEF (%)	54 ± 11	46 ± 12	<.001
HypoMg, n	7(%3.6)	8(%28.6)	.002
Magnesium(mg/dl)	1.96± 0.15	1.73±0.08	<.001

WBC: White blood cell, ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, CKD: Chronic kidney disease, LVEF: left ventricular ejection fraction, GFR: Glomerular filtration rate, LDL-C: low-density cholesterol, HypoMG: Hypomagnesemia

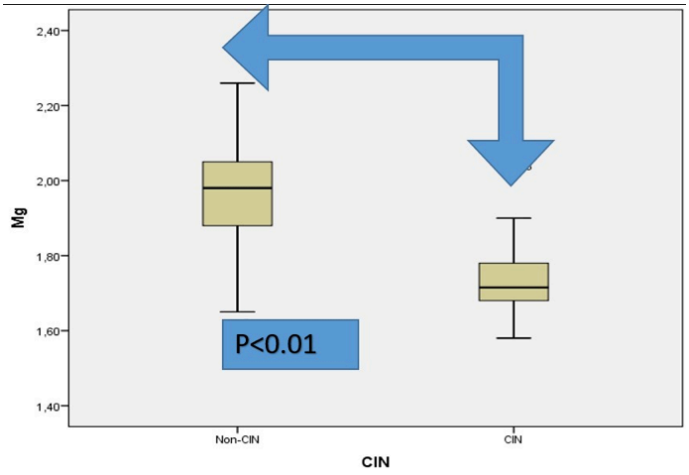

Figure 1. Compared with patients without CIN(Contrast-induced nephropathy), patients with CIN also had lower Mg levels (1.96± 0.15 vs. 1.73±0.08 P<.001).

Logistic regression models were built to assess whether hypoMg contributed to the CIN development. The variables included in the first step of these multivariate analyses were LVEF, presence of diabetes mellitus, AMI, prior MI, baseline eGFR, amount of contrast agent administered, hemoglobin, and Mg level. Multivariate logistic regression analysis revealed baseline Mg levels as independent predictors of CIN after coronary angiography. HypoMg was also an independent predictor of CIN (OR 2.90, 95 % CI 1.42–5.93, P=.004) when introduced into the multivariate model instead of the baseline Mg level.

Discussion

To our knowledge, this is the first study to describe that hypoMg was a risk factor for CIN after coronary angiography. CIN is an essential complication in using iodinated contrast media (1, 11). With an increasing number of diagnostic and therapeutic catheterizations each year, particularly among patients with severe conditions predisposing to CIN, the incidence of CIN will continuously increase.

The present study demonstrated that Mg level was related to the incidence of CIN during hospitalization. Of the 223 patients enrolled, CIN occurred in 28 patients (12.6%). HypoMg was defined as Mg< 1.60 mg/dL. CIN occurred in %53.3 of the patients with HypoMg and %8.9 of those with non-HypoMg (P=<0.001). The incidence of CIN in our study is higher than the results of previous studies(12, 13). Also, due to excluding incomplete patient data, we may have included high-risk patients (DM (30.5%), anemia(%27.4), CKD(%22.9), and CHF (33.6%)) in terms of CIN.

When risk factors were considered, many patients became hypomagnesemia from chronic diuretic therapy combined with low dietary magnesium intake. Patients with long-standing diabetes mellitus also acquire a renal tubular defect for magnesium and become hypomagnesemia. But our study demonstrated that baseline hypoMg was an independent risk factor for CIN in all patients. These associations remained when adjusted for all variables, including CKD, CHF, DM, and medications (Dıuretıc used, etc.).

Several plausible explanations exist for the increased CIN risk in patients with hypoMg. The renoprotective effect of magnesium is likely multifactorial. Besides its role as an antioxidant and coenzyme for compensatory sodium-potassium ATPase (Na+/K+-ATPase or Na+/K+-pump), magnesium has blocked the calcium channel (9). It counteracts vasoconstriction by endogenous catecholamines and potentiates the action of endogenous vasodilators(14-16). The infusion of Mg has increased renal blood flow via an endothelium-dependent release of nitric oxide and its ability as a calcium channel antagonist (17, 18).

Previously Mg has been shown to protect the kidney from contrast media-produced oxygen free radicals(9). In addition, it has been demonstrated that the prophylactic use of intravenous Mg significantly reduces CIN in primary PCI patients(10). These results suggest magnesium replacement in hypomagnesemia may be indicated before diagnostic/interventional studies using contrast media.

The present study has some limitations. Our study is single-center; thus, the results presented here can be biased due to some non-identified center characteristics. Secondly, this is an observational study, so we may have included high-risk patients (DM (30.5%), anemia (%27.4), CKD(%22.9), and CHF (33.6%)) due to excluding incomplete patient data. In addition, because of the observational nature of our study, a causal association between hypoMg and CIN was not completely established, the demonstration of which would further require randomized, controlled trials.

Conclusion

This study demonstrates that hypoMg is associated with an increased risk for CIN.

Disclosure Statement

The authors have no relevant financial or non-financial interests to disclose.

Peer-Review Externally

Peer Reviewed

Support Resources

No financial support was used by authors during this study.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the content of this article.

Ethical Declaration

Ethical permission was obtained from the University of Health Science, Diskapi Yildirim Beyazit Training and Research Hospital Clinical Research Ethics Committee for this study with the date 18.04.2022 and number 135/07, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: N.B.O, S.I, Design: N.B.O, S.I, E.A. ,.Data Collection or Processing: N.B.O, S.I, E.A., F.A, I.G., Analysis or Interpretation: N.B.O, G.G., Literature Search: N.B.O, S.I, E.A., H.F.Ş., I.G, M.A.F, Writing: N.B.O, S.I., G.G

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Original Article

Perivascular administration of hyaluran-cyanoacrylate complex gel for deep venous reflux

Derin venöz reflü tedavisinde hyaluran-siyanoakrilat kompleks jelin perivasküler uygulaması

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Abstract

Aim: Deep venous insufficiency is an important health issue affecting the population worldwide. In this study we aimed to assess the effectiveness and safety of a novel antireflux treatment procedure in patients with primary deep vein insufficiency.

Material and Methods: Between October 2016 and December 2018, 81 valvular leak operations consisting of perivenous hard gel injection were performed in 81 patients with primary deep venous insufficiency. The clinical symptoms of the patients were between C3-C6 according to the CEAP clinical classification. Venous insufficiency associated with only one deep venous valve was verified with Doppler ultrasonography. Patients were assessed with physical and ultrasound examination on the follow-up visits, which were achieved on the third day and at the first, sixth, and twelfth months. The nonexistence of reflux in the treated valve level was defined as the success of the procedure. Any reflux, which lasted 0.5 seconds or more, was regarded as a lack of success.

Results: The ages of the patients ranged between 32 and 78. All the patients had deep venous insufficiency. The follow-up could be achieved in all the patients. The mean volume of the gel administered was 2.4±0.9 ml. The mean procedure duration was 22.3±8.9 (range 14–42) minutes. The procedures could be performed successfully in all of the patients confirmed perioperatively and on the third day of follow-up with the elimination of reflux. The sixth-month follow-up, with the same vein diameter after the treatment without any reflux, revealed the same findings as to the first-month follow-up. The treatment was not associated with any significant morbidity or mortality. The VCSS decreased significantly when preprocedural and twelfth-month VCSS were compared as 21.8 ± 4.8 and 3.8±0.7, respectively ($p<0.001$).

Conclusions: Treatment of venous insufficiency with the novel hard gel injections of hyaluronic acid and n-butyl-cyanoacrylate seems safe, effective, and feasible confirmed with early and midterm follow up results.

Keywords: Venous insufficiency; Femoral vein; Venous valves; Lower extremity; N-butyl-cyanoacrylate.

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Öz

Amaç: Derin venöz yetmezlik dünya çapında popülasyonu etkileyen önemli bir sağlık sorunudur. Bu çalışmada primer derin ven yetmezliği olan hastalarda yeni bir antireflü tedavi prosedürünün etkinliğini ve güvenilirliğini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Ekim 2016-Aralık 2018 tarihleri arasında primer derin venöz yetmezliği olan 81 hastaya perivenöz sert jel enjeksiyonundan oluşan 81 venöz valvüler kaçak operasyonu uygulandı. Hastaların klinik semptomları CEAP klinik sınıflamasına göre C3-C6 arasındaydı. Sadece bir derin venöz kapakla ilişkili venöz yetmezlik Doppler ultrasonografi ile doğrulandı. Hastalar 3. gün, 1., 6. ve 12. aylarda yapılan kontrollerde fizik muayene ve ultrasonografi ile değerlendirildi. Tedavi edilen kapak seviyesinde reflü olmaması işlemin başarısı olarak tanımlandı. 0,5 saniye veya daha uzun süren herhangi bir reflü, başarısızlık olarak kabul edildi.

Bulgular: Hastaların yaşları 32 ile 78 arasında değişiyordu. Hastaların tamamında derin ven yetmezliği vardı. Takip tüm hastalarda sağlanabildi. Uygulanan jelin ortalama hacmi 2,4±0,9 ml idi. Ortalama işlem süresi 22,3±8,9 (dağılım 14-42) dakikaydı. Hastaların tamamında işlem başarıyla uygulandı ve perioperatif olarak ve takibin 3. gününde reflünün ortadan kalkması ile doğrulandı. Altıncı ay kontrolünde, reflü olmaksızın tedavi sonrası aynı damar çapı ile birinci ay kontrolü ile aynı bulgular saptandı. Tedavi, herhangi bir önemli morbidite veya mortalite ile ilişkili değildi. VCSS, işlem öncesi ve 12. ay VCSS karşılaştırıldığında sırasıyla 21,8 ± 4,8 ve 3,8±0,7 olarak anlamlı olarak azaldı ($p<0,001$).

Sonuçlar: Venöz yetmezliğin yeni sert jel hyaluronik asit ve n-bütil-siyanoakrilat enjeksiyonları ile tedavisi güvenli, etkili ve uygulanabilir görünmektedir ve erken ve orta vadeli takip sonuçları ile doğrulanmıştır.

Anahtar Kelimeler: Venöz Yetmezlik; Femoral ven; Venöz kapaklar; Alt ekstremite; N-bütil-siyanoakrilat.

Introduction

Chronic venous insufficiency (CVI) is a condition that impairs patients' quality of life with specific clinical manifestations and symptoms, such as edema, ulcers, and pain. Deep veins in the affected limb can be involved in the disease with reflux in the venous valves, termed deep venous reflux (DVR). The treatment in DVR is mainly compression therapy, but in severe cases, surgery or interventional therapies can be options [1-3].

Etiological classification of the DVR is performed using well-known CEAP classification, where "E" stands for etiology. The secondary reasons of DVR, as in post-thrombotic syndrome (PTS) or trauma (Es) are the most frequent types and seen in nearly 60-85% of cases [4,5]. The valve structure is injured due to inflammation and thrombosis in the vein, leading to a partial or total valve dysfunction. Hence, a direct valve repair is not an option for treatment [6]. On the other hand, attempts for reversal of the reflux by reversal of the dilated venous segment into normal diameters and approximation of the valvular structures may be an option in this particular group to prevent DVR. Such procedures were attempted surgically (7, 8) and with percutaneous means (3, 9).

The application of hard gel injections of hyaluronic acid and n-BCA (n-butyl-cyanoacrylate) over defective deep vein valves between the deep vein and muscle fascia, so called internal compression therapy (ICT) is a unique and novel treatment option [3]. By applying hard gel implants, the goal is to approximate the vein valves to each other. The gel remains over the vein and can shift with the muscle pump helping the malfunctioning valves work appropriately. This paper aimed to verify the effectiveness and safety of internal compression therapy in patients with primary deep valve insufficiency (PDVI) during a single-session procedure.

Materials and Methods

Patient selection

From October 2016 to December 2018, 81 patients who suffered from primary deep venous insufficiency underwent valvular leak operations. Venous insufficiency was associated with only one deep venous valve. CEAP and Venous Clinical Severity Score (VCSS) classifications were used to categorize the patients. Only patients with CEAP clinical scores between C3-C6 were included in the study. The study's ethical approval was obtained (Number: 92198657). Following patient eligibility and obtaining written informed consent, the clinical and ultrasound (US) examinations were performed by a vascular surgeon and an unbiased radiologist.

Patients were assessed by duplex US scanning to verify the superficial, deep, and perforator veins' actual anatomy.

Duplex scanning was conducted in the standing position using the conventional method. Assessment of the reflux was performed using a cuff placed at the calf level, and afterward, the evaluation of the reflux was carried out in the supine position. CEAP, VCSS, and US findings were recorded.

Selection criteria

Deep venous reflux was seen in all patients with duplex scanning. The CEAP classification was Clinical classification 3-6 (C3-6), Etiologic classification was primary (Ep), Anatomic classification deep (Ad), and Pathophysiologic classification reflux (Pr) among patients. Of 81 patients, 53 had superficial/perforator reflux, and these patients were treated before the ICT intervention. Patients with ulcers had lesions that were resistant to standard therapies and superficial and/or perforator vein abolition procedures. The ulcers persisted for at minimum one year or had been recurring in the same interval of more than once, which implied that the ulcer had been existing for more than one year.

The exclusion criteria were advanced limited mobilization, thrombophilic syndrome, post-thrombotic etiology, history of deep vein thrombosis, contraindication to anticoagulant therapy, severe comorbidity, and eligibility for surgical treatments such as femoral transposition or valve transplant, and deep venous reflux <2 seconds [10-14].

Intervention technique

Local anesthesia was used for all procedures, and the interventions were done with the standard sterile method. With the extremity mildly flexed, the patient was positioned supinely before the procedure. The treatment goal is to decrease the diameter of the vein until the space among vein valves closes. Defective deep vein valve positions were verified under US. All the insufficiencies were detected in the suprasaphenous valves in common femoral veins, and the anatomical sites for injections were determined by US (Figure 1). The space between defective valves and the vein caliper were determined (Figure 2).

The ICT (Internal Compression Therapy) Paravalvular Leak Device (Invamed, Ankara, Turkey) mainly consists of two parts. The main part includes a gap-closing kit with a monitored mixing unit, administration unit, and two vials of hyaluronic acid and n-BCA. The distribution part of the device is a system with an aspiration and administration adapter, a distribution line, and 2 units of 6F, 11-cm cannulas (Figure 3). The access to the region between the muscle fascia and the deep vein was done using the Seldinger technique. The access was performed twice, one entry on each side, on opposite sides of the vein to administer ICT hard gel evenly across the deep vein. A 0.035", 45-cm guidewire was introduced and secured just over the deep vein after the access. The needles were removed, and 6F, 11-cm distribution system cannulas were introduced over the wire to both sides of the vein valve.

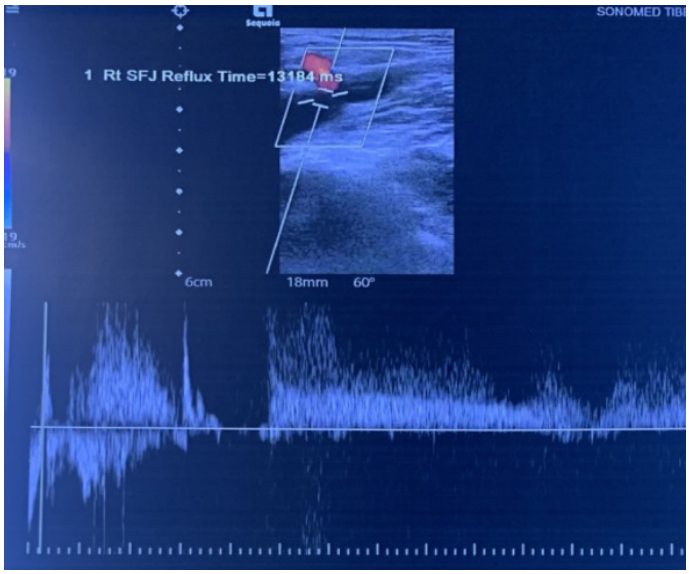

Figure 1: Preoperative doppler ultrasonography revealing reflux of saphenofemoral junction.

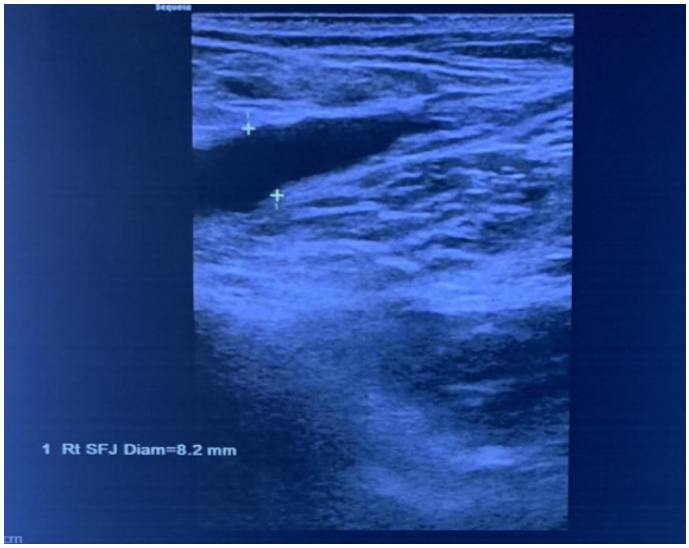

Figure 2: The preoperative saphenofemoral junction diameter on doppler ultrasonography.

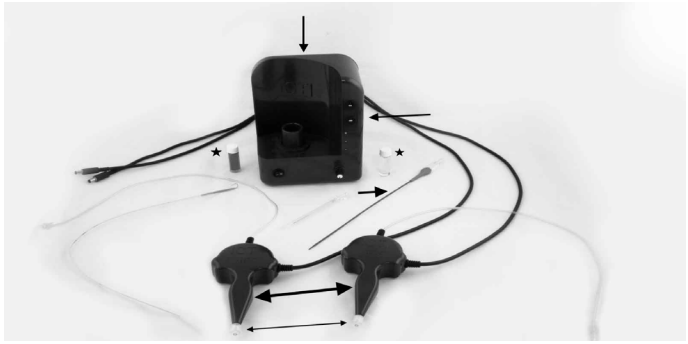

Figure 3: The Internal Compression Therapy (ICT) system. System is composed of a mix unit (down arrow), an injection unit (left arrow), vials containing hyaluronic acid and n-BCA (stars), aspiration and injection connectors (two-sided thin arrow), delivery lines and delivery ports (two-sided arrow), and two 6F-11 cm cannulas (right arrow).

Two separate 2-ml vials of hyaluronic acid and n-BCA come with the ICT kit. The hyaluronic acid and n-BCA were blended for 30 minutes with a preset program in the ICT device mixing unit prior to administering over the valves. The mixed vial was attached to the aspiration adapter while the cannulas were connected to the administration adapter. The ICT system administration unit was triggered and calibrated to the required administration rate. Under US, handled administration started, and the vein caliper reduced to the disparity between the vein caliper and the space between the valves (Figure 4). The aspiration was activated instantly to collect excessive gel if needed. After the space among valves was eliminated, manual compression was applied for 1-2 minutes to the injection site. Then, the valve function and reflux were documented with US (Figure 5). The administration of the hard gel was repeated if the reflux persisted. The cannulas were removed after verifying the competency of the valves. The compression stockings (20-30 mmHg) were utilized just after the procedure, and the patient was encouraged for prolonged use.

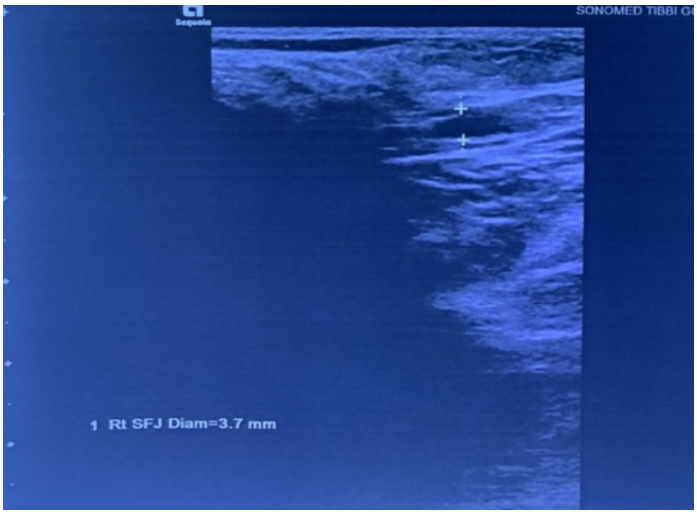

Figure 4: The postoperative saphenofemoral junction diameter on doppler ultrasonography.

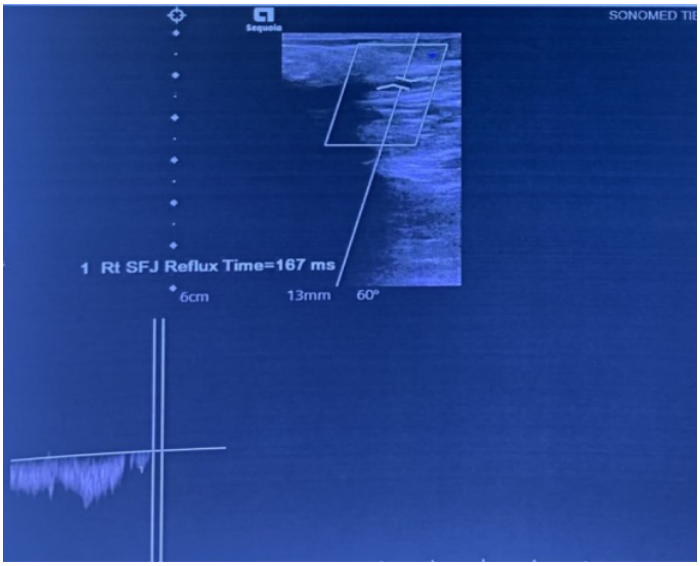

Figure 5: Postoperative doppler ultrasonography revealing reflux of saphenofemoral junction.

Follow-up

Patients were assessed with physical and US examination on the follow-up visits, which were achieved on the third day and at the first, sixth, and twelfth months. The success of the therapy was identified as a patent deep vein without reflux or with reflux, which is not exceeding 0.5 seconds.

Statistical analysis

Statistical analysis was carried out using the SPSS for Windows software package (ver. 22; SPSS Inc. Chicago, IL, USA). All variables were assessed using visual (histograms, probability plots) and analytical (Kolmogorov-Smirnov test) modes to decide if they were normally distributed. Continuous parameters are indicated as the means±SDs for normally distributed parameters and as medians with interquartile ranges for non-normally distributed parameters. Categorical parameters are described as numbers and percentages (n, %). Reference level alterations in VCSS were contrasted between control periods using paired t-test. Kaplan-Meier estimator was used for estimating the total removal of deep vein reflux. P-values <0.05 were assumed to be of statistical significance.

Results

A total of 81 patients (38 male, 43 female, median age: 54; range, 32 to 78 years) with deep venous insufficiency who had VCSS between 10-29 (mean: 21.8 ± 4.8) were enrolled in the study. The mean vein diameter at the valve level was 11.9 ± 2.7 (range 8.9-16.5) mm. The reflux was at least 3 seconds which reached up to 15 seconds (mean: 11.6 ± 3.6 sec) at the valve level. The distance between the valves ranged between 1.9-7.0 (mean: 3.8 ± 1.2) mm. There were 25 (31%) patients at C3, 21 (26%) patients at C4, 24 (30%) patients at C5 and 11 (13%) patients at C6 class according to the CEAP classification. In 43 patients the left leg was intervened where as in the remaining the right leg. Except one popliteal vein, femoral vein was the primary site of intervention. Patient demographics are provided in Table I.

The follow-ups were achieved in all the patients. The mean volume of the gel administered was 2.4±0.9 ml. The mean procedure duration was 22.3±8.9 (range 14–42) minutes. The procedure's achievement amounted to 100%, and just after the procedure and on the third day of follow-up, total elimination of reflux was confirmed. The sixth-month follow-up, with the same vein diameter after the treatment without any reflux, revealed the same findings as to the first-month follow-up. In two patients vein diameters were observed to be increased with a reflux less than 0.5 seconds at the twelfth-month follow-up, described in the study's success criteria.

Table 1: Demographic features of the patients.			
	Mean ± Std (Mean)/ Preoperative	**Mean ± Std (Mean)/ Postoperative**	**n (%)**
Age (years)	54 ± 22.4 (range 32-78)		
Female gender			43 (53)
Male gender			38 (47)
Vein diameter at valve level (mm)	11.9 ± 2.7 (range 8.9-16.5)	3,9 ± 0,8 (range 2.3-7.5)	
Distance between valves (mm)	3.8 ± 1,2 (range 1.9-7.0)		
Reflux (sec)	11.6 ± 3.6 (range 3-15)		
Preoperative CEAP category			
C3			25 (31)
C4			21 (26)
C5			24 (30)
C6			11 (13)
Postoperative CEAP category			
C0			33 (41)
C1			33 (41)
C2			10 (12)
C3			3 (4)
C4			1 (1)
C5			1 (1)
VCSS (p<0.001)	21.8 ± 4.8 (range 10-29)	1,9 ± 1,49 (range 0-7)	
Right leg/Left leg			38/43(47/53)
Symptomatic improvement			75 (92)
Postoperative Deep Vein Thrombosis			-

The treatment was not associated with any significant morbidity or mortality. Minority of the patients experienced pain early after intervention which was controlled with non-steroid anti-inflammatory agents and completely disappeared in all patients by the end of 24 hours. No complications such as ecchymosis, skin pigmentation, hematoma, paresthesia, deep vein thrombosis, or pulmonary embolism were seen after the treatment. In a median interval of 10 (range: 3-18) weeks, all the patients exhibited complete ulcer recovery. The postprocedural caliper of the deep vein was 8.9±1.6 mm. After the operation, all patients had significantly improved VCSS. The preprocedural and twelfth-month VCSS were 21.8 ± 4.8 and 3.8±0.7, respectively (p<0.001). There were 33 patients at C1, 10 patients at C2, 3 patients at C3, 1 patient at C4 and 1 patient at C5 class according to the CEAP classification after 12 months.

Discussion

The current research provides one of the first experiences and preliminary results of the application of hard gel injections of hyaluronic acid and n-BCA (n-butyl-cyanoacrylate) over defective deep vein valves between the deep vein and muscle fascia with a novel equipment, the ICT (Internal Compression Therapy) Paravalvular Leak Device (Invamed, Ankara, Turkey), in the literature. Yavuz et al. conducted the first study in deep venous insufficiency, which evaluated the clinical results of internal compression treatment. They concluded that the postprocedural outcomes were safe and sufficient. We also analyzed the early-term clinical results of this treatment modality in PDVI patients. The results of our study are consistent with the results published by Yavuz et al., which confirmed that for the management of deep venous insufficiency, the internal compression treatment is secure and extremely efficient [3]. During the 12-month monitoring, there were no significant adverse or toxic instances recorded. Until now, there are no mentioned toxic, carcinogenic, or mutagenic consequences of hyaluronic acid or n-BCA with vascular or nonvascular applications [15-18].

Valvuloplasty is rarely the treatment choice due to the feasibility, risks and benefits are discussed in clinical practice up to date. The efficacy of surgical approaches including valvuloplasty, axillary vein transfer, and dacron sleeve in situ are still under debate, and no definite management for deep venous insufficiency is formulated [19-21]. However, perivenous internal compression is easy to perform after a learning period with improved results. According to Ragg et al., hyaluronan (hyaluronic acid) in superficial venous insufficiency, together with sclerotherapy, is suitable to

compress veins. Hyaluronan compression was successful in reducing the diameter of the vein. Moreover, no complications were observed clinically in terms of physical examination and patient comfort during follow-up [9, 17]. N-butyl cyanoacrylate is also shown to be reliable and successful for intravascular use in patients with superficial venous reflux disease [22-26]. In addition to polymerization of the molecule when it interacts with blood, the binding effect of the n-BCA to the vein wall enhanced the collapse of the vein. The binding property of the n-BCA increases when it combines with hyaluronic acid, which is then stabilized by n-BCA over the intended vein segment.

The hard gel administration over the two sides of the vein was aimed to cover the vein's external surface circumferentially. This method permits forming a permanent exoskeleton over the vein, moving together with the muscle fascia, and taking advantage of the muscle pump. There is no fixed volume to be injected over the vein. The administered volume differs according to the patient's duplex US examination, where the distance between valve leaflets is measured. The aim is to provide competence of the valve leaflets.

Treatment of deep venous reflux is still limited and attempts to overcome reflux with interventional techniques still have a low success rate. Moreover, surgical treatment, which seems to be the only option in patients with post-thrombotic etiology, is still controversial [27]. The lack of treatment options forces researchers to develop new techniques [28-31]. A relatively high success rate was achieved in early and mid-term follow up results of our cohort in our study; however, the late results should also be evaluated.

Limitations

Although we report a single-center prospective experience on a novel method, there are many drawbacks in this study. The follow-up times provide only early- and mid-term results with limited information on symptoms. We cannot comment on the effects of parallel development of additional reflux sites, which could be regarded as a late failure of the procedure. Moreover, hospital stay costs involved with returning to work, and overall treatment costs are not calculated. Another limitation may be regarded to the relatively small cohort size. Additionally, the technique requires expertise and good quality duplex US devices. The duplex US quality significantly reduces after polymerization of the hyaluronic acid and n-BCA combination when interacts with the tissue; hence, the approximation of the valves should clearly be visualized and degree of the reflux should not be relied on the red-blue color changes.

Conclusion

In conclusion, the internal compression therapy with the novel ICT (Internal Compression Therapy) Paravalvular Leak Device (Invamed, Ankara, Turkey) seemed safe, effective, and feasible in treating PDVI. The deep vein caliper reduces with the administration of hard gel over the vein wall to form an exoskeleton and prevents valvular leakage. The initial findings are promising; however, comparative randomized clinical trials are warranted to evaluate the long-term results and improve the quality of the system.

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Orijinal Makale

Çocuk yoğun bakımda yatan hastalar için istenen çocuk ve ergen psikiyatrisi konsültasyonlarının değerlendirilmesi

Evaluation of child and adolescent psychiatry consultations requested for patients in the pediatric ıntensive care unit

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Öz

Amaç: Pediyatrik Yoğun Bakım Ünitesinde yatan bedensel hastalığı olan çocuklarda davranışsal-duygusal psikopatolojiler sıklıkla gelişmektedir. Fiziksel hastalığa eşlik eden bu ruhsal durumlar tedaviyi uyumu bozarak olumsuz sonuçlara yol açabilmektedir. Bu çalışmada çocuk yoğun bakım ünitemizde kritik hastalık nedeniyle izlenen hastalar için son 3 yıl içinde istenen çocuk psikiyatri konsultasyonlarının değerlendirilmesi amaçlanmıştır

Gereç ve Yöntemler: Çalışmamızda 2019-2022 yılları arasında Dr. Behçet Uz Çocuk Hastanesi Çocuk Yoğun Bakım ünitesinde izlenen çocuk psikiyatrisi konsültasyonu istenen hastaların verileri geriye dönük olarak taranmıştır. Hastaların demografik özellikleri, bedensel hastalık tanıları, konsültasyonların istenme nedenleri, konsültasyon sonucunda saptanan psikiyatrik tanılar ve bunun sonucunda tedavi uygulanıp uygulanmadığı, verilen bir tedavi olması durumunda hangi medikal tedavilerin tercih edildiği, psikiyatrik tedavi ve izlem sürecine ilişkin veriler kaydedilmiştir

Bulgular: Üç yıllık sürede çocuk yoğun bakımda izlenen çocukların 118'i (%4,9) için psikiyatri konsültasyonu istenmiştir. Konsültasyon istenenlerin çoğu kızdır (%61,9) ve 12 yaş veya üzeri yaşta % 71,4 hasta bulunmaktadır. En sık konsültasyon isteme nedeni özkıyım girişimleri (%33,1) ve depresif görünüm (%25,5) olarak saptanmış olup en sık konulan tanı majör depresif bozukluk ve uyum bozukluğudur. Olguların %31'inde psikotrop ilaç başlanmış olup erkekler ve kızlar arasında anlamlı fark saptanmamıştır.

Sonuç: Bu çalışma bedensel hastalığı olan kritik çocuk yoğun bakım hastalarında ruhsal hastalıkların sık görülmesine rağmen psikiyatri konsültasyonu istenme oranlarının düşük olduğunu saptamıştır. Bu durum yoğun bakım hekimlerinin belirtileri anlama ve değerlendirme konusunda hastaların bilinç durumları ve primer hastalıkları nedeniyle güçlükler yaşadığına işaret etmektedir. Bu nedenle çocuk psikiyatrisi ile birlikte multidisipliner bir yaklaşım izlemeleri ve işbirliği içinde olmaları hastanın tedaviye uyumunu arttırarak yatış sürelerini kısaltacaktır.

Anahtar Kelimeler: çocuk psikiyatrisi; konsültasyon; pediyatrik yoğun bakım; kritik hasta

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Abstract

Aim: Behavioral-emotional psychopathologies often develop in children with physical illness in the Pediatric Intensive Care Unit. These mental conditions accompanying physical illness can lead to negative consequences by disrupting treatment compliance. In this study, it was aimed to evaluate the child psychiatry consultations in our unit.

Material and Methods: Between 2019 and 2022, the data of patients who were followed up in our Pediatric Intensive Care Unit and formally requested a child psychiatry consultation were evaluated retrospectively in this study. The demographic characteristics of the patients, primary diagnoses, reasons for the consultations, psychiatric diagnoses as a result of the consultation were all recorded.

Results: Psychiatric consultation was requested for 118 (4.9%) of the children observed in our unit throughout a three-year period. The majority of individuals requested for consultation (61.9%) were female, and 71.4% were aged 12 or older. Suicide attempts (33.1%) and depressive appearance (25.5%) were the most prevalent grounds for receiving consultation, with major depressive disorder and adjustment disorder being the most common diagnoses. Psychotropic medicines were prescribed in 31% of the patients, with no statistically significant difference between boys and girls.

Conclusion: Although mental disorders are widespread in critically ill pediatric patients, our study indicated that psychiatric initial consultation is low in children with physical illnesses. Therefore, taking a multidisciplinary approach and collaborating with child and adolescent psychiatry will improve patient compliance to the tretament and minimize the length of stay.

Key words: child psychiatry; consultation; pediatric intensive care; critically ill

Giriş

Pediyatrik Yoğun Bakım Ünitesi (PYBÜ) öncelikli işlevi yaşamı idame ettirmek olan yoğun, akut tedavi ile karakterize çoğu zaman kısa dönemli yatışların olduğu birimlerdir. Yoğun bakım biriminde önceliğin tıbbi girişimler olması, zaman kısıtlılığı nedeniyle mahremiyetin ikinci planda kalması nedeniyle çocuklar yatış süreci ve uygulanan tedavilerden psikolojik olarak etkilenebilmektedir [1]. Çocuk yoğun bakım üniteleri akut travma hastalarından, yeni tanı almış ciddi hematolojik hastalıklara, özkıyım girişiminde bulunmuş ergenlerden, kompleks cerrahi operasyon sonrası iyileşme sürecindeki çocuklara ve ventilasyon bağımlı hastalara kadar geniş bir yelpazede çeşitlilik gösteren hastalara hizmet vermektedir. Yoğun bakıma yatış planlı ya da plansız olabildiği gibi bazı çocuklar sağlığına tamamen kavuşup taburcu olurken; bazıları hastanenin diğer bölümlerine ya da palyatif bakım merkezine yönlendirilmektedir. Bazı durumlarda ise hastalar hayatlarını kaybetmektedir. Tüm bu hastaların yatış nedenleri farklı olmakla birlikte hastaneye yatan her çocukta ruhsal bir tepki ortaya çıkar; bu tepkinin düzeyi psikopatoloji oluşma süreci; geçmiş deneyimleri, aile öyküleri, sosyokültürel kökenleri, iletişim kurma becerileri gibi birçok faktöre bağlı şekillenir. Bedensel ve ruhsal hastalıklar bir arada olduğunda ise çocukların muayene, tanı ve tedavi uygulamaları olumsuz etkilenmektedir[1,2,3].

Var olan psikopatolojilerin tedavisi yoğun bakımdaki tedaviye uyumu arttırarak yatış süresini azaltmaktadır. Bu yüzden çocuk yoğun bakım hekimleri bedensel hastalığı olan çocuklarda davranışsal-duygusal durumların da gelişebileceğini düşünerek konsültasyon liyezon psikiyatrisi ile beraber çocukların tedavisinde multidisipliner bir yaklaşım göstermelidir [2].

Yoğun bakımdan istenen psikiyatri konsültasyonlarının çoğu tanısal amaçlı veya düzenleyici, yürütücü vasıftadır. Fakat genel olarak hastaneye yatan çocuk hastalarda ülkemizde konsültasyon isteme oranı diğer gelişmiş ülkelere göre oldukça düşüktür. Bu durum özellikle yoğun bakımlarda ruhsal bozuklukların tanınmasındaki bazı güçlüklerden kaynaklanıyor olabilir. Bu yüzden yoğun bakımda yatan hastalarda çocuk ve ergen liyezon psikiyatrisi uygulamalarının yaygınlaştırılmasında çocuk yoğun bakım hekimleri ile çocuk ve ergen psikiyatrisi arasındaki işbirliği çok önemlidir[2,4,5]. Gerek fiziksel hastalığı nedeniyle yatan çocuklara, gerekse çocukların kritik hastalığı nedeniyle anksiyetesi yüksek ailelerine gerekse çocuk yoğun bakım uzmanlarına yardımcı olmak amacıyla mevcut konsültasyon hizmetleri gözden geçirilerek eksikliklerin giderilmesi yönünde çalışmalara ihtiyaç vardır [2,6,7].

Bu çalışmada bedensel bir hastalık veya belirti nedeniyle çocuk yoğun bakım ünitemize yatırılan psikiyatrik yardım gereksinimi

olan hastaların değerlendirilmesi sonucu elde edilen verilerin hastaların demografik özelliklerine, konsültasyon istenme nedenlerine, ruhsal tanılarına ve tedavilerine göre dağılımlarının incelenmesi amaçlanmıştır.

Gereç ve Yöntemler

Bu çalışmada 2019-2022 yılları arasında Dr. Behçet Uz Çocuk Hastanesi Çocuk Yoğun Bakım ünitesinde izlenen çocuk psikiyatrisi konsültasyonu istenen hastaların verileri kurum yetkililerinden gerekli izinler ve etik kurul onayı alınarak hastane bilgi sistemi üzerinden geriye dönük olarak incelenmiştir. Çalışmaya dahil edilen tüm hastalardan ve ailelerinden bilgilendirilmiş onam formu alınmıştır. Hastaların demografik özellikleri, bedensel hastalık tanıları, konsültasyonların istenme nedenleri, konsültasyon sonucunda saptanan psikiyatrik tanılar ve bunun sonucunda tedavi uygulanıp uygulanmadığı, verilen bir tedavi olması durumunda hangi medikal tedavilerin tercih edildiği, ve psikiyatrik tedavi ve izlem sürecine ilişkin veriler kaydedilmiştir. Çocuk yoğun bakımdan istenen konsültasyonlarda hastaların ruhsal değerlendirilmesi yatak başında çocuk psikiyatri uzmanı ve kıdemli çocuk psikiyatri asistanı tarafından yapılmıştır. Hastaların muayene bulguları hastane bilgi sistemine konsültasyon formuna kaydedilerek anne, baba, takip eden hekim ve hemşire ile de görüşülerek Ruhsal Bozuklukların Tanısal ve İstatistiksel Elkitabı (Diagnostic and Statistical Manual of Mental Disorders) DSM- V kriterlerine göre tanı konulmuştur [8].

İstatiksel analizler için toplanan veriler SPSS (version 22.0, SPSS Inc. Chicago, IL, USA) ile analiz edilmiştir. Değerlendirmede tanımlayıcı istatistiksel yöntemler kullanılmıştır (ortalama, standart deviasyon, % dağılımı). Kategorik değişkenlerin karşılaştırılmasında ki-kare testi kullanılmış, p <0,01 altı anlamlı kabul edilmiştir.

Bulgular

Çocuk yoğun bakım ünitemizde son 3 yılda 18 yaş altı toplam 2400 hasta izlenmiş olup bu kritik hastaların yalnızca 118(%4,9) tanesinden çocuk ve ergen psikiyatrisi konsültasyon istemi yapıldığı saptandı. Konsultasyon istenen hastaların % 38,1'i (n=73) erkek, %61,9'u (n=45) kız olmak suretiyle, en küçüğü 4 yaşında olup yaş ortalaması 12 ±5,0 yıl saptandı. Hastaların %29,6'sı 12 yaş altında iken; % 71,4'ü 12 yaş üzerinde idi.

Çocuk yoğun bakımdan konsültasyon istenen hastaların yatış tanılarına bakıldığında en yüksek oranı % 48 ile özkıyım girişimleri ve % 26 ile kronik hastalıklar oluşturmakta idi. Tüm konsültasyon istenen hastaların % 42'sinin altta yatan kronik hastalığı mevcuttu. Hastaların demografik özellikleri ve yatış tanıları Tablo 1'de özetlenmiştir.

Tablo 1. Konsültasyon istenen çocuklardaki bedensel/yatış hastalık tanıları

Demografik veriler	n=118
Yaş (ay) Median(min-max)	146,5 (48-225)
Cinsiyet	n(%)
Kız	73 (61,9)
Erkek	45 (38,1)
Yatış Süresi(gün)-Median (IQR)	7 (1-246)
Yatış Tanı n(%)	
Septik şok	17(14,4)
Suisid	48(40,7)
Bronkopnomoni	13(11)
Nörolojik hastalıklar	26(22)
Kalp hastalıkları	2(1,7)
Metabolik hastalıklar	2(1,7)
Doğumsal hastalıklar	4(5,1)
Neoplastik hastalıklar	6(3,4)
Kronik Hastalık Tanısı n(%)	
Solunumsal	6(5,1)
KVS	4(3,4)
Nörolojik	24(20,3)
Romatolojik	10(8,5)
Metabolik hastalık	2(1,7)
Psikiyatrik bozukluk	7(5,9)
Hematolojik hastalık	7(5,9)
Kronik hastalık yok	58(4,2)

Konsultasyon isteme nedenleri incelendiğinde ise yoğun bakım ünitesinde en çok akut bedensel sorunlar/travmalar sonucu oluşan özkıyım girişimleri (%33,1; n=39) ve depresif görünüm (%25,5; n=30) nedeniyle konsültasyon istendiği saptandı. Konsultasyon nedenleri erkek ve kızlar arasında karşılaştırıldığında cinsiyete göre anlamlı bir fark olmadığı görüldü(p: 0,037).

Kliniğimizde çocuk psikiyatri konsültasyon hekiminin yaptığı ruhsal değerlendirme sonucunda en sık konulan psikiyatrik tanılar sırasıyla majör depresif bozukluk (%35,6, n=42), uyum bozukluğu(%24,6), anksiyete bozukluğu (%14,4) ve deliryum (%6,8) olarak saptandı. Bu tanıların oranları erkekler ve kızlar arası anlamlı fark göstermedi (p>0,001, Fisher'in kesin $\chi 2$ testi).Hastaların 10'unda (3 erkek, 7 kız) (%8,5) herhangi bir psikopatoloji saptanmadı. Hastaların konsültasyon nedenleri ve konsültasyon sonucu saptanan psikopatolojileri içeren veriler Tablo 2'de gösterilmiştir.

Konsultasyon sonuçlarına göre hastaların % 41,5'ine (n=49) medikal tedavi olarak psikotrop

ilaç başlandığı saptandı. En sık başlanan psikotrop ilaç grubu sırasıyla; antidepresanlar (%19,5,n=23), antipsikotikler (%16,1,n=19), anksiyolitikler(%3,4, n=4) olmuştur(Tablo

3). Değerlendirme sonucu kızların %57,1'ine erkeklerin ise %42,9'una ilaç başlanmış olup aradaki fark anlamlı saptanmamıştır (p=0,374).

Tablo 2. Konsultasyon isteme nedenleri ve konsultayon sonucu saptanan psikiyatrik tanılar

	Toplam n (%)	Erkek n (%)	Kadın n (%)
Kons nedeni			
Suisid girişimi	39(33,1)	27 (30,8)	12 (69,2)
Depresyon	30 (25,5)	14 (46,6)	16 (53,3)
Anksiyete	16(13,6)	6 (37,5)	10 (62,5)
Tedaviye uyumsuzluk	5 (4,2)	5 (100)	0 (0)
Davranış sorunları	9 (7,6)	3 (33,3)	6 (66,7)
Madde kullanımı	2 (1,7)	1 (50)	1 (50)
Deliryum	16 (13,6)	4 (25)	12 (75)
İlaç yan etkisi	1 (0,8)	0 (0)	1 (100)
Psikyatrik tanı			
Major depresif bozukluk	42 (35,6)	16 (38)	26 (62)
Deliryum	8 (6,8)	5 (62,5)	3(62,5)
Anksiyete bozukluğu	17 (14,4)	7 (41,2)	10 (13,7)
Uyum bozukluğu	31 (24,6)	13 (44,8)	16 (55,2)
Konversiyon	5 (4,2)	0 (0)	5 (100)
Madde kullanım bozukluğu	1 (0,8)	1 (100)	0 (0)
Dikkat eksikliği ve hip-eraktivite bozukluğu	4 (3,4)	0 (0)	4(100)
Aktif psikopatoloji yok	10 (8,5)	3 (6,7)	7 (9,6)

Tablo 3. Değerlendirme sonucunda önerilen psikotrop ilaçlar

	n(%)
Psikyatrik ilaçlar	
Yok	69(58,5)
Antidepresan	23(1,5)
Antipsikotik	19(16,1)
Nöroleptik	1(0,8)
Anksiyolitik	4(3,4)
Psikostimülan	2(1,7)
Total	118(100)

Konsultasyon sonucu hastaların %39'unun ailesi ile görüşme yapılmış, %8,5'na sosyal servis konsültasyonu önerilmiş, %29,7'sine ilaç tedavisi başlanmadan davranışsal önerilerde bulunulmuş, %48'inden rekonsultasyon istenmiştir. Konsultasyon istenen hastaların %56,8'ine(n=67) poliklinik kontrolü önerilmiş fakat yalnızca %29 (n=21) hastanın çocuk psikiyatrisi takibine devam ettiği görülmüştür.

Tablo 4. Değerlendirme sonucunda kadın/erkek arası tedavi planı farkları

	Kadın n(%)	Erkek n(%)	p
İlaç tedavisi			0,374
Var	28(57,1)	21(42,9)	
Yok	45(65,2)	24(34,8)	
Davranışsal Öneriler			0,787
Var	21(60)	14(40)	
Yok	52(62,7)	31(37,3)	
Ebeveynle Görüşme			0,323
Var	31(67,4)	15(32,6)	
Yok	42(58,3)	30(41,7)	

Tartışma

Çalışmamızda üç yıllık süre içersinde çocuk yoğun bakımdan istenen 118 çocuk ve ergen psikiyatrisi konsültasyonu değerlendirilmiştir. Bu sayı aynı dönemde yatarak tedavi gören hastaların yaklaşık %4,9'u kadardır. Ülkemizde yapılan diğer çalışmalara bakıldığında ise bu oran Emiroğlu ve ark.'larının yaptığı çalışmada %2,3; Aras ve ark.'nın yaptığı çalışmada %1,7 olarak saptanmıştır[7,9]. Çalışmamızdaki yatan hastalardan çocuk psikiyatri konsültasyonu istenme oranı ülkemiz ile paralellik gösterse de yurtdışında yapılan çalışmalarda bildirilen %25-65 arasında değişen oranlara göre oldukça düşüktür [10,11]. Bunun sebepleri yoğun bakımda çalışan hekimlerin hastanın beraberinde sahip olduğu bedensel kritik hastalığı nedeniyle ruhsal belirtileri anlama ve değerlendirme konusunda güçlükler yaşaması, sınırlı zamanda ve hayati problemlere yönelik hizmet verirken psikiyatrik değerlendirmeye öncelik verememe, mahremiyetin ikinci planda kalması ve çocuk psikiyatrisine erişim sorunları olabilir [2,12,13]. Yatarak tedavi gören çocukların %33-66'sının ruhsal sorunları ortaya çıktığına ilişkin literatür bilgileri göz önüne alındığında; hastanın takibinin tek bir hekim tarafından karşılanması yerine çocuk ve ergen psikiyatrisi ile işbirliğinin sağlanarak ruhsal durumun iyileştirilmesinde sürerliliğin sağlanması kritik hastada büyük önem taşımaktadır[14].

Çalışmamızda en küçük yaş konsültasyon istenen olgu 4 yaş, en büyük ise 17 yaş olup ülkemizde yapılan diğer çalışmalara paralel olarak 12 yaş üstü ergen yaş grubunun konsültasyon istemlerinin %71,4'ünü oluşturduğu görülmüştür[7,13,15]. Bu durum ergenlikte ruhsal problemlerin çocuklara göre daha farkedilebilir olması ve ergenliğin daha hassas ve ruhsal hastalıklar açısından daha kırılgan bir dönem olması ile ilgili olabilir.

Çalışmamızda olguların cinsiyetleri incelendiğinde ise %62 kız olması nedeniyle konsültasyon istenen hastalarda kızların baskınlığı Kandil ve ark.'nın (%62) ve Rezaki ve ark.'nın (%70,6)

çalışmasıyla benzer saptanmıştır[16,17] Nitekim bu sonuçlar farklı cinsiyetteki olgularda ruhsal sorunlar farklı olabileceği gibi, tedavi ekibinin ruhsal problemlere duyarlılığının cinsiyete göre değişmesi ile de ilgili olabilir.

Yoğun bakımda yatan hastalarda hastalık ve yoğun bakımda izlem, ebeveynden ayrılma, başlı başına zor ve uyum gerektiren bir süreçtir. Nitekim bu uyum sürecinde çocukların yaşadıkları emosyonel sorunlara yönelik çocuk psikiyatrisi konsültasyon nedenleri poliklinik hastalarına göre farklılık gösterir[2]. Bu nedenler genel olarak tedavi uyumsuzluğu, ankisiyete, depresif tutum, özkıyım sonrası risk değerlendirmesi, ayırıcı tanı yapılması, ağrı ile baş edememe, ebeveynlere ilişkin sorunlar, deliryum tablosu, ağrılı girişimler öncesi veya kronik hastalık konusunda çocuğun bilgilendirilmesi için olabilir. Bu çalışmada hastalarımızdan en sık özkıyım risk değerlendirilmesi ve depresif görünüm için konsültasyon istenmiştir. Bu durum özkıyım nedeniyle başvuran çocuk yoğun bakım hastalarının rutin olarak risk değerlendirilmesi ve izlem için konsültasyon liyezon psikiyatrisine yönlendirilmesi ile ilgili olabilir[2,18,19]. Literatürdeki diğer çalışmalara bakıldığında ise Şimşek ve ark. yaptığı çalışmada intihar girişimi ve depresif belirtiler; Emiroglu ve ark. yaptığı çalışmada ise emosyonel nedenler(depresif görünüm) için en sık konsültasyon istendiği bildirilmiştir[7,20]. Çalışmamızda deliryum nedeniyle istenen konsültasyonların(%13,6) literatüre göre fazla olması ise oldukça dikkat çekicidir. Pediyatrik yoğun bakım alanında yapılan birçok farklı çalışmada bu oran %5'in altında bildirilmiştir[7,8,20]. Deliryum klinisyenlerce oldukça sık atlanan dalgalı seyirli belirti skalası gösteren akut başlangıçlı bir durum olduğundan tanısal karmaşaya açıktır. Nitekim hastalarımızın %6,8'i bu tanıyı alarak izlem ve tedavisi yapılmıştır. Ortam değişikliklerine uyumu az, duygusal ve dürtüsel olan çocukların deliryum açısından risk altında olduğu bilinmektedir. Deliryum tablosunun hastanın kliniğini ağırlaştırıp mortaliteyi arttıracağı ve yatış süresini uzatabileceği göz önüne alınarak şüphe edilen hastalardan konsültasyon mutlaka istenmelidir[21,22,23].

Çalışmamızda psikiyatrik değerlendirme sonucu en sık konulan tanılar sırasıyla majör depresif bozukluk ve uyum bozukluğu olup bu veriler literatür ile benzerdir. Şimşek ve ark.'ları depresif bozukluk ve uyum bozukluğunu; Aktepe ve ark.'ları depresif bozukluk ve anksiyete bozukluğunu; Alpaslan ve ark.'ları depresif duygudurum ve uyum bozukluklarını; Kandil ve ark.'ları depresif bozukluk ve anksiyete bozukluğunu sırasıyla en sık tanı olarak bildirmişlerdir[12,13,16,20]. Bunun yanında çalışmamızda istenen konsültasyonlar içersinde %8,5 oranında psikopatoloji saptanmamıştır. Ülkemizde yapılan diğer çalışmalarda ise bu oran Kandil ve ark.'larının yaptığı çalışmada %9,52; Çolpan ve ark.'larının yaptığı çalışmada %7,6; Kılıç ve ark.'nın yaptığı çalışmada %38,9 olarak bildirilmiştir[16,24,25]. Bu oranlardaki farklılıklar özellikle kritik hastalığı olan çocuklarda sözel iletişim güçlüğünün psikolojik değerlendirmeyi güçleştirmesi ve tıbbi durumla alakalı oryantasyon bozukluğu nedeniyle olabilir.

Çalışmamızın geneline bakıldığında psikolojik değerlendirme sonucu hastaların yaklaşık yarısından çoğuna (%58) ilaç başlanmadığı saptanmış olup ilaç kullanan hastalarda ise erkekler ve kızlar arasında anlamlı fark olmadığı görülmüştür. En sık başlanan ilaç grubu ise antidepresanlar (SSRI) olup bu durumun en sık konan tanının depresif bozukluk olması ve konsültasyon istenme nedeninin de özkıyım girişimi olması ile ilişkili olduğunu düşünmekteyiz. Literatürdeki diğer çalışmalarda ayaktan çocuk psikiyatrisine başvuran hastalarda ilaç başlanma oranının (%15-19) çalışmamızdaki kritik yoğun bakım hastalarına göre düşük saptanmasının nedeninin polikliniğe başvuran çocukların emosyonel sorunlarının ve mevcut psikiyatrik tanılarının farklılık göstermesi ile ilişkili olabileceğini düşünmekteyiz. Bununla birlikte yoğun bakım yatışı sürmekte olan kritik hastalarda medikasyonun neden olabileceği yan etkiler sebebiyle diğer psikiyatrik müdahalelere öncelik verilmiş olabilir [2,26,27,28].

Çalışmamızda konsültasyon değerlendirmesi sonucu poliklinik kontrolü önerilen hastaların %29'unun ayaktan tedaviyi sürdürdüğü saptanmıştır. Ülkemizde yapılan diğer çalışmalarda tedavinin sürdürülme oranları %34-%70,2 arasında bulunmuştur [15,29]. Çalışmamızda bu oranın daha düşük saptanmasının nedeni çalışmanın bir devlet hastanesinde yapılması ve buraya daha düşük sosyokültürel düzeyde hasta profilinin başvurması olabilir. Bununla birlikte çalışmanın yapıldığı yerin kırsal alanlar da dahil olmak üzere bir çok yerden sevkin kabul edildiği bir hastane olmasından dolayı taburculuk sonrası çocuk psikiyatri hekimine ulaşımda sorunlar yaşanmış olabilir.

Bu çalışmanın kısıtlılıkları arasında retrospektif bir çalışma olması nedeniyle fiziksel hastalık ve psikiyatrik tanılarının elektronik arşiv hasta kayıtlarından elde edilmiş olması olabilir. Öte yandan bu çalışmadan elde edilen veriler çocuk yoğun bakımlarda konsultasyon lizeyon psikiyatrisi ile birlikte çalışma alışkanlığının kazanılması ve hastaların daha doğru değerlendirilmesine katkı sağlayacaktır.

Sonuç

Çocuk yoğun bakım hastalarında kritik hastalık süreci, yoğun bakım yatış sürelerinin uzaması ve çevresel değişikliklere uyum zorluğu nedeniyle ruhsal problemlerin gelişimi oldukça sıktır. Fakat bu oranda konsültasyon istenmediği görülmektedir. Bu noktada çocuk yoğun bakım hekimlerinin farkındalıklarının arttırılmasına yönelik ortak eğitim programlarının düzenlenmesi, çocuk psikiyatrisi ile birlikte multidisipliner bir yaklaşım izlemeleri hastanın tedaviye uyumunu arttırarak yatış sürelerini kısaltacaktır.

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Original Article

The comparison of hemorrhoidal laser procedur and classical (ferguson) surgical hemorrhoidectomy methods

Hemoroidal lazer işlemi ile klasik(ferguson) cerrahi hemoroidektomi yöntemlerinin karşılaştırılması

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Abstract

Aim: Generally, pathological hemorrhoids are more common in patients aged 45-65 years. Treatment options may vary according to the degree of hemorrhoids.We aimed to compare surgical treatment with classical surgical hemorrhoidectomies(CH,Ferguson procedure) and hemorrhoidal laser procedur methods(HeLP)in the treatment of grade III and grade IV hemorrhoids.

Material and Methods: Univariate analyses were performed using the Student's t test for continuous variables and chi-squared test for dichotome variables. Data were analyzed with SPSS™for Windows18(SPSS, Chicago,IL).All cases over the age of 18 and under the age of 65 without any malignancy diagnosis who underwent HeLP and CH methods due to gradeIII, gradeIV hemorrhoid disease were included in the study.

Results: Totally 187 cases included in this study.The patients was 66.8%(n:125,male)vs.female 33.2%(62)($p<0.05$).The distribution of patients according to who underwent HeLP by gender,it was found as[71.8%(n:89)male vs. female28.2%(35) ($p<0.05$)]. For CH this distrubition rate was[male57.1%(n=36)vs.female42.9%(n=27)$P<0.05$]. The complication rates between for procedures weren't found statistically different from each other.CH[(n=66)(Complicative cases 9.5% (n:6)vs. HeLP[(n=116)complicative cases 6.9%(n:8)($p=0.56$)].

The difference between complication rates according to gender is examined;The complication rates of both procedures were similar in both gender too[64.3%(9)vs.35.7%(5)($p=0.8$)].There wasn't statistically significant results found in the comparison made in terms of the choice of procedure in terms of the average age.The patients who underwent CH(40,9±13.7)years old vs.HeLP(38,2±13,4)years old(p:0.2)was found.The bleeding complications were found significantly higher in the HeLP than in the CH[HeLp vs.CH for hematoma;8(89.9%)vs1(11.1%)($p<0.02$)].The effects of HeLP on complications in terms of number of laser shots,wavelength,energy and application time were examined, statistically significant results weren't.

Conclusion: The male population applying for hemorrhoid treatment was found to be significantly younger than females. The male gender preferred the HeLP procedure significantly compared to the females and the complication of hemorrhage was significantly higher in the laser procedure.

Keywords: Hemorrhoids , Laser ,classical hemorrhoidectomy , HeLP,comparison

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Öz

Amaç: Genellikle patolojik hemoroidler 45-65 yaş arası hastalarda daha sık görülür. Tedavi seçenekleri hemoroidin derecesine göre değişiklik gösterebilir. Grade III ve grade IV hemoroid tedavisinde cerrahi tedaviyi klasik cerrahi hemoroidektomi(KH,Ferguson prosedürü) ve hemoroidal lazer işlem yöntemlerini(HeLP) ile karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Tek değişkenli analizler, sürekli değişkenler için Student t testi ve ikili değişkenler için ki-kare testi kullanılarak yapıldı. Veriler SPSS™ for Windows18(SPSS, Chicago,IL) ile analiz edildi. 18 yaş üstü ve altı tüm vakalar Evre III, Evre IV hemoroid hastalığı nedeniyle HeLP ve KH yöntemleri uygulanan malignite tanısı olmayan 65 hasta çalışmaya dahil edildi.

Bulgular: Bu çalışmaya toplam 187 olgu dahil edildi.Hastalar %66.8(n:125,erkek) ve %33.2(62)(p<0.05) kadın idi.Hastaların cinsiyete göre HeLP yapılanlara göre dağılımı, [%71,8(n:89)erkek - kadın %28,2(35)(p<0,05)] olarak bulundu. KH için bu dağılım oranı[erkek %57,1(n=36)vs.kadın %42,9(n=27)P<0,05]. İşlemler arasındaki komplikasyon oranları istatistiksel olarak birbirinden farklı bulunmadı. KH[(n=66)(Komplikatif vakalar %9,5 (n:6) ve HeLP[(n=116)komplikatif vakalar %6,9(n:8))(p=0.56)].

Cinsiyete göre komplikasyon oranları arasındaki fark incelendiğinde; Her iki işlemin komplikasyon oranları her iki cinsiyette de benzerdi[64.3%(9)vs.35.7%(5)(p=0.8)].İstatistiksel olarak anlamlı bir sonuç yoktu. yaş ortalaması açısından işlem seçimi açısından yapılan karşılaştırmada bulundu.KH(40,9±13,7)yaş ile HeLP(38,2±13,4)yaş uygulanan hastalar(p: 0.2) bulundu. Kanama komplikasyonları HeLP'de KH'ye göre anlamlı olarak yüksek bulundu[Hematom için HeLp vs.KH;8(89.9%)vs1(11.1%)(p<0.02)]. Laser atış sayısı, dalga boyu, enerji ve uygulama süresi açısından incelendi, istatistiksel olarak anlamlı bir sonuç çıkmadı.

Sonuç: Hemoroid tedavisi için başvuran erkek popülasyonun kadınlara göre anlamlı olarak daha genç olduğu saptanmıştır. Erkek cinsiyeti kadınlara göre anlamlı olarak HeLP işlemini tercih etmekte ve lazer işleminde kanama komplikasyonu anlamlı olarak daha yüksek bulunmuştur.

Anahtar Kelimeler: Hemoroid , Lazer ,klasik hemoroidektomi , HeLP,karşılaştırma

Introduction

Hemorrhoidal disorders are one of the most common benign anorectal diseases known. The worldwide prevalence of hemorrhoids in the general population has been reported to be 4.4% (1).

HD develops due to the increased blood flow in the superior rectal artery, which causes dilatation of the hemorrhoidal vascular structures. However, the disruption of the supporting tissue also causes the hemorrhoidal pouches to sag downwards(2).

Almost one third of patients with hemorrhoidal complaints apply to the hospital for doctor's advice. It has been stated in the literature that the age distribution generally fits a Gaussian distribution, with the highest incidence between the ages of 45 and 65 and decreasing after the age of 65 (3, 4). In addition, men experience hemorrhoidal disorders more frequently than women (5).

Initially, the treatment approach of HD consists of lifestyle changes (nutrition with fiber foods, etc.) and phlebotonic medical treatment. If conservative treatment is not sufficient, interventional procedures are used in HD treatment(6)]. Open hemorrhoidectomy (HC) intervention was first described and described by Milligan-Morgan (7) in 1937, and it remains the gold standard of interventional therapy for advanced stages of HD today. The most prominent disadvantages are post-operative pain and complications associated with complications resulting from excision of hemorrhoidal tissue(8). For the above reasons, various non-excisional treatments such as rubber band ligation (RBL), mucopexy (MP) or laser treatments are also available(6,9). Laser application without excision was first introduced in 1998 by Barr et al. (10) by an experimental animal study. has been revealed. Karahaliloğlu and et al. were shared in their study results for first and second degree hemorrhoids with the laser obliteration, in 2007(11). On the other hand, although laser applications, which offer an excision-free treatment option, constitute interventional treatments for HD treatment, it has been emphasized in the literature that the level of evidence is low (6, 9). In this study, we aimed to share our results in the current literature by comparing classical hemorrhoidectomy and laser application with hemorrhoid obliteration.

Material and methods

The study was approved by Çukurova University Faculty of Medicine Ethics Committee dated July 22, 2022 the ethics committee decision the number of 124. The patients who underwent laser hemorrhoidoplasty procedure and open

surgical hemorrhoidectomy operations, which were applied to patients with third and fourth degree hemorrhoids between 2020-2022, were examined in addition to demographic features such as age and gender, as well as whether there was a significant factor determining the procedure chosen by the patients, and complications according to the procedures applied. It was also investigated whether there is a difference in terms of complications according to the duration of laser hemorrhoidoplasty and the energy wave length given. However, patients under 18 years of age or older than 65 years ,diagnosed with fissure, fistula, anorectal diseases and malignant diseases, and patients whose data were found to be incomplete or inconclusive were excluded from the study. Continuous variables were reported as mean and standard deviation, while categorical nominal variables were determined as a percentage of the total population. Continuous or discrete variables were considered as independent variables for comparison of differences between groups. In order to reveal the difference between independent groups, discrete variables were evaluated with the χ^2 test or Fischer's exact test for univariate analyzes, while Student's t test was used for the distribution status of continuous variables. Data were analyzed with SPSS™ for Windows 18 (SPSS, Chicago, IL).

Results

The total number of patients is 187; It was determined that the male population applied for the treatment of hemorrhoids significantly compared to the females [125(66.8%) male vs.62(33.2%) (p=0.045)] female (Table 1). It was also revealed that the males significantly preferred the hemorrhoidal laser procedure compared to the females[89(71.8%) vs.35(28.2%), p=0.043](Table 1).

The mean patient age was 39.1±13.5(18-79). The male population applying for hemorrhoid treatment was significantly younger than females [37.3 vs. 42.7 (p=0.014)] (Table 2). When it was examined whether there was an age difference according to the treatment methods chosen by all patients included in the study, no statistically significant difference was found[CH(n=63) (mean age =40.9±13.7) vs HeLP (n=124)(mean age =38.16±13.4) (p=0.2)] (Table 2).

Considering which of the applied procedures led to more complicating results, the complication rates between the procedures were not found statistically different from each other. [Classic hemorrhoidectomy [42.9%(n:6) vs. HeLP 57.1%(n:8)(p=0.56)] (Table3).

When the difference between complication rates according to gender is examined; The complication rates of both procedures were similar in both gender [male 64.3 %(9) vs. female 35.7%(5)(p=0.8)] (Table 4).

Table 1: Distribution of patients who underwent classical hemorrhoidectomy and laser hemorrhoidectomy in terms of gender

The cases who underwent classical hemorrhoidectomy and laser hemorrhoidectomy in terms of gender					
		GENDER		Total	P<0.05
		Male	Female		
CH	63	57.1%(n=36)	42.9%(n=27)	100%(n=63)	0.045
HeLP	124	71.8%(n=89)	28.2()n=35	100%(n=124)	
Total	187	66.8%(n=125)	33.2%(n=62)	100%(n=187)	0.043

Table 2: The comparison of the mean age for all patients by performed procedure and gender

	Comparison of mean age for all patients by gender	P<0.05
Male(n=125)	37.3 ±12.7	p=0.014
Female(=62)	42.7±14.5	
All patients mean age (n=187)	39±13.53	
	Comparison of mean age for all patients by performed procedure	
CH(n:63)	40,8571±13,72525	0.2
HeLP(n:124)	38,1613±13,39177	

Table 3: General complication rates in terms of applied procedures

Procedure* Complication					
			Complication		p<0.05
		n	No	Yes	
Procedure	CH	63	57(90.5%)	6(9.5%)	0.56
	HeLP	124	116(93.1%)	8(6.9%)	
Total cases		187	173 (91.9%)	14 (8.1%)	

Table 4 : Comparison and distribution of complication rates according to gender and procedure

		Complication		Total	P<0.05
		,00	1,00		
GENDER	The number of male cases	116	9	125	0.8
	The complication percentage within males	92,8%	7,2%	100,0%	
	The number of female cases	57	5	62	
	The complication percentage within females	91,9%	8,1%	100,0%	
Total	The number of total cases	173	14	187	
	The complication percentage of total cases	92,5%	7,5%	100,0%	
	The complication distrubition in terms of procedure				
	HeLp vs. CH for hematoma	8(89.9%) vs 1(11.1%)			0.02
	HeLP	Hematoma	8		
	CH		1		
	CH	Abscess	1		
	CH	Pain	2		
	CH	Hematoma and pain	2		

Discussion

Keighley MRB. et al. reported that men are affected by hemorrhoids more frequently than women (12). But furthermore, Parvez Sheikh et al. reported in their study that there was a slightly higher proportion of women in the cohort with hemorrhoidal disease in the general population [(52% versus 56%)(13)]. In our study, the male population was operated more often than the female population due to hemorrhoidal disease [125(66.8%) vs.62(33.2%)(Table 1)]. A.Senagore et al. reported in a study in which they compared laser and classical hemorrhoidectomy involving 86 patients in total, that they did not find a significant difference in preference for the type of procedure in terms of gender(14).Whereas in our study, when we compared the cases who underwent classical hemorrhoidectomy and laser hemorrhoidectomy in terms of gender; It was revealed that male gender preferred laser hemorrhoidectomy method compared to females [71.2%(89) vs.28.8%(36)(p<0.045)].

In terms of classical hemorrhoidectomy, the distribution of male and female cases was found as [57.1%(36) vs. 42.9%(27) (p<0.045)](Table 1). In our study, when the mean age of the patients who had hemorrhoidectomy operation was examined by gender, the mean age of the male gender was significantly lower than that of the female gender [37.3 ±12.7 vs. 42.7±14.5 (p=0.014) (Table 2). In the studies in the literature, it is stated that the highest incidence of hemorrhoidal age distribution is between the ages of 45-65, and it decreases after the age of 65 (3,4). Ismali SA et al. reported in their study that hemorrhoid cases were most common between the ages of 35 and 65. (15). On the other hand; In our study, the mean age of all patients who underwent hemorrhoidal treatment procedure was found to be 39±13.53, similarly (Table 2). There was not found any statistical significance results in comparison of mean age in terms of performed procedure (Table 2). In terms of complication rates; The comparison of the applied the procedures were not found statistically signifinannacy [Classic hemorrhoidectomy [n:6 (9.5%) vs. laser hemorrhoidectomy n:8(6.9%) (p=0.56)] .The overall complication rate of patients who underwent both procedures was 14 (8.1%)(Table 3). Whereas when we examine the distribution of complications as laser hemorrhoidoplasty and surgical hemorrhoidectomy; Interestingly, except for 1 case, almost all hematomas belonged to the laser procedure. Consequently our complication distrubition were hematoma n=9(2.4%), pus n=1(0.3%), pain(n=2 (0.5%), hematoma and pain 2(0.5%). 14 of 187 cases (3.7%) had complications(Table 4). Six cases, including the remaining pain, abscess, pain and hematoma, were seen after the classical hemorrhoidectomy operation (Table 4). When we scanned the literature in terms of complication distribution, after surgical hemorrhoidectomy; It has been stated that the most common complication in post-surgical hemorrhoidectomy is pain. On the other hand, early complications were listed as urinary retention (20.1%), bleeding (2.4-6%) and soft tissue infections (0.5%)(16-18). However, the complications that occur in the long term are respectively; anal fissure(1% -2.6%), anal stenosis(1%), fistula(0.5%), gas and/or stool incontinence (0.4%) development and recurrence of hemorrhoids(16-18). Statistically, hematoma development was significantly higher in laser application than in classical

hemorrhoidectomy. G.Longchamp et al. stated in their study that the most prominent intraoperative complications were bleeding and emphasized that they detected more in HeLP cases(8). In our study too; It was determined that bleeding complications were significantly higher in the hemorrhoidal laser procedure than in the classical hemorrhoidectomy operation. [HeLp vs. CH for hematoma;8(89.9%) vs 1(11.1%) (p<0.02)] (Table 4). In addition, there are studies in the literature stating that bleeding complication is the most common complication and most of them after classical hemorrhoidectomy (CH) (11,19-21) , as well as studies indicating that bleeding is more common after HeLP (8,22-24). In laser hemorrhoidectomy; The thermal effect caused by laser pulses is limited to the mucosa and submucosa and avoids perforation of the rectal tissue caused by overheating(25). Additionally, in this process, the laser beam at this wavelength, by means of a diode laser operating at a wavelength of 980 nm, creates maximum absorption specifically to the chromophores of the hemoglobin. As a result of high energy absorption in the arterial circulation; There is minimal damage to the mucosa in the surrounding tissue crossed by the laser beam and shrinkage of the vessel, however, the "contraction effect" that occurs in the submucosal arteries is the ultimate goal(25). Laser energy causes minimal discomfort to patients, anesthesia is not required for HeLP. If patients require sedation, mild intraoperative sedation can be applied(25). When the effects of laser hemorrhoidectomy on complications in terms of number of shots, wavelength, energy and application time were examined, no statistically significant results were found(Table 5).

Table 5: Showing the effects of laser hemorrhoidectomy on complications in terms of number of shots, wavelength, energy and application time

	Complication	n	Mean	Std. Deviation	P<0.05
Energy (watt)	,00	116	7,0345	,55059	0.68
	1,00	8	7,1250	,58248	
Time (second)	,00	173	126,4740	13,81967	0.28
	1,00	14	131,0714	14,69937	
Shot	,00	116	41,4914	5,42217	0.68
	1,00	8	42,3750	5,65528	
Wavelength	,00	116	661,5517	108,89647	0.79
		8	672,5000	112,34513	

Conclusion

In our study, the male gender preferred the hemorrhoidal laser procedure more frequently and the hemorrhoidal laser procedure created a risk of bleeding compared to the classical surgical method, no significant difference was found in terms of general complications except for these two cases, and it is thought that these results should be investigated with prospective multicenter studies in the next step.

Declaration of congress abstract

This study has not been published anywhere before and has not been presented in any congress.

Ethic

In this retrospective study, national and international ethical rules were complied with.

Conflict of Interest

No conflict of interest was declared by the authors. In addition, no financial support was received for this study.

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Orijinal Makale

Koroner Yavaş Akım Fenomeni Olan Hastalarda Kardiyak Elektrofizyolojik Denge Endeksinin Değerlendirilmesi

Evaluation of İndex of Cardiac electrophysiological Balance in Patients with Coronary Slow Flow Phenomenon

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Öz

Amaç: Koroner yavaş akım (KYA) fenomeni koroner arterlerde anlamlı darlık olmadan yavaş akımla karakterize olan bir klinik antitedir ve koroner anjiyografilerin yaklaşık %3'ünde görülmektedir. KYA'nın nadiren de olsa ventriküler aritmiler ve ani kardiyak ölümle ilişkili olduğu bilinmektedir. Kardiyak elektrofizyolojik denge endexi (index of cardiac electrophysiological balance = iCEB), 12 derivasyonlu EKG'de QT intervalinin QRS süresine bölünmesi ile elde edilen non-invaziv bir parametredir. Bu parametrenin normalden sapmasının malign ventriküler aritmiler ile ilişkili olduğu gösterilmiştir. Bu çalışma ile amacımız KYA olan hastalarda kontrol grubuna göre iCEB farklılığını ve iCEB 'in yavaş koroner akım olan arter sayısı ile ilişkisini değerlendirmektir.

Gereç ve Yöntemler: Çalışmamıza toplamda 189 hasta dahil edildi (KYA: 91, kontrol: 98). KYA olan hastalar tek damar KYA ve çok damar KYA olarak 2 gruba ayrıldı (tek damar KYA:60, çok damar KYA:31). Her iki grubun demografik, klinik, laboratuvar ve elektrokardiyografik parametreleri karşılaştırıldı.

Bulgular: Çalışmaya alınan hastalardan KYA hastalarında median yaş 52 (45-59) kontrol grubunda 50 (43-56) saptandı (p=0,186). KYA hastalarının % 45,1'i ; kontrol hastalarının %62.2 si kadındı (p=0,018) . Median kreatinin düzeyi KYA hastalarında daha yüksek (0,81 vs 0,72, p=0,015) , HDL düzeyi KYA hastalarında daha düşük saptandı (39 vs. 43, p=0,033). Median iCEB değerleri KYA grubunda kontrol grubuna göre anlamlı olarak daha yüksekti (4,18 vs. 4,07, p=0,006). Tek damar KYA ve çok damar KYA hastalarının karşılaştırıldığı analizde bazal karakteristik özellikler arasında fark yoktu ve iCEB değerleri arasında istatistiksel olarak anlamlı fark bulunamadı (4,18 vs. 4,15 p=0,391).

Sonuçlar: Çalışmamızın sonucunda KYA hastalarında iCEB değeri , kontrol grubuna göre anlamlı olarak daha yüksek bulundu. Bununla beraber tek damar KYA ve çok damar KYA hastalarında iCEB değerleri açısından anlamlı fark bulunamadı. KYA'da artmış iCEB 'in görülmesi, bu hasta grubunda ventriküler aritmilerle ilişkilendirilebilir. Bu parametrelerin yakından izlenmesi, olası ventriküler aritmilerin öngörülebilmesi ve yüksek riskli hastalarda daha agresif bir tedavi yaklaşımın sergilenmesi açısından yol gösterici olabilir.

Anahtar kelimeler: Kardiyak elektrofizyolojik denge endexi, koroner yavaş akım, ventriküler aritmi

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Abstract

Aim: Coronary slow flow (CSF) phenomenon is a clinical entity characterized by slow flow without significant stenosis in the coronary arteries and is observed in approximately 3% of coronary angiographies. It is known that CSF is associated, although rarely, with ventricular arrhythmias and sudden cardiac death. The index of cardiac electrophysiological balance (iCEB) is a non-invasive parameter obtained by dividing the QT interval by the QRS time on a 12-lead ECG. It has been shown that the deviation of this parameter from normal is associated with malignant ventricular arrhythmias. Our aim with this study was to evaluate the difference in iCEB in patients with CSF compared to the control group and the relationship of iCEB with the number of arteries with slow coronary flow.

Material and Methods: A total of 189 patients were included in our study (CSF: 91, control: 98). Patients with KYA were divided into 2 groups as single-vessel CSF and multi-vessel CSF (single-vessel CSF:60, multi-vessel CSF:31). Demographic, clinical, laboratory and electrocardiographic parameters of both groups were compared.

Results: The median age of the patients enrolled in the study was 52 (45-59) in CSF patients and 50 (43-56) in the control group (p=0.186). 45.1% of CSF patients and 62.2% of control patients were female (p=0.018). Median creatinine level was higher in CSF patients (0.81 vs 0.72, p=0.015), HDL level was lower in CSF patients (39 vs. 43, p=0.033). Median iCEB values were significantly higher in the CSF group compared to the control group (4.18 vs. 4.07, p=0.006). In the analysis comparing single vessel CSF and multi vessel CSF patients, there was no difference between basal characteristic features and no statistically significant difference was found between iCEB values (4.18 vs. 4.15 p=0.391).

Conclusion: As a result of our study, the iCEB value was found to be significantly higher in CSF patients compared to the control group. However, no significant difference was found in terms of iCEB values in single-vessel CSF and multi-vessel CSF patients. The occurrence of increased iCEB in CSF may be associated with ventricular arrhythmias in this group of patients. Close monitoring of these parameters can be a guide in terms of predicting possible ventricular arrhythmias and demonstrating a more aggressive treatment approach in high-risk patients.

Keywords: İndex of cardiac electrophysiological balance, coronary slow flow, ventricular arrhythmia

Giriş

Koroner yavaş akım fenomeni, en az bir epikardiyal koroner arterde anlamlı darlık olmadan distal arter yatağında gecikmiş opifikasyonla karakterize bir klinik durumdur ve kesin patofizyolojisi bilinmemekle beraber mikrovasküler disfonksiyonla ilişkili olduğu düşünülmektedir. Koroner anjiyogramlarda sıklığı %1-3 arasında bildirilmektedir. Hastalar sıklıkla akut koroner sendrom (AKS) kliniği ile başvurmakta ve yaklaşık %8 'inde kardiyak biyobelirteçlerde yükseklik ile seyretmektedir [1,2]. KYA 'nın objektif değerlendirmesi Thrombolysis in Myocardial Infarction (TIMI) frame sayısı (TFS) ile yapılmaktadır. KYA nın ani kardiyak ölüm ve ventriküler aritmilerle ilişkili olduğu gösterilmiştir [3,4]. Kardiyak elektrofizyolojik denge endeksi (iCEB) son zamanlarda daha sık kullanılan ve kardiyak aritmilerin öngördürücüsü olan non-invaziv bir belirteçtir. iCEB, yüzey elektrokardiyografide (EKG) QT intervalinin QRS süresine bölünmesi ile elde edilir ve hem yüksek olması hem de düşük olmasının aritmiler için öngördürücü olduğu belirlenmiştir. iCEB, EKG'den kolaylıkla ölçülebilmesi nedeni ile klinik kullanım kolaylığı sağlamaktadır [5].

Yakın zamanlı yapılan çalışmalar KYA ile iCEB arasında ilişki olduğunu ortaya koymuştur [6]. Biz bu çalışma ile KYA ile iCEB arasında korelasyon olup olmadığının yanısıra yavaş akım olan koroner arter sayısı ile iCEB arasında ilişki olup olmadığını araştırmayı amaçladık.

Gereç ve Yöntemler

Çalışmamız tek merkezli ,retrospektif ve gözlemsel bir çalışma olarak tasarlandı. Çalışmaya toplamda 189 hasta dahil edildi. Çalışma için etik kurul onayı hastanemizin lokal etik kurulundan alındı(Tarih:09.12.2022 Sayı:275). Bütün hastalardan çalışmaya dahil edileceklerine dair aydınaltılmış onam alındı. Bütün hastaların bazal karakteristik özellikleri, laboratuvar parametreleri ve elektrokardiyografik parametreleri hastane veri tabanından kaydedildi.

Elektrokardiyografik Analiz

Bütün hastaların 12 derivasyonlu EKG'leri supin pozisyonda ve standart olarak 25 mm/s hızve10 mm/mV kalibrasyon ile (Schiller, GermanyBavaria) çekildi. Bazal EKG'ler sinüs ritminde değerlendirildi. Kalp hızı, QRS süreleri ve QT intervalleri 2 kardiyolog tarafından değerlendirildi. Ölçümlerde DII ve V5 lead'leri kullanıldı. En uzun QT intervalleri ve QRS kompleks süreleri analiz edildi. Son olarak QT/QRS oranları (iCEB) hesaplandı.

Koroner Anjiyografi

Koroner anjiyografi işlemi bir girişimsel kardiyolog tarafından femoral veya radiyal perkütan yolla gerçekleştirildi. Koroner

arterler, sağ ve sol oblik planda kraniyal ve kaudal açılarla saniyede 30 kare hızda (30 fps) görüntülenmiş açılar referans alınarak görüntülendi. TFS ölçümü için başlangıç noktası olarak kontrast maddenin koroner arterin her iki kenarına değdiği an, son nokta olarak kontrast maddenin sol ön inen arter (LAD) için mustage denilen, sirkümfleks arter (CX) için en uzun dalın distal bifurkasyonuna ulaştığı an sağ koroner arter (RCA) için posterolateral arterin ilk yan dalını verdiği an alındı. Her üç koroner arter için görüntüler referans alınıp TIMI frame sayısı hesaplandı.

İstatistiksel Analiz

Tüm istatistiksel analizler için IBM SPSS yazılım paketi kullanıldı (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). Norml dağılım gösteren veriler Kolmogorov-Smirnov testi ile değerlendirildi. Normal dağılım sergileyen sayısal değişkenler ortalama ± standart sapma olarak, normal dağılım sergilemeyen değişkenler ise ortanca (medyan) olarak gösterildi. Kategorik değişkenler sayı ve yüzde olarak belirtildi. İki grup karşılaştırmalarında normal dağılım sergilemeyen sayısal değişkenlerin analizinde Mann-Whitney U testi tercih edildi. Kategorik verilerin analizinde ise Ki-kare testi ve Fisher'in kesin Ki-kare testi kullanıldı. İstatistiksel analizlerde $p<0.05$ değeri anlamlı olarak kabul edildi.

Bulgular

Çalışmaya 91 'i koroner yavaş akım , 98'i kontrol grubu olmak üzere toplamda 189 hasta dahil edildi.İki grubun yaş ortalaması benzerdi (p=0,186) . KYA olan hastaların % 45,1' i (n=41); kontrol grubunun %62,2'si (n=61) kadındı. KYA hastalarında median kreatinin değeri kontol grubuna göre daha yüksekti (0,8 vs. 0,71 p=0,015). Median HDL değeri KYA grubunda daha düşüktü (39 vs. 43 p=0,033). Hemoglobin değeri KYA grubunda kontrol grubuna göre daha yüksek iken (15,1 vs 13,8 p<0,001) ,trombosit sayısı KYA grubunda kontrol grubuna göre daha düşük saptandı (241 vs 300 p<0,001). Hastaların bazal karakteristik özellikleri tablo I de gösterilmiştir. KYA olan hastalarda ortanca TFC değeri sol ön inen arter (LAD), sirkumfleks arter (CX) ve sağ koroner arterde (RCA) sırasıyla 36 (36-40), 27 (25-29), 27 (25-28) ; kontrol grubunda sırasıyla 21 (20-24), 19 (18-20), 17 (17-19) olarak ölçüldü (p<0,001). KYA hastalarında ortalama iCEB değeri 4,18 (3,85-4,80) ; kontrol grubunda ise 4,07 (3,66-4,41) bulundu (p=0,006). KYA ve kontrol grubunun EKG parametreleri tablo II'de gösterilmiştir.

91 KYA hastasından 60'ında sadece tek damar; 31'inde ise çok damar yavaş akım mevcuttu. Tek damar ve çoklu damar KYA olan hastaların bazal karakteristik özellikleri ve EKG parametrelerinin karşılaştırılması sonucunda hastaların yaş, cinsiyet ve eşlik eden komorbiditeleri arasında fark olmadığı gözlendi. Tek damar KYA olan hastaların ortanca iCEB değeri 4,18 (3,76-4,70), çoklu damar KYA olan hastaların ortanca iCEB değeri 4,15(3,96-4,87) olarak bulundu. İki grubun iCEB değerleri arasında istatistiksel olarak anlamlı fark bulunamadı (p=0,391). İki grubun bazal karakteristik özellikleri ve elektrokardiyografik parametreleri tablo III' te gösterilmiştir.

Tablo I. Tüm hastaların bazal karakteristik özellikleri ve laboratuvar parametreleri

	Yavaş akım grubu (n:91)	Kontrol grubu (n:98)	P değeri
Yaş (yıl)	52(45-59)	50(43-56)	0,186
Kadın cinsiyet, n(%)	41(45,1)	61(62,2)	0,018
Sigara, n(%)	27(29,7)	23(23,5)	0,335
DM, n(%)	9(9,9)	6(6,1)	0,34
HT, n (%)	7(7,7)	2(2)	0,069
EF (%)	60(60-60)	60(60-60)	0,649
Glukoz (mg/dl)	101(94-111)	98(91-113)	0,406
Üre(mg/dL)	30(25-38)	30(26-36)	0,842
Kreatinin (mg/dL)	0,81(0,66-0,96)	0,72(0,62-0,84)	0,015
Sodyum (mEq/L)	140(138-141)	140(139-141)	0,166
Potasyum (mEq/L)	4,27(4,00-4,60)	4,34(4,10-4,60)	0,290
AST (IU/L)	20(15-25)	19(15-26)	0,623
ALT (IU/L)	19(14-26)	19(15-26)	0,993
Total kolesterol(mg/dl)	171(150-196)	177(156-199)	0,311
Trigliserid (mg/dl)	168(119-243)	160(102-225)	0,252
HDL kolesterol (mg/dl)	39(33-46)	43(34-52)	0,033
LDL kolesterol (mg/dl)	99(82-121)	98(87-121)	0,598
Nötrofil (10^3/uL)	5,15(3.97-6.81)	5,10(3,90-6,27)	0,361
Lenfosit (10^3/uL)	2,32(1.82-3.00)	2,35(1,91-2,96)	0,432
Hemoglobin (g/dl)	15,1(13.9-16.1)	13,8(12,6-15,3)	<0,001
Platelet (10^3/uL)	241(199-285)	300(250-339)	<0,001

DM: diyabetes mellitus, HT: hipertansiyon

Tablo II. Hastaların koroner anjiyografi ve elektrokardiyografik parametreleri			
Paremetreler	Yavaş akım grubu (n:91)	Kontrol grubu (n:98)	p değeri
LAD TFS	36(36-40)	21(20-24)	<0,001
CX TFS	27(25-29)	19(18-20)	<0,001
RCA TFS	27(25-28)	17(17-19)	<0,001
Kalp hızı (atım/dk)	71(65-78)	74(70-80)	0,069
QT (msn)	380(362-402)	376(364-388)	0,131
QTC (msn)	405(394-420)	406(396-419)	0,671
QRS (msn)	90(82-96)	93(84-102)	0,021
iCEB	4,18(3,85-4,80),	4.07(3,66-4,41)	0,006
İCEB: index of cardiac electrophysiological balance, TFS: TIMI Frame sayısı			

Tablo III. Tek damar ve çoklu damar KYA hastalarının bazal karakteristik özellikleri ve elektrokardiyografik parametreleri			
	Tek damar yavaş akım (n:60)	Çoklu damar yavaş akım (n:31)	P değeri
Yaş (yıl)	52(47-59)	52(43-59)	0,801
Kadıncinsiyet, n (%)	26(43,3)	15(48,4)	0,648
Sigara, n(%)	16(26,7)	11(35,5)	0,385
DM, n(%)	4(6,7)	5(16,1)	0,154
HT, n(%)	3(5)	4(12,9)	0,182
Kalp hızı (atım/dk)	71(63-78)	72(66-80)	0,344
QT (msn)	389(362-400)	387(364-406)	0,601
QRS (msn)	90(82-100)	90(80-96)	0,305
iCEB	4,18(3,76-4,70)	4,15(3,96-4,87)	0,391
İCEB: index of cardiac electrophysiological balance, DM: diyabetes mellitus, HT: hipertansiyon KYA: koroner yavaş akım			

Tartışma

Tek merkezli ve koroner anjiyografi temelli olarak yaptığımız bu çalışmada koroner yavaş akımın iCEB değerleri ile ilişkili olduğunu saptadık. Ayrıca bu ilişkinin yavaş akım olan koroner arter sayısından bağımsız olduğunu ve tek damar KYA ile çok damar KYA hastaları arasında iCEB değerleri arasında istatistiksel olarak anlamlı fark olmadığını tespit ettik.

Koroner yavaş akım fenomeni , koroner arterlerde belirgin darlık olmadan distal damar yatağında akımın yavaşlaması ile karakterize olan bir klinik durumdur [7].Tambe ve arkadaşları 1972 yılında ilk kez 6 hastalık bir vaka serisinde anjinal semptomlarla başvuran hastalarda tuhaf bir anjiyografik görünüm saptadıklarını ve bunun olası mekanizmasının endoletyal disfonksiyon olabileceğini belirttiler [8].İlerleyen zamanlarda bu klinik antitenin daha net olarak anlaşılması ile beraber 1996 yılında Gibson ve arkadaşları yavaş akımın kantitatif değerlendirilmesi amacıyla TFS'yi tanımladılar [9].

Daha önceki çalışmalar KYA için birçok farklı patofizyolojik mekanizmayı vurgulasa da en çok üzerinde durulan iki mekanizma endotelyal disfonksiyon ve subklinik aterosklerozdur. Nitekim bu hastalarda yapılan intrakoroner görüntüleme yöntemleri koroner lümende daralmaya yol açmadan iskemiye yol açan longitidunal kalsifikasyonlar olduğunu göstermiştir [10,11].Daha önce yayınlanmış bazı vaka serilerinde KYA'nın ventriküler aritmiler ve ani kardiyak arrestle ilişkili olduğu belirlenmiştir. Yine bazı çalışmalarda KYA'nın QTc ispersiyonu ile ilişkili olduğu bildirilmiştir. Bilindiği gibi QTc dispersiyonu yüzey EKG'deki maksimum ve minimum QT arasındaki farkı ifade eder ve ventriküler repolarizasyon dağılımını gösterir. Artmış QTc dispersiyonunun ventriküler aritmiler ve ani kardiyak ölümle ilişkili olduğu bilinmektedir [12,13]. KYA fenomeni prognostik açıdan genellikle iyi huylu olmasına rağmen daha önce yayınlanan vaka serilerinde miyokard infarktüsü, senkop ve ani kardiyak ölümle presente olabileceği vurgulanmıştır . Daha önceki yayınlar bu hastalarda total mortalitetin %1 in altında olduğunu göstermektedir. Uzun süreli takip verileri akut miyokard infarktüsü (AMI) öyküsü olması, miyokard perfüzyon sintigrafisinde belirgin iskemi olması ve QT uzamasının kötü sonlanımlarla ilişkili olduğunu göstermiştir [14].

iCEB , 12 derivasyonlu EKG de QT/QRS'in ölçülmesi ile elde edilen bir değerdir . ventrikülün depolarizasyonu(QRS) ve repolarizasyonu (QT) arasındaki dengenin ölçülmesine dayalı bir parametredir ve literatürde ilk olarak ilaca bağlı ventriküler aritmilerin öngörüdürülmesi amacıyla kullanılmıştır. Hua Rong Lu ve arkadaşlarının tavşan kalbi ile yaptıkları çalışma sonucuna göre bu dengenin normalden sapması ilaca bağlı aritmilerin öngördürülmesi açısından yüksek değere sahiptir. Bu çalışmada ayrıca iCEB 'in ventriküler ileti yavaşlaması, QT kısalması ve torsades-d-pointes(TdP) dışı VT/VF sıklığında artış ile de ilişkili olduğu saptanmıştır [15]. Tomas Robyns ve arkadaşları , elektrofizyolojik çalışma ile destekledikleri ve 40 hastayı dahil ettikleri bir çalışmada iCEB artışının ventriküler aritmiler için çok iyi bir prediktör olduğunu saptamıştır [5].

KYA'nın elektrokardyografik parametrelerle ilişkili olduğu daha önceki çalışmalarla da gösterilmiştir. Işık ve arkadaşlarının 97 KYA hastasını 103 kontrol hastasıyla karşılaştırarak yaptıkları çalışmada TFS yüksekliğinin frontal QRS-T açısı ile ilişkili olduğu saptanmış ve bu ilişkinin yavaş akım olan koroner arter sayısı ile de arttığı gösterilmiştir. Bilindiği gibi frontal QRS-T açısı ventriküler repolarizasyonun göstergesidir ve bu değerin artışı istenmeyen kardiyak sonlanımlarla ilişkildir [4].

Aşkın ve arkadaşlarının en az bir koroner arterinde KYA fenomeni olan hastaları kontrol grubu ile karşılaştırdıkları bir çalışma sonucuna göre iCEB değeri KYA hastalarında kontrol grubuna göre belirgin olarak yüksek bulunmuştur [6]. Bizim çalışma bulgularımız da bu çalışma sonuçlarıyla uyumlu bulunmuştur. Söz konusu çalışmada KYA olan hastalarda koroner arter sayısı dikkate alınmamıştır. Biz çalışmamızda birden fazla koroner arterinde yavaş akım olan hastalarda tek koroner arterinde yavaş akım olan hastalara göre iCEB değerinin farklı olmadığını saptadık. Bu durum koroner arter sayısından bağımsız olarak azalmış yavaş koroner akımın iCEB ile , dolayısıyla da vetriküler aritmiler ile ilişkili olabileciğini göstermesi açısından önemli bir bulgudur. iCEB 12 derivasyonlu EKG ile kolaylıkla ölçülebilen, non-invaziv, basit ve ucuz bir parametredir. Koroner yavaş akımı olan hastalarda bu parametrenin aritmik olayları öngördürmesi , bu hasta grubunda risk belirlenmesi ve tedavinin yönlendirilmesi açısından faydalı olabileceğini düşünmekteyiz.

Bununla beraber çalışmamızın bazı kısıtlıkları mevcuttur. Bunlardan birincisi tek merkezli ve prospektif bir çalışma olmasıdır. İkinci olarak da sadece EKG verileri üzerinden indirekt bir değerlendirme yapılmış olması ve bu sonuçların klinik olarak desteklenmemiş olmasıdır.

Sonuç olarak biz daha önceki araştırma sonuçları ile uyumlu olarak koroner yavaş akımın iCEB ile ilişkili olabileceği , ayrıca bu ilişkinin yavaş akım olan koroner arter sayısından bağımsız olduğu sonucuna vardık. Daha büyük sayıda hastanın dahil edildiği prospektif çalışmalar hastaların izlemde aritmik olay yaşayıp yaşamadığının da değerlendirildiği klinik sonuçlarla da desteklenmesi durumunda koroner yavaş akım fenomeni olan hastalarda iCEB değerleri hastalara medikal tedavi konusunda ne kadar agresif davranılması gerektiği konusunda yol gösterici olabilir.

Etik Kurul Kararı

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Original Article

Effects of COX 1-2 Inhibitors on Prevention of Rocuronium Injection Pain: Controlled, Randomised, Double Blind Study

COX 1-2 İnhibitörlerinin Roküronyum Enjeksiyon Ağrısının Önlenmesine Etkileri: Randomize, Kontrollü, Çift Kör Çalışma"

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ABSTRACT

Aim: Rocuronium bromide is a painful agent during induction of general anaesthesia. The aim of the study is to investigate the effects of Cyclooxygenase (COX) inhibitors as a resque agent against the rocuronium pain.

Material and Methods: Sixty patients of either sex scheduled for under general anesthesia were enrolled in this study. Patients were allocated into two groups (Group 1: Dexkethoprofen group, Group 2: Control group). Pain was evaluated by during rocuronium injection, patients were scored by a scale showed below. 0; No movement response to injection, 1; Mild movement response to injection, 2; Hand withdrawal response to injection, 3; Arm withdrawal response to injection. We also evaluated the pain with 2 questions when the patient was in the recovery room. Question 1. What was the last feeling before you fall into sleep? and question 2. Did you feel any pain on your hand during medication injection for anesthesia?

Results: There were differences between the groups in terms of total pain score for example in group 1 there were 16 (53%) patients who did not make any movement during rocuronium injection while there were 22 (73%) patients in group 2.There was significant difference in injection rocuronium bromide pain between group 1: dexkethoprofen group, Group 2: control group in terms of the answer to the second question. Patients felt less pain than the control group. In the second question, 16% in group 2 stated that they felt pain, while this rate was observed as 3% in group 1.

Conclusion: The effect of cox inhibitors on rocuronium pain was seen in our study but control group is also effective in reducing pain in vascular width.

Keywords: Rocuronium; injection, pain; cyclo-oxygenase inhibitors.

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ÖZ

Amaç: Roküronyum bromür genel anestezi indüksiyonu sırasında ağrılı bir ajandır. Bu çalışmanın amacı Siklooksijenaz (COX) inhibitörlerinin roküronyum enjeksiyon ağrısına karşı etkilerini araştırmaktır.

Gereç ve Yöntemler: Çalışmaya genel anestezi ile opere olacak toplam 60 hasta dahil edildi. Hastalar iki gruba ayrıldı (Grup 1: Deksketoprofen grubu, Grup 2: Kontrol grubu). Roküronyum enjeksiyonu sırasında hastalar tarafından hissedilen ağrı aşağıda gösterilen bir skala ile puanlandı. 0; Enjeksiyona hareket yanıtı yok, 1; Hafif enjeksiyona hareket yanıtı, 2; Enjeksiyona el çekme yanıtı, 3; Enjeksiyona kol geri çekme yanıtı. Ayrıca hastalara uyanma odasında iken 2 soru ile ağrıyı değerlendirdi. Soru 1. Uyumadan önceki son hissettiğiniz duygu neydi, soru 2. Anestezi için ilaç enjeksiyonu sırasında elinizde herhangi bir ağrı hissettiniz mi?

Bulgular: Toplam ağrı skoru açısından gruplar arasında fark vardı. Roküronyum enjeksiyonu sırasında hareket etmeyen 1. grupta 16 (%53) tane hasta varken 2. Grupta 22 (%73) hasta vardı. Gruplar arasında ikinci soruya verilen yanıt açısından anlamlı fark vardı. Hastalar kontrol grubuna göre daha az ağrı hissettiler. İkinci soruda grup 2'de (%16) ağrı hissettiğini belirtirken bu oran grup 1'de (%3) olarak gözlendi. Brakiyel ven yolundan el dorsumuna göre daha az ağrı hissedildi.

Sonuç: Cox inhibitörleri, rokuronyum ağrısını azaltmada etkili olmakla birlikte damar çapının da ağrı hissedilmesinde etkili olduğu görülmüştür.

Anahtar Kelimeler: Roküronyum; enjeksiyon, ağrı; siklo-oksijenaz inhibitörleri.

Introduction

Due to its favorable pharmacological characteristics, rocuronium is frequently used during the induction and maintenance of general anesthesia [1]. Rocuronium is a painful agent which is mostly preferred muscle relaxant by anesthesiologists due to its rapid onset of action and low rate of adverse events. Even when rocuronium is used after loss of consciousness, some patients reportedly exhibit spontaneous movement of the upper limb and recall injection pain after the surgery [2]. The major disadvantage of rocuronium is injection pain causing withdrawal reaction of the arm and hand. This injection pain is an unconfortable experience for the patients undergoing general anesthesia. In the literature there many agents including lidocaine, ketamine, magnesium sulphate, tramadol, ondansetron and alfentanil were used in trials for alleviation of injection pain but their failure ratio were between 7%-35% [3-5]. The exact mechanism of rocuronium injection pain is stil not clear. Histamine and bradykinin release is a possible mechanism which is pointed out in some published trials [6].

The main mechanism of action of nonsteroidal anti-inflammatory drugs (NSAIDs) is the inhibition of prostaglandin synthesis due to cyclo-oxygenase (COX) inhibition. Dexketoprofen trometamol is a non selective COX inhibitor which has a rapid onset of action. The aim of the study is to investigate the effects of Cyclooxygenase (COX) inhibitors as a resque agent against the rocuronium pain.

Material and Methods

This study conducted as a double blind controlled randomised study. Local ethical consent (No:2018/1634) was obtained from the scientific research ethics committee. Power analysis showed that a sample size of 30 for each group was necessary toill give a power of 0.80 at a level of significance level of =0.05. 60 patients undergoing general anesthesia were enrolled in this study (Figure 1). After obtaining ethical comittee approval patients randomly allocated into two groups. Patients non- allergic to dexketoprofen, 18-60 years old, ASA 1-2-3, 70-90 kg weigh were included to study while patients with pshychiatric and menthal problems were excluded from the study. Closed envelope randomisation method was used as a randomisation method. IV cannulation was performed on hand dorsum or brachial. Patients allocated in Group 1 were administered intravenous dexkethoprofen (50 mg/2ml) and 0.3 mg/kg midazolam 10 minutes prior to general anesthesia induction while patients in Group 2 were applied 2 ml of saline and 0.3 mg/kg midazolam in the premedication room. A third person resident unaware of the study applied this medication to both group 1 and 2. After the patient arrived to the operating theatre and the standart monitarisation performed with ECG, non-invasive blood

pressure and pulse oxymetry General anesthesia was induced with; %2 lidocaine (1mg/kg), 2 mg/kg propofol, and 0.6 mg/kg rocuronium respectively. During rocuronium injection, patients were scored by a scale showed below.

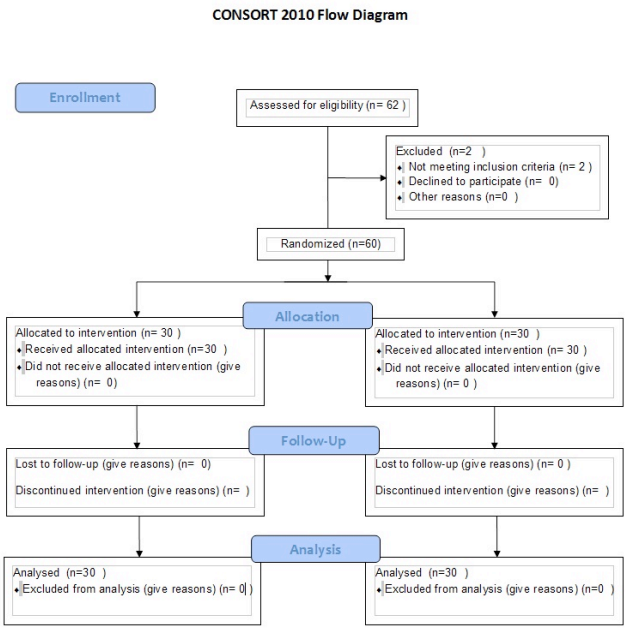

Figure 1. Flow diagram of patient data distribution

Response to rocuronium injection pain scale;

1. No movement response to injection
2. Mild movement response to injection
3. Hand withdrawal response to injection
4. Arm withdrawal response to injection

During intraoperative period; heart rate, mean arterial pressure and SpO2 were recorded in intervals. Patients whose Aldrete score were nine point, asked to answer two questions below in the recovery room.

Question 1.What was the last feeling before you fall into sleep?

a. Nothing

b. Mild

c. Moderate

d. Severe

e. Do not remember

Question 2. Did you feel any pain on your hand during medication injection for anesthesia?

a. Yes b. No c. Do not remember

Statistical Analysis

Version 22.0 of SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) program was used for statistical analysis of the data. Kolmogorov-Smirnov normality test was performed for continuous variables. In comparison of groups, Student-T test was used for continuous variables, while ordered or non-normal variables were evaluated with Man Whitney U test. Chi-square and Fisher's exact tests were used in the analysis of categorical variables. A $p<0.05$ value was accepted for the statistical significance limit.

Results

There was no statistically significant difference in patient characteristics between groups (Table 1). Heart rates during intraoperative period were comparable between groups. (P=0.8) Oxygen saturation and mean arterial blood pressures were also similar.(P=0.30, P=0.65 respectively) In group 1 there were 16 (53%) patients who did not make any movement during rocuronium injection while there were 22 (73%) patients in group 2 (Table 2). The table contains the number of reactions in the Groups. For example, there are 16 people in Group1 who say response, no movement, and they constitute 53.3% of the group. The same number in Group2 is 22 (73.3%) and therefore higher than Group1. Other responses were lower in Group2 than in Group1. It was seen that the reactions in the groups were different. The answers to question 1 are the same in both groups. P = 0.83 Fisher exact test result as p value (Table 3). The answers to Question 2 are different (you read the numbers and percentages from the table) (Table 4). Even those who say I don't remember will be different. P = 0.0290 Fisher exact test result. The veins are not different. P=0.41 Chi-square test Table5).

Table 1. Patient characteristics.

	Group 1	Group 2	P value
Age	43±12	40±13	0.29
BMI	26±3	27±4	0.55
Gender (F/M)	19/11	15/15	0.3

Data were presented as ratios and percentages. A $p<0.05$ value was accepted for statistical significance.

Table 2. Hand and arm movement during rocuronium injection.

	Group 1(n)	Group 2 (n)	Total(n)	P value
No movement	16	22	38	0.047
Mild hand movement	6	0	6	0.015
Hand withdrawal	2	4	6	0.37
Arm withdrawal	6	4	10	0.38
Total	30	30	60	

Data were presented as ratios and percentages. A $p<0.05$ value was accepted for statistical significance.

Table 3. Last feeling before falling into sleep.(Question 1).

	Group 1	Group 2	Total	P value
Nothing	18	18	36	-
Mild pain	2	1	3	0.67
Moderate	1	0	1	1
Severe	0	0	0	-
Do not remember	9	11	20	0.83

The answers to question 1 do not seem different(p=0.83 Fisher exact as p value)

Table 4. Did you feel any pain on your hand during medication injection for anesthesia? (Question2)

	Group 1	Group 2	Total	P value
Yes	1	5	6	0.021
No	21	11	32	0.024
Do not remember	8	14	22	0.68

p<0.05 value was accepted for statistical significance.

Table 5. Intravenous cannulation location.

	Group 1	Group 2	Total	P value
Hand Dorsum	11	8	19	0.41
Brachial	19	22	41	0.40

p<0.05 value was accepted for statistical significance.

Discussion

Nociceptive stimulation can activate the sympathetic nervous system and increase blood pressure or heart rate. Original rocuronium was found to be the independent factor associated with a higher heart rate. However, there were no increases in mean blood pressure 3 minutes after the injection of rocuronium.In our study, we did not find the hemodynamic effect of rocuronium.

Rocuronium is widely used to provide neuromuscular blockade during anesthetic care. Intense pain induced by its intravenous injection is common in the clinical setting [7].

it is a muscle relaxant used in our clinic.

The mechanism of rocuronium-induced pain is unclear. Administration rocuronium following high dose bolus of remifentanil (1 mcg/kg) or fentanyl (1.5 mcg/kg) was also examined. However, high dose bolus of these agents could induce the adverse events such as cough, breath holding, and chest rigidity [8]. Although various techniques have been studied to alleviate rocuronium injection pain, there has been no widely accepted method to date.

Acidic or alkaline solution with high osmolality is known to cause injection pain [9]. Rocuronium is an isotonic solution with a pH value of 4. While normal saline is also buffered to pH 4, it does not cause injection pain. It has also been assumed that pain on rocuronium injection occurs as a result of the release of local mediators, such as kinins, stimulating the venous nociceptors [10.] Histamine and bradykinin release is a possible mechanism which is pointed out in some published trials therefore based on this theory, we aimed to prevent rocuronium pain with these cox inhibitors agents.

According to the answer in second question in our study; COX inhibitors drugs have effect on injection pain in group 1 (Table 3).

We could not achieve a meaningful result in the first question, in which we evaluated rocurum injection pain. The reason why there is less pain in group 2 according to the first question because of the vascular access of 22 patients may be from the brachial vein (Table 5).

Since vascular diameter is reportedly associated with the occurrence of the withdrawal reflex after rocuronium injection [11]. Multivariate analysis was performed to exclude the effects of catheter size and location on vessel diameter at the access site.

In our study, pain was less in the group 2 where rocuronium was applied through the brachial vein. (Table 5)

Conclusion

The effect of cox inhibitors on rocuronium pain was seen in our study but check is also effective in reducing pain in vascular width. We think that there are more dominant etiological causes other than the cyclooxygenase pathway in the etiology of rocuronium pain. Nevertheless, there is a need for further studies with larger patient groups to confirm these results.

Declaration of conflict of interest

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Orijinal Makale

Basit böbrek kistlerinin perkütan aspirasyon ve skleroterapisi: tedavi başarısında etkili faktörler

Percutaneous aspiration and ethanol sclerotheraphy of simple renal cysts: factors affecting treatment success

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Öz

Amaç: Semptomatik böbrek kistlerinin tedavisinde perkütan aspirasyon ve etanol skleroterapinin (PAS) güvenilirliğini, etkinliğini ve uzun dönem sonuçlarını değerlendirmek

Gereç ve Yöntemler: 2004-2020 yılları arasında tedavisinde perkütan aspirasyon ve etanol skleroterapi ile tedavi edilen 82 hasta, 90 kist retrospektif olarak değerlendirildi. Ortalama hasta yaşı 60,6 (28-86 arası) olup, 67 hasta yan ağrısı (%81,8), 7 hasta hipertansiyon (%8,6), 3 hasta hidronefroz (%3,5) nedeniyle tedavi edildi. Ortalama takip süresi 59 aydı (1-220 ay). Girişimden sonra ardışık olarak 1, 3, 6, 12, 18. ve 24. aylarda ve sonrasında yıllık olmak üzere takip edildi.

Bulgular: Teknik başarı %100'dü. Prosedür ilişkili mortalite görülmedi. İşlem sonrası 3 (%3,9) hastada yan ağrısı, 1 hastada (%1,3) hematüri gelişti. Birinci yıl sonunda ortalama kist hacminde azalma %93 olup kistlerin 19'u tamamen kayboldu. Bir yıllık takip sonunda radyolojik tam/tama yakın yanıt 77 hastanın 67'sinde (%78); parsiyel yanıt 13 hastada saptandı. Beş hastada tedaviye radyolojik yanıt yoktu.

Sonuç: Semptomatik böbrek kistlerinin tedavisinde ultrasonografi eşliğinde PAS, basit, iyi tolere edilen bir teknik olup düşük komplikasyon riski ve yüksek teknik başarı ile güvenle uygulanabilir.

Anahtar kelimeler: Etanol, böbrek kisti, skleroterapi, perkütan ablasyon

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Abstract

Aim: To evaluate the effectiveness of percutaneous aspiration and ethanol sclerotheraphy in the treatment of symptomatic simple renal cysts

Materials and Metods: Data of 82 consecutive patients with 90 symptomatic renal cysts who were treated with percutaneous aspiration and ethanol sclerotheraphy between 2004 and 2020 were retrospectively reviewed. The mean age of patients was 60.6 (range, 28-86 years). The indications were flank pain (n=67, 81.8%), hypertension (n=7, 8.6%) and hydronephrosis (n=3, 3.5%). Mean follow up period was 59 (11-220) months. Follow-up examinations were performed 1, 3, 6, 12, 18 and 24 months after the procedure and once every year thereafter.

Result: Technical success rate was 100% (n=82). There is no procedure related mortality. Flank pain occurred in 3 (3.9%), and hematuria occurred in 1 patients (1.3%).

Average cyst volume reduction was 93% at the end of the first year (n=77). The cysts disappeared completely in 19 (24.6%) patients. After one year follow-up, the radiological complete/near complete response rate (>90 %), partial response rate (50-90%) and non-response (<50%) was 78% (67 of 77), 16% (13 of 77), 6% (5 of 77) respectively.

Conclusion: Ultrasound guided percutaneous aspiration and ethanol sclerotheraphy in the treatment of symptomatic simple renal cysts is simple, well tolerated technique and can be used effectively, and safely with high technical success with low complication rates.

Keywords: ethanol, renal cyst, sclerotheraphy, percutaneous ablation

Giriş

Basit kistler, böbrekte en sık rastlanan kitle olmasına rağmen 50 yaşın üstündeki bireylerin hemen hemen yarısına yakınında tek ya da çok sayıda olmak üzere insidental olarak saptanır. Özellikle büyük boyutlara sahip (7 cm üstü) kistler semptom gösterir [1]. Basit böbrek kistlerinin yaş ile birlikte hem boyutlarında hem de sayılarında artış olduğu bilinmektedir [2]. 70 yaş ve üzerindeki bireylerde yaklaşık %22 oranında saptanır ve çoğunun boyutlarının yaklaşık 10 yılda 2 katına kadar çıktığı bilinmektedir [3]. Böbrek kistleri çoğunlukla asemptomatiktirler ancak boyutları arttıkça, bası etkisiyle pelvikaliksiyel sistemde obstrüksiyona, flank ağrısına, hipertansiyona, enfeksiyona, hematüriye veya enfeksiyona neden oldukları durumlarda tedavi gerektirir. [4].

Semptomatik böbrek kistleri perkütan aspirasyon (bir sklerozan ajan ile veya kullanılmadan), perkütan marsupiyalizasyon, açık ve laparoskopik kist açma (dekortikasyon) dahil olmak üzere çeşitli cerrahi ve perkütan yöntemlerle tedavi edilebilir. [5]. Laparoskopik olarak yapılan dekortikasyon işlemi efektif, minimal invaziv bir yaklaşım olup laparoskopik tecrübenin artması ile son yıllarda popülaritesi artan bir yöntemdir.

Perkütan aspirasyon ve skleroterapi (PAS) güvenli ve etkili bir metod olarak tanımlanmıştır. Cerrahinin getirdiği yüksek maliyet ve özellikle ileri yaş grubunda genel anestezi nedenli artan morbidite açısından güvenlidir. [6]. Her ne kadar skleroterapi için farklı ajanlar kullanılabiliyor olsa da etanol yıllardır en yaygın kullanılan, en çok tecrübenin olduğu, etkinliği en çok denenmiş ve en kolay ulaşılan sklerozan ajandır [7].

Bu çalışmada basit renal kistlerin tedavisinde perkütan aspirasyon ve etanol ile skleroterapinin etkinliği, güvenliğini ve uzun dönem sonuçlarını sunmayı, başarıda etkili faktörleri güncel literatür bilgileri ışığında özetlemeyi hedefledik.

Gereç ve Yöntemler

Çalışma Helsinki Deklerasyonu kararlarına, hasta hakları yönetmeliğine ve etik kurallara uygun olarak planlandı. Çalışma öncesinde kurum Klinik Araştırmalar Etik Kurulundan onay alındı (Karar no: BTEDK-07/20). İşlem öncesi tüm hastalarda yazılı ve sözel onam alındı. Retrospektif olarak hastanemiz ve radyoloji arşivi taranarak 2004-2020 tarihleri arasında Radyoloji bölümünde perkütan yolla tedavi edilen böbrek kistleri kaydedildi.

Çalışmaya hastanemizde perkütan yolla Bosniak tip 1 kist tedavisi uygulanan yaş ortalaması 60,6 (28-86 arası) olan 82 hasta (26 kadın, 56 erkek) dahil edildi. Tedavi endikasyonu flank ağrısı (n=67, %81,8), hipertansiyon (n=7, %8,6) ve hidronefroz (n=3, %3,5) olarak belirlendi. Hastaların 5

tanesi asemptomatikti (%4,1). Bu beş hastada tedavi kararı, takipte boyut artışı göstermesi nedeniyle hasta ile beraber kararlaştırılarak planlandı. Öncesinde Tip 1 Bosniak kist tanısını BT/MRG (Bilgisayarlı Tomografi/ Manyetik Rezonans Görüntüleme) ile almış tüm hastalarda tedaviye karar vermek için Ultrasonografi (US) ile kistin/kistlerin içeriği, duvar yapısı ve lokalizasyonu değerlendirildi. Sadece Bosniak Tip 1 kistler çalışmaya dahil edildi. Kistin üç boyutu ölçülerek işlem öncesi kistin hacmi belirlendi. Hastalar semptomları, semptomlarının şiddetini değerlendirmek için detaylı sorgulandı ve medikal hikayeleri kaydedildi. Hastaların yaş, cinsiyet, taraf, kist hacmi Tablo 1'de, semptomları Tablo 2'de yer almaktadır.

Tablo 1. 82 hasta 90 kiste ait demografik, klinik ve görüntüleme bulguları (parantez içleri % değerleri göstermektedir)

ÖZELLİKLER	DEĞER
Yaş	
Ortalama	60.6
Aralık	28 - 86
Cinsiyet	
Kadın	26 (31.8)
Erkek	56 (68.2)
Semptom	
Var	77 (93.9)
Yok	5 (6.1)
Taraf	
Sağ	39 (43.4)
Sol	51 (56.6)
Yerleşim	
Üst	38 (42.2)
Orta	22 (24.4)
Alt	30 (33.4)
Çap (mm)	
Ortalama	69.2 ± 2.7
Aralık	42.7 – 119.5
Çap Aralığı (mm)	
< 50	27 (30.0)
50-100	48 (53.3)
>100	15 (16.7)
Hacim (ml)	
Ortalama	247.5 ± 108.4
Aralık	37.1- 847.9
Hacim Aralığı (ml)	
< 200	29 (32.2)
200-500	48 (53.3)
> 500	13 (14.5)

Tablo 2. Semptom tablosu

	Hasta sayısı (n=82)	Yüzde
Asemptomatik	5	4.1
Yan ağrısı	67	81.8
Hipertansiyon	7	8.6
Hidroüreteronefroz	3	3.5

İşlem Tekniği

Hastaların tamamı işlem sırasında monitorize edildi ve hastalara intavenöz sedasyon uygulandı. Tüm hastalarda işlem US ve floroskopi eşliğinde gerçekleştirildi. Kist büyüklüğü ve kist içeriğine göre PAIR (Puncture, Aspiration, Injection, Reaspiration) (n= 11, %13,4) ve tek seans kateterizasyon (n=71, %86,6) olarak iki farklı teknik ile uygulandı;

PAIR tekniğinde hastalar pron pozisyonunda yatırılıp US ile kist lokalizasyonu belirlendi. Giriş traktı boyunca cilt altı dokular prilokain HCl ile infiltre edildi. US kılavuzluğunda kiste 18 G Seldinger iğnesi ile giriş yapıldıktan sonra kist içeriği 10 ml olmak üzere aspire edildi. Aspire edilen sıvı sitolojik, bakteriyel ve biyokimyasal değerlendirme için kullanıldı. Devamında kist lümenine kontrast madde Iopromide (Ultravist 370 mg/mL, Shering) enjekte edilerek kistogram elde edildi. Kistte ekstravazasyon ve böbrek toplayıcı sistemi ile ilişki olmadığından emin olduktan sonra kist içeriğinin %90'nı aspire edildi ve ilk kist hacminin %30-50 miktarında %95 etanol kist lümenine enjekte edildi. Tek seansta maksimum 200 ml etanol kullanıldı. Etanol 10 dakika boyunca kist lümeninde bırakıldı, ardından tüm etanol aspire edildi ve iğne geri çekildi. Tek seans kateterizasyon tekniğinde ise benzer basamakların ardından ponksiyon sonrası az miktarda kontrast madde kullanılarak kist içine Amplatz Super Stiff kılavuz tel yardımı ile 5-7 Fr pigtail kateter yerleştirildi. Floroskopi ile kavite içine %50 dilüe kontrast madde (Ultravist 370 mg/mL, Shering, Berlin, Germany) uygulanarak kistin şekli, ekstravazasyon varlığı, kist kavitesinin toplayıcı sistem ile ilişkisi değerlendirildikten sonra kist içeriğinin %10'u kalacak şekilde aspire edildi. Ekstravazasyon görülen hastalara skleroterapi uygulanmadı. Ardından az miktarda kontrast madde ile birlikte kist volümünün %30-40 arasındaki miktarda %95 etanol kateter yardımı ile floroskopi kılavuzluğunda kist içine enjekte edildi. Maksimum 200 ml etanol ile skleroterapi yapıldı ve kavite içinde maksimum 10 dakika bekletildi. İşlem sonunda içeriğin tamamı aspire edilip kateter çekildi.

Takip

Hastalar tedaviden sonraki 1., 3., 6., 12., 18., ve 24., aylarda kontrol US tetkikiyle klinik olarak ve radyolojik olarak US ile değerlendirildi. Kontrollerde tedavi edilen kistin hacmi ölçüldü. Toplayıcı sistemlerde gelişebilecek obstrüksiyon kontrol edildi. Birinci yıldan itibaren yıllık olarak işlem başarısı yönünden takip edildi. Ortalama takip süresi 58 ay idi (1-220 ay arası). Hastaların

5'i ilk bir yıl içinde takipleri bıraktı. Birinci yıldan itibaren radyolojik ve semptomatik tedavi yanıtı kalan 77 hastada, tedavi edilen 85 kistte değerlendirildi. İşlem öncesi ve sonrası takiplerde görüntüleme bulguları, kist nüksünü ve kist boyutundaki azalmayı karşılaştırmak için belgelendi. Tedavi öncesi ve sonrası hacim "The Wilcoxon-Pratt testi" ile karşılaştırıldı.

Bulgular

Yaş ortalaması 60,6 (28-86 arası) olan 82 hasta (26 kadın, 56 erkek), 90 kist perkütan olarak tedavi edildi. Teknik olarak tüm hastalarda perkütan aspirasyon ve skleroterapi tedavisi başarılı olarak gerçekleştirildi. Tedavi edilen kistlerin ortalama çapı 69 mm (42-119 mm); kistlerin ortalama hacmi 247 ml (37-847 ml) idi. Hastaların 5'i ilk bir yıl içinde takipleri bıraktı. Kalan 77 hastada, tedavi edilen 85 kistin 1. yıl sonunda işlem sonrası kist hacmi ortalama 17,2 ml idi. Takipte ortalama hacim azalması %93 oldu. Tedaviye yanıt açısından perkütan tedavi öncesi ve sonrası kist hacmindeki azalma istatistiksel olarak anlamlı olarak bulundu ($p < 0,001$). 19 (%24,6) hastada kist takipte tamamen kayboldu. Sitolojik incelemede malignite bulgusu saptanmadı. Ortalama takip süresi 58 ay idi (11-220 ay arası).

Semptomatik ve radyolojik düzelme

Birinci yıl sonundaki takip verilerine göre semptomlar 77 hastanın 67'sinde düzeldi (% 87). On hastanın 1 tanesinde hipertansiyon, 1 tanesinde hidroüreteronefrozda gerileme, 8'inde hissettiği ağrıda azalma olmadı. Ancak işlem öncesine göre ağrı şiddetinde artış ya da semptomlarda progresyon izlenen hasta olmadı. Semptomları düzelmeyen (ağrı ve hidroüreteronefroz) ve kist boyutunda azalma olmayan 3 hastaya 2. Seans skleroterapi yapıldı (iki hastaya 2. ve bir hastaya 4. yılda). Bu hastalarda da semptomatik tam yanıt elde edildi. Hipertansiyon nedeniyle 1 seans tedavi edilmiş semptomatik düzelme olmayan hasta stabil değerlerle seyrettiğinden anti hipertansif tedaviye devam edildi. Semptomatik yanıtı olmayan 6 hastaya ek müdahale uygulanmadı. Son takipte total semptomatik yanıt % 90 olarak saptandı.

Birinci yılın sonunda radyolojik olarak 67 kistin (%78) kist hacminde > %90 küçülme,

13'ünde (%16) %50-90 küçülme, 5'inde (%6) ise < %50 küçülme izlendi. Radyolojik olarak %50-90 küçülme gösteren 13 kistten sadece 6'sında semptom devam ediyordu. Radyolojik olarak < %50 küçülme olan 5 kistin ise 4'ünde kiste bağlı semptomlarda düzelme izlenmezken 1 tanesinde semptomatik düzelme saptandı (Tablo 3 ve Tablo 4).

Tablo 3. Radyolojik düzelme olmayan hastalarda kist hacmindeki azalma % değerleri ve 1. yıl sonunda semptomatik yanıt

Hasta no	Küçülme %	1 yıl sonra semptom
1	18	+
2	20	+
3	21	+
4	31	+
5	45	-

Tablo 4. Radyolojik parsiyel düzelme olan hastalarda kist hacmindeki azalma % değerleri ve 1. yıl sonunda semptomatik yanıt

Hasta no	Küçülme %	1 yıl sonra semptom
1	52	+
2	52	+
3	54	+
4	55	+
5	58	+
6	61	+
7	63	+
8	69	-
9	70	-
10	72	-
11	76	-
12	87	-
13	88	-

Komplikasyonlar

Hastalarda işleme bağlı majör komplikasyon gelişmedi. Hastaların 4'ünde (%5,2) minör komplikasyon gelişti. Hastaların 3 (%3,9) tanesinde işlem sırasında hafif flank ağrısı gelişti. Bir tanesinde ise işlem sonrası 24 saat içinde düzelen hafif hematüri şikayeti oldu (% 1,3).

Tartışma

Basit renal kistler 40 yaşından sonra yaklaşık %20 sıklıkta, 60 yaşından sonra ise yaklaşık %30-35 sıklıkta saptanır [8]. Bu kadar sık görülen ve daha çok ileri yaşlarda, büyük boyutlara ulaşan, çoğu zaman tesadüfen saptanan kistlerin çoğunluğu asemptomatiktir ve tedavi gerektirmez. Nadiren semptomatik olan kistlerin tedavisi ve tedavi seçenekleri tartışmalı bir konudur. Tedavide cerrahi veya perkütan teknikler temel olmak üzere birçok farklı yöntem denenmiştir.

US eşliğinde kist içeriğinin aspire edilmesi basit, kolay ve minimal invaziv bir yöntem olsa da kistin kavitesini çevreleyen sekretuar epitele zarar verilmedikçe sadece perkütan aspirasyon yapılan kistlerde rekürrensin %90 'lara kadar ulaştığı bilinmektedir [9]. Perkütan aspirasyon, son yıllarda giderek daha fazla rapor edilen basit ve güvenilir bir prosedürdür ama skleroterapi olmadan basit drenaj %30-80 nüks oranı ile ilişkilidir [4,10]. Sklerozan ajan

kullanılarak yapılan perkütan tedavi işlemi kist sıvısının yeniden birikmesine neden olan canlı kist duvarını da destrükte ettiği için daha tatmin edici sonuçlar sağlar [11, 12]. Brown D ve ark.'nın 2021 yılında yayınladığı, 1990 – 2020 yıllar arasında 4071 hastanı kapsayan meta analiz çalışmasında perkütan aspirasyon ve skleroterapi tekniği ile tedavi edilen hastaların %87'sinde kist boyutlarında %50'inde fazla azalma ve semptomlarında tam gerileme saptanmıştır [13].

Perkütan tedavi basit renal kistlerin tedavisinde ilk seçenek olarak tercih edilse de bazı çalışmalarda özellikle büyük kistlerin tedavisinde, laparoskopik tedavi ile kıyaslandığında perkütan tedavilerde radyolojik ve rekürrens oranlarının daha fazla olduğu gösterilmiştir. Shao ve ark.'nın araştırmasında, böbrek kistleri etanol ile perkütan tedavi edilen 986 hastadan oluşan grup ve laparoskopik dekortikasyon ile tedavi edilen 208 hastalık grubu karşılaştırdığında, iki grup arasında efektivite ve güvenilirlikte fark saptamasa da özellikle 7 cm'den büyük lezyonlarda rekürrensin PAS grubunda daha yüksek olduğunu bildirmişlerdir. Bu çalışmada PAS grubunda komplet regresyon oranı %91, LD grubunda ise olarak %95 gösterilmiştir ve bu değerler arasında istatistiksel olarak fark saptanmamıştır. Shao ve ark. bir yıllık takipte rekürrens oranı PAS grubunda %8,5 iken LD'de %1,9 belirtmiştir. Ama aynı araştırmada kendilerinin de belirttiği gibi, PAS işlemi sırasında kist içine hacminin yalnız %20'si kadar etanol enjekte edildiğini ve bunun da rekürrens sonuçlarına etki edebileceğini belirtmişlerdir [14]. Güncel pratikte ise kist hacminin %30-50'si kadar etanol uygulanması ile daha iyi sonuçlar aldığımızı biliyoruz. Ayrıca PAS ile kıyaslandığında laparoskopik tedavi yönteminin genel anestezi, işlem süresinin uzunluğu, işlem maliyeti, uzun hastane yatış süresi ve ciddi komplikasyon riskleri gibi dezavantajları vardır. Shao ve ark. kendi çalışmasında komplikasyonlar açısından bilgi vermese de literatürde LD tedavisinde en sık görülen komplikasyonu kanama olarak bildirilmiştir. Bunun dışında organ/doku yaralanmaları, enfeksiyon gelişebilir. Bunlar göz önüne alındığında özellikle yaşlı hastalarda daha sık görülen ve daha büyük boyuta ulaşan kistlerin tedavisinde ilk seçenek özellikle genel anestezi riskleri düşünüldüğünde PAS olmalıdır. Rekürrens daha yüksek oranda gelişse bile, bu daha çok büyük boyutlu kistlerdedir. Uygun teknikle (büyük boyutlu kistlere yüksek miktarda etanol uygulama, maksimum aspirasyon, daha uzun süre etanolü bekletme, PAS prosedürünü aynı seansta birkaç kez ardarda irrigasyon vb.) bunun önüne geçilebilir. Efesoy ve ark. serisinde de PAS ve LD gruplarında semptomatik başarı açısından istatistiksel fark saptanmamıştır (%94,7 vs. %97,6, p=0,498), radyolojik başarı ise sırasıyla %63,2 vs. %95,2'dir [15]. Choi ve ark'nın 2020 yılında yayınladığı çalışmada da radyolojik başarı oranı LD grubunda %97,5, PAS grubunda %60 olsa da, her iki grup arasında semptomatik başarı oranı olarak anlamlı fark saptanmamıştır (sırasıyla %95 ve %90) [16]. Fikrimizce amacımız hastalarda radyolojik düzelme olmamalıdır. Semptomu düzelen ancak kist volümü %50'den daha az küçülme gösteren hastalar tedaviye yanıtsızlık olarak kabul edilmemelidir. PAS minimal invaziv bir yöntem olduğundan ve genel anestezi gerektirmediğinden hastalara bir kaç kez işlemi tekrarlamak morbiditeyi arttırmayacaktır. Bizim serimizde de semptomatik başarı %87 olup literatür ve bu seriler ile benzerdir.

Yıllar içinde ilk olarak %95 etanol kullanılarak perkütan aspirasyon ve skleroterapi yöntemleri denenmiş ve başarılı sonuçlar alınmıştır. Bununla birlikte, çevre dokulara etanol sızıntısı sadece ağrı, ateş, lokal doku korozyonları gibi küçük komplikasyonlara değil, aynı zamanda aseptik apse ve şiddetli merkezi sinir sistemi depresyonu gibi büyük komplikasyonlara da neden olabilir. Bu nedenle zamanla PAS tedavisi için farklı sklerotik ajanlar denenmiştir. İdeal sklerozan ajan kolay ulaşılabilir, düşük maliyetli, düşük ağrı ve yan etki oluşturan ve güvenli bir madde olmalıdır. Polidakanol, asetik asit, OK-432, etanolamin oleat, sodyum tetradesil sülfat, povidione – iodin, n-buthyl siyanoakrilat gibi birçok ajan kullanılmıştır [7]. Bir çoğu ile iyi sonuçlar alınmış olsa da vaka serileri az hastadan oluşmakta ve randomize kontrollü çalışmalar mevcut değildir. 2016 yılında asetik asit (n=42) ile etanolün (n=40) PAS etkinliğini karşılaştıran bir çalışmada kist hacmini azaltmada, total ve parsiyel cevap oranında iki grup arasında fark gözlenmemiştir ve benzer yan etki gözlenmiştir [17]. Agarwal ve ark.'ı polidakanolle (n=20) laparoskopik de-roofingi (n=20) karşılaştırdığı çalışmada istatistiksel olarak benzer etkinlik bildirilmiştir. Polidokanolle %90 komplet regresyon sağlarken, laparoskopi grubunda %95 komplet regresyon olduğu sağlanmıştır [18]. Bleomisin ile tedavi edilen 22 asemptomatik, 31 semptomatik 53 hastada komplikasyon olmaksızın tedaviye %98,5 total cevap olduğu bildirilmiştir. Bu tedaviye yanıt oranları sadece radyolojik yanıtı göstermektedir [5]. Fakat bu çalışmalar gibi birçok farklı araştırmada tedaviye yanıtta belirlenen kriterler yazıdan yazıya değişmekte ve sadece radyolojik cevabı baz olan sonuçlar olduğu görülmektedir. Etanol ile PAS yapılan hastalarda gelişebilecek komplikasyonlardan çekinilse de 2013 yılında Shao ve ark'ın 986 hasta ile yapılmış en fazla hasta sayısına sahip seride

etanole bağlı belirgin komplikasyon bildirilmemiştir [14]. Bu da ilk, en sık ve en yaygın olarak kullanılan sklerozan ajan etanolün güncel verilerle de değerlendirildiğinde halen en güvenilir ajan olduğunu göstermektedir

Bizim serimizde tedavi edilen hastaların %87'sinde kist çapında düzelmeye bakılmaksızın semptomlar kayboldu. Hastaların %92'sinde kist hacminde %50'den fazla azalma oldu. 2021 yılında yayınlanan ve PAS ile ilgili meta-analizde de bizim serimize benzer sonuçlar elde edildi, çapta %50'den fazla azalma toplamın %87,7'sinde saptandı (%92 vs. %87,7). Aynı meta-analizde kist boyutunda azalmadan bağımsız olarak semptomda tam düzelme hastaların %79,6'ında elde edildiği bildirilmektedir [6]. 2021 yılında yayınlanan LD ve PAS sonuçlarını karşılaştıran başka bir meta-analizde LD grubunun daha yüksek semptomatik başarı oranı olduğu saptansa da bu istatistiksel olarak anlamlı düzeyde değildir. Aynı çalışmada LD grubunda radyolojik başarı oranı PAS grubundan yüksektir ve istatistiksel olarak anlamlı bulunmuştur [19]. Bizim düşüncemiz radyolojik yanıttan çok semptomatik yanıtın daha önemli olduğu yönündedir. Radyolojik yanıta bakarak < %50 altında hacimde küçülme tedaviye yanıtsızlık olarak kabul edilse de önemli olan bu grupta da olsa semptomların düzelip düzelmediğidir. Çünkü 2. Seans kararı kistin boyutundan yeterli küçülme sağlanamamasına bağlı değil semptomların düzelip düzelmemesine göre verilecektir.

Tek seans ya da çoklu seans veya farklı teknikler de alternatif uygulamalar arasındadır. 2012 yılında Hamid ve ark. yayınladığı bir çalışmada 25, 50 ve 75 ml etanol sırasıyla <150, 150-300, >300 ml olan kistlere aspirasyon sonrası enjekte edilmiş ve bırakılmıştır. Sonuçları özellikle >300 ml olan grupta yüz güldürücü olmamıştır. Totalde %22 hasta parsiyel semptomatik yanıt, 4 hastada başarısız işlem gerçekleştirilmiştir [20]. Akıncı ve arkadaşlarının 97 hastadan oluşan serisinde etanol ile PAS'da semptomatik başarı oranı %83 olarak bildirilmiştir. Akıncı ve ark. araştırmasında belirttiği gibi bizim serimizde de multipl seans skleroterapi etkinliğine yakın tek seans PAS sonuçlarına (rekürrens ve semptomatik etkinlik açısından) ulaşılmasının sebebi özellikle büyük boyutlu kistlere 200 ml'ye kadar yani kist volümünün %30-50'ı kadar hacimde etanolle ablasyon yapılması, floroskopi ve ultrasonografi eşliğinde işlem yapılması ve işlemlerin tecrübeli bir girişimsel radyolog tarafından gerçekleştirilmesi olabilir [4]. Multipl seansın işlemin rekürensi azalttığı düşünülse de katetere bağlı artan morbidite, uzayan yatış günü, artan maliyet gibi dezavantajları vardır. 2020 yılında yayınlanan laparoskopik de-roofing ve PAS'ı karşılaştıran meta-analize bakıldığında PAS ile tedavi edilen hastalarda ağrı ve ateş dışında komplikasyon görülmemiştir ve laparoskopi ile komplikasyon yönünden istatistiksel anlamlı fark saptanmamıştır [6]. Bizim çalışmamızda da majör komplikasyon ya da etanol ilişkili ciddi bir komplikasyon görülmemiştir.

Bu çalışmanın bazı limitasyonları vardır. Hasta sayısının az oluşu, semptomatik hastaları sübjektif kriterlerle değerlendirmemiz yanında çalışma prospektif ve randomize kontrollü bir çalışma değildir. Bu da seçim kriterlerinde biasa neden olmaktadır. Daha çok sayıda hasta içeren prospektif randomize çalışmalara ihtiyaç vardır.

Sonuç

Etanol ile PAS semptomatik böbrek kistlerinin tedavisinde düşük komplikasyon oranı, maliyeti, tekrar edilebilir oluşu, düşük hastane yatış süresi ve genel anestezi gerektirmemesi nedeniyle ilk tercih edilecek yöntemdir. Düşük rekürrens oranı ve semptomatik tedavi yanıtının yüksek oluşu ile özellikle yaşlı ve komorbiditesi yüksek hastalar için uygun bir seçenektir. Parsiyel yanıt gösteren ya da tedaviye yanıtsız olarak değerlendirilen kistlerin en az 1 yıl süreyle takip edilmesi; bazı hastaların bu sürenin sonunda semptomatik ve radyolojik regresyon gösterebileceği unutulmamalıdır.

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Orijinal Makale

Stent Restenozunu Tahmin Etmede Sistemik İmmün İnflamasyon İndeksinin Rolü

Role of Systemic Immune Inflammation Index in Predicting Stent Restenosis

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Öz

Amaç: Koroner arter hastalığı için implante edilen stentlerin restenozu önemli bir sorun olarak karşımıza çıkmaktadır ve hangi hastalarda gelişebileceği net değildir. Aterosklerotik süreçte ve stent içi restenozda inflamasyon önemli bir rol oynamaktadır. Çalışmamızda stent içi restenozu tahmin etmede Sistemik immün inflamasyon indeksinin (SII) kullanılabilirliğinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışmada Haziran 2019 ile Haziran 2022 yılları arasında akut koroner sendrom veya stabil anjina pektoris ile hastaneye başvurup başarılı stent implantasyonu uygulanmış ve sonrasında 1 yıl içinde stabil anjina pektoris nedeniyle tekrar koroner anjiografi yapılmış hastalar retrospektif olarak incelenmiştir. Hastaların ikinci yapılan koroner anjiografileri öncesinde alınan rutin hemogram testinden SII değeri (Platelet x Nötrofil) / (Lenfosit) formülü ile hesaplanmıştır. Toplam 213 hasta çalışmaya dahil edilmiştir ve hastalar stent içi restenoz olan (n:58) ve restenoz olmayan (n:155) olarak iki gruba ayrılmıştır.

Bulgular: SII ortanca değeri restenoz (+) olan grupta daha yüksek saptandı (920 vs 582, p=0,001). SII değeri ile restenoz arasındaki ilişki ROC eğrisi ile değerlendirildi ve 809 optimal kesme değerinin %60,3 sensitivite ve %64,5 spesifisite ile restenozu tahmin ettiği belirlendi (Eğri altındaki alan: 0,642; %95 GA: 0,559-0,725, p=0,001). Çok değişkenli lojistik regresyon analizinde Diabetes mellitus (OR:2,409, CI %95: 1,228-4,727, p=0,011), hiperlipidemi (OR:2,703, CI %95: 1,335-5,472, p=0,006) ve Log10 SII'nin (OR:3,659, CI %95: 1,360-9,848, p=0,010) stent içi restenozun bağımsız öngördürücüsü olduğu saptandı.

Sonuç: Stent içi restenozda diabet, hiperlipidemi ve inflamasyon önemli rol oynamaktadır. Bir inflamasyon belirteci olan ve kolay hesaplanabilen SII'nin stent içi restenozunun bağımsız öngördürücüsü olduğu görülmüştür. Stent içi restenozu tahmin etmede inflamasyon belirteçlerinin katkısı olabileceği düşünülmelidir.

Anahtar Kelimeler: Sistemik immün inflamasyon indeks, Stent içi restenoz, İnflamasyon, Ateroskleroz

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Abstract

Aim: Restenosis of implanted stents for coronary artery disease is an important problem and it is not clear in which patients it may develop. Inflammation plays an important role in the atherosclerotic process and in-stent restenosis. In our study, we aimed to investigate the usability of the Systemic immune inflammation index (SII) in predicting in-stent restenosis.

Material and Methods: In the study, patients who were admitted to the hospital with acute coronary syndrome or stable angina pectoris and underwent successful stent implantation between June 2019 and June 2022 and then underwent coronary angiography again within 1 year due to stable angina pectoris were retrospectively analyzed. The SII value was calculated by the formula (Platelet x Neutrophil) / (Lymphocyte) from the routine hemogram test taken before the second coronary angiography of the patients. A total of 213 patients were included in the study, and the patients were divided into two groups as those with in-stent restenosis (n:58) and those without restenosis (n:155).

Results: The median level of SII was found to be higher in the group with restenosis (+) (920 vs 582, p=0.001). The relationship between the SII value and restenosis was evaluated with the ROC curve, and the optimal cut-off value of 809 was determined to predict restenosis with 60.3% sensitivity and 64.5% specificity (Area under the curve: 0.642; 95% CI: 0.559-0.725, p=0.001). In multivariate logistic regression analysis, Diabetes mellitus (OR:2.409, CI 95%: 1.228-4.727, p=0.011), hyperlipidemia (OR:2.703, CI 95%: 1.335-5.472, p=0.006) and Log10 SII (OR:3,659, CI 95%: 1.360-9.848, p=0.010) was found to be an independent predictor of in-stent restenosis.

Conclusion: Diabetes, hyperlipidemia and inflammation play an important role in in-stent restenosis. SII, which is an inflammation marker and can be calculated easily, was found to be an independent predictor of in-stent restenosis. It should be considered that inflammation markers may contribute to the prediction of in-stent restenosis.

Keywords: Systemic immune inflammation index, In-Stent restenosis, Inflammation, Atherosclerosis

Giriş

Koroner arter hastalığının altın standart tedavisi haline gelen perkütan koroner girişimlerde koroner arterdeki lezyonlar için stent implantasyonu yapılmaktadır. Ancak implante edilen stenlerde nativ damarlar gibi ateroskleroz ve neointimal hiperplazi nedeniyle stent içi restenoz görülebilmektedir [1]. Stentin proksimal ve distal 5mm'lik segmentleri de içeren stent içi %50 ve üzeri darlıklar stent içi restenoz olarak değerlendirilmektedir [2]. Stent içi restenozu literatürde erken ve geç stent restenozu olarak ikiye ayrılmıştır [3]. Stent içi restenozda aterosklerotik süreç dışında stent malpozisyonu, uygun boyutta stent implante edilmemesi, yeterli stent açıklığı sağlanmaması gibi işlem kaynaklı nedenlere bağlı olabilir. Ancak optimal perkütan koroner işleme ve optimal medikal tedaviye rağmen stent içi restenozlarıyla karşılaşmaktayız. Özellikle diabetes mellitus, hiperlipidemi gibi komorbiditesi olanlarda stent içi restenoz sık olarak izlenmektedir [4]. Erken dönemde stent içi restenozları genellikle işleme bağlı olduğu geç stent restenozlarının da ateroskleroz ve neointimal hiperplaziye bağlı olduğu düşünülmektedir. Stent içi restenozunu öngörebilmek, stent restenozu gelişebilecek hastalara ilaç kaplı stent implante edilmesi, daha yakın takibe çağrılması, sıkı lipidemik ve glisemik kontrol yapılması açısından önemlidir.

Aterosklerozda ve stent içi restenozda inflamasyonun önemi gösterilmiş ve çeşitli inflamasyon parametreleri geliştirilmiştir [5,6]. Sistemik immün inflamasyon indeksi (SII)'de son yıllarda geliştirilen inflamasyon parametrelerinden biridir ve trombosit lenfosit ve nötrofil değerleri ile hesaplanmaktadır. SII, aterosklerotik hastalıklar dışında infeksiyon hastalıkları, kanser gibi hastalıkların prognozunu göstermek içinde son yıllarda kullanılmıştır [7-9]. Bizim çalışmamızdaki amaç stent içi restenozunu tahmin etmede SII'in kullanılabilirliğinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler

Çalışma retrospektif olarak dizayn edilmiştir. Çalışmaya Haziran 2019 ile Haziran 2022 yılları arasında hastanemize akut koroner sendrom veya stabil anjina pektoris ile başvurup perkütan koroner girişim ile başarılı stent implantasyonu uygulanmış ve sonrasında 1 yıl içinde tekrar koroner anjiografi yapılmış hastalar çalışmaya dahil edilmiştir. Hastaların demografik ve klinik değerlerine hastane kayıt sistemi üzerinden ulaşılmıştır. Çalışma Helsinki bildirgesine uygun olarak gerçekleştirilmiştir ve yerel etik kurul onayı alınmıştır

Stent trombozu ile başvuran, daha önce koroner bypass cerrahisi olan hastalar ve ilk perkütan koroner girişimde stent implantasyonu optimal olmayan hastalar çalışma dışı bırakılmıştır. Yine ikili antiplatelet tedaviye şiddetli intoleransı olan veya alerjisi olanlar, hematolojik hastalık öyküsü olanlar, kronik böbrek hastalığı olanlar, şiddetli karaciğer hastalığı

olanlar, trombositopeni ve trombositozu olanlar, antikoagülan kullanan hastalar, aktif enfeksiyonu olan, kronik enflamatuar hastalığı ve malignitesi olanlar çalışma dışı bırakılmıştır.

Stent proksimal ve distal 5 mm'sini kapsayan segmentte %50 ve üzeri darlık olması stent içi restenozu olarak değerlendirilmiştir, Kantitatif ölçüm ile darlık düzeyi hesaplanmıştır. Hastaların ikinci yapılan koroner anjiografi öncesinde alınan rutin hemogram ve biyokimya testleri hastane kayıt sisteminden elde edilmiştir. SII değeri (Platelet x Nötrofil) / Lenfosit formülü ile hesaplanmıştır.

İstatistiksel Analiz

İstatistiksel analizler IBM SPSS Statistics 23 paket programı ile yapıldı. Sürekli değişkenler için veri normal dağılıma uyuyorsa ortalama ± standart sapma olarak, normal dağılıma uymuyorsa medyan [Q1-Q3] ve kategorik değişkenler yüzdeler olarak sunuldu. Normal dağılım gösteren iki bağımsız grubun karşılaştırılması için Student t testi kullanıldı. Normal dağılıma uymayan iki bağımsız grubun karşılaştırılması için Mann Whitney U testi kullanıldı. Kategorik değişkenlerin karşılaştırılması için Ki-Kare testi uygulandı. Stent restenozunda SII'in tanı testi olarak kullanılması, özgüllük ve duyarlılık değerleri ROC eğrisi kullanılarak hesaplandı. P değerleri için <0,05'in altında olması istatistiksel olarak anlamlı kabul edildi.

Bulgular

Toplam 213 hasta çalışmaya dahil edilmiş ve retrospektif olarak incelenmiştir. Hastalar restenoz (+) ve restenoz (-) olarak iki gruba ayrılmıştır. Restenoz (+) grupta yaş ortalaması 57,8 ± 11,6 olan 58 hastadan, Restenoz (-) grupta yaş ortalaması 60,6 ± 12 olan 155 hastadan oluşmaktaydı. Gruplar arasında cinsiyet ve yaş açısından anlamlı fark tespit edilmemiştir. Çalışmaya katılan hastaların demografik, klinik ve laboratuvar verileri Tablo 1'de verilmiştir.

Tablo 1. Hastaların Demografik özellikleri, klinik ve laboratuvar parametreleri

	Restenoz - (n:155)	Restenoz + (n:58)	p
Demografik Veriler			
Yaş (Yıl)	60,6 ± 12	57,8 ± 11.6	0,12
Erkek Cinsiyet, n (%)	118 (76,1)	44 (75,9)	0,55
Komorbidite, n (%)			
Diabetes Mellitus	54 (34,8)	32 (55,2)	0,006
Hipertansiyon	64 (41,3)	24 (41,4)	0,556
Hiperlipidemi	42 (27,1)	24 (41,4)	0,034
Aktif Sigara Kullanımı	54 (24,8)	27 (46,6)	0,08
LVEF %	51,3 ± 10,7	47 ,8 ± 11,8	0,041
Prezentasyon, n (%)			
AKS	100 (64,5)	42 (72,4)	0,178
SAP	55 (35,5)	16 (27,6)	
Anjiografik Bulgular			
Stent Uzunluğu	18,1 ± 5,9	20 ± 5,8	0,047
Stent Çapı	3,2 ± 0,5	3,1 ± 0.5	0,083
İlaç Salınımlı Stent,n (%)	39 (25,2)	13 (22,4)	0,412
Laboratuvar Değerleri			
Hemoglobin, (g/dL)	13,9 ± 1,7	13,8 ± 1,8	0,772
Beyaz küre sayısı, (103/uL)	10,2 ± 4,3	11,7 ± 3,4	0,113
Nötrofil sayısı, (103/uL)	7,12 ± 4,04	8,29 ± 3,42	0,052
Lenfosit sayısı, (103/uL)	2,36 ± 1,65	2,02 ± 0,86	0,138
Trombosit, (103/uL)	225,4 ± 79,9	259,8 ± 104,1	0,011
Kreatinin, (mg/dL)	0,95 ± 0,2	1,02 ± 0,25	0,04
Total Kolesterol, (mg/dL)	180,9 ± 37,6	186,4 ± 54,8	0,537
LDL-Kolesterol, (mg(dL)	110.6 ± 33.6	109 ± 36.6	0,51
HDL-Kolesterol, (mg/dL)	42,3 ± 9,3	33,6 ± 9,8	<0,001
SII	582 [377-1096]	920 [517-1810]	0,001

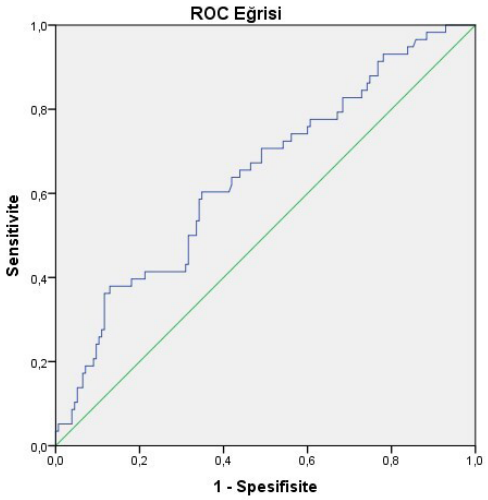
LVEF: Sol ventrikül ejeksiyon fraksiyonu, AKS: Akut koroner sendrom, SAP: Stabil anjina pektoris SII: Sistemik immün-inflamasyon indeksi

Restenoz (+) olan grupta restenoz (-) olan gruba göre daha fazla diabetes mellitus gözlenmiştir (p=0,006). Hipertansiyon, hiperlipidemi ve aktif sigara kullanımı açısından gruplar arasında fark yoktur. Restenoz (+) olan grubun Sol ventrikül ejeksiyon fraksiyonu anlamlı olarak daha düşük olduğu tespit edilmiştir (47 ,8 ± 11,8 vs 51,3 ± 10,7, p=0,041). Her iki grubun anjiografik bulguları karşılaştırıldığında Restenoz (+) olan hastalara daha uzun stent implante edildiği izlenmiştir (20 ± 5,8 vs 18,1 ± 5,9, p=0,047).

Laboratuvar bulguları incelendiğinde restenoz (+) olan grupta platelet sayısı anlamlı olarak daha fazla izlenmiştir (259,8 ± 104,1 vs 225,4 ± 79,9, p=0,011). Restenoz (+) olan grupta kreatinin değeri anlamlı olarak daha fazla olduğu izlenmiştir (1,02 ± 0,25 vs 0,95 ± 0,2, p=0,04). Hastaların lipid profilleri

incelendiğinde ise HDL kolesterol seviyesi Restenoz (+) olan grupta daha düşüktür (33,6 ± 9,8 vs 42,3 ± 9,3, p=<0,001). SII ortanca değeri restenoz (+) olan grupta daha yüksek saptanmıştır (920 vs 582, p=0,001). Gruplar arasında diğer laboratuvar parametreleri arasında anlamlı fark izlenmemiştir.

SII değeri ile restenoz arasındaki ilişki ROC eğrisi ile değerlendirildi (Figür 1). SII'in 809 optimal kesme değerinin %60,3 sensitivite ve %64,5 spesifisite ile restenozu tahmin ettiği belirlendi (Eğri altındaki alan: 0,642; %95 GA: 0,559-0,725, p=0,001).



Figür 1.

Çok değişkenli lojistik regresyon analizinde Diabetes mellitus (OR:2,409, CI %95: 1,228-4,727, p=0,011), hiperlipidemi (OR:2,703, CI %95: 1,335-5,472, p=0,006) ve Log10 SII'nin (OR:3,659, CI %95: 1,360-9,848, p=0,010) stent içi restenozunun bağımsız öngördürücüsü olduğu saptandı (Tablo 2).

Tartışma

Çalışmamızda, klinik uygulamada kolayca kullanılabilecek SII değerinin stent içi restenoz gelişenlerde anlamlı olarak yüksek olduğu tespit edilmiştir ve Diabetes Mellitus, hiperlipidemi ve Log10 SII'nin stent içi restenozunun bağımsız öngördürücüleri olduğu izlenmiştir. Literatürde SII ile koroner arter hastalığı ciddiyeti ve prognozu ilişkilendirilmiş olsa da stent içi restenozu gelişimi ile ilişkisini gösteren ilk çalışmadır [10,11].

Aterosklerozun kronik inflamatuar hastalık olduğu ve gelişiminde inflamasyonun rol aldığı daha önceki çalışmalar ile gösterilmiştir [12]. Son yıllarda nötrofil-lenfosit oranı, trombosit-lenfosit oranı gibi belirteçlerin inflamasyonun göstergesi olduğu ve bunların aterosklerozla ilişkisi olduğu gösterilmiştir [13,14]. Bizim çalışmamızda da benzer şekilde trombosit, nötrofil ve lenfosit değerleri ile bir inflamasyon belirteci olan SII değerleri hesaplanmıştır ve ateroskleroza yol açarak stent restenozuyla ilişkili olduğu gösterilmiştir. Nötrofillerin trombotik süreçleri tetikleyebilir ve aterosklerozda da rol alır [15]. Trombositlerde endotel ile ilişkisi ile homeostaz sağlamanın yanı sıra endotel hücrelerinin aktivasyonuyla inflamatuar süreçlerin başlamasına ve ateroskleroza yol açmaktadır [16].

Tablo 2. Stent restenozunu etkileyen faktörlerin lojistik regresyon analizi

	Tek Değişkenli	Çok Değişkenli
	Odds Oranı (%95 Güven aralığı)	Odds Oranı (95% Güven aralığı)
Stent Uzunluğu	1,053 (1,000-1,108, p=0.048)	1,043 (0.987-1.102, p=0.132)
Kreatinin	4,106 (1,050-16,046, p=0,042)	2,014 (0,457-8,865, p=0,355)
LVEF	0,972 (0,947-0,999, p=0.043)	0,977 (0,948-1,007, p=0,132)
Diabetes mellitus	2,302 (1,246-4,254, p=0.008)	2,409 (1,228-4,727, p=0,011)
Hiperlipidemi	1,899 (1,010-3,570, p=0.046)	2,703 (1,335-5,472, p=0,006)
Log10 SII	4,710 (1,903-11,661, p=0.001)	3,659 (1,360-9,848, p=0,01)

Çalışmamızda literatüre benzer şekilde diabetes mellitusu olan hastalarda daha sık stent içi restenozu olduğu izlenmiştir [17]. Diabetes mellitus pek çok yolak ile ateroskleroza ve stent içi restenoza yol açtığı bilinmektedir. Diabetli hastalarda vasküler düz kas hücrelerinde fenotipik farklılıkların gözlendiği ve bu hastalarda kronik olarak aktive olan IL-1β'nin daha agresif adezyona yol açtığı gösterilmiştir [18]. Ayrıca diabetik hastalarda hiperlipidemi ve makrofajlarda artmış LDL kolesterol alımının hızlı bir ateroskleroza neden olmaktadır [19]. Ateroskleroz gelişiminde ana rol oynayan hiperlipideminin tedavisinde LDL kolesterolün düşürülmesi ve HDL kolesterolünün arttırılması hedeflenmektedir. Özellikle LDL kolesterol seviyesinin yüksek olduğu durumlarda aterosklerozun arttığı ve hızlandığı daha önceki çalışmalarda gösterilmiş [20]. Çalışmamızda benzer şekilde stent içi restenoz gözlenen hastalarda daha fazla hiperlipidemi izlenmiştir. Ancak laboratuvar değerlerine bakıldığı zaman restenoz izlenen ve izlenmeyen grupta benzer oranda LDL kolesterol izlenmiştir, hastalar daha öncesinde koroner arter hastalığı tanısı konduğu için düzenli statin tedavisi aldıkları düşünülmektedir bu nedenle LDL kolesterol açısından anlamlı fark saptanmamış olabilir. Ayrıca çalışmamızda daha önceki çalışmalara benzer şekilde stent içi restenozu olan grupta daha düşük HDL kolesterol düzeyi izlenmiştir [21]. HDL endotel makrofajlarından kolesterol çıkışını sağlamak yanında oksidasyonu, vasküler inflamasyonu ve trombozu azaltarak ateroskleroza karşı koruyucudur [22].

Stent içi restenozu için stent tipi, uzunluğu ve genişliği de önemli faktörlerdir. Son yıllarda geliştirilen yeni jenerasyon ilaç salınımlı stentlerde metal stentlere göre daha az stent restenozu izlenmektedir [23]. Çalışmamızda iki grup arasında stent tipi açısından anlamlı fark izlenmemiştir, bu da çalışma popülasyonunda ilaç salınımlı stentlerin az kullanılmasından kaynaklanmış olabilir. Stent uzunluğu açısından ise restenoz grubunda anlamlı olarak daha uzun stent implante edildiği görülmüştür. Literatürde benzer şekilde lezyon ve stent uzunluğunun stent içi restenozu için bağımsız risk faktörü olduğu gösterilmiştir [24].

Sonuç

Koroner arter hastalığının altın standart tedavisi olan perkütan koroner girişimlerde implante edilen stentlerin restenozu önemli bir sorun olarak karşımıza çıkmaktadır. Aterosklerotik süreçte olduğu gibi stent içi restenozda da diabet, hiperlipidemi ve inflamasyon önemli rol oynamaktadır. Bir inflamasyon belirteci olan ve kolay hesaplanabilen SII'nin stent içi restenozunun bağımsız öngördürücüsü olduğu görülmüştür. Hiperlipidemik ve diabetik hastalar dışında inflamasyon belirteçleri yüksek olan hastalarında stent restenozu açısından değerlendirilmesi önemlidir

Çalışmanın kısıtlılıkları

Çalışmanın bazı kısıtlılıkları mevcuttur. Bunlardan ilki tek merkezli ve retrospektif bir çalışma olması. İkinci olarak inflamasyon indeksinin hastaların ikinci koroner anjiografilerinden önce alınan hemogram testinden hesaplanmamış olması, inflamasyon indeksinin uzun dönem sonuçlarını net olarak ortaya çıkarmamaktadır, akut dönemde kullanılabilirliğini göstermiştir.

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Orjinal Makale

Neoadjuvan tedavi alan rektum kanseri hastalarında tedavi yanıtını predikte eden parametreler var mı?

Is there any parameter for predicting tumour response following neoadjuvant chemoradiotherapy for patients with rectal cancer?

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Öz

Amaç: Lokal ileri rektum kanserlerinde neoadjuvan kemoradyoterapi(NAKRT) standart hale gelmiş olup patolojik tam yanıt (pCR) alınan hastalarda cerrahi yapılmadan izlem seçeneği tartışılmaktadır. Bu çalışmada NAKRT'ye yanıtı predikte edecek faktörleri araştırmayı amaçladık.

Gereç ve Yöntemler: 2011-2021 yılları arasındaki 18 yaş üstü rektum kanseri tanılı 184 hasta retrospektif olarak tarandı. Histopatolojik olarak rektum kanseri olduğu konfirme edilen ve lokal ileri evre olup neoadjuvan tedavi alan 79 hasta mevcuttu. 18 hasta çalışma dışı bıraklıdı, çalışmaya 61 hasta dahil edildi. TNM evrelemesi pelvik MRG (manyetik rezonans görüntüleme) ile yapıldı. Prediktif faktörleri belirlemek için SPSS'de lojistik regresyon modeli kullanıldı.

Bulgular: Çalışmaya 61 hasta dahil edildi. Median yaş 45 (44-89) idi. Hastaların 42(%68.9) si erkek idi. Klinik T evresi 34 (%55.7) hastada T3 ve 23 (%37.7) hastada T4 idi. Klinik N evresi 0, 1 ve 2 olan hastaların sayısı sırasıyla 5(%8.2), 28(%45.9) ve 28(%45.9) idi. Ortalama CEA(karsinoembriyojenik antijen) ve CA 19-9 değerleri sırasıyla 9.69 (std. Deviation:14.95) ve 12.32 (std. Deviation:12.61) idi. 49 (%80.3) hasta kapesitabin eşliğinde, 12 hasta 5-FU(5-Fluorourasil) eşliğinde RT(Radyoterapi) aldı. 40 (%65.6) hastaya LAR(Low anterior rezeksiyon) yapılmıştı. 57 (%93.4) hastanın patolojisi adenokarsinom idi. Patolojik yanıt durumuna bakıldığında 8 (%13.1) hastada tam yanıt ve 48 (%78.7) hastada kısmi yanıt varken 5 (%8.2) hasta tedaviye yanıtsız olarak görüldü.

Sonuç: Bazı çalışmalarda NAKRT ile tedavi yanıtını predikte edecek birtakım faktörler olduğu belirtilmiş olsa da henüz kılavuzlara yansımış ortak kabul edilmiş parametreler yoktur. Bizim çalışmamızda değerlendirilen parametreler arasında patolojik tam yanıtı predikte eden bağımsız bir faktör bulunamadı. 'Neoadjuvan tedavi alan rektum kanseri hastalarında tedavi yanıtını predikte eden parametreler var mı?' sorusuna cevap verecek daha çok sayıda ileri araştırmaya ihtiyaç duyulmaktadır.

Anahtar kelimeler: Kanser, kemoradyoterapi, neoadjuvan tedavi, prediktif faktörler, rektum

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Abstract

Aim: Nonoperative management of rectal cancer is an emerging treatment approach; neoadjuvant chemoradiotherapy (nCRT) has become the standard treatment for locally advanced rectal cancer. The aim of the present research was to examine the parameters that could better understand the response to nCRT for patients with rectal cancer.

Material and Methods: This is a retrospective study which enrolled 184 patients diagnosed with rectal cancer 2011-2021; only 79 of them received nCRT and 18 patients were excluded from the analysis. TNM staging of rectal cancer made by pelvic magnetic resonance imaging. Logistic regression models are used to evaluate predictor variables.

Results: Sixty one patients were included in the final analysis and 68.9% were males with a median age of 45 (44-89) years. T-stage 3 and 4 were: 34 (55.7%) and 23 (37.7%), respectively. The majority of patients had N-stage 1 (45.9%) and N-stage 2 (45,9%) disease at presentation. Median carcinoembryonic antigen level was 9.69±14.95 ng/mL whereas cancer antigen 19-9 level was 12.32±12.61 U/mL. Forty nine (80.3%) patients received concurrent capecitabine with preoperative radiation therapy. Patients undergoing low anterior resection were 40 (65.6%). Eight (13.1%) patients had a pathologic complete response (pCR) while the incomplete response group consisted of 48 (78.7%) patients and no response group had only 5 (8.2%) patients.

Conclusion: Although some studies have stated that there are some factors that will predict the treatment response with NACRT, there are no commonly accepted parameters reflected in the guidelines yet. No independent factor predicting pathological complete response was found among the parameters evaluated in our study.. Further research is needed to address the following question; is there any parameter for predicting tumour response following nCRT for patients with rectal cancer?

Keywords: Cancer, chemoradiotherapy, neoadjuvant therapy, predictive factors, rectum

Giriş

Lokal ileri rektum kanserinde neoadjuvan kemoradyoterapi (NAKRT) standart tedavi olarak kabul edilmektedir. Tedavi altında tümör evresinin gerilemesi, genel sağkalım katkısı ve sfinkter koruyucu cerrahi girişim şansının arttırılması NAKRT'nin avantajları arasında yer almaktadır(1). Neoadjuvan tedaviye kötü veya yetersiz yanıtların uzun dönem takiplerde kötü prognozla ilişkili olduğu bilinmektedir(2). Patolojik tam yanıt (pCR), rezeke edilen dokunun histopatolojik incelemesinde rektum duvarında ve lenf nodlarında canlı tümör hücresinin yokluğu olarak tanımlanmaktadır(3). NAKRT ile patolojik tam cevap oranları %10-40 arasında gözlenmektedir(4). Neoadjuvan tedavi yanıtlarının iyi olmadığı hastalar sfinkter koruma, lokal kontrol ve uzun sağkalımlar elde etme açısından kötü prognostik grup olarak değerlendirilir. Bu noktada hangi hastaların neoadjuvan tedaviden fayda görebileceğini belirlemek tedavi planı açısından yol gösterici olacaktır.

Biz de çalışmamızda, Kliniğimizde neoadjuvan tedavi almış olan rectum kanseri tanılı hastaları inceleyerek tedavi yanıtını etkileyen faktörleri araştırmayı amaçladık.

Gereç ve Yöntemler

2011-2021 yılları arasında Dışkapı Eğitim ve Araştırma Hastanesi (EAH) Tıbbi Onkoloji kliniğinde tedavi gören 18 yaş üstü rectum kanseri tanılı 184 hasta retrospektif olarak tarandı. Histopatolojik olarak rektum kanseri olduğu konfirme edilen ve lokal ileri evre olup neoadjuvan tedavi alan 79 hasta mevcuttu. Verileri eksik olan ve 2. primer kanseri olan hastalar çalışma dışı bıraklıdı. Çalışmaya 61 hasta dahil edildi. Hastaların klinik ve laboratuvar verileri hastane bilgi yönetim sistemi ve hasta dosyaları taranarak kaydedildi. Neoadjuvan tedavi öncesi radyolojik olarak klinik T ve N evreleri, operasyon sonrası pT ve pN evreleri kaydedildi.

İstatistiksel analizler IBM SPSS istatistik programı (IBM SPSS istatistik versiyon 22.0, IBM SPSS, ABD) kullanılarak yapıldı. Hastaların klinik ve demografik özellikleri deskriptif analizlerle incelendi. Kategorik ve numerik değişkenler sayılar ve yüzdeler(n,%) olarak verildi. Sürekli değişkenler normal dağılım durumunda ortalama ± standart sapma, normal dağılıma uymadığında ise median ve aralık olarak verildi. P değeri < 0.05 tüm istatistikler için anlamlı kabul edildi.

Bulgular

Çalışmaya 61 hasta dahil edildi. Median yaş 45 (44-89) idi. Hastaların 42(%68.9) si erkek idi. Klinik T evresi 34 (%55.7) hastada T3 ve 23 (%37.7) hastada T4 idi. Klinik N evresi 0, 1 ve 2 olan hastaların sayısı sırasıyla 5(%8.2), 28(%45.9) ve 28(%45.9) idi. Ortalama CEA (karsinoembriyojenik antijen) ve CA 19-9 de-

ğerleri sırasıyla 9.69 (std. Deviation:14.95) ve 12.32 (std. Deviation:12.61) idi. Kırkdokuz hasta (%80.3) kapesitabin eşliğinde, 12 hasta 5-FU(5-Fluorourasil) eşliğinde RT (Radyoterapi) aldı. Ondokuz hastaya (%31.1) APR (Abdominoperineal rezeksiyon), 40 hastaya (%65.6) LAR (Low anterior rezeksiyon) ve 2 hastaya (%3.3) sol hemikolektomi yapılmıştı. Elliyedi hastanın (%93.4) patolojisi adenokarsinom iken 4 hastanın (%6.6) patolojisi müsinöz karsinom idi. Patolojik yanıt durumuna bakıldığında 8 hastada (%13.1) tam yanıt ve 48 hastada (%78.7) kısmi yanıt varken 5 hasta (%8.2) tedaviye yanıtsız olarak görüldü. Hastaların klinikopatolojik ve demografik verileri tablo 1'de verildi. Patolojik tam yanıtı predikte eden faktörler olarak araştırıldığında yaş, cinsiyet, KRT de kullanılan KT tipi, CEA ve CA 19-9 düzeyleri, klinik T ve N evreleri parametrelerinden hiçbiri istatistiksel anlamlı bulunmadı (Tablo 2).

Tablo 1. Hastaların klinikopatolojik ve demografik verileri

		N	%
cT Evresi	2	4	6,6
	3	34	55,7
	4	23	37,7
cN Evresi	0	5	8,2
	1	28	45,9
	2	28	45,9
Patoloji	adenokarsinom	57	93,4
	müsinöz	4	6,6
Ameliyat tipi	Total	61	100,0
	APR	19	31,1
	LAR	40	65,6
	hemikolektomi	2	3,3
pCR	var	8	13,1
	yok	53	86,9
pT Evresi	0	10	16,4
	1	4	6,6
	2	13	21,3
	3	34	55,7
pN Evresi	0	53	86,9
	1	6	9,8
	2	2	3,3
Cinsiyet	kadın	19	31,1
	erkek	42	68,9
Diferansiyasyon	iyi	6	9,8
	orta	27	44,3
	az	1	1,6
	bilinmiyor	27	44,3
Adjuvan KT	aldı	55	90,2
		6	9,8

Tablo 2. Tam yanıtı etkileyen faktörlerin multivariate analizi

			95% C.I.for EXP(B	
	Sig.	Exp(B)	Lower	Upper
Yaş	,653	1,021	,932	1,119
Cinsiyet	,631	1,646	,216	12,543
CA19.9	,215	1,062	,966	1,167
CEA	,088	,578	,308	1,086
KRT_kt_tipi	,678	,587	,048	7,245
Patoloji	,999	,000	0,000	
cT Evresi	,689	1,501	,205	10,987
cN Evresi	,693	,719	,140	3,690
Nagelkerke R Square:0.29, Hosmer and Lemeshow Test P:0.463				

Tartışma

Rektum kanseri kolorektal kanserlerin üçte birinden fazlasını oluşturmakta ve sıklıkla lokal ileri evrede tanı almaktadır(5). Son yıllarda cerrahi, radyoterapi (RT), kemoterapi (KT) ve moleküler tedavideki hızlı gelişmelere rağmen, lokal nüks veya uzak metastaz nedeniyle tedavi sonuçları hala istenen düzeyde değildir. NAKRT ile lokal nüks kontrol oranları ve sağkalımlar artmakta ancak tedavi yanıt oranları kişiler ve çalışmalar arasında farklılıklar göstermektedir(6). Hangi hastaların NAKRT'den fayda göreceğini predikte edecek faktörlerin bilinmesi, gereksiz tedavi ve tedavi ilişkili toksisitelerin önüne geçmek adına yol gösterici olacaktır.

Fischer ve ark. ve Al Sukhni ve ark. yaptıkları retrospektif çalışmalarda sırasıyla hastaların %71.3'ü ve %62.2'si erkekti ve ortanca yaş 66 ve60 idi(7, 8). Bizim çalışmamızda erkek hasta oranı %68.9 idi ve ortanca yaş 45 idi. Bizim çalışmada hastaların daha erken yaşta oldukları görüldü. Fischer ve ark. İle Al Sukhni ve ark. yaptıkları çalışmada cT2, cT3 ve cT4 ve N0, N1 ve N2 hasta oranı sırasıyla %16.5/10.6, %59.1/78.7 ve %24.4/6.8 idi. N0, N1 ve N2hasta oranları ise sırasıyla %19.5/53.2, %39/41.4 ve %41.5/5.3 idi. Bizim çalışmamızda ise cT2, cT3 ve cT4 oranları sırasıyla %6.6/55.7/37.7 idi. N0, N1 ve N2 hasta oranları ise 8.2/45.9 /45.9 olarak bulundu(7, 8). Al Sukhni ve ark. yaptıkları çalışmada iyi diferansiye, orta derece diferansiye ve kötü diferansiye hasta oranları sırasıyla %8.6, %76.8 ve %13.4 iken bizim çalışmamızda %9.8, %44.3 ve %1.6 iken %44.3 hastanın diferansiyasyon bilgisine ulaşılamadı (8).

Yapılan retrospektif çalışmaların bazılarında multivariate analizde CEA, patolojik tam yanıtı predikte eden bağımsız bir faktör olarak bulunmuşken(7, 9), bazı çalışmalarda ise istatistiksel anlamlı bir ilişki bulunmamıştır (8). Bizim çalışmamızda da CEA ile pCR arasındaki ilişki istatistiksel olarak anlamlı bulunmadı (p:0.088).

Ayrıca çalışmamızda CA 19-9 düzeyleri, radyoterapi ile beraber kul-

lanılan kemoterapotik ilaç, yaş, cinsiyet, klinik T ve N evreleri gibi değerlerle de pCR arasında istatistiksel anlamlı bir ilişki bulunmadı.

Çalışmamızın en başta retrospektif olmasından ileri gelen hasta seçimleriyle ilgili olabilecek bias başta olmak üzere hasta sayısının yetersizliği gibi birtakım limitasyonları mevcuttur. Bağımsız prediktif faktörlerin tayini için patolojik tam yanıtla beraber tama yakın yanıtın değerlendirildiği, daha çok sayıda hastanın katıldığı ve en önemlisi prospektif dizayn edilmiş randomize kontrollü çalışmalara ihtiyaç olduğu bir gerçektir.

Sonuç

Lokal ileri rektum kanserinde neoadjuvan tedavi ve sonrasında cerrahi tedaviyi takiben alınan patolojik tam yanıtların daha iyi lokal kontrol ve daha iyi sağkalımlarla ilişkili olduğu bilinmektedir. Bazı çalışmalarda NAKRT ile tedavi yanıtını predikte edecek birtakım faktörler olduğu belirtilmiş olsa da henüz kılavuzlara yansımış ortak kabul görmüş parametreler yoktur(5, 10). Bizim çalışmamızda değerlendirilen parametreler arasında patolojik tam yanıtı predikte eden bağımsız bir faktör bulunamadı. 'Neoadjuvan tedavi alan rektum kanseri hastalarında tedavi yanıtını predikte eden parametreler var mı?' sorusuna cevap verecek daha çok sayıda hastayı kapsayan prospektif ileri araştırmaya ihtiyaç duyulmaktadır.

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Orjinal Makale

Perkütan endoskopik gastrostomi deneyimlerimiz

Our experiences with percutaneous endoscopic gastrostomy

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ÖZ

Amaç: Perkütan endoskopik gastrostomi (PEG), uzun süreli enteral nütrisyon gerektiren gastrointestinal sistemi aktif olan hastalarda tercih edilen bir yoldur. Cerrahi bir müdahale olması sebebiyle hem akut hem de kronik dönemde komplikasyonlara neden olabilmektedir. Bu çalışmada, deneyimlerimizi ve kliniğimizde yapılan PEG işlemlerinden elde ettiğimiz verileri sunmayı amaçladık.

Gereç ve Yöntemler: Sağlık Bilimleri Üniversitesi Konya Şehir Hastanesi Endoskopi Ünitesi'nde 1 Ocak 2008-31 Aralık 2020 tarihleri arasında PEG yapılan 386 hasta incelendi. İşlem sonrası hasta bilgileri kaydedildi. İlk 1 aylık dönemde PEG'e bağlı komplikasyonlar ve 6 aylık mortalite incelendi.

Bulgular: Hastaların 26'sında (%6,7) kateter çıkış yerinde yara enfeksiyonu, 2'sinde (%0,5) cilt, cilatı seviyede kanama, 7'sinde (%1,8) kateter etrafından sızma, 18'inde (%4,6) çıkma, 6'sında (%1,5) tıkanma görülmüştür. PEG işlemi ile direkt ilişkili, işlem sırası ve yakın dönemde mortalite gözlenmemiştir. 47 (%12) hasta ilk 1 hafta içinde, 113 (%29) hasta ilk 1 ay içinde, 192 (%49) hasta 6 ay içinde ölmüştür. İkiden çok sistemik hastalığı olanlarda 1 aylık mortalite oranı %44 olarak tespit edilmiştir.

Sonuç: Komplikasyon oranlarının düşürülebilmesi için PEG yapılan hastalarda enfeksiyon ile etkin mücadele ve asepsi önerileri önemlidir. Ayrıca tüp tespiti dikkatli yapılmalı ve hasta yakınları ayrıntılı bilgilendirilmelidir.

Anahtar Kelimeler: Perkütan Endoskopik Gastrostomi, komplikasyonlar, nutrisyon

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Abstract

Aim: Percutaneous endoscopic gastrostomy (PEG) is preferred in patients with active gastrointestinal systems who require long-term enteral nutrition. Since it is a surgical intervention, it can cause complications in both acute and chronic periods. In this study, we aimed to present our experience and the data obtained from PEG procedures performed in our clinic.

Material and Methods: 386 patients who underwent PEG were examined between January 1, 2008 and December 31, 2020 in the Endoscopy Unit of the Health Sciences University Konya City Hospital. Patient in formation was recorded after the procedure. In addition, complications related to PEG in the first 1-month period and 6-month mortality were evaluated.

Results: 26 (6.7%) of the patients had an infection at the catheter exit site, 2 (0.5%) had bleeding in the skin, and under the skin, 7 (1.8%) had leakage surrounding the catheter, 18 (4.6%) had a protrusion, and 6 (1.5%) had an occlusion. No mortality was observed directly related to the PEG procedure, during the procedure, and in the recent period. However, 47 (12%) patients died with in the first week, 113 (29%) patients died with in the first month, and 192 (49%) patients died with in six months. In patients with more than two systemic diseases, the 1-month mortality rate was 44%.

Conclusion: Effective infection control and asepsis recommendations are important in patients undergoing PEG to reduce the complication rates. In addition, tube detection should be done carefully, and patient relatives should be informed in detail.

Keywords: Percutaneous Endoscopic Gastrostomy, complications, nutrition

Giriş

Malnütrisyon, cerrahi hastalarda mortalite ve morbiditeyi etkileyen önemli bir faktördür (1). Cerrahi hastalarda beslenme durumunun postoperatif komplikasyonların oluşması ile iyileşme sürecine zarar verdiği, tıbbi tedavi gören hastalarda sağlık bakım maliyetlerinde ve enfeksiyonlarda artışa neden olduğu bilinmektedir (2).

Enteral beslenme, gastrointestinal mukozanın fonksiyonları, bağırsak immünitesi ve floranın devamı için de önemlidir. PEG, uzun süreli enteral nütrisyon gerektiren gastrointestinal sistemi aktif olan hastalarda tercih edilen bir yoldur. PEG tüpleri, uzun süreli oral alımı olmayan hastalarda enteral beslenme, hidrasyon ve ilaç uygulaması için bir yol sağlamak için kullanılır (3). Yapılan bir çalışmada PEG ile beslenmeye başladıktan sonraki iki ay içinde ağırlık stabilizasyonu ve serum albüminin-de artış olduğu ileri sürülmüştür (4).

Cerrahi gastrostomi ile perkütan endoskopik gastrostomi arasında karşılaştırma yapılan çalışmalarda morbidite ve mortalite açısından fark saptanmayan çalışmalar mevcuttur (5). Ancak PEG takılmasının cerrahi gastrostomiye göre morbidite ve mortalite oranının daha düşük olduğunu gösteren çalışmalar da vardır (6). Günümüzde PEG'ler daha basit, ucuz ve komplikasyon oranının düşük olması nedeniyle uzun süreli enteral beslenmenin devamında altın standart olarak uygulanmaktadır. Özellikle genel anestezi gerektirmeden lokal anestezi kullanılarak gerçekleştirilmesi açık gastrostomi yöntemlerine göre önemli bir avantaj sağlar.

PEG endikasyonları arasında nörolojik hastalıkların neden olduğu disfaji, uzun süreli koma, yanıklar, kansere bağlı beslenememe ve nadir de olsa laringofaringeal ve özofageal bölgelerin mekanik obstrüksiyonu sayılabilir. Disfajisi olan hastalarda, 4 haftadan uzun süre oral beslenme mümkün değil ise PEG önerilmektedir. Mekanik obstrüksiyonla seyreden hastalıklarda obstrüksiyon tam ise endoskopik işlemler başarısız olabilir. Bu hasta grubunda cerrahi gastrostomi yapılması gerekebilir. Ayrıca gastrostomi, duodenal yaralanmalarda saptırma ve özofagus yaralanmalarında anastomoz güvenliği için açılabilir.

PEG yerleştirme işleminde en sık kullanılan 2 teknik itme (push) ve çekme (pull) yöntemidir. Bunlardan daha çok kullanılan yöntem Ponsky tarafından 1981 yılında tanımlanan çekme yöntemidir(7). Bu çalışmada, deneyimlerimizi ve kliniğimiz tarafından yapılan PEG işlemlerinden elde ettiğimiz verileri sunmayı amaçladık.

Gereç ve Yöntemler

Bu çalışmada; Sağlık Bilimleri Üniversitesi Konya Şehir Hastanesi Genel Cerrahi Anabilim Dalı'nda 1 Ocak 2008-31 Aralık 2020 tarihleri arasında endoskopi ünitesinde perkütan endoskopik gastrostomi tüpü yerleştirilen 386 hasta incelendi. Genel demografik veriler, ilk bir aylık dönemde PEG kateteri takılmasına bağlı gelişen komplikasyonlar ve altı aylık ölüm oranları incelendi.

Teknik

Tüm PEG işlemleri, pull (çekme) yöntemi kullanılarak ve endoskopi ünitemizde anestezi uzmanı gözetiminde 8 saatlik açlık sonrası monitörizasyonla gerçekleştirildi. İşlem öncesi tüm hastalara lokal anestezi (prilokain hidroklorür) ve sedasyon (midazolam 0,05 mg/kg) uygulandı. Hastalara profilaktik antibiyotik uygulanmadı. Transvers kolonu korumak için distansiyonu olan immobilize hastalara işlem öncesi lavman uygulandı. Gastroduodenoskopi işlemi fiber endoskopi kullanılarak yapıldı. Üst gastrointestinal sistemde endoskopide görülebilen duodenumun ikinci kısmına kadar PEG'i engelleyecek herhangi bir patolojinin olup olmadığı değerlendirildi. Kateterin uygulanacağı bölgeye povidon iyot ve lokal anestezi uygulandı. Endoskop ile karın duvarından transilluminasyon ile karın duvarında uygun bir bölge bulundu. İkinci operatör seçilen bölgeye bir parmağıyla bastığında teyit edildi. İğne mideye gönderildi. Kılavuz tel mideye gönderilerek, tuzak yardımıyla gastrostomi tüpü ağızdan çekilerek mideye gönderildi. İşlem için 18-20 Fr PEG seti kullanıldı. PEG tüpü kendi etrafında dönebilecek kadar sıkıştırılarak karın duvarına yerleştirildi. Endoskop ile tekrar mideye girilerek PEG'in yeri kontrol edildi. Kanama kontrolü yapıldıktan sonra işleme son verildi. Daha sonra ciltteki seviyesi endoskopi notuna yazıldı. Hastanın yattığı klinik ve hasta yakınları durumu hakkında bilgilendirildi.

İstatistik Analiz

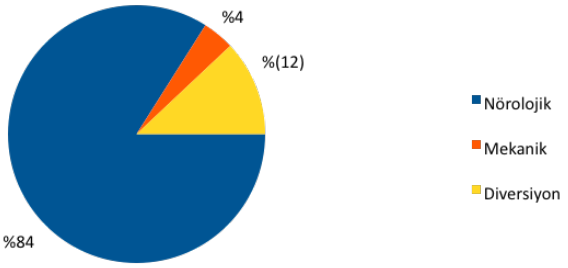
İstatistiksel analiz için Windows için SPSS (Statistical PackagefortheSocialSciences) 22.0 sürümü (IBM Corp, Armonk, NY, ABD) kullanıldı. Nitel değişkenler frekanslar (yüzdeler) olarak sunulurken nicel değişkenler ortalamalar (standart sapmalar) olarak sunuldu.

Bulgular

PEG katateri takılan 386 hastanın 178'i (%46) erkek, 208'i (%54) kadındı. Hastaların yaş ortalaması 70 ± 12.8 idi. 326 (%84) hastaya nörolojik nedenlerden dolayı PEG takıldı, 17 (%4) hastaya ise mekanik nedenlerden dolayı PEG işlemi uygulandı. 43 hastaya ise diversiyon nedeniyle PEG uygulandı (Şekil 1). 386 hastanın 30'unde hipertansiyon, 16'sında diyabet, 32'sinde kalp hastalığı, 75'inde akciğer hastalığı vardı. 82 hastada 2'den daha çok sistemik hastalık mevcuttu (Tablo 1). 386 hastanın 1'inde PEG işlemi yapılamadığından cerrahi olarak ameliyathanede gastrostomi açılmıştır.

Hastaların 26'sında (%6,7) yara enfeksiyonu, 2'sinde (%0,5) kanama, 7'sinde (%1,8) sızma, 18'inde (%4,6) çıkma, 6'sında (%1,5) tıkanma görülmüştür (Şekil 2). Komplikasyonlar ile ek hastalık ve endikasyonlar arasında istatistiksel olarak bir ilişki bulunamamıştır.

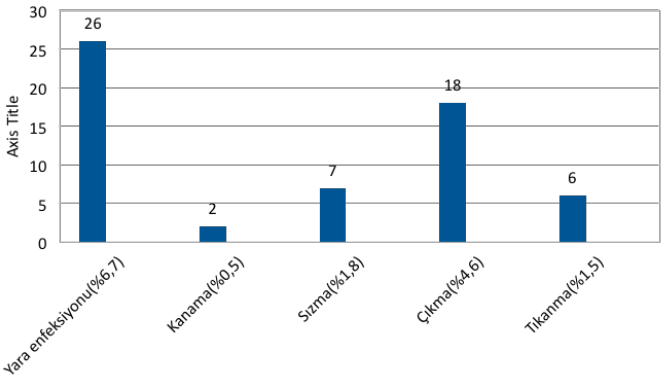
PEG işlemi ile direkt ilişkili mortalite gözlenmemiştir. 47 (%12) hasta ilk 1 hafta içinde, 113 (%29) hasta ilk 1 ay içinde, 192 (%49) hasta 6 ay içinde ex olmuştur. İkiden çok sistemik hastalığı olanlarda 1 aylık mortalite oranı %44 idi. Mekanik nedenlerden dolayı PEG takılan hastaların 1 aylık mortalite oranı %1,1 idi (Tablo 2).



Şekil 1. PEG Endikasyonları

Tablo 1. Hasta sayısı ve ek hastalıklar tablosu

	Erkek	Kadın	Toplam
	178 (%46)	208 (%54)	386
Akciğer hastalığı	43 (%11.1)	32 (%8.3)	75 (%19.4)
Kalp hastalığı	21 (%5.4)	11 (%2.8)	32 (%8.2)
Hipertansiyon	14 (%3.6)	16 (%4.1)	30 (%7.7)
Diyabet	5 (%1.3)	11 (%2.8)	16 (%4.1)
2'den çok hastalık	39 (%10.1)	43 (%11.1)	82 (%21.2)
Ek hastalık yok	56 (%14.5)	95 (%24.6)	151 (%39.1)



Şekil 2. PEG komplikasyonları

Tablo 2. Hastaların mortalite dönem ve sayıları

	Mortalite
1 hafta	47 (%12)
1 ay	113 (%29)
6 ay	192 (%49)

Tartışma

PEG kateter yerleştirilmesinde en sık kullanılan iki yöntem literatürde çekme ve itme yöntemi olarak tanımlanmıştır. Bu tekniklerin karşılaştırıldığı retrospektif bir çalışmada itme tekniğinde %46 olan kısa dönem minör komplikasyonlar çekme tekniğinde %12 olarak gösterilmiş ve uzun dönem majör

komplikasyonlarda fark saptanmamıştır (8). Günümüzde en çok bilinen ve en yaygın kullanılan yöntem çekme yöntemidir. Çalışmamızdaki tüm PEG kateter yerleştirme işlemleri bu yöntemle yapılmıştır. Çalışmamızda kısa dönem komplikasyonların oranı %15,1 'dir ve bu oran literatürdeki oran ile benzerdir. PEG tüpü yerleştirilmesini takiben bildirilen komplikasyon oranları yüzde 10 ile 70 arasında değişmektedir (4,9).

Retrospektif bir çalışmada PEG kateteri yerleştirilen 642 hastada görülen yara enfeksiyonu oranı %3,5 olarak bildirilmiştir (10). Genel cerrahi kliniğinde yapılan başka bir çalışmada bu oran %8,4 olarak bildirilmiştir (11). Çalışmamızda bu oran literatüre benzer şekilde %6,7 olarak belirlenmiştir. Antibiyotik profilaksisi yapılmasının bu oranı daha da azaltacağı kanaatindeyiz. Literatürdeki bazı çalışmalarda yara enfeksiyon oranlarının daha düşük olması, yaş ortalamasının daha düşük olmasından kaynaklanıyor olabilir. Bizim çalışmamızda yara enfeksiyonu olanların yaş ortalaması 68'di. Yaş ortalaması benzer olan çalışmalarda yara enfeksiyon oranı da benzer çıkmıştır (11).

Diyabetin yara enfeksiyonu artırdığı yönünde literatürde çok sayıda bilgi mevcuttur (l2). Ancak bizim çalışmamızda diyabet ile yara enfeksiyonu arasında bir ilişki bulunmamıştır.

Çakır ve arkadaşlarının 700 hasta ile yaptıkları çalışmada %7 oranında yara enfeksiyonu, %2 oranında PEG kenarından kaçak görülmüştür (13).

Gastrostomi tüpünün kenarından sızıntıların hastaların konforunu bozan önemli bir sorun olduğu ve bu sızıntıların yara enfeksiyonuna neden olma ihtimali olduğu bilinmektedir. Bizim araştırmamızda sızıntı oranı %1,8 olup literatürde bildirilen %2-20 arası oranlardan daha düşük olduğu görülmektedir (13,14). İşlem raporunda tüp seviyesinin rutin olarak kaydedilmesi ile birlikte kliniğimizde hasta bakıcı ve yakınlarının bu konuda bilgilendirilmesinin tüpün kenarından sızıntıları azalttığına inanıyoruz.

484 hasta ile yapılan prospektif bir çalışmada, 85 hasta (%18) PEG tüpü yerleştirildikten sonraki iki ay içinde kaybedilmiştir (9). Çalışmamızda ise ilk 1 ay içindeki mortalite %29 olarak tespit edildi. İkiden çok sistemik hastalığı olanlarda ise bu oran %44 çıkmıştır. Mekanik nedenlerden dolayı PEG kateteri takılan hastalarda mortalite %1,1 idi. 6 aylık mortalite oranı %49 tespit edilmiştir. Mortalite oranının yüksek olmasının PEG takılması ile direkt ilişkisi olmayıp hastaların yaşı ve ek hastalıkları ile ilgili olduğu düşünülmüştür.

Sonuç

Sonuç olarak, PEG kateteri yerleştirme prosedürü literatürdeki komplikasyon ve başarı oranlarına uygun olarak genel cerrahi kliniği endoskopi ünitesinde cerrahi veya medikal hastalığı olan hastalarda yapılmaktadır. Bu çalışmada yara enfeksiyonu ve tüp kenarından sızıntıların tüp tespiti ile yakından ilişkili olduğu gözlemlenmiştir. İkiden çok sistemik hastalığı olanların mortalitesinin çok yüksek olduğu görülmüştür.Bu çalışmanın sonucunda biz PEG için antibiyotik profilaksisi öneriyoruz. Ayrıca tüp tespiti dikkatli yapılmalı ve hasta yakınları ayrıntılı bilgilendirilmelidir.

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Bilgilendirilmiş onam formu

Tüm hastalardan bilgilendirilmiş onam alınmıştır.

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Orijinal Makale

YouTube kaynaklı COVID-19 kişisel koruyucu ekipman kullanımı için hazırlanmış Türkçe videoların değerlendirilmesi

Evaluation of youtube-sourced Turkish videos for the usage of COVID-19 personal protective equipment

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Öz

Amaç: COVID-19 hastalarının tanı ve tedavilerinde aktif rol üstlenen sağlık çalışanlarının enfekte olma riskleri yüksektir. Bu risk, kişisel koruyucu ekipmanların [KKE] doğru kullanımıyla azaltılabilir. Bu çalışmada, YouTube KKE kullanım videolarının içerik ve kalite analizlerin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: YouTube'da Aralık 2020'de "COVID-19, kişisel koruyucu ekipman" cümlesiyle arama yapıldı. İlk 10 sayfadaki sonuçlar, 2 araştırıcı tarafından standart bir ölçekle değerlendirilip eğitici ve eğitici olmayan olarak sınıflandırıldı. Eğitici olma özelliği ile video izlenme sayısı, uzunluğu ve yükleme kaynağı arasındaki ilişki değerlendirildi.

Bulgular: Toplam 200 video değerlendirildi. KKE giyme ve çıkarma videolarının yaklaşık yarısı eğitici özelliğe sahipti. Video yükleme kaynağı açısından eğitici ve eğitici olmayan videolar arasında bir fark bulanamadı. KKE giyme ve çıkarma videolarının her ikisinde de eğitici kalitedeki videoların izlenme oranları daha fazlaydı.

Sonuç: COVID-19 salgını sırasında KKE giyme ve çıkarma konusunda YouTube bir öğrenme kaynağı olarak kullanılabilir. Ancak eğitici nitelikteki videolara kolay erişim için YouTube sağlık linki oluşturulmasını önermekteyiz.

Anahtar Kelimeler: COVID-19; kişisel koruyucu ekipman; youtube.

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Abstract

Aim: Healthcare professionals who take an active role in diagnosing and treating COVID-19 patients have a high risk of infection and contamination. This risk can be reduced by correctly using personal protective equipment [PPE]. This study aimed to evaluate the content and quality analysis of YouTube PPE usage videos.

Material and Methods: A search was done on YouTube with the phrase " COVID-19, personal protective equipment" in December 2020. Two researchers evaluated the results in the first ten pages on a standard scale and classified them as educational and non-educational. The relationship between the educational feature and the video's number of views, length, and upload source was evaluated.

Results: A total of 200 videos were evaluated. About half of the PPE donning and doffing videos were educational. No difference was found between educational and non-educational videos in terms of video upload source. Videos of educational quality had higher viewing rates for both putting on and taking off PPE.

Conclusion: YouTube can be a learning resource on wearing and removing PPE during the COVID-19 pandemic. However, we recommend creating a YouTube health link for easy access to educational videos.

Keywords: COVID-19; personal protective equipment; youtube.

Giriş

Türkiye'de 11 mart 2020 tarihinde ilk COVID-19 vakası görülmüş ve aynı tarihte Dünya Sağlık Örgütü [WHO] tarafından SARS-CoV-2 nedenli pandemi ilan edilmiştir [1]. Bu tarihten 27 Kasım 2022 tarihine kadar Türkiye'de toplam 17.042.722 vaka tanımlanmış ve 101.492 COVID-19 kaynaklı ölüm gerçekleşmiştir [2]. Aynı tarih itibarıyla, Türk Tabipler Birliği [TTB] verilerine göre, Türkiye'de COVID-19 nedenli hayatını kaybeden sağlık çalışanı sayısı 556 olarak kayıtlara geçmiştir [3].

COVID-19 enfeksiyonunun başlıca bulaş yolu aerosol olarak tanımlanmakla beraber enfekte yüzeylere temas sonrası mukozal bulaş ve fekal oral yol ile de bulaş olabileceği bildirilmiştir [4]. Bulaşıcı hastalıkların tanı tedavi ve takip aşamalarında aktif rol üstlenen sağlık çalışanlarının COVID-19 hastalığı ile enfekte olma ihtimali normal popülasyona göre yüksektir. Hastalıkları Önleme Merkezi [Center for Disease Control and Prevention-CDC] ve WHO olası ve tanı konulmuş COVID-19 hastalarında aerosal oluşturulan işlemlerde kişisel korucuyucu ekipman kullanımı ile ilgili bir rehber yayınlamıştır [5,6]. Sağlık çalışanlarını ve diğer hastaları COVID-19 enfeksiyonundan korumak için KKE kullanımı tavsiye edilmiştir. Uygun KKE'ların doğru giyilmesi ve çıkarılması ile ilgili prosedürler tanımlanmış ve bu prosedürlerin sağlık çalışanlarına eğitimi konusunda tavsiyeler vermiştir [5,6].

Popüler video paylaşma platformu olan YouTube profesyonel sağlık çalışanlarının kullanımı için hazırlanmış bir çok medya içermektedir [7]. Bu içerikler sağlık profesyonellerinin eğitim ihtiyaçlarını karşılayabilecek nitelikte iyi tasarlanmış doğru ve güncel bilgiyi içerebildiği gibi yanlış ve yanıltıcı nitelikte de olabilir. Youtube video paylaşım platformunun doğru içerik denetimi gibi bir yükümlülüğü olmadığından KKE kulanımı ile ilgili hazırlanmış videolar sağlık çalışanları için eğitici nitelikte olabileceği gibi önemli bir riskte taşımayabilir. Bu araştırmada, YouTube platformunda Türkçe olarak hazırlanmış olan COVID-19 KKE giyme ve çıkarma videolarının, içerik ve kalite analizlerini değerlendirmeyi amaçladık.

Gereç ve Yöntemler

YouTube [https://www.youtube.com; YouTube, LLC, San Bruno; CA; USA] sitesinde 15 Aralık 2022 tarihinde "COVID-19, kişisel koruyucu ekipman" kelimesi ile arama yapıldı. 2020 yılı ve sonrası yayınlanan videolardan, arama kelimesi için ilk 10 sayfadaki videolar, bağımsız iki anestezi hekimi tarafından incelendi. İlk 10 sayfadan sonra arama kelimeleri ile alakasız videoların daha çok gösterilmesi ve daha önce yapılan çalışmalarda izleyicilerin en fazla ilk çıkan videoları izlediklerinin gösterilmiş olması nedenleri ile sadece ilk 10 sayfadaki videoların analizi yapılmıştır [8,9]. Araştırmamız etik kurul kapsam dışındadır.

Çalışma dışı bırakılma özellikleri;

- İlgisiz,
- Reklam içeren,
- Tıbbi içerik olmayan,
- Tekrarlanan videolar.

Videoların uygunluk değerlendirilmesi

Videoların eğitici olmaları bakımından uygun olup olmadıkları, Azer SA'nın belirtmiş olduğu, kriterler modifiye edilerek tespit edildi [Tablo 1]. Bu kriterler video içeriğinin doğruluğu, verilen mesajın netliği, konu hakkında uzman yorumunun olması, eğiticilik ve teknik tasarıma göre 5 major ve 6 minör kriterden oluşmak olup daha önce yapılan birçok çalışmada da kullanılan kriterler olduğu için tercih edildi [10-12] [Tablo 1].

Tablo 1. KKE Değerlendirme Kriterleri
Major kriterler
1. KKE'nin giyme ve çıkarma ilgili içerikler bilimsel olarak doğrudur
2. Görüntüler nettir
3. Kaynak açıkça belirtilmiştir
4. Konu net olarak açıklanmıştır
5. Sesler nettir ve arka planda gürültü yoktur
Minör kriterler
1. Video belirlenen konuyu kapsamaktadır
2. Makul bir indirme süresine sahiptir
3. İçerik oluşturucu hakkındaki bilgiler günceldir
4. Sağlık bilimleri öğrencileri düzeyinde tasarlanmıştır
5. KKE giyme/çıkarma prosedürünün illüstrasyon yerine insan üzerinde gösterilmiştir

Karşılanan major kriterlerin her biri için 2 puan, minör kriterler için ise 1 puan verildi. Major kriterlerin hepsinin karşılanması şartıyla, toplamda 13 puan alan videolar faydalı video olarak değerlendirildi.

Veri Toplama

Her bir video için toplam izlenme sayısı, YouTube'da bulunma süresi, günlük izlenme sayısı, video uzunluğu [saniye], videoların beğenilme/beğenilmeme derecesi ve yükleme kaynağı kaydedildi. Videolara rağbet edilme derecesi, video güç endeksi [VPI] kullanılarak hesaplandı.

VPI=beğenilme derecesi x izlenme derecesi /100

Beğenilme derecesi=beğenme sayısı x 100/ [beğenilme + beğenilmeme]

İzlenme derecesi=izlenme sayısı/gün

Video Yükleme Kaynağı

Videolar yüklenme kaynaklarına göre Üniversite/ Devlet hastanesi ve Özel kurum/ dernek/Kişisel olarak sınıflandırıldı.

Videoların İçerik Açısından Güncelliği ve Doğruluğunun Değerlendirilmesi

Her videonun içeriğinin değerlendirmesini ve KKE giyme ve çıkarma prosedürünü standart hale getirmek ve değerlendirmelere rehberlik etmesi için European Centre for Disease Prevention and Control Guidance referans olarak kullanıldı [13]. KKE giyme ve çıkarma video içerikleri için bakılan parametereler tablo 2 de gösterilmiştir.

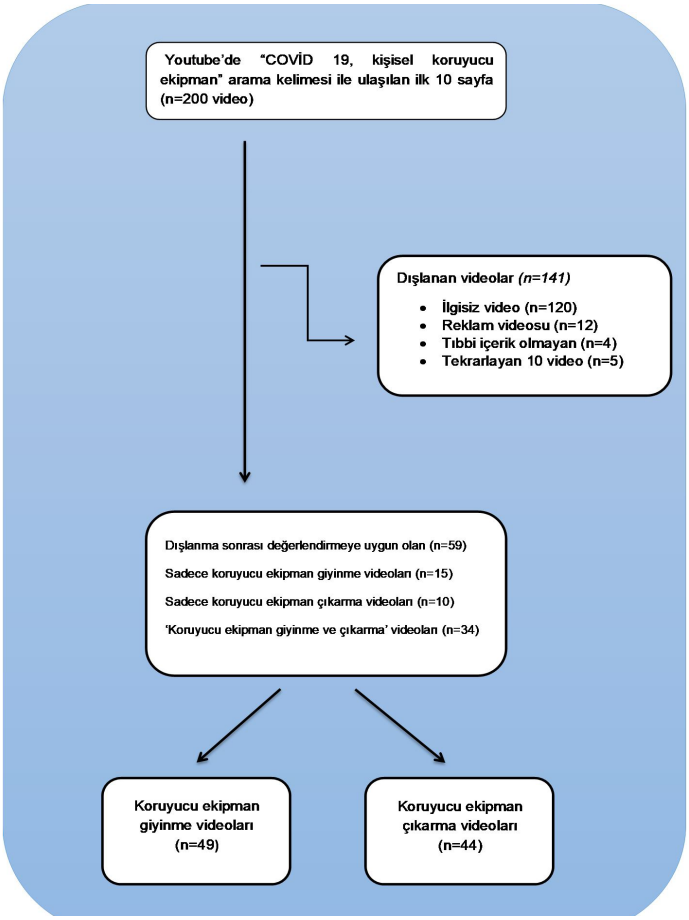
Tablo 2. KKE giyme ve çıkarma video içerik kriterleri	
KKE giyme videoları	KKE çıkarma videoları
1. Önlüğü doğru giyme,	1.Eldivenlerin doğru çıkarılması
2. Maskeyi doğru takma,	2.Göz koruyucunun doğru çıkarılması
3. Maske testi yapılması,	3. Önlüğün doğru çıkarılması
4. Giyinme öncesi malzeme kontrolü yapılması,	4. Temiz alana geçilmesi
5.Göz koruyucuyu doğru giyme	5. Maskenin doğru çıkarılması
6. Eldiveni doğru giyme.	6. Adımlar arası el yıkanması

İstatistiksel Yöntem

Çalışmada elde edilen verilerin analizinde IBM-Statistical Package for Social Sciences [IBM-SPSS Inc., Şikago, IL, ABD] 22.0 programı kullanıldı. Verilerin normal dağılıma uygunluğu 'Shapiro–Wilk testi' ile incelendi. Sürekli değişkenler, dağılım durumlarına göre ortalama ve standart sapma veya [ortanca [25-75 persantil]] olarak, kategorik değişkenler ise sayı ve yüzde olarak ifade edildi. Sürekli değişkenlerin analizinde parametrik test varsayımlarının sağlandığı durumlarda 'Bağımsız gruplarda t testi' uygulanırken, aksi halde 'Mann-Whitney U testi' uygulandı. Toplam video puanı ile temel video özellikleri arasındaki ilişki Pearson ve Spearman korelasyonu ile analiz edildi. Kategorik değişkenlerin analizinde 'Ki kare testi' uygulandı. İstatistiksel anlamlılık düzeyi $p < 0.05$ olarak kabul edildi.

Bulgular

Youtube sitesine "COVID-19, kişisel koruyucu ekipman" arama kelimesi yazılarak, ilk 10 sayfada çıkan 200 video değerlendirmeye alındı. Videoların 141 adeti dışlama kriterlerine göre çalışma dışı kaldı. Bunlardan 120'si ilgisiz, 12 tanesi reklam içeren, 4'ü tıbbi içerik olmayan ve 5'i tekrarlanan videolardı. Böylece çalışmaya 59 video dahil edildi; bunlardan 15'i sadece KKE giyme, 10'u sadece KKE çıkarma ve 34'ü hem KKE giyme hem KKE çıkarma videosu idi. Böylece toplam 49 KKE giyme videosu ve toplam 44 KKE çıkarma videosu değerlendirmeye alındı [Şekil 1].



Şekil 1. Araştırma için uygun YouTube videolarının seçimi

KKE giyme videolarının 23'ü [%46.9] 'eğitici video' olarak değerlendirilirken, 26'sı [%53.1] 'eğitici olmayan video' kategorisinde değerlendirildi. Yükleme kaynağı için bakıldığında, Üniversite/ Devlet hastanesi tarafından yüklenen videoların 14'ü [%46.7] eğitici video, Özel kurum/ dernek/ Kişisel tarafından yüklenenlerin ise 9'u [%47,4] eğitici video idi ve istatistiksel olarak anlamlı fark yoktu [p=0.962]. Video karekteristik özellikleri tüm parametreler için eğitici videolarda daha yüksek skora sahipti. Bu yükseklik 'Video izlenme sayısı', 'video günlük izlenme sayısı', 'video power index', 'total video skoru' istatistiksel olarak anlamlı iken; 'video uzunluğu' ve 'video Youtube'de bulunma süresi' parametreleri istatistiksel olarak anlamlı bulunmadı [p=0,022, p=0,021, p=0,016, p<0,001, p=0,841 ve 0,581] [Tablo 3].

Tablo 3. KKE giyme videolarının, video karakteristik özellikleri ve yükleme kaynağına göre değerlendirilmesi

	Video sayısı	İzlenme sayısı	Video uzunluğu [saniye]	Youtube de bulunma süresi [gün]	Günlük izlenme sayısı	Video power index	Total video skoru	Video yükleme kaynağı	
								Üniversite/ Devlet hastanesi	Özel kurum/ dernek/ kişisel
KKE giyme videoları	49 [%100]	917[280-3187]	168[120-238]	612[593-625]	1,59[0,51-5,08]	1,59[0,51-5,08]	11[9-16]	30 [%100]	19 [%100]
Eğitici videolar	23[%46,9]	2515 [480-5191]	178[123-238]	617[592-626]	4,02[1,03-8,52]	4,02[1,03-8,52]	16[15-16]	14[%46,7]	9 [%47,4]
Eğitici olmayan videolar	26 [%53,1]	783 [248-599]	157[120-275]	610[593-623]	1,34[0,45-1,77]	1,34[0,45-1,77]	9,00[7-10]	16[%53,3]	10 [%52,6]
p değeri		0,022	0,841	0,581	0,021	0,016	<0,001	0,962	

Değişkenler medyan [Q1–Q3] sunuldu ve p < 0.05 istsatistiksel anlamlı olarak ifade edildi.

KKE çıkarma videolarının 20'si [%45.5] 'eğitici video' olarak değerlendirilirken, 24'ü [% 55.5] 'eğitici olmayan video' kategorisinde değerlendirildi. Üniversite ve devlet hastanesi kaynaklı videolarının 12'si [%48] eğitici KKE çıkarma, Özel kurum/ dernek/Kişisel kaynaklı videoların 8'i [%42.1] eğitici çıkarma videolarından oluşmakta olup, aralarında istatistiksel anlamlı fark yok idi [p=0.697]. Video karekteristik özellikleri tüm parametreler için eğitici videolarda daha yüksek skora sahipti. Bu yükseklik 'Video izlenme sayısı', 'video günlük izlenme sayısı', 'video power index', 'total video skoru' istatistiksel olarak anlamlı iken; 'video uzunluğu' ve 'video Youtube'de bulunma süresi' parametreleri istatistiksel olarak anlamlı bulunmadı [p=0,004, p=0,003, p=0,003, p<0,001, p=0,944 ve 0,768] [Tablo 4].

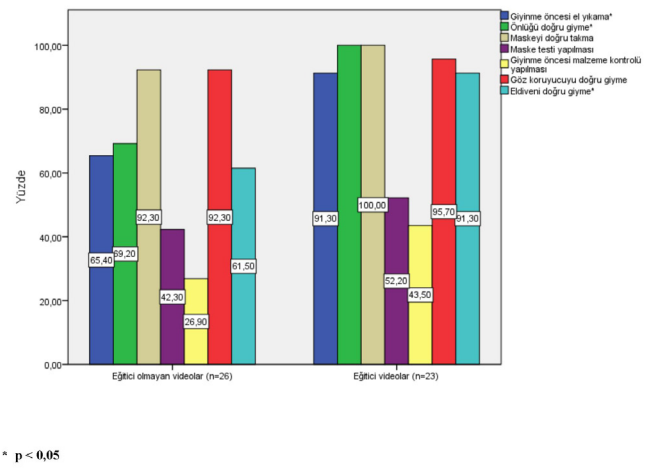
Tablo 4. KKE çıkarma videolarının, video karakteristik özellikleri ve yükleme kaynağına göre değerlendirilmesi

	Video sayısı	Toplam izlenme	Video uzunluğu [saniye]	Youtube de bulunma süresi [gün]	Günlük izlenme sayısı	Video power index	Total video skoru	Video yükleme kaynağı	
									Özel kurum/ dernek/ kişisel
KKE çıkarma videoları	44[%100]	848 [198-2676]	125[104-162]	615[566-624]	1,49[0,32-4,43]	1,49[0,32-4,43]	11,5[8-15,5]	25[%100]	19[%100]
Eğitici videolar	20[%45,5]	2342 [635-3769]	123[107-156]	618[578-623]	3,78[1,09-6,05]	3,78[1,09-6,05]	16[15-16]	12[%48]	8 [%42,1]
Eğitici olmayan videolar	24[%55,5]	420 [86-968]	129[85-166]	613[562-624]	0,78[0,15-1,61]	0,78[0,15-1,61]	8[7-10]	13 [%52]	11 [%57,9]
p değeri		0,004	0,944	0,768	0,003	0,003	<0,001	0,697	

Değişkenler medyan [Q1–Q3] sunuldu ve p < 0.05 istsatistiksel anlamlı olarak ifade edildi

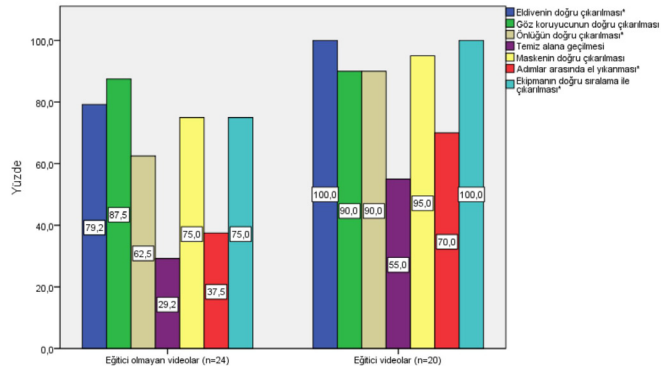
KKE ekipmanları giyme videolarının içerik değerlendirmesine bakıldığında; eğitici videolar tüm parameterleri daha yüksek oranda içermekle birlikte, bu yükseklik 'giyme öncesi el yıkama', 'önlüğü doğru giyme' ve 'eldiveni doğru takma' parametreleri için istatistiksel olarak anlamlı bulundu [p<0.05] [Şekil 2].

KKE ekipmanları çıkarma videolarının içerik değerlendirmesine bakıldığında; eğitici videolar, tüm parameterleri daha yükek oranda içermekle birlikte; 'eldivenin doğru çıkarılması', 'önlüğün doğru çıkarılması' ve 'adımlar arasında el yıkanması' işlemleri eğitici videolarda istatistiksel anlamlı bulundu [p<0.05][Şekil 3].



* p < 0,05

Şekil 2. KKE giyme videolarının içerik açısından değerlendirilmesi



* p < 0,05

Şekil 3. Koruyucu ekipman çıkarma videolarıının içerik açısından değerlendirilmesi

Tartışma

COVID-19 salgını sırasında hastaya müdahale sağlık çalışanları enfekte olma oranı %11 ile %29 arasında değişmektedir [14-16] Sağlık çalışanlarının kontaminasyon ve enfeksiyon riski şüphesiz KKE uygun kullanımı ile azaltılabilir. KKE kullanımı ile ilgili Türkçe Yotube videolarının içerik ve kalite analizlerini yaptığımız çalışmamızda 59 videonun [%28,5] değerlendirmeye uygun olduğunu bulduk. Uygun anahtar kelime ile arama yapılmasına rağmen, videoların %71,5'i çalışma dışına alınmıştır. Bu oran çeşitli çalışmalarda %80 ile %94 arasında tespit edilmiştir [8, 17, 18]. Yazılan arama kelimeleri ile çıkan videolar arasında çalışma dışı bu kadar fazla video çıkması; yüklenen videoların etiketlerinin, video içeriği ile alakasız olması, reklam maksatlı videoların ve tıbbi içerik içermeyen videoların arama sonucu çıkması sebebiyle olduğu tespit edildi. Bu durum YouTube'un Türkçe KKE giyme ve çıkarma konusunda ulaşılabilirliğini ve kullanılabilirliğini kısıtlayabilmekte ve kişilerin konuyla alakasız videolara erişme ihtimalini artırabilmekte dolayısı ile bu videolarının eğitim amaçlı kullanımını kısıtlayabilmektedir.

Geçtiğimiz 10 yılda telekomünikasyon teknolojilerinin gelişimi internet kaynaklı bilgininin, erişim kolaylığı ve çoğunlukla ücretsiz olması nedeniyle popülaritesini giderek arttırdı. Çoğunlukla eğlence ve reklam amacıyla kullanılan internet tabanlı video paylaşım uygulaması olan Yotube, özellikle küresel COVID-19 salgını sürecinde, aynı zamanda bir eğitim aracı olarak da kullanılmaya başlandı. Ancak, YouTube ücretsiz ve kolay ulaşılır olmasının yanında denetimsizdir. Bu nedenle eğitici içeriği her zaman sorgulanabilir. 2015 yılında Madathil ve ark yaptıkları derlemede YouTube'un yanıltıcı bilgiler içerdiği, sıradan kullanıcıların bu bilgiye kolaylıkla ulaştığını ve tartışmalı önemli konularda kullanıcıların karar vermesinde etkili olabileceğini belirtmişti [19]. Araştırmamızda KKE giyme ve çıkarma videolarının sadece yarısının eğitici ve yararlı nitelikte olduğu bulundu. Sağlık alanında yayınlanmış eğitim videolarıyla ilgili yapılan yayınlarda; Üniversite veya tersiyer sağlık merkezlerine ait videolarda yararlılık ve doğruluk oranı, diğerler kurum ve kişilere göre daha yüksek iken, bizim çalışmamızda kurumlar arasında istatistiksel bir farklılık bulunmadı. [20-22]. KKE giyme ve çıkarma alanında hem üniversite/devlet hastanesinin hem de özel kurum/dernek/kişisel kaynaklı gerçekleştirilen yüklemelerin doğru bilgi sunuyor olması kullanıcılar açısından avantaj sağlamaktadır.

YouTube videolarının eğitici olma özelliği ile izlenme sayısı arasında her zaman korelasyon olmayabilir [19,21,22]. Literatürde, bu konuda oldukça farklı sonuçlar mevcuttur [10,19-22]. Araştırmamızda Azer SA ve ark. sonuçlarıyla benzer olarak KKE giyme ve çıkarma videolarının her ikisinde de eğitici özelikte videoların eğitici olmayanlara göre hem günlük izlenme hem de total izlenme sayılarının daha fazla olduğunu tespit ettik. KKE eğitici videoların izlenme sayılarının daha fazla olması, muhtemelen sağlık profesyonellerinin, Covid 19'un yüksek bulaş riski ve mortalite oranı konusundaki farkındalıklarından kaynaklanıyor olabilir.

KKE ekipmanların bulaş riskini en aza indirmek için doğru sıralamayla çıkarılması ve adımlar arası el hiyjeni önemlidir. Çalışmamızda eğitici videoların ekipmanları doğru sıralamayla çıkarılmasının tüm videolarda vurgulandığını; eldivenin ve önlüğün doğru çıkarılması, adımlar arası el hiyjeni sağlanması gibi önemli parametrelerin ise eğitici olamayan videolara göre istatistiksel olarak anlamlı düzeyde yüksek oranda

anlatıldığını tespit ettik [Şekil 3]. Ancak COVID-19 major bulaş yollarından biri olan aerosol içeren partiküllerin mukozal teması ve inhalasyon yolu ile vücuda girmesidir [4]. Bu durum uygun ve doğru maske kullanımıyla engellenebilir. Bu nedenle COVID-19 ilgili birimlerde görev alan sağlık çalışanlarının, cerrahi maskelerden daha iyi koruma sağladığı bilinen N95 ve FFP2 maskeleri kullanması önerilmektedir [6,13]. Maske testi ise aerosol içeren partiküllerin solunmasının önlemek için gerekli bir prosedürdür. Bu araştırmada, tüm videolarda ilgili maskelerin kullanılması teşvik edilirken maske testinin gerekliliğine yeterince vurgu yapılmadığını tespit ettik. Bu oran eğitici videolarda dahi %52 olup eğitici olmayan videolarla istatiksel farklı değildir [Şekil 2]. Bu eksiklik YouTube'nin eğitici olma potansiyelini azaltmaktadır.

Her ne kadar video içeriklerinin değerlendirmeleri bilimsel objektif kriterlere dayansa videonun eğiticilik değerlendirmesinde kullanılan görüntü kalitesi, netlik indirme süreleri gibi bazı kriterlerin öznel olması araştırmanın kısıtlılıkları olarak sıralanabilir.

Sonuç

Sonuç olarak bu araştırma elde edilen veriler neticesinde, Türkçe YouTube KKE giyme ve çıkarma videoları, uygun bir seçim süreci uygulanırsa, sağlık çalışanlarının eğitiminde kullanılabilecek etkili bir kaynak olabilir. Ancak videoların bazı önemli eksiklikler ve yanıltıcı özellikler içerebildiği tespit edildi. Bu eksikliklerin alanında uzman bir ekip tarafından denetlendikten ve gerekli düzeltmeler yapıldıktan sonra yayınlanması uygun olacaktır.

Videonun kullanışlılığı ve izleyicilerin tercihleri arasında önemli ilişkiler bulduk. Uygun bir seçim süreci uygulanırsa, YouTube, COVID-19 salgını sırasında KKE giyme ve çıkarma konusunda, potansiyel bir öğrenme kaynağı olabilir. Bu nedenle, eğitim açısından yararlı olan videolara kolay erişim için YouTube sağlık linki oluşturulmasını önermekteyiz.

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Original Article

Evaluation of the relationship of urinary sodium excretion with metabolic syndrome, hypertension, and graft function in renal transplant patients

Renal transplant hastalarında idrar sodyum atılımının metabolik sendrom, hipertansiyon ve greft fonksiyonu ile ilişkisinin değerlendirilmesi

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ABSTRACT

Aim: To evaluate the relationship between high sodium intake determined by spot urinary sodium excretion with metabolic syndrome, hypertension, and graft function in renal transplant (RT) recipients.

Materials and Methods: 152 RT (35.5% were female) recipients were enrolled. The demographic characteristics, office blood pressure (BP) values, height, weight, body mass index, waist and hip measurements, immunosuppressive drugs, other medications, and biochemical parameters of the patients were recorded. Spot urinary sodium and protein excretions were measured in the RT recipients' first-morning urine. The patients were grouped as low sodium excretion (≤57 mmol/L) and high sodium excretion (≥58 mmol/L) based on the median value.

Results: When the groups were compared according to spot urinary sodium excretion, no difference was found in terms of creatinine values, systolic BP and diastolic BP (p=0.21, p=0.18 and p=0.80, respectively). In the low sodium group, creatinine values were significantly lower (p<0.001), and eGFR was high in female patients (p=0.03). The mean protein in spot urine was lower in women (p=0.03). In the high sodium group, BUN and creatinine levels were significantly higher in male patients than in female patients (p=0.04 and p=0.02, respectively). The ejection fraction was significantly lower in male patients than in female patients (p=0.008). When the spot urinary sodium excretion of patients with and without metabolic syndrome was compared, no difference was found between the two groups (p=0.99).

Conclusion: Spot urinary sodium excretion can an inexpensive and relatively effective screening method that can be used to evaluate sodium intake in RT patients. It can be considered a more valuable follow-up method, especially in RT recipients with male gender, kidney dysfunction, and high BP.

Keywords: Graft function, hypertension, metabolic syndrome, renal transplant, spot urine sodium

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Öz

Amaç: Renal transplant (RT) hastalarında idrar sodyum atılımı ile metabolik sendrom, hipertansiyon, greft fonksiyonu arasındaki ilişkinin değerlendirilmesidir.

Gereç ve Yöntemler: Nakil polikliniğinde düzenli takip edilen 152 RT (%35.5 kadın cinsiyet) alıcısı çalışmaya alındı. Hastaların demografik özellikleri, ofis kan basıncı değerleri, boy, kilo, vücut kitle indeksi, bel ve kalça ölçümleri, immunsüpresif ilaçlar, diğer ilaçlar ve biyokimyasal parametreleri kaydedildi. Tüm RT alıcılarında sabah ilk idrarlarında spot sodyum ve protein atılımları ölçüldü. Hastalar spot idrar sodyum medyan değerine göre düşük sodyum atılımı (≤57 mmol/L) ve yüksek sodyum atılımı (≥58 mmol/L) olarak gruplandırıldı.

Bulgular: Gruplar spot idrar sodyum atılımına göre karşılaştırıldığında kreatinin değerleri, sistolik KB ve diyastolik KB açısından fark bulunmadı (sırasıyla p=0,21, p=0,18 ve p=0,80). Düşük sodyum grubunda; kadınlarda kreatinin değerleri anlamlı derecede düşük (p<0,001) ve eGFR yüksek saptandı (p=0,03). Yüksek sodyum grubunda; BUN ve kreatinin düzeyleri cinsiyete göre karşılaştırıldığında erkeklerde anlamlı derecede yüksek bulundu (sırasıyla p=0,04 ve p=0,02). EF değeri erkeklerde kadınlardan anlamlı derecede düşüktü (p=0,008). Metabolik sendromu olan ve olmayan hastaların spot idrar sodyum atılımları karşılaştırıldığında her iki grupta spot idrar sodyum atılım değerleri arasında fark saptanmadı (p=0,99).

Sonuç: Spot idrar sodyum atılımı, RT hastalarında sodyum alımını değerlendirmek için kullanılabilecek ucuz ve nispeten etkili bir tarama yöntemi olarak görülebilir. Özellikle erkek cinsiyet, böbrek fonksiyon bozukluğu ve yüksek tansiyonu olan RT alıcılarında daha değerli bir takip yöntemi olarak kabul edilebilir.

Anahtar kelimeler: Böbrek nakli, greft fonksiyonu, hipertansiyon, metabolik sendrom, spot idrar sodyum.

Introduction

Metabolic syndrome (MS) is a fatal endocrinopathy starting with insulin resistance, followed by a series of systemic disorders such as abdominal obesity, glucose intolerance or diabetes mellitus (DM), dyslipidemia, hypertension (HT), and coronary artery disease (CAD) [1]. MS is associated with a risk of developing cardiovascular disease [2].

Hypertension, a component of metabolic syndrome, is a common cardiovascular disease and has been indicated as one of the leading causes of death [3]. Numerous observational studies have shown that cardiovascular morbidity and mortality are associated with systolic and diastolic blood pressure (BP) [4]. According to the argument starting with Guyton, the main problem of hypertensive patients is the failure of the kidney to eliminate the excess sodium load taken with a high-salt diet [5]. Beyond raising BP, a high-salt diet is an independent risk factor for target organ damage, leading to fatal cardiovascular events, including stroke, cardiac hypertrophy, diastolic dysfunction, and renal failure [6]. Retention of excess sodium in the kidneys triggers HT. This retention may occur due to congenital or acquired deficiency in nephron number or function [7]. Although the number of cardiovascular disease-related deaths is decreasing thanks to new treatments [8], it remains the leading cause of death in renal transplant (RT) patients [9].

In the non-transplant population, high sodium consumption is generally associated with insulin resistance, metabolic syndrome, and hypertension [10, 11]. The number of studies on the relationship between increased sodium intake and excretion and metabolic syndrome in RT patients is limited. Therefore, in this study, we aimed to investigate whether there is a relationship between daily urinary sodium excretion, an indirect indicator of daily salt intake, metabolic syndrome, hypertension, and graft function in RT patients.

Material and Methods

The study was prospectively carried out on 152 patients over 18 years, who were admitted to the nephrology outpatient clinic between January 2016 and April 2016, underwent renal transplantation, had stable kidney functions, and gave informed consent forms. The patient's gender, age, body weight, height, body mass index, transverse waist circumference, medication use, BUN (blood urea nitrogen), creatinine, sodium, spot urinary sodium, spot urinary protein, estimated glomerular filtration rate (eGFR), fasting blood glucose, insulin, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglyceride, and albumin values were recorded. During the examinations of the patients, the BP measurements were made by a sphygmomanometer in the sitting position after at least 10 minutes of rest. They were recorded as systolic BP (mmHg) and diastolic BP (mmHg). As use of antihypertensive drug or an above BP of 130/85 mm Hg measured during the examination was considered the diagnostic criteria for hypertension.

Metabolic syndrome was diagnosed according to the Adult Treatment Panel III (ATP III) criteria updated in a report of the American Heart Association (AHA)/National Heart, Lung and Blood Institute (NHLBI) in 2005 [1].

At the same time, left ventricular hypertrophy and ejection fractions were recorded by evaluating the reports of transthoracic echocardiography performed in the last year.

The local ethics committee approved the study.

Statistical analysis

The Statistical Package for Social Sciences version 15.0 software was used to evaluate the data. Descriptive statistical data are expressed as frequency (percentage), number and mean±standard deviation, or median (min-max). Kolmogorov-Smirnov test evaluated the distribution properties of the numeric variables. Independent-samples t-test was used for intergroup comparisons of numeric variables with normal distribution, and Mann–Whitney's U test was used for variables without normal distribution. Categorical data were evaluated using the chi-square test. A p-value of <0.05 was considered statistically significant.

Results

The mean age of the patients in the study was 40.7±12.0 years. Of the patients, 64.5% (98 individuals) were male. Left ventricular hypertrophy (LVHT) was detected in 59.2% (71 individuals) of the 120 patients registered in the system and had echocardiography performed in the last year. The mean time after RT was 7.9±6.4 years. The clinical and laboratory characteristics of the patients are shown in Table 1.

The patients were grouped as low sodium excretion (57 mmol/L and below) and high sodium excretion (58 mmol/L and above) based on the median value.

Low Sodium Group: The mean creatinine level was 1.7±0.6 mg/dL in male patients, while it was 1.1±0.4 mg/dL in female patients and was significantly lower in female patients (p<0.001). The mean eGFR value was 53.5±18.5 ml/min/1.73 m^2 in male patients and 65.2±23.9 ml/min/1.73 m^2 in female patients and was significantly higher in female patients (p=0.03). The mean spot urinary protein value was 69.4±97.8 mg/dL in male patients, while it was 33.4±49.5 mg/dL in female patients, and this difference was statistically significant (p=0.03) (Table 2).

High Sodium Group: The mean BUN value was 25.1±11.9 mg/dL in male patients and 19.7±8.9 mg/dL in female patients (p=0.04). The mean creatinine was measured as 1.5±0.6 mg/dL in male patients and as 1.2±0.5 mg/dL in female patients and was found to be significantly higher in male patients (p=0.02). The mean insulin level was 17.1±6.5 µU/mL in male patients, while it was 13.2±5.2 µU/mL in female patients, and this difference was significant (p=0.009). The mean EF measurement was significantly lower in male patients (57.5±5.4) than in female patients (61.0±3.3) (p=0.008) (Table 2).

When the groups were evaluated by sodium levels regardless of gender, there was no significant difference between the measurements (p>0.05) (Table 2).

53.1% (52 individuals) of male patients were in the low sodium group, this rate was 46.3% (25 individuals) in female patients. There was no significant difference between the groups regarding sodium excretion (p=0.42). Of the patients with and without diabetes mellitus, 51.9% (4 individuals) and 48.8% (61 individuals) were in the high sodium group, respectively, and this difference was not significant (p=0.77). Of the patients using and not using a statin, 63.6% (28 individuals) and 45.4% (49 individuals) were in the low sodium group, respectively, and this difference was statistically significant (p=0.04) (Table 3).

Table 1. Clinical and laboratory characteristics of the patients

Characteristics	Patient Group (n=152)
Age, years (Mean ± SD)	40.7±12.0
Female/Male	54/98
Diabetes Mellitus	27 (%17.8)
Use of Statin	44 (%28.9)
Metabolic Syndrome	81 (%53.3)
Tacrolimus	63 (%41.4)
Sirolimus	45 (%29.6)
Cyclosporine	39 (%25.7)
ECHO LVHT	71 (%59.2)
	median (min-max)
Post-Transplant Duration, years	7 (1-36)
BUN, mg/dL	19.5 (7.2-67.5)
Creatinine, mg/dL	1.39 (0.59-4.76)
Albumin, g/dL	4.21 (2.91-4.76)
eGFR, ml/min/1.73 m^2	58.04 (14.81-127.25)
Spot Urine Sodium, mmol/L	57 (7-195)
Spot Urine Protein, mg/dL	21.9 (0.9-544.8)
LDL-cholesterol, mg/dL	124 (22-263)
HDL-cholesterol, mg/dL	47 (17-90)
Triglyceride, mg/dL	162.5 (35-561)
Fasting blood glucose, mg/dL	93 (55-269)
Insulin, µU/mL	16 (4-32)
Systolic Blood Pressure, mmHg	130 (90-170)
Diastolic Blood Pressure, mmHg	80 (60-100)
EF, %	60 (30-71)
BMI, kg/m2	25.53 (15.43-92)
Waist circumference, cm	74 (56-120)

BUN: Blood urea nitrogen; BMI: Body mass index; EF: Ejection fraction; ECHO LVHT: Echocardiography left ventricular hypertrophy; eGFR: Glomerular filtration rate

Table 2. Comparison of the characteristics of the patients according to sodium groups and gender

	Spot Urine Sodium								
	Low (≤57 mmol/L) (Mean±SD)				High (≥58 mmol/L) (Mean±SD)				
	Male (n=52)	Female (n=25)	Total (n=77)	p	Male (n=46)	Female (n=29)	Total (n=75)	p	p*
Age, years	41.7±11.9	39.1±10.8	40.8±1.6	0.37	42.2±12.3	38.0±12.6	40.5±12.5	0.15	0.88
Post-Transplant Duration, years	8.8±6.4	7.9±7.6	8.5±6.8	0.57	6.9±6.3	7.8±5.3	7.2±5.9	0.54	0.23
BUN, mg/dL	23.7±12.1	18.4±7.7	22.1±11.1	0.05	25.1±11.9	19.7±8.9	22.9±11.1	0.04	0.60
Creatinine, mg/dL	1.7±0.6	1.1±0.4	1.5±0.6	<0.001	1.5±0.6	1.2±0.5	1.4±0.6	0.02	0.21
Albumin, g/dL	4.2±0.3	4.1±0.3	4.2±0.3	0.69	4.1±0.3	4.1±0.3	4.1±0.3	0.35	0.20
eGFR, ml/min/1.73 m^2	53.5±18.5	65.2±23.9	57.3±21.1	0.03	59.7±20.3	65.5±27.1	61.9±23.1	0.33	0.20
Spot Urine Protein, mg/dL	69.4±97.8	33.4±49.5	57.7±86.5	0.03	63.1±80.3	41.0±90.1	54.5±84.4	0.27	0.97
LDL-cholesterol, mg/dL	130.7±46.6	122.8±42.1	128.1±45.1	0.47	121.6±35.1	137.8±42.2	127.9±38.5	0.07	0.97
HDL-cholesterol, mg/dL	43.8±11.4	51.5±16.6	46.3±13.7	0.04	42.4±11.3	50.6±10.8	45.6±11.8	0.003	0.72
Triglyceride, mg/dL	196.6±103.6	144.7±3.5	179.7±95.2	0.02	194,3±97.7	149.5±60.1	176.9±87.4	0.01	0.85
Fasting blood glucose, mg/dL	102.4±19.5	100.2±35.4	101.7±25.5	0.72	103.5±38.5	101.5±40.9	102.7±39.2	0.82	0.84
İnsulin, µU/mL	16.9±6.4	14.7±6.3	16.2±6.4	0.15	17.1±6.5	13.2±5.2	15.6±6.3	0.009	0.55
BMI, kg/m2	26.9±9.4	28.1±14.8	27.3±11.2	0.69	25.7±4.1	27.9±13.3	26.5±8.8	0.40	0.65
Waist circumference, cm	78.5±12.2	73.6±12.5	76.9±12.4	0.10	78.7±11.5	75.3±13.2	77.4±12.2	0.25	0.80
SBP, mmHg	131.6±13.9	125.2±13.2	129.5±13.9	0.05	129.1±14.8	122.2±4.6	126.4±15.1	0.05	0.18
DBP, mmHg	80.2±9.5	76.8±9.0	79.1±9.4	0.13	80.0±7.9	76.8±9.9	78.7±8.8	0.14	0.80
EF, %	57.8±7.3	60.1±3.5	58.6±6.3	0.11	57.5±5.4	61.0±3.3	58.9±4.9	0.008	0.76

*Low vs High; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood urea nitrogen; BMI: Body mass index; EF: Ejection fraction; eGFR: Glomerular filtration rate

Table 3. Comparison of sodium levels of patients.

		Spot Urine Sodium		
		Low	High	p
Gender	Male	52 (%53.1)	46 (%46.9)	0.42
	Female	25 (%46.3)	29 (%53.7)	
Diabetes	Presence	13 (%48.1)	4 (%51.9)	0.77
	Absence	64 (%51.2)	61 (%48.8)	
Use of Statin	Presence	28 (%63.6)	16 (%36.4)	0.04
	Absence	49 (%45.4)	59 (%54.6)	
MS	Presence	41 (%50.6)	40 (%49.4)	0.99
	Absence	36(%50.7)	35 (%49.3)	
Tacrolimus	Presence	34 (%54.0)	29 (%46.0)	0.49
	Absence	43 (%48.3)	46 (%51.7)	
Sirolimus	Presence	25 (%55.6)	20 (%44.4)	0.43
	Absence	52 (%48.6)	55 (%51.4)	
Cyclosporine	Presence	16 (%41.0)	23 (%59.0)	0.16
	Absence	61 (%54.0)	52 (%46.0)	
ECHO LVHT	Presence	35 (%49.3)	36 (%50.7)	0.85
	Absence	25 (%51.0)	24 (%49.0)	

ECHO LVHT: Echocardiography left ventricular hypertrophy; MS: Metabolic syndrome

The systolic BP values of the patients using and not using tacrolimus were compared. While the median systolic BP value of the patients using tacrolimus was 120 mmHg, the median value of those who did not was found to be 130 mmHg, and this difference was statistically significant (p=0.036). There was no statistically significant difference when using sirolimus and cyclosporine compared to the systolic BP values. When the diastolic BP values of the patients included in the study were compared by the immunosuppressives they used, there was no statistically significant difference. No difference in sodium excretion between the group with high BP and the other group among the patients using tacrolimus suggests that the elevation of BP due to tacrolimus is independent of sodium.

When the patients with controlled and uncontrolled BP were compared for spot urinary sodium excretion, there was a statistically significant difference between the groups (p<0.001). The median value of the spot urinary sodium excretion level was 66 (IQR 52) mmol/L in patients with controlled BP and 43 (IQR 32) mmol/L in patients with uncontrolled BP. This difference was statistically significant (p<0.001).

Discussion

In this study, we evaluated the relationship between urinary sodium excretion, which is an indirect indicator of daily salt intake, and metabolic syndrome, hypertension, and graft function in RT patients; when the groups were compared according to spot urinary sodium excretion, no difference was found in terms of creatinine values, systolic BP and diastolic BP. In the low sodium group, creatinine values were significantly lower, and eGFR was higher and the mean protein in spot urine was lower in female patients. In the high sodium group, while BUN and creatinine levels were significantly higher and the ejection fraction was lower in male patients than in female patients. When the spot urinary sodium excretion of patients with and without metabolic syndrome was compared, no difference was found between the two groups.

Compared to the general population, the prevalence of MS appears to be higher in renal transplant patients (32%-44.8%) [12, 13]. This study detected MS in 53.3% of renal transplant patients. The spot urinary sodium excretions of the patients with and without metabolic syndrome were compared, and no statistically significant difference could be demonstrated. The absence of a substantial difference in these results may be because spot urinary sodium might have yet to reflect 24-hour urinary sodium fully. The gold standard method for estimating urinary sodium excretion is 24-hour urinary sodium measurement. Although spot urinary sodium yielded similar results with 24-hour urinary excretion in some studies [10, 11], spot urinary sodium may not be an appropriate indicator in RT patients, considering that kidney functions of this group are different from the general population and some immunosuppressive drugs used can differentiate spot urinary sodium excretion.

Similarly, an evaluation performed on people with normal BP (781 patients, BP<130/85 mmHg) in Brazil showed no difference between 24-hour urinary sodium excretions in the comparison of patients with or without MS. Urinary sodium excretion was lower in those with MS than in those without MS [9]. In a study reported from South Korea, no difference was observed between urinary sodium excretion of patients with and without MS [14]. On the contrary, in a study conducted by Unal et al. [15] on 76 renal transplant patients, MS was detected in 52 patients (68.4%), and daily urinary sodium excretion was significantly higher in MS patients. Likewise, Hoffman and Cubeddu [11] showed that 24-hour urinary sodium excretion was significantly increased in patients with metabolic syndrome.

Based on previous studies, we can predict that salt intake is also elevated in the high sodium excretion group. Baudrand et al. [10] showed that high salt intake increases the risk of metabolic syndrome by two times. In addition, they showed that high salt intake was associated with HT, dyslipidemia, insulin resistance, and high glucocorticoid production [10]. Donovan et al. [16] showed that high salt intake was more insulin resistant than low salt intake in euglycemic and normotensive individuals. In this study, "insulin levels" were significantly higher in male patients in the high salt intake group. TG levels of male patients with high insulin were also considerably higher. It is thought that this is caused by increased TG synthesis due to the anabolic effect of insulin on the liver. Because TG-rich HDL cholesterol tends to break down more quickly, HDL cholesterol values are low in these male individuals with high TG levels. Again, BUN and creatinine levels are statistically significantly higher in male patients. These results suggest that male patients in the high-risk group for cardiovascular diseases consume a higher amount of salt than female patients, and spot urinary sodium excretion may be an independent risk factor.

Male patients are expected to have higher mean creatinine levels due to higher muscle mass. Accordingly, creatinine-based eGFR estimations differ similarly. In this study, creatinine levels were significantly lower, and eGFR levels were significantly higher in female patients with low sodium excretion. In this case, it can enable us to predict that low salt consumption may contribute to long-term graft function.

In this study, the mean spot urinary protein was higher in male patients than in female patients. High proteinuria levels in male transplant patients were found in the group with low sodium excretion; suggests that the reason for the low sodium excretion may be related to the protein and sodium restricted diet recommendation in patients with proteinuria. We know that high dietary sodium intake increases albuminuria [17]. Spot urinary sodium of male patients due to both high levels of sodium intake and relatively poor functioning grafts point to male RT patients as a group at higher risk for long-term cardiovascular diseases.

The rate of hypertensive patients among RT recipients appears to be 60-80% or more, and the use of antihypertensive drugs increases over time after kidney transplantation [18]. Hypertension is a major cardiovascular complication and increases graft loss in RT recipients with a systolic BP ≥140 mmHg [19]. This shows the great significance of BP control in RT patients. It may be difficult for patients with a single functional kidney to achieve BP control due to restriction therapy, including immunosuppressive and corticosteroid drugs.

In this study, the relationship between sodium excretions and systolic and diastolic BP, though not statistically significant, was found to be quite substantial when evaluated by gender in the low and high sodium excretion groups. A study reported that 24-hour urinary sodium excretion within one year after kidney transplantation between 1997 and 2009 was associated with systolic and diastolic BP [20]. However, some authors have reported a lack of relationship between sodium excretion and BP [21, 22]. On the contrary, in their extensive study including 660 RT patients, Van den Berg et al. [23] showed that 24-hour urinary sodium excretion increased with systolic and diastolic BP. The relationship between sodium excretion and BP has always been more significant for systolic than diastolic BP in transplant and non-transplant populations [23, 24]. The data of our study show that BP is higher in patient groups with increased sodium excretion, even though it is not statistically significant. Thus, restriction of sodium intake for BP control should be considered crucial. In a cross-sectional study conducted in Japan with 889 patients, a positive gender-independent correlation was found between spot urinary sodium concentrations and systolic BP. In a cross-sectional study conducted in Japan with 889 patients, a positive gender-independent correlation was found between spot urinary sodium concentrations and systolic BP [25]. In a study from England, 23,104 male and female patients between the ages of 45-79 years were analyzed. The spot urinary sodium/creatinine ratio was positively correlated with systolic and diastolic BPs [26]. Daily urinary sodium excretion correlated with diastolic BP, serum glucose concentration, and creatinine clearance. Additionally, although no significant correlation has been found between urinary sodium excretion and systolic BP, their relationship is statistically borderline significant [15]. These data are in line with the data of our study. Here, although spot urinary sodium concentration alone is not an important risk factor, in the presence of the other risk factors that may accompany it, it may be of considerable importance in terms of hypertension and metabolic syndrome.

This study observed no significant difference between systolic and diastolic BP by sodium excretion. When the patients were grouped based on their BP values as controlled (BP<140/90 mmHg) and uncontrolled (≥140/90 mmHg) and compared in terms of spot urinary sodium excretion, a significant difference was found between the groups. The role of sodium in the hypertension mechanism by causing volume load in the body supports this result. Based on these results, we suggest that it is impossible to control BP without salt restriction in renal transplant patients with unregulated BP. That follow-up of salt restriction can be performed with spot urinary sodium.

Our study compared the systolic and diastolic BP of the patients using and not using tacrolimus. The systolic BP of the patients using tacrolimus was significantly lower than those who did not. No correlation was found in the patients used cyclosporine. In a similar study, 80% of controlled HT patients and 50% of patients with uncontrolled HT used tacrolimus as an immunosuppressive drug [22]. Cyclosporine increases systemic and renal (primary afferent arteriolar effect) vascular resistance. The increased release of vasoconstrictors, especially endothelins, is thought to play a substantial role [27]. Therefore, reviewing the immunosuppressive regimen of patients with high spot urinary sodium and uncontrolled BP may be appropriate.

Our study has some limitations. First, our study included a relatively small number of groups with renal transplantation. The patients' 24-hour sodium consumption could not be recorded since reliable information could not be obtained. We did not re-studied spot urinary sodium values to support the initial results of our patients. The BP of the patients was recorded only as the measurements we performed during the follow-up. Thus, masked hypertension (normal in-office BP but elevated out-of-office BP) and white-coat hypertension (high in-office BP but normal BP at home) could not be distinguished. At the same time, the patient's smoking status was not questioned. Although no medication change was made in the last month in the patients in the study, it would be more accurate to record their antihypertensive and diuretic use.

In conclusion, spot urinary sodium excretion is an inexpensive and relatively effective screening method that can evaluate sodium intake in renal transplant patients. It can be considered a more valuable follow-up method, especially in male RT recipients with kidney dysfunction and high BP.

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The authors declare no conflicts of interest to disclose.

The corresponding author's data supporting this study's findings are available upon reasonable request.

The study was approved by the ethics committee of Baskent University Medical Faculty (Date: 15/02/2016, Approval number: KA16/17).

Authors' contributions to the article

Conception and design of the study; TID, SY, CBS

Generation, collection, assembly, analysis, and/or interpretation of data; TID, SY, CBS

Drafting or revision of the manuscript; TID, SY, CBS

Approval of the final version of the manuscript; TID, SY, CBS

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Original Article

Comparison of the hemodynamic effects of etomidate-midazolam and ketamine-midazolam combinations in anesthesia induction in coronary artery bypass surgery

Koroner arter bypass cerrahisinde anestezi indüksiyonunda etomidat-midazolam ve ketamin-midazolam kombinasyonlarının hemodinamik etkilerinin karşılaştırılması

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ABSTRACT

Aim: We aimed to compare the effects of anesthesia induction on hemodynamic parameters of ketamine-midazolam or etomidate-midazolam combinations and coronary artery bypass grafting surgery.

Material and Methods: 40 adult patients undergoing Coronary artery bypass graft (CABG) were randomly allocated into two groups for this prospective randomized double-blinded study. Ketamine group (n = 20) and Etomidate group (n = 20). Intraoperative and postoperative hemodynamic variables, adrenal gland functions and intensive care period were compared after anesthesia induction with etomidate and ketamine.

Results: Perioperative hemodynamic parameters were not significantly different between the groups. Despite similar baseline measurements, cortisol levels were significantly higher 5 minutes after induction, during rewarming, and after Adrenocorticotropic Hormone (ACTH) stimulation test at postoperative day 1 in group ketamine than group etmidate. The groups were not significantly different in terms of duration of postoperative mechanical ventilation, frequency of postoperative delirium, and intensive care unit and hospital lengths of stay.

Conclusion: Ketamine-midazolam combination is an acceptable alternative to etomidate-midazolam combination in terms of hemodynamic stability. Compared with the ketamine-midazolam combination, the etomidate-midazolam combination significantly decreased cortisol levels during the intraoperative and early postoperative periods

Keywords: Coronary artery bypass grafting, hemodynamic instability, adrenal suppression, etomidate, ketamine

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Öz

Amaç: Ketamin-midazolam veya etomidat-midazolam kombinasyonları ile koroner arter bypas greftleme (KABG) cerrahisinin anestezi indüksiyonunun hemodinamik parametreler üzerindeki etkilerini karşılaştırmayı amaçladık.

Gereç ve Yöntemler: KABG cerrahisi uygulanan 40 yetişkin hasta, prospektif randomize çift kör çalışma için rastgele iki gruba ayrıldı. Ketamin grubu (n = 20) ve Etomidat grubu (n = 20). Anestezi indüksiyonu sonrası her iki grupta intraoperatif ve postoperatif hemodinamik değişkenler, adrenal bez fonksiyonları ve yoğun bakım süreci karşılaştırıldı.

Bulgular: Perioperatif hemodinamik parametreler gruplar arasında anlamlı farklılık göstermedi. Benzer başlangıç ölçümlerine rağmen kortizol seviyeleri, indüksiyondan 5 dakika sonra, yeniden ısınma sırasında ve postoperatif 1. gün ACTH (Adrenokortikotropik hormon) stimülasyon testinden sonra grup ketaminde, grup etmidata göre anlamlı derecede yüksekti. Gruplar arasında postoperatif mekanik ventilasyon süresi, postoperatif deliryum sıklığı, yoğun bakım ve hastanede kalış süreleri açısından anlamlı fark yoktu.

Sonuç: Hemodinamik stabilite açısından ketamin-midazolam kombinasyonu, etomidat-midazolam kombinasyonuna göre kabul edilebilir bir alternatiftir. Ketamin-midazolam kombinasyonu ile karşılaştırıldığında, etomidat-midazolam kombinasyonu, intraoperatif ve erken postoperatif dönemlerde kortizol seviyelerini önemli ölçüde azalttır.

Anahtar kelimeler: Koroner arter baypas greftleme, hemodinamik instabilite, adrenal supresyon, etomidat, ketamin

Introduction

During anesthesia induction in cardiovascular surgery, achieving hemodynamic stability should be the primary goal [1, 2]. Different anesthesia induction protocols are administered for this purpose. Etomidate and ketamine are potentially more suitable agents in terms of preventing hypotension, one of the problems that arise during anesthesia induction [3].

Etomidate is among the preferred agents in cardiovascular anesthesia due to the hemodynamic stability it provides. Although this agent is often used as an induction agent, due to its undesirable effects on the synthesis of cortisol in the adrenal gland, practices in the form of recurrent and continuous infusion are avoided [4, 5].

Ketamine increases arterial blood pressure and heart rate by causing sympathetic stimulation in the cardiovascular system (CVS) [6]. It can cause pulmonary artery pressure to increase the burden on the right ventricle by increasing pulmonary vascular resistance [7].

The primary aim of our study is to examine the effects of etomidate-midazolam and ketamine-midazolam combinations used in coronary artery bypass grafting (CABG) surgery anesthesia on hemodynamics, and the secondary aim is to evaluate the etomidate-induced adrenal suppression and ketamine-induced delirium during the intensive care period.

Material and Methods

This study was approved by the Medical and Health Sciences Research Board and Ethics Committee of Baskent University (KA10-114).

The study was a prospective, randomized and double-blinded study. A total of 40 patients who were planned to undergo elective CABG were included in the study. Patients who did not agree to participate in the study, who were younger than 30 years of age or older than 80 years, who had an ejection fraction (EF) rate < 40%, who had an urgent surgical need, who were also planned to undergo a cardiac valve or aorta surgery, who previously used corticosteroids, who had a history of adrenal insufficiency, who used imidazole-type antifungal drugs, who had hypoalbuminemia, who were known to be allergic to study drugs, who had a history of psychotic disorders, who had severe hypertension, which had unstable angina pectoris, who had a chronic renal failure or compensated renal failure, and who had liver failure were not included in the study.

During anesthesia induction, one group was given etomidate 0.3 mg/kg, the other group was given ketamine 1 mg/kg, and both groups were given midazolam 0.025 mg/kg through a peripheral venous access. In addition to those, during induction, they were given fentanyl 10 mcg/kg, as well as vecuronium bromide 0.1 mg/kg as a myorelaxant drug. Both groups were given 1 ml of lidocaine 2% before induction to prevent pain caused by etomidate injections. To maintain anesthesia, the patients were given fentanyl at a rate of 15 mcg/kg/h, and isoflurane 0.5–1.5% in 40% oxygen + 60% air mixture. Systolic, diastolic, average arterial pressures and heart rates were recorded immediately before the anesthesia induction (at minute 0) and during the first 5 minutes after induction at intervals of 1 minute, followed by recordings at intervals of 15 minutes.

Blood was drawn prior to and after induction, and during the warming phase (when body temperature was at 35 °C) for cortisol and ACTH measurements. In order to compare the effects of etomidate and ketamine on steroid synthesis in the adrenal gland, the patients were subjected to ACTH stimulation tests with 1 mg of Synacthen Depot (ACTH synthetic product) i.m. on days 1 and 4. Basal samples of blood were drawn before stimulation tests, and blood was drawn for serum cortisol at the 2nd and 3rd hours after Synacthen Depot injections.

Durations of postoperative mechanical ventilation and intensive care, the need for analgesia, blood pressures, heart rates, inotropic agents that were used, antihypertensives, sedatives and their maximum and minimum amounts, discharge times, and additional problems were recorded.

The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) scale was used to investigate the delirium that could be caused by the use of ketamine.

Statistical analysis

The main goal of the study was to achieve >15% reduction in blood pressure after induction compared to the initial average blood pressure. In this respect, during the calculation of the sample size, it was seen that it was sufficient to include 18 patients in each group in order for the alpha value to be .80 and the p value to be 0.05. Considering that there may be a 10% difference during the study in normal conditions, 2 patients were added to this number. Consequently, 20 patients were included in each group. The data were examined with the help of the SPSS statistics program. For within-group comparisons, Friedman and Wilcoxon tests were used. And for between-group comparisons, Mann-Withney U tests were carried out for numerical parameters, and Chi-square tests for categorical parameters. $p < .05$ was considered significant.

Results

Considering the demographic characteristics of the groups, the proportion of women to men in the etomidate group was found to be 1/19, and in the ketamine group, it was 9/11 (p=0.04). This difference was caused by randomization. The demographic characteristics and systemic diseases of the patient groups are summarized in Table 1.

Table 1. According to the groups of patients' demographic characteristics, coexisting systemic diseases

	Ketamine (n=20)	Etomidate (n=20)	P
Age (years) ± SD	62,6 ± 7,9	60,9 ± 10,3	0,523
Body weight (kg) ± SD	78,7 ± 10,8	80,2 ± 11,8	0,724
Gender (female) %	45	5	0,040
Systemic Disease			
Diabetes mellitus %	45	35	0,748
Hypertension %	85	75	0,695

In both groups, durations of surgeries; maximum doses of positive inotropic and vasodilator drugs, intravenous fluid, blood and blood products given during surgery; hemodynamic variables; and the amounts of urine during surgery were similar (Table 2).

Table 2. According to the groups of patients surgery, cardiopulmonary bypass and aortic clamp times, the maximum inotropic drug dose during surgery, the intravenous fluid, the amount of blood and blood products, hemodynamic changes occurring during surgery, patients urine volume (mean ± standard deviation [95% confidence interval] or the number [%]).

	Ketamine (n=20)	Etomidate (n=20)	P
Surgical time (minutes) ± SD	252,8 ± 38,6	265,5 ± 40,5	0.239
CPB time (minutes) ± SD	86,2 ± 17,2	92,9 ± 26,5	0.685
Aortic clamp time (minutes) ± SD	52,0 ± 16,5	56,0 ± 15,4	0.685
Maximum dopamine infusion (mcg / kg / min) ± SD	5,3 ± 2,6	5,5 ± 2,2	0.685
Maximum perlinganit infusion (mcg / kg / min) ± SD	7,9 ± 3,7	9,9 ± 3,4	0.351
Intraoperative ES (unit) ± SD	1,8 ± 0,5	2,0 ± 0,3	0.290
Intraoperative FFP (unit) ± SD	1,6 ± 0,5	1,7 ± 0,8	0.405
Intraoperative crystalloid (ml) ± SD	512 ± 445	275 ± 412	0.083
Intraoperative colloid (ml) ± SD	525 ± 111	500 ± 000	0.317
Intraoperative urine volume (ml) ± SD	1078 ± 534	927 ± 408	0.448
Intraoperative bradycardia %	5	5	1
Intraoperative hypertension %	30	30	1
Intraoperative hypotension %	50	20	0,096

CPB: Cardiopulmonary Bypass, ES: Erythrocyte Suspension, FFP: Fresh Frozen Plasma

There were no significant differences between the groups in terms of the systolic, diastolic, and average arterial pressures, heart rates, and percentages of oxygen saturation recorded immediately before the anesthesia induction (at minute 0) and during the first 5 minutes after induction at intervals of 1 minute, followed by recordings at intervals of 15 minutes for 60 minutes (p> 0.05)

Blood ACTH and cortisol levels measured before induction were similar between the ketamine-midazolam and etomidate-midazolam groups (p>0.05). Cortisol levels were found to be suppressed in the etomidate-midazolam group compared to the ketamine-midazolam group at the 5th

minute after induction and while warming up during the CPB (while the body temperature was 35 °C) (p<0.05). At the 5th minute, the average amount of blood cortisol was measured to be 8.2 mcg/dl in the etomidate-midazolam group, and 11.1 mcg/dl in the ketamine-midazolam group (p=0.04). During the CPB warming phase (while the body temperature was 35 °C), the amount of blood cortisol was measured to be 10.0 mcg/dl in the etomidate-midazolam group and 28.3 mcg/dl in the ketamine-midazolam group (p=0.02). Contrary to the amounts of cortisol suppressed in the etomidate-midazolam group, the amounts of ACTH were significantly increased at the 5th minute after induction and while warming up during CPB (while the body temperature was 35 °C), compared to the ketamine-midazolam group (p<0.05). The average amount of ACTH at the 5th minute was measured to be 27.7 pg/ml in the etomidate-midazolam group and 13.0 pg/ml in ketamine-midazolam group (p=0.018). During the CPB warming phase (while the body temperature was 35 °C), the amount of ACTH was measured to be 59.7 pg/ml in the etomidate-midazolam group and 30.7 pg/ml in the ketamine-midazolam group (p=0.038). Blood cortisol levels in the etomidate-midazolam group were found to be suppressed compared to the ketamine-midazolam group during the ACTH stimulation test on the first day after surgery (p<0.05). In the etomidate-midazolam and ketamine-midazolam groups, the amount of blood cortisol before the ACTH stimulation test was 12.6 mcg/dl and 26.5 mcg/dl, respectively (p=0.048); the amount of blood cortisol at the first hour after the ACTH stimulation was 30.3 mcg/dl and 42.9 mcg/dl, respectively (p=0.05); blood cortisol 2 hours after the ACTH stimulation test was measured to be 31.4 mcg/dl and 46.5 mcg/dl, respectively (p=0.011). During the ACTH stimulation test on the 4th day, blood cortisol levels were similar in both groups (Table 3). In both groups; Postoperative mechanical ventilation duration, intensive care time, hospital duration, inotrope, and antihypertensive agent usage amount were found to be similar (Table 4).

The patients were assessed in terms of postoperative delirium, with the help of the CAM-ICU scale consisting of the headings of sudden changes in consciousness, attention disorder, thought/orientation disorder, and lost consciousness levels. There were no signs of delirium in the postoperative period among the patients in either of the groups who were assessed under four headings.

Table 3. Amounts of ACTH and cortisol during surgery according to the groups of patients, the 1st and 4th day after surgery, according to the ACTH stimulation test and blood cortisol levels (mean ± standard deviation [95% confidence interval])

	Ketamine (n=20)	Etomidate (n=20)	P
ACTH (pg/ml) ± SD			
Beginning	8,7 ± 4,7	11,9 ± 5,8	0.070
5 minutes after induction	13,0 ± 10,9	27,7 ± 27,0	0.018
Re-warming (35 ° C)	30,7 ± 23,9	59,7 ± 55,2	0.038
Cortizol (mcg/dl) ± SD			
Beginning	7,3 ± 3,5	5,5 ± 1,8	0.118
5 minutes after induction	11,1 ± 5,1	8,2 ± 3,2	0.040
Re-warming (35 ° C)	28,3 ± 32,9	10,0 ± 4,1	0.002
1st day ACTH stimulation test (pg/ml) ± SD			
Initial cortisol	26,5 ± 25,7	12,6 ± 8,32	0.048
1 hour after stimulation	42,9 ± 21,0	30,3 ± 4,5	0.050
After 2 hours stimulation	46,5 ± 21,7	31,4 ± 4,1	0.011
4th day ACTH stimulation test (pg/ml) ± SD			
Initial cortisol	18,0 ± 11,7	20,0 ± 12,6	0.725
1 hour after stimulation	41,1 ± 16,2	38,8 ± 8,4	0.588
After 2 hours stimulation	43,3 ± 15,2	42,8 ± 10,6	0.914

ACTH: Adrenocorticotropic hormone

Table 4. Postoperative mechanical ventilation, intensive care, hospital time, use of inotropes, antihypertensive agents for groups.

	Ketamine (n=20)	Etomidate (n=20)	P
Mechanical ventilation (hours) ± SD	21,8 ± 3,3	22,1 ± 3,9	0.976
ICU LOS (days) ± SD	3 ± 1,17	3 ± 1,07	0.818
Hospital LOS (days) ± SD	10,4 ± 2,3	10,1 ± 2,5	0.442
Maximum dopamine (mcg / kg / min) ± SD	5,2 ± 2,8	5,1 ± 2,1	0.453
Maximum perlinganit (mcg / kg / min) ± SD	4,3 ± 2,1	5,1 ± 2,1	0.189

ICU: Intensive care, LOS: length of stay

Discussion

The combination of ketamine and midazolam was concluded to be able to be used as an alternative induction agent to the combination of etomidate and midazolam in patients who undergo CABG surgery without causing any hemodynamic instability. In our study, in the etomidate-midazolam group, it was shown that adrenal suppressants developed after the intraoperative etomidate injection and in the ACTH stimulation tests on day 1. No significant difference was found

between the two groups in the ACTH stimulation test on day 4. There was no significant difference between the two groups, either, in terms of postoperative delirium that we compared with the help of the CAM-ICU scale, which we thought might be related to ketamine. Duration of postoperative mechanical ventilation, intensive care and hospital stay, blood and blood products that were given, and positive inotropic amounts were also similar between the two groups.

Hemodynamic instability that can occur after induction of anesthesia significantly increases morbidity and duration of hospital stay [8-10]. Post-induction hypotension can set the stage for major complications such as cerebrovascular disease (CVD) and myocardial infarction (MI) with high mortality and morbidity [11, 12]. In the retrospective study of Reich et al. examining 2152 patients, the effects of intraoperative hemodynamic variables on mortality, CVD and myocardial damage were examined in patients undergoing CABG surgery, and hemodynamic instability was reported to be a predictor of myocardial injury, CVD, and mortality after surgery [13]. In our study, decreases in systolic, diastolic and average arterial pressures were detected in both the etomidate-midazolam group and the ketamine-midazolam group after induction compared to the initial levels. However, no significant difference was found between the two groups. In within-group comparisons, compared to the initial values in the etomidate-midazolam group, in the first 60 minutes after induction of anesthesia, systolic blood pressure, diastolic blood pressure and average blood pressure was found to decrease more frequently than those in the ketamine-midazolam group. The number of heart beats in the ketamine-midazolam group decreased significantly in the first 60-minute period after anesthesia induction in within-group comparisons, whereas it was unchanged in the etomidate-midazolam group. Ketamine affects CVS through the adrenergic central pathway. For this reason, it is used together with medicines that suppress the central nervous system, such as benzodiazepines. In our study, midazolam was administered to both groups in order to ensure standardization. During the first 60 minutes after induction, the reductions in blood pressures in the etomidate group and the reductions in heart rates in the ketamine group were thought to be associated with midazolam.

Etomidate infusion, which was administered in 1984 for the first time by Wagner et al. to 5 patients, was shown to decrease cortisol levels [14]. In a study conducted on rats, it was shown to inhibit 11β-hydroxylase. In a study conducted in 1985 by Duthie et al. comparing etomidate and thiopental in 12 patients to undergo minor surgery under general anesthesia, it was shown that a dose of bolus etomidate caused 11β-hydroxylase inhibition. In their study conducted in 2003, Annane et al. reported that the response in 94.4% of the patients given a single dose of etomidate was impaired in the corticotropin stimulation test, whereas this rate was 71% in the group that did not receive etomidate [15, 16].

Etomidate can facilitate further suppression of cortisol, which should be released with adrenal suppression, and as a result, facilitate the development of serious postoperative complications on the one hand; and on the other, it can help protect the balance between the oxygen delivery and consumption of the myocardium and prevent deterioration in the immune system in the postoperative period as it prevents the rise in stress hormones [17-19]. Morel et al. carried out a prospective study where they compared hemodynamic results of etomidate and propofol induction on 100 patients undergoing CABG surgery. They reported that the cortisol response was suppressed in the etomidate group, but the patients in the etomidate group were hemodynamically more stable, and there was no difference between the two groups in terms of postoperative pulmonary and renal complications [20]. In our study, the blood cortisol levels were found to be suppressed in the etomidate-midazolam group compared to the ketamine-midazolam group in the postoperative ACTH stimulation tests on the first day after anesthesia induction and after surgery, whereas there was no difference between the groups in the ACTH stimulation test on the 4th day.

During waking after ketamine induction, agitation was observed in some of the patients, and this condition was linked to the hallucinogenic effect of ketamine. The incidence of hallucinations varied between 5% and 30%. The incidence was increased among females, with high doses and rapid injection. Premedication with benzodiazepines may be able to reduce hallucinations [21]. In our study, both groups were assessed based on the CAM-ICU delirium scale in the postoperative period. There were no findings of delirium during the first postoperative week both in the etomidate-midazolam group and in the ketamine-midazolam group.

There are various limitations to our study. Preoperative hospital duration was not evaluated. The number of men and women was not equal in the etomidate-midazolam group. The difference in the proportion of women and men in the etomidate-midazolam group was thought not to affect the intraoperative cortisol and

ACTH amounts, and the results of the ACTH stimulation tests on the first and fourth days due to the fact that the women included in the study were in their postmenopausal period, and therefore their ovaries were not hormonally active. The two groups were not compared with a third control group in terms of intraoperative cortisol and ACTH amounts, and the results of the ACTH stimulation tests on the first and fourth days.

Conclusion

In our study comparing the hemodynamic effects of etomidate-midazolam and ketamine-midazolam combinations in anesthesia induction in coronary artery bypass grafting surgery, it has been concluded that the combination of ketamine-midazolam can be used as an alternative induction agent to the combination of etomidate-midazolam without causing any hemodynamic instability or adrenal suppression, in patients who are planned to undergo CABG surgery.

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Original Article

Achilles tendon surgery from the perspective of patients: an ınstagram study

Hasta perspektifinden aşil tendon cerrahisi: bir ınstagram çalışması

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Abstract

Aim: The use of social media, especially Instagram, has become widespread in the medical field. The aim of this study was to evaluate Achilles tendon surgery from patients' perspectives by examining public posts on Instagram.

Material and Methods: A retrospective analysis was made of the Instagram posts of patients with the hashtags #achillestendonsurgery and #achillestendonrepair between December 2018 and October 2021. In total, 234 posts (181 photographs, 53 videos) were evaluated and compared in terms of gender, sharing format (video, photo), sharing tone (negative, positive, neutral), content (activities of daily living, rehabilitation, cast/brace, hospital room, surgical site), country and popularity (the number of views for videos,and the number of likes for photographs).

Results: Posts in video format and a positive tone, posts on the rehabilitation process, and posts about male patients were found to have higher numbers of likes and views than other posts. The content of the shares were respectively; activity of daily living 36.8%(n=86), physical therapy 29.9%(n=70), cast/brace 20.1%(n=47), surgical site 7.7%(n=18), and hospital room 5.6%(n=13). The media tone of the posts was 40.2%(n=94) positive, 6.4%(n=15) negative, and 53.4%(n=125) neutral.

Conclusions: Patients avoided making negative posts on their Instagram after Achilles tendon surgery, and often shared experiences of postoperative rehabilitation processes and daily living activities.

Keywords: achilles tendon, social media, Instagram, physical therapy

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Öz

Amaç: Sosyal medya, özellikle de instagram, tıp alanında yaygın olarak kullanılmaya başlamıştır. Bu çalışmanın amacı, Instagram'daki aşil tendon cerrahisi ile ilgili herkese açık hasta paylaşımlarını incelemek ve aşil tendon cerrahisini hastaların bakış açısıyla değerlendirmektir.

Gereç ve Yöntemler: Aralık 2018 ve Ekim 2021 tarihleri arasında, #achillestendonsurgery ve #achillestendonrepair etiketleri kullanılan, hastalara ait Instagram gönderileri, geriye dönük olarak analiz edildi. Toplam 234 gönderi (181 fotoğraf, 53 video) cinsiyet, biçim (video, fotoğraf), paylaşım tonu (olumsuz, olumlu, nötr), içerik (günlük yaşam aktivitesi, rehabilitasyon, alçı/korse, hastane odası, cerrahi alan), ülke ve popülerlik (videoların görüntülenme sayısı ve fotoğrafların beğeni sayısı) açısından değerlendirilmiştir.

Bulgular: Video formatındaki ve pozitif tondaki paylaşımların, rehabilitasyon süreci ile ilgili paylaşımların ve erkek hastalara ait paylaşımların diğer paylaşımlara göre daha fazla beğeni ve izlenme aldığı tespit edildi. Paylaşımların içeriği sırasıyla; günlük yaşam aktivitesi %36,8(n=86), rehabilitasyon %29,9(n=70), alçı/breys %20,1(n=47), ameliyat yeri %7,7(n=18), hastane odası %5,6(n=13) idi. Gönderilerin tonu %40,2(n=94) olumlu, %6,4(n=15) olumsuz ve %53,4(n=125) nötrdü.

Sonuçlar: Hastalar aşil tendonu ameliyatından sonra Instagram'da olumsuz paylaşımlar yapmaktan kaçınmışlardır. Ameliyat sonrası rehabilitasyon süreçleri ve günlük yaşam aktivitelerine ilişkin deneyimlerini sıklıkla paylaşmışlardır.

Anahtar Kelimeler: aşil tendonu, sosyal medya, Instagram, fizyoterapi

Introduction

Surgery performed in the treatment of Achilles tendon injuries may result in wound problems, poor performance especially in athletes, and prolonged rehabilitation[1]. The outcomes of these surgeries have been examined in many studies according to clinical and biomechanical outcomes and patient satisfaction[2-4]. However, these studies have often been categorical with the participation of one or more physicians, and have not reflected the patient's perspectives.

Internet and social media usage, especially Facebook, Twitter, and Instagram, has increased in recent years, and the number of users has reached billions[5]. One of the free social media applications, Instagram, with more visual sharing such as photos and videos, has reached 1 billion subscribers, and 500 million users access Instagram daily[6]. On these platforms, people can freely share their posts, share opinions with their followers, like other posts or make positive or negative statements. The posts are placed in a stream with the algorithms determined by Instagram according to the words or word groups expressed as hashtags.

As the use of social media has become widespread, many studies have been conducted, especially in the field of orthopedics and traumatology. Social media usage in anterior cruciate ligament surgery, hip arthroscopy, shoulder arthroscopy, total joint arthroplasty, scoliosis surgery, and pilon fractures has been investigated[7-12]. When evaluated in terms of the use of Instagram, it was evident that after Achilles tendon surgery, visual posts, photographs (surgical site, cast, brace), or videos (rehabilitation process) could be made quite often, and patients would share their feelings.

This observational social media study investigated and analyzed the shared content of Achilles tendon surgery posts on Instagram. The study hypothesis was that patients would primarily share media with a positive tone centered on rehabilitation and activities of daily living after surgery. It was expected that Instagram would be a valuable tool to examine patients' perspectives, their satisfaction, and the treatment steps they like or with which they have difficulties.

Material and Methods

A search and retrospective evaluation was made of hashtags with the terms #achillestendonsurgery and #achillestendonrepair on public Instagram (San Francisco, California) posts in a 3-year period (December 2018 - October 2021).

A third-party application (Picodash, San Francisco, California) was used to analyze the mobile-based Instagram database on a web-based platform to view the images on a personal computer instead of a smartphone. Searches were repeated with another third-party web application of Instagram (Iconosquare, Limoges, France) to ensure no posts were missed on the Picodash platform. All data analyses were performed using Microsoft Excel (Redmond, Washington).

From a total of 473 posts, those belonging to professional groups such as physicians (n=68), physiotherapists (n=46), personal trainers (n=23), podiatrists (n=21), commercial accounts (n=60), and those where it could not be determined from which country they were shared (42) were excluded.

In total, 234 posts(181 photographs and 53 videos) met the inclusion criteria for this study (Figure 1).The posts were evaluated and compared in terms of gender, sharing format (video, photograph), tone (negative, positive, neutral), content (activities of daily living (ADLs), rehabilitation, cast/brace, hospital room, surgical site), country and popularity (the number of views for videos, the number of likes for photographs). The results were evaluated by two reviewers (M.O and B.B), with each reviewer evaluating all the posts. If there was any disagreement, it was resolved by formal discussion of the posts with other authors.

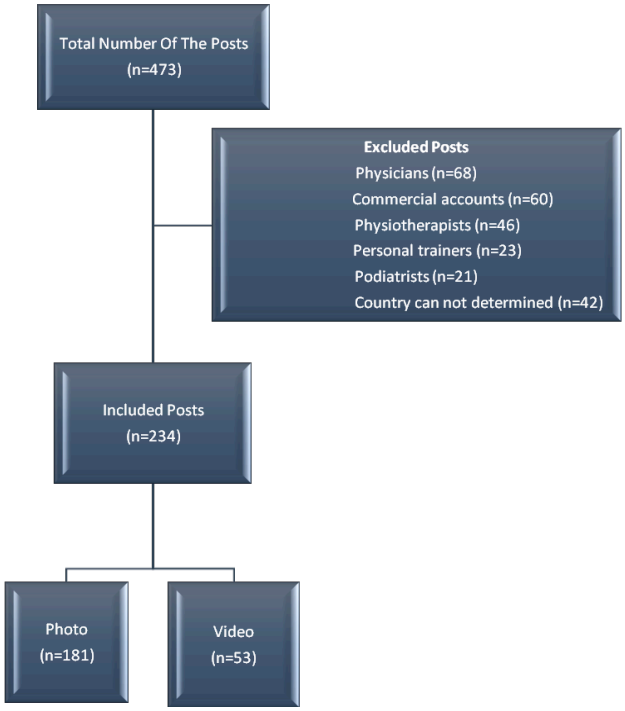

Figure 1. Post Chart

Data obtained in the study were analyzed using SPSS vn.22 for Windows software. Values were stated at a 95% confidence interval (CI). Data were recorded as a percentage, arithmetic mean, and standard deviation values. Conformity of the data to normal distribution was analyzed with the Kolmogorov–Smirnov test. Popularity and groups (Media format, tone, timing, gender content) were evaluated with the Mann–Whitney U and Kruskal Wallis tests. A value of $p<0.05$ was considered statistically significant.

Results

In terms of sharing formats, 77.4%(n=181) of the posts were photographs, 22.6%(n=53) were videos. 73.1%(n=171) were female and 26.9%(n=63) were male(Table 1). The media tone of the posts was 40.2%(n=94) positive, 6.4%(n=15) negative, and 53.4%(n=125) neutral. Most of the shares were from the postoperative period 96.6%(n=226), and the rest were from the preoperative period 3.4%(n=8). The content of the shares were respectively; activity of daily living 36.8%(n=86), physical therapy 29.9%(n=70), cast/brace 20.1%(n=47), surgical site 7.7%(n=18), and hospital room 5.6%(n=13) (Figure 2). Posts in video format, a positive tone, posts on the rehabilitation process, and posts about male patients were found to have a greater number of likes and views than other posts (Table 2). Most of the posts were from the USA 81.6%(n=191), Australia 3%(n=7), and China 2.6%(n=6).

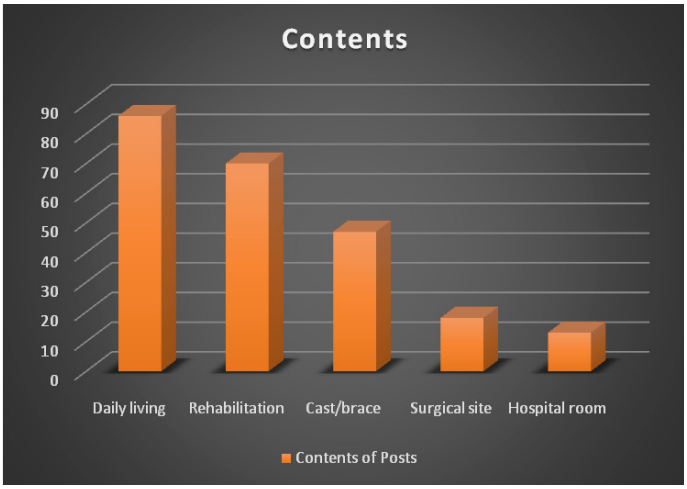

Figure 2: Content Of Posts

Table 1. Study Results		
Media format	Photo	181 (%77.4)
	Video	53 (%22.6)
Media tone	Positive	94 (%40.2)
	Negative	15 (%6.4)
	Neutral	125 (%53.4)
Timing	Preoperative	8 (%3.4)
	Postoperative	226 (%96.6)
Content	Physical therapy	70 (%29.9)
	Daily living	86 (%36.8)
	Cast/brace	47 (%20.1)
	Hospital room	13 (%5.6)
	Surgical site	18 (%7.7)
Gender	Male	63 (%26.9)
	Female	171 (%73.1)
Popularity	121±312.4	(1-3257)

Table 2. Popularity Of Posts				
	Groups	Mean ± SD	Min-max	P value
Media format	Photo	58.1 ± 192	1-2131	0.000*
	Video	335.8± 498	9-3257	
Media tone	Positive	183.7± 445.5	6-3257	
	Negative	45.8 ± 95.3	2-354	0.001*
	Neutral	82.9 ±168.4	1-1113	
Timing	Preoperative	60.1 ± 54.9	6-175	0.682*
	Postoperative	123.2 ± 317	1-3257	
Content	Physical therapy	216± 444.2	3-3257	
	Daily living	75 ±172.2	1-1105	
	Cast/brace	118.3± 346	4-2131	0.000*
	Hospital room	45. ±47	3-175	
	Surgical site	33.1 ± 36.9	4-164	
Gender	Male	215.7± 520.4	4-3257	0008*
	Female	86.1 ± 174.4	1-1113	

Discussion

The use of social media, especially Instagram, has been increasing in the last decade and has become widespread in the field of healthcare services and among patients[6]. Patients generally use social media to obtain medical advice or information about diseases, share their personal experiences in the treatment process, and communicate with their physicians. Instagram shares of patients about their diseases are free shares that have been made without limitations or classifications, as in satisfaction scales used in clinical studies. Therefore, social media applications, especially Instagram, could be used as a new and different tool for measuring and evaluating patients' perspectives on their diseases and treatment processes. It was observed in this study that most of the Instagram posts about Achilles tendon surgery had a neutral or positive tone. The patients generally shared in the postoperative period and mostly shared their experiences of daily living activities and physiotherapy processes.

In a social media study on hip arthroscopy, public Instagram and Twitter posts over one year were examined[8]. It was found that most of the posts were in a positive tone (52.9%) and were shared in the postoperative period (89.4%). The rehabilitation process was shared by 63.7%, activities of daily living by 17.9%, and most posts originated from the USA (65%). However, in the current study, patients mostly shared about activities of daily living, and most importantly, most of their posts were in neutral tones. The reason for this difference was that the sources of the shares examined by the two studies were different. All posts related to hip arthroscopy, including commercial, professional, and physician posts, were examined but only patient posts were examined in this study. It was expected that positive tones would be shared from the accounts of physicians and healthcare providers, primarily used for promotional or informational purposes.

In a retrospective comparative study by Rizkalla et al., the Instagram posts of patients about pilon fractures were examined, and the majority of posts were found to be in a positive tone (88.8%)[11]. Those posts were only divided into positive and negative tones, whereas the current study classified the shares into positive, negative, and neutral tones. As neutral tones were not included in the previous study, a detailed result comparison could not be made, but the rate of posts with a negative tone was similar. Compared with the current study, it was observed that 66.8% vs 29.9% of the posts were shared during the rehabilitation process, and 26.6% vs 36.8% included activities of daily living. This was attributed to the rehabilitation period of pilon fractures being much more complicated and painful than Achilles tendon surgery, so patients want to demonstrate their success in this challenging process more. Most of the posts were made by females (59.3%), as in this study(73.1%).

In an observational social media study, Ramkumar et al. investigated the nature of the shared contents of total joint arthroplasty(TJA) patients[10]. The timing, tone, and content of posts were compared between hip and knee arthroplasties, and it was observed that most TJA posts on Instagram had a positive tone during the postoperative period. The contents mainly reflected the rehabilitation process, daily living activities, and surgical site images. The total knee arthroplasty(TKA) posts focused more on rehabilitation and wound healing, and total hip arthroplasty (THA) posts included more ADLs. In that study, only positive and negative tones were included, and although the rate of positive tones was higher than in the current study, the results were determined to be similar when the shares containing neutral tones were added. THA patients shared fewer posts containing the surgical site than TKA patients because of the difficulty in imaging. This was also determined to be the reason why patients who underwent Achilles tendon surgery shared the surgical area less frequently. Patients mostly shared their rehabilitation processes and daily living activities instead of surgical site posts.

The results of this study showed that the rate of postoperative sharing was as high as 96.6%. This high rate was considered due to the examination of patient shares only. Achilles tendon rupture is an acute and painful condition, so patients do not have the opportunity to share social media posts before surgical care[13]. Furthermore, preoperative or intra-operative and educational or commercial posts not related to the operation process were mainly made in professional accounts of physicians and healthcare providers[14]. When the contents of the patient posts were evaluated, it was seen that mostly daily living activities (36.8%) and rehabilitation processes (29.9%) were shared, and the surgical site shares were less than expected (7.7%). This result showed that patients who underwent Achilles tendon surgery focused more on clinical and

functional outcomes than aesthetic appearance. The region of origin of the posts was evaluated, and 81.6% of the posts were seen to originate from the USA. As the study was carried out by searching for an English hashtag, it was considered normal to have more posts from an English-speaking country.

When the popularity of the shares was evaluated, the shares in video format had a high rate of likes, but the number of views rather than the likes was examined. Therefore, the objectivity of this statistical difference was questionable, as it was not possible to evaluate the number of people who watched the video and liked it. Posts in the rehabilitation process containing cast/brace had more likes than other contents. As expected, it was observed that the posts with a positive tone received more likes than the negative posts, and it was found that the posts made by males were more popular than those by females.

This study have several limitations. First, the shares examined in the study were found through hashtags, but the rate of hashtag usage on Instagram was 53%[15]. This showed that there were undoubtedly many shares in the same period that were not included in the study. Second, people tend to portray their lives more positively on social media, so objectively, it will not be possible to evaluate patients' satisfaction through social media alone. Third, the number of posts was limited because only public posts were examined, private posts could not be reached, and only posts with English hashtags were examined.

Conclusion

The patients avoided making negative posts on Instagram after Achilles tendon surgery. They often shared about postoperative rehabilitation processes and daily living activities. By examining social media posts, it may be possible to evaluate patients' perspectives on their diseases and what the disease truly means to them.

Conflict of Interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

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Orijinal Makale

Çocuk ve adolesanlarda konjonktival nevüse yaklaşım

Approach to conjonctival nevus in children and adolescents

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Öz

Amaç: Bu çalışmanın amacı pediatrik ve adolesanlarda konjonktival nevüslerin seyrini ve olası yaklaşım yöntemlerini belirlemektir.

Gereç ve Yöntemler: Ocak 2021- Kasım 2022 Ankara Şehir Hastanesi oküler onkoloji birimine danışılan konjonktival nevüslü çocuk ve ergenler çalışmaya dahil edildi. 18 yaşından büyük ve kronik sistemik hastalığı olanlar çalışmaya dahil edilmedi. Toplam 35 hastanın yaş ortalaması 12 (standart sapma: 2.1; aralık, 7-17) idi. Büyüme gösteren, pigmentasyon artışı olan, eksizyonel biyopsi gerektiren lezyonların lokalizasyonları, patolojik tanıları araştırıldı.

Bulgular: Toplam 35 hastanın %54' ü erkek %46'sı kadındı. Etkilenen gözlerin % 54.2'si sağ, %45.71'i sol taraftaydı. Nevüslerin %62.8'i bulbar konjonktivada, %25.7'i limbusda, %11.4'ü de karünkülde lokalizeydi. %54.28'inde nazal kadranda, %34.28'inda temporal kadranda, %5.71'inde tüm kadranlarda lokalizasyon görüldü. Nevüslerin %71.42'sinde kist gözlendi. Besleyici damar sadece 10 hastada görüldü (%28.57). Lezyon içerisinde vaskülarizasyon %34.28 hastada gözlemlendi. Hastaların ilk başvuruda %74.28'inde büyüme şikayeti mevcuttu. Takip imkanı bulunmayan, aile endişesi ve malignensi şüphesi olan 26 hastaya ilk tanıda eksizyonel biyopsi uygulandı. Geride kalan 9 hasta takip edildi. 3 hastaya takiplerde lezyonda büyüme ve pigmentasyon artışı nedeniyle eksizyonel biyopsi uygulandı. Geride kalan 6 hasta halen takip edilmektedir. Lezyon boyutunda ve kalınlığında 12 aylık takip sonrasında değişiklik yoktur. Eksizyonel biyopsiler etraf dokuları travmatize etmeden uygulandı. Çıkarılan 29 konjonktival nevüsün 15'i (%52) compound nevüs, 8'i intrastromal nevüs (%27), 5'i junctional nevüs (%17), 1 tanesi de kombine nevüs olarak gelmiştir. Malign lezyon saptanmamıştır.

Sonuç: Çocuklarda konjonktival nevüsde büyüme pek sık değildir ve çıkarılan lezyonların çoğu benign karakterdir. Oftalmoloji pratiğinde takiplerde büyüme göstermeyen lezyonlar takip edilebilmekle beraber, çoğu zaman pigmentasyon artışı, büyüme göstermesi, enflamasyon bulguların görülebilmesi ve özellikle ebeveynlerin tedirginlikleri nedeniyle çıkarılmaları uygun görülmektedir.

Anahtar kelimeler: konjonktiva, nevüs, çocuk, adolesan

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Abstract

Aim: The aim of this study is to determine the course of conjunctival nevi in pediatrics and adolescents and possible approaches

Material and Methods: Children and adolescents with conjunctival nevus who were consulted to Ankara City Hospital ocular oncology unit between January 2021- November 2022 were included in the study. Patients older than 18 years of age and with chronic systemic diseases were not included in the study. The mean age of 35 patients was 12 (standard deviation: 2.1; range, 7-17). The localizations and pathological diagnoses of the lesions showing growth, increased pigmentation and requiring excisional biopsy were investigated.

Results: 46% of the 35 patients were female and 54% were male. 54.2% of the affected eyes were on the right, 45.71% were on the left side. 62.8% of the nevi were localized in the bulbar conjunctiva, 25.71% in the limbus, and 11.4% in the caruncle. Lesion localization was seen in the nasal quadrant in 54.28%, in the temporal quadrant in 34.28%, and in all quadrants in 5.71% of the patients. Cysts were observed in 71.42% of the nevi. The feeding vessel was seen in only 10 patients (28.57%). The vascularization within the lesion was observed in 34.28% of patients. 74.28% of the patients had complaints about lesion enlargement at the first admission. Excisional biopsy was applied to the 26 patients in cases of family concern, suspicion of malignancy, and when follow-up was not possible. The remaining 9 patients were followed up. Excisional biopsy was performed in 3 patients due to enlargement and increased pigmentation in the lesion during follow-up. The remaining 6 patients are still being followed up. There was not any change in the size and thickness of the lesions after 12 months of follow-up. Excisional biopsies were performed without traumatizing the surrounding tissues. The histopathological results of 29 removed conjunctival nevi were compound nevi in 15 (52%) patients, intrastromal nevi in 8 patients (27%), junctional nevi in 5 patients (17%), and combined nevi in 1 patient. No malignant lesion was detected.

Conclusion: Enlargement of the conjunctival nevus is uncommon in children and most of the excised lesions are benign. In ophthalmology practice, although lesions that do not grow can be followed up, it is often considered appropriate to remove them because of increased pigmentation, growth, signs of inflammation, and especially because of parents' concern.

Key words: conjunctiva, nevus, child, adolescent

Giriş

Konjonktival nevüs, konjonktivanın en sık görülen pigmentli tümörüdür. En sık bulbar konjonktivada, değişken derecelerde pigmentasyon gösteren, hafif kabarık lezyonlardır. Biyomikroskopta ince şeffaf kistik alanlar içerdiği gözlenir ve melanomlardan ayırımında önnemli bir bulgudur. Birinci ve ikinci dekatlar en sık görüldükleri yaş aralığıdır ve puberte, gebelik gibi hormonal durumların ve UV ışınlarının etkisiyle lezyon boyutlarında ve pigment yoğunluğunda artış görülebilir. Mevcut nevüsün aniden büyümesi veya renk değişimi adolesan yaş grubunda sıktır ve konjonktivada papiller reaksiyon eşlik etmektedir. Biyopsi yapıldığında lenfosit, plazma hücresi ve eozinofillerden oluşan yoğun bir inflamatuar hücre infiltrasyonu görülmektedir [1].

Konjonktival tümörlerin çocuklarda görülen tümörlerin %61'ini oluşturduğu ABD merkezli yeni bir çalışmada gösterilmiştir [2]. Bu nedenle konjonktival tümörlerden olan nevüslerin tanı ve takibi önemlidir. Histolojik olarak nevüslere baktığımızda, küçük modifiye melanositlerden oluşan nevüs hücrelerinin konjonktivada kümeler oluşturduğunu görürüz. Deri nevüsünde gördüğümüz gibi, lezyonun gelişim evresine göre, epitelyal bileşke yerinde (Junctional nevus), subepitelyal bölgede veya her iki alana uzanacak şekilde (Compound nevus) yerleşim gösterir. İntrastromal nevüs de ise nevüs hücreleri stromada kümelenmiştir [3].

Klinik olarak nevüslerle karşılaştırıldığında konjonktival melanomlar daha kalındır ve taban çapları daha geniştir. Ayrıca melanomlarda kist görülmez, belirgin besleyici damar mevcuttur ve iç yapıda belirgin vaskülarizasyon vardır [2]. Ayrıca, palpebral konjonktiva, plika ve karünkül gibi atipik lokalizasyonlarda lezyonun görülmesi ve korneanın pigmentli lezyonla tutulması melanom şüphesini artırmaktadır [4].

Nevüsün doğal seyri ile ilgili yapılan 2 büyük çalışmada görülme yaşının 30 yaş sonrası olduğu belirtilmiştir. Nevüslerin çoğu

bulbar konjonktivada interpalpebral aralıkta temporal veya nazal tarafta görülmüştür. Büyüme görülse bile malignensi ile ilişkilendirilmemiştir [5].

Özellikle çocuklarda konjonktival nevüslerin takibi ile ilgili net yaklaşım bulunmamaktadır. Belirli aralıklarla takipleri gerekmektedir ancak hastane ulaşımı zor olan hastalarda düzenli takipler çoğu zaman hem pahalı hem de istenilen sürelerde olamamaktadır. Bu çalışmanın amacı çocuk ve adolesanlarda konjonktival nevüslerin seyri ve nevüslere yaklaşım anlatılmaya çalışılacaktır.

Gereç ve Yöntemler

Ocak 2021- Kasım 2022 Ankara Şehir Hastanesi oküler onkoloji birimine danışılan konjonktival nevüslü çocuk ve ergenler çalışmaya dahil edildi. 18 yaşından büyük ve kronik sistemik hastalığı olanlar çalışmaya dahil edilmedi. İlk vizitte eksizyon yerine gözlem yapılacak hastalarda en az iki ardışık fotoğraflama yapıldı. Belirli izlem zamanı belirlenmedi. Demografik bilgilerden yaş, cinsiyet, klinik bulgular olarak tümörün hangi tarafta olduğu, geçmiş tıbbi öykü kaydedildi. Lezyon özellikleri olarak pigmentasyon derecesi, lezyon lokalizasyonu, boyutu, kistlerin varlığı, besleyici damar varlığı, lezyon damarlanması incelendi. Tanımlayıcı istatistikler, normal dağıldığında ortalama ± standart sapmayı (SD) normal dağılmadığında medyanı(çeyrekler arası aralık (IQR)) tahmin etmek için kullanıldı.

Sonuçlar

Toplam 35 hastanın %54'ü erkek %46'sı kadındı. Etkilenen gözlerin % 54.2'si sağ, %45.71'i sol taraftaydı. İlk başvuruda ortalama yaş 12 olarak saptandı (SD:2.1; aralık 7-17). Tablo 1'de hastaların ilk başvuruda oküler ve nevüs özelliklerini özetlemektedir.

Nevüslerin %62.8'i bulbar konjonktivada (22/35), %25.71'i limbusda (9/35), %11.4'ü de karünkülde (4/35) lokalizeydi. %54.28'inde nazal kadranda, %34.28'inda temporal kadranda lokalizasyon görüldü. 1 hastada inferior, 1 hastada süperior tutulum mevcuttu. 2 hastada tüm kadranların tutulduğu Ota nevüs mevcuttu.

Nevüslerin %71.42'sinde kist gözlendi. Besleyici damar sadece 10 hastada görüldü (%28.57). Lezyon içerisinde vaskülarizasyon %34.28 hastada gözlemlendi (12/35). Hiçbir hastada kornea tutulumu izlenmedi.

Hastaların ilk başvuruda %74.28'inde büyüme şikayeti mevcuttu (26/35). Takip imkanı bulunmayan, aile endişesi ve malignensi şüphesi olan 26 hastaya ilk tanıda eksizyonel biyopsi uygulandı. Geride kalan 9 hasta takip edildi. 3 hastaya da takiplerde lezyonda büyüme ve pigmentasyon artışı nedeniyle eksizyonel biyopsi uygulandı. Geride kalan 6 hasta halen takip edilmektedir. Lezyon boyutunda ve kalınlığında 12 aylık takip sonrasında değişiklik yoktur. Eksizyonel biyopsiler etraf dokuları travmatize etmeden uygulandı. Çıkarılan toplam 29 konjonktival nevüsün 15'ü (%52) compound nevüs, 8'i intrastromal nevüs(%27), 5'i junctional nevüs(%17), 1 tanesi de kombine nevüs olarak gelmiştir. Malign lezyon saptanmamıştır.

Tablo 1. Hastaların demografik özellikleri ve konjonktival nevüs yönetiminin özeti

	Sayı (%)
Demografik özellikler	
Yaş ± SD, aralık, yıl	12 ± 2.1(7-17)
Kadın	16 (%46)
Erkek	19 (%54)
Yönetim	
Gözlem	6 (%17.15)
Eksizyonel biyopsi	29 (%82.85)
Eksizyon sebebi	
Hasta isteği	26 (%74.28)
Melanom şüphesi	
Takiplerde büyüme	3 (%8.57)
Takiplerde pigmentasyon artışı	3 (%8.57)
Histolojik tip	
Kompound nevüs	15 (%52)
Junctional nevüs	5 (%17)
Kombine nevüs	1 (%2.85)
Intrastromal nevüs	8 (%27)
Melanom	0

Tablo 2. İlk muayenede tüm nevüslerin oküler ve nevüs bulguları

	Sayı (%)
Oküler/nevüs bulguları	
Sağ göz	19 (% 54.2)
Sol göz	16 (%45.71)
Nevüs lokasyon	
Bulbar	22 (%62.8)
limbus	9 (%25.71)
Karünkül	4 (%11.4)
Kadran	
Temporal	12 (%34.28)
Nazal	19 (%54.28)
Süperior	1 (%2.85)
İnferior	1 (%2.85)
Ota nevüs (tüm kadranlar)	2 (%5.71)
Kist varlığı	25 (%71.42)
Besleyici damar varlığı	10 (%28.57)
Vaskülarizasyon varlığı	12 (%34.28)

Tartışma

Pek çok çalışma ve bu çalışmada da görüldüğü üzere lezyonların çoğu bulbar konjonktivada görülmektedir. Hangi kadranların tutulduğuna bakıldığında, lezyonların daha çok nazal (%54.28) ve temporal kadranda (%34.28) lokalize

olmaları da diğer çalışmalarla uyumluluk göstermektedir [4,5]. Benign karakterdeki nevüslerin kistik özellikleri melanom ayırıcı tanısında klinisyene yardımcı olmaktadır [4]. Bu çalışmada da hastaların %71.42'sinde kist saptanmıştır. Eksize edilen nevüslerin %52'si compound nevüs olarak gelmiştir, bunu intrastromal (%27) ve junctional nevüs (%17) takip etmiştir. Özellikle erişkinlerde yapılan diğer çalışmalarda da compound nevüs histopatolojik incelemelerde bu çalışmadaki gibi daha sık görülmüştür [2,4,5]. Negretti ve ark'larının [6] çocuklarda yaptıkları çalışmada, lezyonların %96'sının bulbar konjonktivada, hem temporal (53%) hem nazal (42%) kadran tutulumu ile olduğu gösterilmiştir. Bununla beraber tars, forniks veya inferior bulbar konjonktiva tutulumu görülmemiştir. Bizim çalışmamızda da bulbar konjonktiva tutulumu %62.8 hastada görülmüştür. Bununla beraber farklı olarak %25.71 limbus (9/35), %11.4 karünkül (4/35) lokalizasyonu mevcuttur. Ayrıca 1 hastada inferior, 1 hastada da süperior bulbar konjonktiva tutulumu izlenmiştir. Negretti ve ark'larının çalışması 20 yaş altı grupta yapılmıştır ve lezyonların histopatolojisine baktıklarında compound nevüs %66 oranında gözlemlenmiştir [6]. Aynı çalışmada kist görünümü %82 hastada saptanmıştır ve bu bulgunun lezyonun benign karakterini gösterdiğini vurgulamışlardır. Besleyici damar %27, lezyon içerisindeki vaskülarizasyon %31 hastada saptanmıştır. 1 hastada korneal tutulum görülmüştür. Bizim çalışmamızda da compound nevüs hastaların %52'sinde, kist mevcudiyeti %71.42, lezyon vaskülarizasyonu %34.28 hastada görülmüştür. Hiçbir hastada kornea tutulumu saptanmamıştır. Çalışmamızda eksizyon kararı verilirken lezyonlarda kalınlık ve pigmentasyon artışı ilk planda ele alınırken hasta ve yakınlarının talebi ile takip edilebilecek lezyonları da eksize etmek gerekmiştir. Takip imkanının olmadığı hasta sayısının yüksek oluşu bu kararı vermede etkili olmuştur. Lezyonların malign formasyona dönüşümünde güneş maruziyeti önemli olmasından dolayı coğrafi olarak yoğun güneş alan ülkemizde bu lezyonların takip edilmesinden ziyade cerrahi olarak çıkarılması daha uygun gibi görülmektedir.

Levecq ve ark'larının yaptığı çalışmada da %83 hasta isteği ile eksizyon yaptıklarını belirtmişlerdir. Negretti ve ark'ları da bu oranı %75 olarak belirtmişlerdir. Bizim çalışmamızda da hasta ve yakınlarının isteği önemli olmuştur ve eksizyon kararı verilmesinde %74.28 hastada etkili olmuştur. Bununla beraber Shields ve ark'larının [4] yaptığı çalışmada sadece %10 oranında kozmetik sebeplerle eksizyon yapılmıştır. Bu çalışmada hasta yaş grubunun düşük olması, ebeveynlerin karar vermede etkili olduğunu göstermiştir. Büyük ihtimalle hastaların yaşı büyüdükçe kozmetik sebepler ön plana çıkmaktadır. Negretti ve ark'larının çalışmasında lezyonlarda büyüme düşük oranda çıkmıştır (8.5%) [6]. Bizim çalışmamızda da lezyonlarda büyüme ebeveynlerin tarifi ile değerlendirilmiş ve bundan dolayı ilk tanı anında eksizyon yapılması gerekmiştir. Histopatoloji sonuçlarının benign karakterde raporlanması aslında bu nevüslerin malign dönüşüm göstermediğini sadece enflamasyona sekonder büyüme ve pigmentasyon artışı gibi olduğunu ortaya koymaktadır. Bundan dolayı çoğu çalışmada çocukluk çağı konjonktiva tümörleri takip edilirken, takip zorluğu olan ülkelerde ebeveynlerin de isteği ile eksizyon kararı ilk muayenede verilmektedir. Zamir ve ark'ları da çocuklardaki konjonktival nevüslerin %75'inin enflamasyon bulguları ile beraber olduklarını ve bu durumun özellikle alerjik/vernal konjonktivit hikayesi olan çocuklarda daha çok görüldüğünü belirtmişlerdir [7]. Bizim çalışmamızda takip edilen hastalara bakıldığında 2 hastanın Ota nevüsü nedeniyle takip edildiği görülmüştür. Ota nevüs trigeminal sinirin 1 ve 2. dallarının innerve ettiği bölgelerde pigmentasyon artışı ile karakterizedir çoğunlukla Asya kökenli kişilerde görülen konjonktiva ve cilt tutulumu ile olan bir melanositozdur. Lezyonlar genellikle konjenitaldir, ancak erişkin dönemde dahi başlangıç olabilir [8]. Klinik olarak trigeminal sinirin 1. ve 2. dallarının innerve ettiği deri bölgelerinde düzensiz sınırlı mavi-gri renkli maküler pigmentasyon görülülür. Bu lezyonlarda malign dönüşüm riski bulunmaktadır.

Sonuç

Hastaların ilk muayeneleri sonrasında mevcut lezyonların eksizyon yapılmasının ardından benign histopatolojik sonuçlarla karşılaşılması aslında bu hastaların takip edilebileceğini ortaya koymaktadır. Benign karakterde lezyonların da büyüme ve pigmentasyon artışı gösterebileceği ve bunun enflamasyon ile oluşabileceği düşünülmektedir. Yani her büyüme veya pigmentasyon artışı malign transformasyon olarak değerlendirilmemelidir.

Sonuç olarak, çocuklarda konjonktival lezyonların çoğu benign karakterdedir ve cerrahi olarak çıkarılmadan takip edilebilirler.

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Orijinal Makale

Koroner Bypas Cerrahisi Sonrasında Gelişen Safen Ven Greft Darlıklarına Perkütan Girişim Yapılan Hastalarda Majör Olumsuz Kardiyovasküler Olaylar ile Serum Fibrinojen Düzeyi Arasındaki İlişki

Relationship Between Fibrinogen Levels and Major Adverse Cardiovascular Events in Patients Undergoing Percutaneous Intervention for Saphenous Vein Graft Stenoses After Coronary Bypass Surgery

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ÖZ

Amaç: Koroner arter bypas greft (KABG) cerrahisi sonrasında gelişen safen ven greft (SVG) hastalığına perkütan girişim ile revaskülarizasyon sağlanan bireylerde uzun dönem kardiyovasküler sonuçlar ve mortaliteyi öngördürmede, aterosklerozun patogenezinde rol oynayan serum fibrinojen seviyesinin değerini aydınlatmak amaçlandı.

Gereç ve Yöntemler: Perkütan koroner girişim (PKG) yolu ile safen ven greft darlıklarına müdahale edilen hastalar retrospektif olarak tarandı. Toplamda 115 hasta çalışmaya dahil edildi. Majör olumsuz kardiyovasküler olay (MACE) varlığına göre 56 hasta (+), 59 hasta (-) olarak değerlendirildi. Her iki grubun PKG öncesi fibrinojen düzeyleri belirlenerek MACE ve fibrinojen değerleri arasındaki ilişki incelendi.

Bulgular: Ortalama takip süresi 42,5 ay olan çalışmada beyaz küre ve serum fibrinojen değerleri, MACE'nin olduğu grupta diğer gruba oranla istatistiksel olarak anlamlı derecede yüksek bulundu (p=0,001). Fibrinojen yüksekliği ve hipertansiyonun bağımsız olarak MACE oluşumuna neden olduğu saptandı (sırasıyla p=0,001 CI: 1,880-6,142; p=0,005 CI: 0,076-0,632). Fibrinojen değerinin 2,75 gr/L'nin olması, %76,2 sensitivite ve %62,7 spesifite ile bağımsız olarak MACE oranlarının öngördürücüsü olarak bulundu (AUC 0,793 CI:0,710-0,875).

Sonuçlar: Serum fibrinojen düzeyinin, safen ven greft darlıklarına yapılacak girişimsel tedavi öncesi değerlendirildiğinde, ölüm ve istenmeyen kardiyak klinik son noktaları öngörmede faydalı olabileceği sonucuna varıldı.

Anahtar Kelimeler: Fibrinojen; Safen ven hastalığı; Ateroskleroz

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Abstract

Aim: We aimed to elucidate the long term cardiovascular outcomes and predicted mortality value of high fibrinogen levels, which is related to the pathogenesis of atherosclerosis, in individuals undergoing percutaneous revascularization of saphenous vein graft disease after coronary bypass surgery.

Material and Methods: Patients with saphenous vein graft stenoses treated with percutaneous coronary intervention were retrospectively reviewed. A total of 115 patients with severe saphenous vein graft lesion were included. Of all the participants, 56 patients experienced major adverse cardiac events (MACE) and 59 of them were not during the follow up. The relationship between major adverse cardiac events and fibrinogen levels was analyzed.

Results: In the study with a mean follow-up period of 42.5 months, white blood cell and serum fibrinogen values were significantly higher in the group with MACE compared to the other group (p=0.001). Elevated fibrinogen levels and hypertension were independently associated with MACE (p=0.001 CI: 1.880-6.142; p=0.005 CI: 0.076-0.632, respectively). A fibrinogen value of 2.75 g/L was found to be an independent predictor of MACE rates with 76.2% sensitivity and 62.7% specificity (AUC 0.793 CI: 0.710-0.875).

Conclusion: In patients admitted with saphenous vein graft disease, pre-procedural fibrinogen level was significantly associated with long-term mortality and adverse cardiac clinical end points. We conclude that serum fibrinogen level may be useful in predicting high-risk patients with saphenous vein disease.

Keywords: Fibrinogen; Atherosclerosis; Saphenous vein graft disease

Giriş

Güncel tıp dünyasında koroner arter hastalığında (KAH) geliştirilen girişimsel metotlar ile hastalığın tedavisinde çok büyük ilerleme sağlanmıştır. Koroner arter bypass (KABG) cerrahisi, stabil KAH tedavisinde yaygın olarak kullanılan bir yöntemdir. Ancak operasyon sonrası 10 yıllık süreçte safen ven greftlerinin (SVG) sadece %61'i anlamlı aterosklerotik hastalıktan etkilenmemiş durumdadır [1]. Redo cerrahinin, ilk yapılan KABG cerrahisi ile karşılaştırıldığında 3 kat daha yüksek perioperatif mortaliteye sahip olması nedeniyle gün geçtikçe yapılırlığı azalmaktadır [2] ve perkutan koroner girişim (PKG) ile revaskülarizasyon, tekrarlayan cerrahiye zorunlu bir alternatif olmaya başlamıştır.

SVG darlıklarına yapılan PKG distal mikroembolizasyona bağlı olarak no-reflow gelişmesi ve periprosedürel miyokard infarktüsü (MI) nedeni ile komplikasyon oranı yüksek, riskli koroner girişimlerdendir [3]. SVG'lerdeki yüksek arteriyal basınca karşı adaptif bir mekanizma olan "arterizasyon" süreci, greftlerde oluşan intimal hiperplazi ile sonuçlanır ve bu durum ateroskleroz gelişimine zemin oluşturur. Devam eden süreçte aktive olan inflamatuar ve koagülatuar mediyatörler aterosklerozun ilerlemesine katkı sağlar [4]. Bir çalışmada SVG PKG sonrası 5 yıllık takipte no-reflow gelişen hastaların MI ve ölüm riski, iyi ileri yönlü akımı olan hastalara oranla daha yüksek bulunmuştur [5]. SVG hastalığında çoğu hasta için PKG tercih edilse de, yeniden müdahale kararı ve yöntem seçimi (PKG'ye karşı KABG), revaskülarizasyonun uygunluğu, risk altındaki alan, komorbiditeler ve hastanın klinik durumu dikkate alınarak multidisipliner bir kalp ekibi tarafından değerlendirildikten sonra bireyselleştirilmelidir [6].Tüm bu nedenlerden dolayı yüksek riskli hastaların belirlenebilmesi önem arz etmektedir.

Tıp literatürü incelendiğinde artmış fibrinojen düzeyinin stabil KAH ve stent restenozu gibi durumlarda gelişebilecek olumsuz kardiyak olaylar için prognostik önemi olduğu gösterilmiştir [7,8]. Benzer şekilde artmış fibrinojen ve beyaz küre düzeyleri no-reflow gelişiminde etkilidir [9]. Değişik çalışmalarda bahsedildiği üzere, viskozite [10], Von Willebrand faktör [11], doku plazminojen aktivatörü [12], fibrin d-dimerleri [13] gibi koagülasyon elemanlarının ve bir akut faz proteini olan serum amiloid A'nın [14] kardiyovasküler olayların görülme sıklığında etkili olduğu bilinmektedir.

Biz bu çalışmada SVG hastalığı olan ve PKG ile revaskülarizasyon sağlanan bireylerde, yaygın ve kolay ulaşılabilir bir parametre olan fibrinojenin uzun dönem kardiyovasküler sonuçları öngördürücü değerini aydınlatmayı amaçladık.

Gereç ve Yöntemler

Çalışma için Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi Kardiyoloji Kliniği Kateter Laboratuvarında Aralık 2009 ile Şubat 2015 tarihleri arasında koroner anjiyografi (KAG) sonrası SVG PKG yapılan hastalar retrospektif olarak

incelendi. Akut koroner sendrom (AKS) kliniği ile başvuran, aktif enfeksiyonu olan, otoimmün hastalık öyküsü olan, serebrovasküler hastalık öyküsü olan, aktif malignite tanısı olan, karaciğer ve böbrek yetmezliği olan hastalar dışlanarak toplamda SVG PKG yapılan 115 hasta çalışmaya dahil edildi. Çalışma, Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi araştırma ve etik kurulu tarafından onaylandı. (04/09/2014 tarihli ve 322 sayılı toplantı)

Hastaların takip bilgileri poliklinik kontrolleri ve telefon görüşmeleri ile elde edildi. Hastaların verileri, hastane otomasyon sistemi ve kateter laboratuvarı arşivinden edinildi. Yapılan SVG girişimlerinin verileri geriye dönük şekilde anjiyografi kayıtlarından belirlenip oluşturuldu. Hastalar MACE varlığına ve yokluğuna göre iki gruba ayrıldı. MACE; ölüm, MI, serebrovasküler olay, hedef damar revaskülarizasyonu ve kardiyak nedenli hospitalizasyon olarak tanımlandı.

Hipertansiyon (HT) tanısı tekrarlayan ölçümlerde tansiyon değerinin > 140/90 mmHg olması veya mevcut antihipertansif tedavi altında olma olarak belirlendi. Hiperlipidemi total kolesterol değerinin >200 mg/dl olması veya antilipid tedavi alması olarak belirlendi. Diyabetes mellitus (DM) tanısı çoklu ölçümlerde açlık serum glukoz düzeyinin > 126 mg/dl olması veya halen antidiyabetik tedavi alması olarak belirlendi.

Fibrinojen düzeyleri Sysmex CA-7000 Coagulation Analyzer cihazı ile ölçüldü. Tam kan sayımı analizi için Coulter Counter LH Serisi (Beckman Coulter Inc, Hialeah, Florida) kullanıldı. Sol ventrikül ejeksiyon fraksiyonu (LVEF) Philips EPIQ 7G cihazıyla, modifiye edilmiş Simpson yöntemi kullanılarak hesaplandı.

İstatistiksel Analiz

İstatistik analizler SPSS (v.17 ; SPSS Inc., Chicago, Illinois, USA) programı ile yapıldı. Sayısal değişkenler için tanımlayıcı istatistikler, kategorik değişkenler için ise sayı tabloları oluşturuldu. Sayısal değişkenlerin dağılım paternini test etmek için Kolmogorov–Smirnov metodu kullanıldı. Kategorik değişkenler arasında fark analizi Ki – kare analizi ile yapıldı. Normal dağılımın sağlandığı durumlarda fark analizleri Student's t-testi ile yapılırken, normal dağılımın sağlanmadığı durumlarda Mann Whitney U kullanıldı. Devamlı iki değişken arasındaki ilişki Pearson's veya Spearman's korelasyon analizi ile değerlendirildi. Fibrinojen düzeyinin MACE varlığı ile olan ilişkisini analiz etmek için tek ve çoklu değişkenli lojistik regresyon modelleri kullanıldı. Öngörülen klinik son noktaların en iyi kestirim değerini belirlemek için ROC (receiver-operating characteristic) eğrisi kullanıldı. Analizlerde p<0,05 değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular

Hastaların ortalama takip süresi 42,5 aydır. Tablo 1'de gösterildiği üzere cinsiyet, sigara kullanımı, yaş, hiperlipidemi, LVEF açısından iki grup arasında anlamlı farklılık saptanmadı (p>0,05). Dahil edilen 115 hastadan 56 hasta MACE (+), 59 hasta MACE (-) olarak belirlendi. Risk faktörleri göz önüne alındığında DM ve HT açısından iki grup arasında anlamlı farklılık saptandı. MACE (+) olan grupta diyabetik ve hipertansif hasta oranının daha yüksek olduğu görüldü (p değeri sırasıyla 0,030 ve 0,032). Kullanılan stent tipi ve girişim yapılan safen ven lokalizasyonu açısından iki grup benzer özelliklere sahipti (p>0,05). Ancak her iki grupta da çıplak metal stent kullanımı, ilaç salınımlı stent kullanımına göre bariz olarak daha fazlaydı.

Kan parametreleri değerlendirildiğinde açlık kan glukozu, kreatinin, total kolesterol, LDL, HDL, trigliserid değerleri arasında istatiksel olarak anlamlı farklılık bulunmadı (p>0,05) (Tablo 2.). Beyaz küre ve fibrinojen değerleri MACE (+) hastalarda istatistiksel olarak yüksek bulundu (p değeri sırasıyla 0,01 ve 0,001).

MACE oluşumuna katkıda bulunan faktörler (DM, HT, stent tipi, safen ven lokalizasyonu, fibrinojen) çoklu değişkenli lojistik regresyon analizine alındığında fibrinojen ve hipertansiyonun bağımsız olarak MACE oluşumuna neden olduğu saptandı (sırsıyla p=0,001 CI: 1,880-6,142; p=0,005 CI: 0,076-0,632). MACE öngörmede prediktif olduğu düşünülen fibrinojen düzeyi değerlendirildiğinde iki grup arasında istatistiksel anlamda farklılık bulundu (p<0,001) (şekil 1). Fibrinojen değerinin 2,75 gr/L olması, %76,2 sensitivite ve %62,7 spesifite ile bağımsız olarak MACE oranlarının öngördürücüsü olarak saptandı (AUC 0,793 (CI:0,710-0,875). (Tablo 3.) (Şekil 2).

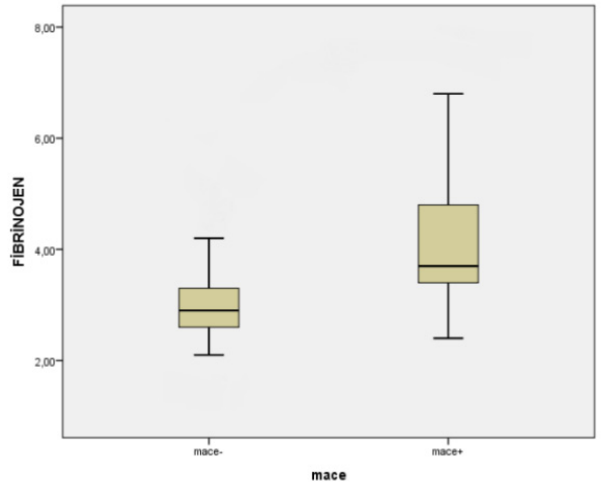
Tablo 1. Bazal Karakteristik Özellikler

	MACE (-) (n=59)	MACE (+) (n=56)	P değeri
Yaş (yıl)	63,5±9,2	64,5±9,1	0,35
Erkek, n(%)	46 (78)	36 (64,3)	0,78
Hipertansiyon, n(%)	34 (57,6)	40 (71,4)	0,032
Diyabetes mellitus, n(%)	20 (33,8)	27 (48,2)	0,030
Sigara kullanımı, n(%)	35 (53,8)	39 (55,5)	0,153
Dislipidemi, n(%)	38 (64,4)	34 (60,7)	0,68
Aile Hikayesi, n(%)	15 (25,4)	16 (28,5)	0,85
Stent Tipi, n			
-Düz Metal Stent	48	50	0,231
-İlaç Kaplı Stent	11	6	0,156
SVG Lokalizasyonu, n			
-LAD	9	15	0,199
-LCX	27	18	0,178
-RCA	23	23	0,673
LVEF (%)	47,4±11,4	46,2±11,1	0,557

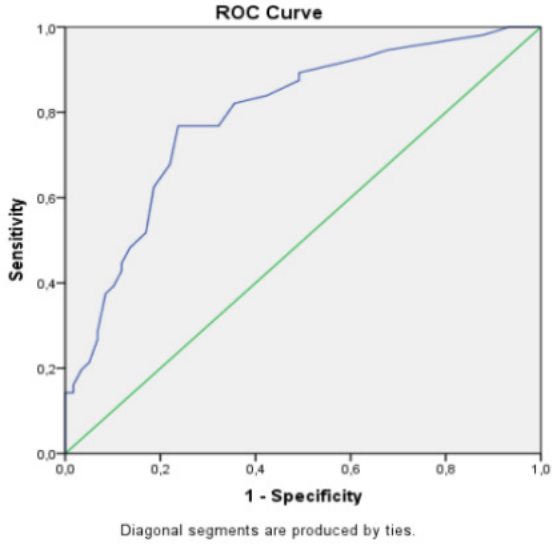
LAD : Sol ön inen arter, LCX : Sol sirkümfleks arter, RCA: Sağ koroner arter, SVG: Safen ven greft, LVEF: Sol ventrikül ejeksiyon fraksiyonu

Tablo 2. Labaratuvar Bulguları			
	MACE (-) (n=59)	MACE (+) (n=56)	P değeri
Glukoz, mg/dl	130 ± 68,7	132,9 ± 62,3	0,814
Üre, mg/dl	44,56	44,70	0,964
Kreatinin, mg/dl	1,04	2,66	0,231
LDL, mg/dl	121,8 ± 67	118,8 ± 40,9	0,78
HDL, mg/dl	42,6 ± 10,6	40,8 ± 12,6	0,406
Trigliserid, mg/dl	194,3 ± 23,5	156,4 ± 69,9	0,208
WBC, $x10^3/mm^3$	7,4 ± 1,6	8,4 ± 1,7	0,01
Fibrinojen, g/L	3,08 ± 0,76	4,10 ± 1,16	0,001
LDL: Düşük yoğunluklu lipoprotein, HDL: Yüksek yoğunluklu lipoprotein, WBC: Beyaz küre sayısı			

Tablo 3. MACE ile İlişkili Çoklu Değişkenli Lojistik Regresyon Analizi			
Değişkenler	B	95%CI	P
Fibrinojen	3,398	1,880-6,142	0,001
Hipertansiyon	0,219	0,076-0,632	0,005
Diabetes mellitus	0,686	0,270-1,744	0,428



Şekil 1. MACE (+) ve MACE (-) Gruplarının Fibrinojen Düzeylerinin Karşılaştırması



Şekil 2. Fibrinojen Düzeyinin MACE Oranlarının Öngörülmesindeki Değerini Gösteren ROC Eğrisi

Tartışma

KAH dünya genelinde mortalite ve morbiditenin ilk sırada gelen nedenidir [15]. Dolayısıyla risk sınıflaması yapılarak yüksek riskli hastaların tespit edilmesi önem arzetmektedir. Bu sayede risk faktörleri kontrol altına alınarak hem kardiyovasküler ölümlerin, hem de ölümcül olmayan koroner olayların azaltılabileceği bilinmektedir.

KABG cerrahisi, KAH olan hastalarda 50 yılı aşkın süredir yaygın şekilde uygulanmaktadır [16]. Maalesef cerrahiden yaklaşık 10 yıl sonra hastaların üçte birinde gelişen anginal sempomlar ve AKS nedeniyle tekrardan KABG ya da PKG gereksinimi doğmaktadır[17].

KABG öyküsü olan hastalarda yapılan PKG'in sonuçları, KABG olmamış hastalarla kıyaslandığında daha kötüdür [18]. Fakat redo-KABG yapılan hastalarda mortalite ilk cerrahiye nazaran 2-4 kat daha fazladır[19]. PKG yerine tekrar cerrahi işlem genellikle kullanılan greftlerin tıkandığı, LVEF'nin düştüğü, native arterlerinde total tıkanıklık bulunan ve bunun yanı sıra arteryel grefti tıkanan vakalarda ön plana çıkmaktadır [20].

SVG yetersizliği yaygın olmasına rağmen bu greftler KABG sırasında hala en sık kullanılan greftler olarak kalmaya devam etmektedirler [21]. Maalesef safen ven hastalığı gelişmesi durumunda yapılacak PKG işleminde bir takım kısıtlılıklar bulunmaktadır. SVG'de meydana gelen plak morfolojileri nativ koroner arterlerdekine göre lipidden daha zengin, daha yumşak ve rüptüre olmaya daha meyillidir, bu nedenle stent ve balon basıncının neden olduğu mekanik yaralanmaya daha hassastır [22]. Tüm bu sebeplerden dolayı SVG hastalığına yapılan PKG yüksek riskli olarak kabul edilmektedir. Bu açıdan bakıldığında bu hastaların risk sınıflaması oldukça önemlidir.

Çalışmamızda SVG'e PKG sırasında düz metal stent veya ilaç kaplı stent kullanılması hastaların MACE sonuçları açısından anlamlı bir farklılığa neden olmadığı görüldü. Benzer şekilde 6 randomize kontrollü çalışmanın incelendiği bir metaanalizde tüm nedenlere bağlı mortalite, kardiyovasküler mortalite, stent trombozu, MI ve hedef damar revaskülarizasyonu açısından ilaç kaplı ve düz metal stent kullanımı arasında fark bulunmamıştır [23]. Bu veriler çalışmamızla paralellik göstermektedir.

Çalışmamızda demografik ve klinik özellikler ile fibrinojen düzeyi arasındaki ilişki değerlendirildiğinde DM ve HT varlığı fibrinojen düzeyi ile benzer olarak MACE (+) gözlenen grupta daha yüksek bulunmuştur. Tip 2 diyabeti olan hastaların büyük bir kısmında fibrinojen yüksekliği mevcuttur. Hiperfibrinojenemi HbAıc'den bağımsız olarak tip 2 DM hastalarında artmış kardiovaskuler riske neden olabilir [24].

Ayrıca sigara kullanımı, artmış vücut kitle indeksi, ve sınırlı fiziksel aktivite tip 2 DM'da birbirinden bağımsız olarak yüksek plazma fibrinojeni ile alakalıdır [25,26].

Çalışmamızda fibrinojen düzeyinin yanında beyaz küre sayısı da MACE ile ilişkili bulunmuştur. Kardiyovasküler hastalıklar ve artmış beyaz küre sayısı birlikteliği mevcut literatür verileriyle de paralellik göstermektedir. Akinyelure OP ve arkadaşlarının yapmış olduğu çalışmada yükselmiş inflamasyon belirteçleri artmış kardiyovasküler risk ile ilişkili bulunmuştur [27,28].

Daha önceki çalışmalarda fibrinojen yüksekliğinin tekrarlayan kardiyovasküler olaylarla ilişkili olduğu gösterilmiştir [29]. Fakat Jun Wang ve arkadaşlarının yaptığı bir çalışmada plak hassasiyeti intravasküler optik koherans tomografi ile değerlendirilmiş ve kolay yaralanabilir plak mevcudiyeti fibrinojen düzeyi ile ilişkili bulunmamıştır [30]. Çalışmamız ve literatürdeki diğer çalışmaların verileri göz önünde bulundurulduğunda fibrinojen yüksekliğinin kardiyovasküler kötü sonlanımlara olan katkısı genel inflamatuar yanıt, damar yapısı ve stent mevcudiyeti gibi birçok faktörle ilintili olduğu düşünülmektedir.

Kısıtlılıklar

Mevcut çalışmanın bazı kısıtlılıkları vardır. En önemlisi çalışmaya alınan hasta sayısının az olmasıdır. Diğer bir kısıtlılığımız ise çalışmanın retrospektif olarak yapılmış olmasıdır. Yine mevcut çalışmanın çok merkezli olarak planlanmamış olması kısıtlılıklar arasında sayılabilir.

Sonuç

Hem çalışmamızdaki veriler hem de literatürde yer alan diğer çalışmalar göz önüne alındığında kardiyovasküler hastalıklar için önemli olan risk faktörlerinin çoğunun yüksek fibrinojen düzeyi grubundaki hastalarda yoğunlaştığı söylenebilir. Bununla beraber fibrinojen ucuz, kolay ulaşılabilir bir belirteçtir. Çalışmamızda serum fibrinojen düzeyinin, SVG darlıklarına yapılacak girişimsel tedavi öncesi değerlendirildiğinde, ölüm ve istenmeyen kardiyak klinik son noktaları öngörmede faydalı olabileceği sonucuna varıldı, dolayısıyla işlem öncesi bakılacak fibrinojen düzeyleri risk sınıflaması açısından öngördürücü olabilir.

Maddi Destek ve Çıkar İlişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur.

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Original Article

Evaluatıon of Obstetrıc Results of Pregnancy Who Applıed Ankara Educatıon and Research Hospıtal Gynecology and Obstetrıcs Clınıc Pregnancy School (Mode of Delıvery)

Ankara Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği Gebe Okulunda Eğitim Alan Gebelerin Obstetrik Sonuçlarının Değerlendirilmesi (Doğum Şekli)

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Abstract

Aim: Recently cesarean section rate has increased significantly all over the world. The information provided by the healthcare provider during pregnancy follow-up is important for the pregnant women to decide on the delivery method. In particular, information about normal birth; may help reduce rising cesarean rates by curbing fears of obscurity and widespread public rhetoric. The aim of this study is to investigate the effect of the education given by the prenatal school on the delivery method preferred by the pregnant women.

Material and Methods: This descriptive study includes equal number of nulliparous pregnant women who applied to Ankara Training and Research Hospital Gynecology and Obstetrics outpatient clinic, who attended or did not attend the prenatal school between January 2020 and November 2022. The effect of education on decision making was investigated by comparing delivery methods according to the status of being educated in the pregnancy school and the primary cesarean section rate of the same number of nulliparous pregnant selected from among the uneducated pregnant women who gave birth in the same period in our clinic were compared.

Results: In our study, 44 (81.5%) of the 54 nulliparous pregnant women who received education gave normal birth, while 33 (61.1%) of 54 those who did not receive education gave birth normally. A statistically significant difference was found between the two groups in terms of delivery mode ($p<0.05$).

Conclusion: It was thought that the education given in the pregnancy school may be a factor in reducing the primary cesarean section rates.

Keywords: Prenatal School, Cesarean, Normal Birth, Education

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Öz

Amaç: Son yıllarda sezaryen oranı tüm dünya genelinde önemli ölçüde artış göstermektedir. Gebelerin doğum yöntemine karar vermesinde gebelik izlemleri sırasında sağlık personeli tarafından yapılan bilgilendirmeler önem taşır. Özellikle normal doğumla ilgili olan bilgilendirmeler; bilinmezlikten ve halk arasındaki yaygın söylemlerden kaynaklanan korkuları engelleyerek artan sezaryen oranlarını azaltmaya yardımcı olabilir. Bu çalışmanın amacı gebe kadınlarda gebe okulu ile verilen eğitimin gebenin tercih etmiş olduğu doğum yöntemine etkisini araştırmaktır.

Gereç ve Yöntemler: Tanımlayıcı tipteki bu araştırma, Ankara Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum polikliniğine başvuran nullipar gebelerden Haziran 2020 ve Kasım 2022 tarihleri arasında gebe okuluna katılım sağlayan ve katılmayan eşit sayıdaki gebeyi içermektedir.

Gebe okulunda eğitim alma durumu ve aynı dönemde kliniğimizde eğitim almamış gebe kadınlar arasından aynı sayıda nulipar gebelerde primer sezeryan oranı karşılaştırılarak doğum metoduna karar vermede eğitimin etkisi araştırıldı.

Bulgular: Çalışmamızda 54 nulipar eğitim alan gebeden 44'ü (%81.5) normal doğum yaptı, 54 nulipar eğitim almayan gebeden 33'ü (%61.1) normal doğum yaptı. Doğum metodu açısından istatistisel olarak iki grup arasında anlamlı fark tespit edildi ($p<0.05$).

Gebe okulunda Ocak 2020 - Kasım 2022 arasında eğitim almış toplam 54 nullipar gebenin primer sezaryen oranı ile kliniğimizde aynı dönemde doğum yapan eğitim almamış gebeler içerisinden seçilen aynı sayıda nullipar gebenin primer sezaryen oranı karşılaştırıldı.

Sonuç: Çalışmamızda değerlendirilen eğitim alan 54 nullipar gebenin 44'ü (%81,5) normal doğum yaparken eğitim almayanların ise 33'ü (%61,1) normal doğum yapmıştır. İki grup arasında doğum şekli açısından istatistiksel olarak anlamlı bir fark bulunmuştur. Bu verilerden yola çıkarak gebe okulunda verilen eğitimin primer sezaryen oranlarını azaltmada bir etken olabileceği düşünülmüştür.

Anahtar Kelimeler: Gebe Okulu, Sezeryan, Normal Doğum, Eğitim

Introduction

Pregnancy and childbirth; even if there are physiological conditions, they cause anxiety in pregnant women due to the risks they pose. Information provided by medical personnel during pregnancy follow-up is important for pregnant women to decide on the mode of delivery. Information, especially related to normal vaginal birth, can help reduce the increasing cesarean section rates by preventing fears caused by the decency and widespread discourse among the public. Information, especially related to normal childbirth, can help reduce the increasing cesarean section rates by preventing fears caused by the decency and widespread discourse among the public. According to World Health Organization (WHO) data, education and follow-up during pregnancy is determined as 68%, while this rate is 98% in developed countries (1).

With the trainings received during pregnancy, it is ensured that women are healthy both in the birth process and in the postpartum period. In the field of medical indications, the preference of women for cesarean section with social indication is increasing rapidly. WHO / World Health Organization recommends keeping cesarean section rates below 15% (2).

In our country, the Ministry of Health has started to establish prenatal schools in hospitals in order to reduce the rate of cesarean section in the field of medical indication and to prepare pregnant women for birth more consciously and to act consciously in newborn care. In this context, prenatal schools provide training in a certain period and certificates are issued to those who attend (3).

It was determined that among the factors affecting the cesarean section preferences of women, social, psychological and environmental factors other than fear were under the influence (4). Childbirth preparation and support trainings aim to reduce the rate of cesarean section except for medical indications (5). The aim of our study is to investigate whether there is an effect in the form of birth with the trainings given in the prenatal school established in our hospital.

Material and Methods

The research was planned as a retrospective observational

study. It was designed in Ankara Training and Research Hospital Gynecology and Obstetrics Clinic to cover the period of January 2020-November 2022. The study included nulliparous pregnant women aged 20-49 who were educated at the prenatal school of Ankara Training and Research Hospital Gynecology and Obstetrics clinic. The same number of nulliparous patients who did not receive education in the prenatal school at the same time were randomized and designed as the control group. Ages, education levels, working status, type of delivery, cesarean rate, indications of cesarean were recorded using hospital archive files and hospital automation system retrospectively. The delivery mode of pregnant women who gave birth in Ankara EAH Gynecology and Obstetrics Service, who received education in a prenatal school and who did not receive any education were compared.

The study was carried out with the permission of – University/ Training and Research Hospital, Noninvasive Clinical Ethics Committee (Date: 23.11.2022, Decision No: E-93471371-514.99). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

SPSS for Windows, version 23.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Whether the assumption of homogeneity of variances is provided with the Kolmogorov-Smirnov test will be investigated with the Levene test. Descriptive statistics expressed as mean ± standard deviation or median (25th percentile-75th percentile) for continuous and discrete numerical variables, and as number of cases and (%) for categorical variables. Student-t test will be used in parametric tests and Mann-Whitney U test will be used in non-parametric tests. Categorical variables will be evaluated with Pearson's χ 2 or Fisher Freeman Halton tests. For p≥0.05, the results will be considered statistically significant.

Results

The mean age of 54 pregnant women who received training was 27.52±4.7 years, and 54 pregnant women who did not receive any education was 25.7± 5.3 years (Table 1). There was no statistically significant difference between the two groups (p>0.05). While 44 (81.5%) of the trainees gave birth normally, 10 (18.5%) gave birth by cesarean section. Of those who were not educated, 33 (61.1%) gave birth normally, while 21 (38.9%) gave birth by cesarean section (Table 2). Accordingly, a statistically significant difference was found between the group that received education and the group that did not receive education in terms of the mode of delivery (Fisher's Exact test; p=0,033<0,05) (Figure 1).

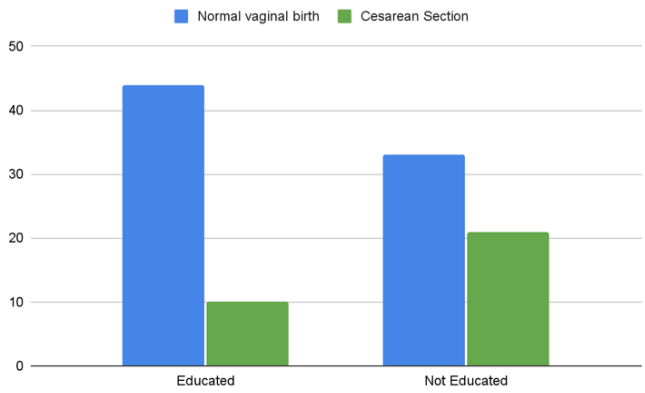

Figure 1. Comparison of the educated and non-educated groups in terms of mode of delivery

Table 1. Distribution of demographic characteristics of the participants

	Educated (n=54)		Not educated (n=54)	
Age (mean±SD)	27.52±4.7		25.7± 5.3	
Education level n % Primary education	14	25,9%	18	33,3%
High school	34	63,0%	33	61,1%
Master's degree	6	11,1%	3	5,6%
Working Status n %				
Working	32	59,3%	25	46,3%
Not Working	22	40,7%	29	53,7%

Table 2. Comparison of the educated and non-educated groups in terms of mode of delivery

	Educated (n=54)		Not educated (n=54)		P
	n	%	n	%	
Normal vaginal birth	44	81,5%	33	61,1%	0,033*
Cesarean birth	10	18,5%	21	38,9%	
*: p<0,05					

Among the pregnant women who received training, 60% of the cesarean indications are fetal distress, 30% multiple pregnancy, and 10% non-progressed labor. 45% of cesarean section indications in uneducated pregnant women are fetal distress, 33.3% non-progressive labor, and 19% social indications (Table 3). Although there was no statistically significant difference between the educated and uneducated groups in terms of cesarean section indications (Chi-square test; p=0.087>0.05), it was not seen any cesarean section with social indications in those who received education.

Table 3. Comparison of the educated and non-educated groups in terms of cesarean section indications

Cesarean indication	Educated (n=10)		Not educated (n=21)	
Failure to progress	1	10,0%	7	33,3%
Fetal distres	6	60,0%	9	42,9%
Multiple pregnancy	3	30,0%	1	4,8%
Social endication, etc	0	0,0%	4	19,0%

There was no statistically significant difference between those who received education and those who did not, in terms of educational status (Chi-square test; p=0.393>0.05) (Table 1). Similarly, there was no statistically significant difference in terms of working status between those who received education and those who did not (Chi-square test; p=0.172>0.05) (Table 1). Groups were homogeneous in terms of working status.

Discussion

According to WHO data, cesarean section rates are increasing rapidly in the world. In Turkey, this rate has reached 35% today. In previous years, cesarean section rates were seen as the lowest 21.2% in the past, and reached 48% in 2013 when it was the highest (1, 6).

Pregnancy and childbirth pose great fears for expectant mothers. It is very common today for expectant mothers to want a cesarean section due to fear of childbirth. It has been found that there is a 35% decrease in cesarean section requests in pregnant women who received prenatal school education (7). It was revealed in a study conducted in Rome that education level is an important factor in cesarean section request, and it was found that pregnant women at primary education level had a 24% higher cesarean section request than those at university level (8). In our study, the cesarean section request of the patients was not evaluated, but there was no significant difference between the two groups in terms of educational status. However, when the educational status of the patients who continue their prenatal school education is evaluated, it is seen that there are patients in every education level. Prenatal school is thought to be effective and successful not only for pregnant women with a high education level, but also for those with a low education level.

Sipahi M. compared pregnant women who received pregnancy training and those who did not, and no significant difference was found between the two groups in terms of delivery type. However, it was observed that the rate of cesarean section was higher in pregnant women who did not receive education (9). In our study, although the rate of cesarean section of pregnant women who did not receive education in prenatal school was lower than the country average, it was determined that it was higher than those who received education in a pregnant school. As the patient's knowledge about birth increased, there may have been a decrease in the cesarean section rates due to the decrease in their anxiety, increase in their resilience and increase in their compliance.

In a study investigating the effect of prenatal school education on birth anxiety, it was shown that the education received reduced birth anxiety in pregnant women (10). It has been reported that the main reason for these concerns is the lack of information about childbirth (11, 12). When cesarean section indications were evaluated in our study, although there was no significant difference between the two groups, cesarean section performed for social indications did not occur in the patients who received training. In the uneducated group, 20% of the patients who had cesarean section were performed due to social indications. It is seen that the education given in the prenatal school reduces the cesarean sections for social reasons rather than the cesarean sections for medical reasons, as expected.

The most important limitation of our study was the low number of patients, and the most important reason for this was the disruption of prenatal school studies during the Covid-19 pandemic.

In conclusion, prenatal school probably reduces the anxiety of pregnant women about childbirth by making the obscurity of birth more fearless for patients. As a result, the education given in the prenatal school is effective in reducing the cesarean section rates.

Ethics Committee Approval

The study was carried out with the permission of –University/ Training and Research Hospital, Noninvasive Clinical Ethics Committee (Date: 23.11.2022, Decision No: E-93471371-514.99)

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version

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Original Article

Multidisciplinary differences in approaches to patients undergoing breast examination and evaluation of collaborations

Meme muayenesi yaptıran hastalara yaklaşım ve işbirliğinin değerlendirilmesinde multidisipliner farklılıklar

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Abstract

Aim: The purpose of this study is to examine the outpatient clinics of patients admitted to the hospital for breast examinations and the diagnostic process after these applications. It also the seconder aim is the comparison between the general surgery (GS) outpatient clinic and other non-general surgery clinics , for the diagnosis of the breast cancer.

Material and Methods: The patients who came to the GS, internal medicine (IM), and obstetrics and gynecology (OG) outpatient clinics of our hospital between January1, 2015, and June15, 2019, were examined retrospectively. Continuous variables were reported as the mean and standard deviation, whereas categorical nominal variables were expressed as a percentage of the total population.

Results: Between January1, 2015, and June15, 2019, the total number of mammograms required for breast examination was 7998.Of these, 1769 were GS,456 were IM, and 5773 of them were OG outpatient clinics. The mean age was 48±2.3 years in GS, 48±6.7 years in IM, and 47±3.9 years in OG outpatient clinics (p>0.05). The distrubition of the number of malignant breast cases are GS: 43, OG: 21, IM: 5, respectively. In total, 69 breast cancer diagnoses were made. In terms of clinical dominance, the general surgery clinic has emerged as the most effective clinic in putting breast malignancy [AOR: 0.34 (0.21-0.54) (P <0.001)]. Among patients with mammography BIRADS 4 and 5, the risk of malignancy was higher than in those with BIRADS 0-1-2-3 [AOR: 0.81 (0.72-0.9) (P <0.001)].

Conclusion: We believe that the most important cornerstone for the diagnosis of breast diseases, especially concerning malignancy is physical examination, anamnesis, and imaging techniques through which interclinic collaboration.

Keywords: Breast cancer, physical examination, interclinic collaboration

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Öz

Amaç: Bu çalışmanın amacı meme muayenesi için hastaneye başvuran hastaların polikliniklerini ve bu uygulamalar sonrasındaki tanı sürecini incelemektir. İkincil amacı da meme kanseri tanısı için genel cerrahi (GC) poliklinikleri ile diğer genel cerrahi dışı kliniklerin karşılaştırılmasıdır.

Gereç ve Yöntemler: Hastanemizin 1 Ocak 2015-15 Haziran 2019 tarihleri arasında genel cerrahi(GC), Dahiliye (IM), Kadın Hastalıkları ve Doğum (OG) polikliniklerine başvuran hastalar retrospektif olarak incelendi. Sürekli değişkenler ortalama ve standart sapma olarak rapor edilirken, kategorik nominal değişkenler toplam popülasyonun yüzdesi olarak ifade edildi.

Bulgular: 1 Ocak 2015-15 Haziran 2019 tarihleri arasında meme muayenesi için gerekli olan toplam mamografi sayısı 7998'dir. Bunların 1769'u Gc, 456'sı IM ve 5773'ü OG polikliniklerdir. Yaş ortalaması Gc'de 48±2,3, IM'de 48±6,7, OG polikliniklerinde 47±3,9 idi (p>0,05). Malign meme vaka sayılarının dağılımı sırasıyla GC: 43, OG: 21, IM: 5 şeklindedir. Toplamda 69 meme kanseri teşhisi konulmuştur. Klinik hakimiyet açısından genel cerrahi kliniği meme kanseri koymada en etkili klinik olarak ortaya çıkmıştır [AOR: 0,34 (0,2-0,54) (P <0,001)]. Mamografi BIRADS 4 ve 5 olan hastalarda malignite riski BIRADS 0-1-2-3 olanlara göre daha yüksekti [AOR: 0,81 (0,72-0,9) (P <0,001)].

Sonuç: Özellikle maligniteyi ilgilendiren meme hastalıklarının tanısında en önemli mihenk taşının klinikler arası işbirliği ile yapılan fizik muayene, anamnez ve görüntüleme teknikleri olduğuna inanıyoruz.

Anahtar kelimeler: Meme kanseri, fizik muayene, klinikler arası işbirliği

Introduction

The second most common cancer in the world is breast malignancy. It constitutes 10.4% of the cancer incidence counted in both genders and was ranked fifth among cancer deaths (1). It has been reported that breast cancer caused 502,000 deaths worldwide in 2005, accounting for 7% of cancer deaths and almost 1% of all fatal cases (2). Almost a quarter of women experience breast disease throughout their lives (1,2). More women face the risk of breast cancer because of improvements in the life span of people as a result of advances in health systems worldwide. Most women who come to the surgical outpatient clinic complaining of pain in the chest, a lump, or discharge from the nipple (3). There are several methods for the diagnosis of a breast lump, such as mammography, ultrasonography, and fine-needle aspiration cytology, all of which have both medical and financial costs (4). On the other hand, clinical evaluation is both cheap and noninvasive. The patient may be critical as the first step in identifying cases in the meeting with the doctor (5). Evaluating the suspected breast mass as soon as possible and with the correct diagnosis will reduce the mortality and morbidity associated with the disease caused by breast malignancy. Therefore, clinical evaluation is a valuable diagnostic tool. Since clinical examination requires funds and/or facilities for more sophisticated diagnostic methods, it is much more prominent in the diagnosis in rural areas (6). A systematic approach with clinical examination criteria is also important to reduce unnecessary patient admissions or patient expenditures. More importantly, it is essential for the clinician to diagnose malignancy more accurately and to plan the surgical treatment of patients as an outpatient or inpatient. A mass in the chest is a very worrying situation for the patient. Because of this; Reliable, non-invasive and rapid diagnostic examinations help reduce current anxiety and provide an advantage in early diagnosis. The clinical examination is a simple method to detect breast masses and their nature as it is inexpensive and noninvasive and if found to be accurate, might be of great value as a diagnostic tool.

As we briefly emphasized above, we want to examine the approaches of clinics to this step by considering that breast examination is as least as important as a physical examination is in other diseases of medicine. The primary purpose of this study was to examine the incidence of breast cancer among patients who came to different clinics for breast examination and to examine the approaches of each clinic to this patient group. The second purpose of this study was to evaluate the contribution of clinical examination toward the diagnosis of breast cancer.

Material and Methods

On July 10, 2019, and with the study number 90057706-799-E375, permission was obtained from the Etlik Zübeyde Hanım Obstetrics and Gynecology Training and Research Hospital Medical Education Unit. Between January 1, 2015, and June 15, 2019, mammography reports were screened using the Breast Imaging-Reporting and Data System (BI-RADS). Patients

who came to general surgery (GS), internal medicine (IM), and gynecology outpatient (OG) clinics of our hospital for breast examination were retrospectively analyzed. Continuous variables were reported on average and standard deviation, while categorical nominal variables were determined as a percentage of the total population. The distribution status of cases was evaluated by the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for continuous variables or the Student's t-test for independent groups. A Chi-square test will be used for binary variables, or Fisher's exact test will be performed for statistical comparisons between clinical situations according to distribution status. The final results will be achieved by binary multiple regression. Values of p <.05 will be considered statistically significant.

A total of 8024 mammography records were screened after excluding unclear or missing data. The accuracy of clinical assessment at an outpatient facility was determined by comparison with the mammography.

Results

The total number of patients who underwent mammography examination for mammography was 7998. According to clinical distribution, 1769 of them were GS, 456 of them were IM, and 5773 of them were OG outpatient clinics (Figure 1). The mean age was 48 ± 2.3 years in GS, 48 ± 6.7 years in IM, and 47 ± 3.9 years in OG outpatient clinic (p >.05). Of the 1769 patients admitted to GS, 43 patients had malignancy. Malignancy was diagnosed in 21 OG after mammography examination, and malignancy was detected in five patients after mammography examination in the IM clinic (Table1). In terms of clinical dominance, the general surgery clinic has emerged as the most effective clinic in putting breast malignancy [AOR: 0.34 (0.21,0.54) (P <0.001)]. Among patients with mammography BIRADS 4 and 5, the risk of malignancy was higher than in those with BIRADS 0-1-2-3 [AOR: 0.81 (0.72,0.9) (P <0.001)](Table2).

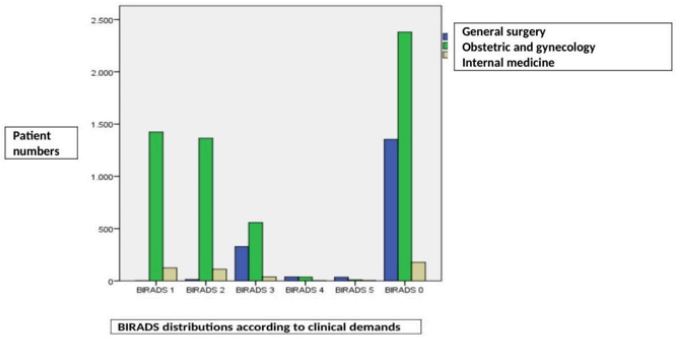

Figure 1: Graph of mammography results by BIRADS distributions

Table 1. The distribution of patient mammograms

	Internal medicine	Obstetrics and gynecology	General surgery	Total number (n)	P <.05
Age (Mean ± SD)	48 ± 6.7	47 ± 3.9	48 ± 2.3		0.13
BIRADS 0	177	2380	1375	3932	
.001					
BIRADS I	124	1424	2	1550	
BIRADS II	111	1365	14	1490	
BIRADS III	37	558	328	923	
BIRADS IV	3	36	15	54 (0.7%)	
BIRADS V	4	10	35	49 (0.6%)	
Meme USG	427	516	815		
The number of malignant breast cases after pathology report	[5 (1.1%) vs. 451 (89.9%]	[21 (0.4%) vs. 5752 (99.6%)]	[43 (2.43%) vs. 1726 (97.57%)]	69 (0.86%)	.01
Total number of mammograms	456	5773	1769	7998	

Table 2. Malignancy risk ratios in terms of clinic and BIRADS distrubitions

		Malign Cases	Benign Cases	P<0.05	Adjusted odds ratio [Exp(B)]	P<0.05
Clinic codes	GS	(90% CI)/Adjusted mean	1726(21.8%)	0.001	0.34(0.21,0.54)	0.001
	OG	difference (90% CI)	P<0.05			
	IM	5 (7.2%)	451(5.7%)			
	Total	69(100%)	7929(100%)			
BIRADS4,5 vs BI-RADS0-1-2-3		67/125(97.1%) vs 2*(2.9%)	0.001	0.81(0.72,0.9)	0.001	
*BIRAD-S 0 cases						

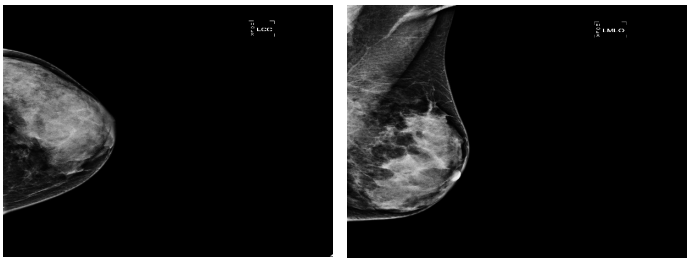

Figure 2a (mediolateral) and **2b** (oblique) mammograph results are samples for BI-RADS 0 breast malignancy.

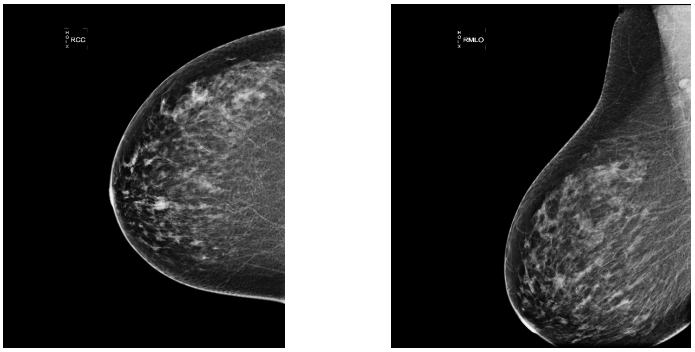

Figure 3a (Right craniocaudal) and **3b** (right mediolateral oblique) BI-RADS 0 mammography diagnosed with malignancy, after surgery.

Discussion

This study is one of the rare studies that investigated the interdisciplinary relationship between routine breast cancer examinations and additional exams that were also important since they included a high number of cases. When we examined the world literature, Huang and colleagues in a study of 1.2 million Chinese women, stated cancer detection rates for urban women (0.6/1000) and rural women (0.5/1000) (7). On the other hand, when we examined other studies in other fields, we found rates to be lower than in the early breast and cervical cancer detection program in the USA (8,9). According to the United Kingdom, (5.4/1000 to 6.7/1000 in the National Health Service Breast Screening Program (NHS-BSP) (10,11) and Canada [Cancer detection rates in the Canadian National Breast Screening Study (CNBSS) data (2.5/1000 to 7.9/1000) CNBSS 2 (3.5/1000)] were found (12,13). The malignancy rate detected in our study was 0.86%, or 8.6/1000, and was consistent with the results of these studies. In addition, Jiagge et al. found that the high incidence of breast cancer among women, especially in low- and middle-income countries (LMICs), is higher because of insufficient sociocultural barriers and early detection programs (14). Sylla and Wild reported that especially suboptimal transportation increased breast cancer mortality (15). With regard to the correct diagnosis of breast masses, Masooda and colleagues reported that breast examination, mammography, and pathological examination after resection of suspicious masses are three important cornerstones (16). Among our series two cese were BIRAD-S 0 and they final pathological results with malignancy (Figure 2a-2b and 3a-3b). More importantly, these two patients belonged to the general surgery clinic. Although BIRADS 0 lesions do not pose a clear risk for malignancy, they cannot be said to be very innocent. Because there is no clear situation in terms of benignity such as BIRAD-S 1 and BIRAD-S 2. Triple evaluation is a very useful diagnostic tool for the successful identification of breast cancer patients and has increased the diagnosis of breast cancer patients by 99.3%. Triple evaluation was particularly useful in detecting most breast cancers at an early stage: Phase I or Stage II (T1 or T2: N0 or N1, M0) (16). In our opinion that especially in cases where mammography is ambiguous, such as BI-RADS 0 lesions, early malignancies can be detected in these lesions, as we see in the GS clinic, thanks to physical examination, anamnesis and radiological imaging. Brown et al. emphasized the use of a multidisciplinary approach that involves GS, OG, and oncology clinics to provide balanced care (17). We think that interclinic cooperation is important for the diagnosis of breast cancer and the distribution of patients referred to the GS clinic with the diagnosis of breast cancer. Because, in our study, we found that 21 patients (30.4%) were referred to the GS clinic with the diagnosis of breast cancer from the OG clinics and the other five cases were referred from IM clinics with interclinic collaboration, especially regarding screening and early diagnosis of breast cancer. Although the OG clinic is thought to have the lowest rate of diagnosing mammographic breast cancer malignancy according to the number of mammographies requested, we attribute this to referrals to the OG clinic of women who are in the perimenopausal period, especially those in the 45-55 year age group. At this point, we see that OG clinics have also performed an important screening task. Therefore, the coordination of the OG clinic with the GS outpatient clinic is of particular importance. Population-based studies have demonstrated that mammography is successful in early diagnosis and can reduce breast cancer mortality (18, 19, 20). In a Cochrane review analysis, it was stated that mammography screening for breast cancer decreases breast cancer mortality. On the other hand, although its effectiveness is not apparent, the estimated relative risk reduction in breast cancer mortality is 15% (21).The American Cancer Society (ACS) also recommends performing a clinical breast examination and mammography in the early diagnosis

of breast cancer (22). Also, the ACS emphasized that women should know how a normal breast is, and healthcare providers need to be informed about the changes that might occur in the early stages of breast diseases and the importance of breast self-examination (BSE). On the other hand, the Cochrane Review does not suggest that screening by BSE has a beneficial effect (23). As part of their periodic medical examinations, the ACS recommends clinical breast examinations every year for women aged 20 to 39 years, and preferably every year for women over the age of 40 years. For women over 40 years of age, an annual mammogram is recommended and continues as long as a woman has good health (24). In our opinion, clinical examination is very important, and if possible, a clinical guideline should be provided to the radiologist who will perform the mammography or ultrasound before the patient is directed to radiology. For this reason, breast examination performed in clinics other than GS should be directed to the GS policlinic after the mammography examination. In our study, other clinics directed patients after mammography to the GS policlinic and accounted for 37.68% of the total number of patients. The clinical breast examination, mammography, anamnesis, and interclinic communication are essential components not to overlook in early stage breast cancer. In our country, mammography for diagnosis and evaluation is paid by the state-financed health insurance programs, and routine mammograms may be requested by family medicine centers (25). However, Dündar et al. stated in their study that only 27%-39% of the women could perform BSE, 23.4% had no information about breast cancer, 27.9% did not have any knowledge of BSE, and 75% had no previous history of breast examination. At the end of their study, Dündar et al. emphasized that 89.3% of cases had not had mammography performed (26).

Conclusion

In our opinion, although the rates of mammography and BSE are much higher today, we think that the clinical breast examination remains low because of direct mammography and breast ultrasound preference. This means that anamnesis, physical examination, radiological examination, and the absence of triple hair foot can lead to delays in diagnosis.

Conflict of interest

The authors declares none any conflict of interests.

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Original Article

The Mediterranean Diet Effects on Atrial Premature Complexes.

Akdeniz Diyetinin Atriyal Prematür Kompleks Üzerine Etkileri.

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Abstract

Aim: The aim of this study was to evaluate the relationship between atrial premature complexes (APC) and Mediterranean diet score. Rhythm disturbances in the heart significantly affect the patients' quality of life.

Material and Methods: This study was conducted on 50 patients with palpitations who were referred to the cardiology outpatient clinic and had more than 10000 APC per day as a result of a 24-hour holter, and 50 patients who presented with palpitations but had less than 10,000 APC in the holter. Diet quality was determined by scoring method (5, 6-9 and ≥10 points) 'Mediterranean Diet Adaptation Scale' and compared between groups.

Results: There was no difference between the two groups in terms of clinical and demographic characteristics. Mediterranean diet scores were lower in patients with APC ≥10.000/day ($p<0.001$). A significant negative correlation was found between APC and Mediterranean diet score ($p<0.001$, $r = -0.560$).

Conclusion: The protective role of Mediterranean diet type nutrition on the frequency of APC was clearly observed in our study. This study, which is one of the limited numbers of studies examining the relationship between the Mediterranean diet and APC, may be helpful in understanding the pathophysiology of APC.

Keywords: Atrial premature complexes; Mediterranean diet score; Arrhythmia

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Öz

Amaç: Bu çalışmanın amacı, atriyal prematüre kompleksler (APK) ile Akdeniz diyeti skoru arasındaki ilişkiyi değerlendirmektir. Kalpteki ritim bozuklukları hastaların yaşam kalitesini önemli ölçüde etkiler.

Gereç ve Yöntemler: Bu çalışma, çarpıntı şikayeti ile kardiyoloji polikliniğine başvuran ve 24 saatlik holter sonucu günde 10000' den fazla APK' si olan 50 hasta ve çarpıntı şikayeti ile başvuran ancak APK' si 10.000' den az olan 50 hasta üzerinde yapıldı. Diyet kalitesi puanlama yöntemi (5, 6-9 ve ≥10 puan) 'Akdeniz Diyeti Uyum Ölçeği' ile belirlendi ve gruplar arasında karşılaştırıldı.

Bulgular: İki grup arasında klinik ve demografik özellikler açısından fark yoktu. APK ≥10.000/gün olan hastalarda Akdeniz diyeti skorları daha düşük bulundu ($p<0.001$). APC ile Akdeniz diyeti puanı arasında anlamlı bir negatif korelasyon bulundu ($p<0.001$, $r = -0.560$).

Sonuç: Akdeniz diyeti tipi beslenmenin APK sıklığı üzerindeki koruyucu rolü çalışmamızda net bir şekilde gözlendi. Akdeniz diyeti ile APK ilişkisini inceleyen sınırlı sayıdaki çalışmalardan biri olan bu çalışma, APK' nin patofizyolojisinin anlaşılmasında yardımcı olabilir.

Anahtar Kelimeler: Atriyal prematüre kompleks; Akdeniz diyeti puanı; Aritmi

Introduction

Typical dietary habits and style of societies surrounding the Mediterranean; includes high consumption of fruits, vegetables, monounsaturated fats, fish, whole wheat, legumes, and nuts, as well as low consumption of red meat[1]. This type of healthy diet has the potential to have anti-arrhythmic effects with anti-inflammatory, antioxidant, and cytoprotective effects[2]. Previous studies have identified the protective effect of the Mediterranean diet on atrial fibrillation[3]. Antiarrhythmic effects associated with foods frequently used in the Mediterranean diet, such as fruits, walnuts, and olive oil, have been identified. However, The number of studies examining the antiarrhythmic effects of the Mediterranean diet still needs to be increased.

Atrial premature complexes (APC) is a common arrhythmia generally considered benign. It has been reported that the prevalence is up to 73% in young individuals and 100% in healthy elderly individuals[4]. Despite their benign concept, APCs are more common in patients with underlying cardiac conditions such as coronary heart disease, chronic rheumatic heart disease, left ventricular dysfunction, hypertension, and hyperthyroidism. In addition, rapid APCs from arrhythmogenic foci in the pulmonary veins often precede AF attacks in patients with paroxysmal atrial fibrillation (AF)[5].

The increased burden of premature atrial contractions (APCs) and subclinical atrial tachyarrhythmias have been shown to be strong and independent predictors of incident AF and associated complications as the effect of LA structural remodeling[6], indicating the critical role of atrial electric activity in triggering AF and maintenance[7].

This study aims to evaluate the relationship between frequent APCs and Mediterranean diet score.

Material and Methods

In this study, patients who complained of palpitations in the cardiology outpatient clinic at Süleyman Demirel University between December 2018 and September 2019 and who had more than 10.000 APCs daily and also had less than 10.000 APCs. Seventy-two hours prior to the Holter test, caffeine-containing beverages, stimulants, and medications that can alter cardiac rhythm were discontinued. Many publications and guidelines recommend a cut-off value of 10,000/day for catheter ablation or medical therapy[8]. A total of 163 patients were reviewed by the cardiologist, and the study was completed when both groups reached 50 patients. The "Mediterranean diet compliance questionnaire" is a valid questionnaire for Mediterranean populations[9]. Questions were asked by the researcher in the Mediterranean diet compliance questionnaire (Table 1)[10]. The portion amounts consumed by people were assessed using colored representations of foods. The scoring system was used to evaluate the consumption of fish, monounsaturated fats, fermented milk products, whole grains, vegetables, fruits, legumes, nuts, and red meat on average (5, 6–9, or ≥10 points)[10]. Individuals with higher scores were considered to eat more consistently with the

Mediterranean diet. The body weight (kg), height (cm), and waist circumference (cm) of the individuals were taken per the measurement technique, and body mass index (BMI) was calculated according to these measurements. By dividing the body height by the height square, the BMI was determined. The waist-to-length ratio is a measure of body fat distribution calculated by dividing waist size by the height ratio. Patients with hypertension were defined as having a systolic/diastolic blood pressure of 140/90 mmHg or higher and/or taking antihypertensive medication. Diabetes mellitus was defined as patients with fasting plasma glucose level ≥126 mg/dL or actively using oral antidiabetic and/or insulin. Hyperlipidemia was defined as a total cholesterol level ≥200 mg/dL. Patients with active infection, secondary tachycardia, congestive heart failure, symptomatic congenital heart disease, symptomatic valvular heart disease, diagnosed coronary artery disease, diagnosed psychiatric disorder, and eating disorders such as anorexia, neurosis, and bulimia were excluded from the study. In order to conduct the study, necessary patient consent and ethics committee permission were obtained.

Table 1. Validated 14-item Questionnaire of Mediterranean diet adherence.

Questions	Criteria for 1 point
1. Do you use olive oil as main culinary fat?	Yes
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)?	≥4 tbsp
3. How many vegetable servings do you consume per day? (1 serving : 200 g [consider side dishes as half a serving])	≥2 (≥1 portion raw or as a salad)
4. How many fruit units (including natural fruit juices) do you consume per day?	≥3
5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving: 100–150 g)	<1
6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g)	<1
7. How many sweet or carbonated beverages do you drink per day?	<1
8. How much wine do you drink per week?	≥7 glasses
9. How many servings of legumes do you consume per week? (1 serving : 150 g)	≥3
10. How many servings of fish or shellfish do you consume per week? (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish)	≥3
11. How many times per week do you consume commercial sweets or pastries (not home-made), such as cakes, cookies, biscuits, orcustard?	<3
12. How many servings of nuts (including peanuts) do you consume per week? (1 serving 30 g)	≥3
13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomatoand onion, leek, or garlic and simmered with olive oil)?	≥2

Statistics analysis

All statistical analyses were performed using SPSS for Windows version 19.0 (SPSS, Chicago, IL). The number of each group was adjusted to 50 patients. We calculated the minimum number of individuals that should be sampled with 90% power and 0.05 Type-I error as at least 44 (R 3.0.1. open source program). The primary effect variable was calculated as ± 0.18. For the descriptive statistics of the data, mean, standard deviation, rate, and frequency values were used. The Kolmogorov–Smirnov test was used to evaluate whether the distribution of continuous variables was normal. For the analysis of parametric data, Student's t-test was used. For the analysis of nonparametric data, the Mann–Whitney U test was used. The v2 test was used to compare the categorical variables between groups. Pearson correlation analysis was used for correlation analysis to assess the correlation between the number of APC and Mediterranean diet score. Statistical significance was defined as $p<0.05$.

Results

The basic parameters of both groups are shown in Table 2. There was no difference between the two groups regarding clinical and demographic characteristics. However, Mediterranean diet scores were lower in patients with APC ≥10,000/day ($p<0.001$). The significant negative correlation between the number of APCs and the Mediterranean diet score is shown in Figure 1 ($p<0.001$, $r= -0.560$).

Table 2. Baseline general and clinical characteristics of the study population			
Variables	APC group (n=50)	Control group (n=50)	p value
Age,years	51.0 ± 10.5	55.1 ± 9.4	0.214
BMI, kg/m2	33.1 ± 3.6	27.7 ± 4.2	<0.001
Waist circumference, cm	92.5 ± 11.6	85.1 ± 9.9	<0.001
Smoking, n (%)	22 (44.0)	15 (30.0)	0.147
Hypertension, n (%)	7 (14.0)	4 (8.0)	0.338
Hyperlipidemia, n (%)	13 (26.0)	10 (20.0)	0.476
Diabetes Mellitus, n (%)	7 (14.0)	5 (10.0)	0.538
Female, n (%)	28 (56.0)	33 (66.0)	0.305
Married, n (%)	25 (50.0)	20 (40.0)	0.315
Ejection Fraction, (%)	625 ± 3.2	61.5 ± 6.2	0.502
Education level, n (%)			0.643
Literate	11 (20.0)	12 (24.0)	
Middle School	24 (44.0)	38 (20.0)	
High School and above	15 (36.0)	19 (38.0)	
Physical activity			0.703
Sedentary (<600 METs-min/week)	36 (72.0)	32 (64.0)	
Inactive (600-3000 METs- min/week)	14 (38.0)	17 (34.0)	
Active (>3000 METs- min/week)	0 (0.0)	1 (2.0)	
Mediterranean diet score	3.8 ± 2.3	5.5 ± 2.1	<0.001
Data are given as mean ± standard deviation or number (%) [n (%)], BMI: Body mass index, METs: Metabolic Equivalent Minutes			

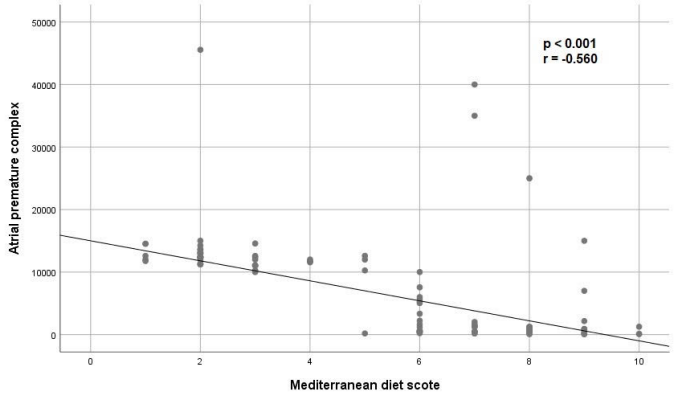

Figure 1. The correlation between Mediterranean diet score and atrial premature complexes

Discussion

In our study, Mediterranean diet scores were lower in patients with APC ≥10,000/day than in patients with APC <10,000/day. In addition, our study showed a statistically significant and negative correlation between the Mediterranean diet score and the number of APCs. This study is one of the few studies examining the potential antiarrhythmic effects of the Mediterranean diet.

Many studies in recent years have shown that there is a close relationship between diet and cardiovascular diseases[11]. The Mediterranean diet is recognized as one of the healthiest diets worldwide in terms of the prevention of cardiovascular diseases and metabolic syndrome. People living in the Mediterranean region show moderate ethanol, low consumption of meat and meat products, and high consumption of vegetables, fruits, fish, nuts, whole wheat, and legumes[12]. The primary source of fat in this diet is olive oil, and the main components of the Mediterranean diet have been shown to have potential cardiovascular protective effects, such as antioxidant and anti-inflammatory effects[13]. The number of studies investigating the Mediterranean diet and its potential antiarrhythmic effects is limited[14]. Due to heavy fish consumption, the Mediterranean diet is rich in n-3 polyunsaturated fatty acids (n-3 PUFA). The ATTICA study showed that long-term fish consumption of healthy individuals in the Mediterranean region was associated with protection from arrhythmias[15, 16]. A large-scale study by Mattioli et al. showed that adopting a Mediterranean diet and antioxidant intake enhanced the spontaneous conversion of atrial fibrillation to sinus rhythm[17]. In addition, low adoption of the Mediterranean diet was associated with the development of persistent atrial fibrillation, and high adoption of the Mediterranean diet was associated with the prevention of atrial fibrillation[18].

Etiology of cardiac arrhythmias is associated with alcohol or tobacco use and a marked increase in myocardial oxidative stress in addition to the risk factors such as myocardial infarction, congestive, heart failure, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, Coxsackie virus, higher CHA2DS2-VASC score.

Chong et al. showed that patients with frequent APCs are at greater risk for new AF onset and other adverse cardiovascular events, including ischemic stroke, heart failure, and mortality[19]. Various studies have indicated that supplements such as N-acetylcysteine, polyunsaturated fatty acids (n-3 PUFA), and antioxidant vitamins may be effective in preventing both postoperative AF (POAF) and ventricular extrasystole[20]. Costanzo et al. demonstrated that a Mediterranean diet similar to a long-term intense antioxidant diet reduces the risk of POAF after cardiac surgery [21]. Studies on potential nutritional impacts on heart rhythm are becoming more prevalent in the literature. An essential part of a healthy diet, n-3 PUFA has been shown in numerous studies to have positive effects on the cardiovascular system[22]. Animal studies and in vitro research have both shown that n-3 PUFA has anti-arrhythmic properties[23]. In an electrophysiological study, fish oil consumption decreased the frequency of induced ventricular fibrillation in marmoset monkeys[24]. It has been demonstrated that n-3 PUFA alters the conductivity of ion channels in the cell membrane of cardiomyocyte cultures, reducing the development of arrhythmias [25]. Additionally, n-3 PUFA may have an impact on sodium and calcium currents that traverse cardiac cell membranes and regulate heart rhythm [25]. n-3 PUFAs are thought to prolong the idle time of these channels and reduce their conductivity[25]. Moreover, incorporating n-3 PUFA into myocyte cell membrane phospholipids can reduce vulnerability to arrhythmias by affecting the production of various eicosanoids, thereby preventing ventricular fibrillation during myocardial ischemia and reperfusion.

Conclusion

This investigation into the connection between the Mediterranean diet and APC may aid in our understanding of the pathophysiology of the condition and lead to further research. Although there are few effective medical treatments for APC, the Mediterranean diet may play a protective function and be crucial to understanding its etiology. Turkey is mainly agricultural, and 20% of the nation has a Mediterranean climate. The Mediterranean diet also has a "sustainable" structure, making it an important nutritional reference for current and future generations. The nation's economy and public health may gain from the spread of the Mediterranean diet as a health policy. A multidisciplinary strategy with a specialized team may be more effective in preventing and treating the disease than a single medical therapy method. In light of these findings, maintaining a Mediterranean diet and nutritional lifestyle throughout one's life may help to lower the prevalence of APC and other arrhythmias.

Our study has some limitations, including a cross-sectional design, a small sample size, and no MACE follow-up data. In addition, this study is a retrospective screening study and depends on the memory factor. Therefore, multicenter prospective longitudinal studies with bigger sample sizes should be used to validate our findings.

Authors' Note

All authors made substantial contributions to conception and design of the study, and acquisition, analysis and interpretation of data, drafting or revising the manuscript to include important intellectual content, and approval of the final version of the manuscript readily to be published.

Conflict of Interest Statement

The author(s) do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.

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Ethical statement

The study protocol was approved by the Suleyman Demirel University Clinical Trials and Ethics Committee.

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Original Article

Relationship between the Castelli risk indeces and the presence and severity of ischemia in non-geriatric patients with suspected coronary artery disease

Koroner arter hastalığı şüphesi olan non-geriatrik hastalarda Castelli risk indeksleri ile iskeminin varlığı ve şiddeti arasındaki ilişki

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Abstract

Aim: This study aimed to investigate the relationship between ischemia severity and Castelli risk indices (CRI) levels in non-geriatric patients with suspected coronary artery disease (CAD) referred to myocardial perfusion scintigraphy (MPS) with gated single photon emission computed tomography (SPECT).

Material and Methods: This retrospective study included 417 non-geriatric patients referred to SPECT MPS for suspected CAD at the Cardiology Clinic between January 2019 and January 2021. Patients were divided into normal, mild, moderate, and severe ischemia groups according to MPS. CRIs were calculated as follows: CRI-I = total cholesterol / high-density lipoprotein cholesterol (HDL) ratio; CRI-II = low-density lipoprotein cholesterol / HDL ratio.

Results: The CRIs levels were higher in ischemia group than non-ischemia group. Increase in CRI-II level was associated with increased ischemia severity. Increased CRI-II level was found to be an independent predictor of mild, moderate and severe ischemia group, but CRI-I was similar in moderate and severe ischemia groups. The threshold value of CRI-II for predicting the presence of ischemia was >2.1 (Area under the curve [AUC] ± standard error = 0.787 ± 0.02, sensitivity = 79.5%, specificity = 71.4%). The threshold values of CRI-II showed a gradual increase in predicting the severity of ischemia.

Conclusion: CRI-II offers offers gradually increasing threshold values in distinguishing patients with suspected CAD but without perfusion defects or determining its severity in the case of ischemia. CRI-II can be a potential screening tool for patients with suspected CAD and it can be used for risk stratification.

Keywords: Castelli risk index, coronary artery disease, ischemia, lipids.

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Öz

Amaç: Bu çalışmada, kapılı tek foton emisyonlu bilgisayarlı tomografi (SPECT) ile miyokardiyal perfüzyon sintigrafisine (MPS) yönlendirilen koroner arter hastalığı (KAH) şüphesi olan non-geriatrik hastalarda iskemi şiddeti ile Castelli risk indeksleri (CRI) arasındaki ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif çalışmaya Ocak 2019 ile Ocak 2021 arasında Kardiyoloji Kliniğinde KAH şüphesi nedeniyle SPECT MPS'ye yönlendirilen 417 non-geriatrik hastayı dahil edildi. Hastalar MPS'ye göre normal, hafif, orta ve ağır iskemi gruplarına ayrıldı. CRI düzeyleri CRI-I = toplam kolesterol / yüksek yoğunluklu lipoprotein kolesterol (HDL) oranı; CRI-II = düşük yoğunluklu lipoprotein kolesterol / HDL oranı olarak hesaplandı.

Bulgular: CRI seviyeleri iskemi grubunda iskemisi olmayan gruba göre daha yüksekti. CRI-II seviyesindeki artış, artan iskemi şiddeti ile ilişkili saptandı. Artmış CRI-II düzeyi, hafif, orta ve ağır iskemi grubu için bağımsız bir belirteç olarak bulundu, ancak CRI-I, orta ve ağır iskemi gruplarında benzerdi. CRI-II'nin iskemi varlığını öngörme eşik değeri >2,1'dir [Eğri altındaki alan (AUC) ± standart hata = 0,787 ± 0,02; duyarlılık = %79,5; özgüllük = %71,4]. İskeminin ciddiyetini öngörmede CRI-II'nin eşik değerleri kademeli bir artış gösterdi.

Sonuçlar: CRI-II, KAH şüphesi olan ancak perfüzyon kusurları veya normal koroner arterleri olmayan hastaları ayırt etmede ve iskemi ciddiyetini belirlemede kademeli artan eşik değerler sunar. Bu nedenle, CRI-II KAH şüphesi olan hastalar için potansiyel bir tarama aracı olabilir ve risk sınıflandırması için kullanılabilir.

Anahtar kelimeler: Castelli risk indeksi, iskemi, koroner arter hastalığı, lipid.

Introduction

Coronary artery disease (CAD), which develops as a result of narrowing or occlusion of the coronary arteries due to atherosclerosis, is an important cause of mortality as well as being an important cause of global health burden and expenditures [1]. Evaluation of CAD requires both anatomical and functional information. Radionuclide cardiac imaging methods, especially myocardial perfusion scintigraphy (MPS), provide high-level evidence for the diagnosis and prognosis of CAD [2]. MPS, which is frequently used in clinical routine for diagnosis and risk determination or treatment planning in CAD, offers superiority in reducing the number of unnecessary coronary angiography (CAG) despite its radiation risk and cost. However, it is not easy to access because it is not available in every hospital [3]. Therefore, the use of easy, cheap and accessible markers among screening methods has an increasing importance [4].

Early diagnosis of atherosclerosis and determination of risk lesions in the coronary arteries have an important place in reducing cardiovascular diseases [5]. It is known that lipid metabolism plays an important role in the initiation and acceleration of atherosclerosis [6]. Lipid profiles are among the traditional risk factors for CAD [7]. Castelli risk indices (CRI) derived from lipid parameters have been shown to exhibit superior diagnostic performance in predicting cardiovascular diseases and events. CRI-I index obtained by dividing total cholesterol by high-density lipoprotein (HDL) cholesterol reflects the coronary plaques formation [8], while CRI-II obtained by dividing low-density lipoprotein (LDL) cholesterol by HDL cholesterol has been shown to be an excellent marker for cardiovascular risk [9]. Despite these prognostic findings of CRIs, to the best of our knowledge, we could not find any study evaluating the relationship between CRIs and severity of ischemia.

We hypothesized that CRIs levels could be easy, cheap and accessible markers for the classification of severity of ischemia due to atherosclerosis, which is play a role in the pathogenesis of CAD. This study aimed to investigate the relationship between ischemia severity and CRIs levels in non-geriatric patients with suspected CAD referred to MPS with gated single photon emission computed tomography (SPECT).

Material and Methods

This retrospective study included patients with suspected CAD who were referred for SPECT MPS in XXXXXX Hospital Cardiology Clinic between January 2019 and January 2021. The study initiated with the approval of the XXXXXX Hospital Ethics Committee (Date: 02.2023, Decision No: E1-23-3325) and was carried out in accordance with relevant ethical guidelines and the Declaration of Helsinki (revised in 2013, Brazil). Because of retrospective design, the waiver of informed approval was deemed appropriate by the ethics committee that approved the study.

Study Population

A total of 1512 non-geriatric patients with suspected CAD were assessed retrospectively and 1095 patients who did not meet the inclusion criteria were excluded. Exclusion criteria were geriatric age (>65 years), a history of any systemic inflammatory or autoimmune disease, history of CAD, history of myocardial infarction or heart failure, thyroid dysfunction, liver or kidney diseases, active hepatitis, malignancy, renal failure, history of anti-inflammatory or chronic corticosteroid or nephrotoxic drugs, pregnancy or delivery within the last 90 days, and missing clinical data. After the exclusion process, 417 patients were included in this study.

The hospital's electronic information system and patient files were used to gather clinical data. In repeated measurements, blood pressure of > 140 / 90 mmHg or use of anti-hypertensive drugs was defined as hypertension, and a fasting plasma glucose level of ≥ 126 mg/dL or use of anti-diabetic drugs was defined as diabetes mellitus.

Laboratory Measurements

The hospital's electronic information system and patient files were used to gather demographic and clinical data. Blood samples were taken at the time of admission and during follow-up and were measured using a Beckman Coulter LH 780 device (Mervue, Galway, Ireland). Levels of hemoglobin (photometrically), platelets (impedance method), C-reactive protein (CRP) (immunoturbidimetric method), albumin (bromocresol green method), triglycerides and total cholesterol (enzymatic colorimetric method), and HDL (homogeneous enzymatic colorimetric method) were determined. The Friedewald formula was used to determine LDL levels [10]. CRIs were calculated as follows: CRI-I = total cholesterol / HDL ratio; CRI-II = LDL / HDL ratio.

Myocardial Perfusion Imaging

Myocardial perfusion assessment had a 2-day stress and rest imaging protocol involving the use of technetium 99-m methoxy-isobutylisonitrile (Tc-99m MIBI). Radiopharmaceutical agents were administered on the peak hyperemia period or modified Bruce protocol during the peak exercise. An infusion of dipyridamole (0.142 mg/kg/min) or adenosine (0.28 mg/min) was administered for stress imaging. All imaging was initiated 30 to 45 minutes after injection of 15 to 20 mCi Tc-99m MIBI. If any perfusion defect was suspected in the stress images of the patients, a similar dose injection was applied to transmit the rest imaging.

SPECT Imaging Protocol

All images were acquired via low energy high resolution SPECT computed tomography (CT) scanner (GE Infinia Hawkeye 4, GE Healthcare, Buckinghamshire, UK) collimators, including 256×256 matrix utilizing 20% energy window focused on 140.5 keV photopeak of Tc-99m. Images were taken in a position where the patients were lying in the position of supine with their arms raised above their heads. Noise reduction and relative risk parameters were utilized for the images created via SPECT/CT analysis. The images were then reconstructed on workstation. After completion of each acquisition, a low dose CT scan of chest (120 kV, 20 mAs, pitch 0.938, collimation 16 ×1.25) was made to obtain a map of attenuation automatically applied through the processing software to allow for the correction of the emission data. The dataset of MPS was remapped via the attenuation map in CT to create the attenuation-corrected images.

The ischemia degree was classified by percentage of ischemia obtained in MPS images. According to this; zero was defined as "No ischemia", "Mild ischemia" if the percent ischemia is <5%, "moderate ischemia" if the percent ischemia is 5–9.9%, and "Severe ischemia" if the percent ischemia is ≥ 10%. Patients without ischemia were considered as the normal group.

Statistical Analysis

IBM SPSS Statistics for Windows 20.0 (IBM Corp., USA) was utilized in the analysis of all data obtained in this study. In light of the results of the Kolmogorov-Smirnov test, numerical data with normal distribution were identified and presented as mean ± standard deviation, while data found to have non-normal distribution were presented as median values with interquartile ranges (IQR). The Mann-Whitney U test and Student T-test were utilized when comparing two groups of data with normal distribution. For comparisons between more than two groups, the ANOVA (post-hoc: Benferroni test) and Kruskall-Wallis H test (post hoc: Dunn's test) were utilized according to the normality of the distribution. Categorical variables were assessed with numbers with percentages (%), and Fisher exact and Chi square tests were utilized in drawing comparisons between these groups of data. Stepwise multivariable multinomial logistic regression analysis was assessed to identify any possible independent predictors of severity of ischemia. Receiver operating characteristic (ROC) curve analysis was performed to evaluate diagnostic performance and results are presented with area under the curve (AUC), standard error (SE), sensitivity, and specificity. Threshold values were calculated with the Youden index method. Values of $p < 0.05$ were considered statistically significant.

Results

A total of 417 patients, 235 males and 182 females, with a mean age of 57.8 ± 6.7 years were included in the analysis. The baseline characteristics of the patients are presented in Table 1. Ischemia was detected in 73.6% (n = 307) of the patients referred to MPS. Severe ischemia was detected in 10.6% (n = 44) of all patients, moderate ischemia in 26.9% (n = 112) and mild ischemia in 36.2% (n = 151). The rates of diabetes mellitus (46.6% vs. 32.7%, p = 0.013) and hypertension (68.1% vs. 52.7%, p = 0.004) were higher in ischemia group. The rate of angiotensin-converting enzyme inhibitor (ACEi) / angiotensin receptor blockers (ARBs) and β-blocker users were higher in ischemia group. Median CRI-I and median CRI-II (3.8 vs. 2.3, p < 0.001) levels were higher in ischemia group than non-ischemia group (For CRI-I =3.8 vs. 2.3, p < 0.001; For CRI-II =3.0 vs. 1.7, p < 0.001) (Table 1).

Table 1. Demographic and laboratory findings associated with the presence of ischemia.

Variables	Study population n=417	Ischemia		p
		No n=110	Yes n=307	
Demographic findings				
Age, years	57.8 ± 6.7	57.3 ± 7.9	58.1 ± 6.2	0.282
Gender, n (%)				
Male	235 (56.4)	54 (49.1)	181 (59.0)	0.073
Female	182 (43.6)	56 (50.9)	126 (41.0)	
Smoking (%)	226 (54.2)	57 (51.8)	169 (55.0)	0.560
Diabetes mellitus, n (%)	179 (42.9)	36 (32.7)	143 (46.6)	0.013*
Hypertension, n (%)	267 (64.0)	58 (52.7)	209 (68.1)	0.004*
Drugs, n (%)				
ACEi / ARBs	218 (52.3)	47 (42.7)	171 (55.7)	0.019*
β-blocker	195 (46.8)	37 (33.6)	158 (51.5)	0.002*
CCBs	138 (33.1)	32 (29.1)	106 (34.5)	0.302
Diuretics	102 (24.5)	26 (23.6)	76 (24.8)	0.815
Oral antidiabetic drug	153 (36.7)	36 (32.7)	117 (38.1)	0.315
Laboratory findings				
Hemoglobin, g/dL	13.2 ± 1.5	13.3 ± 1.3	13.2 ± 1.6	0.539
Neutrophil, x109/L	4.8 ± 1.4	4.2 ± 1.2	5.0 ± 1.4	<0.001*
Platelet count, x109/L	240.0 ± 64.4	233.7 ± 73.5	242.3 ± 60.5	0.228
Lymphocyte, x109/L	2.2 ± 0.7	2.2 ± 0.7	2.2 ± 0.7	0.985
Monocyte, x109/L	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	<0.001*
RDW, %	13.9 ± 1.5	13.7 ± 1.4	13.9 ± 1.5	0.542
HDL, mg/dL	44.1 ± 9.7	48.9 ± 11.7	42.4 ± 8.2	<0.001*
LDL, mg/dL	112.6 ± 38.4	90.4 ± 35.6	115.5 ± 40.8	<0.001*
Triglycerides, mg/dL	136 (105-198)	114 (91-130)	166 (118-218)	<0.001*
Creatinine, mg/dL	0.8 (0.7-0.9)	0.8 (0.6-0.9)	0.8 (0.6-1.0)	0.427
CRP, mg/dL	0.4 (0.2-0.7)	0.3 (0.2-0.5)	0.5 (0.2-0.8)	<0.001*
CRI-I	3.1 (2-5.5)	2.3 (1.8-3.1)	3.8 (2.6-5.7)	<0.001*
CRI-II	2.8 (2.2-3.5)	1.7 (1.2-2.4)	3.0 (2.2-3.6)	<0.001*

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P <0.05 shows statistical significance.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; CRI, Castelli risk index; CRP, C-reactive protein; HDL, high density lipoprotein; LDL, low density lipoprotein; RDW, red cell distribution width.

Multivariable regression analysis results, which included findings related to the presence of ischemia, showed that hypertension (OR = 1.88; p = 0.015), monocytes (OR = 5.16; p = 0.041), and CRI-II (OR = 2.33; p < 0.001), were independent predictors for the presence of ischemia. The threshold value of CRI-II for predicting the presence of ischemia was >2.1 (AUC ± SE = 0.787 ± 0.02, sensitivity = 79.5%, specificity = 71.8%). CRI-II levels showed superior diagnostic performance in predicting the presence of ischemia (Figure 1).

Table 2. Independent predictors for presence of ischemia.

	Univariable Regression			Multivariable Regression		
	OR	95% CI	p	OR	95% CI	p
Gender						
Male	ref			ref		
Female	0.67	0.43-1.04	0.074	-	-	-
Diabetes mellitus	1.79	1.14-2.83	0.012*	-	-	-
Hypertension	1.91	1.23-2.98	0.004*	1.88	1.13-3.15	0.015*
Neutrophil	1.56	1.30-1.85	<0.001*	-	-	-
Monocyte	2.82	1.40-4.05	<0.001*	2.56	1.07-4.26	0.041*
CRP	1.38	1.04-1.75	<0.001*	-	-	-
CRI-I	1.94	1.60-2.36	<0.001*	-	-	-
CRI-II	2.30	1.81-2.92	<0.001*	2.33	1.80-3.00	<0.001*
				Nagelkerke R2=0.386; p < 0.001*		

In the multivariate regression analysis, the effects of age and drugs were adjusted. * P <0.05 shows statistical significance.
Abbreviations: CI, confidence interval; CRI, Castelli risk index; CRP, C-reactive protein; OR, odds ratio.

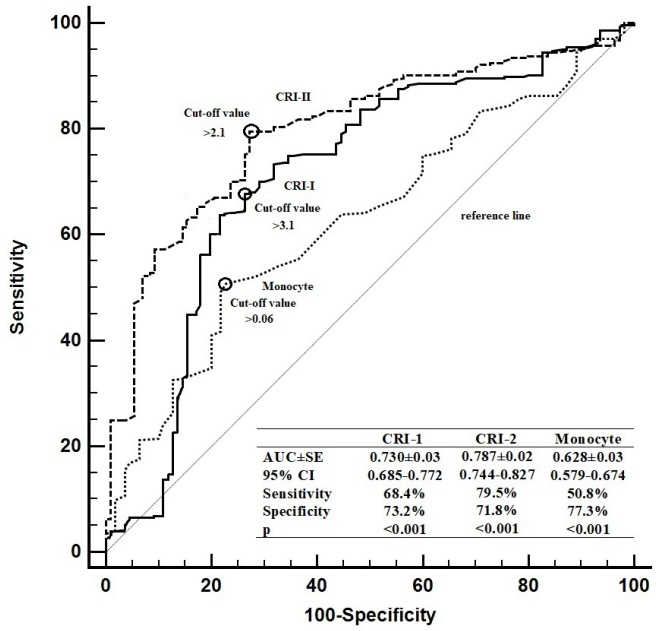

Figure 1. Diagnostic performance assessment of CRI in predicting presence of ischemia.

The rates of diabetes mellitus and hypertension were similar in moderate and severe ischemia groups, while their rates were higher than mild ischemia and non-ischemia group. The rates of diabetes mellitus and hypertension were similar in mild ischemia and non-ischemia group. Median CRI-I level was similar in moderate and severe ischemia groups, while it was higher compared to mild ischemia and non-ischemia group. Median CRI-II level was lower in the normal group than other ischemia groups, while it increased as the severity of ischemia increased (Table 3).

The results of the multivariable regression model analysis, which included the findings related to severity of ischemia, are presented in Table 4. An increased CRI-II levels was independent predictors of mild ischemia group (vs. normal groups) (OR = 2.29, p < 0.001) moderate ischemia group (vs. mild ischemia groups) (OR = 1.98, p = 0.002) and severe ischemia group (vs. moderate ischemia group) (OR = 1.77, p = 0.003). Diagnostic performance assessment of CRI in predicting severity of ischemia is shown in Table 5. Accordingly, it was determined that the threshold values of CRI showed a gradual increase in predicting the severity of ischemia.

There was a positive correlation between CRI-I levels and neutrophil level (r = 0.284, p = 0.023), platelet level (r = 0.271, p = 0.031), and CRP level (r = 0.288, p = 0.018). CRI-II levels were also positively correlated with neutrophil level (r = 0.308, p = 0.001), platelet level (r = 0.292, p = 0.018) and CRP level (r = 0.314, p < 0.001).

MPS results were normal in 79 patients with CRI-II levels of <2.1. These patients constituted 18.9% of all population.

Discussion

The main findings of this study, which evaluated for the first time the relationship between the CRI and presence and severity of ischemia in patients with suspected CAD referred to MPS, were as follows: 1) Higher CRI levels were detected in patients with ischemia, while CRI-II levels was correlated with ischemia severity, but not CRI-I. 2) CRI-II was a co-independent predictor of presence and severity of ischemia (3) CRI-II threshold levels showed a gradual increase in predicting ischemia severity.

MPS is a non-invasive imaging method that is frequently used in the diagnosis of CAD and in monitoring the effectiveness of interventional or medical treatment [11].. However, a significant

Table 3. Demographic and laboratory findings associated with the grade of ischemia.

Variables	Normal (No Ischemia) n=110	Severity of Ischemia			p
		Mild n=151	Moderate n=112	Severe n=44	
Demographic findings					
Age, years	57.3 ± 7.9	57.8 ± 6.6	58.1 ± 5.6	58.5 ± 5.5	0.257
Gender, n (%)					
Male	54 (49.1)	73 (48.3)	78 (69.6)	30 (68.2)	0.001*
Female	56 (50.9)	78 (51.7)	34 (30.4)	14 (31.8)	
Smoking (%)	57 (51.8)	78 (51.7)	63 (56.3)	28 (63.6)	0.491
Diabetes mellitus, n (%)	36 (32.7)	64 (42.4)	57 (50.9)	22 (50.0)	0.036*
Hypertension, n (%)	58 (52.7)	89 (58.9)	86 (76.8)	34 (77.3)	<0.001*
Drugs, n(%)					
ACEi / ARBs	47 (42.7)	64 (42.4)	79 (70.5)	28 (63.6)	<0.001*
β-blocker	37 (33.6)	62 (41.1)	68 (60.7)	28 (63.6)	<0.001*
CCB	32 (29.1)	49 (32.5)	41 (36.6)	16 (36.4)	0.564
Diuretics	26 (23.6)	35 (23.2)	28 (25.0)	13 (29.5)	0.834
Oral antidiabetic drug	36 (32.7)	55 (36.4)	44 (39.3)	18 (40.9)	0.698
Laboratory findings					
Hemoglobin, g/dL	13.3 ± 1.3	13.3 ± 1.6	13.2 ± 1.6	13.2 ± 1.8	0.168
Neutrophil, x109/L	4.2 ± 1.2	4.7 ± 1.4	5.3 ± 1.5	5.2 ± 1.4	<0.001*
Platelet, x109/L	233.7 ± 73.5	234.8 ± 59.2	246.3 ± 55.8	257.9 ± 74.8	0.109
Lymphocyte, x109/L	2.2 ± 0.7	2.2 ± 0.6	2.2 ± 0.7	2.1 ± 0.6	0.726
Monocyte, x109/L	0.6 ± 0.2	0.6 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	<0.001*
RDW, %	13.7 ± 1.4	13.8 ± 1.6	13.9 ± 1.3	13.8 ± 1.6	0.278
HDL-C, mg/dL	48.9 ± 11.7	43.1 ± 8.0	42.4 ± 8.6	39.0 ± 7.5	<0.001*
LDL-C, mg/dL	90.4 ± 35.6	110.8 ± 42.0	125.3 ± 38.6	127.0 ± 34.0	<0.001*
Triglycerides, mg/dL	114 (91-130)	135 (102-175)	164 (118-240)	175 (123-230)	<0.001*
Creatinine, mg/dL	0.8 (0.6-0.9)	0.8 (0.7-0.9)	0.8 (0.6-1.0)	0.9 (0.8-1.0)	0.215
CRP, mg/dL	0.3 (0.2-0.5)	0.3 (0.2-0.6)	0.6 (0.3-1.0)	0.9 (0.5-1.3)	<0.001*
CRI-I	2.3 (1.8-3.1)	3.0 (2.4-4.6)	3.8 (2.7-5.5)	3.9 (2.7-6.0)	<0.001*
CRI-II	1.7 (1.2-2.4)	2.2 (1.6-3.0)	2.9 (2.3-3.6)	3.4 (2.6-4.2)	<0.001*

Numerical variables were shown as mean ± standard deviation or median (IQR). Categorical variables were shown as numbers (%). * P <0.05 shows statistical significance. Bold characters indicate the difference between groups.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; CRI, Castelli risk index; CRP, C-reactive protein; HDL, high density lipoprotein; LDL, low density lipoprotein; RDW, red cell distribution width.

proportion of patients with suspected CAD may have normal MPS findings, as demonstrated in current study. Considering both the radiation risk and high costs in these patients with normal MPS results [3, 12], there is a need for easy and accessible biomarkers without radiation risk for the classification of patients with suspected CAD in clinical practice.

CAD is primarily caused by atherosclerosis, while atherosclerosis-related diseases often have a poor prognosis [13]. It is known that mechanisms such as lipid accumulation in the arterial intima, activation of inflammatory cells such as monocytes and T lymphocytes, and production of matrix proteins play a role in the pathogenesis of atherosclerosis [14, 15]. This is consistent with the detection of impaired lipid metabolism, elevated monocytes and CRP levels in patients with presence or severity of ischemia. Previous studies have demonstrated the role of CRI created from lipid profiles in predicting cardiovascular disease. Zhang et al. [16] reported that CRI-I, which reflects coronary plaque formation, is associated with the risk of ischemic stroke in both men and women. Dai et al. [17] reported that aortic calcification exhibits a positive correlation with both CRI-I and CRI-II. Afsin et al. [18] showed that CRI-II is an independent predictor of slow coronary flow. Although these findings support that CRI can be an important screening tool in predicting CAD, there are studies reporting the opposite. In a study conducted with non-ST-segment elevation myocardial infarction patients, it was reported that there was a low correlation between CAD severity and CRI-I, but CRI-II did not show a significant relationship [19]. On the other hand, previous studies have reported a positive correlation between the myocardial damage and extent of CAD [20-22]. In the current study, CRI levels were higher in patients with ischemia. While CRI-II showed significant differences in ischemia severity, CRI-I did not provide a significant diagnostic distinction in patients with moderate and severe ischemia. However, this study,

Table 4. Independent predictors for presence and severity of ischemia.

	Univariable Regression			Multivariable Regression		
	OR	95% CI	p	OR	95% CI	p
Mild (ref: Normal)						
Gender						
Male	ref					
Female	1.03	0.63-1.68	0.905	-	-	-
Diabetes mellitus	1.51	0.91-2.52	0.114	-	-	-
Hypertension	1.28	0.78-2.11	0.318	-	-	-
Neutrophil	1.34	1.10-1.63	0.003*	1.26	1.02-1.55	0.032*
Monocyte	2.09	0.46-9.44	0.338	-	-	-
CRP	1.05	0.96-1.12	0.718	-	-	-
CRI-I	2.05	1.64-2.56	<0.001*	-	-	-
CRI-II	2.34	1.80-3.05	<0.001*	2.29	1.76-2.98	<0.001*
				Nagelkerke R2 = 0.302; p < 0.001*		
Moderate (ref: Mild)						
Gender						
Male	ref					
Female	0.41	0.24-0.68	0.001*	-	-	-
Diabetes mellitus	1.35	1.02-2.15	0.049*	-	-	-
Hypertension	2.30	1.34-3.98	0.003*	2.07	1.16-3.70	0.014*
Neutrophil	1.35	1.13-1.61	0.001*	-	-	-
Monocyte	2.05	1.22-3.10	<0.001*	-	-	-
CRP	2.72	1.69-3.85	<0.001*	2.65	1.22-3.98	0.024*
CRI-I	1.64	1.09-2.20	0.012*	-	-	-
CRI-II	1.85	1.32-2.40	<0.001*	1.98	1.45-2.50	0.002*
				Nagelkerke R2 = 0.324; p < 0.001*		
Severe (ref: Moderate)						
Gender						
Male	ref					
Female	1.07	0.51-2.27	0.859	-	-	-
Diabetes mellitus	0.96	0.48-1.94	0.920	-	-	-
Hypertension	1.03	0.45-2.36	0.948	-	-	-
Neutrophil	0.98	0.77-1.26	0.913	-	-	-
Monocyte	0.56	0.09-3.25	0.520	-	-	-
CRP	2.25	1.16-4.37	0.016*	2.40	1.21-4.78	0.013*
CRI-I	0.99	0.88-1.12	0.975	-	-	-
CRI-II	1.72	1.20-2.46	0.003*	1.77	1.22-2.55	0.003*
				Nagelkerke R2=0.270; p < 0.001*		

In the multivariate regression analysis, the effects of age and drugs were adjusted. * P <0.05 shows statistical significance.
Abbreviations: CI, confidence interval; CRI, Castelli risk index; CRP, C-reactive protein; OR, odds ratio.

which presented the relationship between CRI and ischemia severity, supported the prognostic role of CRI-II.

Inflammatory activation can accelerate atherosclerosis [23]. Following tissue damage, an inflammatory response causes macrophages to accumulate in the damaged tissue. It has also been suggested that HDL may inhibit leukocyte activation and migration [24]. Activated monocytes transform into macrophages by engulfing oxidized LDL cholesterol molecules. HDL cholesterol plays a role in reducing monocyte activation and reversing the effects of oxidized LDL [25, 26]. This results in the secretion of pro- and anti-inflammatory cytokines and increased CRP production. Thus, an inflammatory response accelerates atherosclerosis [27]. This mechanism was consistent with the positive correlation between CRIs and markers of inflammation. Previous studies reported a positive correlation between CRP levels and ischemia severity in CAD patients [28-30]. These mechanisms may explain the diagnostic performance power of CRI-II derived from LDL and HDL cholesterol levels. Moreover, CRI-II offered a gradual threshold values for distinguishing ischemia severity. Before the referral of patients with suspected CAD to MPS, CRI-II can be an inexpensive and easy screening tool to predict the severity of ischemia beyond presence of ischemia. In addition, the threshold value of the CRI-II level in predicting the presence of ischemia could have prevented 19% of all patients from being referred to MPS and the risk of radiation.

Table 5. Diagnostic performance assessment of CRI in predicting severity of ischemia		
ROC Curve findings	CRI-I	CRI-II
Mild (ref: Normal)		
AUC±SE	0.733±0.03	0.774±0.03
95% CI	0.686-0.784	0.719-0.824
Sensitivity	70.2%	80.8%
Specificity	75.1%	72.7%
Cut-off point	>2.9	>2.1
p	<0.001	<0.001
Moderate (ref: Mild)		
AUC±SE	0.704±0.04	0.700±0.04
95% CI	0.640-0.760	0.637-0.760
Sensitivity	70.6%	78.7%
Specificity	69.4%	65.3%
Cut-off point	>3.7	>2.8
p	<0.001	
Severe (ref: Moderate)		
AUC±SE	0.539±0.5	0.689±0.04
95% CI	0.457-0.619	0.609-0.763
Sensitivity	70.5%	%75.5
Specificity	40.3%	%68.7
Cut-off point	>3.9	>3.3
p	0.459	<0.001
Abbreviations: AUC, area under the curve; CI, confidence interval; CRI, Castelli risk index; SE, standard error.		

Although this study is the first study evaluating the relationship between CRI and MPS, it has some limitations. Initially, it had a single-center and retrospective design. Second, the coronary angiography results of the patients could not be evaluated. Finally, this study did not include patients with a history of CAD and acute coronary syndrome.

Conclusion

High CRI-II levels are an independent predictor of severity of ischemia beyond presence of ischemia. CRI-II offers an important threshold value in distinguishing patients with suspected CAD but without perfusion defects or normal coronary arteries. CRI-II can be a potential screening tool for patients with suspected CAD and can be used for risk stratification.

Conflicts of Interest

The author declare they have no conflicts of interest.

Funding

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Ethics approval

The study was performed in accordance with the Declaration of Helsinki, and was approved by the Ankara City Hospital Clinical Research Ethics Committee (Decision Date/No: 02.2023/ E1-23-3325).

Informed Consent

The need for informed consent was waived under the approval of the Local Ethics Committee due to the retrospective design.

Availability of Data and Material

The data that support the findings of this study are available on request from the corresponding author, [B.D].

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Original Article

The Prognostic Values of Graded Prognostic Assessment (GPA) Index In Advanced Stage NSCLC Patients With Brain Metastasis

Beyin Metastazlı İleri Evre KHDAK Hastalarında GPA İndeksinin Prognostik Değeri

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ABSTRACT

Aim: Graded Prognostic Assessment (GPA) is a new prognostic index for patients with brain metastases. Brain metastasis is a common site of metastasis in lung cancers. Lung cancer-specific GPA scoring system is used. We aimed to assess the prognostic and predictive significance of Graded Prognostic Assessment (GPA) score in non small-cell lung cancer patients with brain metastasis.

Material and Methods: This study was designed as a hospital-based retrospective observational case-series study. A total of 95 patients with brain metastatic NSCLC patients who were followed in two different oncology centers in Turkey between 2015 and 2021 have been included into this study. They were divided into 3 groups according to their GPA scores.

Results: The median age of the patients was 62 (range 44-89) years The patients were divided into 3 groups according to their GPA scores. 24 (25.2 %) patients had ''0-1'' GPA score, 54 (56,8 %) patients had ''1,5-2'' GPA score and 17 (18 %) patients had ''2,5-3'' GPA score. The median follow-up time was 11 months and 89 (93.7%) patients died during follow-up. Overall survival (OS) was 8 months. Patients in the low (0-1) GPA scores had worst overall survival than those with higher GPA scores (4.7, 12.6 and 18.5 months respectively and p=0,001).

Conclusion: In this study, we have shown that GPA score is useful in evaluating the prognosis of NSCLC patients with brain metastasis..

Keywords: GPA, Lung Cancer, Brain Metastasis

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Öz

Amaç: Derecelendirilmiş Prognostik Değerlendirme (GPA), beyin metastazı olan hastalar için yeni bir prognostik indekstir. Beyin metastazı, akciğer kanserlerinde sık görülen bir metastaz bölgesidir. Akciğer kanserine özgü GPA skorlama sistemi kullanılmaktadır. Beyin metastazı olan küçük hücreli dışı akciğer kanseri hastalarında Kademeli Prognostik Değerlendirme (GPA) skorunun prognostik ve prediktif önemini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu çalışma, hastane tabanlı retrospektif gözlemsel vaka serisi çalışması olarak tasarlandı.Bu çalışmaya 2015-2021 yılları arasında Türkiye'de iki farklı onkoloji merkezinde izlenen beyin metastatik KHDAK'li toplam 95 hasta dahil edildi. GPA puanlarına göre3grubaayrıldılar.

Bulgular: Hastaların ortanca yaşı 62 (44-89) idi. Hastalar GPA'larına göre 3 gruba ayrıldı. 24 (%25,2) hastanın GPA'sı "0-1", 54 (%56,8) hastanın GPA 'sı "1,5-2" ve 17 (%18) hastanın GPA skoru "2,5'-3" arsasındaydı. Medyan takip süresi 11 aydı ve takipte 89 (%93,7) hasta öldü. Genel sağkalım (OS) 8 aydı. Düşük (0-1) GPA skorlarındaki hastalar, daha yüksek GPA skorlarına sahip olanlara göre en kötü genel sağ kalıma sahipti (sırasıyla 4.7, 12.6 ve 18.5 ay vep=0,001).

Sonuç: Bu çalışmada beyin metastazı olan KHDAK hastalarının prognozunu değerlendirmede GPA skorunun yararlı olduğunu gösterdik.

Anahtar Kelimeler: GPAİ, Akciğer Kanseri, Beyin metastazı

Introduction

Lung cancer is the most common type of lung cancer and leading cause of cancer death worldwide [1-3]. At the time of diagnosis, approximately 50% of patients are in the metastatic stage. Metastasis to the brain is one of the most common and serious complications of this disease [4,5]. According to conservative estimates, 10% to 30% of lung cancer patients will develop brain metastases. Previously, survival after the development of brain metastases was poor and patıents wıth braın metastas represent a hıghly heterogenıc group. Prognostic scoring systems are used for patients with brain metastases. These scoring systems can be used to identify patients who are candidates for current treatments as well as predict prognostic grouping and expected survival times.

In 1997 Gaspar at al demonstrated for the first time a scoring system for patients with brain metastases [6]. A newer prognostic index for patients with brain metastases is the Graded Prognostic Assessment (GPA) [7]. This prognostic index was originally developed from a database of study patients with different tumor types with brain metastases [8,9]. The original GPA was validated and refined with diagnosis-specific prognostic indices [10]. A series of GPA studies have revealed that survival and the factors that predict survival differ greatly depending on the diagnosis. Age, KPS, extracranial metastases, and the number of brain metastases were significant prognostic factors for survival in lung cancer with brain metastases. The aim of this study was to evaluate the prognostic and predictive importance of GPA scores in non small cell lung cancer patients with brain metastases.

Material and Methods

This study was designed as a hospital-based retrospective observational case-series study. Total of 95 patients were included into the study from Radiation Oncology Departments of Okmeydani Research and Training Hospital and Dr. Ersin Arslan Research and Training Hospital between the years of 2015 and 2021. Non small cell lung cancer patients with brain metastasis were included to the study. Demographic features and treatment modalities were recorded from patient electronic files. Variables considered included the 4 used by the existing DS-GPA (patient age, KPS, extracranial metastases, and the number of brain metastases) and was shown in table-1.

Table 1. GPA Scoring Criteria

Prognostic Factor	0 Point	0.5 Point	1 Point
Age, y	≥70	<70	NA
KPS	<70	80	90-100
ECM	Present		Absent
Brain metastases, No	>4	1-4	NA

Abbreviations
KPS: Karnofsky Performance Status
ECM: Extracranial metastasis

Statistical Analysis

All results were presented as the rate for categorical values or mean and median for continuous variables. Clinical and statistical significant correlation between continuous

variables was calculated by Spearman's rank correlation test, rs (spearman's correlation coefficient) and p value (2-tailed) were noted. Overall survival (OS) was defined as the time from diagnosis time to the date of death. Survival curves were estimated according to the Kaplan-Meier method, and log-rank tests were used for univariate statistical comparisons. Adjusted Hazard Ratio (HR) and 95% confidence interval (95% CIs) were used for estimation. All statistical data were analyzed using the SPSS version 17.0, and a p value of <0.05 was considered statistically significant.

Results

The median age of the patients was 62 (range 44-89) years and 74 (77.9%) patients were male. All of the patients (n: 95) had brain metastasis. Majority of patients had Karnofsky Performance Status 80 and 90 (n=44, 46,3% and n=35, 36,8 % respectively). 55 (57.9 %) patients had extracranial metastasis. While 60 (63,2 %) patients had a single brain metastasis, 35 (36,8 %) patients had more than 1 brain metastasis. The patients were divided into 3 groups according to their GPA scores. 24 (25.2 %) patients had "0-1" GPA score, 54 (56,8 %) patients had "1,5-2" GPA score and 17 (18 %) patients had "2,5-3" GPA score. Patient characteristics and GPA scores are shown in table 2.

Table 2. Patient characteristics and GPA Scores

Characteristics	N %
Median age	62 (44-89) years old
Gender	
Men	74 (77.9)
Women	21 (22.1)
KPS	
60	4 (4.2)
70	12 (12.6)
80	44 (46.3)
90	35 (36.8)
Cranium Metastasis Count	
Single Lesion	60 (63.2)
>1	35 (36.8)
Extracranial Metastases	
Yes	55 (57.9)
No	40 (42.
Bone Metastases	
Yes	74 (59.2)
No	51 (40.1)
GPA Score	
0-1	24 (25.2)
1,5-2	54 (56,8)
2,5-3	17 (18)
Final Status	
Alive	6 (6.3)
Exitus	89 (93.7)

The median follow-up time was 11 months and 89 (93.7%) patients died during follow-up. Overall survival (OS) was 8 months (Figure 1). Patients in the low (0-1) GPA scores had worst overall survival than those with higher GPA scores (4.7, 12.6 and 18.5 months respectively and p=0,001). Survival rates by the 3 prognostic classes are detailed in Table 3 and illustrated in the Figure-2

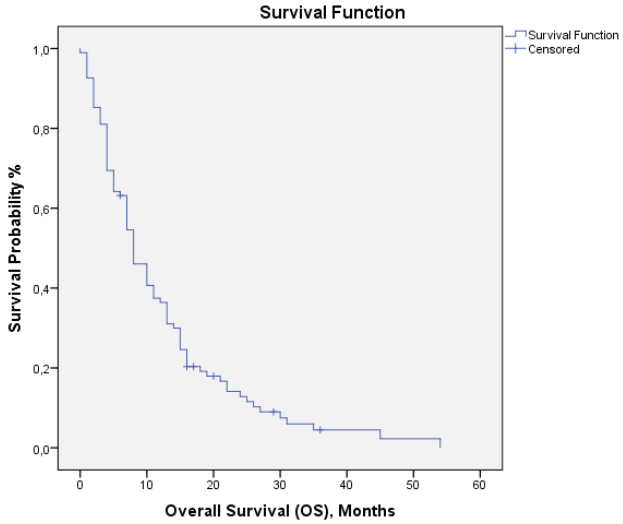

Figure 1.

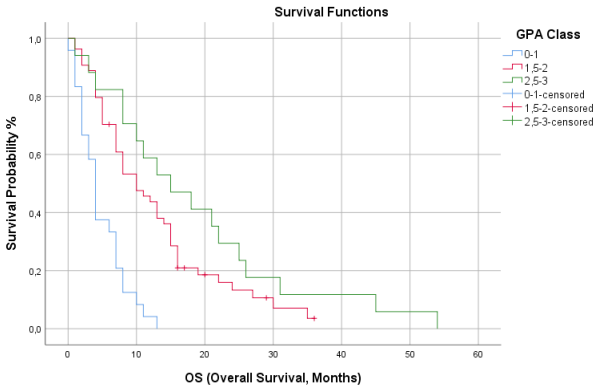

Figure 2

Table 3. Relationship between GPA Scores with Overall Survival

GPA Scores	Median OS	
	Months	p
0-1 (Low)	4	0,001a
1,5-2 (Intermediate)	10	0,001a
2,5-3 (High)	15	0,001a

Abbreviations
a Statistically Significant
GPA : Graded Prognostic Assessment
OS Overall Survival

Discussion

In this study, the GPA scores of 95 NSCLC patients with brain metastasis were analyzed retrospectively. The results showed that the GPA score was an independent prognostic factor in these patients. In our study, we showed that patients with low GPA scores had worse prognosis.

During the past 25 years, multiple prognostic models have been developed. The Radiation Therapy Oncology Group's (RTOG) Recursive Partitioning Analysis (RPA) was first used in 1997 by Gaspar et al in their foundational study on a prognostic index for patients with brain metastases [6]. In this trial, They established 3 distinct prognostic classes based on Karnofsky Performance Status, age, and control of primary and metastatic disease. Sperduto et al. devised the GPA in 2008, using data from 1960 participants in 5 phase 3 Radiation Therapy Oncology Group trials [7]. The GPA index also took into account the number of brain metastases (BM) in addition to the first three RPA criteria. Based on a second, independent, multi-institutional retrospective analysis of 4,259 additional patients with brain metastases from breast carcinoma, small-cell and non-small-cell lung carcinoma, GI cancers, melanoma, and renal cell carcinoma, the original GPA was validated and improved with diagnosis-specific prognostic indices [11,12].The diagnosis specific GPA, a later iteration released in 2012, maintained the 4-point scoring system but added sophistication and placed more attention on the primary location of origin and related criteria [13]. There were identified four illness classes, and the median survival time ranged from 3.0 to 14.8 months.

This was revised in 2017 to include molecular profiling for NSCLC, further highlighting the biologic heterogeneity of NSCLC BM [14]. The inclusion of the lung GPA based on contemporary molecular profile would be very helpful in the initial patient evaluations and aid in the creation of fresh paradigms for the choice and administration of therapeutic modalities. We also determined the prognostic importance of the GPA index in our study. however, performing these analyzes with molecular subtyping will provide a better separation of prognostic groups.

The our study has some considerable limitations. First, as with any retrospective study, unpredictable biases may have influenced our results and the number of patients was low. Second, no evaluation was made according to molecular subtypes in our study.

In conclusion, the results of our study showed that GPA score is useful and cost-effective prognostic marker in evaluating the prognosis of NSCLC patients with brain metastasis and should therefore be included in routine clinical practice for these patients.

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Orijinal Makale

Varikoselektomi operasyonu sonrası işe geri dönüş zamanı ve iş günü kaybı

Back to work time and loss of working days after varicoselectomy operation

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ÖZ

Amaç: Varikoselektomi operasyonları çoğunlukla 20-35 yaşları arasında uygulanmaktadır. Bu yaş grubu aynı zamanda etkin iş gücü için de oldukça önemlidir. Varikoselektomide iş günü kaybı üzerine literatürde çalışma bulunmamaktadır. Bu çalışmamızla varikoselektomi ameliyatının iş günü kaybına etkisi üzerine farkındalık oluşturmak ve literatüre katkıda bulunmayı amaçladık.

Gereç ve Yöntemler: Aksaray Özel İnova Hastanesi'nde 07.03.2019-14.10.2022 tarihleri arasında varikoselektomi yapılan 77 hasta çalışmaya dahil edildi. Varikoselektomi tek cerrah tarafından subinguinal yöntem kullanılarak, Carl-Zeiss operasyon mikroskopu (Carl Zeiss, Thornwood, NY) ile 10'luk büyütme altında uygulandı. Hastaların erken dönem komplikasyonları ve iş günü kaybı ameliyat sonrası 10. gün ve 1. ay kontrollerinde sorgulandı. Araştırma verilerinin istatistiksel analizi için Statistical Package for Social Sciences (SPSS), sürüm 22.0 (SPSS Inc. Chicago, ABD) bilgisayar paket programı kullanıldı. $p < 0.05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: Hastaların ortalama yaşı 27,01 ± 4,91 yıl; ve ortalama VKİ 24,72 ± 4,21 kg/m^2 . Hastaların 42'sinde (54,5) grade 3 varikosel mevcuttu. Çalışmamızda mikroskopik varikoselektomi operasyonu sonrası iş günü kaybını (16,09 ± 14,27) gün olarak tespit ettik. Ameliyat sonrası 21 (%27,3) hastada erken dönem komplikasyon tespit edildi. Eğitim durumu, komplikasyon ve cerrahi deneyim ile iş günü kaybı arasında istatistiksel anlamlı ilişki saptanmadı(p>0,05). İş türü, medeni durum ve erken dönem komplikasyonların çeşitleri ile iş günü kaybı arasında istatistiksel anlamlı farklılık bulundu (p:0,014, p:0,03 ve p:0,02; sırasıyla).

Sonuç: Mavi yakalı çalışanların varikoselektomi operasyonu sonrası beyaz yakalı çalışanlara göre işe dönüş zamanı birkaç gün daha uzun olmaktadır. Yaklaşık olarak varikoselektomi sonrası çalışanlar 15 gün sonra işbaşı yapabilmektedir. Bu konuda prospektif, daha büyük merkezlerin geniş vaka serilerine ihtiyaç olduğu kanaatindeyiz.

Anahtar Kelimeler: iş günü kaybı; varikoselektomi; mikrocerrahi

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ABSTRACT

Aim: Varicocelectomy surgeries are mostly performed between the ages of 20-35. This age group is also essential for an effective workforce. However, there is no study on the loss of working days in varicocelectomy. With this study, we aimed to raise awareness regarding the effect of varicocelectomy surgery on the loss of working days and to contribute to the literature.

Material and Methods: This study included 77 patients who underwent varicocelectomy at Aksaray Private Inova Hospital between 07.03.2019 and 14.10.2022. Varicocelectomy was performed by a single surgeon using the subinguinal method with a Carl-Zeiss operating microscope (Carl Zeiss, Thornwood, NY) under 10x magnification. The early complications and the loss of working days were questioned at the postoperative 10th-day and 1st-month follow-ups. Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc. Chicago, USA) computer package program was used to analyze research data. $p<0.05$ was considered statistically significant.

Results: The mean age and BMI of the patients were 27.01±4.91 and 24.72±4.21 kg/m^2. Grade 3 varicocele was present in 42 (54.5) patients. The mean loss of working days was 16.09± 14.27 days after microscopic varicocelectomy. Postoperative early complications were detected in 21 (27.3%) patients. No statistically significant relationship was found between education status, complications, surgical experience, and loss of workdays ($p>0.05$). However, significant differences were found regarding work type, marital status, early complications, and lost work days (p:0.014, p:0.03, and p:0.02, respectively).

Conclusion: After varicocelectomy, blue-collar employees return to work a few days longer than white-collar employees. Employees can return to work after approximately 15 days after varicocelectomy. We believe that prospective, more extensive case series are needed in this regard.

Keywords: lost working days; varicocelectomy; microsurgery

Giriş

Varikosel, en sık görülen ve düzeltilebilen erkek kaynaklı infertilite sebebidir[1]. Değişik çalışmalarda farklı değerler bulunmasına rağmen genel popülasyonda yaklaşık %12-15, infertil popülasyonda ise yaklaşık %30-35 oranında görülmektedir[2]. Meta-analizleri de içeren geniş çaplı çalışmalarla palpabıl varikoselin onarımının fertilite üzerine oldukça olumlu etki yaptığı gösterilmiştir[3]. Varikoselin embolizasyon gibi nadir başvurulan cerrahi olmayan yöntemlerin yanında açık ve laparoskopik yöntemleri de içeren cerrahi tedavisi standart tedavi protokolü olarak uygulanmaktadır. Açık cerrahi teknikler içerisinde ise mikroskop yardımıyla 4 ile 20 kat cerrahi sahanın büyütülmesine olanak sağlayan mikrocerrahi varikoselektomi, daha düşük nüks ve komplikasyon oranları sebebi ile altın standart olarak kabul edilmektedir[4].

Varikoselektomi operasyonları çoğunlukla 20-35 yaşları arasında uygulanmaktadır[5]. Bu yaş grubu aynı zamanda etkin iş gücü için de kritik bir öneme sahiptir. Birçok cerrahi ve hastalık için işe dönüş ve iş gücü kaybı üzerine literatürde çalışma bulunmaktadır[6]. Ancak gündelik üroloji pratiğinde yoğun bir şekilde uygulanan mikroskopik varikoselektomi operasyonu sonrası işe dönüş ve iş gücü kaybı üzerine literatürde çalışma bulunmamaktadır. Bu çalışmamızla mikroskopik varikoselektomi ameliyatının iş gücü kaybına etkisi üzerine farkındalık oluşturmak ve literatüre katkıda bulunmayı amaçladık.

Gereç ve Yöntemler

Çalışmamız Helsinki Bildirgesi prensiplerine uygun olarak hazırlanmış olup, 24/11/2022 tarihinde, Aksaray Üniversitesi Klinik Araştırmalar Etik Kurul Başkanlığı tarafından incelenmiş ve oy birliğiyle etik açıdan uygun görülmüştür (Etik kurul onay numarası: 144-SBKAEK/ 2022/19-04). Bütün hastalardan operasyon öncesi aydınlatılmış onam formu imzalı olarak alınmıştır.

Aksaray Özel İnova Hastanesi'nde 07.03.2019-14.10.2022 tarihleri arasında varikoselektomi endikasyonu konulduktan sonra varikoselektomi yapılan ve aktif çalışan 80 hastanın verileri retrospektif olarak incelendi. Ağrı sebebi ile varikoselektomi yapılan 3 hasta çalışma dışı bırakılarak toplam 77 hasta çalışmaya dahil edildi. Hastaların demografik verileri, iş türü, iş günü kaybı, varikosel tarafı, varikosel derecesi,

skrotal doppler ultrasonografi bulguları, varikoselektomi için tercih edilen anestezi türü ve erken dönem komplikasyonları kaydedildi. Erken dönem komplikasyonlar enfeksiyon(yara yeri enfreksiyonu veya epididim-orşit), hematom, post-spinal baş ağrısı, ağrı(insizyon veya skrotal) ve skrotal ödem olarak 5 gruba ayrıldı. Varikoselektomi tek cerrah tarafından subinguinal yöntem kullanılarak, Carl-Zeiss operasyon mikroskopu (Carl Zeiss, Thornwood, NY) ile 10'luk büyütme altında uygulandı. Hastalar operasyon gününün ertesi sabahı taburcu edildi. Taburcu olurken hastalara böbrek fonksiyon testleri kontrol edilerek sefpodoksim 200 mg tb 2x1, diklofenak 50 mg tb 2x1 şeklinde standart olarak reçete edildi. Hastalara 10 gün boyunca skrotal elevasyon, aralıklı skrotuma soğuk uygulama ve en az 15 gün cinsel ilişkiye girilmemesi önerildi. Cerrahın öğrenme eğrisi açısından hastalar deneyime göre 2 gruba ayrıldı. Hastaların erken dönem komplikasyonları ve iş günü kaybı ameliyat sonrası 10. gün ve 1. ay kontrollerinde sorgulandı. Hastaların demografik ve klinik verileri ile iş günü kaybı arasındaki ilişki değerlendirildi.

İstatistiksel Analizi

Araştırma verilerinin istatistiksel analizi için Statistical Package for Social Sciences (SPSS), sürüm 22.0 (SPSS Inc. Chicago, ABD) bilgisayar paket programı kullanıldı. Verilerin dağılımı Kolmogorov-Smirnov testi ile test edildi. Tanımlayıcı istatistikler bölümünde kategorik değişkenler sayı, yüzde olarak sunuldu. Parametrik olmayan veriler ortalama± SS olarak rapor edilir. Normallik analizinin bir sonucu olarak, gruplar arasında karşılaştırmalı analiz için Mann-Whitney U Testi kullanıldı. Bağımsız gruplar arasında kategorik değişkenlerin karşılaştırılmasında Ki-kare testi kullanıldı. p <0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular

Dahil edilme kriterlerine göre 77 erkek hasta istatistiksel analize dahil edildi. Hastaların demografik özellikleri, klinik ve laboratuvar değerleri Tablo 1'de gösterilmiştir. Hastaların ortalama yaşı 27,01 ± 4,91 yıl; ve ortalama VKİ 24,72 ± 4,21 kg/m2. Fizik muayenede hastaların 42' sinde (54,5) grade 3 varikosel mevcuttu. Ameliyat sonrası 21 (%27,3) hastada erken dönem komplikasyon gelişti (Tablo 1).

İş günü kaybı ile hastaların demografik ve klinik verileri arasındaki ilişki Tablo 2'de gösterilmiştir. Eğitim durumu, komplikasyon ve cerrahi deneyim ile iş günü kaybı arasında istatistiksel anlamlı ilişki saptanmadı(p>0,05). İş türü, medeni durum ve erken dönem komplikasyonların çeşitleri ile iş günü kaybı arasında istatistiksel anlamlı farklılık bulundu (p:0,014, p:0,03 ve p:0,02; sırasıyla) (Tablo 2).

Mavi yakalı ve beyaz yakalı hasta grupları arasında demografik ve klinik verilerinin karşılaştırılması Tablo 3'de sunulmuştur. Gruplar arasında yaş, erken dönem komplikasyonlar, komplikasyon alt başlıkları ve cerrahi deneyim açısından istatistiksel anlamlı fark saptanmadı(p>0,05). VKİ ve iş günü kaybı mavi yakalı grupta istatistiksel anlamlı yüksek saptandı (p:0,04 ve p:0,014). Gruplar arasında eğitim durumu karşılaştırılmasında; mavi yakalı hasta grubunda ilk-orta öğretim (%42,6) ve lise-ön lisans (%46,8), beyaz yakalı grupta ön-lisans (%43,3) ve üniversite mezunu (%50) yüksek saptandı(p<0,001). Medeni durumu evli olanların oranı mavi yakalı grupta (%80,9), beyaz yakalı gruba(%50) göre istatistiksel anlamlı yüksek saptandı(p:0,004) (Tablo 3).

Tablo 1: Hastaların Demografik, Klinik Ve Laboratuar Sonuçları

	Ortalama± SD; n (yüzde)
Yaş, yıl	27,01 ± 4,91
VKİ, kg/m²	24,72 ± 4,21
İş günü kaybı, gün	16,09 ± 14,27
Variköz ven çapı, mm	3,46 ± 0,69
Eğitim durumu	
İlk-orta öğretim	22 (28,6)
Lise-ön lisans	35 (45,5)
Üniversite mezunu	20 (26)
Medeni durum, E/B	53/24
İş türü	
Mavi yakalı	47 (61)
Beyaz yakalı	30 (39)
Varikoselektomi öyküsü	2 (2,6)
Varikosel grade	
1	2 (2,6)
2	33 (42,9)
3	42 (54,5)
Varikosel taraf	
Sol	65 (84,4)
Sağ	3 (3,9)
Bilateral	9 (11,7)
Anestezi türü	
Spinal anestezi	33(42,9)
Genel anestezi	44(57,1)
Erken dönem komplikasyonlar	
Enfeksiyon	8 (10,4)
Hematom	2 (2,6)
Post-spinal başağrısı	3 (3,9)
Ağrı	5 (6,5)
Skrotal ödem	3 (3,9)
VKİ; vücut kitle indeksi	

Tablo 2: İş Günü Kaybı İle Demografik Ve Klinik Verilerin Karşılaştırılması

	İş günü kaybı, gün± SD	p
İş türü		0,014
Mavi yakalı	16,77 ± 12,36	
Beyaz yakalı	14,33 ± 16,50	
Eğitim durumu		0,24
okur-yazar değil	0	
İlk-orta öğretim	20,14 ± 20,64	
Lise-ön lisans	14,57 ± 10,33	
Üniversite mezunu	13,25 ± 9,89	
Medeni Durum		0,03
Evli	17,40 ± 15,61	
Bekar	12,33 ± 9,18	
Erken dönem komplikasyonlar	0,02	
Enfeksiyon	25,63 ± 26,38	
Hematom	11 ± 4,24	
Post-spinal başağrısı	6 ± 1,73	
Ağrı	8,6 ± 4,72	
Skrotal ödem	18,33 ± 10,41	
Komplikasyon		0,87
Yok	15,63 ± 12,39	
Var	16,33 ± 18,14	
Cerrahi deneyim		0,87
ilk 38 vaka	16,76 ± 16,35	
İkinci 39 vaka	14,9 ± 11,56	

Tablo 3: İş Türü ile Demografik Ve Klinik Verilerin Karşılaştırılması

İş türü	Mavi yakalı(n:47)	Beyaz yakalı(n:30)	p
Yaş, yıl	27,11 ± 4,28	26,37 ± 5,99	0,51
VKİ, kg/m^2	25,34 ± 4,2	23,41 ± 4,11	0,04
İş günü kaybı, gün	16,77 ± 12,36	14,33 ± 16,5	0,014
Eğitim durumu			<0,001
İlk-orta öğretim	20 (42,6)	2 (6,7)	
Lise-ön lisans	22 (46,8)	13 (43,3)	
Üniversite mezunu	5 (10,6)	15 (50)	
Medeni Durum			0,004
Evli	38 (80,9)	15 (50)	
Bekar	9 (19,1)	15 (50)	
Erken dönem komplikasyonlar			0,07
Enfeksiyon	3 (27,3)	5 (50)	
Hematom	2 (18,2)	0 (0)	
Post-spinal başağrısı	0 (0)	3 (30)	
Kasık ağrısı	3 (27,3)	2 (20)	
Skrotal ödem	3 (27,3)	0 (0)	
Komplikasyon			0,34
Yok	36 (76,6)	20 (66,7)	
Var	11 (23,4)	10 (33,3)	
Cerrahi deneyim			0,14
ilk 38 vaka	20 (42,6)	18 (60)	
İkinci 39 vaka	27 (57,4)	12 (40)	

VKİ; vücut kitle indeksi

Tartışma

Varikosel esasında skrotum içinde pampiniform venöz pleksusta anormal genişleme ile meydana gelen varistir. Etyolojisi net olarak aydınlatılamamış olmakla birlikte patofizyolojisinde ise artmış testiküler sıcaklık, hipoksi, oksidatif stres ve toksik metabolitelerin reflüsü gibi nedenlerle spermatogenezin bozulması üzerinde durulmaktadır[7-9]. Varikosel onarımının cerrahi endikasyonu olarak Avrupa Üroloji Birliği kılavuzlarında, palpabıl varikoseli olup anormal semen parametreleriyle birlikte çocuk isteği olan erişkinler ve ipsilateral testis boyutlarında küçülme olan adolesanlar, şeklinde belirtilmiştir[10]. Donovan ve ark. tarafından popülarize edilen laparoskopik varikoselektomi, Palomo tekniği olarak da bilinen açık yüksek retroperitoneal ven ligasyonu gibi cerrahi yöntemlerin yanında, Marmar ve ark. tanımladığı subinguinal mikroskopik varikoselektomi nüks ve hidrosel gibi komplikasyonların daha az görülmesi sebebi ile diğer yöntemlerin bir adım önüne çıkmıştır[11-13].

Günümüzde birçok hastalığın, cerrahi yöntemin ve hatta sağlıklı popülasyonun yaş ve diğer demografik özelliklerinin sosyoekonomik etkilerini araştıran çalışmalar mevcuttur[14, 15]. Bu tarz araştırmalarla ülkelerin karar alıcıları gelecek projeksiyonları yapabilmekte, sağlık profesyonelleri ve akademik çevreler ise en doğru ve etkin yöntemin hangisi olduğuna karar vermek için yoğun bir çaba sarf etmektedir. Sağlık alanında maliyetler hesaplanırken doğrudan ve dolaylı maliyetler olarak kabaca iki ana gruba ayrılmaktadır. Doğrudan maliyetleri yatarak tedavi, ayaktan tedavi, ve ilaç maliyetleri gibi unsurlar oluştururken, dolaylı maliyetleri ise iş günü kaybı, bakıcı maliyetleri ve diğer maliyetler oluşturmaktadır[16]. Baş ağrısı gibi bütün insanların gündelik hayatında görülebilecek bir semptomdan, Ankilozan spondilit gibi romatolojik hastalıklara kadar iş gücü kaybı üzerine araştırmalar yapılmıştır [17, 18]. Üroloji özelinde ise, benign prostat hiperplazisinde HoLEP (Holmium laser enucleation of the prostate) operasyonunun ve onkolojik bir operasyon olan radikal prostatektomide kullanılan robot yardımlı laparoskopik cerrahi yönteminin iş günü kaybı üzerindeki etkilerini araştıran çalışmalar mevcuttur [19, 20]. Ancak görece üroloji pratiğinde sıklıkla uygulanan mikroskopik varikoselektomide iş günü kaybı üzerine literatürde çalışma bulunmamaktadır. Çalışmamızda, güncel üroloji pratiğinde çok sık uygulanan mikroskopik varikoselektomi operasyonu sonrası iş günü kaybını (16,09 ± 14,27) gün bulduk.

Birçok farklı çalışmada işçi, sürücü, operatör ve aktif

operasyonlara katılan askerleri barındıran mavi yakalı iş kolları ile yönetici, ofis çalışanları, bankacılık gibi alanları barındıran beyaz yakalı iş kolları arasında uygulanan tedavinin etkinliği açısından farklılıklar gözlenmiştir[21, 22]. Bizim çalışmamızda da mavi yakalı grup ile beyaz yakalı grup arasında iş günü kaybı açısından fizik güç yoğun çalışan mavi yakalı grubun iş günü kaybı daha fazla bulunmuştur (16,77 ± 12,36; 14,33 ± 16,50; p:0,014). Bu duruma mavi yakalılarda daha sıklıkla skrotal ödem görülmesi de etki etmiş olabileceği gibi bu grupta VKİ'nin daha fazla olması ile evli olan hastaların görece fazla olması da nedenler olarak karşımızda durmaktadır. Ayrıca mavi yakalı grupta iş günü kaybının ve komplikasyon oranlarının nispeten yüksek olmasında eğitim seviyesinin beyaz yakalı gruba göre daha düşük olmasından dolayı post-op dönem için cerrahın önerilerine tam uyamama ve hijyene dikkat etmemelerinin de rolü gözönünde bulundurulmalıdır. Ghanem ve ark. mikroskopik varikoselektomi yaptıkları hastalarının iş günü kayıplarını 1±0,4 gün olarak bulmuşlar ancak bunun operasyon sonrası taburculuğa kadar geçen gün olduğu tespit edilmiştir [23]. Bizim çalışmamızda ise iş günü kaybı tüm gruplarda (16,09 ± 14,27) gün gibi yüksek bulunmuş olup bu sonuçta literatürden yüksek olan erken dönem özellikle yara yeri enfeksiyonu ve skrotal ödem gibi komplikasyonlarımızla birlikte Türk toplumunun operasyon sonrası işe başlama konusunda batı toplumlarına göre daha defansif bir tavır sergilemesinin de etkili olduğunu düşünmekteyiz[24].

İş günü kayıpları ve post-op komplikasyon görülmesi açısından cerrahın ilk 38 vakası ile ikinci 39 vakası arasında anlamlı bir farklılık görülmemiş olup literatürle uyumlu olarak bulunmuştur[24]. İş günü kaybı açısından evli grubun bekar gruba göre (17,40 ± 15,61; 12,33 ± 9,18; p:0,03) daha kötü bir durumda olmasında ise evli hastaların post-op dönem cinsel ilişki perhizine dikkat etmedikleri gözlemlenmiştir. Çalışmamızda erken dönem komplikasyon olan grupla olmayan grup arasında iş günü kaybı açısından anlamlı farklılık saptanmazken (16,33 ± 18,14 ;15,63 ± 12,39; p: 0,87), komplikasyonların alt gruplarında enfeksiyon ve skrotal ödem ile diğer gruplar arasında anlamlı farklılık saptanmıştır(p:0,02) (Tablo 2).

Çalışmamızın retrospektif karakteri, operasyonların mikroskopik cerrahi öğrenme eğrisinin başlarında olması, Türkiye'nin nispeten küçük bir şehrindeki özel klinikte uygulanmış olması gibi dezavantajları barındırması, vaka sayısının görece az olması gibi kısıtlayıcı tarafları bulunmaktadır.

Sonuç

Mavi yakalı çalışanların varikoselektomi operasyonu sonrası beyaz yakalı çalışanlara göre işe dönüş zamanı birkaç gün daha uzun olmaktadır. Yaklaşık olarak bu operasyon sonrası çalışanlar 15 gün sonra işbaşı yapabilmektedir. Çalışmamızın varikoselektomi gibi üroloji pratiğinin sık uygulanan bir ameliyatı sonrası iş günü kaybı gibi sosyoekonomik açıdan önemli bir konuda literatüre katkı sağlayacağını düşünmekteyiz. Bu konuda prospektif dizaynlı, daha büyük merkezlerin geniş vaka serilerine ihtiyaç olduğu kanaatindeyiz.

Maddi destek ve çıkar ilişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkara dayalı ilişkisi yoktur.

Yazarların katkıları

MEŞ: protokol/proje geliştirme, veri toplama, veri analizi ve metin yazma/düzenleme. MK: protokol/proje geliştirme, istatistiksel analiz ve taslak yazımı. MY: protokol/proje geliştirme, taslak yazımı. Tüm yazarlar sonuçları tartıştı ve makale yazımı hakkında yorum yaptı.

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Orijinal Makale

Kronik Pulmoner Problemli Hastalarda Kostaklavikular Brakiyal Pleksus Bloğunun Diyafram Hareketi ve Analjeziye Etkileri: Retrospektif Analiz

Effects of Costoclavicular Brachial Plexus Block on Diaphragm Excursion and Analgesia in Patients with Chronic Pulmonary Problems: A Retrospective Analysis

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ÖZ

Amaç: Çeşitli seviyelerden yapılan brakiyal pleksus blokları, postoperatif analjezi için artroskopik omuz cerrahisinde yaygın olarak kullanılmaktadır. Ancak, bloğun uygulandığı seviyeyle ilişkili yüksek hemidiyafragmatik paralizi insidansı, pulmoner fonksiyon bozukluğu olan hastalarda kullanımı sınırlamaktadır. Paradoksal olarak, pulmoner patolojili hastalarda analjezi için kullanılacak sistemik opioidlerin oksijenasyonu bozabileceği düşünüldüğünde analjezi yönetimleri özellikli hastalardır. Son araştırmalar frenik siniri koruyucu brakiyal pleksus blok yaklaşım alternatiflerini araştırmaktadır. Bu retrospektif çalışma ile, ultrasonografi eşliğinde uygulanan kostaklavikular bloğun bilinen pulmoner patolojisi olan hastalardaki analjezik etkinliğinin ve diyafram fonksiyonlarına etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya Ocak 2020-Temmuz 2022 tarihleri arasında, kronik pulmoner problemi olan, kostaklavikular blok ve genel anestezi kombinasyonu ile anestezi yönetimleri gerçekleştirilen artroskopik omuz cerrahisi geçiren vakalar dahil edildi. Demografik veriler, cerrahi endikasyonlar, uygulanan genel anestezi yöntemi, komplikasyonlar/yan etkiler, vizual analog skala skorları, analjezi süreleri, uygulanan anestezi tekniği için hasta ve cerrah memnuniyeti ile diyafram fonksiyonları retrospektif olarak kayıtlardan incelendi. Blok uygulanan tarafta hemidiyafram fonksiyonları; diyafram tutulumunun derecesi > %75 ise "tam paralizi", %25,1-74,9 ise "kısmi paralizisi" ve < %25 ise "paralizi yok" olarak değerlendirildi.

Bulgular: Çalışmaya dahil edilen 21 hastanın dördü Bankart, diğerleri rotator kaf rüptürü endikasyonuyla opere edilmişti. Hastalarda komplikasyon gözlenmedi. Anestezi tekniğiyle ilgili hem hasta (%71,4) hem cerrah (%100) memnuniyet oranları yüksekti. Diyafram ekskürsiyon oranları %25'ten düşüktü ve dolayısıyla hemidiyafragmatik paralizisinin gerçekleşmediği görüldü. Kostaklavikular blokla ortalama 470 dakika postoperatif analjezi sağlandı.

Sonuçlar: Kostaklavikular blok, pulmoner patolojisi olan artroskopik omuz cerrahisi geçirecek hastalarda diyafram fonksiyonunu korurken, etkin cerrahi ve postoperatif analjezi sağlamıştır.

Anahtar kelimeler: brakial pleksus blok; diyafram; analjezi; akciğer hastalıkları

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Abstract

Aim: Brachial plexus blocks are widely used for post-operative analgesia in shoulder surgery. The high risk of hemidiaphragmatic paralysis limits its use in patients with pulmonary dysfunction. In patients with pulmonary diseases, the management of pain requires special approaches since systemic opioids may also decrease oxygenation. Latest studies search for alternative methods for phrenic nerve preserving brachial plexus block. This retrospective study aims to analyze the analgesic efficacy and diaphraghmatic effects of ultrasound guided costoclavicular block in patients with pulmonary diseases.

Material and Methods: The study includes patients with pulmonary diseases underwent arthroscopic shoulder surgery under general anesthesia combined with costoclavicular block between January 2020 and July 2022. The demographic data, operation indications, general anesthesia method, complications, visual analog scale scores, the duration of analgesia, diaphragm functions, rate of patient and surgeon satisfaction survey was collected from the records and analyzed retrospectively. The diaphragm functions which were evaluated as complete paralysis ≥ 75%, partial paralysis 25.1-74.9%, no paralysis ≤ 25% were documented.

Results: Four of the 21 patients underwent Bankart surgery, while the others were operated due to rotator cuff rupture. No complications were observed in the patients. Rate of patient (71.4%) and surgeon (100%) satisfaction about the anesthesia method was high. Since the diaphragm excursion rates were below 25%, it was observed that hemidiaphragmatic paralysis did not occur. An average of 470 minutes of postoperative analgesia was noted.

Conclusion: While preserving diaphragmatic function, a costoclavicular block provided effective surgical and postoperative analgesia in pulmonary pathology patients undergoing arthroscopic shoulder surgery.

Keywords: brachial plexus block; diaphragm; analgesia; lung diseases

Giriş

Artroskopik omuz cerrahisinde önceleri tercih edilen genel anestezi, yerini iyi bir iyileşme ve rehabilitasyon sağlamasının yanı sıra intraoperatif ve postoperatif ağrının giderilmesindeki avantajları nedeniyle periferik sinir bloklarına bırakmıştır [1,2]. Bu hastaların en önemli şikayeti ağrı ve ağrıya sekonder gelişen hareket kısıtlılıklarıdır [3]. Dolayısıyla hastaların öncelikli beklentileri postoperatif dönemde ağrılarının sonlanması olsa da, cerrahinin yarattığı travmanın eklenmesiyle bu süreç uzayabilmektedir.

Farklı seviyelerden yapılan brakiyal pleksus blokları (BPB) ile hastalarda yüz güldürücü sonuçlara ulaşılmıştır [4]. Fakat bu uygulamaların da farklı komplikasyonları mevcuttur. Anatomik olarak özellikle klavikula üzerinden yapılan bloklarda, frenik sinirin etkilenerek blok tarafında hemidiyafragmatik paraliziye (HDP) yol açması bu komplikasyonlardan biridir [5]. Diyafram tutulumu, pulmoner fonksiyonu normal hastalarda klinik veya monitörizasyona yansıyan sorunlara yol açmasa da, pulmoner problemli hastalarda yakın gözlem gerektiren komplikasyonları beraberinde getirebilmektedir [6, 7, 8]. Dolayısıyla hem ağrının hem de uygulanan sistemik analjeziklerin spontan solunumu zorlaştırıp solunumun baskılanmasına yol açmasıyla, ağrıya pulmoner problemler de eşlik edebilmektedir. Farklı seviyelerden yapılan BPB'lerde ise frenik sinire olan mesafenin değişmesiyle tutulum azalmakta ve solunum komplikasyonları engellenebilmektedir.

İnfraklaviküler brakiyal pleksus bloğunun bir varyantı olan kostaklaviküler brakiyal pleksus bloğu (KKB), üst ekstremite anestezisi ve postoperatif analjezi için umut verici sonuçlarıyla popülerlik kazanmıştır. Kostaklaviküler yaklaşım 2015 yılında tanımlanmış, teknik açıklama ve kadavra anatomik çalışmaları yayınlanmıştır. Tekniği tanımlayan Karmakar ve ark. bu teknikle bir komplikasyonla karşılaşmadan 100'den fazla blok gerçekleştirmişlerdir [9,10]. Kostaklavikular brakiyal pleksus bloğunda, komplikasyon riskinin azaldığı ve blok kalitesinin arttığı gösterilmiş olup, genel anestezinin yüksek riskli olduğu hastalarda etkin cerrahi anestezi için kullanımının bildirildiği vaka sunumları da mevcuttur [11-13].

Bu retrospektif çalışmada, KKB ve genel anestezi kombinasyonu

ile artroskopik omuz cerrahisi geçiren pulmoner problemli hastaların; diyafram fonksiyonları, analjezi süreleri, komplikasyon/yan etkileri ile hasta-cerrah memnuniyetinin araştırılması ve literatür eşliğinde sunulması amaçlanmıştır.

Gereç ve Yöntemler

Bu tek merkezli, retrospektif çalışma Gazi Üniversitesi Tıp fakültesi Yerel Etik Kurul onayı (05/07/2022 tarihli ve 2022-881 nolu) alındıktan sonra, Gazi üniversitesi Tıp Fakültesi Anesteziyoloji ve Reanimasyon AD, Ortopedi ve Travmatoloji ameliyathanesindeki hasta verileriyle gerçekleştirildi. Çalışmaya Ocak 2020-Temmuz 2022 tarihleri arasında, kronik pulmoner problemi olan, KKB ve genel anestezi kombinasyonu ile anestezi yönetimleri gerçekleştirilen artroskopik omuz cerrahisi geçiren vakalar dahil edildi. Verilerine ulaşılamayan ve diyafram hareketleri değerlendirilememiş hastalar çalışma dışı bırakıldı.

Kliniğimizde tüm periferik bloklar, Logiq E R7 (GE, Wisconsin, ABD) ultrasonografi (USG) ve sinir stimülatörü (Stimuplex HNS 12, Braun, Almanya) eşliğinde gerçekleştirilmektedir. Ve standart olarak tüm BPB'lerde USG ile hem blok uygulamasından önce hem de 30 dakika sonra, normal ve derin inspiryum sırasındaki diyafram hareketleri USG motion (M) modunda ölçülerek kaydedilmektedir.

Kostaklavikular brakiyal pleksus bloğu uygulamasında, hastalar supin ve kol 90° abdüksiyonda pozisyonlandırılır ve klavikula orta noktasının altında, medial infraklaviküler fossa üzerinde USG ile tarama yapılır. Aynı pozisyonda prob hafifçe öne doğru yatırılır, görüntü brakiyal pleksusun üç kordunun (lateral, medial, posterior), aksiller arterin lateralinde görselleştirilmesine kadar optimize edilir. Blok iğnesinin ucu, lateralden mediale in-plane yaklaşımla üç kordun ortasına gelene kadar ilerletilir. Sinir stimülatöründe 0,3-0,5 mA arasında deltoid kas kontraksiyonu görüldüğünde her 5 mL'de bir aspire edilerek toplam 20 mL %0,375 bupivakain uygulanır. Bloklar, 30 dakika sonra pin-prick testi ve motor muayene ile değerlendirilerek blok kalitesi kontrol edilir.

Tüm blok uygulamalarında; komplikasyonlar/yan etkiler, 0-10 arasında 11 puanlık bir ölçekle ağrı skorları (Vizual Analog Skala [VAS]: hayal edilebilecek en kötü ağrı,10 puan; hiç ağrı olmaması, 0 puan), ilk analjezik gereksinimine kadar geçen süre (analjezi süresi), ek analjezik ihtiyacı, kullanılan analjezik ilaçlar (morfin, aldolan ve/veya non-steroidal antiinflamatuar ilaçlar [NSAİİ]), hasta ve cerrah memnuniyetleri ("Kesinlikle tercih ederim", "belki tercih ederim" ya da "tercih etmem" ifadeleri ile) değerlendirilmektedir.

Verilere anestezi takip fişleri, USG kayıtları, ortopedi ameliyat notları ve servis izlem formlarından ulaşıldı. Tıbbi kayıtlardan toplanan veriler arasında; demografik veriler, operasyon tarafı, cerrahi endikasyonlar, uygulanan genel anestezi yöntemi vardı. Kostaklavikular brakiyal pleksus bloklarıyla ilişkili olarak; komplikasyonlar/yan etkiler, VAS skorları, diyafram fonksiyonları, analjezi süreleri ve uygulanan anestezi tekniği için ise hasta/cerrah memnuniyeti retrospektif olarak kayıtlardan incelendi. Blok uygulanan taraftaki (hemidiyafram) diyafram fonksiyonları, daha önceki bir çalışmamız referans alınarak diyafram tutulumunun derecesi; > %75 ise "tam paralizi", %25,1-74,9 ise "kısmi paralizi" ve < %25 ise "paralizi yok" olarak değerlendirildi [3].

İstatistiksel analiz

Araştırma verilerinin istatistiksel analizleri için Statistical Package for Social Sciences (SPSS), Windows için sürüm 26.0 (SPSS Inc. Chicago, USA) bilgisayar paket programı kullanıldı. Tanımlayıcı istatistiklerde kategorik değişkenler sayı ve yüzde verilerek, sürekli değişkenler ise ortanca ve minimum maksimum ile belirtildi. Sürekli değişkenlerin normal dağılıma uygunluğu ise görsel histogram ve Kolmogorov-Simirnov testi kullanılarak değerlendirildi.

Bulgular

Artroskopik omuz cerrahisi için KKB ve genel anestezi kombinasyonu uygulanan kronik pulmoner problemli 27 hastanın dosyası incelendi ve altı hasta verilerdeki eksiklikler nedeniyle çalışma dışı bırakılarak, 21 hasta çalışmaya dahil edildi. Hastaların demografik özellikleri, operasyon tarafları ve omuz artroskopisi için endikasyonları Tablo I'de sunulmaktadır. Bankart nedeniyle opere edilen dört hasta dışındaki hastalar, rotator kaf rüptürü nedeniyle opere edilmişti.

Çalışmaya dahil edilen tüm hastalara kliniğimizde standardize edilmiş KKB uygulanmıştı. Yeterli cerrahi analjezi ve blok kalitesi sağlanan hastalara genel anestezi altında operasyon gerçekleştirilmişti. Tercih edilen genel anestezi ajanları ile ilgili detaylar Tablo II'de verilmiştir. Hiçbir hastada komplikasyon gelişmediği görüldü. Hem hastalar (%71,4) hem de cerrahlar (%100), anestezi tekniği ile ilgili olarak yüksek memnuniyet oranları bildirmişlerdi.

Blok önce ve sonrasında normal ve derin inspiryumdaki diyafram ekskürsiyon oranlarının tüm hastalarda %25'in altında olduğu, dolayısıyla HDP'nin gerçekleşmediği görüldü (Tablo III).

Ayılma ünitesinde ise ameliyat çıkışında VAS'ı 3'ün üzerindeki hastaların ikisine iv morfin, birine ise im dolantin uygulandığı saptanmıştır.

Tablo I. Demografik veriler, n (%)	
Cinsiyet	
Kadın	15 (71,43)
Erkek	6 (28,57)
ASA	
II	16 (76,2)
III	5 (23,8)
VKİ, (kg/m2)	
İnce (<18.5)	1 (4,8)
Normal (18.5-24.9)	14 (66,7)
Aşırı kilolu (25-29.9)	4 (19)
Obez (≥30)	2 (9,5)
Operasyon tarafı	
Sağ	11 (52,4)
Sol	10 (47,6)
Cerrahi endikasyon	
Bankart	4 (19)
Rotator kaf rüptürü	17 (81)
VKİ: Vücut-kitle indeksi	

Tablo II. Anestezi yönetimi, komplikasyonlar ve hasta/cerrah memnuniyeti, n (%)	
Kostaklavikular blok (standart)	21 (100)
Genel anestezi	
Propofol+nmb+remifentanil	14 (66,7)
Pentotal+nmb+remifentanil	7 (33,3)
Komplikasyon	-
Hasta memnuniyeti	
Kesinlikle tercih ederim	15 (71,4)
Belki tercih ederim	3 (14,3)
Tercih etmem	3 (14,3)
Cerrah memnuniyeti	
Kesinlikle tercih ederim	21 (100)
Belki tercih ederim	-
Tercih etmem	-
nmb: nöromusküler blokör	

Tablo III. Diyafram hareketi (ekskürsiyonu), VAS skorları ve postoperatif analjezi süreleri	
Normal inspiryum, n (%)	
≤ 25	21 (100)
25.1-74.9	-
≥ 75	-
Derin inspiryum, n (%)	
≤ 25	21 (100)
25.1-74.9	-
≥ 75	-
Ayılma VAS değerleri, n (%)	
0	13 (61,9)
0-3	5 (23,8)
>3	3 (14,3)
Postoperatif analjezi süreleri, dk [median (min-max)]	470 (15-680)
VAS: Vizual Analog Skala	

Tartışma

Bu retrospektif çalışmada, omuz cerrahisi geçiren kronik pulmoner problemli hastalarda KKB'nin öncelikle diyafram fonksiyonları üzerine etkileri, ikincil olarak ise analjezi süresi, yan etki/komplikasyonlar, hasta-cerrah memnuniyeti ve ek analjezik ihtiyaçları değerlendirilmiş olup, hiçbir hastada HDP ve komplikasyon gelişmediği aynı zamanda hastaların büyük çoğunluğunda da yeterli postoperatif analjezinin sağlandığı görülmüştür.

Brakiyal pleksus blokları artroskopik omuz cerrahisinde etkili postoperatif analjezi sağlamalarına rağmen, özellikle interskalen yaklaşım hemen her zaman frenik sinir tutulumu nedeniyle HDP ile sonuçlanmaktadır [14-17]. Ultrasonografi kılavuzluğunda interskalen bloğun en yaygın tekniği, C5 ve C6 köklerinin yaklaşık krikoid kıkırdak seviyesinde, transvers proseslerin arkasından çıktıkları yerin hemen distalinde, ön ve orta skalen kaslar arasındaki olukta uzandıkları yerde görüntülenmesini içerir ve interskalen oluktaki C5 ve C6 köklerini hedefler [18]. Frenik sinir ve C5 sinir kökü, erişkinlerde krikoid kıkırdak seviyesinde anatomik olarak 1,8-2 mm mesafe ile ayrılır ve frenik sinir boyun köküne daha mediale doğru ilerlediğinden aralarındaki mesafe her cm'de 3 mm daha artar. Bu nedenle frenik sinirin krikoid kıkırdak seviyedeki bloklarla tutulması ve pulmoner komplikasyonların gelişmesi şaşırtıcı değildir [19]. Frenik sinir tutulum riskini daha da azaltmak için, mümkün olduğu kadar distale lokal anestezik enjekte etmek ihtiyatlı görünmektedir [18].

Ultrasonografi kılavuzluğunda rejyonal anestezinin en büyük avantajlarından biri sağladığı gelişmiş anatomi bilgisi olmuştur. Ayrıca anatomik işaretlere olan bağımlılığımızı ortadan kaldırırken, yeni blok tekniklerinin geliştirilmesine ve mevcut olanların da iyileştirilmesine olanak sağlamıştır. Diyaframın solunum ile hareketinin USG eşliğinde değerlendirilmesi invaziv olmayan ve kolay uygulanabilen bir tanı aracıdır. Qaiser ve ark. çalışmalarında, diyafram hareketinin değerlendirilmesi için USG kullanımını açıklamışlar ve sonografik olarak belirlenen diyafram hareketlerini ve dolayısıyla diyafram fonksiyonlarını, spirometrik ölçümlerle (FEV1/FVC) güçlü bir şekilde ilişkili bulmuşlardır [20].

Ultrasonografinin sağladığı diğer avantajlarla birlikte frenik sinir tutulumunu önlemek için enjeksiyon yerini frenik sinirden uzakta tutacak, USG klavuzluğunda alternatif yaklaşımlı bloklar denenmiştir. Omuz cerrahisi için interskalen bloğa benzer etkili süperior trunkus bloğu, geleneksel interskalen bloğa göre enjeksiyon yeri frenik sinirden uzakta olduğundan diyaframı koruduğu düşünülen bloklardan biri olabilir. Süperior trunkus bloğunun interskalen blokla karşılaştırıldığı bir çalışmada HDP, interskalen grupta %97,5, superior trunkus grubunda ise %76,3 oranında gözlenirken (p=0.006); interskalen gruptaki %72,5 orana kıyasla, superior trunkus grubundakilerin sadece

%5,3'ünde tam diyafram tutulumu geliştiği bildirilmiştir. Ayrıca başlangıca göre spirometri değerlerindeki azalma da, interskalen grupta anlamlı olarak daha fazla bulunmuştur [16].

İnfraklaviküler ve aksiller gibi daha distal BPB'lerin, supraklaviküler gibi daha proksimal bloklara göre yaygın olarak kabul edilen bir avantajı frenik sinir tutulum insidansının daha düşük olmasıdır. Bu oran supraklaviküler blokta %0-67, infraklavikülerde ise %0-26 olarak bildirilmiştir [21].

Kostaklaviküler brakiyal pleksus bloğu, brakiyal pleksusun kostaklaviküler boşlukta yüzeysel olarak bir demet halinde düzenlendiği kordları hedef alan, yakın zamanda tanımlanmış ve USG kılavuzluğunda yapılan bir bloktur [9]. Kostaklaviküler boşluktaki avantajlı topografik görünüm, düşük blok başarısızlık oranıyla brakiyal pleksusa kolay ve güvenli erişim sağlar. Erişkinlerde uygulanan KKB ile, cerrahi anestezi ve brakiyal pleksusun ana sinirlerinin duyusal ve motor blokajında hızlı başlangıç için %97'lik bir başarı oranı bildirilmiştir [22]. Lateral sagittal infraklavikular blokla karşılaştırıldığında da, kostaklaviküler yaklaşımın daha hızlı sensorimotor blok başlangıcı sağladığı gösterilmiştir [23]. Genel anestezi ile birlikte KKB uygulanan çalışma hastalarımızda; ayılma odası VAS değerlerinin sadece hastaların %14,3'ünde 3'ün üzerinde olduğu ve KKB ile ortalama 470 dakika postoperatif analjezi sağlandığı görülmektedir. Sağladığı etkin postoperatif analjezi, pulmoner komplikasyon riskini artırabilecek sistemik opioid analjezik ihtiyacını azaltması açısından, çalışmamızı yürüttüğümüz özellikli hasta popülasyonunda önemlidir.

Kostaklaviküler brakiyal pleksus bloğu, daha yaygın olarak uygulanan diğer bloklarla karşılaştırıldığında, HDP ile ilgili veriler nispeten az da olsa sonuçlar umut vericidir. Supraklaviküler blokile karşılaştırıldığında daha distal yaklaşımlı olan KKB'nin, diyafram paralizisini azalttığı bildirilmiştir [24]. Hemidiyafragmatik paralizi gelişimi üzerine supraklavikular ile KKB'nin etkilerinin karşılaştırıldığı bir kohort analizde, KKB uygulanan 118 hastadan 3 (%2,5)'ünde ve supraklaviküler brakiyal pleksus bloğu uygulanan 197 hastadan 47'sinde (%39,8) HDP gözlenmiş ($p < 0,001$), hem brakiyal pleksus blok yaklaşımı hem de enjekte edilen lokal anestezik hacmi ile HDP gelişimi arasında da anlamlı ilişkili bulunmuştur [25]. Hong ve ark. çalışmalarında KKB'nin, supraklaviküler bloğa kıyasla HDP riskini azaltabileceğini düşünmüşler ve KKB uygulanan hastalarda supraklaviküler blok uygulananlara göre pulmoner fonksiyonların daha fazla korunduğu sonucuna varmışlardır [26]. Kliniğimizde USG kılavuzluğunda yaptığımız BPB'lerde diyafram tutulumunu göz ardı etmemek için, USG ile diyafram hareketlerini rutin olarak değerlendirmekteyiz. Pulmoner problemli hastalarda KKB ile postoperatif analjezi sağladığımız çalışmamızda, USG ile hem normal hem de derin inspiryumda diyafram hareketlerindeki azalmanın %25'ten az olduğunu yani hiç diyafram paralizisi gelişmediğini gözlemledik.

Carioca ve ark. KKB uygulanan pediatrik vakalarda komplikasyon insidansını 1:200 (%0.5) olarak bildirilmiştir [25]. Mevcut çalışmamızda ise hiç komplikasyon gelişmemiştir.

Ultrasonografi kılavuzlu BPB'lerde düşük hacimlerde lokal anestezik kullanımının, frenik sinir tutulumunu önlemede etkili olacağı düşünülerek yapılan çalışmalarda, düşük hacimlerde lokal anestezik kullanımının frenik sinir tutulum insidansını azalttığı ancak ortadan kaldırmadığı gösterilmiştir [5,27]. Konvansiyonel interskalen BPB sonrası HDP insidansı, 20 mL veya daha fazla lokal anestezik hacmi ile %100'e kadar çıkmaktadır. Bu insidans 5-10 mL lokal anestezik kullanımıyla %45'e kadar düşürülebilse de, buna perioperatif analjezinin süre ve gücünde klinik olarak anlamlı bir azalma eşlik eder ve ayrıca daha az tecrübeli ellerde başarısız blok riski taşıyabilir [16]. Güngör ve ark. anestezik teknik olarak superior trunkus bloğu (20 mL) ile birlikte klinik standartlara göre daha düşük lokal anestezik hacmi kullandıkları interskalen BPB'nin (10 mL), tek başına geleneksel interskalen BPB'ye (30 mL) kıyasla daha az HDP'ye yol açtığını göstermişlerdir [3].

Bu çalışma, retrospektif tek merkezli tasarımı ve küçük boyutu ile sınırlıdır. Çalışmaya dahil edilen denek sayısının az olması bir sınırlama olabilse de, tüm hastalardaki diyafram ölçümlerinde tutulumunun %25'in altında yani derecelendirmede "paralizi yok" olarak bulunması, yüksek hasta-cerrah memnuniyeti ile hiçbir hastada komplikasyon gelişmemesinin çalışma bulgularımızı güçlendirdiğini düşünmekteyiz. Yine de bulgularımızı doğrulamak için daha büyük popülasyonlarla prospektif klinik çalışmalara ihtiyaç vardır.

Sonuç

Sonuç olarak KKB, HDP'ye neden olmadan diyafram fonksiyonları korurken, yüksek hasta-cerrah memnuniyeti ile etkin cerrahi ve postoperatif analjezi sağlamıştır. Ayrıca sağladığı postoperatif analjezik etkisi ile pulmoner komplikasyonları artırabilecek sistemik opioid kullanımını da azaltmıştır. Tüm bu avantajları nedeniyle, özellikle sınırlı pulmoner fonksiyonları olan hastalarda tercih edilebilecek bir BPB yaklaşımı olabileceği düşünülmüştür.

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Original Article

Comparıson of preoperatıve bowel preparatıon models of patıents who underwent surgery for colorectal cancer

Kolorektal kanser nedeniyle ameliyat giren hastaların ameliyat öncesi bağırsak hazırlık modellerinin karşılaştırılması

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Abstract

Aim: The most prevalent cancer in society is colorectal cancer (CRC). Studies aiming to lower surgical morbidity and mortality have found a significant contribution from preoperative bowel preparation. Models for bowel preparation included mechanical cleaning, the use of antibiotics, and control groups. We compared preoperative bowel preparation for elective colorectal cancer and evaluated its effects in this study.

Material and Methods: Preoperative bowel preparation model was used to prospectively split 144 patients (n=144) with colorectal cancer into four groups. Patients in the first group (Group I) underwent mechanical bowel preparation (MBP), followed by oral antibiotic therapy (OAB) and MBP in the second group (Group II), intravenous antibiotic therapy (IVAB), MBP, and OAB in the third group (Group III), and no bowel preparation in the fourth group (Group IV). Demographic information, anastomotic leakage, surgical site infection, intraabdominal abscess, postoperative ileus, and death were compared between patients.

Results: Groups I, II, III, and IV of the study each had 35 patients, 38 patients, 35 patients, and 36 patients, respectively. There was no statistically significant difference between the four groups when the groups were evaluated by age, gender, and ASA (American Society of Anesthesiologists) score ($p > 0.05$). There were significant differences between surgical site infection (SSI), intraabdominal abscess, and anastomosis leaking (p0.05). Mortality and postoperative ileus did not differ significantly ($p > 0.05$).

Conclusion: We consider that the bowel preparation approach of mechanical colon cleansing and antibiotic administration is appropriate for patients who have had surgery owing to elective CRC.

Keywords: Colorectal cancer, bowel preparation, surgery

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Öz

Amaç: Toplumda en sık görülen kanser kolorektal kanserdir (KRK). Cerrahi morbidite ve mortaliteyi azaltmayı amaçlayan çalışmalar, preoperatif barsak hazırlığının önemli bir katkısını bulmuştur. Bağırsak hazırlığı için modeller arasında mekanik temizlik, antibiyotik kullanımı ve kontrol grupları yer alıyordu. Bu çalışmada elektif kolorektal kanser için preoperatif barsak hazırlığını karşılaştırdık ve etkilerini değerlendirdik.

Gereç ve Yöntemler: Kolorektal kanserli 144 hastayı (n=144) prospektif olarak dört gruba ayırmak için preoperatif barsak hazırlama modeli kullanıldı. Birinci gruptaki hastalara (Grup I) mekanik barsak hazırlığı (MBH), ikinci gruba (Grup II) oral antibiyotik tedavisi (OAB) ve MBH, üçüncü gruba intravenöz antibiyotik tedavisi (IVAB), MBH ve OAB uygulandı. grup (Grup III) ve dördüncü grupta (Grup IV) barsak hazırlığı yapılmadı. Hastalar arasında demografik bilgiler, anastomoz kaçağı, cerrahi alan enfeksiyonu, karın içi apse, postoperatif ileus ve ölüm karşılaştırıldı.

Bulgular: Çalışmanın Grup I, II, III ve IV'ünde sırasıyla 35 hasta, 38 hasta, 35 hasta ve 36 hasta vardı. Gruplar yaş, cinsiyet ve ASA (American Society of Anesthesiologists) puanına göre değerlendirildiğinde dört grup arasında istatistiksel olarak anlamlı fark yoktu (p> 0,05). Cerrahi alan enfeksiyonu (CAE), intraabdominal apse ve anastomoz kaçağı arasında anlamlı fark vardı (p0.05). Mortalite ve postoperatif ileus arasında anlamlı fark yoktu (p > 0.05).

Sonuç: Elektif KRK nedeniyle ameliyat olmuş hastalarda mekanik kolon temizliği ve antibiyotik uygulamalarının barsak hazırlığı yaklaşımının uygun olduğunu düşünüyoruz.

Anahtar Kelimeler: Kolorektal kanser, bağırsak hazırlığı, cerrahi

Introduction

Although some studies suggest that bacterial colonization in the colon improves the recovery of anastomoses, other research indicates that these bacteria aggravate the situation in cases of potential anastomotic leaking and result in sepsis [1,2]. It is generally known that using antibiotics disturbs both the pathogenic and beneficial bacteria in the intestine, and it takes months for the disrupted intestinal flora to recover. Even with microperforations, harmful microorganisms in the colon can cause diffuse peritonitis and secondary interventions [3].

Without bowel preparation, patients with a high fecal load in the colon get contaminated, and fecal contamination causes postoperative problems ranging from surgical site infections to intra-abdominal sepsis [4]. Colorectal surgery's optimal preoperative bowel preparation regimen is still up for debate. Although some articles demonstrate that elective surgeries performed without any kind of preparation have similar complication rates, especially in trauma patients, it has led to a long period of avoiding bowel preparation, bowel preparation due to fecal contamination has been indicated [5]. While some articles advocate for bowel preparation, other approaches, based on publications on trauma and emergency surgery, do not. Additionally, there are several suggestions made by organizations that recommend bowel preparation, including mechanical bowel preparation (MBP) and/or the use of antibiotics [6].

Additionally, the use of MBP, oral antibiotics (OAB), and intravenous antibiotics (IVAB) is suggested [7]. In this study, we compared four different bowel preparation models (MBP, MBP + OAB, MBP + OAB+ IVAB, control group) of patients who underwent elective surgery for CRC in our clinic to compare the postoperative mortality and morbidity rates.

Material and Methods

The study was carried out in a prospective randomized design. This study comprised 144 patients who underwent elective colorectal cancer surgery in our clinic between 2017 and 2019. Ethical approval was obtained from the local ethics committee (Ref Nr: 2019-115). According to their hospitalization protocol number, the patients were randomly assigned. Depending on the application time, MBP, MBP+OAB, MBP+OAB+IVAB, and control groups were developed, accordingly. In the clinic, four distinct surgical teams carried out the operations. Figure 1 displays a flowchart for the study.

The patients in the MBP group (Group I) (n=35) had two 45 ml sodium phosphate enemas, one 8 hours and one 2 hours before the surgery, as mechanical colon cleansing.

MBP + OAB group (Group II) (n=38) patients had two 45 ml sodium phosphate enemas as mechanical colon cleansing: one 8 hours and one 2 hours before surgery. At 22:00, a 500 mg metronidazole and 1 g ceftriaxone oral tablet were administered as an oral antibiotic.

Preoperatively, the patients in the MBP + OAB + IVAB (Group III) (n=35) group received two 45 ml sodium phosphate enemas as

mechanical colon cleansing: one 8 hours and one 2 hours before surgery. At 2:00, 500 mg of metronidazole and 1 g of ceftriaxone were given orally, and 1 g of ceftriaxone was given intravenously.

The control group (Group IV) (n=36) received no preparation.

The patients in four groups had their demographic information and ASA (American Society of Anesthesiologists) scores analyzed. Patients' mortality rates were documented and compared, along with post-operative anastomotic leakage, wound infection, ileus, intra-abdominal abscess, and rates of ileus.

By performing lower and upper abdomen computed tomography (CT) on patients with defense and/or rebound as well as high CRP and WBC values in the daily physical examination, post-operative anastomotic leakage was identified. Patients with hyperemia and purulent drainage at the incision site were diagnosed with SSI. Patients with no gastric output for 72 hours after surgery, vomiting, and air-fluid level on standing direct abdomen X-ray were diagnosed as post-operative ileus. An intra-abdominal abscess was diagnosed as organized abscess formation in three contrast abdominal CT scans. The 30-day postoperative mortality rate is the number of mortality postsurgical.

The study excluded patients who had emergency surgery for a colorectal tumor. Patients whose colon cleansing or antibiotic treatment was not completed were not included in the study. Patients who underwent surgery for recurring tumors were not included in the investigation. Patients under the age of 18 were not included in the study.

In compliance with the 1964 Helsinki Declaration and its most recent revisions, this study was conducted. Consent was gained from both awake and unconscious patients' first-degree relatives.

Statistical Analysis

Statistical software NCSS 11(Number Cruncher Statistical System, 2017 Statistical Software) was used for the statistical analysis. Continuous variables were given as mean±SD values or median and interquartile ranges and categorical variables were given as frequencies and percentages. The Chi-square test was used when comparing the categorical variables. Where appropriate, categorical variables were evaluated with the Fisher-Freeman Halton test. Kolmogorov Smirnov test used the normal distribution of continuous variables and the Mann-Whitney U test was used for the comparison of nonparametric variables. Statistically significant parameters were compared again in double groups. P values of 0.05 below were accepted as statistically significant.

Results

170 patients were included in the study. 26 patients were excluded from the study. Of these, 14 had ileus, and 5 had tumor perforation and were operated on urgently. Of the 7 patients excluded from the study; 3 were tumor recurrence, 2 were under the age of 18, and 2 were incomplete antibiotic protocol. Of the 144 patients who were operated on for CRC, 73 were female and 71 were male. All patients were operated on electively. There was no statistically significant difference in age (p=0.208) and gender (p=0.987). There were 35 (24.31%) patients in Group I, 38 (26.39%) patients in Group II, 35 (24.31%) patients in Group III, and 36 (25%) patients in Group IV.

Tumor location was observed in 71 patients in the rectum,27 patients in the right colon, 29 patients in the sigmoid colon, and 17 patients in the left colon. There was no significant difference in tumor location between the groups (p=0.503). There was no statistically significant difference in ASA score (p=0.068) between the groups. The demographics and clinical features of patients are shown in Table 1.

Table 1. Demographics and clinical features of patients.

Parameter	Mechanical Bowel Preparation (Group I) (n=35)	Oral Antibiotic and Mechanical Bowel Preparation (Group II) (n=38)	Intravenous Antibiotic, Oral Antibiotic and Mechanical Bowel Preparation (Group III) (n=35)	Control (Group IV) (n=36)	P value
Age (Mean±SD)	60,69±12,4	66,34±10,41	63,77±11,32	64,33±13,55	0,208
Gender ,n(%)					
Female	17 (48,57)	19 (50,00)	18 (51,43)	19 (52,78)	0,987
Male	18 (51,43)	19 (50,00)	17 (48,57)	17 (47,22)	
ASA(Mean±SD)	2,26±0,44	2,5±0,51	2,51±0,56	2,31±0,47	0,068
Tumor location, n(%)					
Rectum	17 (48,57)	15 (39,47)	21 (60,00)	18 (50,00)	0,503
Right colon	4 (11,43)	8 (21,05)	5 (14,29)	10 (27,78)	
Sigmoid colon	9 (25,71)	8 (21,05)	6 (17,14)	6 (16,67)	
Left colon	5 (14,29)	7 (18,42)	3 (8,57)	2 (5,56)	

Anastomotic leaking affected 16 patients (11.11%) (Table 2). There were anastomotic leakage 4 patients in Group I, 1 patient in Group II,1 patient in Group III, and 10 patients in Group IV. There was a significant difference between the groups (p=0.002) (Table 3). In the comparison of the two groups, the difference between the control group and the groups that administered antibiotics (Groups II–III) was statistically significant (p=0.006 and p=0.010, respectively). Between Group I and Group IV, there was no statistically significant difference (p=0,152) (Table 4). There was no statistically significant difference between the 27 (18.75%) postoperative ileus patients and the control group (p=0,165). Ten of the post-operative ileus patients were in Group I, six were in Group II, three were in Group III, and eight were in the control group.

Table 2. Postoperative outcomes of patients

Parameter		n	%
Anastomotic leakage	(-)	128	88,89
	(+)	16	11,11
Post-operative ileus	(-)	117	81,25
	(+)	27	18,75
Intra-abdominal abscess	(-)	130	90,28
	(+)	14	9,72
Surgical site infection	(-)	120	83,33
	(+)	24	16,67
Mortality	(-)	141	97,92
	(+)	3	2,08

Table 3. Outcomes and complications associated with bowel preparation

Parameter	Mechanical Bowel Preparation (Group I)		Oral Antibiotic and Mechanical Bowel Preparation (Group II)		Intravenous Antibiotic, Oral Antibiotic and Mechanical Bowel Preparation (Group III)		Control (Group IV)		P value
	n	%	n	%	n	%	n	%	
Anastomotic leakage	4	11,43	1	2,63	1	2,86	10	27,78	0,002
Post-operative ileus	10	28,57	6	15,79	3	8,57	8	22,22	0,165
Surgical site infection	10	28,57	3	7,89	2	5,71	9	25,00	0,015
Intra-abdominal abscess	5	14,29	1	2,63	1	2,86	7	19,44	0,030
Mortality	1	2,86	0	0	0	0	2	5,56	0,323

Tablo 4. Dual comparison outcomes of groups

Parameter		Group I Group II	GroupI Group III	Group I Group IV	Group II Group III	Group II Group IV	Group III Group IV
Anastomotic leakage	P value	0,306	0,353	0,152	0,510	0,006	0,010
Surgical site infection		0,045	0,026	0,942	0,924	0,090	0,055
Intra-abdominal abscess		0,166	0,200	0,792	0,510	0,051	0,066

Infection at the surgical site affected 24 patients. There were 10 patients in Group I, 9 patients in the control group, and 5 patients in the antibiotic-receiving groups (Groups II to III). The difference in SSI between the groups was statistically significant (p=0.015). Although there was no statistically significant difference between Group I and Group IV (p=0.942), there was a significant difference between Group I and the receiving antibiotic groups (Groups II-III) when comparing the dual groups (p=0.045 and p=0.026, respectively). The intra-abdominal abscess was observed in 5 patients in Group I, 1 patient in Group II,1 patient in Group III, and 7 patients in Group IV. There was a statistically significant difference in intra-abdominal abscesses between the groups (p=0.030). In the double groups' comparison, there was no statistically significant difference between the groups. Three patients died and there was no significant difference in mortality (p=0.323). Of the 3 patients who died, 2 were from Group IV, and 1 was from Group I.

Discussion

Colorectal cancer (CRC) is the third most common cancer in the community. Mortality from CRC accounts for 10% of all cancer deaths [8]. The incidence of CRT is similar in both sexes. Of the

patients included in our study, 71 (49.31%) were male and 73 (50.69%) were female, which is consistent with the literature. In this study, the median age of the patients was 63.84±12.01 and there was no statistically significant difference (p=0.208). It is most common in the literature between 60-75 years of age [9]. The ASA score is the most consistent assessment parameter available. There was no statistically significant difference in ASA score (p=0.068) between the groups. The absence of statistically significant differences in terms of ASA score, age, and gender indicates that the groups in the study were homogeneously distributed in terms of postoperative complications.

Anastomotic leaks following a CRC operation can have devastating effects, often resulting in an increased risk of local recurrence and decreased overall survival in patients [10]. In our study, the overall anastomotic leak rate was 11.11%. Anastomotic leakage was observed in 4 patients in Group I, 1 patient in Group II, 1 patient in Group III, and 10 patients in Group IV (p=0.002). The anastomotic leakage rate was higher in the control group than in the others. In binary comparison, there was a significant difference between Group IV and the receiving antibiotic groups (Group II-III) (p=0.006 and p=0.010, respectively), there was no significant difference between Group I and the receiving antibiotic groups (Group II-III) (p=0.306 and p=0.353, respectively). In addition, there was no statistically significant difference in anastomotic leakage in our analysis between Group I and Group IV (p=0.152). MBP decreases the bacterial load but not the bacterial concentration in the colon [11]. Some studies have consistently failed to demonstrate that MBP alone provides any protection against anastomotic leakage [12,13]. Scarborough et al. [14] stated in their study, the MBP+OAB group and the no prepare group were compared and there was a significant difference (p=0.001). But there was no significant difference between MBP and the no prepare group. Also, Midura et al. [15] stated in their study, the MBP+OAB group and the no prepare group were compared and there was a significant difference (p<0.001). McSorley et al. [16] stated in their study that the İVAB+OAB+MBP group and İVAB+MBP group were compared and there was a significant difference (p<0.001). This meta-analysis underlines that preoperative oral antibiotic prophylaxis, in combination with mechanical bowel preparation and i.v. antibiotic prophylaxis was associated with a significant reduction in rates of anastomotic leakage. But, in our study, there was no significant difference between anastomotic leakage between Group II and Group III (p=0.510). This may be related to the small number of patients in the study sample. We believe that MBP and antibiotics (oral and/or iv) should be used in combination when evaluating our results.

Ileus may develop after surgery in patients undergoing colorectal surgery. This condition determines clinical recovery and therefore contributes to post-operative morbidity. Also, the ileus is a risk factor for anastomotic leakage [17]. In the present study, postoperative ileus was observed in 27 patients in all groups (p=0.165). MBP group had a higher rate than the others. There were mixed results in the literature [18,19].

Hata et al. [18] stated in their study that they found no difference between OAB and İVAB in terms of ileus. According to Garfinkle et al. [19] in their study, they showed that the MBP+OAB group was more effective for ileus but there was no statistically significant difference between MBP and no preparation. No clear consensus is the data regarding post-operative ileus.

Many strategies have been adopted in attempts to reduce SSI (mechanical cleaning, oral/iv antibiotic, and different combinations of these). Mechanical cleaning reduces the fecal load of the colon. It is believed that antibiotics cleanse the intestinal flora. Intestinal flora includes aerobic and anaerobic bacteria. Therefore, we used a combination of metronidazole and ceftriaxone in our study. IV antibiotic prophylaxis has become a standard practice for colorectal surgery, oral antibiotics have not been demonstrated but studies are showing that oral antibiotics reduce SSI [20,21]. The present study indicates that decreased rates of SSI are found in patients who received a mechanical bowel prep combined with antibiotics before elective colorectal surgery. In this study, there was a significant difference in SSI between the MBP group and receiving antibiotics (Group II, Group III) (p=0.045 and p=0.026, respectively). Toh et. al [22] showed that the MBP+OAB group was more effective than the MBP group for SSI. MBP alone has been shown in studies to not affect SSI [23]. In our study, SSI was higher in Group I as well (n=10). In 2018, McSorley et al. [16] revealed that lower SSI was seen in the IVAB+OAB+MBP group (p<0.001). Moreover; in 2018, Kaslow et al. [24] stated that the MBP+OAB group and OAB group were compared, and SSI was significantly reduced in the MBT+OAB group. Our analysis has shown that the addition of IV antibiotics to combined mechanical and oral antibiotic preparation carries the lowest risk concerning SSI development.

Infective complications are an important cause of morbidity and mortality in colorectal surgery. An intra-abdominal abscess is one of them. In the present study, the intra-abdominal abscess was observed in 14 patients. In our

study, receiving antibiotic groups was associated with lower rates of abscess (n=2) and there was a statistically significant difference between the groups (p=0.030) but in double comparison, there was no significant difference between the study groups. In the study of Hata et al. [18], the IV+OAB group was compared with the IV group and no difference was found in terms of an abscess (p=0.465). Moreover, the result of the study is parallel with the experience of the Michigan Surgical Quality Collaborative Colectomy Project by Kim et al [25]. in 2014. In the study, 1914 patients were compared. The study demonstrates that patients who received oral antibiotics and MBP had fewer organ space infections than those who did not have bowel preparations. Our analysis has shown that there is no benefit in the use of MBP and no preparation. Although there was no significant difference in double comparisons, our results suggest that more benefit was achieved with a combination of antibiotic (oral±iv) + MBP.

There was no difference between the groups in terms of mortality (p=0.323). No mortality had been when taking antibiotics in the study. Whereas different results are seen in some studies published in the literature [16,19]. McSorley et al.[16] showed that mortality was significantly lower in the İVAB + OAB + MBP group than in the İVAB + MBP group (p<0.001). Also, Garfinkle et al. [19] found a difference in MBP and no preparation groups in dual comparisons (like OAB and no preparation, MBP+OAB and no preparation).

Our study had several limitations. The major limitation of our study is the small number of patients. Apart from this, the inclusion of all patients who underwent laparoscopic and open surgery in our study and the fact that the surgery was performed by four different teams may have caused a limitation in terms of standardization.

In conclusion, we think that antibiotic and mechanical bowel cleansing should be done together as a perioperative cleaning model. There is a need for further studies with larger series on the subject.

Conflict Of Interests

All authors declare no competing interests.

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Authorship Contributions

Conceptualization (BK, MAB); data curation and formal analysis (BK, MAB, CS); interpretation of data (BK, MAB); statistical analysis (BK, MAB, CS); writing – draft (BK, MAB, CS); writing – review and editing of manuscript (BK, MAB, CS); final approval (all authors).

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Original Article

The comparison of pain intensity in the patients undergoing thermal and non-thermal ablation of lower extremity veins for chronic venous insufficiency with visual analogue scale

Kronik venöz yetmezlik nedeniyle alt ekstremite venlerine termal ve termal olmayan ablasyon uygulanan hastalarda ağrı şiddetinin görsel analog skala ile karşılaştırılması

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Abstract

Aim: To compare the procedural pain intensity measured with VAS in patients undergoing thermal or non-thermal ablation of lower extremity veins for chronic venous insufficiency (CVI).

Material and Method: Patients who underwent a venous procedure, either thermal or non-thermal, in our clinic between June 2022 and December 2022 evaluated for inclusion to this retrospective study. The patients with available complete medical records in the database of the health center were included. Patients who had a history of deep venous thrombosis, thrombophlebitis, a venous intervention or who underwent open surgical venous procedure were excluded. Patients were asked to draw a line representing the intensity of the procedural pain on visual analogue scale (VAS).

Results: A total of 183 patients were evaluated and 60 (100%) patients whom complete medical records were available were included. The non-thermal ablation group included 30 (50%), the thermal ablation group included 30 (50%) patients. There were 14 (46.67%) males in non-thermal ablation group, 12 (40.00%) in thermal ablation group (P=0.602). The mean age in the non-thermal ablation group was 47.10 ± 9.84 years, 44.70 ± 8.84 years in the thermal ablation group (P=0.324). The procedure duration was significantly longer in thermal ablation group (22.70 ± 4.45 min in non-thermal ablation group vs 33.10 ± 3.64 min in thermal ablation group, P<0.001). VAS score was significantly higher in thermal ablation group (46.63 ± 15.76 in non-thermal ablation group vs 61.13 ± 10.65 thermal ablation group, P=0.001).

Conclusion: The endovenous non-thermal ablation of vena saphena magna (VSM) with cyanoacrylate is a more comfortable and less painful alternative for the thermal ablation technique for the patients with CVI.

Keywords: Chronic venous insufficiency; cyanoacrylate; radiofrequency; vena saphena magna; thermal ablation.

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Öz

Amaç: Kronik venöz yetmezlik için alt ekstremite venlerine termal veya termal olmayan ablasyon uygulanan hastalarda VAS ile ölçülen işlemsel ağrı yoğunluğunu karşılaştırmak

Gereç ve Yöntemler: Haziran 2022 ile Aralık 2022 tarihleri arasında kliniğimizde termal veya termal olmayan venöz girişim uygulanan hastalar bu retrospektif çalışmaya dahil edilmek üzere değerlendirildi. Sağlık merkezi veri tabanında tıbbi kayıtları tam olan hastalar dahil edildi. Derin ven trombozu, tromboflebit, venöz girişim öyküsü olan veya açık cerrahi venöz girişim uygulanan hastalar çalışma dışı bırakıldı. Hastalardan görsel analog skala (VAS) üzerinde işlem sırasındaki ağrının şiddetini temsil eden bir çizgi çizmeleri istendi.

Sonuçlar: Toplam 183 hasta değerlendirildi ve tıbbi kayıtları eksiksiz olan 60 (%100) hasta dahil edildi. Termal olmayan ablasyon grubu 30 (%50), termal ablasyon grubu 30 (%50) hastayı içeriyordu. Termal olmayan grupta 14 (%46,67), termal ablasyon grubunda 12 (%40,00) erkek vardı (P=0,602). Ortalama yaş termal ablasyon uygulanmayan grupta 47,10 ± 9,84, termal ablasyon uygulanan grupta 44,70 ± 8,84 idi (P=0,324). İşlem süresi termal ablasyon grubunda anlamlı olarak daha uzundu (termal olmayan grupta 22.70 ± 4.45 dk ve termal ablasyon grubunda 33.10 ± 3.64 dk, P<0.001). VAS skoru termal ablasyon grubunda anlamlı olarak yüksekti (termal ablasyon olmayan grupta 46,63 ± 15,76 ve termal ablasyon grubunda 61,13 ± 10,65, P=0,001).

Tartışma: Kronik venöz yetmezlikli hastalarda vena safena magna'nın (VSM) siyanoakrilat ile endovenöz termal olmayan ablasyonu, termal ablasyon tekniğine göre daha konforlu ve daha az ağrılı bir alternatiftir.

Anahtar Kelimeler: Kronik venöz yetmezlik, siyanoakrilat, radyofrekans, vena safena magna, termal ablasyon

Introduction

Varicose veins are the enlarged subcutaneous veins mostly seen in the lower extremity and mainly caused by the chronic venous insufficiency (CVI). The prevalence of varicose veins of the lower extremity is about 25.1%, chronic venous insufficiency is about 16% and it is slightly higher in women (1,2). Clinical manifestations and symptoms vary from eczema, hyperpigmentation, leg heaviness, pedal swelling, pain and chronic ulcers which significantly diminish the quality of life of patients (3,4).

There are thermal and non-thermal treatment options for CVI. Non-thermal treatment modalities include venoactive drugs such as flavonoids, calcium dobesilate, etc., sclerotherapy, glue ablation (cyanoacrylate), compression stockings and vein stripping (5–7). Thermal treatment options include ablation of the vein with the heat energy of radiofrequency, laser, and steam (8,9). A tumescent anesthesia is generally needed for thermal modalities and non-thermal interventions are usually performed under local anesthesia (6,9–11).

Visual analogue scale (VAS) is a psychometric response measurement tool to evaluate subjective characteristics or attitudes such as pain or symptom severity in medicine. It has been used in several medical studies to evaluate the pain before or after a procedure or during the course of a disease (12–14).

Herein, we aimed to compare the procedural pain intensity measured with VAS in patients undergoing thermal or non-thermal ablation of lower extremity veins for chronic venous insufficiency.

Material and Methods

Patients who underwent a venous procedure, either thermal or non-thermal, in our clinic between June 2022 and December 2022 evaluated for inclusion to this retrospective study. The patients with available complete medical records in the database of the health center were included in this study. Patients who had a history of deep venous thrombosis, thrombophlebitis, a venous intervention or who underwent open surgical venous procedure were excluded. Preprocedural informed consent was taken from all of the patients. Local ethical committee approval was taken to conduct the study.

Patients were asked to express the intensity of pain they felt during the procedures by drawing a line starting from point 0 to point 100 on a VAS. It was explained to the patients that the longer the line, the more intense the pain.

The procedure length was measured starting from the first vein puncture until completion of the vein ablation and recorded. The length of the treated vein segment was measured with a sterile ruler in the procedure. All patients were checked for the presence of a non-diagnosed venous thrombosis and the diameter of the target veins were measured to check the indication for intervention in the beginning of the procedures.

The procedures

All procedures were done in the operating room. Non-thermal ablation procedures were performed under local anesthesia. Thermal ablation procedures were performed under spinal anesthesia or femoral nerve block of the target extremity and radiofrequency-powered catheters were used in all of them.

In non-thermal ablation procedures, after proper cleaning and covering the surgical site with surgical cloths, the vena saphena magna (VSM) was accessed with a micro puncture introducer set. A 0.035-inch J guidewire was inserted with the guidance of ultrasonography probe into the vein. Then a 5F introducer sheath was advanced over the J guidewire followed by introduction of the 4F delivery catheter. The delivery catheter was filled with cyanoacrylate and attached to the injection gun of the system. The system injected 0.3 cc cyanoacrylate in every pressing of the trigger for 5 seconds. The catheter was pulled back 2 cm per second while pressing the trigger of the delivery gun. In this method, 0.03 cc cyanoacrylate was delivered in every centimeter of the vein. Extrinsic pressure was applied over the vein for proper adhesion of the vessel wall. The following products were used in the non-thermal venous ablation procedures Venex (Vesta Medical Devices, Ankara, Turkey), VariClose Vein Sealing System (Biolas, Ankara, Turkey) and Musyan (Neogenix, Ankara, Turkey).

In the thermal ablation procedures, tumescent anesthesia was also applied in addition to the spinal anesthesia or femoral nerve block to prevent skin thermal injury. A solution of 35 mg lidocaine in a 500 ml saline was used for the tumescent anesthesia and it was injected around the target vein under ultrasonography guidance. In these procedures, the VSM was cannulated near the most distal point of the venous reflux and the catheter tip was placed 1.5 to 2 cm distal to the saphenofemoral junction under ultrasonography guidance. All the thermal procedures were done with 7 cm radiofrequency-powered heat generating coils (ClosureFast, Medtronic, Minneapolis, USA and FCare, Berchem, Belgium). The radiofrequency (RF) catheter was passed through the vein with the application of the thermal energy in every 7 cm long segments with an overlap of 0.5 cm and the energy was applied for 20 seconds in every segment. Extrinsic pressure was applied over the vein during the procedures.

All the patients were transferred to the inpatient ward and discharged in the same day. All procedures were resulted with technical success.

Statistical analysis

The Statistical Package for The Social Sciences (SPSS version 16.0 Inc., Chicago, IL, USA) software was used to statistical analyzation of the data. Categorical data were expressed as numbers and percentages. Continuous data were presented as mean ± standard deviation (SD). The Kolmogorov-Smirnov test was used to test the normality of data distribution. Categorical data were tested with Chi-square and Fisher's Exact tests and continuous data were tested with independent samples t-test. The non-parametric continuous data were tested with Mann-Whitney U test. P values <0.05 was accepted as statistically significant.

Results

A total of 183 patients were evaluated. The complete medical records of 60 (100%) patients were available and they were included in this study. The first group (non-thermal ablation) consisted of the patients (n=30) who underwent non-thermal venous ablation procedures and the second group (thermal ablation) consisted of the patients (n=30) who underwent thermal venous ablation procedures. There were 14 (46.67%) males in the first group and 12 (40.00%) males in the second group (P=0.602). The mean age in the first group was 47.10 ± 9.84 years and 44.70 ± 8.84 years in the second group (P=0.324). There were no statistically significant differences between the groups in regard to the preoperative variables. The preoperative data were presented in Table 1.

The number of patients who received local anesthesia were significantly higher in non-thermal ablation group (26 (86.67%) patients in non-thermal ablation group vs 1 (3.33) patient in thermal ablation group, P<0.001). The numbers of patients who received spinal anesthesia or femoral nerve block were significantly higher in thermal ablation group (3 (10.00%) patients in non-thermal ablation group vs 12 (40.00%) patients in thermal ablation group and 1 (3.33%) patient in non-thermal ablation group vs 17 (56.67%) patients in thermal ablation group respectively, P<0.001). The procedure duration was significantly longer in thermal ablation group (22.70 ± 4.45 min in non-thermal ablation group vs 33.10 ± 3.64 min in thermal ablation group, P<0.001). VAS score was significantly higher in thermal ablation group (46.63 ± 15.76 in non-thermal ablation group vs 61.13 ± 10.65 thermal ablation group, P=0.001). The postoperative data were presented in Table 2.

Table 1. Preoperative data			
	Non-Thermal ablation (n=30)	Thermal ablation (n=30)	P value
Male n (%)	14 (46.67)	12 (40.00)	0.602
Age years mean ± SD	47.10 ± 9.84	44.70 ± 8.84	0.324
Diabetes mellitus n (%)	7 (23.33)	6 (20.00)	0.754
Hypertension n (%)	5 (16.67)	3 (10.00)	0.445
Smoking n (%)	7 (23.33)	12 (40.00)	0.165
COPD n (%)	2 (6.67)	1 (3.33)	0.550
Bilateral venous insufficiency n (%)	12 (40.00)	9 (30.00)	0.417
CAD n (%)	11 (36.67)	23.33)	0.260
Urea mg/dl mean ± SD	30.64 ± 9.39	29.62 ± 10.01	0.684
Creatinine mg/dl mean ± SD	0.81 ± 0.32	0.75 ± 0.14	0.345
Glucose mg/dl mean ± SD	106.87 ± 31.67	96.77 ± 22.84	0.162
Venous reflux duration sec mean ± SD	5.47 ± 3.40	4.97 ± 4.97	0.585
Reflux duration other extremity mean ± SD	4.67 ± 2.64	6.56 ± 3.50	0.174
VSM diameter mm mean ± SD	5.99 ± 1.12	6.45 ± 1.35	0.159
VSM diameter other extremity mm mean ± SD	6.15 ± 1.01	6.23 ± 1.91	0.888
CEAP Classification n (%) C2	22 (73.33)	20 (66.67)	0.769
C3	5 (16.67)	8 (26.67)	
C4a	2 (6.67))	1 (3.33)	
s C4b	1 (3.33)	1 (3.33)	

COPD: Chronic obstructive pulmonary disease; CAD: Coronary artery disease; SD: Standard deviation; VSM: Vena saphena magna;

Table 2. Postoperative data				
		Non-Thermal ablation (n=30)	Thermal ablation (n=30)	P value
Treatment extremity n (%)	Right	9 (30.00)	13 (43.33)	0.105
	Left	21 (70.00)	15 (50.00)	
	Bilateral	0	2 (6.67)	
Anesthesia type n(%)	Local	26 (86.67)	1 (3.33)	<0.001
	Spinal	3 (10.00)	12 (40.00)	
		1 (3.33)	17 (56.67)	
Procedure duration mins mean ± SD		22.70 ± 4.45	33.10 ± 3.64	<0.001
Length of treated segment cm mean ± SD		31.17 ± 6.60	30.97 ± 5.75	0.784
VAS score mm mean ± SD		46.63 ± 15.76	61.13 ± 10.65	0.001

SD: Standard deviation; VAS: Visual analogue scale.

Discussion

According to the results of this study, non-thermal ablation of the lower extremity varicose veins was less painful and could be done in a shorter time when compared to the thermal ablation technique. The length of the vein to be treated had no effect on the pain perception or the duration of the procedures in this study.

Endovenous ablation of the saphenous vein (both thermal and non-thermal) for the treatment of chronic venous reflux is a widely used method and it is recommended as the first treatment choice for lower extremity chronic venous insufficiency (CVI) in the guidelines of the Society for Vascular Surgery, American Venous Forum, and European Society for Vascular Surgery (8,15). There are many advantages of the endovenous treatment methods of CVI reported in the literature over the open surgery such as higher patient comfort, lower postprocedural pain, lower rates of complications and faster recovery of the patients to the daily life (16–19).

Thermal and non-thermal venous ablation techniques have their advantages and disadvantages. Thermal ablation needs tumescent anesthesia which prolongs the procedural time, causes patient discomfort, hematoma and ecchymosis but it has lower risk of postablation thrombus extension to saphenofemoral junction (20). Non-thermal ablation technique is based on the polymerization of cyanoacrylate after its contact with plasma and blood and causes the closure of the target

vein (21). It is more comfortable for the patients because there is no thermal energy involved in its mechanism and there is no significant postprocedural side effects or complications reported in the literature (7). But Proebstle et al reported in 8 (21%) of the 38 patients undergoing non-thermal ablation of the saphenous veins postprocedural thrombus extension through the saphenofemoral junction (22). Both methods are used in our clinic in routine venous ablation procedures and it is the operating surgeon's call which method will be used.

In a randomized trial including 222 patients, the efficacy, procedural comfort and postprocedural complications after radiofrequency ablation (RF) and cyanoacrylate embolization (CAE) for symptomatic GSV incompetence were compared. After three months, the closure rates were 99% in CAE and 94% in RFA. The intensity of the pain during the procedures were similar in both groups. But there was less ecchymosis in the treated region after CAE in comparison to RFA (P<0.01) (23).

There are some studies comparing another thermal energy based endovenous ablation technique, the endovenous lase ablation (EVLA), with the RFA technique in terms of procedural pain, ecchymosis and tenderness. Almeida et al (24) treated 87 veins in 69 patients with either ClosureFast or 980-nm EVLA for CVI in their randomized study. They reported significantly lower scores related with pain, ecchymosis and tenderness in ClosureFast group at 46 hours, 1 week and 2 weeks. They also reported more prevalent minor complications in EVLA group (P=0.210). Sheperd et al (25) treated 131 CVI patients randomly either with EVLA or RFA. They reported lower postprocedural pain scores over 3 days in RFA group (26.4 ± 22.1 mm for RFA vs 36.8 ± 22.5 mm for EVLA, P=0.010). The most common choice of thermal ablation technique in our center is also the RFA technique.

In their study Morrison et al (23) reported lesser mean procedure time in CAE group than RFA group (24 vs 19 minutes, P<0.01). On the contrary, Bozkurt et al (20) compared 156 CVI patients treated with EVLA and 154 CVI patients treated with CAE and reported lower mean procedure time in CAE group (33.2 ± 5.7 minutes in EVLA group vs 15 ± 2.5 minutes in CAE group, P<0.001). The mean procedure time was significantly lower in non-thermal ablation (CAE) group in our study.

In thermal endovenous ablations, a mean local anesthesia volume of 10 – 12 ml/cm administration to the perivenous space is recommended for the tumescent anesthesia in the literature (26). Another anesthesia technique is the combination of general anesthesia with supraglottic device and tumescent anesthesia in EVLA procedures to reduce patients' discomfort and pain (27). In their study Lafçı and Budak (28), compared the patients undergoing RFA for CVI under general anesthesia or spinal anesthesia. They reported significantly lower pain scores at 1 hour in spinal anesthesia group (0.1 cm vs 1.7 cm, P<0.001). Also duration in the operating room and surgery times were significantly lower in spinal anesthesia group (45.2 ± 0.2 minutes versus 43.9 ± 0.4 minutes, P<0.01; and 28.1 ± 0.2 minutes versus 26.5 ± 0.3 minutes, P<0.001, respectively). The anesthesia types used in the groups were significantly different in our study. The non-thermal ablations (CAE) were performed in local anesthesia because there was no thermal energy application in the procedure and the main source of pain in the procedure was the vein puncture for vascular access. The thermal ablations were performed either under spinal anesthesia or femoral nerve block because the thermal energy application was a painful procedure. Also perivascular tumescent anesthesia was also administered in addition to spinal anesthesia or femoral vein block to prevent skin burns and reduce postprocedural discomfort.

Limitations of the study

The main limitations of this study was its retrospective nature and it was a single center study. Also only one type of thermal ablation was used in this study. We did not measure the total tumescent anesthetic agent volume administered in the patients.

Conclusion

The endovenous non-thermal ablation of GSV with cyanoacrylate is a more comfortable and less painful alternative for the thermal ablation technique for the patients with CVI. We think that more prospective randomized studies should be conducted including larger patient populations on this subject.

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Original Article

The Anatomical Landmarks in Endonasal Endoscopic Optic Nerve Decompression Surgery: An Anatomical Study

Endonazal Endoskopik Optik Sinir Dekompresyon Cerrahisindeki Anatomik Belirteçler: Anatomi Çalışması

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Abstract

Aim: Optic nerve decompression can be applied for many pathologies that affect the optic canal and the optic nerve. Optic nerve decompression via endonasal endoscopic method is very popular in nowadays with the developments in endoscopic surgery.

Material and Methods: In this study, the lateral opticocarotid recess (LOCR) and the medial opticocarotid recess (MOCR) which are important anatomical landmarks used during transsphenoidal approach to the opticocarotid region were evaluated. The relations of these anatomical landmarks with each other and with important surrounding landmarks such as optic nerve were examined.

Results: MOCR were observed in all cadavers on the right side and in 4 of 5 cadavers on the left side. The superior border of the LOCR was measured as 4.85±1.94 mm in average on the right side and 3.93±1.11 mm in average on the left side. The inferior border of the LOCR was measured as 4.72±2.11 mm in average on the right side and 3.98±1.67 mm in average on the left side. The linear distance between the LOCR and the MOCR was measured as 3.11±1.41 mm in average on the right side and 2.46±1.36 mm in average on the left side.

Conclusion: It is necessary for a safe surgery to reveal the anatomical landmarks and to know the detailed anatomy of this region during optic nerve decompression.

Keywords: Optic nerve; optic canal; decompression; landmarks; endoscopic

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Öz

Amaç: Canalis opticus'u ve nervus opticus'u etkileyen pek çok patoloji için nervus opticus dekompresyonu yapılmaktadır. Endonazal endoskopik yol ile yapılan nervus opticus dekompresyonu, endoskopik cerrahideki gelişmeler ile de günümüzde oldukça revaçtadır.

Gereç ve Yöntemler: Bu çalışmada opticocarotid bölgeye transsfenoidal yaklaşım sırasında kullanılan ve önemli anatomik belirteçler olan materal optikorarotid recess (LOCR) ve medial opticocarotid recess (MOCR) incelendi. Bu anatomik belirteçlerin birbiri ile olan ve nervus opticus gibi önemli çevre anatomik yapılar ile olan ilişkileri değerlendirildi.

Bulgular: MOCR sağ tarafta tüm kadavralarda ve sol tarafta 5 kadavranın 4 tanesinde belirgin olarak izlendi. LOCR superior kenarı sağ tarafta ortalama 4,85±1,94 mm ve sol tarafta ortalama 3,93±1,11 mm aralığında ölçüldü. LOCR inferior kenarı sağ tarafta ortalama 4,72±2,11 mm ve sol tarafta ortalama 3,98±1,67 mm aralığında ölçüldü. LOCR ile MOCR arasındaki lineer mesafe sağ tarafta ortalama 3,11±1,41 mm ve sol tarafta ortalama 2,46±1,36 mm aralığında ölçüldü.

Sonuçlar: Nervus opticus dekompresyonu sırasında anatomik belirteçlerin ortaya konulabilmesi ve bölgenin detaylı anatomisinin bilinmesi güvenli bir cerrahi için gereklidir.

Anahtar Kelimeler: optik sinir; optik kanal; dekompresyon; belirteç; endoskopik

Introduction

Optic nerve decompression is performed for pathologies that affect the optic canal and the optic nerve such as tumors, trauma, infections, vascular pathologies and sinus lesions [1].

Optic nerve decompression was firstly perfomed by Dandy in 1922 [2]. Optic nerve decompression via transethmoidal approach was firstly perfomed by Sewall [3]. Optic nerve decompression via endonasal endoscopic approach, which is a good option for pathologies that affect the optic canal especially inferiorly and medially, is also very popular in nowadays with the developments in endoscopic surgery [1, 4].

Optic nerve decompression via endonasal endoscopic approach has some advantages that it provides a panoromic view to the sellar region, does not require brain retraction, does not leave behind any incision scar and has a relatively short surgical time [1, 5, 6]. However, this surgical technique has also some possible and serious complications such as neurovascular injury (the optic nerve or the ophthalmic artery injury) [7]. For this reason, it is extremely necessary to know the detailed anatomy of this region and to be aware of the anatomical landmarks that play a key role for a safe surgery.

In this study, the lateral opticocarotid recess (LOCR) and the medial opticocarotid recess (MOCR), which are important anatomical landmarks used during the transsphenoidal approach to the opticocarotid region, were examined. The relationships of these anatomical landmarks with each other and with other important surrounding anatomical structures such as the optic nerve were also evaluated.

Material And Methods

This study was performed on a total of five (n=5) adult head cadavers in Ankara University School of Medicine, Department of Anatomy (Surgical Neuroanatomy Laboratory). Five fresh frozen cadaver heads stored at (-21)-(-5) ^{0}C and with colored silicone intravascular were used. Cadaver heads were fixed in the neutral position and examined by using the binostral approach with the Storz 0-degree rigid endoscope. (Karl Stroz SE&Co. Tuttlingen, Germany).

Transsphenoidal endoscopic approach were performed to all of the five cadaver heads. The mucosa of the sphenoid sinus was removed and the bony structure was revealed. LOCR and MOCR, the two important anatomical landmarks that located in the sphenoid sinuses of the cadavers were revealed and examined with an endoscope (Figure 1).

Measurements were made of the superior and inferior borders of the LOCR, which has a triangular shape. The relationships between the LOCR, internal carotid artery and optic nerve were revealed in all cadavers (Figure 2). The linear distance between MOCR and LOCR was measured. Each step of the anatomical dissection was recorded with digital cameras.

Results

LOCR, carotid protuberance and optic protuberance were observed bilaterally in all of the five cadavers. MOCR was clearly observed in all cadavers on the right side and in four out of five cadavers on the left side.

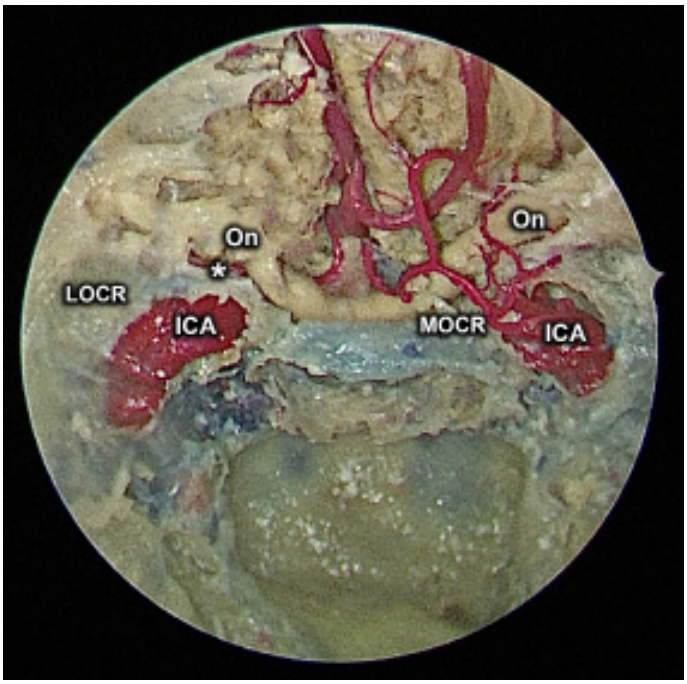
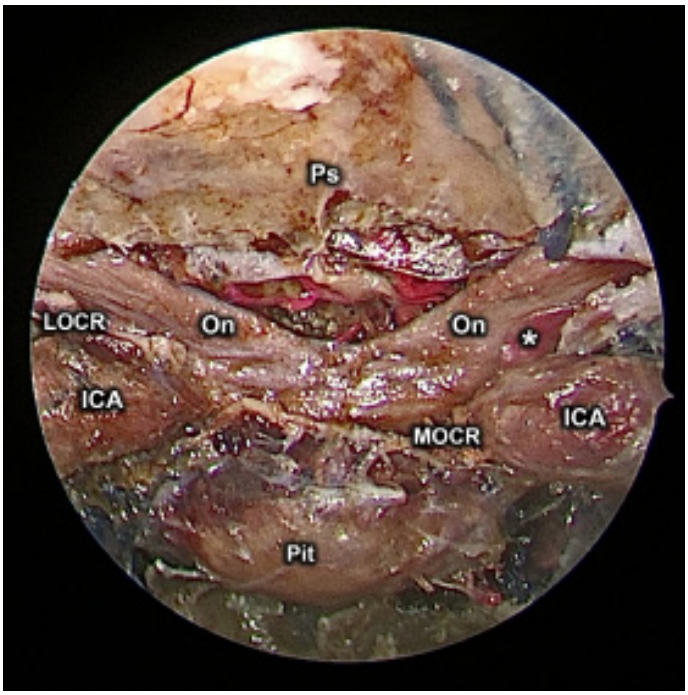


Figure 1: Opticocarotid region. The optic nerve decompression was performed bilaterally and internal carotid arteries were skeletonized. MOCR: Medial opticocarotid recess, LOCR: Lateral opticocarotid recess, On: Optic Nerve, ICA: Internal carotid artery, *: Ophthalmic artery



The superior border of the LOCR ranges between a minimum of 3.22 mm and a maximum of 7.28 mm (mean 4.85±1.94 mm) on the right side and between a minimum of 2.37 mm and a maximum of 5.48 mm (mean 3.93±1.11 mm) on the left side (Table 1).

Table 1: The measurements of superior border of LOCR

	Right (mm)	Left (mm)
Cadaver 1	6.10	5.48
Cadaver 2	7.28	4.02
Cadaver 3	3.64	4.19
Cadaver 4	3.22	2.37
Cadaver 5	4.01	3.61
Average	4.85±1.94	3.93±1.11

The superior border of the LOCR ranges between a minimum of 2.09 mm and a maximum of 6.92 mm (mean 4.72±2.11 mm) on the right side and between a minimum of 1.79 mm and a maximum of 6.41 mm (mean 3.98±1.67 mm) on the left side (Table 2).

Table 2: The measurements of inferior border of LOCR

	Right (mm)	Left (mm)
Cadaver 1	6.92	6.41
Cadaver 2	6.88	4.32
Cadaver 3	3.78	4.08
Cadaver 4	2.09	3.33
Cadaver 5	3.95	1.79
Average	4.72±2.11	3.98±1.67

The linear distance between LOCR and MOCR ranges between a minimum of 1.97 mm and a maximum of 5.25 mm (mean 3.11±1.41 mm) on the right side and between a minimum of 1.61 mm and a maximum of 4.49 mm (mean 2.46±1.36 mm) on the left side (Table 3).

Table 3: The measurement of the distance between LOCR and MOCR. *: In Cadaver 3, MOCR could not be determined on the left side and therefore it could not be measured.

	Right (mm)	Left (mm)
Cadaver 1	5.25	4.49
Cadaver 2	3.89	2.08
Cadaver 3	1.97	-*
Cadaver 4	2.24	1.61
Cadaver 5	2.24	1.66
Average	3.11±1.41	2.46±1.36

Discussion

In the literature, many landmarks have been described that can be used during the approaches to the sellar and opticocarotid regions [1,4,8,9]. Optic nerve is a cone-shaped projection on the superolateral wall of the sphenoid sinus during the endoscopic approach [8]. LOCR, an important anatomical landmark used to identify the optic nerve, is the pneumatisation of the optic strut that separates the optic canal from the superior orbital fissure, and it is more prominent compared to MOCR [1,8]. Locatelli et al. defined LOCR as the most prominent anatomical landmark in determining the

optic nerve, the internal carotid artery and the ophthalmic artery [10]. Li et al emphasized that the superior and lateral walls of the sphenoid sinus can be confused with optic protuberance in endoscopic views, and therefore LOCR is a stronger predictor than the optic protuberance [7]. In this study LOCR, carotid protuberance and optic protuberance were identified bilaterally in all five cadavers.

LOCR has a triangular shape and borders of this triangle are determined by optic nerve superiorly, internal carotid artery inferiorly and orbital apex and inferior orbital fissure laterally [8]. The optic nerve has four segments: intracranial, intracanalicular, intraorbital and intraocular [11]. The length of the superior border of the LOCR corresponds to the intracanalicular part of the optic nerve. In this study, the mean length of the superior border was measured as 4.85±1.94 mm on the right side and 3.93±1.11 mm on the left side.

The clinoidal part of the internal carotid artery is located on the inferior part of the LOCR (Figure 2). Internal carotid artery injury is one of the most serious complications that can be encountered during optic nerve decompression via endonasal endoscopic approach. In this study, the mean length of the inferior border was measured as 4.72±2.11 mm on the right side and 3.98±1.67 mm on the left side.

MOCR is a teardrop-shaped bony recess. It corresponds to the medial intersection of the paraclinoid carotid canal and the preforaminal segment of the optic nerve [8]. According to the study by Yilmazlar et al, MOCR is the least prominent anatomical landmark in the sphenoid sinus and could be detected at 25 of 30 cadavers on the right side and 22 of 30 on the left side [4]. Ozcan et al stated in their study that the reveal of MOCR provided the preservation of subchiasmatic and infundibular branches during dissection [12]. In this study by Ozcan et al, MOCR was determined in 24 of 29 cadavers on the right side and in 19 of 29 cadavers on the left side [12]. In our study, MOCR was clearly observed in all of the cadavers on the right side and in 4 of the 5 cadavers on the left side.

Ozcan et al defined a prominent sulcus between MOCR and LOCR [12]. The decompression of the optic canal can be achieved by following this sulcus, which is located between the optic nerve and the internal carotid artery [4]. Ozcan et al classified the cadaver specimens with a distance less than 3 mm between LOCR and MOCR as Type 1 and the cadaver specimens with a distance more than 3 mm as Type 2 [12]. According to this study, 19 of 29 cadavers were classified as Type 1 on the right side and in these specimens, the average distance between LOCR and MCOR was measured as 2.26±0.50 mm. In the same study, 10 of 29 cadavers were classified as Type 2 on the right side and the average distance between LOCR and MOCR was measured as 6.64±0.10 mm. On the left side, 17 of 29 cadavers were classified as Type 1 and the average distance between LOCR and MOCR was measured as 2.26±0.40 mm on the left side. 12 of 29 cadavers were classified as Type 2 and the average distance between LOCR and MOCR was measured as 6.79±0.90 mm on the left side [12]. In this study, the mean distance between LOCR and MOCR was 3.11±1.41 mm on the right side and 2.46±1.36 mm on the left side. Additionally, anatomical exposure of the optic canal and the orbital apex is very important, and major complications can be reduced and previous results affecting outcomes were recently reported [13].

Conclusion

Optic nerve and optic canal can be affected by many sellar and parasellar pathologies such as tumors, trauma, infections, vascular pathologies and inflammatory processes. Anatomical landmarks located in the sphenoid sinus play a major role during endonasal endoscopic surgery to this region. To be able to reveal these landmarks and to know the detailed anatomy of this region is necessary for a safe surgery.

Conflict of interest

None

Financial suppor

None

Ethical Approval

Conducting scientific studies on cadavers or cadaveric body parts, contribution to education and science is not “human subjects” research and do not require ethical approval. The authors would like to express their sincere gratitude to the donors and their families for their and does not require review IRB review and approval.

Author Contributions

Tugba Morali Guler, Gokmen Kahilogullari, Ayhan Comert wrote the main manuscript text. Tugba Morali Guler, Hazan Basak, Yigit Gungor, Mehmet Yilmaz, Suha Beton, Gokmen Kahilogullari, Ayhan Comert collected the data. Tugba Morali Guler, Gokmen Kahilogullari, Ayhan Comert analyzed the data, and all authors reviewed the manuscript.

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Original Article

Efficacy of intravenous ibuprofen and acetaminophen on postoperative pain and tramadol consumption in laparoscopic cholecystectomy: prospective, randomized, double-blinded clinical trial

Laparoskopik kolesistektomide intravenöz ibuprofen ve asetaminofenin postoperatif ağrı ve tramadol tüketimi üzerine etkinliği: prospektif, randomize, çift kör klinik çalışma

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Abstract

Aim: Many techniques, including multimodal analgesia, have been used to manage postoperative pain after laparoscopic cholecystectomy (LC). Although the number of studies using intravenous (IV) ibuprofen is still limited, ibuprofen has been shown to have a potential role in managing postoperative pain. The primary outcome of this study is to evaluate and compare the impact of IV forms of ibuprofen and acetaminophen on 24-hour postoperative opioid consumption and pain management in patients undergoing LC. The second outcome of the study is to evaluate the impact of ibuprofen and acetaminophen on opioid-related adverse events (ORAE).

Materials and Methods: This study was a prospective, randomized, double-blind clinical trial. Following ethical committee approval, 70 patients aged 18 to 65, American Society of Anesthesiology (ASA) score I- II, and those scheduled for LC were enrolled in the study. Patients were randomly divided into two groups. The control group (n=35) received 800 mg IV ibuprofen (group I) in 100 mL saline during surgery, while the acetaminophen group (n=35) received 1000 mg (group A). In the postoperative period, all patients received a patient-controlled analgesia (PCA) device with tramadol. The PCA device was set to a bolus dose of 10 mg and had a lockout time of 15 minutes. A blinded pain nurse assessed postoperative analgesia at the 1st, 2nd, 4th, 6th, 12th, and 24th hours using a numerical rating scale (NRS). The incidence of postoperative nausea and vomiting (PONV), total tramadol consumption, and the need for additional analgesics during the 24-hour postoperative period were recorded.

Results: Seventy patients who underwent LC participated in this study. The use of analgesic medications was statistically lower in group I than in the other group A. NRS scores between the IV ibuprofen and acetaminophen groups were statistically similar at the 1st, 2nd, 4th, 6th, 12th, and 24th hours postoperatively ($P>0.05$). 24-hour opioid consumption was statistically significantly higher in group A than in group I ($P<0.05$). PONV rates were similar in the ibuprofen and acetaminophen groups ($P>0.05$). ORAEs were similar between groups.

Conclusion: Ibuprofen as part of tramadol-based multimodal analgesia reduced tramadol consumption compared to acetaminophen during the first 24 hours postoperatively following elective LC surgery. The IV ibuprofen-tramadol combination appeared superior to an acetaminophen-tramadol combination. ORAEs were similar in both groups.

Keywords: Ibuprofen, acetaminophen, postoperative pain, analgesia, laparoscopic cholecystectomy

Abbreviations: ASA= American Society of Anesthesiologists, IV= intravenous, NRS= Numerical rating scale, PCA= patient-controlled analgesia, PONV= postoperative nausea and vomiting syndrome, ORAE= opioid-related adverse events

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Öz

Amaç: Laparoskopik kolesistektomi (LC) sonrası postoperatif ağrıyı yönetmek için multimodal analjezi de dahil olmak üzere birçok teknik kullanılmıştır. İntravenöz (IV) ibuprofen kullanan çalışmaların sayısı hala sınırlı olsa da, ibuprofenin postoperatif ağrı yönetiminde potansiyel bir rolü olduğu gösterilmiştir. Bu çalışmanın birincil amacı, LC uygulanan hastalarda IV ibuprofen ve asetaminofen formlarının postoperatif 24 saatlik opioid tüketimi ve ağrı yönetimi üzerindeki etkisini değerlendirmek ve karşılaştırmaktır. Çalışmanın ikincil amacı, ibuprofen ve asetaminofenin opioidle ilişkili advers olaylar (ORAE) üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntemler: Bu çalışma prospektif, randomize, çift kör bir klinik çalışmaydı. Etik kurul onayı alındıktan sonra yaşları 18 ile 65 arasında değişen, American Society of Anesthesiology (ASA) skoru I-II olan ve LC planlanan 70 hasta çalışmaya alındı. Hastalar rastgele iki gruba ayrıldı. Ameliyat sırasında kontrol grubu (n=35) 100 mL salin içinde 800 mg IV ibuprofen (grup I), asetaminofen grubu (n=35) 1000 mg (grup A) aldı. Postoperatif dönemde tüm hastalara tramadollü hasta kontrollü analjezi (HKA) cihazı verildi. PCA cihazı, 10 mg bolus dozuna ayarlandı ve 15 dakikalık bir kilitleme süresine sahipti. Kör bir ağrı hemşiresi, postoperatif analjeziyi sayısal derecelendirme ölçeği (NRS) kullanarak 1, 2, 4, 6, 12 ve 24. saatlerde değerlendirdi. Postoperatif 24 saatlik dönemde postoperatif bulantı ve kusma insidansı, toplam tramadol tüketimi ve ek analjezik ihtiyacı kaydedildi.

Bulgular: Bu çalışmaya LC uygulanan 70 hasta katıldı. Analjezik ilaç kullanımı grup I'de grup A'ya göre istatistiksel olarak daha düşüktü. İV ibuprofen ve asetaminofen grupları arasında NRS skorları postoperatif 1, 2, 4, 6, 12 ve 24. saatlerde istatistiksel olarak benzerdi (P>0.05) . 24 saatlik opioid tüketimi grup A'da grup I'e göre istatistiksel olarak anlamlı derecede yüksekti (P<0.05). POBK oranları ibuprofen ve asetaminofen gruplarında benzerdi (P>0.05). ORAE'ler gruplar arasında benzerdi.

Sonuç: Tramadol bazlı multimodal analjezinin bir parçası olarak ibuprofen, elektif LC cerrahisini takiben postoperatif ilk 24 saat boyunca asetaminofene kıyasla tramadol tüketimini azaltmıştır. IV ibuprofen-tramadol kombinasyonu, asetaminofen-tramadol kombinasyonundan avantajlı olarak izlendi. ORAE'ler her iki grupta da benzerdi.

Anahtar kelimeler: İbuprofen, asetaminofen, postoperatif ağrı, analjezi, laparoskopik kolesistektomi

Introduction

Laparoscopic cholecystectomy (LC) is the most common abdominal surgery in developed countries. It is the gold standard surgical technique for gallstone disease [1]. This procedure has less postoperative pain, better cosmetic outcomes, faster healing, and earlier mobilization [2].

Several factors are involved in the development of pain after LC. This pain is quite complex and is generally considered visceral. Factors involved in developing this pain include irritation of the phrenic nerve due to the insufflation of CO_2 into the abdominal cavity, distension of the abdomen, incisions at the ports, and trauma associated with removing factors [3].

Postoperative pain is an acute sensation associated with an inflammatory process associated with surgical trauma that decreases as the tissue heals. Successful postoperative analgesia is known to prevent most pain-related effects on the patient, such as the inability to breathe comfortably, increased workload on the cardiovascular system, thromboembolic events with delayed mobilization, and increased stress response with activation [4,5].

Opioids play a crucial role in pain management by acting on the central nervous system, but they cannot block the inflammatory aspect of pain [6]. Eliminating the inflammatory response can reduce the need for opioids and strengthen the control of postoperative processes [7,8]. Opioid use has been associated with severe adverse effects, including respiratory depression, postoperative pruritus, urinary retention, gastrointestinal events, sedation, and allergic reactions [9]. Combining nonsteroidal anti-inflammatory drugs (NSAIDs) with opioids may also reduce adverse effects and the required opioid dose [10-13]. The ASA Task Force on Acute Pain Management reports that opioids in combination with NSAIDs, COXIBs, or acetaminophen may be superior to opioid use alone [5].

Nonsteroidal analgesics such as ibuprofen and other analgesics such as acetaminophen have long been used to reduce pain and inflammation in various conditions. These agents prevent the stimulation of pain receptors in response to injury by inhibiting the conversion of arachidonic acid to prostaglandins [14].

The IV form of ibuprofen has been used in the United States since 2009 for treating mild and moderate pain and severe pain in combination with opioids [15,16]. Ibuprofen is a propionic acid derivative that like other NSAIDs, has anti-inflammatory, antipyretic, and analgesic effects. Compared with other NSAIDs, it has a lower side effect profile on the gastrointestinal tract and cardiovascular

system due to its balanced COX-1 and COX-2 inhibition [17]. Because of the inherent risk of bleeding during surgery, drugs inhibiting COX are generally accepted reluctantly [18].

Acetaminophen is the most commonly used analgesic, administered orally or intravenously. Because its gastrointestinal and cardiovascular side effects are few, it can be safely used in patient populations with other diseases in addition to the primary pathology leading to surgery. However, its lack of anti-inflammatory effect may not be sufficient to relieve inflammatory symptoms [19].

The present study aims to evaluate and compare the impact of IV forms of ibuprofen and acetaminophen on pain management and opioid consumption in patients undergoing surgery LC.

Material and Methods

Following ethical committee approval, 70 ASA stage I- II patients aged 18 to 65 who were scheduled for LC were enrolled in this prospective, randomized, double-blind study. Informed consent was obtained from all individual participants included in the study. Before surgery, patients were informed about the medications in the study, the NRS for pain assessment, and the use of the PCA device.

The same anesthetic protocol was used in both groups, and all LC surgeries were performed laparoscopically by the same surgical team using the same technique. Data collected included age (years), gender, height (cm), weight (kg), BMI, ASA score, duration of anesthesia (minutes), and duration of surgery (minutes). Patients with a score above ASA 3, with a history of renal, hepatic, and cardiovascular disease, gastrointestinal bleeding, peptic ulcer or inflammatory bowel disease, diabetes, or other neuropathic disease, patients with a weight of less than 40 kg, a BMI greater than 35, an allergy to acetaminophen, long-term use of NSAIDs and opioids, a history of oral anticoagulants, a platelet count < 80.000, inability to use a PCA device, and those who discontinued the medication required for the study for any reason, as well as those who were pregnant, were excluded from the study.

Patients were randomly divided into two groups. Group I (ibuprofen group, n = 35) received 800 mg IV ibuprofen, and group A (acetaminophen group, n = 35) received 1000 mg IV acetaminophen after intubation. The study drugs were administered in 100 mL saline. In all patients, a standardized general anesthesia protocol was performed by an experienced anesthesiologist. Electrocardiogram (ECG), heart rate (HR), peripheral oxygen saturation (SpO_2), and noninvasive blood pressure monitoring were performed in all cases, and all measurements were recorded at 5-minute intervals during surgery. After preoxygenation (100%, 4 L/min O_2 for 3 min), propofol (1-2 mg/kg), rocuronium (0.8mg/kg), and fentanyl (0.1 µg/kg) was administered during induction of anesthesia via IV at doses calculated according to ideal body weight. End-tidal carbon dioxide ($EtCO_2$) was monitored continuously after intubation. Tidal volume and ventilation rate were adjusted to maintain arterial blood $EtCO_2$ partial pressure at 35-45 mmHg, and 0.1-0.2 µg/kg fentanyl was titrated as needed for analgesia when HR and mean arterial blood pressure (MAP) increased 20% above baseline during surgery. Anesthesia was maintained with 2-3% sevoflurane in both groups. Inhalation in a 0.5 O_2 oxygen-air mixture was discontinued at the onset of skin suturing, and the fresh gas flow was changed to 1.5 L/min oxygen for both groups. Remifentanil IV infusion 0.05-0.2 µg/kg/min was administered to maintain anesthesia. Granisetron 10-20 µg/kg IV was administered to all groups approximately 10 min before the end of surgery. At the end of the surgery, 0.05-0.07 mg/kg neostigmine methyl sulfate and 0.02-0.03 mg/kg atropine sulfate were administered as antagonists of muscle relaxants. Tracheal extubation was performed when extubation criteria were fully met in the operating room, and the patient was then transferred to recovery room.

Postoperative Analgesia Management

Patients in two groups received their medications over a 24-hour period postoperatively. They were connected to a PCA device in the recovery room. The tramadol-prepared PCA device was programmed for a 15-minute lockout and a bolus dose of 10 mg without basal infusion, which was maintained for 24 hours. NRS scores for pain (NRS 0= no pain, NRS 10= worst possible pain) and tramadol doses consumed were recorded the 1st, 2nd, 4th, 6th, 12th, and 24th hours postoperatively. A blinded pain nurse performed a postoperative follow-up of the patients. The incidence of ORAE and bleeding related to protocol medications was analyzed. The adverse effects of ibuprofen, acetaminophen, and opioids were recorded.

Statistical Analysis

The study's sample size was calculated using the G*Power program (v3.1.9.2). We conducted a pilot study with five patients in our clinic. According to this pilot study, the postoperative opioid consumption in these patients was 83±22 mL, considered clinically significant. Therefore, a difference of 20 mL between the two groups was detected with a power of 80% and 0.05 error with 20 patients in each group. Considering a 20% failure rate, we included 35 patients in each group using the double-block randomization method.

Shapiro-Wilk test and QQ plots were evaluated to test normality. Comparisons of continuous variables for normal and non-normal distributed variables were run by using Student's t and Mann Whitney U tests between groups. To understand if the distributions of group factors categories are homogenous among categories of nominal variables, chi-square or Fisher's exact tests were used. The difference between the two groups, 6-time points, and the interaction of these two main effects

were tested with two-way repeated measures of ANOVA. The sphericity assumption was performed by using Mauchly's test sphericity. As a violation of this assumption, Wilk's Lambda statistic was used as multivariate test results. General descriptive statistics are summarized as median (minimum and maximum) for continuous variables. A "p" value of less than 0.05 was considered statistically significant, and IBM SPSS Statistics for Windows, Version 20.0. were used for all these statistical analyses.

Results

Each group in this study included 35 patients and the patient allocation is outlined in the consort flow diagram (Fig. 1). Baseline demographics, except for gender, duration of the operation and antiemetic consumption were similar between groups and showed no statistical difference (p>0.05) (Table 1). In particular, the doses of opioid consumption at 4, 12, and 24 hours were significantly higher in group A than in group I (Table 2) (Fig. 2). The cumulative doses of tramadol consumption according to PCA doses are higher in acetaminophen groups than ibuprofen group (Fig. 3). Pain scores (NRS) in group I and group A at the 1st, 2nd, 4th, 6th, 12th, and 24th hours were similar (p > 0.05). Only the 24-hour pain score was significantly higher in group I than in group A (p < 0.05) (Table 3).

From the 1st to the 24th hour, pain scores decreased radically in both groups, and the groups behaved in parallel in time. Although there was no statistical difference between the groups, the ibuprofen group was above the acetaminophen group from the 1st to the end of the 24th hour (Fig 4). The incidence of ORAEs and bleeding is similar in both groups (p>0.05) (Table 4).

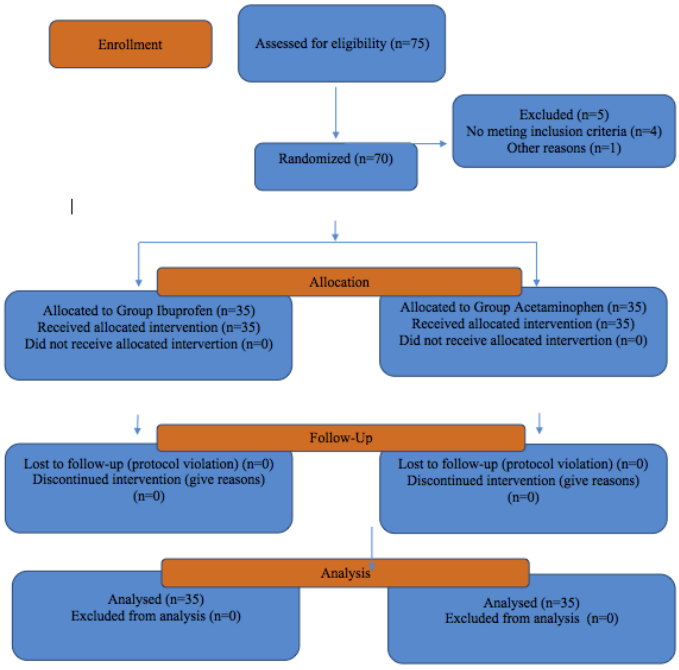

Figure 1. Consort flow diagram of the study

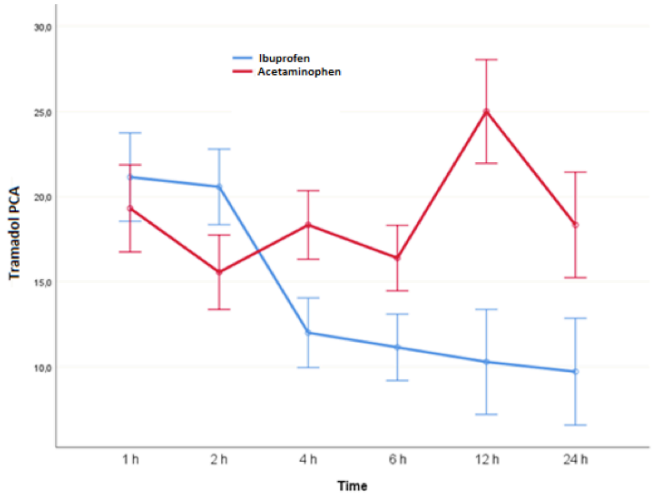

Figure 2. Time graph of tramadol patient control analgesia (PCA) use

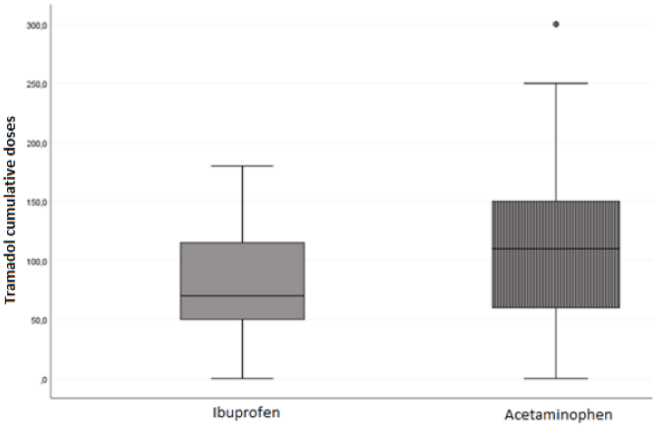

Figure 3. Tramadol cumulative doses of groups

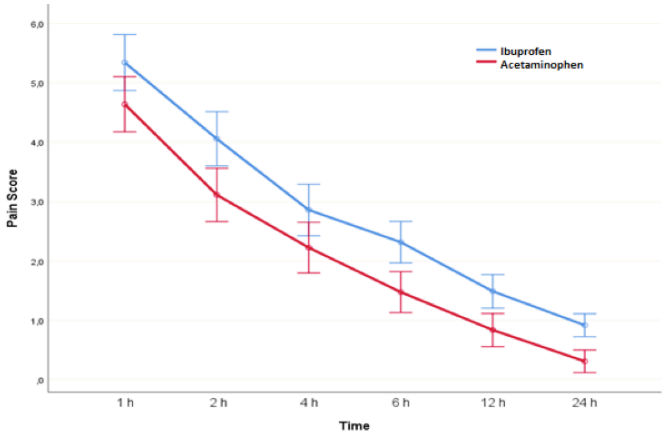

Figure 4. Pain scores of groups over time

Table 1. Demographic characteristic of study patients

	Group I (n=35)	Group A (n=35)	p
Age, year	50.09±13.38	46.92±11.04	0.280
Gender (M/F)	6/29	16/19	0.013#
Weight, kg	71.4±13.2	73.86±15.57	0.476
Height, cm	164.17±7.39	167.78±9.36	0.077
BMI (kg/m2)	26.51±4.77	25.99±3.53	0.604
ASA status (I/II)	11/24	8/27	0.560
Duration of the operation, min	81.29±28.24	74.86±15.65	0.418
Antiemetic consumption	0.86±1.24	0.97±1.28	0.878

ASA=American Society of Anesthesiologists, BMI=Body mass index
Independent t test results are expressed as mean ± standard deviation or as numbers of patients
#p< 0.05 independent t test

Table 2. Postoperative tramadol consumption of the patients with respect to the groups

Time	Group I (n=35)	Group A (n=35)	p
1 h	20(0-50)	20(0-70)	0.514
2 h	20(0-60)	10(0-40)	0.197
4 h	10(0-50)	15(0-50)	0.040
6 h	10(0-40)	10(0-50)	0.062
12 h	10(0-40)	20(0-120)	0.001
24 h	0(0-60)	10(0-70)	0.021
Cumulative doses	70(0-180)	110(0-300)	0.069

Mann Whitney U test results are expressed as median (min-max)

Table 3. The Pain Intensity of the Patients According to the Groups Based on the NRS

Time	Group I (n=35)	Group A (n=35)	p
1 h	6(0-9)	4(0-9)	0.242
2 h	5(0-10)	3(0-8)	0.186
4 h	2(0-8)	2(0-8)	0.534
6 h	2(0-8)	1(0-6)	0.216
12 h	1(0-8)	0(0-4)	0.182
24 h	0(0-6)	0(0-4)	0.033

NRS= Numerical Rating Scale.
Mann Whitney U test results are expressed as median (min-max)

Table 4. The comparison of the incidence of ORAE and bleeding between groups

	Group I (n=35)	Group A (n=35)	* p
Breathing depression	0	0	1.000
Confusion	0	0	1.000
Urinary retention	0	0	1.000
Nausea /Vomiting	20	19	0.712
Pruritus	0	0	1.000
Dyspepsia	0	0	1.000
Constipation	0	0	1.000
Bleeding	0	0	1.000

ORAE= Opioid-related adverse events
Values are expressed as numbers, *p> 0.05

Discussion

This study demonstrates that administering ibuprofen to treat postoperative pain in surgery LC reduces opioid consumption more than acetaminophen. Ibuprofen did not cause any serious adverse events, and it was well tolerated.

Several studies [23-25] recommend multimodal analgesic regimens. Multimodal analgesia reduces the dosage and adverse effects of analgesics, allowing safer pain management, improving the quality of analgesia, and leading to better functional outcomes [5]. IV acetaminophen and ibuprofen are essential options, either alone or in combination, for treating pain and fever and reducing opioid use. Furthermore, confirmed by the World Health Organization's pain ladder [26], which specifies the use of these medications and regional anesthesia as the first choice to relieve acute pain [19].

Many previous studies have favored IV acetaminophen and ibuprofen as part of multimodal analgesic treatment [24,25] for postoperative pain. Tramadol is an a typical opioid and affects both the μ-opioid receptor agonist and an inhibitor of monoamine neurotransmitter reuptake. Tramadol's analgesic and pharmacologic effects are similar to those of other opioids [11]. Because of the beneficial effects of tramadol, it was preferred as part of the multimodal analgesic protocol in this study. We also compared two different combinations of the drugs (IV ibuprofen-tramadol and IV acetaminophen-tramadol) for treating mild and moderate-to-severe pain as an adjunct to opioids. Results showed that total tramadol consumption after surgery was significantly lower in the ibuprofen group compared with the acetaminophen group [27]. The IV form of ibuprofen has been studied in patients undergoing orthopedic surgery, abdominal hysterectomy, or LC; it is reported to be relatively safe and effective [21,23,28].

Kayhan et al. [29] stated that the administration of 800 mg IV ibuprofen to treat postoperative pain in morbidly obese patients undergoing bariatric surgery did not significantly reduce opioid consumption compared with IV acetaminophens but resulted in lower pain intensity. In our study, opioid consumption was significantly reduced compared with acetaminophen infusion, but patients' pain scores did not differ between the two drug groups.

In contrast to our study, Sparber et al. found that preemptive administration of ibuprofen significantly decreased postoperative pain scores in patients undergoing laparoscopic inguinal hernias but did not affect opioid consumption [30].

In addition, Erdi et al. [31] demonstrated in their study of

patients undergoing LC that mean abdominal pain scores were not significantly different in the ibuprofen and acetaminophen groups but were significantly lower than in the control group.

The use of IV ibuprofen and acetaminophen was associated with a reduction in total morphine consumption compared with the control group, according to Akbas et al. study. Also, the use of IV ibuprofen significantly reduced total morphine consumption compared with control and acetaminophen [32]. The study by Ekinci et al. [33] has a control group besides the ibuprofen and acetaminophen group. They suggested that IV ibuprofen resulted in lower pain scores and opioid consumption compared with acetaminophen postoperatively in the first 24 hours in patients undergoing LC surgery. In addition, it reduced the need for rescue analgesics and ORAE. Therefore, IV ibuprofen may have a more potent analgesic effect than IV acetaminophen in postoperative pain management [33]. At the same time PONV and pruritus were more common in the control group than in other groups in terms of adverse effects. Notably, the group I had a lower incidence of nausea than group A. This study showed that the IV form of ibuprofen reduced pain scores and opioid consumption in the 24-hour postoperative period compared with acetaminophen. In addition, rescue analgesic utilization was significantly lower in those in the ibuprofen group [33].

Ahiskalioglu et al. [28] reported that a single preventive dose of IV ibuprofen significantly decreased VAS scores and the incidence of PONV by 45%, as well as the side effects of opioid use in LC patients. Because they compared the control group and ibuprofen in this study, they were able to calculate the effect on side effects. In our study, none of our patients had cardiac or renal side effects, respiratory depression, pruritus, confusion, or bleeding.

One limitation of the study is the absence of a control group. The second limitation is that we did not record anesthesia time. Another limitation, the study could have been performed with a larger sample size and as a multi-center study.

Conclusion

The administration of ibuprofen during surgery for the treatment of postoperative pain reduces opioid consumption more than acetaminophen. Ibuprofen was well tolerated, and no serious adverse events were observed; however, our sample size was too small to draw any definite conclusions. In patients requiring postoperative pain control in LC, ibuprofen may be a safe and valuable alternative to acetaminophen.

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None.

Ethical Statement

Institutional approval was obtained before article submission from Baskent University Institutional Review Board. Project no: KA15/346

Declaration of Competing Interest

No conflict of interest.

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Orijinal Makale

Ankara Eğitim ve Araştırma Hastanesi Hasta Deneyimi Anketi Analiz Raporu

Ankara Training and Research Hospital Patient Experience Survey Analysis Report

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Öz

Amaç: Hastanemizde kalite ölçütlerinden olan "Hasta Memnuniyet Anketi" önemli bir kalite göstergesidir. Bu çalışmada amacımız, Ankara Eğitim ve Araştırma Hastanesi Hasta Deneyimi Anketi Analiz Raporunu değerlendirmeyi, hastalarımızın poliklinik, yataklı servis, acil servisteki memnuniyetlerini değerlendirerek hizmet kalitesinin artırılmasında neler yapılabileceğini, memnuniyetsizlik durumunun nedenlerini gözden geçirmektir.

Gereç ve Yöntemler: Sağlıkta Kalite Standartları gereği Türkiye'de tüm hastanelerde hasta memnuniyetini belirlemek ve hizmet kalitesini arttırmak amacıyla yapılan hasta memnuniyet anketleri uygulaması, 2019 yılından itibaren "Anket Uygulama Rehberi Versiyon 2"ye göre yapılmaktadır. Araştırmamız Ankara Eğitim ve Araştırma Hastanesinde 1 Ocak 2020-31 Aralık 2020 tarihleri arasında yatan hasta, ayaktan hasta ve acil servis hastalarına uygulanmıştır. Anket Sağlık Bakanlığı tarafından yayınlanan ayaktan hasta memnuniyet anketi, yatan hasta memnuniyet anketi, acil servise başvuran hasta memnuniyet anketi örneği kullanılarak yapılmıştır. Çalışmamız telefonla yapılmış anket çalışmasının retrospektif analizini içermektedir.

Bulgular: 2020 yılı içinde yatarak tedavi gören 383 hastaya, ayaktan tedavi gören 384 hastaya, acil servise başvuran 384 hastaya, toplamda 1151 hastaya anket uygulanmıştır. Hasta memnuniyet oranımız yatan hasta için ortalama %96,82, ayaktan hasta için %95,84, acil servis için %95,58'dir. Yaklaşık %5 oranında temizlik ve fiziki koşullar ile ilgili memnuniyetsizlik bildirilmiştir.

Sonuç: Hasta memnuniyeti sağlık kurumlarında hizmet kalitesini değerlendirmede kullanılan temel bir kriterdir. Bu çalışmada fiziki koşullar ve temizliğin hasta memnuniyetinde önemli faktörler olduğu görülmüştür.

Anahtar Kelimeler: hasta memnuniyet; kalite; sağlık hizmetleri; hastane

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Abstract

Aim: "Patient Satisfaction Questionnaire", which is one of the quality criteria in our hospital, is an important quality indicator. In this study, our aim is to evaluate the Ankara Training and Research Hospital Patient Experience Questionnaire Analysis Report, to evaluate the satisfaction of our patients in the outpatient clinic, inpatient service, and emergency service, and to review what can be done to increase the service quality, and the reasons for the dissatisfaction.

Materıal and Methods: In accordance with the Quality Standards in Health, the application of patient satisfaction surveys, which is carried out in order to determine patient satisfaction and increase service quality in all hospitals in Turkey, has been carried out according to "Survey Application Guide Version 2" since 2019. Our research was applied to inpatients, outpatients and emergency room patients between January 1, 2020 and December 31, 2020 in Ankara Training and Research Hospital. The survey was conducted using the example of outpatient satisfaction survey, inpatient satisfaction survey, and patient satisfaction survey who applied to the emergency department published by the Ministry of Health. Our study includes a retrospective analysis of a telephone survey.

Results: In 2020, a questionnaire was applied to a total of 1151 patients, of which 383 inpatients, 384 outpatients and 384 patients who were admitted to the emergency service. Our average patient satisfaction rate is 96.82% for inpatients, 95.84% for outpatients, and 95.58% for emergency services. Dissatisfaction with cleanliness and physical conditions were reported at a rate of approximately 5%.

Conclusıon: Patient satisfaction is a basic criterion used to evaluate the quality of service in health institutions. In this study, physical conditions and cleanliness were found to be important factors in patient satisfaction.

Keywords: patient satisfaction; quality; health service; hospital

Giriş

Hastane hizmetlerinden hasta memnuniyeti, hastane hizmetlerinin etkinliğinin ve kalitesinin en önemli göstergelerinden biridir. Hasta memnuniyeti anketleri, sağlık yöneticilerine ve politika yapıcılara mevcut durumu, süreç iyileştirme programlarının nitelik ve nicelik farkındalığını ve kalite iyileştirmeyi değerlendirmek için değerli veriler sağlayabilir [1].

Hastanın hastaneye başvurduğu andan itibaren yönlendirilmesi, resmi işlemleri, çalışanların iletişimi, bekleme süreleri, bekleme lokalizasyonu, muayeneye geliş şekli, doktorun ve hemşirenin iletişimi, muayenesi, bilgilendirilmesi, fiziki alt yapının temizliği, acildeki müdahale süresi, servislerde yatış süresi, yataklı serviste yemek hizmeti, temizlik, doktor ve hemşire bakım süreci hastaların memnuniyetinde bir ölçek olabilmektedir. Bu ölçeklere göre memnuniyetsiz olunan alanların yapılan anketlerle belirlenerek yönetim ve çalışanlar tarafından düzeltici ve önleyici faaliyetlerle giderilmesi amaçlanmıştır [2-5].

Hastanemizde kalite ölçütlerinden olan "Hasta Memnuniyet Anketi" önemli bir kalite göstergesidir. Sağlık Bakanlığı'nın yayınladığı kalite standartlarında yol gösterici olarak hizmetin iyileştirilmesini ve eksikliklerinin giderilmesini, paralelinde hasta memnuniyetini artırmayı sağlamak için önemli bir parametredir [5].

Bu çalışmada amacımız, Ankara Eğitim ve Araştırma Hastanesi Hasta Deneyimi Anketi Analiz Raporunu değerlendirmeyi, hastalarımızın poliklinik, yataklı servis, acil servisteki memnuniyetlerini değerlendirerek hizmet kalitesinin artırılmasında neler yapılabileceğini, memnuniyetsizlik durumunun nedenlerini gözden geçirmektir.

Gereç ve Yöntemler

Sağlıkta Kalite Standartları gereği Türkiye'de tüm hastanelerde hasta memnuniyetini belirlemek ve hizmet kalitesini arttırmak amacıyla yapılan hasta memnuniyet anketleri uygulaması, 2019 yılından itibaren "Anket Uygulama Rehberi Versiyon 2"ye göre yapılmaktadır [5]. Bu rehbere göre randomize seçilen telefon numaralarından pandemi nedeniyle telefonla anket yapılmıştır. Çalışmamız Ankara Eğitim ve Araştırma Hastanesi yerel Etik Kurulu tarafından onaylanmıştır. Çalışma Helsinki İlkeler Deklerasyonu'na (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirilmiştir. Hastaların onamı telefonla sözel olarak alınmıştır. Anketler; 18 yaşından büyük, bilinci açık hastaların kendisine, bilinci kapalı hastalar için hasta yakınlarına uygulanmıştır. Psikiyatri hastaları ve terminal dönemdeki hastalar için anket uygulanmamıştır. Bu hastaların yakınlarına anket uygulanmıştır. Dahil edilecek kişiler

randomizasyon yöntemi ile seçilip, telefon görüşmesi sonucu anket uygulamasını kabul eden hastalardan oluşmaktadır.

Araştırmamız Ankara Eğitim ve Araştırma Hastanesinde 1 Ocak 2020-31 Aralık 2020 tarihleri arasında yatan hasta, ayaktan hasta ve acil servis hastalarına uygulanmıştır. Anket Sağlık Bakanlığı tarafından yayınlanan ayaktan hasta memnuniyet anketi, yatan hasta memnuniyet anketi, acil servise başvuran hasta memnuniyet anketi örneği kullanılarak yapılmıştır. Bu anketlerde yatan hasta için 15, acil servis için 18, ayaktan hasta için 18 soru olarak uygulanmıştır. Çalışmamız telefonla yapılmış anket çalışmasının retrospektif analizini içermektedir.

"Hasta Deneyimi Anketleri" hastanın tetkik ve tedavi işlemlerinin tamamlanması ve sağlık kuruluşundan ayrılmasını takiben "Telefon Görüşmesi" yöntemi ile uygulanmıştır.

Anket, telefon görüşmesi ile;

• Aramalarda anketör kendisini ve sağlık kuruluşunu tanıtarak, karşı tarafa kim tarafından arandığı konusunda bilgi verdi

• Sorulan sorulara net ve objektif cevaplar alabilmek ve kişilerin kendilerini güvende hissetmeleri için anketi cevaplayan kişilerin kimlik ve iletişim bilgileri alınmadı ve sorulmadı.

• Sorulara verilecek cevapların gizli tutulacağı konusunda kişi bilgilendirildi.

• Anketin amacı, ne için yapıldığı anlatıldı.

• Ankette yer alan soruların kişi tarafından anlaşıldığından emin olundu.

• Anket tamamlandıktan sonra kişiye değerli katkılarından dolayı teşekkür edildi ve görüşme sonlandırıldı.

Anketör kalite biriminden görevlendirilmiş memurdu ve anketin özellikleri ve uygulama esasları hakkında eğitim almıştı, eğitimler kayıt altına alınmıştı.

İstatistiksel Analiz

Anketlerde "likert ölçeği" kullanıldı. 5 tamamen katılıyorum, 4 katılıyorum, 3 kararsızım, 2 katılmıyorum, 1 kesinlikle katılmıyorum olarak değerlendirildi. Çalışmadan elde edilen veriler, Microsoft Excel Çalışma Programı kullanılarak analiz edildi. Çalışma verileri değerlendirilirken tanımlayıcı istatistiksel yöntemleri (frekans (n) ve yüzde (%) cinsinden) hesaplandı.

Ankete katılan hastaların demografik verileri Tablo 1'de gösterilmiştir. 2020 yılı içinde yatarak tedavi gören hasta sayısı 80202'dir. Bu sayının anket rehberi evren tablosundaki karşılığına göre 75000-100000 başvuru sayısına karşılık gelen örneklem sayısı 383'dür. Bu sayı 12 aya bölündüğünde anket yapılacak hasta sayısı aylık 32'ye denk gelmektedir.

Tablo 1: Ankete katılan hastaların demografik verileri

Ayaktan Hasta	n=384
Yaş Aralığı (yıl)	18-88
Kadın/Erkek	220(57.2)/164(42.8)
Eğitim Durumu	
İlkokul	150 (39.0)
Ortaokul	75 (19.5)
Lise	91 (23.6)
Üniversite	53 (13.8)
Yüksek Lisans	25 (6.5)
Yatan Hasta	n=383
Yaş Aralığı (yıl)	18-93
Kadın/Erkek	222 (57.9)/161(42.0)
Eğitim Durumu	
İlkokul	85 (22.1)
Ortaokul	119 (30.9)
Lise	105 (27.3)
Üniversite	60 (15.6)
Yüksek Lisans	15 (3.9)
Acil Hasta	n=384
Yaş aralığı (yıl)	18-95
Kadın/Erkek	283 (73.6)/101 (26.4)
Eğitim Durumu	
İlkokul	91 (23.8)
Ortaokul	110 (28.6)
Lise	107 (27.8)
Üniversite	57 (14.8)
Yüksek Lisans	19 (4.9)

2020 yılında hastanemize başvuran ayaktan hasta sayımız 498.999 hastanın tablo karşılığı olan 384 hastaya ve acil servisimize başvuran 233.328 hastanın tablo karşılığı olan 384 hastaya uygulanmıştır. Bu sayılarda aylık 32'ye denk gelmektedir. 2020 yılında acil servise başvuran hasta sayısı 233.328'dir. Bu sayının anket rehberindeki evren tablosundaki karşılığına göre 250.000-500.000 başvuru sayısına karşılık gelen 384'tür. Bu sayı 12 aya bölündüğünde anket yapılacak hasta sayısı 32'ye denk gelmektedir. Anket rehberinde belirtilen anket yapılmayacak olan hasta gruplarına ek olarak Bakanlığın duyurusuna istinaden Covid-19 hastaları da anket uygulaması dışında tutulmuştur. Toplamda 1151 hasta alınmıştır. Anketlerde demografik veri olarak yaş, cinsiyet, eğitim durumu, kaydedilmiştir. Hasta memnuniyet oranımız yatan hasta için ortalama %96,82, ayaktan hasta için %95,84, acil servis için %95,58'dir.

Anketler yıl ortalaması olarak soru bazında incelendiğinde;

Yatan hastaların "Hastane genel olarak temizdi" sorusuna %5 oranında "Katılmıyorum" derken, "Odadaki eşyalar çalışır durumdaydı" sorusuna ise %1 oranında "Katılmıyorum" cevabı verdiği görülmüştür.

Ayaktan hastaların "Hastane genel olarak temizdi" sorusuna %6 oranında "Katılmıyorum" cevabı verirken, "Odadaki eşyalar çalışır durumdaydı" sorusuna ise %1 oranında "Katılmıyorum" cevabı verdiği görülmüştür.

Acil servise başvuran hastalar arasında "Acil servis genel olarak temizdi" sorusuna %9 oranında, "Muayene olacağım doktoru kendim seçtim" sorusuna %3 oranında, "Bekleme alanlarının fiziki koşulları yeterliydi" sorusuna ise %2 oranında katılmıyorum cevaplarının verildiği görülmüştür.

Tartışma

Hastanemizde yapmış olduğumuz anket çalışmasında 1151 kişi ile görüşüldü ve yatan hasta, ayaktan hasta ve acil servis memnuniyet oranımızın yüksek olduğu gözlendi. Memnuniyetsizlik oranı düşüktü. Ayaktan hastada %3 oranında muayene olacağım doktoru kendim seçtim maddesinde katılmıyorum cevabı alındı. Yatan hasta, ayaktan hasta ve acil serviste genel olarak hastane temizliğinden sırası ile %1, %6 ve %9 oranında memnuniyetsizlik mevcuttu. Ayrıca acil serviste %2 oranında fiziki koşulların yetersizliği bildiridir. Bunlara yönelik olarak temizlikle ilgili analiz yapıldığında temizlik personel sayısında azalmaların yaşandığı gözlendi. Azalma sebepleri ise pandemi nedeniyle hastalanmalar, emeklilikler, başka kurumlara görevlendirilmeler ve temizlik için verilen eğitimlerin anlaşılabilirliğinin düşük olabilmesi idi. Buna yönelik ilgili mercilerle irtibatta bulunularak temizlik personelinin sayısının artırılması planlandı. Acil servis bekleme alanları için fiziki koşulların yetersizliği maddesi için düzenleyici tadilatlar planlandı. Odadaki eşyaların çalışır durumda olmadığının tespiti için denetim ekipleri ile irtibata geçilerek fonksiyonel olmayan eşyalar belirlenerek değişimi için gerekli işlemler başlatıldı.

Diğer bir etken ise pandemi hastanesi olmamız nedeniyle hasta yoğunluğunun artması idi. Yine pandemiye bağlı olarak personelin sık sık yer değiştirmesi ve oryantasyon problemi yaşaması memnuniyetsizlikte bir etken olarak gözlemlendi.

Pamukkale Üniversitesi Tıp Fakültesinde yapılan çalışmada gözlendiği gibi hekim ilgi ve zaman ayrılması, mahremiyete saygı gösterilmesi, bilgilendirmede genel memnuniyet bildirilmiştir [3]. Bizim çalışmamızda da bu maddelerde memnuniyet yüksekti. Katılan hastaların çoğunda muayene edeceği doktoru kendisinin seçememesi bizim çalışmamızda da düşük oranda da olsa memnuniyetsizliği gösteriyordu. Ancak Pamukkale Üniversitesinde düşük oranda olduğu için genel memnuniyeti etkilemediğini düşünmüşlerdir. Aynı şekilde bizim de memnuniyet oranına göre istatistiksel anlamlı gözükmemektedir.

Özer ve ark. yapmış olduğu bir çalışmada hasta memnuniyetinin sağlık kurumlarında hizmet kalitesini değerlendirmede kullanılan temel bir kriter olduğu, bireylerin sosyodemografik özellikleri ve tedavi sürecine ilişkin faktörlerden etkilendiği bildirilmiştir [4]. Bizim çalışmamızda da memnuniyetsizlik maddeleri tek tek ele alınarak düzeltici önleyici faaliyet başlatılarak önlenmesi için çalışma başlatılmıştır. Aynı konuda Ankara Üniversitesi Tıp Fakültesi İbni Sina Hastanesinde yapılan araştırmada poliklinik bazında değerlendirme yapılmış, hasta memnuniyet ölçümünün hastanenin daha iyiye gitmesinin sağlanmasında yararlı olacağı kanaati bildirilmiştir [6].

Erdem ve ark. Elazığ ilinde 4 hastanedeki hasta memnuniyeti ve hasta bağlılığı üzerine yaptıkları incelemede hasta memnuniyetinin hasta bağlılığı üzerinde olumlu etkileri olduğunu bildirmişlerdir [7]. Hastanemizde yapılan yatan hasta anketinde hastanemizi aileme ve arkadaşlarıma tavsiye ederim sorusu hasta bağlılığının göstergesidir. Bizim hastanemizde de hasta memnuniyeti hasta bağlılığı ile paralellik göstermektedir.

Van Yüzüncü Yıl Üniversitesi Medikososyal birimine başvuran birinci basamakta yapılan hasta memnuniyeti çalışmasında hastaların aile hekimliği ilkelerine uygun olarak dinlenilmeye ve bilgilendirilmeye önem verdikleri bildirildi. Memnuniyeti etkileyen başlıca faktörlerin hastanın dinlenmesi, yeterli zaman ayrılması, tüm vücut muayenelerinin yapılması ve hastalıkla ilgili yeterli bilgi verilmesi olarak bildirilmiştir. Hastanın gelirinin hastanın doktor yanında kendini güvende hissetmesi ile direk ilgisi olduğu kaydedilmiştir [8]. Bizim hasta popülasyonumuz sosyokültürel düzeyi daha düşük bir popülasyondur. Araştırma yılında Şehir Hastanesinin hizmete başlamış olması ve çevredeki hastanelerin kapanmış olması, bu bölgede sosyoekonomik seviyesi düşük hasta popülasyonunun Şehir Hastanelerine ulaşamayıp bizim hastanemizde yeterli sağlık hizmetine ulaşabilmesi de memnuniyet oranımızı artırmış olabilir.

İstanbul'da bir tıp fakültesinde yatan hastaların memnuniyet düzeyi araştırıldığında, yatan hastaların çok büyük bölümünün hastaneden memnun olduğu bildirilmiştir. Genel memnuniyet düzeyini etkileyen en önemli iki faktörün odaların durumu ve doktorların becerileri olduğunu, bununla birlikte sağlık hizmetlerinin kalitesine önem verilmesi ve hasta memnuniyeti ölçümünün rutin olarak yapılması gerektiğini bildirmişlerdir [9]. Bizim hastalarımızın memnuniyet düzeyi de fiziki koşullardan etkilenmiştir.

Bjertnaes ve ark. çalışmasında hasta memnuniyetinin önemli komponentlerinin hemşirelik hizmetleri deneyimi ve doktorların deneyimi olduğunu bildirmişlerdir [10]. Bizim

hastanemiz de deneyimli eğitim kadrosuyla yıllardır bu bölgede hizmet veren ve yüzlerce hekim ve hemşire yetiştirmiş bir Eğitim ve Araştırma Hastanesidir. Hasta memnuniyeti ve tercih edilirliğimizin en önemli komponentinin personel tecrübemiz olduğunu düşünmekteyiz.

Sonuç

Sonuç olarak hasta memnuniyeti sağlık kurumlarında hizmet kalitesini değerlendirmede kullanılan temel bir kriterdir. Bu çalışmada fiziki koşullar ve temizliğin hasta memnuniyetinde önemli faktörler olduğu görülmüştür.

Maddi destek ve çıkar ilişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarın herhangi bir çıkar dayalı ilişkisi yoktur.

Teşekkür: Hastanemiz Kalite sorumlusu Op. Dr. Süheyla Aydoğmuş ve hastanemiz kalite birimine katkı ve destekleri için teşekkür ederim.

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Review

The renin-angiotensin system in fructose-induced metabolic syndrome

Fruktozla oluşturulan metabolik sendromda renin-anjiyotensin sistemi

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Abstract

The widespread use of fructose in processed foods is accepted to cause an increase in metabolic syndrome characterized by insulin resistance, abdominal obesity, hypertriglyceridemia, and hypertension. Fructose-induced metabolic syndrome is also associated with various diseases such as type 2 diabetes, cardiovascular diseases, and non-alcoholic fatty liver disease (NAFLD). The renin-angiotensin system (RAS) has essential roles in blood pressure regulation, fluid-electrolyte homeostasis, cell growth, and glucose homeostasis. Angiotensin I (Agt I) and angiotensin II (Agt II), which are derived from angiotensinogen by renin and angiotensin-converting enzyme (ACE), respectively, are essential players of RAS. Experimental and clinical studies showed that excessive fructose consumption causes activation in RAS. Increased Agt II in fructose-induced metabolic syndrome initiates insulin resistance by disrupting the insulin signaling pathway and thus predisposes to type 2 diabetes, hypertension and NAFLD. Angiotensin 1-7 (Agt 1-7), which is formed from Agt II by angiotensin-converting enzyme 2 (ACE2) has contra-balancing effects to Agt II as well as regulatory effects on insulin resistance and hepatic fat accumulation.

Keywords: fructose; metabolic syndrome; insulin resistance; renin-angiotensin system

Öz

Fruktozun işlenmiş gıdalarda yaygın olarak kullanılması insülin direnci, abdominal obezite, hipertrigliseridemi ve hipertansiyon ile karakterize olan metabolik sendromun artmasına neden olmaktadır. Fruktozla oluşturulan metabolik sendrom tip 2 diyabet, kardiyovasküler hastalıklar ve alkole bağlı olmayan yağlı karaciğer hastalığı (NAFLD) gibi çeşitli hastalıklara zemin hazırlamaktadır. Renin-anjiyotensin sistemi (RAS), kan basıncının düzenlenmesi, sıvı-elektrolit homeostazı, hücre büyümesi ve glikoz homeostazı üzerinde önemli rollere sahiptir. Renin ve anjiyotensin dönüştürücü enzim (ACE) tarafından anjiyotensinojenden türetilen anjiyotensin I (Agt I) ve anjiyotensin II (Agt II), RAS'ın temel bileşenleridir. Deneysel ve klinik çalışmalar, aşırı fruktoz tüketiminin RAS aktivasyonunu artırdığını göstermiştir. Fruktozla oluşturulan metabolik sendromda artan Agt II, insülin sinyal yolunu bozarak insülin direncini başlatmakta ve böylece tip 2 diyabet, hipertansiyon ve NAFLD'e zemin hazırlamaktadır. Anjiyotensin dönüştürücü enzim 2 (ACE2) tarafından Agt II'den oluşturulan anjiyotensin 1-7 (Agt 1-7), insülin direnci ve hepatik yağ birikimi üzerinde düzenleyici etkilerin yanı sıra Agt II'ye karşı dengeleyici etkilere sahiptir.

Anahtar Kelimeler: fruktoz; metabolik sendrom; insulin direnci; renin-anjiyotensin sistemi

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Introduction

Metabolic syndrome, which is characterized by hyperinsulinemia, hyperlipidemia, abdominal obesity, and hypertension, is becoming a worldwide health problem [1,2,3]. This syndrome affects more than thirty percent of the population in various regions of the world [4-6]. The presence of this syndrom predisposes to the development of many diseases such as type 2 diabetes [7] cardiovascular [7], and non-alcoholic fatty liver disease (NAFLD) [8]. Many factors including high carbohydrate intake, and low physical activity play a role in the development of metabolic syndrome. Insulin resistance, hypertriglyceridemia and abdominal obesity are major indicators in the progression of this syndrome [9]. Insulin released from beta cells of the pancreas activates the insulin receptors and affects glucose and lipid metabolism by phosphorylating proteins involved in the insulin signaling pathway such as insulin receptor substrates (IRS-1 and IRS-2) [10]. Insulin resistance may be mainly attributable to the disruption of this signaling pathway. The changes in the expression of IRS-1 and IRS-2 in metabolic diseases such as type 2 diabetes demonstrated that insulin resistance is one of the most critical factors in developing these diseases [11,12]. Similarly, abdominal obesity or visceral fat accumulation is one of the underlying causes of metabolic syndrome [13]. The adipose tissue distribution is crucial in metabolic syndrome [14]. Particularly, the increase in abdominal fat mass is a risk factor for metabolic and cardiovascular diseases [15,16,17].

Changing dietary habit is one of the responsible factors for developing metabolic syndrome [18]. In today's diets, the consumption of sugars containing fructose has become quite common [19]. High-fructose intake in the diet suppresses the insulin signaling pathway and causes insulin resistance [20-24]. Fructose metabolism, unlike glucose, is not suppressed by the feedback mechanism, and de novo lipogenesis is directly stimulated by the monosaccharide [25,26]. Therefore, fructose induces lipogenesis and leads to worse results in metabolic syndrome compared to other sugars [25-27]. The observation of an increase in visceral adipose tissue with the consumption of fructose-sweetened beverages, has proven that fructose is closely associated with metabolic syndrome and abdominal adiposity [27-29]. Therefore, high fructose administration has become a common dietary method for conducting an experimental metabolic syndrome model in animals [30].

The renin-angiotensin system (RAS) plays a vital role in regulating blood pressure and fluid-electrolyte balance [31]. Angiotensinogen, which is produced in the liver as a precursor compound of this system, is converted to angiotensin I (Agt I) by the renin enzyme released from the kidney. Then, the angiotensin-converting enzyme (ACE) in the lung converts Agt I to Agt II [31,32]. Agt II exerts the well-known effects such as vasoconstriction, promotion of cell growth and inflammation by activating the angiotensin II type 1 receptor (AT1R). Angiotensin II type 2 receptors (AT2R) has opposite effects to Agt II on AT1R [33]. Angiotensin 1-7 (Agt 1-7), another critical RAS component, is formed from Agt II by the angiotensin-converting enzyme 2 (ACE2). This component has a contra-balancing effect to Agt II via Mas receptor (MasR) [31]. In addition to being systemically expressed, RAS components are locally presented in various tissues such as adipose, heart, kidney, pancreas, and brain [33-35]. Increased local RAS activity contributes to systemic RAS action and accelerate the effects of this system. High-fructose consumption activates local and systemic RAS components [36]. In fructose-induced metabolic syndrome, increased RAS activity is one of the fundamental causes of exacerbation of insulin resistance [26], cardiovascular side effects [26,37], and NAFLD [38]. Here, we presented preclinical and clinical evidence showing the effects of systemic and tissue components of RAS in the progression of fructose-induced metabolic syndrome and its complications.

1.The effect of the renin-angiotensin system on insulin resistance in fructose-induced metabolic syndrome

Insulin is an important hormone synthesized in the β cells of the pancreas and stimulates glucose utilization in peripheral tissues [39,40]. This hormone initiates the intracellular insulin signaling pathway by phosphorylating IRS-1 and IRS-2 after binding to the insulin receptor. Phosphorylated IRS-1 and IRS-2 activate phosphoinositide-3-kinase and convert phosphoinositol diphosphate to phosphoinositol triphosphate. Phosphoinositol triphosphate activates protein kinase B (Akt). Akt translocates GLUT4 to the plasma membrane and promotes glucose transportation, regulating glycogen synthesis and gluconeogenesis [10,12,40,41]. In metabolic syndrome, this signaling pathway of the insulin hormone is suppressed and the glucose utilization in the target tissue is not as much as in the physiological state. This situation is determineted as insulin resistance [42]. Studies have demostrated that high-fructose diet causes insulin resistance by reducing the expression of proteins in the insulin

signaling pathway such as IRS-1 [22-24], IRS-2 [23], and Akt [22] in various tissues. The increase in RAS activation by fructose consumption is one of the factors that play an important role in the occurrence of these effects. Supportingly, the fact that high-fructose intake induces the gene expression of various RAS components such as angiotensinogen, Agt II, ACE, AT1R in various studies [43,44]. RAS is involved in the etiology of insulin resistance, which is an important determinant of metabolic syndrome. In particular, Agt II, which is increased by RAS activation, decreases phosphoinositide-3-kinase sensitivity by increasing serine phosphorylation and decreasing tyrosine phosphorylation of IRS-1. This condition reduces Akt formation, as well as the transport of glucose transporters to the membrane and glucose entry into the cell [36,45]. At the same time, increased level of vasoconstrictor Agt II decreases glucose uptake by decreasing blood flow to insulin-sensitive tissues [30]. Based on this information, Rabie and colleagues have indicated that in a rat model of metabolic syndrome induced by a 60% high-fructose diet for twelve weeks, blocking the RAS at renin and Agt II receptor levels by aliskiren and telmisartan improved plasma glucose levels and insulin sensitivity. In addition, it has been shown that the gene expression levels of peroxisome proliferator-activated receptor-α (PPAR-α) and peroxisome proliferator-activated receptor-γ (PPAR-γ), which are important transcription factors in insulin sensitivity, were increased in rats treated with aliskiren and telmisartan [46]. Similarly, in an in vivo study, a 60% high-fructose diet for eight weeks was used to induce a rat model of metabolic syndrome for evaluating the effects of aliskiren, a direct renin inhibitor, on insulin sensitivity. The preventive and treatment effects of renin inhibition were assessed by administering aliskiren at the first day of the experiment or the fourth week of the experiment. The results show that renin inhibition increases insulin sensitivity by lowering glucose as well as insulin levels measured on 56. days in aliskiren-administered groups [47]. In another study evaluating acute and chronic losartan (angiotensin receptor antagonists) treatment, rats were administered a 60% fructose diet for two weeks. The findings of study indicated that chronic losartan treatment reduced hyperinsulinemia in fructose-fed rats [48]. Similarly, the effects of delapril (an ACE inhibitor) and TCV-116 (angiotensin receptor antagonists) were studied in rats fed a 66% fructose diet and in essential hypertensives individuals. Both ACEI (angiotensin-converting enzyme inhibitor) and ARB (angiotensin receptor antagonists) treatments improved insulin resistance as assessed by the steady-state glucose level in fructose-fed rats or by the glucose-clamp method in individuals with essential hypertensives [49]. These studies demonstrate that inhibition of Agt II formation or receptor interaction improves insulin sensitivity in fructose-dependent metabolic syndrome.

Agt 1-7 is another important RAS component formed from Agt II by the ACE2 enzyme. This component improves metabolic parameters such as glucose homestasis and insulin sensitivity by balancing the effects of Agt II through Mas receptors. An animal study evaluated whether Agt 1-7 improves metabolic parameters in 10% fructose-fed rats. After six weeks diet of 10% fructose, the authors measured systolic blood pressure and the levels of insulin, triglyceride, and glucose, they also evaluated the insulin signaling pathway at the level of IR/IRS-1/PI3K/Akt. Fructose-fed rats displayed hypertension, hyperinsulinemia, and hypertriglyceridemia as well as decreased insulin signaling through the IR/IRS-1/PI3K/Akt pathway. However, six weeks of Agt 1-7 treatment normalized all alterations, including insulin resistance, via a mechanism that could cover the modulation of insulin signaling [50]. In a study examining the effects of chronic Agt 1-7 treatment, the rats were fed a high fructose/low magnesium diet for 24 weeks. After six months, improved glucose tolerance, better insulin sensitivity, and lower serum triglycerides were observed in Agt 1-7-treated rats compared to control groups. Similar effects were observed in rats exposed to a high fructose diet for five months followed by short-term (4 weeks) treatment with Agt 1-7 [51]. In another study examining the effect of Agt 1-7 in a metabolic syndrome model, the rats were fed a 10% fructose diet for 6 weeks. During the last 2 weeks of the high fructose feeding period, rats were treated with Agt 1-7 and Mas receptor antagonist A-779. The results of the study showed that Agt 1-7 treatment reduces systolic blood pressure, plasma insulin and triglyceride levels, which are increased by high-fructose diet. Furthermore, it was observed that Agt 1-7 treatment increased the phosphorylation of insulin signaling pathway components such as Akt, and AS160 (Akt substrate) and GSK-3β (glycogen synthase kinase-3β) which is responsible for glycogen synthase in skeletal muscle, adipose tissue, and liver. Also, the reversing effects of Mas receptor antagonist A-779 suggests that Agt 1-7 ameliorates the metabolic effects through the Mas receptor [52].

On the other hand, Agt II activates nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, which leads to increased production of reactive oxygen species (ROS) by

AT1R effects [45,46,53,54]. This activates the Nf-kB pathway, which consequently increases the transcription of cytokines such as TNF-α [46] (Figure 1). These cytokines further inhibit insulin signaling by increasing the cytokine signal 3 expression [53]. In a study in rats fed a 60% fructose diet for eight weeks, it was investigated whether fructose consumption induces the NADPH oxidase enzyme, which increases intracellular ROS levels, by RAS activation. In the study, it was determined that plasma insulin, Agt II, triglyceride and vascular NADPH enzyme levels have increased in fructose-fed rats, which reversed by losartan treatment. In AT1a knock out rats, it was observed that the levels of p22phox, gp91phox and p67phox subunits of NADPH oxidase enzyme have decreased in fructose-fed rats. These results suggest that the increased NADPH enzyme activation with fructose consumption is mediated by RAS [54]. In the comparison of the effects of renin inhibition and angiotensinogen receptor blockade, both aliskiren and telmisartan improved blood glucose, plasma insulin, HOMA-IR, insulin sensitivity, dyslipidemia, hypertension, oxidative stress, and inflammatory parameters such as Nf-kB and TNF-α leves in the fructose-fed rats [46]. These findings suggest that inhibition of any component of the RAS pathway alleviates insulin resistance of fructose-fed rats through improving of insulin signaling and inflammation and oxidative stress.

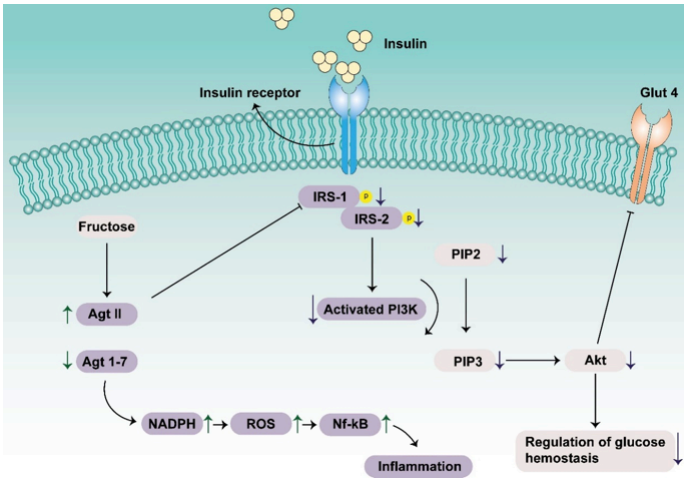

Figure 1. Schematic representation of the effects of Agt II, which increases with fructose consumption, on insulin resistance. Agt II: Angiotensin II, Agt 1-7: Angiotensin 1-7, IRS-1: Insulin receptor substrate-1, IRS-2: Insulin receptor substrate-2, PI3K: Phosphoinositide-3-kinase, PIP2: Phosphoinositol diphosphate, PIP3: Phosphoinositol triphosphate, Akt: Protein kinase B. NADPH: Nicotinamide adenine dinucleotide phosphate, ROS: Reactive oxygen species

2. Relationship between the renin-angiotensin system and abdominal obesity in fructose-induced metabolic syndrome

The distribution of adipose tissue is more important than the amount of adipose tissue in metabolic diseases [55]. Determining the fat distribution is highly important although body mass index (BMI) is seen as a primary tool in evaluating the risk possibilities of metabolic syndrome [16]. In particular, quantitative analysis of visceral fat distribution has been found to be crucial for the assessment of obesity-related metabolic and cardiovascular risks [56]. Abdominal obesity, a dangerous fat accumulation, is associated with an increased risk of multiple chronic diseases, including diabetes, coronary hearth disease, hypertension and stroke [57]. It has been shown in various studies that high-fructose consumption increases the accumulation of abdominal fat [58,59]. In a study in which female rats were fed isocalorically with fructose or glucose solutions for seven months, it was found that fructose feeding produced an increase in body weight due to hyperleptinemia and white adipose tissue hypertrophy [29]. In assessement of subcutaneous and visceral adipose tissue changes in a fructose-induced metabolic syndrome model of adult rats, it was shown that a high-fructose diet increased non-esterified fatty acids, lipid peroxidation, epididymal and mesenteric white adipose tissue volumes. Although mean adipocyte volume in subcutaneous adipose tissue was lower, adipocyte volume in intraabdominal adipose tissue was higher in rats fed a high-fructose diet compared to control rats. Also, the high-fructose diet decreased the ratio of p-Akt/Akt in rats. These data suggest that a high-fructose diet is a severe risk factor for metabolic diseases [60]. It is also known that high-fructose consumption increases the expression of RAS components such as angiotensinogen, Agt II, ACE, AT1R in adipose tissue [44]. For instance, it was determined that rats fed a 66% fructose diet for 14 days had increases in blood pressure and adipose tissue AT1R mRNA levels [61]. Molecular studies, showed that angiotensinogen, ACE, and AT1R gene expressions were increased in the adipose tissue of rats fed a 60% fructose diet for eight weeks [44]. In addition, a 10% fructose diet for nine weeks increased AT1R but decreased AT2R expressions [62]. The results of these studies show that RAS mediators in adipose tissue are involved in fructose-induced metabolic syndrome.

Activated RAS components promote adipocyte differentiation by reducing adipocyte number but increasing adipocyte size. RAS blockade was suggested to improve differentiation of adipocytes [63]. A study tested the effect of RAS blockade

on insulin sensitivity and adipocyte size in fructose-fed rats. Fructose-fed rats had a lower insulin sensitivity, which was recovered by the treatments with temocapril and olmesartan, an angiotensin-converting enzyme inhibitor, and Agt II type 1 receptor blocker, respectively. Also, adipocyte sizes showed negative correlations with the insulin sensitivity [64]. Aliskiren-mediated renin inhibition significantly decreased Agt II level in visceral fat and adipocytes of fructose-fed rats [65]. Similarly, the administration of captopril significantly reduced abdominal fat accumulation in rats fed a 60% fructose diet for 20 weeks [66].

3. Development of hypertension in fructose-induced metabolic syndrome

Hypertension is one of the characteristic features of the metabolic syndrome. It is known that systolic hypertension occurs in metabolic syndrome induced by high-fructose diet [67,68]. Numerous studies have shown that fructose feeding in rodents increases arterial blood pressure [69-73]. A relationship between fructose -sweetened beverages and hypertension has also been established in various clinical studies [74-77]. A study investigating the effects of 60 grams of fructose or glucose on blood pressure in healthy young adults showed that fructose significantly increased blood pressure, heart rate, and cardiac output compared to glucose [76]. Similarly, another study reported that consuming 200 grams of fructose daily for two weeks increased systolic and diastolic blood pressure in 74 healthy men [77]. RAS is one of the essential mediators in regulating blood pressure [31]. Agt II, the main component of the RAS, plays an essential role in the pathogenesis of hypertension associated with fructose-induced metabolic syndrome [78]. Agt II via binding to AT1R produced a vasoconstriction in fructose-fed hypertensive rats [79]. Studies have shown that both Agt II [78] and AT1R [80] receptors are upregulated in fructose-fed rats, suggesting that the functional interactions of Agt II and AT1R increase systolic blood pressure in fructose-induced metabolic syndrome [79]. At the molecular level, a 60% fructose diet inducing changes in AT1R mRNA levels in rat aorta and heart tissue has been found to cause hypertension. Moreover, ACE inhibitor captopril reversed this event by decreasing aortic AT1R mRNA level [81]. In a study investigating Agt II produced by chymase, fructose-fed rats were shown to have increased systolic, diastolic and mean blood pressures [82]. Another study examining fructose-dependent variations of cardiac and aortic RAS components indicated that administrating 10% fructose solution for nine weeks increases blood pressure and ACE and AT1R expressions, but decreases ACE2 and AT2R expressions in male rats [83]. A 66% fructose diet in rats for 14 days increased cardiac hypertrophy, and blood pressure. Angiotensin receptor bloker treatment decreased the hypertrophy, and blood pressure suggesting a central role for Agt II signaling in fructose consumption [84]. In the other study, it has been also shown that a 60% fructose diet for eight weeks led to left ventricular hypertrophy in rats with severe aortic regurgitation possibly through the hypertrigliseridemia [85]. The acute and chronic losartan treatments reduced the cardiac hypertrophy observed in fructose-fed rats suggested that Agt II mediates mitogenic effects in this dietary intervention [48]. In addition, fructose appears to increase salt and Agt II sensitivities by modulating the Na/H channel activity in the proximal tubule thereby causing hypertension [86]. All together, these studies revealed that RAS is essential in hypertension observed in fructose-induced metabolic syndrome.

4. NAFLD in fructose-induced metabolic syndrome

NAFLD, which is considered the liver component of the metabolic syndrome, includes a wide range of pathological conditions from simple steatosis to nonalcoholic steatohepatitis, fibrosis and cirrhosis [87]. The global prevalence of this disease is estimated to be around 32% [88]. The primary manifestation of the disease is accumulated triglyceride droplets (>5%) in the cytoplasm of hepatocytes [89,90]. Triglyceride accumulation in the liver is directly affected by carbohydrate metabolism [91]. In particular, increased fructose intake has been heavily implicated in NAFLD [92]. Studies have shown that high-fructose flow to the liver accelerates the development of the disease by disrupting normal hepatic carbohydrate metabolism and causing de novo triglyceride synthesis [93,94]. At the same time, the role of RAS is very important in the development of NAFLD. While insulin resistance and de novo lipid synthesis occur in the first stage of this disease, inflammation plays a major role in the second step. Increased Agt II expression causes the development of the disease by increasing both insulin resistance and de novo lipid synthesis as well as inflammation [95] (Figure 2). There are various studies showing increased RAS system activity in the presence of NAFDL [38,96]. In a study 15% fructose diet for 21 weeks it was reported an inrease in hepatic steatosis

and liver weight as well as serum triglyceride, insulin, ACE, and Agt II levels. Moreover, at the molecular level, the fructose diet affects transcription factors such as sterol regulatory element-binding proteins 1 and 2 (SREBP-1c, SREBP-2), PPARα and fatty acid synthase (FAS) levels. All these showed that fructose consumption increases RAS components' levels and insulin resistance and thus leads to the development of NAFLD [38]. In addition, the ACE2/Agt 1-7/Mas axis is thought to have regulatory effects on NAFLD formation by inhibiting hepatic insulin resistance and liver lipogenesis [96]. A rodent study indicates that a rat model of NAFLD, created by a 20% fructose diet for eight weeks, appears to have a high ratio of liver weight/body weight and increased serum and hepatic triglyceride levels and fat droplet numbers in the liver. In line with this, Attia et al. suggest that the fructose diet enhances the Agt II protein level and reduces the protein levels of ACE2 and Agt (1-7) and Mas receptors. While fat accumulation in the liver is considered the first step in the development of NAFLD, as it has been mentioned above, inflammatory cytokines and oxidative stress are also important players in the pathogenesis of NAFLD. Abnormal cytokine production and decreased antiinflammatory RAS components such as Agt 1-7 may also contribute to NAFLD progression [96], which is supporting with treatment studies' findings of ACEI or ARB on hepatic fibrosis and steatosis [97-99]. In a mechanistic study investigating the interactions between the RAS and the NAFLD, it was determined that ACEIs or ARBs administrations reduce liver stiffness in the patients with NAFLD compared to the control group [97]. Moreover, RAS inhibition may prevent fibrosis progression in the livers of patients with type 2 diabetes [98]. In a experimental study, telmisartan administration decreased triglyceride and HOMA-IR levels and attenuated cytoplasmic degeneration in a rat model of 10% fructose-induced NAFLD [99]. The efficacies of amlodipine, a calcium channel blocker, captopril, an ACE inhibitor, and bezafibrate, an antihyperlipidemic, on hepatic triglyceride levels were compared in a 60% fructose diet-induced NAFLD model. Amlodipine treatment showed no significant effect on hepatic triglyceride and macrovesicular steatosis levels. However, the effects of captopril and bezafibrate on macrovesicular steatosis appeared to be correlated with decreased hepatic triglyceride levels [100]. These findings suggest that fructose-induced NAFLD is involved in abnormal RAS activity.

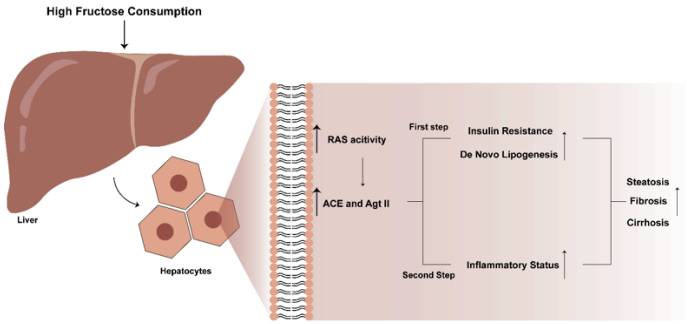

Figure 2. Schematic representation of the development of fatty liver disease due to increased RAS activity with high-fructose consumption. RAS: Renin angiotensin system, Agt II: Angiotensin II, ACE: Angiotensin- converting enzyme

Conclusion

High-fructose consumption may contribute to a significant increase in the prevalence of metabolic syndrome. The activity of systemic and local RAS components has increased in fructose-induced metabolic syndrome. Overexpression of Agt II and AT1R provokes insulin resistance, hypertension, and lipogenesis, leading to the emergence of cardiometabolic complications and NAFLD in fructose-induced metabolic syndrome. Conversely, the reduction in compensatory RAS components including ACE2, Agt 1-7, and AT2R, with fructose consumption exacerbates the complications of the metabolic disorder.

Ethics Approval

Not applicable.

Declaration of conflict of interest

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Contribution of The Authors

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Review

Mitochondrial Transplantation and Transfer, from past to future expectations

Mitokondri Nakli ve Transferi, geçmişten gelecek beklentilere

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Abstract

Mitochondria, with their unique roles in cell energy metabolism, continue to be studied by years of research. Mitochondrial transfer can be summarized as the process of transferring isolated mitochondria to the damaged tissue. In this way, it is aimed to improve the mitochondrial dysfunction in areas with impaired mitochondrial functions such as heart damaged tissue. Although there are many studies on this subject, especially cardiomyocytes, the protective effects of the application in processes such as myocardial ischemia and reperfusion injury continues to be investigated. Although there are different procedures for transferring the isolated mitochondrin to the damaged tissue, many studies have reported positive results regarding the application. In this review, it is aimed to look at the subject from a wide window, while examining the studies done in this field in the literature.

Keywords: Mitochondrial transfer, Mitochondrial transplantation, Mitochondria, Tissue injury

Öz

Hücre enerji eldesinde üstlendikleri eşsiz rolleri ile mitokondri yıllardır devam eden araştırmalar ile incelenmeye devam etmektedir. Mitokondriyal transfer hasarlanmış dokuya izole edilmiş olan mitokondrinin transfer edilme süreci olarak özetlenebilir. Bu sayede kalp hasarı olan doku gibi mitokondrial fonksiyonları bozulmuş bölgede mitokondrial disfonksiyon durmunun düzeltilmesi amaçlanmaktadır. Bu konu ile ilgili özellikle kalp dokusunda birçok çalışma olmakla beraber uygulanın miyokardial iskemi, reperfüzyon hasarı gibi süreçlerde koruyucu etkinliği araştırılmaya devam etmektedir. İzole edilen mitokondrin hasarlı dokuya aktarılmasında farklı prosedürler bulunmakla birlikte, birçok çalışmada uygulama ile ilgili olumlu sonuçlar bildirlmektedir. Derlemede literatürde bu alanda yapılmış olan çalışmalar incelenmekle birlikte konuya geniş bir penceren bakılması hedeflenmiştir.

Anahtar kelimeler: Mitokondriyal transfer, Mitokondriyal transplantasyon, Mitokondri, Doku hasarı

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Introduction

Mitochondria are unique structures that can be called energy units for cells, in addition to meeting the energy needed by the body through mitochondrial electron transport chains and oxidative phosphorylation. It can be said that the organelle plays a central role between pathological and physiological issues in terms of associating processes such as homeostasis and energy metabolism in normal tissue with issues such as neurodegeneration and immunity (1).

In general terms; Mitochondrial transplantation can be defined as the transfer of isolated mitochondria to damaged tissue. Mitochondrial transplantation has entered the literature with various experimental studies as a method for the treatment of mitochondrial damage in different tissues and organs. Mitochondrial damage and dysfunction is defined as an important cause of cardiac dysfunction in patients with myocardial ischemia-reperfusion injury. Although this functional change occurs during ischemia, an increase is also observed during restoration of myocardial blood flow and oxygen distribution to the tissue. It is known that this condition shortens the contractions and lifetimes of myocardium (1). The first studies on the method date back to 2009. The results regarding the ischemic heart tissue in the rabbit model were shared in those years. In the light of the data obtained, it is known that isolated mitochondria are transplanted to the damaged myocard in the rabbit model following Langerdorff perfusion (2). With ongoing studies, the method has been defined as mitochondrial transplantation and it has been shared that this application provides a decrease in the levels of biochemical markers observed after myocardial damage in the infarct area, as well as the decrease that can be seen in the basic heart function. In addition to these data, the experiences obtained also indicate that the frozen and thawed mitchondria suffer a loss of function. With previous experiences it is shown that, unlike the studies that will continue, the transferred mitochondria remained in the intercellular space and did not interact with the cardiomyocyte. Although the mechanism of action of mitochondrial transfusion is still not fully explained; It is suggested that the method reduces the levels of oxidative damage measurable by lipid peroxidation products in the lesion area. It is not yet clear whether this reduction is the primary result of the method or a protective effect originating from the mitochondria.

In the next step in experimental animal studies; in vivo effects of mitochondrial transplantation in a rabbit heart ischemia-reperfusion model is experienced. In this study, mitochondrias obtained from skeletal muscle tissue of the same subject were transplanted, and this method led to a decrease in myocardial infarct area in damaged myocardial tissue after 30 minutes of local ischemia, within 2 hours of reperfusion and 4 weeks of follow-up. Regular follow-ups with echocardiography have demonstrated that the heart exhibits normal contractile function 10 minutes after the start of reperfusion in mitochondria transplanted subjects. On the other hand, in the control group, hypokinesia was observed in the ischemic area for 4 hours. With the results of this study also penetration of Mitotraker Red (CMXRos) (a specific staining method for mitochondria) marked mitochondrias in cardiomyocytes and other cells, were detected. With these datas, it was declared that the transplanted mitochondria did not only stay in the intercellular space, but also penetrated into the cells, and it was continued to be investigated in the ongoing studies how the uptake pathways and cell integrity could continue (3).

There are varied data on the in-vitro results of the methods in different experimental models with mitochondria transplantation. For instance, Masuzawa et al. investigated the penetration of mitochondria isolated from human tissue into 2-day-old rat cardiomyocytes. Mitochondria were detected in heart muscle cells in studies with Transmission Electron Microscope (TEM). In the same study, when rat liver tissue was incubated with mitochondria transplanted heart muscle cells for 4 hours; a 2-fold increase in liver cell respiration rate was detected and shared. These results suggested that mitochondria transplantation restores impaired cell energy resources as a result of ischemia/reperfusion (3). In a different study conducted in 2014, researchers transplanted mitochondria into rat heart muscle cells called P0 that did not contain mitochondria, and as a result, they found an increase in respiratory rate and life span in these cells (4). Following this results, in a different model H9c2 cell culture was cultured with mitochondria obtained from the same cell line or from a different cell line, L6 cells. In this study, standard cell culture medium (DMEM) containing more than 1mM Ca+2 was preferred and the medium was supplemented with pyruvate and glutamine. As a result of the experiment, an increase in basal and maximum cell respiration rates was shared in the presence of carbonylcyanide-p-trifluoromethoxyphenylhydrazone (FCCP) (5).

Encouraging results of in-vitro studies have facilitated different experimental models of mitochondrial transplantation for

cardiac ischemia. Results obtained with these studies have declared the protective effect of mitochondria in ischemia model (6) even in the circulation via the coronary artery (7).

In the first studies on mitochondrial transplantation, promising data draws attention. In the light of these data, it is seen that the studies trying to clear up the pathways showing the effect of the procedure were examined in the following years. In 2017 we can see data sharing that transplanted mitochondria; equalizes the functions of endogenous mitochondria with reduced function. This method contradicts the classical information that high calcium levels, which are characteristic of the extracellular media environment, cause loss of mitochondrial function (8). Possible hypotheses that attempt to explain this divergent finding in the following years are explored below.

Promising data on experimental models led to clinical trials. In 2017, important data about the method were shared in the literature. Pediatric cardiac surgeon Sitaram M. Emani and researcher McCully processed mitochondrial transplantation in infants with ischemic heart damage. It was performed in individuals aged between 2 days and 2 years, followed by extracorporeal membrane oxygenation (ECMO). As a result of the application to 5 patients, 3 of them had tolerated the ECMO application for 30-50 hours and were followed up for a few months. After mitochondrial transplantation, which was applied to two 6-day and 4-year-old patients, a significant improvement was observed in the cardiac functions of those patients, but the patients died eventually (9). These data were criticized with cautious optimism in the literature.

In order to better interpret the experimental studies and results related to the method, it is seen that they are classified under 3 headings (1, 10):

1) Pre-Ischemia

2) Before reperfusion

3) During reperfusion

1) Mitochondrial transplantation before ischemia:

The first study with this technique was performed by Guariento et al. Researchers declared the results of female Yorkshire pig model, which the left coronary artery was cannulated and 1 x 109 mitochondria were transplanted once and in every 5 minutes for a total of 60 minutes. 15 minutes after the end of the injection, regional ischemia was occured by clamping the left anterior descending branch for 30 minutes. Subsequently, the protective efficacy of mitochondrial transplantation before ischemia was evaluated by providing reperfusion for 120 minutes. Coronary blood flow and heart ejection fraction values increased significantly 30 minutes after ischemia, and these values remained constant until the end of reperfusion. Significant reduction in infarct area was detected with improvement in heart muscle functions in single and continuous applications. Also, a significant decrease was detected in infarct size/area at risk (IS/AAR) values. No difference was detected when the continuous application was compared with the one-time application. The data obtained were interpreted as mitochondrial transplantation before ischemia can prevent myocardial ischemia-reperfusion injury and reduce mortality-morbidity rates in individuals with ischemia-reperfusion injury (11).

2) Mitochondrial transplantation before reperfusion:

The first experimental model in the literatüre analyzing mitochondrial transplantation before reperfusion was performed in the rabbit model by Mc Cully et al. The research team transplanted the mitochondria they isolated from the left ventricle to the damaged area in ischemic heart tissue. Mitochondria transplantation was completed before Langendorff perfusion in the experiment. With the data obtained by this research results of the technique were shared as cardioprotectivity and improved ATP levels (2). In the following years, the same method was performed in animal in-vivo ischemia-reperfusion injury model by Masuzawa et al. Mitochondrias obtained from autologous pectoralis major were transplanted into the ischemic area formed in the heart tissue. As a result of the experiment, significant reductions in myocardial infarct markers, including creatine kinase MB (CK-MB), cardiac troponin I (cTnI), and caspase-3, were observed in the mitochondria transplant group. Also, a decrease in IS/AAR ratio values was detected in the same study (3). Kaza et al., the same mitochondrial transplantation method was preferred. In the pig model, autologous transplantation of mitochondria obtained from the pectoralis major muscle was performed. Before reperfusion, transplantation was performed to the ischemic remainder formed in the heart, and the results were evaluated with both light and electron microscopy. As a results of this research, it was observed that the damage was not evident in the transplanted group. In addition, while a decrease in myocardial infarction area and the IS/AAR ratio values were reported, there was an increase in CK-MB and cTnI levels in the control group (6).

3) Mitochondrial transplantation during reperfusion:

Blitzer et al. introduced a different cardiac ischemia model in an animal model to investigate mitochondrial transplantation during reperfusion. After 120 minutes of perfusion, autologous mitochondria transplantation was completed. Following the completion of the transplantation, another 120 minutes of perfusion was applied. Ejection fraction, short axis shortening rate and area change score values were found increased with the echocardiographic examination. Also, mitochondrial transplantation application provided during perfusion may cause an increment in long-term morbidity and mortality of patients scheculed for cardiac surgery (10).

Different delivery methods of mitochondria in experimental studies:

1)Using Injection: It can be defined as a simple method applied using Tuberculin syringe with a standard 18-, 28-, or 32-gauge needle or an insulin syringe with a 28-gauge needle (3, 12). This technique is preferable in conditions which there is no need for an additional suture during heart surgeries and it does not cause additional damage to the myocardium. In studies on rabbit heart tissue, mitochondrial structures marked with MitoTracker were detected in the area of injection and 2-3 mm around of it. Transplanted mitochondria were seen in the area close to cardiomyocytes. 1-2 hours after the injection, the mitochondrial structure was found to be integrated into the cardiomyocyte and close to the sarcomere (between the z-line and the sarcomere) . Immune reaction and arrhythmia were not observed contrary to the increase in ATP levels (6, 13). In a different study performed with injection, by Orfany et al., the mitochondrial structure was taken into the cell by actin-dependent endocytosis. Although the injection route is feasible, it should be taken into account that there may be a need for injection into different areas (13, 14) which could be associated with additional damage for cardiac musle tissue.

2)Using Intracoronary Perfusion: In this method, exogenous mitochondria are distributed in a general way via the coronary artery instead of a prominent area. With this technique mitochondria transplantation can be completed for a general area in a short time through the coronary artery unlike the injection method. However, compared to direct injection method, both methods had cardioprotective effects with no significant differences. Considering a wider effect, it can be thought that this method may be a more appropriate choice for cases with a diagnosis of multiple cardiovascular diseases (2, 7, 12, 13, 15).

3) Inherent Mitochondrial Transfer Mechanism in Cells: It can be thought that transfer of mitochondria via stem cell route may be a preferable method for mitochondria-dependent diseases. Bone marrow dependent stem cells are highly effective for this method with their high expression levels. Although Miro1 is a calcium-dependent protein structure, it binds the mitochondrial structure to the dynein protein, allowing the mitochondria to move with the microtubules in the cell. Miro1 expression in stem cells can expand the distribution of donor cells. The view that stem cells can heal recipient cells by mitochondrial transfer can be identified among the different features of the method. In the literatüre it is declared that stem cells with Miro1 expression have wide mitochondrial distribution ability as well as a healing effect on epithelial damage, while this feature has been found to be absent in Miro1 gene knockout (MSCmiroLo) subjects (16, 17). It is known that bone marrow-derived stem cells can be effective in mitochondria transfer in neurons damaged as a result of spinal cord injury. It is stated in the literature that the main mechanism during this transfer is related to the gap junction structure. As a result of transferring mitochondria to neurons with stem cells, there is an increment of ATP levels in the cell and lactate dehydrogenase activation but with a decrease in apoptosis levels. Application of mitochondria transplantation using stem cells may be promising for patients with spinal cord injury (18).

4) Effect of Drug Delivery System: Application methods for mitochondria transfer may have uncertainities for the patient due to their invasiveness. In order to maximize the results of mitochondria transplantation, it is of great importance to develop the use of auxiliary drugs in the transport of mitochondria to the target tissues or organs. Using PEP-1 modified mitochondria structures (PEP-1-MITO) increases the uptake of mitochondria into the target cell. It has been reported that mitochondrial function improved within days, reactive oxygen species (ROS) decreased, and membrane potential improved in cocultures of fibroblast cells obtained from patients with myoclonic epilepsy, provided with PEP-1-MITO, compared to the untreated control group (15, 19). In a different study conducted in the rat Parkinson model, after autologous/allogeneic PEP-1-MITO injection, the exercise capacity of the subjects improved, as well as an improvement in the expression of substantia nigra respiratory chain complex protein (20). In addition to these effects mentioned, the anti-tumoral effect after mitochondrial transplantation supported by PEP-1 is among the data shared in the literature. These effects can be exemplified as inhibition of breast cancer cell proliferation and improvement of chemotherapy sensitivity (21). (Diseases related with Mitochondrial Transplantation are summarized in Table -1 (1))

Table 1: Application of Mitochondrial Transplantation for Various Diseases with related sources of m itochondriai transfer models, results and references (1)

Disease Models	Sources of Mitochondria	Transfer Modes	Results	References
PD	PC12 cells and human osteosarcoma cells	PEP-1-MITO	Mitochondrial complex I protein and mitochondrial dynamics restored	(20)
Type 2 diabetes	Pectoralis major muscles	Infusion through aorta	ATP content increased significantly and myocardial infarction area apparently decreased	(22)
HIRI	Allogeneic liver	Intrasplenic injection	ALT, apoptosis markers, and ROS production decreased	(23)
HL	Hepatoma cells	Caudal vein injection	Serum transaminase activity and cholesterol levels decreased	(24)
ALI	Gastrocnemius muscle BMSCs	Pulmonary artery infusion, tracheal atomization, GJIC	Dynamic compliance and inspiratory capacity significantly increased; alveolar ATP concentration rose	(25, 26)
PAH	Femoral artery smooth muscle cells	Intravenously injected	Inhibited pulmonary vasoconstriction; reduced pulmonary vascular remodeling	(25, 27)
SCI	Soleus muscles	Direct injection in medial gray matter	Acute bioenergetics of maintaining injured spinal cord	(28)
MCAO	hUC-MSCs	ICV	Reduced astrocyte proliferation and microglia activation; reduced infarct size	(29)
Eye disease	MSCs	Cocultivate	Reduced the loss of retinal ganglion cells	(30, 31)
ALI	Muscles of mice	Injected into the muscles of the hind limbs	Improved skeletal muscle injury and 10 enhanced hind limb function	(14)
DD	Hippocampus	Intravenously injected	Significantly reduced the activation 39 of astrocytes, microglia, and neuroinflammatory factors; increased the expression of brain-derived neu- rotrophic factor	(32)
AKI	BMSCs	Injected into renal cortex	Cellular oxidative stress decreased; promoted the regeneration of renal tubular cells	(33)
Mammary cancer	143B osteosarcoma cybrids	PEP-1-MITO	Weakened the vitality of MCF-7 breast cancer cells; improved the sensitivity of chemotherapy	(21)
Infertility	Oocyte precursor cell	Injection into follicular plasma	Increased in vitro fertilization rate	(34, 35)
Septicemia	L6 muscle cells and UC-MSCs	Intravenously injected	Improved the survival rate of spleen in sepsis and bacterial clearance; reduced apoptosis and inflammatory response	(36)

(ALT, alanine aminotransferase; AKI, acute kidney injury; ALI, acute limb ischemia; BMSCs, bone marrow stem cell, DD, dysthymic disorder; HL, hepatic lipidosis; HIRI, hepatic ischemia–reperfusion injury; hUC, human umbilical cord; MCAO, Middle Cerebral Artery Occlusion; MSCs, Mesenchymal stem cells; PAH, pulmonary arterial hypertension; PD, Parkinson's disease; ROS, reactive oxygen species; SCI, spinal cord injury.)

Regarding the mentioned topic, multifunctional mitochondrial targeting liposome nanodevice, ie, the MITO-Porter system was developed by Yamada et al. Considering that the transplanted structure combines with the cell, divides within the cell and shares some biological molecules belonging to the cell, Yamada and his team developed the MITO-Porter and aimed to combine with the mitochondria and be transplanted. The basic mechanism of action can be classified under 3 headings (1):

1) MITO-Porter surface is modified by positively charged cell-penetrating peptide R8.

2) It binds to mitochondria with negative membrane potential via MITO-Porter electrostatic interaction.

3) MITO-Porter associates with the mitochondrial membrane and is transported as a complete structure

All data support that the application of mitochondrial transplantation before ischemia or after reperfusion may be an adjunct method. It is known that the method is effective for ischemic damage in skeletal muscle and lung tissue as well as cardiac muscle (10, 11, 14, 25). In addition, data on the use of the method in the diagnosis of pulmonary hypertension (27, 37), different neurodegenerative diseases (20) and even depression (32) and schizophrenia (38). In addition to the long history declaring the results of the technique and scientific data obtained in different models, the therapeutic

mechanisms related to the mitochondrial transplantation method are still unclear (8). It can be said that the need for studies to explain the effects of the method continues in order for the results of the method to be more predictable and thus to accelerate clinical applications.

Uncertainties about the method

With the help of trial data especially after 2018, it is clear that opinions about the mechanism of mitochondrial transplantation perspective have widened (19). In the light of the hypotheses shared in the literature, mitochondria can remain healthy in the extracellular environment and they can penetrate into cells to repair the impaired ATP production. In the method in which mitochondria are applied with the blood circulation, the mitochondria penetrate the endothelium of the blood vessel before entering the cell (8)

There are basically two questions about the method mentioned by Mc Cully et al. The first of these is the continuation of mitochondrial functions at high Ca+2 levels, as mentioned in the previous chapters. As it is known, at high Ca+2 levels, mitochondria irreversibly lose their ATP synthesis capacity and NAD-dependent respiration abilities. This feature is mainly due to the high membrane potential of mitochondria and the MCU protein (calcium ion carrier protein) properties. The high level of Ca42 in the medium ultimately leads to an increase in permeability at the inner mitochondrial membrane level, and this is known as the permeability transition. Salt and sugar (sucrose, mannitol) groups are added to the incubation medium in order to maintain the osmotic balance. However, with the opening of the pores, the concentration between the medium and the mitochondrial matrix is equalized, resulting in swelling of the mitochondrial structure. The outer membrane, which is shorter than the inner membrane (due to its cristae structure), is broken down first, and this step is followed by the destruction of the inner membrane. As a result of these events, not only the membrane potential decreases, but also NAD/NADPH is lost from the matrix, making oxidation of substrates such as pyruvate and malate impossible. Two possibilities can be considered to explain the survival of mitochondria at high Ca+2 levels: the Ca+2 transporter being blocked or the membrane potential completely destroyed. In a study conducted in 2020, it was shown that the pyruvate and malate oxidizing properties of skeletal muscle mitochondria and its properties for ATP synthesis were lost primarily in standard medium (140 mM Na+, 5 mM K+, and 1 mM Ca+2); it was shared that these properties could be preserved following the blocking of the Ca+2 carrier protein (40).

A second question about the mitochondria transplantation procedure is the continuation of cellular integrity after mitochondria enter the cell. Mc Cully et al., shared that mitochondrias are taken into cells by endocytosis (41). Similar data on the uptake of mitochondria are available in the literature; however, the mechanism for maintaining the integrity of mitochondria after penetration into the cytoplasm remains unclear. To demonstrate the post-transplant robustness of exogenous mitochondria, McCully and colleagues used mitochondria loaded with iron complexes. These complexes were detected in pig heart tissues 4 weeks after transplantation. This result, however, cannot be considered conclusive evidence for mitochondrial robustness. Because it is known that macrophages can maintain iron complexes in phagosomes a few weeks after stem cell administration (42). When in-vitro and in-vivo studies are compared, it is detected that the number of intact mitochondria were found in cardiomyocytes is less in in-vivo studies. When considered together with the data obtained, it is still not clear by which mechanisms the mitochondria, which are few in number, can provide a significant increase in energy production in cardiac muscle cells (3). One view of the efficacy of mitochondrial transplantation is also related to mitochondrial transfer. This situation, in which mitochondria only act as a carrier, is called mitochondrial transformation (43). In some studies in the literature, detection of progression in cardiac functions 10 minutes after mitochondria presentation eliminates the effects of DNA transfer (2, 3, 7).

Another view regarding the method is that after mitochondria transplantation, even autologous, there is a limited immune response in the region. It is known that innate immunity perceives mitochondria and its components as pathogens (44). Studies by Mc Cully et al did not detect an increment in inflammatory markers or proinflammatory cytokine levels. Similarly, no immune response was detected in the rabbit model that was planned with intraperitoneal mitochondria transplantation. However, the local immune response observed in the area of mitochondrial transplantation cannot be ignored according to the literature. In this response, besides neutrophil and macrophage activation in the damaged area, cytokine activation, which affects regional regenerative processes, is important. Along with all the information, the need for experimental data supporting this hypothesis continues (4, 8).

Although there are shared data in the literature on mitochondrial transplantation, the need for evidence for the

transition to clinical applications of the method continues. Experimental animal models in which cardioprotective effects are studied have been studied by a limited team, and the methodological differences between clinical and experimental research models raise questions. While it has been reported that mitochondrial transplantation is performed a few days (up to 15 days) after ischemia in clinical applications; it is found that this time is limited to hours (2 hours) in experimental models (10). Assuming that exogenous mitochondria penetrate cells during the transplantation process, different objections arise regarding the effect of this process on ATP production. The first of these is to ensure the continuation of mitochondrial functions in an environment containing high Ca+2 concentrations. However, the fixation of a very limited number of exogenous mitochondria to the dysfunctional mitochondria structures found in large numbers in the cell is still not clearly explained. Although there is still very limited data in the literature with these processes, the current data still cannot explain these questions clearly. In the light of all the data, although the cardioprotective effects of the existing methods are promising, the need for experimental studies for clinical applications continues (8).

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Case Report

Robot-Assisted Management of Spontaneous Intramural Left Atrial Hematoma Mimicking an Atrial Mass

Atrial Kitleyi Taklit Eden Spontan İntramural Sol Atrial Hematomun Robot-Asiste Tedavisi

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Abstract

Spontaneous Intramural left atrial hematoma that mimics a primary or metastatic cardiac tumor is a very rare entity. We report a case of a 60-year-old man suffering from chronic myeloid leukemia, who was admitted for prolonged chest pain and fatigue. Transthoracic echocardiography revealed a left atrial mass in close proximity to the posterior mitral annulus and failed to provide an ethiological diagnosis. Surgical management was utilized to outrule the atrial neoplasm and to prevent emboli, obstruction and mitral valve insufficiency. This is the first case in the literature in which robot-assisted minimally invasive surgery was adopted to manage such a rare entity.

Keywords: intramural left atrial hematoma, robot-assisted, minimally invasive

Öz

Primer veya metastatik kalp tümörünü taklit eden spontan intramural sol atriyal hematom çok nadir bir antitedir. Uzun süreli göğüs ağrısı ve halsizlik şikayeti ile başvuran 60 yaşında kronik miyeloid lösemi hastası bir erkek hastayı sunuyoruz. Transtorasik ekokardiyografide sol atriyumda posterior mitral anulusa yakın bir kitle saptandı ve etyolojik tanı konulamadı. Atriyal neoplazmı ekarte etmek, kitle obstrüksiyonunu ve mitral kapak yetmezliğini önlemek için cerrahi tedavi uygulandı. Bu, literatürde robot yardımlı minimal invaziv cerrahinin bu kadar nadir görülen bir durumu yönetmek için kullanıldığı ilk vakadır.

Anahtar kelimeler: İntramural sol atrial hematom, robotik cerrahi, minimal invazif

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Introduction

Left atrial intramural hematoma (LAIH) is a rare occurrence that has been documented as associated with percutaneous coronary interventions or surgical cardiac procedures, radiofrequency ablations, mitral annular calcification3, myocardial infarction, blunt chest trauma and dissecting aneurysm of the aorta1-5. The robot-assisted minimally invasive approach, increasingly popular in recent years, was used to surgically manage this case of spontaneous LAIH mimicking a left atrial mass; until now, the literature contains no reports of this approach to managing this rare entity.

Case Report

A 60-year-old man presented to our hospital with prolonged atypical chest pain, progressive shortness of breath and fatigue. At the time of admission, his haemodynamic status was stable and electrocardiogram, chest X-ray findings were normal. Subsequent laboratory tests revealed a white blood cell count of 66,54 K/uL (normal value: 4,23-9,07). Transthoracic echocardiography (TTE) revealed a left atrial mass (4,7 x 2,5 cm) attached to the posterior wall and inter-atrial septum in close proximity to the posterior mitral annulus, and minimal pericardial effusion (Figure 1).

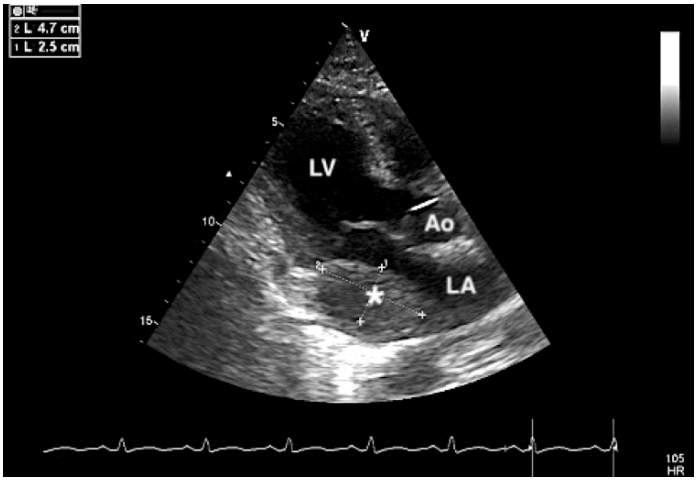

Figure 1: Modified parasternal long-axis transthoracic echocardiogram (preoperative). *Left atrial mass (4,7 x 2,5 cm) attached to the posterior wall and inter-atrial septum. LA, Left Atrium; Ao, Aorta; LV, Left Ventricle.

Increased mitral inflow velocity and prolonged pressure halftime on pulsed wave Doppler recordings indicated a blockage of the blood flow to the left ventricle. No color flow was observed through the mass. Bone marrow biopsy, immunohistochemichal evaluation, genetic testing and translocation analysis showed BCR-ABL translocation t(9;22) p210 transcription positive chronic myeloid leukemia. A left atrial neoplasm (primary or metastatic) was the presumptive diagnosis, and surgical exploration was planned. Coronary angiography revealed normal coronary arteries.

After the patient was appropriately positioned, the right lung was deflated. A 3- to 4-cm right inframammary thoracotomy lateral to the nipple was made and the pleural cavity was entered through the 4th intercostal space (ICS). Trocars were placed in the third and fifth ICS. A working port and camera trocar were placed through the incision. Considering that a dynamic mitral retractor might be necessary during the operation, another trocar was inserted through the submammary 4th ICS. Femoral arterial and venous cannulation was made to establish perfusion. An additional second venous drainage cannula was inserted percutaneously in the SVC via right internal jugular vein. Cardiopulmonary bypass was established and pericardial entry and suture retractions were made. External inspection of the mediastinium showed no evidence of infiltrating mass or pericardial adhesions. Antegrade cardioplegia needle placement in the ascending aorta was followed by introduction of a transthoracic aortic cross clamp (Chitwood clamp) through the transverse sinus in the 2nd ICS in the posterior axillary line and deployed. Myocardial protection was provided by systemic cooling (28°C) and cold-blood cardioplegia. Left atriotomy was made and an intramural mass was observed in the posterior wall of the LA bulging into the cavity. No infiltration in and outside of the LA wall was found. The endocardium was incised and several pieces of yellow-cream colored elastic tissue were excised from a non-encapsulated cavity (Figure 2). Association of the mass with the posterior wall resulted in a cavity because of the seperation of the endocardium and epicardium. The posterior wall was repaired with bovine pericardial patch (Figure 3).

Histopathological examination of the surgical specimens confirmed fragments of organized thrombus and adjacent normal myocardial wall. There was no evidence of active inflammation, hydaditosis, endocarditis, amyloidosis, tumor, vascular malformation and cultures of the specimen were negative for bacteria and fungus. Postoperative course was uneventful. Predischarge TTE showed no residual hematoma and an intact- patched LA wall with no mitral insufficency (Figure 4).

Figure 2: Intraoperative image. MV, Mitral Valve; *, yellow-cream colored elastic tissue localized in the posterior left atrial wall; dotted line, left atrial wall.

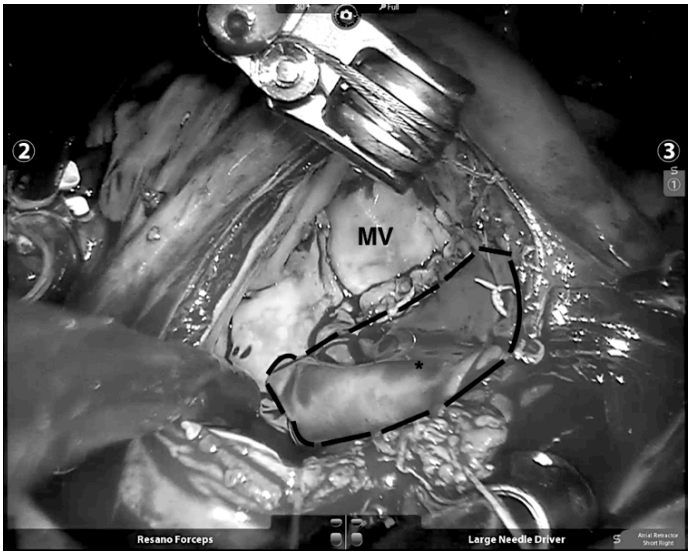

Figure 3: Intraoperative image. *, bovine pericardial patch; MV, Mitral Valve

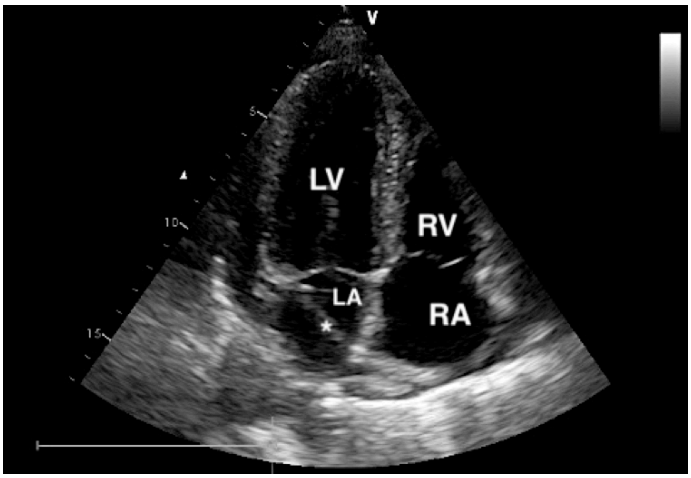

Figure 4: Apical four-chamber transthoracic echocardiogram, postoperative. *intact bovine pericardial patch; LA, Left Atrium; RA, Right Atrium; RV, Right Ventricle; LV, Left Ventricle.

Discussion

Since spontaneous LAIH is a very rare entity, its true incidence is unknown. Even the best imaging techniques sometimes fail to differentiate the diagnosis, and as in the present case, histological confirmation via surgical exploration is required.

Generally the literature concerning LA hematoma includes only case reports. LA hematoma can occur very rarely spontaneously, as in our case, as well as secondary to complications in cardiac surgery or percutaneous interventions and ablation of atrial tachyarrhythmias2,6-8. It has also been associated with amyloidosis, blunt chest trauma, mitral annular calcification, mitral annular abscess, dissecting aortic aneurysm2,6-8. LAIH generally originates from posterior LA wall due to the lower quantitiy of fibrous tissue and because the posterior leaflet of the mitral valve is more prone to calcification2. Altough the position of the LAIH in our case is consistent with the literature, no patient or procedural factors was found. TTE remain as the first-line study in differential diagnosis9.

Due to lack of previous experience and established protocols management of this entity is challenging in terms of timing and approach. In this case, presumptive diagnosis was left atrial neoplasm. As TTE indicated blocked blood flow to the left ventricle and potential hemodynamic instability, surgical intervention was chosen as the best management option.

The most common intracardiac tumor to have been successfully excised using robotic technology has been the left atrial myxoma10. Robotic system affords excellent exposure, magnification and flexibility. The operative technique mimics that of a mitral valve procedure. Improved surgical exposure, reduced postoperative pain, shorter hospitalization, lower mortaliy and perioperative complication rates have been reported as major advantages of robotic approach11. Our case is the first case of spontaneous LAIH that was managed via robot-assisted minimally invasive surgical intervention.

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Olgu Sunumu

Tear Trough Ligamentin Anatomik Varyasyonu, Kadavra Direksiyonu Vaka Sunumu

Anatomical variation of the tear trough ligament, a case report of cadaveric dissection

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Öz

Göz altında yaş alma belirtileri yirmili yaşlardan sonra ortaya çıkar. Yaş alma ile birlikte göz altında çukurlaşma ve renk değişimi görülür. Tear trough deformitesi ameliyatlı ve ameliyatsız estetik müdahale ile düzeltilebilir. Tear trough deformitesinin sebebinin, çöküntünün hemen altında bulunan tear trough ligamentine bağlı olduğu gösterilmiştir. Gözaltı ve yanak bölgesindeki lateral sınırda ise orbitalis retaining ligament gösterilmiştir. Tear trough ligamenti medialde midpupiler hat hizasına kadar devam eder. Midpupiler hat hizasından sonra ise orbitalis retaining ligament iki yaprak olarak başlar. Bu ligamentlerin cerrahi olarak direksiyonu ile veya dolgu uygulaması ile düzeltilmesi mümkündür. Tear trough ligamenti ve orbitali retaining ligamenti daha önce kadavra diseksiyonlarında tanımlanmıştır. Kadavra direksiyonu vaka sunumuzda mevcut tanımın aksine tear trough ligamentinin midpupiler hat hizasına ulaşmadan iki yaprağa ayrıldığı gösterilmiştir. Tear trough ligamentinin anatomik varyasyonun olması, estetik olarak bu bölgenin düzeltilmesinde göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Tear trough ligament, orbitalis retaining ligament, palpebromalar oluk

Abstract

The signs of aging lower eyelids appear after the age of twenties. With aging, depression and color change are seen under the eyes. Tear trough deformity can be corrected with surgical and non-surgical aesthetic intervention. It has been shown that the cause of the tear trough deformity is due to the tear trough ligament located just below the depression. The orbitalis retaining ligament is shown at the lateral border of the under palpebromalar region. Tear trough ligament continues medially to midpupil level. After the midpupil, the orbitalis retaining ligament begins as two leaves at lateral side. It is possible to correct tear trough deformity with surgical dissection or hyaluronic asid filler injection.

Tear trough ligament and orbital retaining ligament have been described previously in cadaveric dissections. In our cadaveric dissection case report, contrary to the current definition, it was shown that the tear trough ligament splits into two leaves before reaching the mid-pupillary level. The anatomical variation of the tear trough ligament should be considered in the aesthetic correction of this region.

Keywords: Tear trough ligament, orbitalis retaining ligament, palpebromalar groove

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Giriş

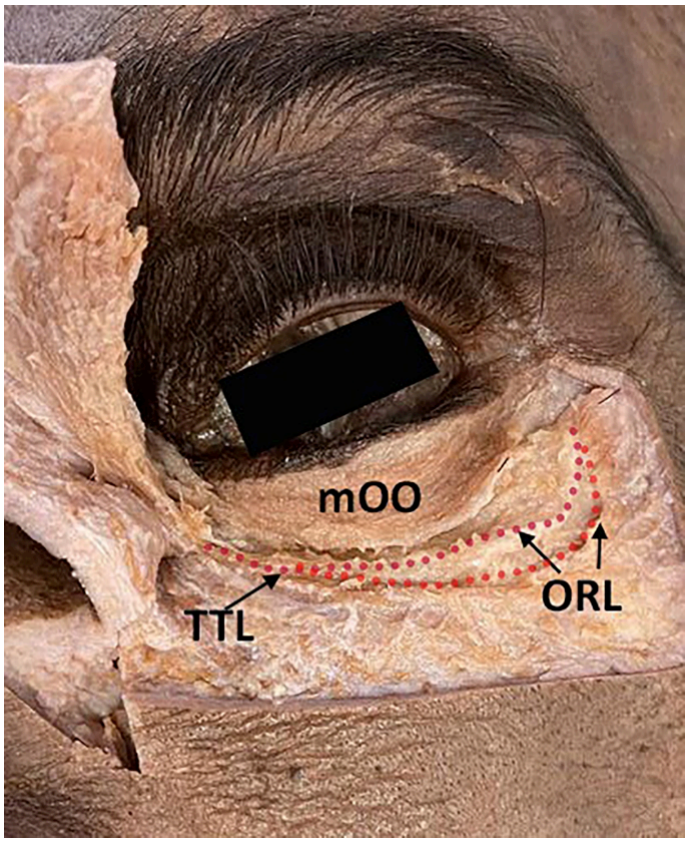
Göz çevresi ve yanak bölgesinin morfolojik olarak ayrım noktasında orbitomalar oluk bulunur. Bu oluğun belirginliği yaş ile artar. Bu bölgenin iç kısmında yer alan çöküntüye tear trough denilir. Tear trough türkçe anlamı göz yaşı oluğu anlamına gelir. Yapılan anatomik çalışmalarda tear trough bölgesinde tabanında bulunan kemik yapıdan deriye kadar uzanan ligament olduğu gösterilmiş (1). Tear trough ligamenti (TTL) musculus (m) orbicularis oculinin palpebral ve orbital bölümleri arasında bulunur. TTL cantus medialis hizasından başlayıp midpupiler hat hizasına kadar devam eder. Midpupiler hat hizasında iki yaprak halinde cantus lateralis'e kadar orbitalis retaining ligament (ORL) uzanır. TTL daha kısa ve dens yapıda bulunurken, ORL daha uzun ve gevşek yapıdadır. Her iki ligament'de kemikten cilde uzanır. (2,3) Bu bölgede yaşlanmayla birlikte m. orbicularis'de gevşeme görülür. Tear trough ligament ve orbitalis retaining ligament m. orbucularis oculi'ye yapıştığı alanda çökmeye neden olur. (8) Bu bölgeye yapılacak cerrahi girişimlerde ve cerrahi dışı girişimlerde düzgün bir hat elde etmek bu ligamentin ve çevre yapıların anatomisinin iyi bilinmesi ile mümkün olacaktır.

Olgu

Kadavra diseksiyonu Ankara Üniversitesi Anatomi Anabilim Dalı laborutarında yapılmıştır. Çalışmada 55 yaş erkek fikse kadavra diseke edilmiştir. Sol periorbital bölgede subsilier ve zigoma seviyesinde cilt insizyonu yapılıp cilt subkutan doku arası TTL ve ORL ye kadar direksiyonla kaldırıldı. Takiben m. orbicularis oculi diseksiyon ile kaldırıldı. Diseksiyon sırasında ligamentler görüldü ve korundu. M. orbicularis oculi tabanda ligamentler korunacak şekilde tamamen kaldırıldı ve tabanda ligamentlerin maksiller kemiğe yapıştığı alan değerlendirildi.

Diseksiyonda TTL'nin literatürde olduğunun aksine midpupiler hat hizasına ulaşmadan iki yaprağa ayrıldığı izlendi (Figür 1). TTL'nin saat 7 hizasında iki yaprağa ayrıldığı izlendi. TTL midpupiler hat hizasından 8.2 mm medialinde iki yaprağa ayrıldığı izlendi.

TTL medial cantus hizasından orbital rim'den 3 mm, midpupil hizasında ORL'nin üst kolu 4 mm, lateralde ORL lateral cantus hizasında orbital rim'den 6 mm uzaklıkta ölçüldü.



Figür 1. mOO musculus orbicularis oculi, TTL tear trough ligament, ORL orbitalis retaining ligament

Tartışma

Göz çevresi yaş almanın ilk görüldüğü bölgedir. Yaş alma ile birlikte göz altında çökme görülebilir. Bu alan alt göz kapağı estetiği sırasında düzeltilebileceği gibi erken dönemde hyaluronik asit bazlı dolgu enjeksiyonu ile de düzeltilebilir. (4,5) Bu alanın cerrahi düzeltilmesinde TTL ve ORL genellikle cerrahi olarak diske edilir. (3) Tekrar yapışmasını engellemek için ve çöküntüyü düzeltmek için cerrahi sırasında yağ grefti uygulanabilir. (6) Gözaltı oluğunun ameliyatsız yani dolgu enjeksiyonu ile düzeltilmesi cerrahiden daha sık uygulanmaktadır. Tear trough deformitesinin ilk belirtileri başladığında oluğa dolgu enjeksiyonu yapılarak gözaltı yanak birleşkesinin daha düzgün geçişi sağlanabilir. (4,5,7)

Bu bölgenin cerrahi ve dolgu enjeksiyonu ile düzeltilebilmesi için anatomisinin çok iyi bilinmesi gerekir. Yapılan diseksiyonda TTL midpupile kadar uzanmamaktadır. TTL daha dens bir ligament olduğu için diseksiyonu ORL den daha zordur. Cerrahi sırasında sınırlarının bilinmesi veya olası varyasyonlarının olabileceğinin bilinmesi cerraha yol gösterici olacaktır. Literatürde mevcut

anatomik çalışmalarda TTL'nin midpupile kadar uzandığı gösterilmiş ama hiçbir varyasyonu tanımlanmamıştır. Olgu sunumuzda daha önce görülmeyen TTL varyasyonu görülmüştür.

Bölgenin dolgu ile düzeltilmesi sırasında anatomisinin bilinmesi de önemlidir. TTL daha kısa olduğu için TTL bölgesine yapılacak dolgu enjeksiyonun en derin tabakaya yani direk kemik üzerine yapılması gerekir. ORL bölgesinde ise iki yaprağın olması ve ORL'nin uzun olması nedeniyle dolgu enjeksiyonu yüzeysel önerilir. Ayrıca ORL'nin iki yaprağının tam ortasına yapılacak derin dolgu enjeksiyonu deformitenin derinliğini artıracaktır.

Yapılan direksiyonda TTL ve ORL'nin varyasyonu gösterilmiştir. Olgumuzda TTL klasik olarak midpupiler hat hizasına kadar uzanmamaktadır. Gözaltı bölgesinde ameliyatlı veya ameliyatsız estetik müdahale öncesinde TTL ve ORL'nin varyasyonları göz önünde bulundurulmalı, gerekirse hastanın anatomisine uygun yaklaşım seçilmelidir.

Teşekkür

Yazarlar, anatomik araştırmaların yapılabilmesi için bedenlerini bilime bağışlayanlara içtenlikle teşekkür eder. Bu tür araştırmalardan elde edilen sonuçlar, potansiyel olarak insanlığın genel bilgisini artırabilir ve bu da daha sonra hasta bakımını iyileştirebilir. Bu nedenle, bu bağışçılar ve aileleri en büyük minnettarlığımızı hak ediyor.

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Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.

Etik kurallar: Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. Turkish Journal of Clinics and Laboratory gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Teşekkür yazısı: Varsa kaynaklardan sonra yazılmalıdır.

Maddi destek ve çıkar ilişkisi: Makale sonunda varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmelidir. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları "Cumulated Index Medicus" ta kullanılan stile uymalıdır. Kaynak sayısının araştırmalarda 25 ve derlemelerde 60, olgu sunumlarında 10, editöre mektupta 5 ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce köşeli parantez kullanılarak belirtilmelidir. Örneğin [4,5]. Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

Şekil ve tablo başlıkları: Başlıklar kaynaklardan sonra yazılmalıdır.

4. Şekiller: Her biri ayrı bir görüntü dosyası (jpg) olarak gönderilmelidir.

Makalenin basıma kabulünden sonra "Dizginin ilk düzeltme nüshası" sorumlu yazara e-mail yoluyla gönderilecektir. Bu metinde sadece yazım hataları düzeltilecek, ekleme çıkartma yapılmayacaktır. Sorumlu yazar düzeltmeleri 2 gün içinde bir dosya halinde e-mail ile yayın idare merkezine bildirecektir.

Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

Özpolat B, Gürpınar ÖA, Ayva EŞ, Gazyağcı S, Niyaz M. The effect of Basic Fibroblast Growth Factor and adipose tissue derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end to end anastomosis rat model. Turk Gogus Kalp Dama 2013; 21: 1010-19.

Kitaptan yapılan alıntı;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Tek yazar ve editörü olan kitaptan alıntı;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams&Wilkins; 1996: 46-60.

Çoklu yazar ve editörü olan kitaptan alıntı;

Schulz JE, Parran T Jr: Principles of identification and intervention. In:Principles of Addicton Medicine, Graham AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams&Wilkins; 1998:1-10.

Eğer editör aynı zamanda kitap içinde bölüm yazarı ise;

Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag;1988:45-67.

Doktora/Lisans Tezinden alıntı;

Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

Sitenin adı, URL adresi, yazar adları, ulaşım tarihi detaylı olarak verilmelidir.

DOI numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of Complementary and Alternative Medicine into Family Practice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

Diğer referans stilleri için "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References" sayfasını ziyaret ediniz.

Bilimsel sorumluluk beyanı: Kabul edilen bir makalenin yayınlanmasından önce her yazar, araştırmaya, içeriğinin sorumluluğunu paylaşmaya yetecek boyutta katıldığını beyan etmelidir. Bu katılım şu konularda olabilir:

a. Deneylerin konsept ve dizaynlarının oluşturulması, veya verilerin toplanması, analizi ya da ifade edilmesi;

b. Makalenin taslağının hazırlanması veya bilimsel içeriğinin gözden geçirilmesi

c. Makalenin basılmaya hazır son halinin onaylanması.

Yazının bir başka yere yayın için gönderilmediğinin beyanı: "Bu çalışmanın içindeki materyalin tamamı ya da bir kısmının daha önce herhangi bir yerde yayınlanmadığını, ve halihazırda da yayın için başka bir yerde değerlendirilmede olmadığını beyan ederim. Bu, 400 kelimeye kadar olan özetler hariç, sempozyumlar, bilgi aktarımları, kitaplar, davet üzerine yazılan makaleler, elektronik formatta gönderimler ve her türden ön bildirileri içerir."

Sponsorluk beyanı: Yazarlar aşağıda belirtilen alanlarda, varsa çalışmaya sponsorluk edenlerin rollerini beyan etmelidirler:

1. Çalışmanın dizaynı

2. Veri toplanması, analizi ve sonuçların yorumlanması

3. Raporun yazılması

Kontrol listesi:

1. Editöre sunum sayfası (Sorumlu yazar tarafından yazılmış olmalıdır)

2. Başlık sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Yazarlar, kurumları, sorumlu yazar posta adresi, tüm yazarların e-mail adresleri, sorumlu yazarın telefon numarası)

3. Makalenin metin sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Özet/anahtar kelimeler, Summary/keywords, makale metni, kaynaklar, tablo ve şekil başlıkları, tablolar, şekiller)

4. Tablo ve grafikler metin içinde olmalıdır.

5. Şekiller (En az 300 dpi çözünürlükte) ayrı bir veya daha fazla dosya halinde gönderilmelidir.