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AMAÇ

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

KAPSAM

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AIM

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

SCOPE

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1. Yazarlar

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

a. Yırtıcı veya Sahte Dergiler

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

2. Dergiler

a. Gizlilik

Dergilere gönderilen yazılar, yazarın özel, gizli mülkü olan ayrıcalıklı iletişimdir ve yazarlar, bir yazının ayrıntılarının herhangi birinin veya tamamının erken ifşa edilmesiyle zarar görebilir.

Bu nedenle editörler, el edilip edilmediği ve incelenip değerlendirilmediği, inceleme sürecindeki içeriği ve durumu, gözden geçirenlerin eleştirisi ve nihai kaderi de dahil olmak üzere yazarlar ve gözden geçirenler dışındaki kimseyle paylaşılmamalıdır. Üçüncü şahıslardan yazılar ve yasal işlemlerde incelemeleri kullanma talepleri kibarca reddedilmeli ve editörler mahkeme celbi olarak bu tür gizli materyalleri temin etmemek için elinden geleni yapmalıdır.

Editörler, hakemlerin yazıları, ilgili materyalleri ve içerdikleri bilgileri kesinlikle gizli tutmaları gerektiğini de açıkça belirtmelidir. Hakemler ve editöryal personel, yazarın çalışmasını kamuya açık olarak tartışmamalı ve hakemler, makale yayınlanmadan önce yazarların fikirlerini uygun görmemelidir. Hakemler makaleyi kişisel kullanımları için saklamamalı ve makalelerin basılı kopyalarını imha etmeli ve incelemelerini gönderdikten sonra elektronik kopyaları silmelidir.

Bir makale reddedildiğinde, yerel yönetmeliklerde saklama gerekmedikçe dergilerin kopyalarını editör sistemlerinden silmeleri en iyi yöntemdir. Reddedilen yazıların kopyalarını tutan dergiler, bu uygulamayı Yazarlar Bilgilendirmesinde açıklamalıdır.

Bir makale yayınlandığında, dergiler, çalışmalarla ilgili gelecekteki soruları cevaplamak için, yerel düzenlemelere bağlı olarak, asıl başvuru, gözden geçirme, gözden geçirme ve yazışmaların kopyalarını en az üç yıl süreyle ve muhtemelen kalıcı olarak saklamalıdır.

Editörler hakemlerin ve yazarların izni olmadan hakemlerin yorumlarını yayınlamamalıdır. Dergi politikası yazarları gözden geçirenin kimliğine karşı koruyacaksa ve yorumlar imzalanmadıysa, söz konusu kimliği hakemlerin ifade ettiği yazılı izin olmadan yazara veya başkalarına ifşa edilmemelidir.

Sahtekarlık veya sahtekarlık iddiası varsa gizliliğin ihlal edilmesi gerekebilir, ancak editörler yazarları veya hakemleri bu konuda istekli olduklarını bildirir ve gizlilik aksi takdirde onurlandırılmıdır.

b. Zamanlama

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

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c. Hakem Değerlendirmesi

Hakem değerlendirmesi, dergilere sunulan yazıların, genellikle editöryal personelin bir parçası olmayan uzmanlar tarafından eleştirel bir değerlendirilmesidir. Tarafsız, bağımsız, eleştirel değerlendirme, bilimsel araştırma da dahil olmak üzere tüm bilimsel çalışmaların özünü oluşturduğu için, hakem incelemesi, bilimsel sürecin önemli bir uzantısıdır. Hakem değerlendirmesinin gerçek değeri tartışılmaktadır, ancak süreç bilimsel topluluk üyeleri arasında bir makale için adil bir duruşma yapılmasını kolaylaştırmaktadır. Daha pratik olarak, editörlerin hangi yazıların dergileri için uygun olduğuna karar vermelerine yardımcı olur. Hakem değerlendirmesi genellikle yazarların ve editörlerin raporlama kalitesini iyileştirmelerine yardımcı olur. Sistemlerin yerinde olmasını sağlamak derginin sorumluluğundadır.

Uygun hakemlerin seçimi için hakemlerin, sadece e-posta için ek materyaller de dahil olmak üzere, makalenin değerlendirilmesine ilişkin tüm materyallere erişebilmesini sağlamak ve hakem değerlendirmelerinin bağlamda uygun bir şekilde değerlendirilmesini ve yorumlanmasını sağlamak editörün sorumluluğundadır.

Hakemli bir dergi, gözden geçirilmek üzere gönderilen makaleleri göndermekle yükümlü değildir ve eleştirilenlerin önerilerini olumlu veya olumsuz olarak izlemekle yükümlü değildir. Bir derginin editörü sonuçta tüm içeriğin seçiminden sorumludur ve editöryal kararlar, derginin uygunluğu gibi bir makalenin kalitesiyle ilgili olmayan konulardan haberdar edilebilir. Bir editör, eserin bütünlüğü ile ilgili endişeler ortaya çıktığında kabul edildikten sonra da dahil olmak üzere herhangi bir anda herhangi bir makaleyi reddedebilir.

Dergiler, incelemeye gönderdikleri yazıların sayısı ve türleri, her bir yazı için aradıkları gözden geçirenlerin sayısı ve türleri, inceleme sürecinin açık veya kör olması ve inceleme sürecinin diğer yönleri bakımından farklılık gösterebilir. Bu nedenle ve yazarlara sunulan bir hizmet olarak dergiler, hakem inceleme sürecinin bir tanımını yayınlamalıdır.

Dergiler bir makaleyi kabul etme veya reddetme kararını nihai olarak gözden geçirmeli ve hakemlerin hakemlerinin dergilerine katkısını kabul etmelidir. Editörler, hakemlerin yorumlarını aynı makalenin hakemleri ile paylaşmaya teşvik edilir, böylece hakemler inceleme sürecinde birbirlerinden öğrenebilirler.

Hakem değerlendirmesinin bir parçası olarak, editörlerin araştırma protokollerini, protokolden ayrırsa istatistiksel analiz planlarını ve / veya projeye özgü çalışmalarla ilgili sözleşmeleri incelemeleri teşvik edilir. Editörler, yayın için bu tür çalışmaları kabul etmeden önce yazarları bu tür belgeleri yayın sırasında veya sonrasında kamuya açık hale getirmeye teşvik etmelidir. Bazı dergiler, bu belgelerin kamuya kabul edilmesinin bir koşulu olarak ilan edilmesini gerektirebilir.

Bağımsız veri analizi ve kamuya açık verilerin mevcudiyeti için günlük gereklilikleri, bu revizyon sırasında yayınlanmıştır; bu, yayın öncesi ve sonrası hakem incelemesi için verilerin mevcudiyetinin önemine dair gelişen görüşleri yansıtmaktadır. Bazı dergi editörleri şu anda yayın için çalışmalarını kabul etmeden önce bağımsız bir biyoistatistikçi tarafından deneme verilerinin istatistiksel analizini talep etmektedir. Diğerleri yazarlardan çalışma verilerinin üçüncü şahıslar tarafından görüntülemek ve / veya yeniden analiz etmek için kullanıp kullanamayacağını belirtirken, başkaları da yazarların verilerini gözden geçirmek veya yeniden analiz için başkalarıyla paylaşmasını teşvik eder veya talep eder. Her dergi, potansiyel yazarların kolayca erişebileceği bir yerde veri analizi ve kayıt için kendi spesifik gereksinimlerini oluşturmalı ve yayınlamalıdır.

Bazı insanlar gerçek bilimsel hakem değerlendirmesinin sadece bir bildiri yayımlandığı tarihte başladığına inanmaktadır. Bu bağlamda, tıbbi dergiler, okuyucuların yayınlanmış makaleler hakkında yorum, soru veya eleştiriler sunma mekanizmasına sahip olmalı ve yazarların uygun şekilde cevap vermeleri ve dergi verilerinin talepleri ile işbirliği yapmaları ya da bildiri ile ilgili ek bilgi talep etmeleri gerekir. yayından sonra ortaya çıkar (bkz. Bölüm III).

d. Bütünlük

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

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Yazım Kuralları

Yazarlar, kaynakların doğruluğundan kendileri sorumludur.

Kaynaklar ayrı bir sayfaya yazılmalı ve yazı içinde geçiş sırasına göre numaralandırılmalıdır.

Cümle içerisinde isim verilmeyecek ise kaynak numarası cümle sonunda, nokta işaretinden önce üstsimge şeklinde verilmelidir.

"profilaksisinde kullanılır², Fields ve ark.²⁸ sağlıklı....."

Dergi kaynaklarında yıl, cilt, başlangıç ve bitiş sayfaları verilirken kitap kaynaklarında ise sadece yıl belirtilmelidir. "Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology. 1999;91:109-18.

İkiden fazla peş peşe gelen kaynak var ise ilk ve son olanları, aralarına "-" işareti konarak verilmelidir:

'İhtiyatla hareket etme eğilimi olarak tanımlanmıştır¹⁻³.'

Kaynaklarda yazarların tam soyadları ve adlarının ilk harfleri yazılmalıdır.

"İlginel MT, Tunay DL, Güneş Y. Epilepside perioperatif yönetim ve anestezi. Arşiv Kaynak Tarama Dergisi. 2018;27:39-69."

Kaynaktaki yazar sayısı 3 veya daha az ise tüm yazarlar belirtilmeli, yazar sayısının daha fazla olduğu durumlarda ilk 3 yazarın sonuna "et al." ibaresi konularak kaynak yazılmalıdır. "Koivuranta M, Läärä E, Snäre L, et al. A survey of postoperative nausea and vomiting. Anaesthesia. 1997;52:443-9."

Kaynak bir dergi ise;

Yazar Soyadı büyük harfle tam olarak yazılmalı, adı ise sadece ilk harf ve büyük olacak şekilde yazılmalı. Makalenin başlığı. Derginin Index Medicus'a uygun kısaltılmış. Yıl;Cilt:ilk sayfa numarası-Son sayfa numarası

"İlginel MT, Tunay DL, Güneş Y. Epilepside perioperatif yönetim ve anestezi. Arşiv Kaynak Tarama Dergisi. 2018;27:39-69."

Kaynak bir kitap ise;

Yazar(lar)ın soyadı adının başharf(ler)i. Kitabın adı. Kaçınıcı baskı olduğu. Basım yeri: Basım Yılı. Basımevi.

"Ropper AH, Brown RH. Adams and Victor's Principles of Neurology. 8th ed. New York, McGraw-Hill, 2007.'

Kitaptan bir bölüm kaynak olarak kullanılmış ise;

Bölüm yazar(lar)ının soyadı adının başharf(ler)i. Bölüm başlığı. İnkıtabın adı. Kaçınıcı baskı olduğu. (Ed y ada Eds. Editör(ler)in ad ve soyadlarının başharf(ler)i): Bölümün ilk sayfa numarası-son sayfa numarası. Basım yeri, Yayınevi, Baskı yılı.

"Phillips MK, Gain P. Hypertension and stroke. In Hypertension: Pathophysiology and Management, 2nd ed (EdsJH Laragh, BM Brenner):495-8. London, Ran Press, 1985."

Web sitesi kaynak olarak gösterilmiş ise;

Web sitesinin adı. Available from: Web sitesinin adresi. (accessed date)

"World Health Organisation. (WHO). Obesity and overweight. Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/> Erişim tarihi: 15 Kasım 2017."

Kaynak tez ise;

Yazarın soyadı adının başharfi. Tezin başlığı (tez). Tezin yapıldığı şehir adı, Üniversite adı (üniversite ise), Yılı. "Tunay M. Kilolu ve obez kadınlarda grup görüşmelerinin vücut ağırlığına, iyilik haline ve sağlık denetim odağına etkisi (Uzmanlık tezi). Adana, Çukurova Üniversitesi, 2015."

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EDİTÖRDEN

Dergimiz tekrar yayın, intihal, uydurma veri vb. etik ihlallerde COPE kılavuzunu referans olarak kabul etmekte ve belirtilen algoritmalara uygun olarak inceleme yapmaktadır. Makaleler dergimize yollandıktan sonra en çok kullanılan ve alanında kabul gören intihal tespit programınca (Ithenticate) kontrol edilmektedir. Buna rağmen makaleler bazen yüksek oranda benzerlik taşısa bile intihal tespit programınca fark edilememektedir.

Yazar(lar) sunulan makalenin yazar(lar)ın özgün çalışması olduğunu beyan ederken, telif hakkı ihlali nedeniyle üçüncü şahıslarca istenecek hak talebi veya açılacak davalarda "Çukurova Anestezi ve Cerrahi Bilimler Dergisi ve Dergi Editörlerinin" hiçbir sorumluluğunun olmadığını, tüm sorumluluğun yazar(lar)a ait olduğunu, ayrıca makalede hiçbir suç unsuru veya kanuna aykırı ifade bulunmadığını, araştırma yapılırken kanuna aykırı herhangi bir malzeme ve yöntem kullanılmadığını ve etik kurallara uygun hareket edildiğini taahhüt ettikleri onam formunu da dergimize yollamaktadırlar.

Dergimizin 31 Aralık 2020 tarihinde yayınlanan sayısında, Niğde Ömer Halisdemir Üniversitesi Niğde Zübeyde Hanım Sağlık Yüksekokulundan Kezban Koraş Sözen tarafından gönderilen "Ameliyat sonrası derlenme ünitesinde görülen erken dönem komplikasyonların değerlendirilmesi" başlıklı makale yayımlanmıştı.

Bahse konu makale, bir doktora tezinden atıfta bulunulmamış alıntılar içerdiğinden yayından çekilmiştir.

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Uzm. Dr. Merthan Tunay

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INVESTIGATION OF THE RELATIONSHIP BETWEEN EPICARDIAL FAT TISSUE THICKNESS AND HEMOGLOBIN A1c LEVELS

EPIKARDİYAL YAĞ DOKUSU KALINLIĞI İLE HEMOGLOBİN A1c DEĞERLERİ ARASINDAKİ İLİŞKİNİN İNCELENMESİ

 Fatih Aydın,  Özge Turgay Yıldırım

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Abstract

Introduction: There is a linear relationship between Epicardial adipose tissue (EAT) thickness and cardiovascular diseases and diabetes mellitus (DM). However, the relationship between HbA1c, which is a direct measure of blood sugar regulation in DM and EAT has not been questioned. In this study, the relationship between EAT and HbA1c was investigated.

Materials and Methods: A total of 90 patients who were admitted to our cardiology clinic were included in the study consecutively. The EATs of the patients were measured by echocardiography and compared with their HbA1c values.

Results: Body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT ($p<0.05$)

Conclusion: In this study, it was shown that there is a direct relationship between HbA1c and EAT, and it was emphasized that EAT can guide the follow-up of preclinical diabetes and glucose control.

Keywords: Epicardial adipose tissue, diabetes mellitus, hemoglobin A1c

Öz

Amaç: Epikardiyal yağ dokusu (EYD) kalınlığı ile kardiyovasküler hastalıklar ve diabetes mellitus (DM) arasında doğrusal bir ilişki vardır. Fakat DM'de kan şekeri regülasyonunun doğrudan bir ölçüsü olan HbA1c ile EYD arasındaki ilişki sorgulanmamıştır. Bu çalışmada EYD ile HbA1c arasındaki ilişki sorgulandı.

Materyal ve Metot: Kardiyoloji kliniğimize başvuran toplam 90 hasta ardışık olarak çalışmaya dâhil edildi. Hastaların EYD'leri ekokardiyografi ile ölçüldü ve onların HbA1c değerleri ile karşılaştırıldı.

Bulgular: Vücut kitle indeksi, açlık kan şekeri, HbA1c, vücut ağırlığı ile EYD arasında doğrusal bir ilişki bulundu ($p<0.05$).

Sonuç: Bu çalışmada, HbA1c ve EYD arasında doğrudan bir ilişki olduğu gösterildi ve EYD'nin prelinik diyabetin takibinde ve glikoz kontrolünde rehberlik edebileceği vurgulandı.

Anahtar kelimeler: Epikardiyal yağ dokusu, diabetes mellitus, hemoglobin A1c

Introduction

The adipose tissue ingrained between the myocardium and visceral pericardium is defined as epicardial adipose tissue (EAT) and it has similar biologically features to visceral adipose tissue^{1,2}. Increased thickness of EAT has associated with the presence of diabetes mellitus (DM), coronary artery disease (CAD) and metabolic syndrome³.

Diabetes mellitus (DM) is a chronic multisystem disease that is common all over the world and its prevalence is increasing markedly⁴. The DM leads to many complications like cardiovascular disease, diabetic neuropathy and retinopathy, chronic kidney disease⁵⁻⁷. In order to control the DM complications and determine its prognosis, there is a need for diagnostic methods that will monitor whether diabetes is under long-term control and determine the treatment protocol accordingly.

Hemoglobin A1c has been relevant as an indicator of mean blood glucose concentrations and has a significant role in evaluating DM control. The close relationship between cardiovascular risk and HbA1c levels has also been broadly presented^{8,9}. The relationship of EAT on DM and cardiovascular diseases has been previously examined in many studies^{10,11}. However, we could not find any study examining the relationship between EAT and HbA1c in our literature research. If a direct relationship can be found between these two parameters, which are indicators of cardiovascular diseases, it will be possible to predict both how well long-term sugar regulation of DM is achieved and a cardiovascular complication that may occur due to DM in the future. In this study, it was aimed to investigate whether there is a relationship between HbA1c and EAT, which are two independent parameters known to be directly related to cardiovascular diseases and DM.

Materials and Methods

This prospective cohort study was conducted at a tertiary hospital in Turkey. A total of 90 (52 diabetics and 38 nondiabetics-the control group) patients who were admitted to our cardiology clinic included between February 2021 and May 2021 were included in the study consecutively. Patients with echogenic anomalies, left ventricular dysfunction, any effusion, abnormal thyroid function were excluded from the study. Participants were divided into two groups; group 1 had 52 patients with DM (the patient group), and group 2 consisted of 38 non-diabetic patients (the control group). All participants were informed and obtained consent before study. This study was approved by the local ethics committee.

Echocardiography examination was performed on all participants. After at least eight hours of fasting, blood samples were taken from the antecubital vein and sent to the laboratory. All participants' blood pressures were measured on the physical examination. Systolic blood pressure ≥ 140 mmHg, diastolic ≥ 90 mmHg, or a need for antihypertensive medication was defined as hypertension. Total cholesterol ≥ 220 mg/dl and/or triglyceride ≥ 150 mg/dl was defined as hyperlipidemia. Diagnosis of DM was based on the criteria of American Diabetes Association¹².

The transthoracic echocardiography was performed using an echocardiographic device (Hitachi Arietta 750) with the patient in the left lateral decubitus position, with a 3.0-MHz transducer. Echocardiographs were performed by two cardiologists. We measured the EFT from the parasternal long-axis view as the echo-free space on the free wall of the right ventricle to the epicardium at end-systole¹³. We chose the thickest area of epicardial fat to measure the EFT. We noted the mean point of the three cardiac cycles.

- *Statistical analysis*

The data is shown as mean \pm standard deviation or median (interquartile range) for continuous variables and as proportions for categorical variables. Homogeneity of group variances are tested by the Levene test and distribution of the data for normality is tested by the Shapiro–Wilk test. Normally distributed continuous variables are tested with t-test and Mann Whitney U test is used for the variables which are not normally distributed. Categorical variables are examined using Chi-square test. Linear regression analysis was used to evaluate the explanatory power of the variables on epicardial adipose tissue thickness. p-values <0.05 were considered statistically significant.

Results

The mean age of the study population was 54.26 ± 14.17 and 52.2% (n=47) was

female. The diabetic patients constituted 57.8% (n=52) of the patients and 42.2% (n=38) of the patients were non-diabetic. The study groups were statistically similar in term of gender, hypertension, cardiovascular diseases, and atrial fibrillation ($p > 0.05$). Dyslipidemia was more common ($p=0.001$), and body mass index were significantly higher in diabetic patients ($p=0.002$). The comparison of the study groups can be found in Table 1.

Epicardial adipose tissue was thicker in diabetic patients compared to normal population (4.7 ± 2.2 mm vs. 2.5 ± 1.8 mm, respectively, $p<0.001$). Body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT ($p<0.05$) (Table 2). Scatter-dot graphs of EAT between HbA1c and BMI can be found in Figure 1 and 2.

Linear regression analysis was performed to detect the explanatory power of age, HbA1c, FBG, creatinine, BMI on epicardial adipose tissue. Regression analysis revealed that age, HbA1c and BMI are independently associated with EAT thickness (Table 3).

Table 1. Baseline characteristics and laboratory results of the study groups.

	Diabetic patients (n=52)	Non-diabetic patients (n=38)	p
Age, mean \pm SD, y	57.0 (52.0-65.0)	48.5 (41.0-62.2)	0.030
Female	31 (59.6%)	16 (42.1%)	0.100
Hypertension	27 (51.9%)	12 (31.6%)	0.054
Cardiovascular diseases	11 (21.1%)	6 (15.8%)	0.521
Dislipidemia	24 (46.1%)	5 (13.1%)	0.001
Atrial fibrillation	5 (9.6%)	2 (5.3%)	0.446
Height, m	1.65 ± 0.01	1.69 ± 0.08	0.030
Weight, kg	79.7 ± 12.8	74.7 ± 14.8	0.094
Body mass index	29.5 ± 5.03	26.0 ± 4.9	0.002
Glucose, mg/dL	114.0 (97.0-133.5)	92.5 (88.0-97.2)	<0.001
Hemoglobin A1c	6.6 (6.0-7.97)	5.0 (4.8-5.1)	<0.001
Creatinine, mg/dL	0.88 (0.77-1.02)	0.78 (0.70-0.88)	0.004
Epicardial adipose tissue	4.7 ± 2.2	2.5 ± 1.8	<0.001

Table 2. Pearson correlation analysis of epicardial adipose tissue and other variables

	p	r
Body mass index (kg/m ²)	0.001	0.345
Fasting blood glucose	0.004	0.298
HbA1c	<0.001	0.470
Creatinine	0.166	0.147
Height	0.816	0.025
Weight	<0.001	0.398

Table 3. Linear regression analysis of the variables associated with epicardial adipose tissue.

Variable	Odds Ratio	95% Confidence Interval	p-value
Age	0.215	0.002 – 0.068	0.037
HbA1c	0.330	0.152 – 0.786	0.004
Fasting blood glucose	0.021	-0.010 – 0.012	0.844
Creatinine	0.009	-1.908 – 2.101	0.924
Body mass index	0.094	0.009 – 0.178	0.031
Constant		-6.824 – -1.003	0.009

Discussion

The present study finds that body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT.

Many studies have shown the relationship of EAT with glucose intolerance, metabolic syndrome, high blood pressure, and atherosclerosis^{10,14-16}. Epicardial fat is also associated with diabetes mellitus¹¹. Similar to previous studies, we found thicker EAT in patients with DM and those with high BMI. In this study, we found a positive correlation between fasting blood glucose and HbA1c. To our knowledge, this has not been questioned in previous studies.

Before discussing the possible mechanisms on the pathophysiology of this relationship, we would like to say that this relationship may provide a practical benefit to clinicians. Because examining EAT is both a simple and practical method. And even if

the fasting blood glucose is normal and diabetes is not diagnosed in individuals with high EAT thickness, it should be kept in mind that HbA1c may be high, and the patients can be diagnosed and treated in the prediabetes period.

HbA1c is described as the stable bring closer of glucose to the N-terminal valine of the β -chain of hemoglobin. The process of HbA1c formation consists of an irreversible structural rearrangement step and a reversible hemoglobin glycation step and happens continuously in vivo along the entire lifetime of erythrocytes (120 days), depending on plasma glucose levels¹⁷.

There are studies showing that HbA1c is associated with the development of cardiovascular disease even in people who do not have DM or cardiac disease yet¹⁸. Both EAT and HbA1c are associated with cardiovascular disease independent of diabetes. Also, EAT is increased in individuals with T2 DM independently of total body fat or BMI¹⁹. Similarly, another

study found that type 1 DM was associated with an increase in EAT independent of BMI and hyperlipidemia²⁰. Both EAT and HbA1c are associated with cardiovascular disease independent of diabetes. Therefore, it was not surprising that the two were positively correlated with each other.

There are many reasons for the linear relationship between HbA1c and epicardial adipose tissue. We think that the first of these is an indirect mechanism due to the increased cardiovascular risk factors like obesity, HT. However, in a study it was shown that EAT was correlated with insulin resistance and impaired glucose tolerance²¹. Adipose tissue secrete pro-inflammatory substances like TNF- α and PAI-1. Systemic micro-inflammation increases insulin resistance and causes the onset and exacerbation of atherosclerosis²². As this inflammation leads to atherosclerosis, thick EAT may have a direct effect on HbA1c by increasing the level of glycated hemoglobin independent of obesity and DM.

EAT's free fatty acids uptake and release capacity is bigger than the other visceral adipose tissue and it has a higher rate of insulin-induced lipogenesis than the other visceral adipose depots^{23,24}.

This study has some limitations. First of all, it was done with a small group. Since other factors such as BMI, hyperlipidemia, and CAD that may affect EAT have not been ruled out, it have not been determined how much the relationship between EAT and HbA1 is affected by other factors.

In conclusion, this study is the first to show a direct relationship between HbA1c and EAT. It has been shown that EAT can guide the follow-up of preclinical diabetes and glucose control. In addition, EAT was thicker in the DM group compared to the Control group.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical approval

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THE RELATIONSHIP BETWEEN PERSISTENT PAIN AND TACTILE SENSORY AND PAIN PRESSURE THRESHOLDS IN POSTMASTECTOMY BREAST CANCER PATIENTS: A PRELIMINARY REPORT

POSTMASTEKTOMİ MEME KANSERLİ HASTALARDA PERSİSTAN AĞRI İLE TAKTİL DUYUSAL VE AĞRI BASINCI EŞİKLERİ ARASINDAKİ İLİŞKİ: BİR ÖN RAPOR

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Abstract

Introduction: Persistent postmastectomy pain is common among breast cancer patients. The relationship of persistent postmastectomy pain (PPP) with sensory loss and increased pain sensitization remains unclear. In this study, we investigated the relationship between PPP and tactile sensory thresholds and pain pressure thresholds in postmastectomy breast cancer patients.

Materials and Methods: Patients were divided into two groups according to the presence and absence of PPP. On both the operated and non-operated sides, pain pressure thresholds (breast, arm, and forearm) were assessed using an algometer, and tactile sensory thresholds (scar region, breast upper outer quadrant, axillary region, median cutaneous nerve and intercostobrachial nerve regions, forearm, and hand) were measured using the Semmes–Weinstein monofilament test. The differences between the operated and nonoperated sides were calculated to investigate whether there was a relation between pain sensitivity and sensory loss and PPP.

Results: PPP was detected in 31 (64.6%) of 48 patients. There was a statistically significant difference in the tactile sensory thresholds and pain pressure thresholds of the operated and non-operated sides ($P < 0.001$). There was no statistically significant difference between the pain pressure thresholds and tactile sensory thresholds of the groups with and without PPP. There was a weak positive correlation between the mean pain intensity and side to side difference in tactile sensory thresholds measured from the axillary region ($P = 0.046$, $r = 0.289$).

Conclusion: Axillary region sensorial loss and PPP may be linked in postmastectomy cancer patients. Pain sensitization and loss of sensation do not seem to be associated with PPP.

Keywords: Persistent postmastectomy pain syndrome, tactile sensory threshold, pain pressure threshold, pain sensitization, sensorial deficit

Öz

Giriş: Persistan postmastektomi ağrısı meme kanseri hastaları arasında yaygındır. Persistan postmastektomi ağrısının duyu kayıp ve artan ağrı duyarlılığı ile ilişkisi belirsizliğini korumaktadır. Bu çalışmada postmastektomi meme kanseri hastalarında persistan postmastektomi ağrısı ile taktil duyu eşikleri ve ağrı basıncı eşikleri arasındaki ilişkiyi araştırdık.

Gereç ve Yöntemler: Hastalar persistan postmastektomi ağrısı varlığına ve yokluğuna göre iki gruba ayrıldı. Hem opere ve nonopere taraflardaki ağrı basıncı eşikleri (meme, kol ve önkol) bir algometre cihazıyla, taktil duyu eşikleri ise (skar bölgesi, meme üst dış kadran, aksiller bölge, median kutanöz sinir ve interkostobrakiyal sinir bölgeleri, önkol ve el) Semmes – Weinstein monofilaman testiyle ölçüldü. Opere ve nonopere taraflar arasındaki farklar hesaplanarak, ağrı duyarlılığı ve duyu kayıp ile PPP arasında ilişki olup olmadığı araştırıldı.

Bulgular: Çalışmaya 48 hasta dahil edildi, hastaların 31'inde (%64,6) persistan postmastektomi ağrısı saptandı. Opere ve nonopere tarafların dokusal duyu eşikleri ve ağrı basıncı eşikleri arasında istatistiksel olarak anlamlı bir fark vardı ($P < 0.001$). Grupların ağrı basıncı eşikleri ile dokusal duyu eşikleri arasında istatistiksel olarak anlamlı bir fark yoktu. Ortalama ağrı şiddeti ile aksiller bölgeden ölçülen opere ve nonopere tarafların taktil duyu eşik farkları arasında zayıf düzeyde pozitif korelasyon saptandı ($P = 0.046$, $r = 0.289$).

Sonuç: Aksiller bölgedeki duyu kayıp ve persistan postmastektomi ağrısı, postmastektomi kanser hastalarında ilişkili olabilir. Ağrı duyarlılığı ve duyu kaybı ise persistan postmastektomi ağrısı ile ilişkili görünmemektedir.

Anahtar Kelimeler: Persistan postmastektomi ağrı sendromu, taktil duyu eşik, ağrı basınç eşiği, ağrı duyarlılığı, duyu kayıp

Introduction

Breast cancer is the most common type of cancer in women. Worldwide, the incidence of breast cancer is 27-94 per 100,000¹. PPP defined by the International Association for the Study of Pain as chronic pain in the anterior aspect of the thorax, axilla, and/or upper half of the arm beginning after a mastectomy and persisting for more than 3 months after the surgery². According to the International Association for Study of Pain, the prevalence of persistent postmastectomy pain (PPP) in breast cancer patients is 40–89%³. PPP in breast cancer can be moderate-to-severe and have a negative impact on quality of life (QoL)⁴. Gottrup et al. investigated the potential association of PPP with sensory changes and pain sensitization in 15 breast cancer patients with pain and 11 breast cancer patients without pain⁵. They found that thermal sensory thresholds were higher on the operated side in both groups and that pain sensitization was higher in the group with pain. Andersen et al. assessed the relationship between sensory function and PPP, following patients from the

preoperative period to postoperative 1 year⁶. They showed that areas of increased hypoesthesia were related to pain at rest and that pain developed with movement. In the same study, movement-related pain on the operated and nonoperated sides differed due to a difference in pain pressure thresholds (PPTs). In addition, they revealed that sensorial thresholds and PPTs are related with sensory impairment.

In the literature, the findings of studies on the relationship between nerve damage and PPP are contradictory⁵⁻⁷. In our study, we aimed to evaluate the relationship between the presence, intensity, and impact of PPP and PPTs and tactile sensory thresholds (TSTs).

Materials and Methods

This cross-sectional prospective study was conducted in accordance with the Declaration of Helsinki. This study was carried out in the University of Health sciences, Konya Training and Research Hospital between August 2019 and October 2020. Ethical approval was received from the ethics committee of the medical faculty

of Necmettin Erbakan University (IRB approval number: 2019/1995; date: 7 July 2019). The written informed consent obtained from all the participants.

Volunteer patients aged 18–80 years who had been diagnosed with breast cancer and presented for a routine follow-up 3–60 months postsurgery in the general surgery breast unit were included in the study. Patients with a history of bilateral breast cancer, cancer recurrence, reconstructive breast surgery, cognitive impairment, thoracic and/or lower cervical radiculopathy, metastasis, and breast reconstructive surgery were excluded. In addition, those with severe psychiatric diseases, central nervous system diseases, progressive neurological diseases, upper extremity lymphedema, frozen shoulder, noncancerous chronic pain syndrome were excluded. Finally, patients who were pregnant and patients who had used gabapentinoids, antidepressant drugs, or painkillers within the last 24 h were excluded from the study.

Data were obtained on patient age, cancer side and stage, surgery time, history of chemotherapy and radiotherapy, pain area (breast, axillary region, and arm), and pain treatment history. The Brief Pain Inventory Short Form (BPI SF) was used to assess PPP severity and PPP-related effects. Also, patients completed the European Organization for Research and Treatment of Cancer and Quality of Life Group BR-23 (EORT QLQ BR-23) questionnaire.

The BPI SF is an easy-to-understand pain assessment questionnaire that the participant can complete unaided. The BPI SF consists of two subsections, one which evaluates pain intensity and the other which assesses pain-related effects. Using the BPI SF, the patients provided information about their pain levels in the previous 24-h period, average pain levels during this 24-h period, and current pain levels. A 0–10 numerical rating scale was used to rate pain severity, where 0 denoted “no pain” and “10” denoted “the most severe pain you have experienced.” To assess the impact of pain

on functional skills, using a 0–10 numerical scale, the patients were asked to rate the effect of pain on the following factors: working life, daily living activities, emotional state, mood, sleeping, walking capacity, and social relationships⁸. We used the threshold values of pain severity determined by Serlin et al.⁹.

In our study group, we examined TSTs and PPTs of both the operated and non-operated sides. To assess PPTs, using an algometer, a simple, routine pain threshold measuring instrument, PPTs in the following areas were assessed: scar, arm (deltoid midpoint), and forearm (lateral epicondyle 2 cm distally). The investigator placed the algometer on the site to be examined and pressed against the site in a vertical direction while increasing the force at a constant rate of 1 kg/cm². The participants were instructed to express pain either by saying stop or by raising their hands when they felt slight discomfort. The algologist gradually increased the pressure by 1 kg/cm²/s until the participants felt the first sensation of pain (PPT). A maximum pressure of 22 kg/cm² was applied for all the participants.

The EORT QLQ BR-23 questionnaire has 23 items, which include functional scales (body image, sexual functioning, sexual enjoyment, and hopes) and symptom scales (systemic therapy side effects, breast-related pain/skin problems-/disorders, arm-related pain/problems-/dysfunction symptoms, and hair loss). The breast symptom and arm symptom subscale scores are calculated. Higher scores on the functional scales indicate better overall QoL, whereas higher scores on the symptom's scales indicate poorer QoL¹⁰.

To evaluate TSTs, the Semmel–Weinstein test was used. The researcher started with the smallest monofilament and applied it to the largest filament in the correct order, but the researcher stopped the test when the smallest monofilament tested was detected by the patient and recorded the value. Using this screening tool, TSTs of the scar region, upper outer quadrant of the breast, axillary

region, intercostobrachial nerve region, medial cutaneous nerve region, and forearm and hand on both the operated and nonoperated sides were assessed. In addition, side to side differences in PPTs were calculated by extracting the operated side PPTs from the non-operated side PPTs to reveal whether pain sensitivity may be related to PPP. Side to side differences in TSTs were calculated by extracting nonoperated side TSTs from operated-side TSTs to reveal whether sensory loss may be related to PPP.

Patients were divided into two groups according to the presence and absence of

PPP to investigate whether there is a relationship presence of pain with side to side differences of the PPTs and TSTs.

A post hoc sample size analysis was performed after the finalization of the study. A power analysis was conducted using the G-power software package, Version 3.1.6 (Franz Faul, Kiel University, Kiel, Germany) power analysis was used. Forty-eight patients were included in the final analysis. The power of the study was 0.99, with an effect size of 0.71 and level of 0.05. The statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY).

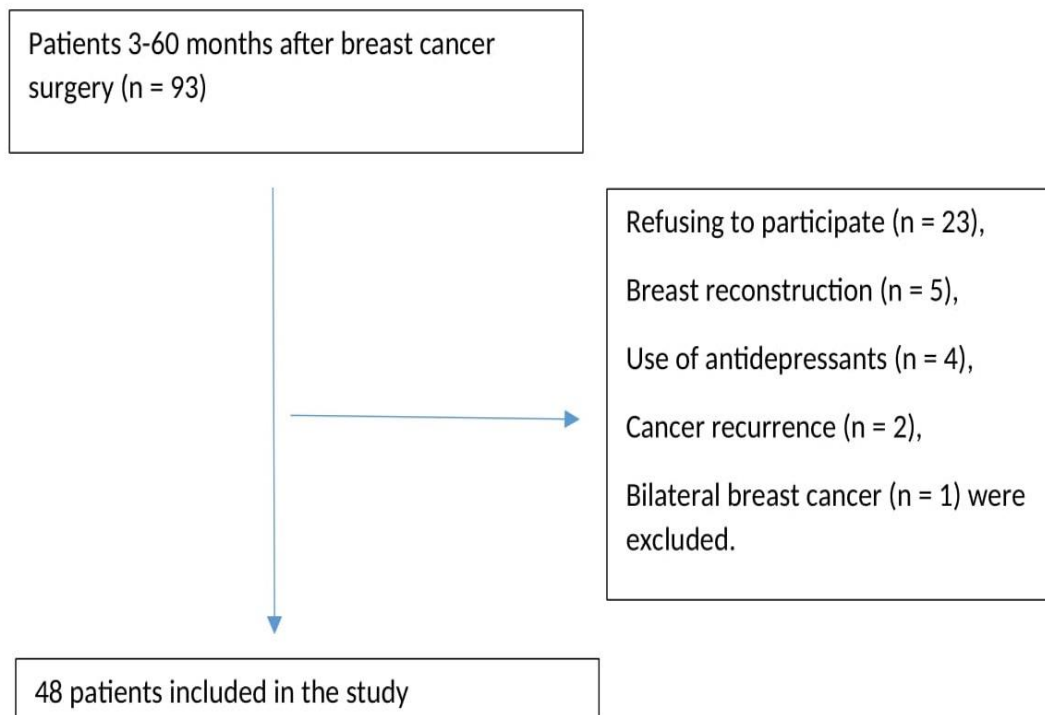


Figure 1: Flowchart

There were no missing data. The Shapiro–Wilk test was used to evaluate the distribution of the data. Descriptive data, with frequencies (*n*) and percentages (%) are presented for categorical variables. For normally distributed numerical data, mean (standard deviation) is presented, together with their 95% confidence intervals (CIs). For non-normally distributed numeric data, minimum-maximum values, together with their 95% CIs, are presented. A chi-square test was used to compare categorical variables between independent groups. A *T*-test or Mann–Whitney *U* test was used to compare numerical data between independent groups, depending on whether the data were normally distributed or not. The relationship between the numerical data was evaluated using Spearman’s correlation analysis. A *P* value of < 0.05 was considered statistically significant.

Results

Forty-eight breast cancer patients with a mean age of 51.53 (\pm 8.08) years in a postoperative period of 11.0 (3.0–38.0) months were included in the study (Fig. 1). Cancer staging in the preoperative period was stage 1 in 20 (41.7%) patients, stage 2 in 17 (35.4%) patients, and stage 3 in 11 (22.3%) patients. In total, 44 (91.7%) patients had received chemotherapy, and 40 (83.3%) patients had received radiotherapy. Thirty-one (64.6%) patients had PPP, the painful area was in the breast in 9 (29.03%) patients; axillary region in 8 (25.1%) patients; arm in 6 (19.35%) patients; and breast together with axillary region and arm areas in 8 (25.1%) patients. Based on the cut-off values determined by Serlin for pain severity, 21 (43.8%) patients had moderate-to-severe pain. The mean pain intensity was 3.75 ± 2.98 [2.67–4.82]. The BPI SF pain interference score was 1.28 (0.0–7.45) [1.26–3.02].

The patients were divided into two groups that with PPP (*n* = 31) and without PPP (*n* = 17). There was no difference in age

between the groups ($z = 0.313$, $P = 0.754$). There was no difference in a history of chemotherapy, radiotherapy, lymph node dissection type, or surgery type between groups ($\chi^2 = 0.406$, $P = 0.607$; $\chi^2 = 0.180$, $P = 0.595$; $\chi^2 = 0.603$, $P = 0.436$; and $\chi^2 = 0.091$, $P = 0.763$, respectively).

There was a statistically significant difference in the TSTs (Table 1) and PPTs (Table 2) of the operated and nonoperated sides. There was no statistically significant difference in the TSTs and PPTs of the operated and nonoperated sides between groups (Table 3).

There was a weak positive correlation between the mean PPP intensity and side to side differences in the TSTs of the axilla ($P = 0.046$, $r = 0.289$). There was no statistically significant correlation between the mean PPP intensity and side to side differences in the TSTs of the hand, forearm, median cutaneous nerve region, intercostobrachial nerve region, breast upper outer quadrant, and scar regions or the PPTs of the scar region, arm, and forearm areas ($P = 0.837$, $r = -0.030$; $P = 0.672$, $r = 0.063$; $P = 0.705$, $r = 0.056$; $P = 0.059$, $r = 0.691$; $P = 0.586$, $r = 0.081$; $P = 0.439$, $r = -0.114$; $P = 0.949$, $r = 0.010$; $P = 0.870$, $r = 0.024$; and $P = 0.535$, $r = 0.092$, respectively).

There was no statistically significant correlation between the pain interference score and side to side differences in the TSTs of the hand, forearm, median cutaneous nerve region, intercostobrachial nerve region, axilla, upper outer quadrant of the breast, and scar region, as well as side to side differences in the PPTs of the scar region, arm, and forearm ($P = 0.990$, $r = -0.002$; $P = 0.569$, $r = 0.084$; $P = 0.775$, $r = 0.042$; $P = 0.901$, $r = 0.018$; $P = 0.115$, $r = 0.230$; $P = 0.519$, $r = 0.095$; $P = 0.767$, $r = -0.004$; $P = 0.448$, $r = 0.103$; $P = 0.462$, $r = 0.109$; and $P = 0.141$, $r = 0.216$, respectively).

Table 1. Tactile sensory thresholds of different regions of the operated and nonoperated sides

Area		Tactile sensory thresholds			
		Median	Min-Max	95% C.I.	P
Hand	Operated	2.69	2.56-4.31	2.76-3.17	0.005
	Healthy	2.56	2.56-4.31	2.67-3.03	
Arm	Operated	2.83	2.56-4.31	2.96-3.33	0.007
	Healthy	2.83	2.56-4.31	2.89-3.24	
Medial cutaneous	Operated	3.61	2.82-4.56	3.35-3.71	0.001
	Healthy	3.22	2.83-4.31	3.19-4.49	
Intercostobrachialis	Operated	3.72	2.83-4.56	3.47-3.83	<0.001
	Healthy	3.22	2.83-4.31	3.22-3.52	
Axilla	Operated	4.08	2.56-5.46	3.77-4.19	<0.001
	Healthy	3.61	2.83-4.31	3.37-3.66	
Breast upper outer quadrant	Operated	3.84	2.83-4.56	3.60-3.92	<0.001
	Healthy	3.61	2.83-4.31	3.34-3.60	
Scar	Operated	4.17	2.83-5.46	4.07-4.48	<0.001
	Healthy	3.41	2.83-4.31	3.34-3.62	

Table 2. Pain pressure thresholds of different regions of the operated and nonoperated sides

Area		Pain Pressure Thresholds			
		Median	Min-Max	95% C.I.	P
Scar	Operated	4.50	2.00-20.00	4.50-7.44	<0.001
	Healthy	10.00	4.00-20.00	4.49-11.88	
Arm	Operated	8.50	4.00-20.00	8.51-12.30	<0.001
	Healthy	12.00	6.00-20.00	11.36-14.89	
Forearm	Operated	9.50	4.00-20.00	9.52-13.23	<0.001
	Healthy	12.50	6.00-20.00	12.04-15.50	

Table 3. Side differences in pain pressure thresholds and tactile sensory thresholds in the patients with and without persistent postmastectomy pain

	Area	PPP	Side to side difference			
			Median	Min-Max	95% C.I.	P
Tactile sensory thresholds	Arm	without	0.00	0.00-2.24	-0.50-0.56	0.660
		with	0.00	0.00-1.28	0.01-0.25	
	Forearm	without	0.00	0.00-0.78	-0.02-0.25	0.975
		with	0.00	0.00-0.78	0.01-0.17	
	Medial cutaneous	without	0.00	0.00-0.78	0.01-0.34	0.641
		with	0.00	-0.39-1.25	0.07-0.31	
	Intercostobrachial	without	0.00	0.00-1.34	0.11-0.58	0.702
		with	0.24	0.00-1.25	0.21-0.49	
	Axilla	without	0.23	0.00-2.00	0.15-0.81	0.178
		with	0.47	-1.25-1.25	0.31-0.65	
	Breast upper outer quadrant	without	0.23	-0.23-1.29	0.11-0.52	0.360
		with	0.39	0.00-2.26	0.24-0.58	
	Scar	without	0.86	0.00-1.96	0.54-1.21	0.364
		with	0.72	0.00-1.52	0.51-0.86	
Pain Pressure Thresholds	Scar	without	3.00	0.00-15.00	1.98-6.13	0.820
		with	3.00	0.00-16.00	2.79-5.79	
	Arm	without	1.00	0.00-11.00	0.63-3.96	0.891
		with	1.00	0.00-12.00	1.19-3.52	
	Forearm	without	0.00	-1.00-10.00	0.20-3.68	0,416
		with	1.00	0.00-11.00	1.08-3,05	

Discussion

In line with the literature^{3,4}, we found that 64.6% of the patients had PPP, and 43.8% had moderate-to-severe pain. In this study, the PPTs on the operated side were lower than those on the non-operated side, and there was no correlation between side to side differences in PPTs and PPP intensity. In addition, there was no statistically significant difference in PPTs between the patients with and without PPP. Mustonen et

al. showed that postmastectomy patients with neuropathic pain had lower PPTs on the affected side than the non-operated side¹¹. In a previous research, lower PPTs on the affected side were associated with peripheral sensitization and defined as secondary hyperalgesia¹². Similar to the findings of our study, Andersen et al.⁶ reported no difference in PPTs of postmastectomy patients with and without pain. Fernandez-Lao et al.¹³ detected no difference between operated and non-operated sides in PPTs of the

zygapophyseal joint (C5-C6), deltoid, second metacarpal joint, and tibialis anterior in postmastectomy cancer patients. They found a moderate negative correlation between low deltoid PPTs and axillary/shoulder pain intensity. Considering the findings of our study and those in the literature, peripheral sensitization may not be related to PPP severity.

In this study, in line with the literature¹³, TSTs on the operated side were higher than on the non-operated side. We found no statistically significant difference in the TSTs of those with and without PPP. In terms of side to side differences, TSTs were higher in the axillary region in the patients with PPP. There was a positive correlation between the difference in sensory thresholds between the operated and non-operated sides in the axillary region and increased pain intensity and a negative correlation with arm symptom on QoL. Similar to the findings of our study, Vilholm et al.¹⁴ found that thermal sensory thresholds in breast cancer patients were higher on the operated than nonoperated side after a mastectomy. In the same study, they reported that thermal sensory loss in a PPP group was higher than in a non-PPP group. In line with the literature⁶, in our study, hypoesthesia was common among all patients, irrespective of the presence or absence of pain. The “intact nociceptor hypothesis” has been put forward to explain hypoesthesia in postmastectomy patients^{15, 16}. Our findings suggested that tactile loss of sensation in the axillary region had a negative effect on QoL. Previous research showed that sensory re-education treatment could lead to functional gains in patients with upper extremity peripheral nerve injury and pain accompanied by upper extremity neuropathic pain^{17, 18}. Future studies could focus on improving functionality and relieving pain severity in patients postmastectomy via sensory re-education treatment.

Our study has some limitations. The cross-sectional design of the study was a

limitation. Both the presence and severity of PPP change over time. A better understanding of the relationship between sensory impairment and postmastectomy pain syndrome can be obtained by repeated measurements of pain and sensation during both the presurgery and postsurgery periods, with a long-term follow-up required. Another limitation was that the sensorial deficit was examined only via TSTs. Assessment of dynamic mechanical allodynia, hot-cold sensory thresholds, vibration thresholds could shed additional light on hyperesthesia in postmastectomy patients. Finally, there may be participant bias related to patients’ willingness to participate in the study. Those with sensory problems and/or pain would have been more likely to agree to volunteer, which may have affected the study results.

There was no relationship between the presence and severity of PPP, sensory loss, and pain sensitization operated in breast cancer patients. We conclude that in patients with increased loss of sensation in the axillary region, PPP may be more severe, with negative impacts on QoL. Given the reported value of sensory re-education programs in enhancing functionality^{17, 18}, studies are needed to assess the potential of such programs in improving functionality and reducing pain severity in breast cancer patients with PPP.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical approval

The ethics committee of the medical faculty of Necmettin Erbakan University (IRB

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A CONSIDERATION OF THE MYTH OF THE LUNAR EFFECT ON THE MYOCARDIAL INFARCTION: A RETROSPECTIVE COHORT STUDY

MİYOKARD ENFARKTÜSÜ ÜZERİNDEKİ AY ETKİSİ EFSANESİNİN DEĞERLENDİRİLMESİ: RETROSPEKTİF KOHORT ÇALIŞMASI

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Abstract

Introduction: In our medical center, we observed that myocardial infarction of proximal lesions occurs more frequently on some days and distal lesions occur more frequently on others. Along with this curiosity, our aim was to study whether the lunar cycle, location and distance from the Earth are related with the location of coronary occlusion, myocardial infarction type, and the shear force.

Materials and Methods: The movements of the lunar cycle day by day, hour by hour, and the Moon's distance from the Earth, were calculated. These parameters were then compared with myocardial infarction subtypes and culprit lesion location.

Results: Culprit lesion location (the distance from the coronary artery ostium and the vertical/horizontal direction according to Earth's gravity line) was not statistically significantly different according to the position of the Moon ($p=0.32$ and $p=0.49$). In the subgroup analysis, there was a statistically significant difference between the left anterior descending artery and the right coronary artery according to the Moon's hourly movement ($p=0.02$).

Conclusion: In conclusion, our analysis found that there is no association between culprit lesion location and the mechanical effects of the lunar cycle.

Keywords: Coronary occlusion, myocardial infarction, moon

Öz

Giriş: Merkezimizde, bazı günlerde proksimal lezyonlara bağlı bazı günlerde de distal lezyonlara bağlı miyokard enfarktüsünün daha sık meydana geldiğini gözlemledik. Bu merakla birlikte, bu çalışmada ay döngüsünün, yerin ve Dünya'dan uzaklığın koroner oklüzyonun yeri, miyokard enfarktüsü tipi ve sürtünme kuvveti ile ilişkili olup olmadığının incelenmesi amaçlanmıştır.

Gereç ve Yöntemler: Ay döngüsünün hareketleri günden güne, saatten saate ve Ayın Dünya'dan uzaklığına göre hesaplandı. Bu parametreler daha sonra miyokard enfarktüsü alt tipleri ve sorumlu lezyon lokalizasyonu ile karşılaştırıldı.

Bulgular: Sorumlu lezyon yeri (koroner arter ostiumundan uzaklık ve Dünya'nın yerçekimi çizgisine göre dikey / yatay yön) Ayın konumuna göre istatistiksel olarak anlamlı derecede farklı değildi ($p=0,32$ ve $p=0,49$). Alt grup analizinde, Ayın saatlik hareketine göre sol anterior inen arter ile sağ koroner arter arasında istatistiksel olarak anlamlı bir fark vardı ($p=0,02$).

Sonuç: Sonuç olarak, analizimiz sorumlu lezyonun lokalizasyonu ile ay döngüsünün mekanik etkileri arasında bir ilişki olmadığını göstermiştir.

Anahtar Kelimeler: Ay, koroner oklüzyon, miyokard enfarktüsü

Introduction

Acute myocardial infarction (AMI) is one of the most common mortal disease¹. The total occlusion of coronary arteries causes ST elevation myocardial infarction (STEMI). Factors that cause the total occlusion of a coronary artery have always been a matter of curiosity for physicians. Therefore, many studies have been conducted on this area^{2,3}.

The lunar cycle has many effects on animal and human physiology⁴. Mostly, these have been attributed to hormonal changes and circadian rhythm⁵. Only a few studies have been conducted to show its mechanical effects⁶. Myocardial infarction (MI) and lunar cycle (LC) relevance has been observed in a some studies⁷. These studies were designed to discover whether the LC was associated with MI frequency. However, the association between myocardial infarction subtypes, coronary artery occlusion sites, and the LC have not been studied before.

In our medical center, we observed that on some days MI of proximal lesions occur more frequently and distal lesions occur more frequently on others. Along with this curiosity, our aim was to study whether the lunar cycle, location, and distance from the Earth are related with the coronary occlusion site, myocardial infarction type, and shear force.

Materials and Methods

- *Study Design and Patient Population*

This was a retrospective cohort single center study which used our center database. 554 STEMI or Non-STEMI patients with a least one totally occluded coronary artery were included in the study. The date and exact hour of the onset of ischemia related symptoms were obtained from hospital records. Patients'

demographic information, chronic diseases, and drugs were recorded. Patients with missing information were excluded from the study. This retrospective study is in accordance with the June 1964 Declaration of Helsinki. The conduct of this study was approved by the Institutional Review Board at regional university (E-25403353-050.99-134591).

- *Coronary Angiography*

Coronary angiography (CAG) images were analyzed by two cardiology specialists. All patients were diagnosed with STEMI or at least one total coronary artery occlusion. For other coronary arteries, 70%, stenosis, or greater, denotes that the vessel is diseased. The number of stents and balloons applied to the culprit artery was also recorded. All culprit lesions were classified according to the BARI classification⁸.

The coronary arteries were classified as proximal, mid, and distal for the calculation of the mechanical impact. In addition, the arteries were classified as horizontal or vertical according to the direction of the Earth's gravity (Table 1).

- *Lunar Cycle*

Lunar cycle was calculated according to 3 parameters. For all these parameters, our city was selected as the center of all events and the absolute time for the Moon's location was calculated according to the onset of ischemic symptoms. A popular internet site (www.mooncalc.org) was used to find the Moon's exact location at the event time. The first parameter is concerned with the movement of the Moon on its orbit. In this parameter, the effects of Moon's gravity on patients were compared with that of the Sun's. The Moon's movement on its orbit is completed in 28 days.

Table 1. Culprit lesion classification according to the distance to the coronary ostium and the Earth's gravity

Classification	According to the distance to the coronary ostium			According to the Earth's gravity	
	Proximal	Mid	Distal	Horizontal	Vertical
BARI Classification	1,12,18,28	2,13,15,16,19,20	3,4,5,9,14,19a,21,23	1,3,4,5,9,11,12,15,18,23,28	2,13,14,16,19,20,21

The position closest to the sun was tagged as day 14 and the farthest was as 0. Day by day, this movement has a value between 0 and 14 (Figure 1). The second parameter was the gravitational force of the moon on the patient according to distance between the Moon and our center. Normally, gravitational force is calculated with the formula $F = G \times M1 \times M2 / R^2$ (G: universal gravitation constant, M1: the Moon's mass, M2: the Earth's mass, and R: distance)⁹. In this formula, as only the distance is variable, we compared only the distance between the Moon and the Earth (Figure 2). The third parameter was the Moon's net gravitational force on patients accompanying with the Earth's. The Earth

has a fixed gravitational force on our city, so, we decided to compare the Moon's gravity force hour by hour. The gravitational force of the Moon parallel to the direction of the Earth's gravity according to surface was calculated. If the Moon had risen, from the perspective of our center, its gravity was assumed as positive, and when the Moon had set and was behind the Earth, its gravity was assumed as negative. We assumed the Moon's gravitational force as 20000 units and we multiplied this force with the sinus of the angle between the Moon and the Earth. As a result, we found values between -19549 and 19390 (Figure 3).

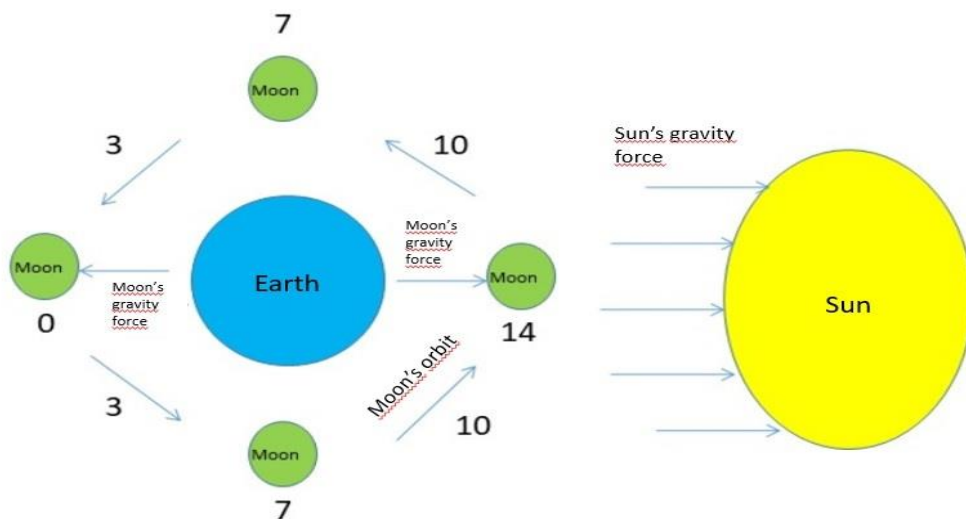


Figure 1. Figure 1 shows the Moon's movement on its orbit day by day and the Moon's net gravitational force on the Earth according to the Sun's gravity.

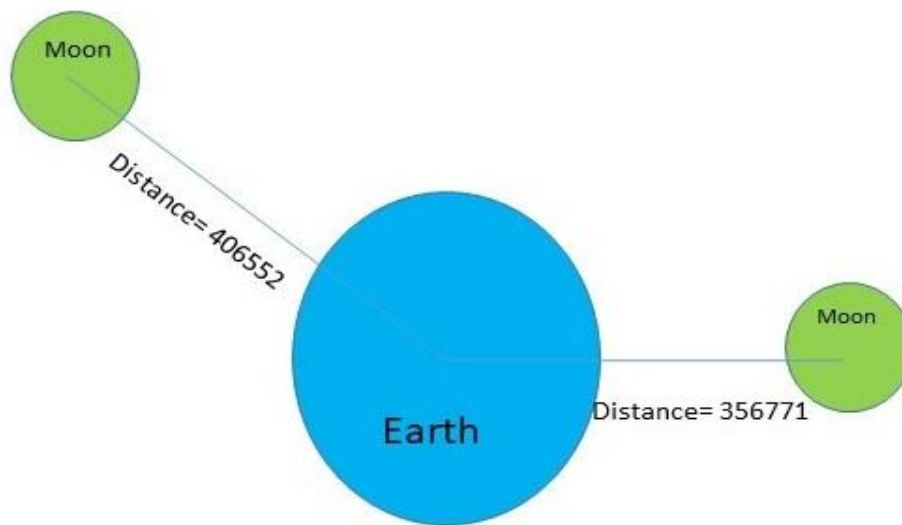


Figure 2. Figure 2 shows the Moon's distance from the center of the Earth.

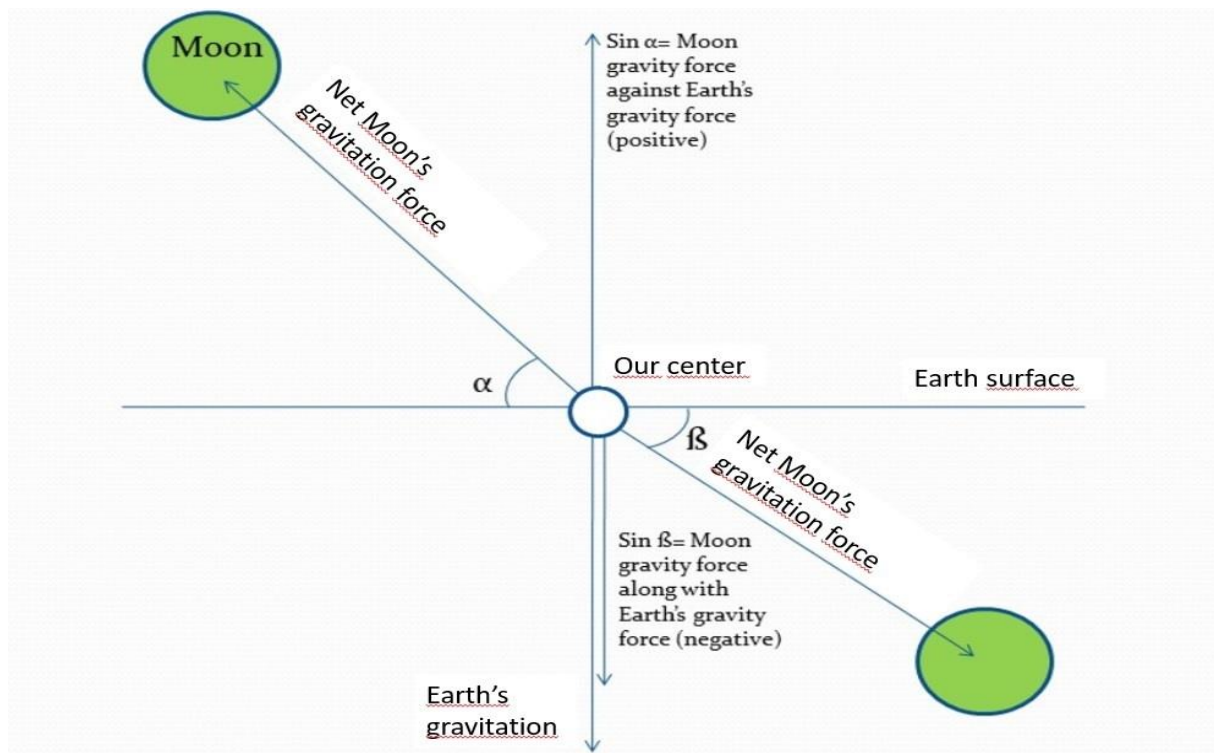


Figure 3. Figure 3 shows the Moon's net gravitational force on our city according to the Earth's gravity.

- *Statistical Analyses*

Categorical and continuous data were expressed as ratio (%) and median (range). Homogeneity of the groups were compared with Kolmogorov-Smirnov and Levene's test. These were compared by the chi-square, T-test, and One-way ANOVA tests, respectively. After finding a statistically significant difference according to One-way ANOVA, subgroup analyses were performed with the Tukey test to compare the subgroups. In addition, bivariate correlation analyses were performed to compare the Moon's movements and coronary lesion's locations. IBM SPSS Statistics for Windows v23 was used for statistical analyses. P values <0.05 were considered statistically significant.

Results

The baseline characteristics of all patients are shown in Table 2. The median age was 60 (29-62) years and male patients were more dominant (76.9%). Most of the patients came to our clinic with anterior and inferior MI. Furthermore, half of patients had only one diseased coronary artery that was the culprit vessel. (53.2%) (Table 2). Culprit lesions were grouped as vertical or horizontal according to the direction of the Earth's gravity. These groups were compared with the Moon's orbital movement, daily movement, and distance from the Earth. All groups were homogeneous (Levene's test), and there were no statistically significant differences between groups (Table 3). For another perspective, the culprit lesions were grouped as proximal, mid, and distal according to the distance from the ostium of the artery. Again, these groups were compared with the Moon's orbital movement, daily movement, and distance from the Earth. All groups were

homogeneous and, again, there were no statistically significant differences between them (Table 4).

Finally, we compared the culprit vessel with Moon's orbital movement, daily movement, and distance from the Earth. All groups were homogeneous. The Moon's orbital movement and daily movement were statistically significantly different (Table 5). However, the Tukey test showed that there were statistically significant differences between the subgroups according to orbital movement. However, the Tukey test showed that left anterior descending (LAD) artery and right coronary artery (RCA) culprit lesions were statistically significantly different according to the Moon's daily movement ($p=0.02$) (Table 6).

Bivariate correlation analyses showed that there was no correlation between three type of the Moon's physical effects (distance, daily and hourly movement) and culprit lesions location (Table 7).

Discussion

In this present study, we found that the Moon's orbital movement, daily movement, and distance from the Earth are not associated with culprit lesion location. However, in our subgroup analysis, we found that the Moon's hourly movement is associated with LAD or RCA total occlusion.

In the literature, researchers have mostly studied the association between lunar phases and myocardial infarction frequency and there are conflicting results on this issue. Eisenburger et al., Wende et al and Kanth et al. found that lunar phases are not associated with MI frequencies^{5,10,11}. In addition, Takagi et al. analyzed 7 studies and found similar results¹².

Table 2. The baseline and angiographic characteristics of patients (n=554)

Clinical Parameters	Number (%)	Angiographic Parameters	
		Number of Stent Implants	Number (%)
Gender (Male)	426 (76.9%)	0	80 (14.4%)
Smoker	288 (52%)	1	350 (63.2%)
Hypertension	385 (69.5%)	2	99 (17.9%)
Diabetes Mellitus	261 (47.1%)	3	18 (3.2%)
History of Coronary Artery Disease	94 (17%)	4	6 (1.1%)
Congestive Heart Failure	118 (21.3%)	7	1 (0.2%)
Atrial Fibrillation	19 (3.4%)	Number of Diseased Arteries	
Type of Myocardial Infarction		1	295 (53.2%)
Anterior MI	205 (37%)	2	175 (31.6%)
Inferior MI	245 (44.2%)	3	84 (15.2%)
Lateral MI	15 (2.7%)	Culprit Lesion According to the Earth's Gravity	
Posterior MI	9 (1.6%)	Horizontal	288 (52%)
Non-STEMI	80 (14.4%)	Vertical	266 (48%)
		Culprit Lesion According to Ostial Distance	
		Proximal	214 (38.6%)
		Mid	267 (48.2%)
		Distal	73 (13.2%)

*MI: myocardial infarction, STEMI: ST elevation myocardial infarction

Table 3. Comparison of the Moon's distance, daily and hourly movement with culprit lesion location according to the direction of the Earth's gravity

Culprit Lesion Location				
According to the Direction of the Earth's Gravity	Vertical	Horizontal	<i>p</i>	LTEoV
Moon's Movement on its Orbit, Day by day (Daily tagged between 0-14)	7.11±4.14	6.82±3.98	0.41	0.32
Moon's Movement According to the Earth's Daily Movement, Hour by Hour (Unit)	-19.48 ±10823.25	39.61±11585.83	0.95	0.08
Distance (Kilometers)	384754.94±16120.27	385174.9±15524.47	0.75	0.24

- Parameters were given as mean ± standard deviation, LTEoV: Levene's Test Equality of Variance

Table 4. Comparison of the Moon's distance, daily and hourly movement with culprit lesion location according to coronary ostial distance

Culprit Lesion Location					
According to Coronary Ostial Distance	Proximal	Mid	Distal	<i>p</i>	LTEoV
Moon's Movement on its Orbit, Day by Day (Daily tagged between 0-14)	6.83±3.98	7.17±4.15	6.55±3.96	0.42	0.49
Moon's Movement According to the Earth's	774.04 ±11434.11	-32.36±10681.62	-	0.17	0.08
			2065.45±12321.66		

Daily Movement, Hour by					
Hour (Unit)					
Distance (Kilometers)	385214.93±1	384768.1±16104.22	385015.18±15259.	0.95	0.34
	5667.13		4		

- Parameters were given as mean ± standard deviation, LTEoV: Levene's Test Equality of Variance

Table 5. Comparison of the Moon's distance, daily and hourly movement with culprit coronary artery

Culprit Vessel	LAD	CX	RCA	<i>p</i>	LTEoV
Moon's Movement on its Orbit, Day by Day (Daily tagged between 0-14)	7.17±4.07	7.58±4.04	6.39±4.0	0.027	0.70
Moon's Movement According to the Earth's Daily Movement, Hour by Hour (Unit)	1470.21±11	-506.78±10701.971	-1370.18±11228.1	0.025	0.42
Distance (Kilometers)	384965.56±15628.62	384670.83±16377.26	385141.93±15758.867	0.969	0.59

- Parameters were given as mean ± standard deviation
- LTEoV: Levene's Test Equality of Variance

Table 6. Subgroup analyses of the comparison of the Moon's daily and hourly movement with culprit coronary artery

			95% Confidence					
			Mean			Interval		
Dependent Variable			Difference	Std. Error	<i>p</i>	Lower	Upper	
			(I-J)			Bound	Bound	
Moon's Movement on Its Orbit Day by Day (Daily tagged between 0- 14)	Tukey	LAD	CX	-0.303	0.474	0.799	-1.42	0.81
			RCA	0.812	0.382	0.086	-0.09	1.71
		CX	LAD	0.303	0.474	0.799	-0.81	1.42
			RCA	1.115	0.486	0.057	-0.03	2.26
	HSD	LAD		-0.812	0.382	0.086	-1.71	0.09
		RCA	CX	-1.115	0.486	0.057	-2.26	0.03
		LAD	CX	2069.876	1308.475	0.254	-1005.12	5144.87
			RCA	2834.030	1055.160	0.020	354.34	5313.72
Moon's Movement According to Earth's Daily Movement Hours by Hours (Unite)	Tukey	CX	-2069.876	1308.475	0.254	-5144.87	1005.12	
		RCA	764.154	1340.234	0.836	-2385.48	3913.79	
	HSD	LAD	-2834.030	1055.160	0.020	-5313.72	-354.34	
		RCA						
		CX	-764.154	1340.234	0.836	-3913.79	2385.48	

LAD: Left anterior descendent artery, CX: Circumflex artery, RCA: Right coronary artery

Table 7. Correlation analyses of the Moon's movements and culprit lesion's locations

Correlation Analyses		Proximal-Distal	Vertical-Horizontal
Hourly Movement	Correlation	-0.75	0.003
	p	0.076	0.951
	Number	554	554
Distance	Correlation	-0.008	0.013
	p	0.846	0.755
	Number	554	554
Daily Movement	Correlation	-0.002	-0.002
	p	0.965	0.965
	Number	554	554

Furthermore, Segan et al. conducted a study to research the association between STEMI outcomes and lunar phases¹³ and found no relevance between these parameters. However, in another study, researchers found that MI frequencies were comparable with lunar phases⁷. In our study we wanted to investigate not only MI frequency, but also the culprit vessel type and culprit lesion location. In the light of the conflicting results mentioned, we established our study with a different approach. We compared the Moon's daily gravitational force against Sun's. If Sun and Moon were on the same side of the Earth, we assumed that they had an additive effect, and we tagged this situation with the number 14. In contrast, if Sun and Moon were on opposite sides, we assumed that they had a negative effect on each other, and we tagged this situation with number 0. The Moon's daily orbital movement was also tagged between 0 and 14 (the Moon's orbital movement is completed in 28 days). We found no statistically difference for culprit vessel

type and culprit lesion location with this calculation.

Most of the studies explained lunar effects on myocardial infarction with non-mechanical effects. In one study, researchers found that the difference in the Moon's gravitational force affects MI frequencies⁶. From the perspective of our study, this difference might also be associated with mechanical effects. With this in mind, we considered that the shear stress difference on coronary lesions according to gravitational force variation was worth investigating. However, there were no statistically significant differences for culprit vessel type and culprit lesion location according to the Moon's distance that influences its gravitational force on the Earth.

Different from previous studies, we thought that the Moon's location at the time of the onset of symptoms may influence coronary artery total occlusion. Especially, that shear stress in line with the Earth's gravity (vertical) may affect the location of total

occlusion. If the Moon had risen, from the perspective of our center, we assumed that the Moon decreased the Earth's gravity force on patients. and, if Moon had set and was behind the Earth, it had additive effect on the Earth's gravitational force for patents (Figure 3). We found that, neither culprit lesion in the vertical side of the coronary artery nor the distance from the coronary ostium (proximal/mid/distal) were statistically significantly different. However, we found that if the Moon had risen and was above our city, LAD occlusion was statistically higher compared with RCA occlusion, and vice versa if the Moon was behind the Earth. In our opinion, RCA feeds mostly the inferior side of the heart and the Moon's additive force with Earth's gravity creates much more shear stress on this coronary artery but, this comment should be investigated further in the subsequent studies.

There are some limitations that should be mentioned. Firstly, this is a retrospective study. In the future, cross-sectional or prospective studies on this issue are needed. Secondly, this study was completed at only one center and had a limited patient number. In subsequent studies, more patients will increase the statistical significance. Thirdly, in this study, we only considered culprit lesion locations, however, long term outcome results associated with lunar effects will be more valuable. Finally, we assumed the patient's symptom onset time as the coronary event onset time. However, this is subjective data that may be influenced by the patient's pain feeling perspective, as such, in further studies, more objective data may be selected.

Conclusion

In conclusion, we found no relationship between lunar effects and culprit lesion locations in myocardial infarction. As a result, the myth of the lunar effects on myocardial infarction seems irrational and should be reconsidered.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical approval

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WHEN TO IMPLEMENT PHARMACEUTICS POLICIES: DEDUCTIONS FROM THE PERIODICALLY INTEGRATED AVERAGE COST PER PRESCRIPTION DATA

İLAÇ POLİTİKALARI NE ZAMAN UYGULANMALI: PERİYODİK BÜTÜNLEŞİK REÇETE BAŞINA ORTALAMA MALİYET VERİSİNDEN ÇIKARIMLAR

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Abstract

Introduction: Pharmaceuticals are integral to the healthcare; therefore, dynamics of their prices affects not only firms but the wellbeing of the public as well. Consequently, this study aims to investigate the dynamics of the pharmaceutical prices as well as the effect of shocks on the series for the purpose of policy implementation, exploiting the periodic structure of the series.

Materials and Methods: The study focuses on the end user prices hence the price data is taken as average price of prescriptions. The data is a time series obtained from Social Security Institution's Monthly Statistical Bulletins and includes the period 2008m12 - 2020m02. The series is investigated using periodic models.

Results: The series depicts strong periodicity, moreover it is found out to be periodically integrated. Consequently, the monthly average price of prescriptions is modeled using periodically integrated autoregressive models. The time varying accumulations of shocks of the models indicate the shocks on spring and summer months have the most severe effect such that it may change the stochastic trend of the series. Additionally shocks on winter have large, long-run impacts.

Conclusion: The shocks can occur intentionally as government policies on pharmaceuticals or unintentionally such as pandemics, unexpected fluctuations in exchange rates. On one hand intentional shocks in winter have larger long run effects, but such shocks are less likely to change the dynamics of the series. On the other hand, unintentional shocks at winter should be dealt carefully since their effect is going to be long lasting. Finally the models agree that policy shocks in spring and summer seasons are more likely to be successful whereas policy makers must take swift action when an unintentional shock occurs in these seasons.

Keywords: Pharmaceuticals pricing policies, average cost of prescriptions, periodic autoregression

Öz

Giriş: İlaçlar, sağlık hizmetlerinin ayrılmaz bir parçasıdır, bu nedenle fiyatlarının dinamikleri sadece firmaları değil, halkın refahını da etkiler. Bu çalışma, serinin periyodik yapısından yararlanarak, politika uygulaması amacıyla ilaç fiyatlarının dinamiklerini ve şokların seriler üzerindeki etkisini araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Çalışma, son kullanıcı fiyatlarına odaklandığından, fiyat verileri ortalama reçete maliyeti olarak alınmıştır. Veriler, Sosyal Güvenlik Kurumu Aylık İstatistik Bültenlerinden alınan bir zaman serisi olup 2008m12- 2020m02 dönemini içermektedir. Seri, periyodik modeller kullanılarak incelenmiştir.

Bulgular: Serinin güçlü bir periyodiklik gösterdiği, ayrıca periyodik entegre olduğu tespit edilmiştir. Sonuç olarak, reçetelerin aylık ortalama fiyatı, periyodik olarak entegre edilen otoregresif modeller kullanılarak modellenmiştir. Modellerin zamana göre değişen şok birikimleri, ilkbahar ve yaz aylarındaki şokların serinin stokastik eğilimini değiştirebilecek şekilde en şiddetli etkiye sahip olduğunu göstermektedir. Ek olarak, kış şoklarının uzun vadede büyük etkileri vardır.

Sonuç: Şoklar, devletin eczacılık politikalarına yönelik politikaları olarak kasıtlı veya pandemi, döviz kurlarında beklenmeyen dalgalanmalar gibi kasıtsız olarak ortaya çıkabilir. Bir yandan, kışın kasıtlı şokların daha uzun vadeli etkileri vardır, ancak bu tür şokların serinin dinamiklerini değiştirmesi daha az olasıdır. Öte yandan, kışın istenmeyen şoklar, etkileri uzun süreli olacağından dikkatli davranılmalıdır. Son olarak modeller, ilkbahar ve yaz mevsimlerindeki politika şoklarının başarılı olma olasılığının daha yüksek olduğu, ancak bu mevsimlerde kasıtsız bir şok meydana geldiğinde politika yapımcıların hızlı hareket etmesi gerektiği konusunda hemfikiridir.

Anahtar Kelimeler: İlaç fiyatlandırma politikaları, ortalama reçete maliyeti, periyodik otoregresyon

Introduction

Healthcare system in Turkey has undergone a total overhaul in 2003 with the launch of the Health Transformation Program (HTP). The private sector's share began to increase with the inauguration of HTP. Adopting various models of public-private partnership projects, which were applied in 1990's around the world, as the main tool of financing, especially the construction and administration of city hospitals since 2013, distanced the provision of health services from the dominance of the state in the sector¹. Additionally HTP is suggested to be proceeding in a positive direction regarding patients².

The effects of state losing its dominance in the sector, and suggestions regarding the patients are investigated in the literature. The overall change in health outcomes, variables and scope of the HTP or health reforms implemented in Turkey has been well researched^{3,4,5}. However the specific effects of these changes on the

pharmaceutical market have been largely overlooked⁶.

Turkey experienced a significant increase in total pharmaceutical sales from US\$ 2.5 billion in 2002 to US\$ 8.0 billion in 2012 as a consequence of the improved access to healthcare services following the implementation of the HTP initiated in 2003⁷. The expenditure on pharmaceuticals would have been even greater, unless the pricing mechanism had been changed during the implementation of HTP⁷. In 2006, the pharmaceutical positive list was integrated into health insurance plans and reference pricing was established⁸. In order to reduce pharmaceutical spending a global budget, which will be in effect for three years between 2010 until the end of 2010 is negotiated where SSI holds rights to further public rebates of drugs on the aforementioned positive list unless the budget is met⁸. A further measure to reduce pharmaceutical expenditure has been the encouragement of generic medicine utilization^{9,10}.

Pharmaceutical expenditure provides only one facet of the impact of HTP on

pharmaceutical market as well as the perspective of pharmaceuticals' overall utilization: the economic one. Pharmaceutical expenditure is essentially influenced by both prices and volumes of the drugs¹¹. Hence, this study aims to investigate the dynamics of the price of medicines per prescription. Furthermore this study examines the impact of (policy) shocks on the series, in order to establish the optimal timing for implementation of policies regarding the price of pharmaceuticals.

Materials and Methods

The data on average cost per prescription is obtained from Social Security Institution's (SSI) Monthly Statistical Bulletins (SGK, Aylık İstatistik Bültenleri) which are publicly available. The data is a time series which calculates the average price in Turkish Liras and consists of the period 2008m12 - 2020m02. In other words, the average price per prescription series starts on December 2008 and ends in February 2020, has monthly frequency and has 135 observation points. A time series plot of the data is available at figure 1.

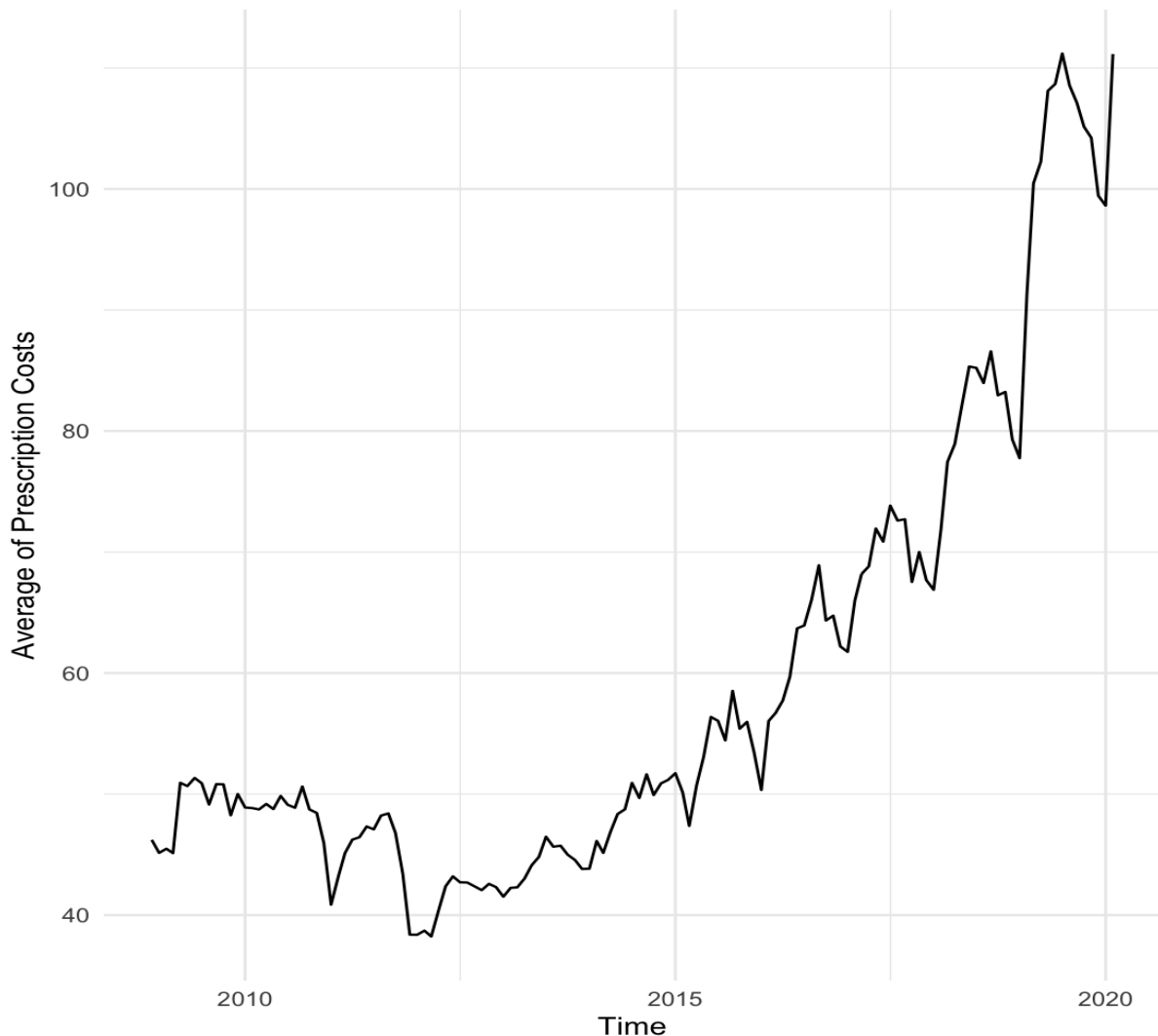


Figure 1. Time series plot of the average cost per prescription in TL

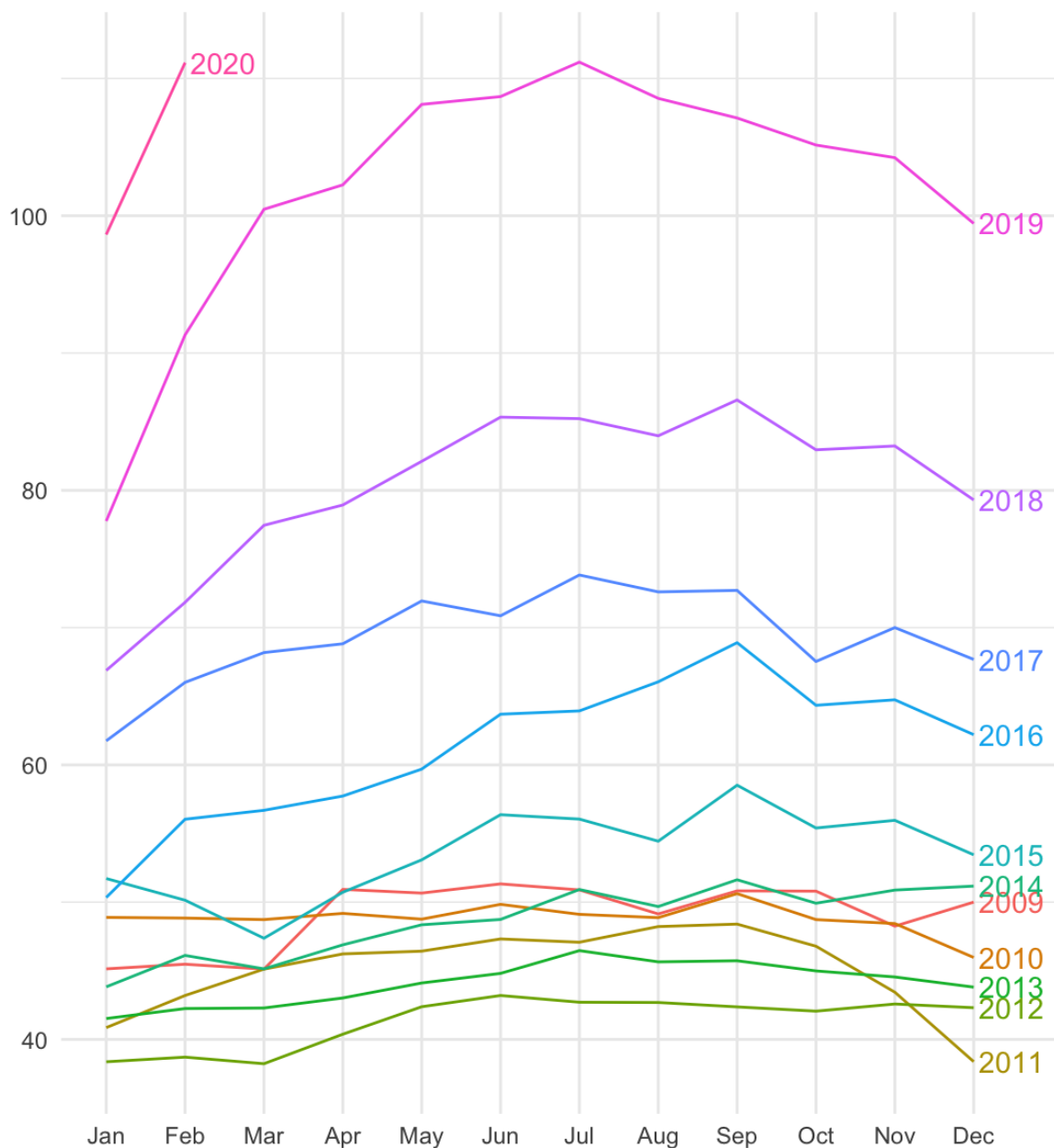


Figure 2. Seasonal plot of the the average cost per prescription

The figure shows that average cost per prescription has characteristic trait which are the upward trend and the oscillations in the series. The seasonal plot of the series in figure 2 cements this observation. In figure 2 instead of a continuous plot from start to end, each year's observations are laid out against the months for each year separately. The 2nd figure clearly indicate that there is an increasing trend, since the observations

for each month is higher than observations at the same month in previous years. Furthermore the periodic movement in the series becomes more apparent in figure 2, especially in recent years the average prices in summer months and at beginning of fall have higher values than.

Many studies filter out such periodic motions in a time series due to the problems

it creates in empirical analysis. However periodicity is an important feature of a series and investigation of it may unravel characteristics of the series which may not be noticed otherwise. Consequently the dynamics of average cost of prescriptions investigated using periodic autoregressive models (PAR) in this study. PAR models by construction take periodic fluctuations, which arise due to seasonality in this case, into account. Due to inclusion of separate AR models such models can handle both cyclic and seasonal patterns better than seasonal ARMA models¹².

A simple PAR model of order p or PAR (p) in short, can be written as follows

$$y_t = \phi_{1s}y_{t-1} + \dots + \phi_{ps}y_{t-p} + \varepsilon_t ; s = 1, 2, \dots, 12, \\ t = 1, 2, \dots, n, \quad \varepsilon_t \square iid(0, 1) \quad (1)$$

where n is the number of observations which is 135 in this case. The PAR(p) model includes 12 different autoregressive model of order p, or AR(p) models, one for each month of the year. Therefore, for a monthly series, equation (1) can be rewritten with the more convenient multivariate notation or monthly vector notation.

$$\Phi_0 Y_{s,T} = \Phi_1 Y_{s,T-1} + \dots + \Phi_p Y_{s,T-p} + \varepsilon_T, \\ \varepsilon_T \square iid(0, 1) \quad (2)$$

where $\Phi_0, \Phi_1, \dots, \Phi_p,$ are the (12×12) matrices which contain the parameters in equation (1). The parameters in the matrices defined as follows

$$\Phi_0(i, j) = \begin{cases} 1, i = j \\ 0, j > i \\ -\phi_{i-j,i}, j < i \end{cases}$$

$$\Phi_k(i, j) = -\phi_{i+4k-j,i}$$

for $i, j = 1, 2, \dots, 12$ and $k = 1, 2, \dots, P$.

This notation is especially useful since it is used to calculate the time varying impact of shocks, which is also a (12×12) matrix. The time varying impact of shocks reveal an crucial feature of the series; it is used to determine the relationship between stochastic trend and seasonal fluctuation¹³.

The cumulative effect of the shocks becomes more severe in the month corresponding to the row with the highest values in the impact matrix. Therefore, fluctuation in the stochastic trend of the series is more likely to occur. Similarly, the month corresponding to the column with the highest values has the largest long-run effect¹⁴.

Modeling the series with PAR model if the series is periodically integrated, creates severe problems. Periodic integration is a form of nonstationarity that arises for existence of unit root in the series which is periodic. Non-stationarity is a characteristic of a time series which, simply put, indicates the distributional properties of the time series does not remain the same throughout the series¹⁵. It indicates that any shock on the series have lasting effect, the impact of the shock does not fade away. In other word the impact of the shock jumps one month to the next. In case of periodic integration the shock jumps from same month to the same month in consecutive years, skipping the observations in between¹⁶.

Periodic integration is tested in two steps. First the null hypothesis of the existence of unit root in the series is tested. If this null hypothesis cannot be rejected, either the series has a long run unit root or a seasonal unit root. If the series has long run unit root the series must be estimated an periodic autoregressive with integration (PARI) model or periodically integrated autoregressive (PIAR) model. The second step is to establish whether the series is guided by PARI process or PIAR process. In order to distinguish among PARI and PIAR processes the following null hypothesis is tested; $H_0: \alpha_s = 1$ and $H_0: \alpha_s = -1$ where α_s are seasonally varying parameters in the periodically differenced representation of equations (1) and (2). If both null hypothesis are rejected the PIAR model is chosen. The time varying impact of shocks can be calculated for PIAR model as well. It works the same way mentioned previously; the rows give information on

severity of the shocks, whereas columns give information on long-run effect. Finally, for modeling purposes two different deterministic components are considered throughout the study. The first deterministic component SI+GT indicates seasonal intercept (SI) and global trend (GT) is added to the model. The second deterministic component SI+ST indicates seasonal intercept (SI) and seasonal trend (ST) is added to the model. SI, which is present in both deterministic components, simply tells us that the series moves around a non-zero value that depends on the month. Moreover the trend, which is discernible in figures 1 and 2, in the series must be controlled for in the models. The trend might be either due to seasonal factors, which can be controlled for with the incorporation of ST into the model, or due to a long-run factor that is globally present in the series, which can be controlled for with the incorporation of GT into the model. The deterministic components prevent any wrong conclusion that might arise due to omission of these cases.

Results

The time series plot is in figure 1 and 2 indicate periodicity in the average cost of prescriptions, this can be formally tested with an F-test. The existence of periodicity at any lag (order of the model) can be tested with the null hypothesis $f_{is} = f_i$ which states the series is not periodic for $s=1,2,\dots,12$ and $i=1,2,\dots,p$; against the alternative hypothesis of periodicity. The null hypothesis implies no periodicity, so AR (p) model is a good approximation. The alternative hypothesis, on the other hand, implies the periodic fluctuations exist in the series and PAR(p) model should be chosen. The results of this test for the average cost of prescriptions are reported in table 1. For the sake of robustness of findings models of order 1,2 and 3 is considered under both of the aforementioned deterministic components. The result of the test indicates

the null hypothesis is rejected, thus the series are periodic in all cases addressed in table 1.

Table 1. Test for periodicity in the autoregressive parameters

deterministic component	order of the model	test statistics	degrees of freedom	p-value
SI+GT	1	9.70	(11,120)	<0.001
SI+ST	1	3.36	(11,109)	<0.001
SI+GT	2	6.13	(22,118)	<0.001
SI+ST	2	3.13	(22,107)	<0.001
SI+GT	3	4.52	(33,116)	<0.001
SI+ST	3	2.68	(33,105)	<0.001

Table 2 reports the findings on model selection criteria. Although working with more models provides more robust findings, the main disadvantage is the confusion due to the large number of results derived from tests and estimation of the models. Reducing the number of models one works with using statistical criteria helps clear the confusion.

Table 2. Model Selection

Deterministic Component	Criteria	Order of the Model		
		p=1	p=2	p=3
SI+GT	BIC	616.3774	645.5174	678.4377
	F-next	1.5745295	1.1380867	0.7423004
	p-value	0.1118186	0.3414765	0.7056932
SI+ST	BIC	651.0958	669.9589	694.0901
	F-next	1.9799833	1.3873362	0.8843325
	p-value	0.0357786	0.1916612	0.5669620

For each alternative model mentioned in table 1, F-next test and Bayesian Information Criterion (BIC) is employed to select appropriate models. F-next tests whether model of order one higher that estimated is more appropriate. For example, F-next test on PAR(p) models checks whether PAR(p+1) should be chosen. The p-value reported below F-next in the table is the one calculate for this test. F-next test helps to select only among various orders of a model; the other criteria, BIC, can help one to choose The BIC can identify optimal model among various functional forms. In other words BIC can be used to choose the model that deterministic component that fits the data. The smaller the BIC is the better the model characterized the series. In table BIC clearly favors PAR(1) regardless of deterministic component. Furthermore BIC prefers the model with SI+GT instead of the PAR model with SI+ST. In short, BIC advocates PAR(1) with SI+GT deterministic terms. The F-next test is considered separately for each form of the deterministic term. For the case of SI+GT, the p-values of the tests for each order are greater than 5%, which suggest that PAR(1) is the best choice. However for the case of SI+ST p-value of the test for the PAR(1) model is less that 5%, this indicates that the null hypothesis of PAR(1) is rejected in favor of PAR(2) model with the same set of deterministic models. Consequently these findings indicate PAR(1) with SI+GT to be the optimal model. Furthermore for the sake of robustness of the findings PAR(2) with SI+ST is also considered in the study, since the F-next test supports order 2 for the case of SI+ST.

Table 3 reports results of the seasonal heteroskedasticity test which is a diagnostic of the selected models. Heteroskedasticity arises when the variance of residuals on the model is not constant. Consequently any test on a model with heteroskedasticity problem is unreliable. The test checks the null hypothesis of no heteroskedasticity against the alternative of the problem

existing in the model. Therefore a p-value greater that 5% means that there is no heteroskedasticity in the model. Fortunately any of the selected PAR models are devoid of heteroskedasticity problem, since the p-values are greater than 5%.

Table 3. Periodic Heteroskedasticity Test

deterministic component	order of the model	test statistics	degrees of freedom	p-value
SI+GT	1	1.09	(11,133)	0.3759
SI+ST	2	1.46	(11,132)	0.1559

The next step in the modeling of the average cost per prescriptions is the investigation of unit root in the series. For this purpose two separate tests are conducted; first tests whether there is unit root in the series, and the second test whether it is a long run unit root are a periodic unit root. Unit root in a series states that the series is nonstationary; any shock on the series does not die down.

Table 4. Single Unit Root in PAR(p) model

deterministic component	order of the model	test statistics	Critical values		
			5%	10%	
SI+GT	1	LR	0.41	9.24	7.52
		LR _τ	0.64	-2.41	-2.57
SI+ST	2	LR	1.46	12.96	10.50
		LR _τ	-1.21	-3.41	-3.12

The test of single unit root in PAR(p) model in table 4 is the aforementioned test, which establishes the existence of the unit root in the series. LR and LR_τ test statistics

reported in the table both indicate that the series has unit root. The next step is therefore to establish whether this unit root is a long-run unit root or periodic unit root. This test is reported in table 5. The test in table 5 tests null of long run unit root against periodic unit root. The test results reject the null hypothesis in favor of periodic unit root.

The unit root tests clearly indicate periodic unit root, therefore the series are called periodically integrated. Therefore such series have to be modeled with methods that

can take periodic integration into account, which PIAR is one of them. As a result the series are modeled with PIAR(1) with SI+GT and PIAR(2) with SI+ST. The matrix of time varying accumulation of shocks of the PIAR(1) and PIAR(2) are reported in table 6 and 7 respectively. As mentioned previously the rows of time varying accumulation of shocks matrix has information on the intensity of a shock while the columns have information on the long-run impact of the shock.

Table 5. Test of Periodic Unit root

deterministic component	order of the model	the null hypothesis	test statistics	degrees of freedom	p-value
SI+GT	1	$\alpha_s = 1$	9.74	(11,121)	<0.001
		$\alpha_s = -1$	1938.35	(11,121)	<0.001
SI+ST	2	$\alpha_s = 1$	2.1	(11,97)	0.0268
		$\alpha_s = -1$	10.55	(11,97)	<0.001

Table 6. Time varying accumulation of shocks for PIAR(1)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Jan	1.000	0.833	0.723	0.755	0.716	0.733	0.731	0.773	0.810	0.871	0.885	0.971
Feb	1.200	1.000	0.867	0.906	0.859	0.880	0.877	0.928	0.972	1.045	1.062	1.166
Mar	1.384	1.153	1.000	1.044	0.990	1.014	1.011	1.070	1.121	1.205	1.225	1.344
Apr	1.325	1.104	0.958	1.000	0.949	0.972	0.968	1.025	1.073	1.154	1.173	1.287
May	1.397	1.164	1.010	1.054	1.000	1.024	1.021	1.080	1.131	1.216	1.237	1.357
Jun	1.364	1.136	0.986	1.029	0.976	1.000	0.997	1.055	1.105	1.188	1.207	1.325
Jul	1.369	1.140	0.989	1.033	0.980	1.003	1.000	1.058	1.108	1.192	1.211	1.329
Aug	1.293	1.078	0.935	0.976	0.926	0.948	0.945	1.000	1.047	1.126	1.145	1.256
Sep	1.235	1.029	0.892	0.932	0.884	0.905	0.902	0.955	1.000	1.075	1.093	1.199
Oct	1.148	0.957	0.830	0.867	0.822	0.842	0.839	0.888	0.930	1.000	1.017	1.116
Nov	1.130	0.941	0.816	0.852	0.809	0.828	0.825	0.874	0.915	0.984	1.000	1.097
Dec	1.029	0.858	0.744	0.777	0.737	0.755	0.752	0.796	0.834	0.896	0.911	1.000

Table 7. Time varying accumulation of shocks for PIAR(2)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Jan	1.000	0.821	0.685	0.669	0.654	0.676	0.680	0.723	0.775	0.754	0.844	0.935
Feb	1.219	1.000	0.834	0.815	0.797	0.824	0.829	0.881	0.944	0.918	1.029	1.140
Mar	1.460	1.198	1.000	0.977	0.955	0.987	0.993	1.056	1.131	1.101	1.233	1.366
Apr	1.495	1.227	1.024	1.000	0.978	1.011	1.017	1.081	1.158	1.127	1.262	1.399
May	1.529	1.254	1.047	1.022	1.000	1.033	1.040	1.105	1.184	1.152	1.290	1.430
Jun	1.479	1.214	1.013	0.989	0.968	1.000	1.006	1.069	1.146	1.115	1.249	1.384
Jul	1.471	1.207	1.007	0.983	0.962	0.994	1.000	1.063	1.139	1.108	1.241	1.375
Aug	1.383	1.135	0.947	0.925	0.905	0.935	0.941	1.000	1.072	1.043	1.168	1.294
Sep	1.291	1.059	0.884	0.863	0.844	0.873	0.878	0.933	1.000	0.973	1.090	1.207
Oct	1.327	1.089	0.908	0.887	0.868	0.897	0.902	0.959	1.028	1.000	1.120	1.241
Nov	1.185	0.972	0.811	0.792	0.775	0.801	0.806	0.856	0.918	0.893	1.000	1.108
Dec	1.069	0.877	0.732	0.715	0.699	0.723	0.727	0.773	0.828	0.806	0.903	1.000

In table 6, the PIAR(1) model indicates that any shocks on March, May, June and July have a stronger effect on the series. Therefore any intentional shocks such as policy shocks on the series are more likely to be effective. Then the column of the table 6 are checked, the shocks on winter months (November, December and January) have the largest long-run impact. The findings on shocks regarding PIAR(2) in table 7 are in consensus with the aforementioned results with a slight difference. PIAR(2) model indicates impact to shocks becomes more severe any shocks on March, April, May, June and July, Addition to March, May, June and July mentioned for the PIAR(1) model, PIAR(2) model includes April into the list of months when impact of shocks are most severe. The findings on the columns of the model are in total agreement with the PIAR(1) model, attesting the shocks on winter months have larger long-run effects.

The impact of policy shocks are investigated in this study using PIAR model. This model is constructed through a tedious modeling process which can be summarized as follows;

- i. periodicity of the series is tested,
- ii. optimal functional form of the model is selected,
- iii. existence of heteroskedasticity in the selected models are tested,
- iv. the series is tested for unit root, where the series are found out to be periodically integrated, and
- v. The series are modeled as PIAR.

The model selection process indicated PIAR(1) with the deterministic terms SI+GT to be the optimal model, we further continued to use PIAR(2) with SI+ST the check the robustness of the results. After the modeling process the impact of shocks are investigated via the time varying accumulation of shocks matrix. The findings indicate any shocks on spring and summer has a more severe impact that shocks on any other months. Furthermore the long-run impact of the shock on winter months is found to be higher.

Discussion

The shocks mentioned in this study stem from policy interventions, exogenous foreign factors such as increasing the cost of transportation of pharmaceuticals or exchange rate fluctuations. In other words shocks might be intentional such as policy interventions, as well as unintentional. The findings in this study imply that any policy implemented on spring and summer seasons are more likely to be effective whereas policies implemented in winter season have longer lasting effect. Furthermore any undeliberate shocks on these seasons should be considered carefully. We especially recommend swift action against exogenous (unintentional) and detrimental shocks on the price of prescriptions which occur on spring and summer seasons. Additionally policies against the (unintentional) shocks on winter must be deliberated and implemented carefully since the shocks on these months have larger and longer effect.

Conclusion

PIAR(1) and PIAR(2) models are employed to model average cost per prescription, which is good indicator of pharmaceutical prices. These models are further employed to examine the impact of shocks on the average cost per prescription series. The shocks can occur intentionally as government policies on pharmaceuticals or unintentionally such as pandemics, unexpected fluctuations in exchange rates. The models indicate that spring and summer are the most likely seasons when policy implementations which reduce the price of drugs are most likely to succeed; since during period fluctuation in the stochastic trend of the series is more likely to occur. However any unintentional shocks in these months must be dealt swiftly, before the shocks effect the prices.

Conflict of Interest

Opinions expressed are solely authors' and do not express the views or opinions of the institutions the authors are affiliated with. The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

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THE EFFECT OF COVID 19 PANDEMIA ON THE SOCIAL LIFE OF HEALTH WORKERS

COVID 19 PANDEMİSİNİN SAĞLIK ÇALIŞANLARININ SOSYAL YAŞAMINA ETKİSİ

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Abstract

Introduction: While Covid -19 disease exhausted healthcare professionals physically and psychologically, it also affected their family, economic and social situations. Based on this view, we aimed to evaluate how and how much the social lives of healthcare professionals have changed.

Materials and Methods: An online questionnaire was applied to 182 people working our hospital. The study questionnaire consisted of two parts, the first part contained 5 questions and the second part 10 questions, totaling 15 questions. These questions define the participants and the ways of transmission of the disease, the distribution of daily activity increases outside of work, individual isolation rates, change in shopping habits, family and relatives relations, ability to continue the profession, health It consisted of questions to measure their perspective on social support given to their employees.

Results: 182 healthcare professionals voluntarily participated in our survey. Participants consisted of 36 doctors, 105 nurses and 41 technicians. The response of the majority of the participants was that they spent most of their time on TV and mobile telephony. Participants were asked how the frequency of grocery shopping was affected during the pandemic, and the majority responded to the question of how the majority was affected.

Conclusion: The social lives, habits and family relationships of healthcare professionals have been affected by the Covid-19 pandemic. In the light of many publications on this subject, it will be beneficial to increase the support that will increase the motivation of healthcare professionals.

Keywords: Covid 19, pandemic, healthcare professionals, social life

Öz

Giriş: Covid -19 hastalığı sağlık çalışanlarını fiziksel ve psikolojik olarak yorarken ailelerini, ekonomik ve sosyal durumlarını da etkiledi. Bu görüşten yola çıkarak sağlık mesleği mensuplarının sosyal hayatlarının nasıl ve ne kadar değiştiğini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Hastanemizde çalışan 182 kişiye online anket uygulandı. Çalışma anketi iki bölümden oluşmakta olup, birinci bölüm 5 soru ve ikinci bölüm 10 soru olmak üzere toplam 15 sorudan oluşmaktadır. Bu sorular, katılımcıları ve hastalığın bulaşma yollarını, günlük aktivite artışlarının iş dışı dağılımını, bireysel izolasyon oranlarını, alışveriş alışkanlıklarındaki değişimi, aile ve akraba ilişkileri, mesleğe devam etme becerisini, sağlığı tanımlayan sorulardan oluşuyordu. Çalışanlarına verilen sosyal desteğe ilişkin bakış açıları ölçüldü.

Bulgular: Araştırmamıza 182 sağlık uzmanı gönüllü olarak katıldı. Katılımcılar 36 doktor, 105 hemşire ve 41 teknisyenden oluşuyordu. Katılımcıların büyük çoğunluğunun cevabı, zamanlarının çoğunu televizyon ve cep telefonu ile geçirdikleri yönündeydi. Salgın sırasında market alışverişi sıklığının nasıl etkilendiği soruldu ve çoğunluğun nasıl olduğu sorusuna çoğunluk etkilendiği yanıtı verdi. Sonuç: Sağlık mesleği mensuplarının sosyal yaşamları, alışkanlıkları ve aile ilişkileri Covid-19 salgınından etkilenmiştir. Bu konudaki birçok yaygın ışığında sağlık çalışanlarının motivasyonunu artıracak desteğin artırılması faydalı olacaktır.

Anahtar Kelimeler: Covid 19, pandemi, sağlık çalışanları, sosyal yaşam

Introduction

Covid 19 disease has captured the whole world. The fact that the treatment of the disease has not yet been found has increased the socioeconomic damages of the pandemic. The disease first started in Wuhan region of China and spread rapidly all over the world¹. Healthcare professionals were the most affected by this process. In line with the recommendations made to healthcare professionals, they provided service for hours with personal protective equipment that was not used frequently before the pandemic². The pathogenicity of Covid 19 disease was examined and after it was shown that it could be transmitted from person to person, some of the employees isolated themselves³. Of course, life had changed for an unknown period of time. Total 348 493 Covid19 positive patients found to this day in Turkey until 9296 that the death has been reported⁴. While Covid -19 disease exhausted healthcare professionals physically and psychologically, it also affected their family, economic and social situations. Based on this view, we aimed to evaluate

how and how much the social lives of healthcare professionals have changed.

Materials and Methods

An online questionnaire was applied to 182 people working our hospital. On the first page of the questionnaire applied, a short explanation about the study was included, and after this part, the participants who wanted to continue voluntarily approved the study and sent the online form back to the researchers with the same online system, but the participants who wanted to leave were given the option of not continuing after the explanation part. The study questionnaire consisted of two parts, the first part contained 5 questions and the second part 10 questions, totaling 15 questions. These questions define the participants (age, gender, occupation, working year, marital status) and the ways of transmission of the disease, the distribution of daily activity increases outside of work, individual isolation rates, change in shopping habits, family and relatives relations, ability to continue the profession, health It consisted of questions to measure their perspective on social support given to their employees.

- *Ethical approval*

The study was conducted in accordance with the Declaration of Helsinki; Ethics committee approval was obtained from Kastamonu health sciences scientific research and publication ethics committee (Ethics Approval Number: 2020-4/3).

- *Statistical analysis*

SPSS version 22 (IBM) was used to analyze the data obtained from the participants. Frequency and ratio calculations were made with descriptive analysis.

Results

182 healthcare professionals voluntarily participated in our survey. Participants consisted of 36 doctors, 105 nurses and 41 technicians. The majority of our doctor and nurse participants were between the ages of 31-45 and had 11-20 years of professional experience. The majority of our technician participants were in the 18-30 age group, from healthcare professionals with 0-10 years of experience. The demographic data distribution of the participants can be seen in Table 1. (Table 1) The second part of our questionnaire was to evaluate the social lives of healthcare professionals. In this

section, participants were asked questions evaluating how much Covid 19 affects the lives of healthcare professionals. Participants' responses are presented in Table 2. (Table 2)

In the second part of our questionnaire, the participants were asked whether the healthcare workers are in the risk group. Except for one participant in the nurse group, all participants answered this question in the direction that they were in the risk group.

The most important means of protection from Covid -19 disease for the participant were questioned. Most of the participants stated that masks and personal protective equipment are the most important means of protection. (Doctor: 21, Nurse:59, Technician: 21). Maintaining social distance has been the second preferred method across the groups. (Doctor: 12, Nurse: 30, Technician: 14). Frequent washing of hands and the use of gloves were preferred in the third place. (Doctor: 3, Nurse: 16, Technician: 6). In our survey, none of the participants thought that the use of sperm and glasses is the most important method of protection. Participants were asked which one they spent more time outside the hospital than before during the Covid-19 pandemic.

Table 1. Demographic distribution of the participants

Total Participants		Doctor n(%)	Nurse n(%)	Technician n(%)	Total n
Gender	Female	15 (%13.6)	75(%68.1)	20(%18.1)	110
	Male	21(%29.1)	30 (% 41.6)	21 (% 29.1)	72
Marital Status	Married	30 (%24.3)	66 (%53.6)	27 (% 21.9)	123
	Single	6 (% 10.1)	39(% 66.1)	14(%23.7)	59
Age Range	18-30	2 (%3.7)	34 (%64.1)	17 (%32)	53
	31-45	27 (25.9)	63 (% 60.5)	14 (% 13.4)	104
	>45	3 (% 100)	0	0	3
Professional Experience	0-10	14 (% 19.1)	41(% 56.1)	18(% 24.6)	73
	11-20	15 (% 20.8)	46(% 63.8)	11(% 15.2)	72
	>20	7 (% 18.9)	18 (%48.6)	12(% 32.4)	37
Additional Disease	Yes	6 (% 14.2)	22 (% 52.3)	14 (%33.3)	42
	No	83 (% 59.2)	27 (%19.2)	140	

Table 2. Distribution of respondents to Survey / Part 2 questions

Survey Questions- Part 2	Participants' Answers	Doctor n:36(%)	Nurse n:105(%)	Technician n:41(%)	Total n=182
Are health workers in the risk group?	Yes	36 (% 19.8)	104(%57.5)	41(%22.7)	181
	No	0(%0)	1(%100)	0(%0)	1
What do you think is the most important way of preventing Covid-19 disease?	Washing hands / Gloves	3(%12)	16(%64)	6(%24)	25
	Mask / Protective equipment	21(%20.8)	59(%58.4)	21(%20.8)	101
	Use of protective sper / glasses	0(%0)	0(%0)	0(%0)	0
	Maintaining social distance	12(%21.5)	30(%53.5)	14(%25)	56
During the Covid-19 pandemic, which one did you spend more time than before?	TV / Mobile phone	26(%20)	78(%60)	26(%20)	130
	Book	6(%25)	12(%50)	6(%25)	24
	Sport	0(%)	3(%37.5)	5(%62.5)	8
	Cooking	4(%20)	12(%60)	4(%20)	20
Did you isolate yourself during the pandemic?	Yes	19(%14.9)	81(%63.8)	27(%21.3)	127
	No	17(%30.9)	24(%43.7)	14(%25.4)	55
What kind of isolation did you apply?	I was separated from my family	10(%12.9)	45(%58.5)	22(%28.6)	77
	I spent time in a separate room at home	9(%18.7)	34(%70.8)	5(%10.55)	48
	I stayed with my friend	0(%0)	2(%100)	0(%0)	2
How was your grocery shopping frequency affected during the pandemic?	Increased	7(%26.9)	14(%53.9)	5(%19.2)	26
	Decreased	19(%15.4)	80(%63.3)	27(%21.3)	126
	Didn't change much	10(%33.4)	11(%36.6)	9(%30)	30
Did any of your relatives, whom you do not meet frequently because of your healthcare professional status, convey their concerns about you?	Yes	33(%19.6)	101(%60.2)	34(%20.2)	168
	No	3(%21.5)	4(%28.5)	7(%50)	14
How were your family relationships affected during the pandemic?	Pozitive	3(%13.6)	10(%45.5)	9(%40.9)	22
	Negative	12(%14.4)	59(%71.2)	12(%14.4)	83
	Not changed	21(%27.7)	36(%46.7)	20(%25.6)	77
Leaving the profession or retiring early, etc. did you have any ideas like	Yes	11(%18.6)	34(%57.6)	14(%23.8)	59
	No	25(%20.4)	71(%57.7)	27(%21.9)	123
How did the support of healthcare professionals by the community (applause, thanks from social media, etc.) affect you?	I am pleased	11(%17.4)	37(%58.7)	15(%23.9)	63
	I am not affected	13(%24.7)	28(%50.6)	13(%24.7)	54
	I found insufficient	12(%18.4)	40(%61.6)	13(%20)	65

The response of the majority of the participants was that they spent most of their time on TV and mobile telephony (Doctor: 26, Nurse: 78, Technician: 26). While the doctor and technician participants preferred to read books at the second frequency, nurse participants were observed to be equal in the second place, namely reading books and cooking. (Doctor: 6, Nurse: 12, Technician: 6). While the doctor and nurse participants preferred to cook at the third frequency, the technicians preferred the option of doing sports. While the nurse was the fourth choice of the participants, none of the doctor participants preferred the option to do sports. (Doctor: 0, Nurse: 3, Technician: 5). Chart1

The participants were asked whether they applied isolation during the pandemic process, and if so, what kind of isolation they preferred. Most of the participants stated that they were separated from their families. (Doctor: 10, Nurse: 45,

Technician: 22). The second preferred option was that I spent time in a separate room at home.

Participants were asked how the frequency of grocery shopping was affected during the pandemic, and the majority responded to the question of how the majority was affected. (Doctor: 19, Nurse: 80, Technician: 27).

The majority of participants answered yes to the question of whether any of your relatives, whom you do not meet frequently because of your health worker, convey their concerns for you. (Doctor: 33, Nurse: 101, Technician: 34).

While the answer of the majority of the doctor and technician group to the question of how your family relationships were affected during the pandemic, the response of the majority of the nurse group was that it was negatively affected. (Doctor: 21, Nurse: 59, Technician: 20). (Chart 2)

Chart 1: ‘During the Covid-19 pandemic, which one did you spare more time than before?’ ‘Participants’ responses to the question

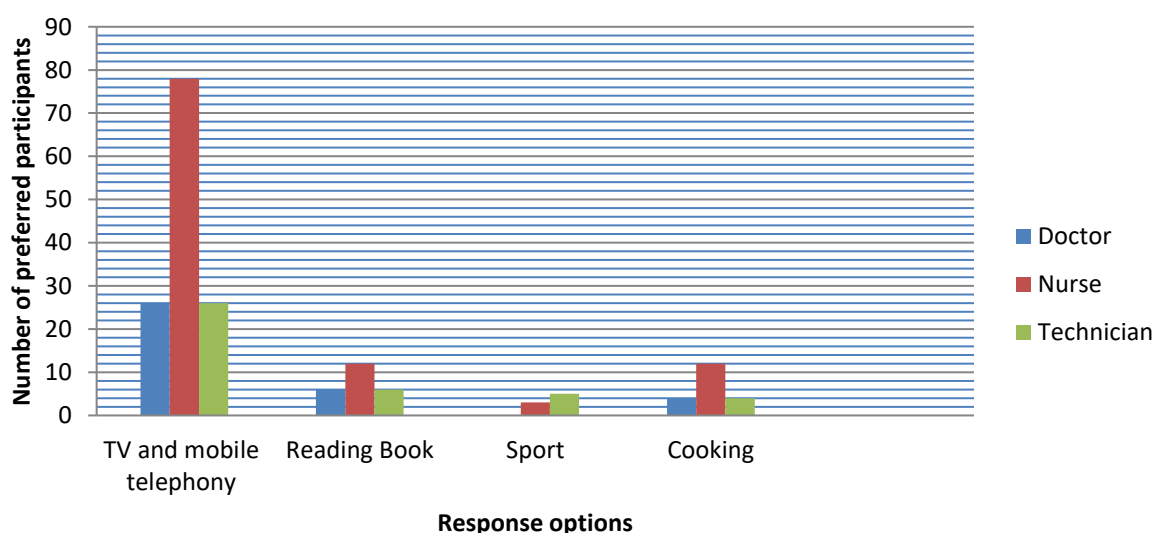


Chart 2. Participants' responses to the question of how your family relationships were affected during the pandemic

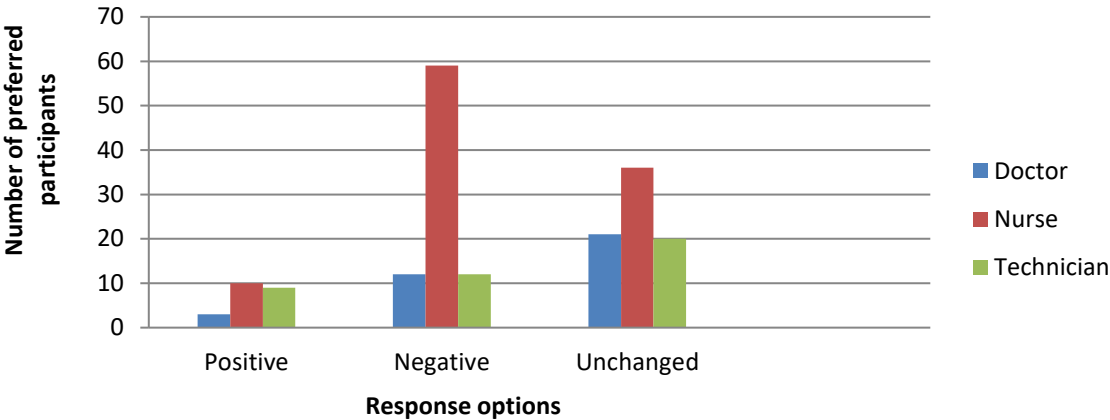
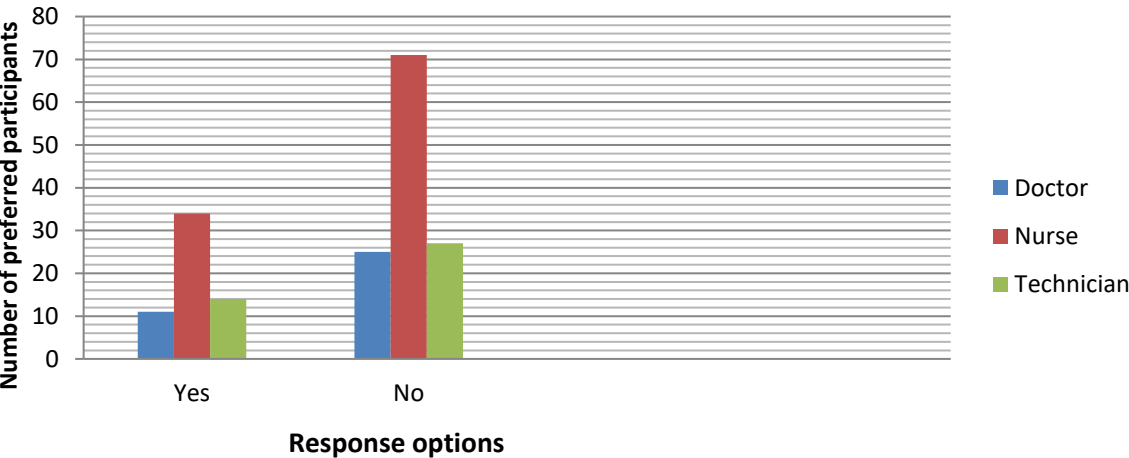


Chart 3: Leaving the profession or retiring early, etc. Participants' responses to the question such as "Have you had ideas?"



Leaving the profession or retiring early, etc. As for the question of whether you have any ideas, the majority answer of all groups was no. . (Doctor: 25, Nurse: 71, Technician: 27). (Chart 3)

The participants were asked how the support of healthcare professionals by the society (applause, thanks from social media, etc.) affected you and the majority of

each group responded differently, 13 people from the doctor group chose the not affected option, 40 people from the nurse group stated that they found it inadequate, and the majority of 15 people in the technician group they reported that they were satisfied with the response.

Discussion

As a result of our survey study, the responses of the participants were classified one by one. Healthcare workers were first asked whether the healthcare workers are in the risk group in part two of our questionnaire. The purpose of this post was to determine the level of awareness of their situation and almost all of our participants reported that they were in the risk group. In early February 2020, the National Health Commission of the People's Republic of China reported that a total of 3387 people, including 23 healthcare professionals, died from Covid-19 out of 77,262 patients ⁵. These numbers gradually increased healthcare deaths in the later dates of the pandemic. An article published in Italy started by describing the 100th doctor who died due to Covid 19 disease ⁶. In this case, healthcare workers are in the high-risk group with their deaths.

While SARS-CoV-2 can be transmitted from person to person through droplets, it can also be transmitted from contaminated items or contaminated air ⁷. However, the best way of protection is not to be exposed to the virus ⁸. In our study, social distance was the second most preferred option. Considering the fact that healthcare professionals cannot keep social distance from their patients in this regard, personal protective equipment and mask option, which is the most common answer given by the participants, is the most important method of protection for healthcare professionals.

Social media was the most frequently used form of communication during the Covid-19 pandemic. Some studies have stated that social media has positive effects during the pandemic period as it enables information to reach everyone quickly ⁹. Some studies have reported that exposure to social media during pandemic exacerbation may have negative effects on mental health ¹⁰. As a result, the power of social media in terms of human relations and information sharing is

indisputable. In our study, the most preferred option was that more time was spent in social media in this period.

Contagiousness of the Covid -19 disease is usually the incubation period of 1-14 days, while the average is 5-6 days, while the longest reported is 24 days ¹¹. During the pandemic process, employees in high-risk units applied themselves to isolation. In one study, 89% of people believed isolation reduced deaths from Covid-19, 8% were unsure, and only 3% stated that they thought isolation could not reduce the number of deaths from Covid-19¹². In our survey, all of the groups preferred isolation. We can see what you do.

During the pandemic period, people stopped their transactions with the community together with the fear of infection. According to a study conducted in Italy, 75.8% of the society, which is a large part of the society, uses the supermarket, 26% from the grocery / market and 9% uses online delivery. 11.8% preferred to have someone else do the shopping. 54%, which is more than half of the society, stated that they now reuse more than 30% of food ¹³. In our questionnaire, we see that most of our healthcare professionals choose the option that states that they reduce it to our question, which evaluates the frequency of grocery shopping.

We thought that even your relatives whom you do not meet frequently because of your health care worker might convey their concerns to you, and we made this a question in our survey. Most of the participants reported that they were sought by their relatives. In addition to putting family relations into the center in creating a buffer against Covid-19 disease and its accompanying vital risks, there are studies to increase resistance to pandemic to family beliefs and close relationships¹⁴. Ideas such as quitting the profession or retiring early, etc., can come to our mind during difficult times. In this period when we, as a country, were fighting the epidemic, it was a gratifying result that most of our healthcare

workers did not want to retire or resign. Intensive care workers following critical Covid-19 patients may show severe depression, anxiety and insomnia symptoms¹⁵. There are studies reporting that healthcare workers have a feeling of burnout, and we think that psychological supports that increase the motivation of healthcare workers will be useful¹⁶.

In our study, it was questioned how the support of healthcare professionals by the society (applause, thanks from social media, etc.) affects healthcare workers, and we observed that the distribution between groups for all options was very close to each other so that there were options to be satisfied, not affected, and inadequate.

The social lives, habits and family relationships of healthcare professionals have been affected by the Covid-19 pandemic. In the light of many publications on this subject, it will be beneficial to increase the support that will increase the motivation of healthcare professionals.

Conflict of Interest

The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

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Ethical approval

Ethics committee approval was obtained from Kastamonu health sciences scientific research and publication ethics committee (Ethics Approval Number: 2020-4/3).

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HEAD AND NECK LYMPHANGIOMAS IN ADULTS: A SINGLE CENTER'S EXPERIENCE

ERİŞKİNLERDE BAŞ VE BOYUN LENFANJİOMLARI: TEK MERKEZ DENEYİMİ

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Abstract

Introduction: To reveal the clinicopathologic features of adult head and neck lymphangiomas that underwent surgical resection in our hospital.

Materials and Methods: All surgical resection materials of patients aged older than 18 years from the head and neck region that were examined at our clinic between 2008 and 2020 were retrospectively reviewed. Cases diagnosed as lymphangioma were included in the study.

Results: Of the 34 lymphangiomas included in the study, 17 were from females and 17 from males. The ages of the patients ranged between 19 and 76 years. The median lymphangioma size was 0.8 cm. Lesions were located on the face in 15 (44.1%) patients, in the oral cavity in nine (26.5%) patients, on the neck in six (17.6%), on the orbital and periorbital region in three (8.8%), and the ear in one (2.9%) patient. All lesions larger than 1.5 cm were located in the neck or oral cavity. All lesions in the oral cavity were diagnosed as cavernous lymphangioma. All four cystic lymphangiomas were identified in the neck. Lymphangioma recurred in two cases; no malignant transformation was detected.

Conclusion: Head and neck lymphangiomas are not uncommon in adults, they can be seen at any age, even in elderly patients. Cystic lymphangioma is often seen in the neck and cavernous lymphangioma in the oral cavity. Total surgical resection provides both treatment and definitive diagnosis. Recurrence can be seen, but malignant transformation is not expected.

Keywords: Lymphangioma; head and neck; cavernous lymphangioma; cystic lymphangioma; lymphangioma circumscriptum

Öz

Giriş: Hastanemizde cerrahi rezeksiyon uygulanan erişkin baş boyun lenfanjiomlarının klinikopatolojik özelliklerini ortaya koymayı amaçladık.

Gereç ve Yöntem: 2008-2020 yılları arasında laboratuvarımızda incelenen 18 yaş üstü hastaların baş boyun bölgesinden yapılan tüm cerrahi rezeksiyon materyalleri retrospektif olarak incelendi. Lenfanjiyom tanısı konulan olgular çalışmaya dahil edildi.

Bulgular: Çalışmaya dahil edilen 34 lenfanjiomdan 17'si kadın, 17'si erkekti. Hastaların yaşları 19 ile 76 arasında değişmekteydi. Medyan lenfanjiyom boyutu 0,8 cm idi. Lezyonlar 15 (%44,1) hastada yüzde, dokuz (% 26,5) hastada ağız boşluğunda, altı (% 17,6) hastada boyunda, üç hastada (% 8,8) orbital ve perioküler bölgede, bir hastada (%2,9) kulakta lokalize idi. Lenfanjiyomların 16'sı (%47,0) lenfanjiyoma sirkumskriptum, 14'ü (%41,2) kavernöz lenfanjiyom ve dördü (%11,8) kistik lenfanjiyom olarak tanımlandı. 1.5 cm'den büyük tüm lezyonlar boyun veya ağız boşluğunda yerleşmişti. Ağız boşluğundaki tüm lezyonlara kavernöz lenfanjiyom tanısı konuldu. Dört kistik lenfanjiyomun tamamı boyunda tespit edildi. Lenfanjiyom iki olguda nüksetti; malign transformasyon saptanmadı. Sonuç: Baş boyun lenfanjiyomları erişkinlerde nadir değildir, her yaşta görülebilirler. Kistik lenfanjiyomlar sıklıkla boyunda ve kavernöz lenfanjiyomlar ağız boşluğunda görülür. Total cerrahi rezeksiyon hem tedavi hem de kesin tanı sağlar. Nüks görülebilir ancak malign transformasyon beklenmez.

Anahtar Kelimeler: Lenfanjiyom; baş ve boyun; kavernöz lenfanjiyom; kistik lenfanjiyom; lenfanjiyoma sirkumskriptum; vasküler malformasyon

Introduction

Lymphangiomas are not considered as true neoplasms, they are thought to be malformations that occur as a result of a communication failure of lymphatic channels with the venous system. Congenital and early childhood lymphangiomas favor developmental malformations and genetic abnormalities also play a role¹. Although the etiology is not well known in adults, it may occur secondary to infection, trauma and iatrogenic injuries². Lymphangiomas are frequently observed in the pediatric age group and most frequently in the head and neck. Although most patients are aged younger than 2 years, lymphangiomas are also seen in adults³. It is slightly more common in males¹.

Lymphangiomas may be superficially or deeply located. Superficial lymphangiomas are known as lymphangioma circumscriptum, and deep lymphangiomas as cavernous or cystic⁴. Radiologic investigations are useful in diagnosis, but the definitive diagnosis is affirmed by histopathologic examination of surgical

resection materials. Sclerotherapy or surgical excision can be used in treatment^{5,6}. While evaluating the treatment options, it is taken into consideration whether the lesion is suitable for complete resection due to its location, size, and its relationship between vessels and vital organs. It is important not to have residual lesions during surgical resection because of the risk of recurrence of incomplete resections⁷.

In this study, we aimed to reveal the clinicopathologic features of adult head and neck lymphangiomas that underwent surgical resection in our hospital.

Materials and Methods

Ethical approval was obtained for the study from the Ethics Committee of KTO Karatay University, Faculty of Medicine (2020/007). The study was conducted in accordance with the principles of the Helsinki Declaration.

All excisional biopsy materials of patients aged over 18 years from head and neck region that were examined at the Pathology

Clinic of Konya Education and Research Hospital between August 1st, 2008, and August 1st, 2020, were retrospectively reviewed. Cases diagnosed as lymphangioma were included in the study. Clinical and pathologic information such as the age and sex of the patients, location and size of the lesions, and follow-up information were obtained from patient files.

Statistical analyses were performed using the SPSS 22.0 for Windows software package (SPSS, Chicago, IL, USA). The Shapiro-Wilk test was used for examining continuous variables with normal and abnormal distribution, and one-way analysis of variance (ANOVA) was used for normally distributed continuous variables. The Kruskal-Wallis test was used for abnormally distributed continuous variables. When the Kruskal-Wallis test indicated statistically significant differences, the causes of the differences were determined by using a Bonferroni-adjusted Mann-Whitney U test. Continuous variables are presented as mean \pm standard

deviation (SD) or median (min-max), and categorical variables are presented as the number of cases and percentage.

Results

Samples from a total of 34 patients were included in the study; 17 were female and 17 were male. The median age of the patients was 52 (range, 19-76) years. The median lymphangioma size was 0.8 (range, 0.3-5) cm. Lesions were located on the face in 15 (44.1%) patients, in the oral cavity in nine (26.5%), on the neck in six (17.6%), the orbital and periorcular region in three (8.8%), and the ear in one (2.9%) patient. The age, sex, and tumor size distributions of the patients according to lesion locations are given in Table 1. Of the lymphangiomas, 16 (47.0%) were defined as lymphangioma circumscriptum, 14 (41.2%) as cavernous lymphangioma, and four (11.8%) as cystic lymphangioma.

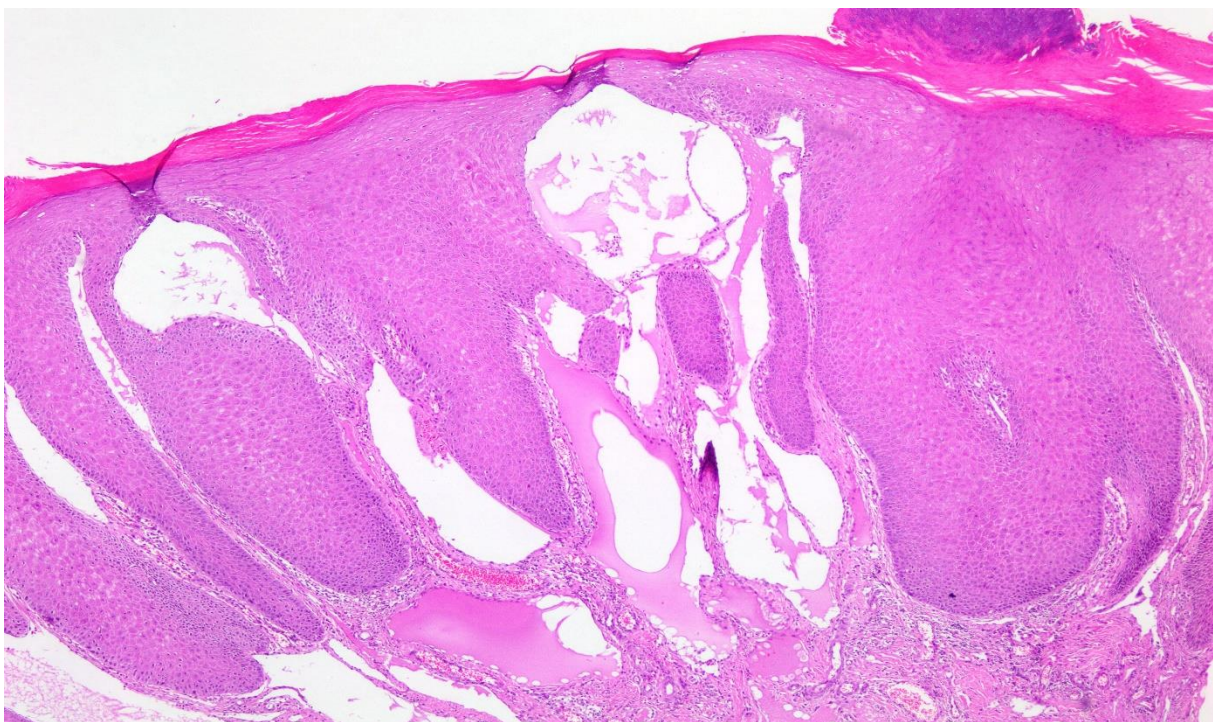


Figure 1. Lymphangioma circumscriptum: Hyperkeratosis, acanthosis and papillomatosis of the epidermis and markedly dilated lymphatic channels containing homogenous eosinophilic proteinaceous material in the papillary dermis. H&E x100

Table 1. The age, sex and tumor size distributions of the patients according to the lesion locations of head neck lymphangiomas.

Location (n)	Age (year)	Sex	Size(cm)
	Median (min-max)	Female/Male	Median (min-max)
Head			
• Face (n=15)	53 (19-68)	10/5	0,6 (0.3-1,5)
• Oral cavity (n=9)	43 (28-62)	5/4	1.7 (0.3-3)
• Orbital and periocular (n=3)	54 (48-62)	1/2	0,3 (0,3-0,6)
• Ear (n=1)	62	0/1	0.7
Neck (n=6)	35 (24-76)	1/5	3 (0,9-5)

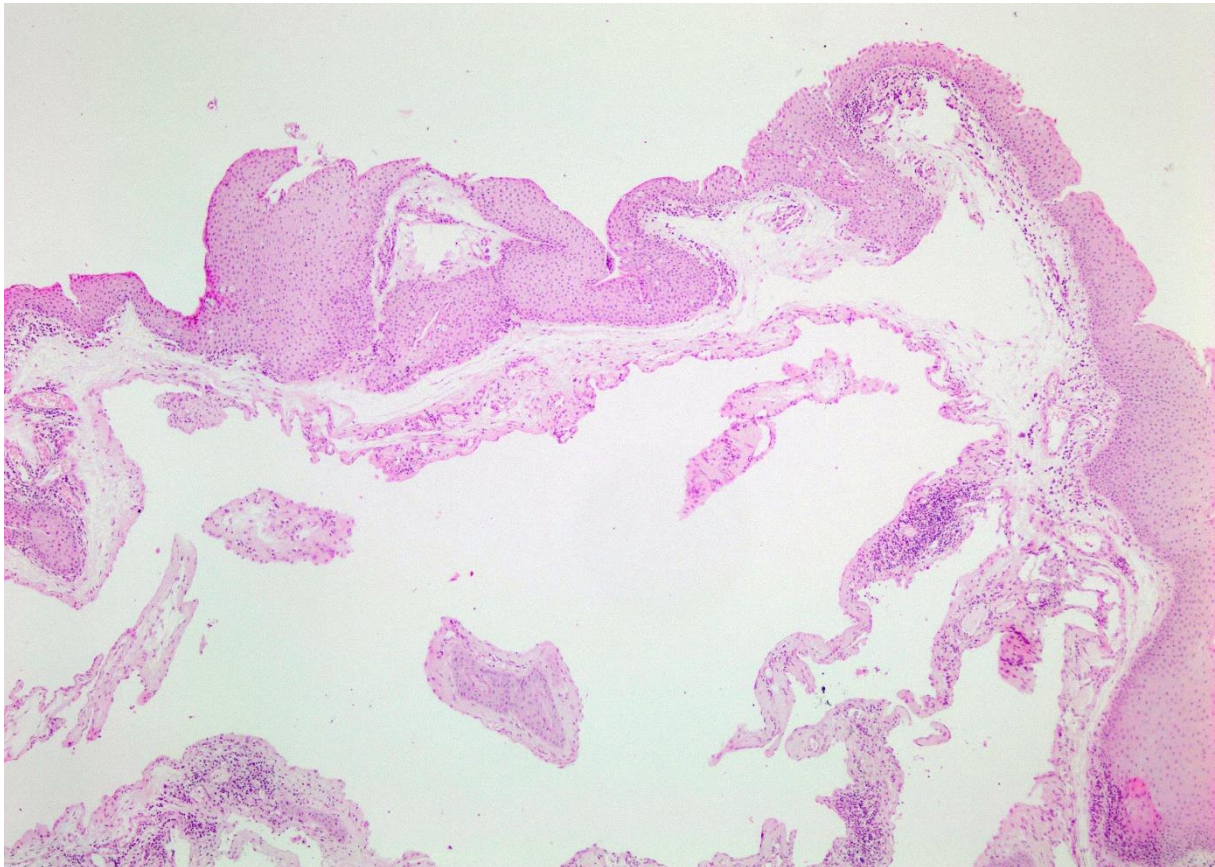


Figure 2. Cavernous lymphangioma in the conjunctiva: Lesion composed of dilated lymphatic vessels. H&E x40

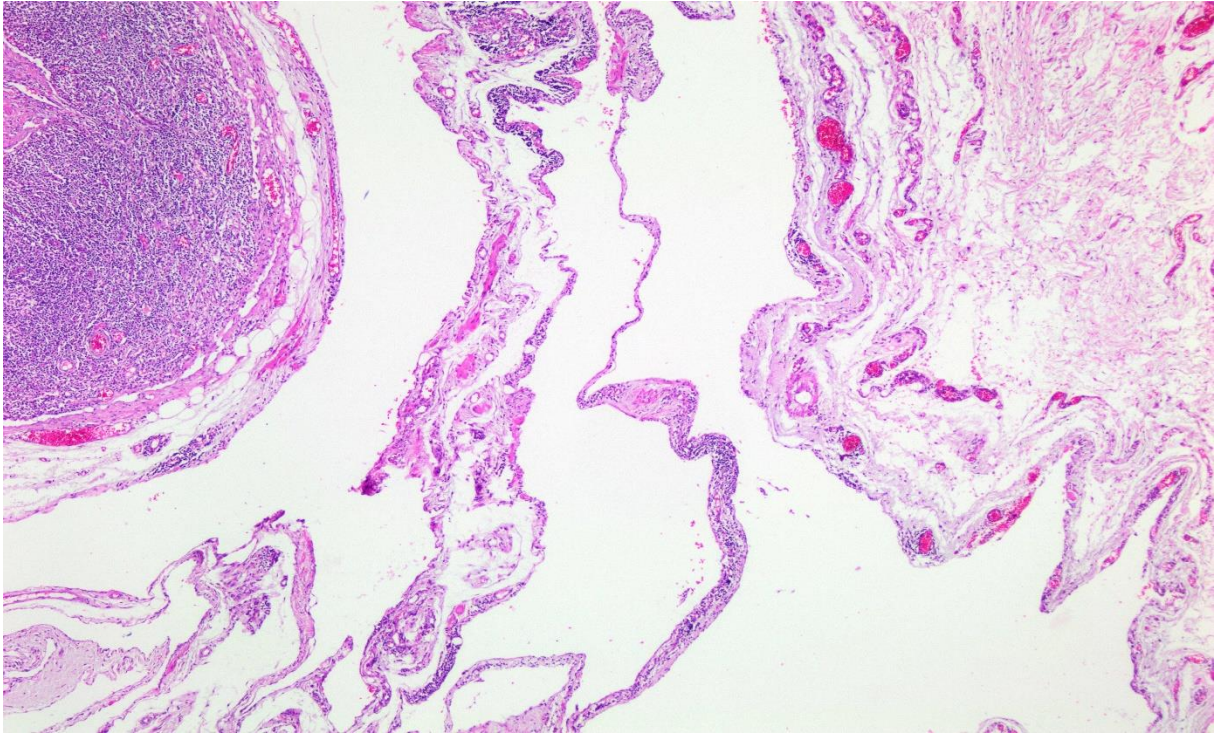


Figure 3. Cystic lymphangioma: Lesion composed of ectatic lymphatic vessels of different sizes lined with flattened endothelium. Lymphoid aggregates of varying densities are observed in septae. H&E x100.

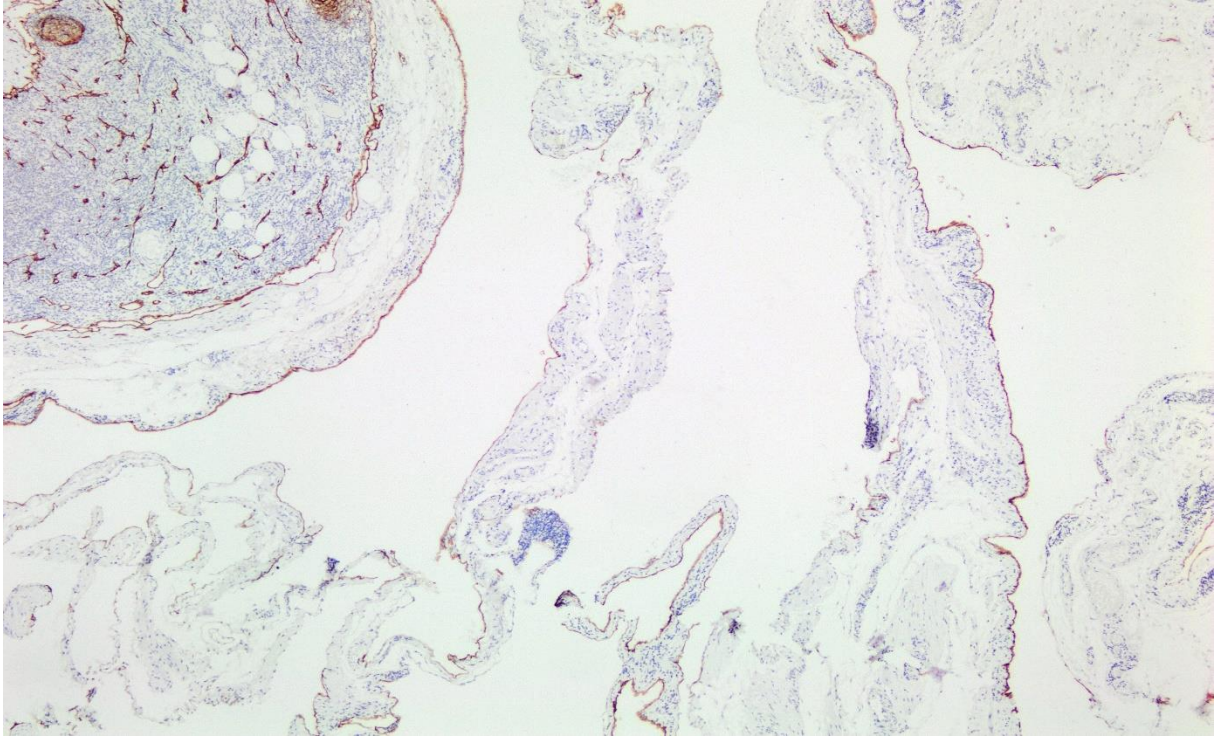


Figure 4. Cystic lymphangioma: D2-40 positivity in the endothelium lining the dilated vessels forming the lesion. D2-40 x100

Three of the lymphangiomas located on the face were defined as cavernous lymphangiomas and 12 as lymphangioma circumscriptum (Figure 1). All lesions in the oral cavity were diagnosed as cavernous lymphangioma. One of the oral lesions was located on the tongue. One of the orbital and periocular lesions was located on the conjunctiva, which was defined as cavernous lymphangioma (Figure 2). The other two lesions were located in the eyelids and were determined as lymphangioma circumscriptum, histopathologically. The lesion identified in the ear was lymphangioma circumscriptum. Four of the lesions located in the neck were cystic lymphangioma, one was cavernous lymphangioma, and the other was lymphangioma circumscriptum (Figure 3). All lesions larger than 1.5 cm were located in the neck or oral cavity. All of the lymphangiomas in the oral cavity were cavernous. All of the cystic lymphangiomas were located in the neck. Lymphangiomas were multiple in two cases, one on the face and the other in the oral cavity. There were no patients with a family history of lymphatic malformation. Genetic examinations were not performed in any patients. Patients with superficial lymphangioma presented with pale or pink vesicular lesions on the skin. The other patients presented with a painless, growing mass. All patients had cosmetic symptoms but none had symptoms related to compression of surrounding tissues such as dysphagia, dyspnea, and voice disorder. Immunohistochemical D2-40 and CD31 were positive in all patients (Figure 4). The follow-up period of the patients ranged from 5 months to 65 months; no malignant transformation was detected in any patients. Lymphangioma recurred in two patients. One case was 4.5 cm in size and a cervical cystic lymphangioma. The other patient with recurrence had an oral cavernous lymphangioma 3 cm in size. Sclerotherapy with bleomycin was administered to both patients.

Discussion

Lymphangiomas are benign malformations frequently seen in children. Sixty-five percent of lymphangiomas are congenital and 80% occur in the first two years of life². Although lymphangiomas primarily occur in children and young adults, they can be encountered at any age and have been reported in adults⁸. The oldest patient in our series was a 76-year-old male.

Lymphangiomas can affect superficial or deep tissues and they are in generally grouped as superficial and deep subject to the depth and size of lymphatic channels. Superficial lymphangiomas are defined as lymphangioma circumscriptum, deep lymphangiomas include cavernous and cystic lymphangiomas. Lymphangioma circumscriptum is mostly seen on the skin of the extremities. They usually present as multiple clusters of pale, pink or red vesicles. Histopathologically, hyperkeratosis and acanthosis of the epidermis are observed and dilated lymphatic channels containing eosinophilic proteinaceous material in the papillary dermis is distinctive. The presence of lymphatic fluid in these dilated channels is critical in distinguishing lymphangioma circumscriptum from angiokeratoma, which has a similar appearance but contains blood in the vessel lumen⁹. In our series, lymphangioma circumscriptum was located on the face, periocular, and ear skin, and all patients presented with a pink or pale vesicle on the skin. The largest lymphangioma circumscriptum in our series was 1 cm in diameter and in one patient it was multiple.

Cavernous lymphangiomas are most commonly observed in the head and neck, followed by the gastrointestinal tract, mesentery, retroperitoneum, extremities, groin and axilla¹⁰⁻¹⁵. Cavernous lymphangiomas, which consist of enlarged lymphatic vessels, usually cause painless, growing swellings. All of the lesions we detected in the oral cavity were cavernous

lymphangiomas. We also described a cavernous hemangioma on the face and in one patient on the conjunctiva.

Cystic lymphangiomas are lesions seen in the neck, axilla, groin, and abdomen, presenting as large cystic masses, also called cystic hygromas¹⁶⁻¹⁸. Microscopy examinations of cystic lymphangiomas reveal that these lesions are composed of ectatic lymphatic vessels of different sizes, which are lined with flattened endothelium. In addition, lymphoid aggregates of varying densities are observed in septae. In some cases, lymphoid cells can even form lymphoid follicles³. Cystic lymphangiomas, like cavernous lymphangiomas, also present as a mass of painless, growing, swellings. Cervical cystic lymphangiomas can cause dyspnea, dysphagia or voice changes due to compression of the trachea, larynx or esophagus.

Although various treatment modalities are defined, surgical resection still seems to be the best treatment option for lymphangiomas. However, complete surgical resection of head neck lymphangiomas may be difficult or impossible. When cervical lymphangiomas are close to the upper airways and great vessels, and when they are too large, total surgical resection may not be performed or surgical complications may develop. Surgical resection may not be possible because deformity and loss of function may occur in lesions located in the retropharynx, tongue-base or oral-floor¹⁹. Especially in lymphangiomas for which complete surgical resection cannot be performed, the recurrence rate is around 39%. Recurrence may occur even after many years, but malignant transformation has not been reported²⁰. In cases where complete resection is difficult or impossible due to the location of the lesion, other treatment methods such as sclerotherapy, radiotherapy, cryotherapy, electrocoagulation or laser applications can be performed. Bleomycin or doxycycline can be used as a sclerosing agent^{5,6}. These

treatment methods can be preferred either alone or together with surgery.

Lymphangiomas in adults can be clinically confused with dermoid cysts, branchial cleft cysts, lymph node neoplasms, and especially cystic metastatic lymph nodes³. In addition, teratoma, dermoid cyst, thyroglossal duct cyst, and neurofibroma should be kept in mind in the differential diagnosis of lymphangiomas²¹. Histopathologically, lymphangiomas are similar to hemangiomas and both consist of dilated vascular structures. However, it is typical to have homogeneous eosinophilic material in lymphangiomas, whereas there is blood in the dilated vessels in hemangiomas. Panendothelial immunohistochemical markers such as CD31 and CD34 are positive in both lymphangiomas and hemangiomas, and markers such as D2-40, vascular endothelial growth factor receptor 3 and podoplanin are specific for lymphatic vessels, which is useful in distinguishing lymphangiomas from hemangiomas²². D2-40 was used in all of our cases and an immunoreaction was detected in all of them in the endothelium lining the dilated vessels forming the lesion. In conclusion, head and neck lymphangiomas are not uncommon in adults. They can be seen at any age, even in elderly patients. The lesions are generally asymptomatic and cause cosmetic problems. Cystic lymphangioma is often seen in the neck and cavernous lymphangioma in the oral cavity. Total surgical resection provides both treatment and definitive diagnosis. Recurrence can be seen, but malignant transformation is not expected.

Conflict of Interest

The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

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Ethical approval

Ethical approval was obtained for the study from the Ethics Committee of Karatay University, Faculty of Medicine (2020/007). All procedures performed in this study were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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REKÜRREN LARİNGEAL PAPİLLOMATOZİSTE GÜNCEL TEDAVİ YAKLAŞIMLARI

CURRENT MANAGEMENT APPROACHES FOR RECURRENT LARYNGEAL PAPILLOMATOSIS

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Öz

Laringeal papillomlar, solunum yolunun farklı yerlerinde epitel hücrelerinde aşırı büyümeye neden olan viral bir enfeksiyonun neden olduğu iyi huylu bir lezyondur. Etken Human Papilloma Virüsüdür. Standart tedavi yöntemi lezyonların cerrahi olarak eksizyonudur. Lazer, mikrodebrider, soğuk cerrahi aletler veya bunların kombinasyonu kullanılarak genel anestezi altında operasyon gerçekleştirilir. Cerrahi tedavi ile kontrol altına alınamayan olgularda adjuvan tedavi seçenekleri planlanır.

Anahtar kelimeler: Rekürren laringeal papillomatosis, human papilloma virüs, rekürren respiratuvar papillomatosis

Abstract:

Recurrent laryngeal papillomas are the benign lesions caused by a viral infection with overgrowth of epithelial cells in different parts of the respiratory tract. It is caused by the human papillomavirus. Standard treatment method is surgical excision of the lesions. Laser, microdebrider, cold surgical instruments or combinations can be used in operation under general anesthesia. Adjuvant treatment options are planned in cases that cannot be controlled by surgical treatment.

Keywords: Recurrent laryngeal papillomatosis, human papillomavirus, recurrent respiratory papillomatosis

Giriş

Rekürren respiratuar papillomatozis olarak da bilinen laringeal papillomatozis, çocuklarda larinksin en sık görülen benign epitelyal neoplazmidir. Respiratuar trakt epitelinin benign proliferasyonu ile karakterizedir. Tekrarlama oranının yüksek olması ve komşu solunum yollarına yayılma eğilimi nedeniyle tedavisi ve yönetimi zor bir patolojidir.

Hastaların yaşına bağlı olarak juvenil başlangıçlı veya yetişkin başlangıçlı olarak incelenir. On iki yaş altı juvenil başlangıçlı laringeal papillomatozis olarak kabul edilirken, 12 yaş üzeri başlangıç yetişkin başlangıçlı laringeal papillomatozis olarak kabul edilir. Juvenil başlangıçlı papillomatozis olgularında bulaş doğum esnasında vertikal geçiş ile yakından ilişkilidir. Annenin ilk doğumunun olması, genital siğil varlığı ve ilk doğan çocuk olması risk faktörleri arasındadır¹. Erişkin başlangıçlı papillomatoziste risk faktörlerinin ise cinsel partner sayısı ile ilişkili olduğu gözlenmiştir¹.

Juvenil başlangıçlı laringeal papillomatozis daha agresif seyirlidir. Hava yolu obstrüksiyonuna neden olma, birden fazla bölge tutulumu ve sık cerrahi müdahalelere ihtiyaç duyma oranı daha yüksektir. Yetişkin başlangıçlı olan ise daha selim seyirli olma eğilimindedir. Yine de bazı erişkin başlangıçlı tipler çoğunlukla HPV alt tipine bağlı olarak agresif seyirli olabilmektedir.

Rekürren Laringeal papillomatozis (RLP), viral bir etiyolojinin neden olduğu bir hastalıktır. Etken Human Papilloma virüsüdür (HPV). HPV, epitel hücrelerini enfekte etme eğiliminde, Papovaviridea ailesinden deoksiribonükleik asit (DNA) içeren zarfsız bir virüstür. Pek çok alt tipi olmasına rağmen, HPV 6 ve HPV 11'in kondiloma lata ile ilişkili olduğu görülmüştür. HPV 16 ve 18 in aksine düşük malignite potansiyeline sahiptir. Literatür, popülasyonun %5'inin larinksinde HPV DNA taşıdığını ancak yalnızca küçük bir

kısımında RLP geliştiğini tahmin etmektedir². HPV 11'in, HPV 6'ya göre daha agresif bir kliniğe neden olduğunu gösteren çalışmalar mevcuttur³. Ayrıca RLP hastalarında %2 oranında malign dejenerasyon olabileceğine dair çalışmalar mevcuttur⁴.

Fiberoptik nazofaringolarinoskop, ameliyat öncesi tanı ve diğer ayırıcı tanıları ayırt etmek için faydalıdır. Muayene esnasında saplı veya sapsız olabilen pembemsi üzüm benzeri yapılar olarak gözlenirler. Vokal kordlar, psödostratifiye epitelden stratifiye epitele geçiş bölgesidir. Bu nedenle, respiratuar epitelde her yerde görülebilmekle birlikte, vokal kordlar papillom lezyonlarının çok sık görüldüğü bir yerdir. Hastalık için tamamen kür şansı neredeyse yoktur. Tedavide amaç hava yolu açıklığını sağlamak ve ses kalitesinin korunmasıdır. Hastalar genellikle bir yılda birden fazla kez cerrahi tedaviye gereksinim duyar. Cerrahi ile kontrol altına alınamayan hastalarda adjuvan tedavilere yer verilir. Tanının ilk beş yılında ortalama ameliyat sayısının yılda 5,1 olduğu, 15 yıl sonra ise yılda 0,1'e düştüğü bildirilmiştir⁵.

RLP, tedavisi ve yönetimi zor bir hastalıktır. Geleneksel tedavi yöntemi cerrahidir. Genel anestezi altında, lazer, mikrodebrider veya soğuk cerrahi aletler kullanılarak operasyon gerçekleştirilir.

• Cerrahi yöntem

RLP için standart tedavi yöntemi lezyonların cerrahi olarak eksizyonudur. Cerrahinin amacı yeterli hava yolu açıklığını sağlamak ve ses kalitesini sürdürmektir. Papillomların daha geniş kapsamlı eksizyonunun, rekürrens oranını azaltmadığı görülmüştür⁶. Aksine agresif eksizyon, mukozal hasarı arttıracığından HPV ile enfekte olan hücrelerin varlığını arttırabilir. Normal dokuya verilen hasarı en aza indirmek için özen gösterilmelidir. Ön ve arka komissür tutulumu durumunda, cerrahinin sınırlı yapılması ve aşamalı cerrahi endikedir.

Hava yolu riski bu hastalarda ciddi bir endişe kaynağıdır. Bu hastalarda trakeostomiden kaçınmak gerekir. Fleksible bronkoskop veya videolaringoskop ile endotrakeal entübasyon önceliklidir. Trakeostomi, lezyonun daha hızlı alt hava yollarına yayılımına neden olabileceğinden, solunum yolu obstrüksiyonu riski olmadan tercih edilmemelidir. Trakeostomi kaçınılmazsa, hava yolu açıklığı sağlandıktan sonra en kısa zamanda dekanulasyon planı yapılmalıdır¹.

Cerrahi tedavide lazerler, elektrikli aletler, soğuk aletler ve bunların kombinasyonu kullanılabilir. Lazerlere kıyasla soğuk enstrümanlarda, komplikasyon oranında artış ve ses kalitesinde düşüş bildirilmiştir⁷.

- *Lazerler*

Süspansiyon mikrolaringoskopi eşliğinde lazer ile lezyon eksizyonu cerrahide altın standarttır.

Lazer cerrahisinin çeşitli avantaj ve dezavantajları vardır. Soğuk cerrahi aletlere göre daha iyi hemostatik özelliğe sahiptir ve daha uzun çalışma mesafelerinde çalışmaya olanak sağlar. Bununla birlikte yüksek kurulum ve bakım maliyetlerine sahiptir. Beraberinde trakea yaralanmalarına, trakeoözefageal fistül oluşumuna ve hava yolu yanıklarına neden olabilir.

İki çeşit lazer kategorisi vardır. Karbondioksit (CO₂) ve Thulium lazerler gibi suyu hedefleyen kesici /ablatif lazerler ve Potasyum Titanil fosfat (KTP) gibi hemoglobini hedefleyen fotoanjolitik lazerlerdir⁸. Günümüzde CO₂ lazer RLP olgularında en sık tercih edilen lazer çeşididir. CO₂ lazerin fotoabsorbsiyon özelliğinin yanında düşük düzeyde derin doku penetrasyonuna ve yeterli doku vaporizasyonuna sahip oluşu nedeniyle tercih sebebidir. Kesme, koterizeasyon ve vaporize etme etkisi oldukça iyidir.

- *Mikrodebrider*

Mikrodebriderler, lazer kullanımına bağlı olası riskler (trakea yaralanmaları, hava

yolu yanıkları gibi) nedeniyle son zamanlarda popülerlik kazanmıştır. Hızlı dönen bıçakları ve aspirasyon yapabilmesi nedeniyle hızlı bir debridman sağlar. Sıklıkla lazerler ile kullanılır. Mikrodebriderler papillomların büyük bir kısmını çıkartır. Ardından lazer ile hemostaz ve koterizasyon sağlanır. Termal yaralanma olmaması ve cerrahi süreyi kısaltma nedeniyle mikrodebrider kullanımı avantajlıdır.

- *Adjuvan terapiler*

RLP olgularında primer tedavi cerrahidir. Ancak cerrahi tedavi ile kontrol altına alınamayan olgularda adjuvan tedavi gereksinimi olabilir. Kesin bir endikasyon olmamakla birlikte yıl içerisinde 4-5'ten fazla cerrahiye ihtiyaç olan hastalarda cerrahlar adjuvan tedavi seçeneğini düşünüyor. Adjuvan tedavi seçenekleri arasında sidofovir, bevasizumab, fotodinamik terapi, interferon, indol 3 karbinol ve proton pompa inhibitörleri vardır. En sık kullanılan tedavi interferon alfa 2 iken, yüksek yan etkileri nedeniyle sidofovir bu ilacın yerini almıştır.

- *İnterferon*

İnterferon tedavisi RLP olgularında kullanılan ilk sistemik tedavilerden biridir⁶. İnterferonlar viral enfeksiyonlar da dahil olmak üzere çeşitli uyaranlara yanıt olarak lökositlerden salınan antijen üretimini arttıran ve immün hücreleri aktive eden proteinlerdir. İnterferon kullanımıyla birlikte rekürrenslerin azaldığını gösteren çalışmalar olmakla birlikte, tedavinin rekürrensi uzun dönemde azaltmadığını gösteren çalışmalar da mevcuttur⁶. Nörolojik bozukluklar, zihinsel problemler, trombositopeni, karaciğer enzim yükselmesi, böbrek fonksiyon bozukluğu, lökopeni, saç dökülmesi, ateş gibi yan etkileri mevcuttur. Sistemik ve lokal yan etkileri nedeniyle kullanımı sınırlıdır.

- *Sidofovir*

Sidofovir, DNA polimerazı inhibe ederek DNA virüslerinin replikasyonunu bloke eden bir sitozin nükleotid analogudur. Sitomegalovirüs, Herpes Simpleks virüs tip 1 ve 2, Varisella Zoster virüs, Epstein-Barr virüs, Human Herpes virüs tip 6 ve 8, Human Papilloma virüs ve adenovirüslere karşı potent bir etkiye sahiptir. RLP hastalarının tedavisinde 1998 yılından beri kullanılmaktadır.

İlaç genel anestezi altında mikrolaringoskopi eşliğinde yapılan operasyon sonrası papillomların derecesine göre değişen miktarlarda (2,5- 37,5 mg/ml) intralezyonel enjekte edilir, 3mg/kg dozu geçmemelidir. İntralezyonel enjeksiyon iyi tolere edilir ve sistemik toksisitesi azdır. 3-4 hafta aralıklarla uygulanır⁹.

Sidofovir kullanımıyla lezyonların gerilediği, rekürrens oranlarının ciddi oranda azaldığı, remisyona sağlandığı gösterilmiştir. Yapılan bir kohort çalışmasında, RLP hastalarında intralezyonel sidofovir enjeksiyonunun 24 aya kadar hastalıkta stabilizasyon ve %89 tam remisyona sağladığı gösterilmiştir⁹⁻¹⁰.

HPV 11 ve 6'nın larinks skuamöz hücreli karsinomuna neden olduğunu gösteren çalışmalar mevcuttur. HPV 6 ve 11 nedenli rekürren laringeal papillomatozis hastalarında malign transformasyon gelişimi %2-3 oranındayken, sidofovir sonrası displazi gelişimi %1.48'dir¹¹. Yapılan çalışmalar, HPV enfekte hastalarda sidofovir kullanımının displastik değişimi indüklediğini göstermektedir¹¹⁻¹².

- *Bevasizumab*

Bevasizumab, insan vasküler endotelial büyüme faktörü A (VEGF-A)'yı inhibe ederek anjiogenezi inhibe eden rekombinant bir monoklonal antikordur. 2004 yılında FDA onayı almıştır ve metastatik kanserlerde anjiogenez inhibitörü olarak kemoterapide kullanılmıştır. Tümörlerde kan akımını engeller ve tümör büyümesinde

yavaşlamaya neden olur. Yapılan bir çalışmada, papillom dokularında VEGF-A ve reseptörleri VEGFR-1 ve 2'nin güçlü mRNA ekspresyonu gözlenmiştir¹³. Bu gözlem üzerine papillomatozis hastalarında bevasizumab kullanımı değerlendirilmiştir. Bevasizumab, viral DNA ve apoptoz üzerine bir etkiye sahip değildir, anjiogenezi etkileyerek tümör büyümesini engeller. 2009 yılında Nagel ve arkadaşları intralezyonel bevasizumabın laringeal papillomatoziste kontrolü sağladığını bildirmiştir¹⁴. Son zamanlarda agresif papillomatozis hastalarında sistemik ve lokal bevasizumab kullanımını ve güvenliğini bildiren çalışmalar mevcuttur¹⁵⁻¹⁶. Viral enfeksiyonu ortadan kaldırmaz ancak lezyonların küçülmesine neden olur. Son yıllarda yapılan çalışmalar 200'den fazla hastada uygulanan KTP lazer ve intralezyonel bevasizumab enjeksiyonundan sonra komplikasyon gelişmemesi ve olumlu klinik sonuçlar alınması, bu tedavi yaklaşımının tedavi seçenekleri arasında listenin başlarına getirmiştir¹⁷⁻¹⁸.

- *Selekoksisib*

Selekoksisib; osteoartrit, romatoid artrit, ankilozan spondilit, yetişkinlerde akut ağrı, ağrılı menstrüasyon ve juvenil romatoid artrit belirti ve semptomlarını tedavi etmek için kullanılan siklooksijenaz-2 (COX-2) selektif nonsteroid antiinflamatuvar ilaçtır. Papillom dokusunda COX-2'nin aşırı ekspresyonu gözlenmiştir ve bu artışın epitelyal büyüme faktörü reseptörü (EGFR) ve fosfatidilinositol 3 kinaz (PI-3K) sinyalinin bir sonucu olduğu öne sürüldü¹⁹. Limsukon ve arkadaşları, papillomların EGFR, COX-2 ve prostaglandin E2'yi aşırı eksprese ettiğini öne sürerek 150 mg/gün dozunda erlotinib (tirozin kinaz inhibitörü) ve 400mg/gün dozunda selekoksisib kombinasyonunu kullanmışlardır ve trakeal ve ana bronşial yayılımı olan bir rekürren laringeal papillomatozis hastasını bu kombinasyon ile başarılı bir şekilde tedavi etmişlerdir²⁰.

Bunun ardından randomize çift körlü bir çalışma yakın zamanda tamamlanmıştır (NCT 00571701). Birincil sonuç verilerine göre selekoksib tedavisinden sonraki 12. ay değerlendirmesinde, başlangıca kıyasla papillom büyüme oranında bir değişiklik olmadığı görülmüştür. İkincil sonuç verilerine göre ise selekoksib verilen hastalarda yaş, cinsiyet ve HPV alt tipinin karşılaştırılmasında papillom büyüme oranında azalmaya neden olmadığını gösterdi.

- *PD-1 İnhibitörleri (Pembrolizumab)*

Lökositlerin yüzeyinde bulunan programlanmış hücre ölüm proteini 1 (PD-1), antijen sunan hücreler (APC) üzerindeki PD-L1 ve PD-L2 ligandlarına bağlandığında bağışıklık sistemini negatif olarak düzenler. PD-L1'in HPV ilişkili baş boyun skuamöz hücreli karsinomlarında aşırı eksprese edildiği görülmüştür. Pembrolizumab gibi PD-1 inhibitörleri, PD-1 ve ligandları arasındaki etkileşimi bloke eder ve HPV ile ilişkili baş boyun skuamöz hücreli karsinomları dahil olmak üzere çok sayıda tümörde klinik etkinliğe sahiptir. Bu durum araştırmacıları HPV'nin neden olduğu RLP hastalarında da bu ilacın etkinliğini araştırmaya da sevk etmiştir. Halen süren bir klinik çalışma mevcuttur (NCT02632344)).

- HPV Aşısı

Şu an güncel olarak 2 HPV aşısı mevcuttur. Biri, HPV-16 ve HPV-18'in L1 kapsid proteinlerine karşı tasarlanmış bir bivalan aşı, diğeri ise HPV-6, HPV-11, HPV-16 ve HPV-18'e karşı profilaktik bir etkiye sahip kuadrivalan aşıdır. Bivalan aşı HPV-16 ve HPV-18'e karşı olması nedeniyle serviks kanserlerinden korusa da HPV-6 ve HPV-11'in neden olduğu RLP'yi etkilemez. Kuadrivalan aşı ise HPV'nin RLP etyolojisinde tanımlandığından beri hastalık yönetiminde kullanılmaya başlandı²¹. Retrospektif olarak yapılan bir çalışmada, kuadrivalan aşı yapılan 20 RLP hastasında

%65 oranında tam veya kısmi remisyon ve cerrahi müdahaleler arasında 3,1 aylık bir artış raporlamışlardır²². Yapılan olgu sunumlarında kuadrivalan aşı ile tedavi edilen papillomatozisli hastalarda, ameliyat aralarında artış ve azalan nüks oranları bildirildi²³.

Sonuç

Rekürren laringeal papillomatozis, hem yetişkinleri hem de çocukları etkileyebilen solunum yollarının kronik bir durumudur. Birinci basamak sağlık hizmeti hekimleri, acil servis hekimleri, kulak burun boğaz uzmanları, enfeksiyon hastalıkları uzmanları ve anestezi uzmanlarını içeren bir ekip tarafından yönetilmelidir. Birincil tedavisi cerrahidir. Cerrahide lazerler, elektrikli aletler, soğuk aletler ve bunların kombinasyonu cerrahın deneyimine ve hastane koşullarına göre seçilebilir. Hava yolu riski taşıyan hastalarda fleksible bronkoskop veya videolaringoskop ile endotrakeal entübasyon önceliklidir. Trakeostomi kaçınılmazsa en kısa sürede dekanülasyon planı yapılmalıdır. Adjuvan tedaviler, cerrahinin hastalığı kontrol edemediği durumlarda kullanılır ve adjuvanların etkinliği, cerrahi prosedürler arasındaki zaman aralığını artırmakla sınırlıdır.

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INFORMATION AND SUPPORT NEEDS OF FIRST-DEGREE FEMALE RELATIVES OF BREAST CANCER PATIENTS

BİRİNCİ DERECE YAKINLARINDA MEME KANSERİ OLAN KADINLARIN BİLGİ VE DESTEK GEREKSİNİMLERİ

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Abstract

Introduction: The aim of this study was to assess information and support needs (ISNs) of first-degree relatives (FDRs) of women with breast cancer.

Materials and Methods: This descriptive and cross-sectional study was conducted in a university hospital's general surgery ward between January and June 2017. The population of the sample consisted of FDRs of women diagnosed with breast cancer and admitted to the hospital ward. The sample consisted of 110 female relatives of the patients, who met the inclusion criteria and agreed to participate in the study. The data was collected with face-to-face interviews using a Personal Information Form and the Information and Support Needs Questionnaire (ISNQ). The results were analyzed using descriptive statistics.

Results: The mean scores of importance of information needs (3.68 ± 0.36) was higher than the mean scores of importance of support needs (3.24 ± 0.58). In addition, the mean scores of meeting the information needs (2.28 ± 0.35) was higher than the mean scores of meeting the support needs (1.93 ± 0.34).

Conclusion: The findings of the study suggest that the information needs were regarded as more important than the support needs, and the information needs were met more often than the support needs.

Nurses should record the family histories of FDRs of breast cancer patients, assess these histories in light of the danger for breast cancer and meet the information needs of the relatives.

Keywords: Breast cancer, high-risk women, first-degree relatives, information and support needs, nursing.

Öz

Giriş: Bu çalışma, birinci derece yakınlarında meme kanseri olan kadınların bilgi ve destek gereksinimlerini (ISNs) belirlemek amacıyla yapılmıştır.

Gereç ve Yöntem: Araştırma, bir üniversite hastanesinin Genel Cerrahi Servislerinde Ocak-Haziran 2017 tarihleri arasında tanımlayıcı ve kesitsel olarak yürütülmüştür. Araştırmanın evrenini bu tarihler arasında servise yatan meme kanserli kadın hastaların birinci derece kadın yakınları (FDRs), örneklemini ise araştırma kriterlerine uyan ve araştırmaya katılmaya gönüllü olan toplam 110 hasta yakını kadın oluşturmuştur. Veriler “Kişisel Bilgi Formu” ve “Bilgi ve Destek Gereksinimleri Ölçeği” kullanılarak yüz yüze görüşme tekniği ile toplanmıştır. Verilerin analizinde tanımlayıcı istatistikler (sayı, yüzde, ortalama ve standart sapma) kullanılmıştır.

Bulgular: Araştırmada kadınların bilgi gereksinimlerinin önemi puan ortalamalarının (3,68±0,36) destek gereksinimlerinin önemi puan ortalamalarına göre (3,24±0,58) daha yüksek olduğu bulunmuştur. Aynı zamanda, kadınların bilgi gereksinimlerinin karşılanma düzeyi puan ortalamalarının da (2,28±0,35) destek gereksinimlerinin karşılanma düzeyi puan ortalamalarından (1,93±0,34) daha yüksek olduğu tespit edilmiştir.

Sonuç: Sonuç olarak, kadınların bilgi gereksinimlerinin, destek gereksinimlerinden daha çok önem taşıdığı ve bilgi gereksinimlerinin karşılanma düzeylerinin, destek gereksinimlerinin karşılanma düzeylerinden daha yüksek olduğu saptanmıştır.

Anahtar Kelimeler: Meme kanseri, yüksek riskli kadınlar, birinci derece yakınlar, bilgi ve destek gereksinimleri, hemşirelik.

Introduction

Breast cancer is the most common cancer in women, and is a serious source of concern¹⁻². It affects annually more than 1.5 million people worldwide, and also ranks first among the deaths caused by cancer in women³.

As with other types of cancer; genetic, hormonal, and environmental factors all together cause to the formation of breast cancer⁴. A genetic factor is the most important non-changeable factor in the formation of breast cancer⁵⁻⁶. 15% of female patients with breast cancer have a family history⁷. It appears that having a family history increases the risk of having breast cancer 1,8 times if a FDR has the disease, and 2,9 times if two people in the family have the disease⁸⁻⁹. FRDs may not always be able to cope with the increased risk, face difficulties, and manage the process¹⁰⁻¹¹. Therefore, active screening programs for early diagnosis of women at high risk plays an important role in reducing breast cancer mortality rates¹²⁻¹³. To diagnose cancer in the early phase, each community should determine own specific

breast cancer risks, determine the risk groups, and execute the screening programs regularly. Assessing and meeting the ISNs of high-risk women and monitoring these groups has been an important step recently in preventing breast cancer¹⁴⁻¹⁵.

Information, counselling, and emotional support needs of female FDRs of women with breast cancer are increasing, and these women are more vulnerable to stress caused by perception of high cancer risk¹⁶. Studies also indicate that it is important to meet this information and support to facilitate coping with stress factors related to breast cancer¹⁷⁻¹⁹.

Nurses, as a part of the healthcare personnel who spend the most time with the relatives of the patients, such as during the early diagnosis stage and the treatment, should not forget they have the responsibility of giving evidence-based education related to the risk factors and the breast health to the women^{18,20}. Cognizant of the support needs of the relatives of the patients it is important that nurses also keep informing them and reflect these needs into the care process. This research was conducted to determine the ISNs of FDRs of women with breast cancer and to have a contribution to the existing literature.

Materials and Methods

- *The Population and the Sample of the Study*

The population of the research consisted of FDRs of women who were diagnosed by breast cancer and were admitted to the general surgery ward during January and June 2017. The sample of the study consisted of 110 female relatives of the patients who met the inclusion criteria and gave consent to contribute to this research.

The inclusion criteria for the study were:

1. Agreeing to participate in the study,
2. Being at least 18 years old,
3. Being able to communicate,
4. One or more relatives having breast cancer,
5. Not having breast cancer herself.

- *Data Collection*

The data was composed using face-to-face meetings after giving the participants information about the study and gaining informed consent. The data was gathered using a Personal Information Form developed by the researchers in line with the literature, and the ISNQ and lasted for approximately 30 minutes. A pilot study was conducted with 10 women, and the data obtained from these interviews were not included in the study.

- *Personal Information Form*

The personal information form included 11 questions such as age, educational position, marital position, occupational position, economic level, and questions related to breast cancer awareness, such as the number of relatives with breast cancer and the relationship, breast self-examination practice frequency, previous support

received regarding breast cancer risks, and the person giving the support.

- *Information and Support Needs Questionnaire (ISNQ)*

The ISNQ was developed by Chalmers et al. (2001) to assess the ISNs of FDRs of women with breast cancer. The questionnaire is a Likert type scale and consists of two scales: "Importance of Needs" and "Meeting Needs"^{21,22}.

1. Importance of Needs Scale: This scale consists of 29 items. First 18 items of the scale assess information needs, and the remaining 11 items assess the support needs²¹⁻²². Each item of the scale scores between 1 and 4 (response options 1 to 4 range from "not important" to "very important").

2. Meeting Needs Scale: The same items as in the Importance of Needs Scale are used in this scale, however, this scale assesses the level of the needs met. Each item is scored between 1 and 4 (response options 1 to 4 range from "not met at all" to "fully met")²¹. The Cronbach Alpha of Importance of Needs scale modified to Turkish by Zorukos and Karayurt (2008) was 0.81, and 0.83 for Meeting Needs Scale¹⁸. The Cronbach alpha of Importance of Needs Scale was 0.88 in our study, and 0.86 for Meeting Needs Scale.

- *Ethical Approval*

Permission was obtained via e-mail from Zorukos Tokkaya, who conducted the reliability and validity tests for Turkish. An approval from the Cukurova University's Non-Invasive Clinic Research Ethics Committee (Decision no:14 Date: 04.11.2016) was also obtained to conduct this study, and necessary institutional permissions were obtained from the hospital management where the data was

gathered. In addition, verbal consents were obtained from the participants who agreed to take part in the study, upon informing them regarding the study.

- *Analysis of the Data*

The data were analyzed by means of Statistical Package for the Social Sciences (SPSS) 20.0 program. The results were analyzed using descriptive statistics (frequency, percentage, mean, and standard deviation).

Results

The mean age of the women contributing in the research was 41.31 ± 14.54 , 30,9 % of the participants were between the age of 31 and 45, 34.5% were primary school graduates, 60.9% were married, and 80% lived in nuclear families. 76.3% of the women were unemployed, and 64.5% of the women reported their incomes being equal to their expenditure. 82.7% of the women had one relative with breast cancer, and 45.5% reported their mother having breast cancer. Findings regarding breast self-examination practices revealed that 44.5%

of the women did not perform breast self-examination. 69.1% of the women reported they had not received any support previously related to the risk of breast cancer. The participants stated having received support previously from doctors (19.1%) and nurses (4.6%). The scale contains 29 items in overall. The primary 18 objects are related to the information needs, and the remaining 11 objects represent the support needs. The mean scores of the importance of the information needs of the participants were higher (3.68 ± 0.36) than the mean scores of the importance of support needs (3.24 ± 0.58). The mean scores for meeting the information needs (2.28 ± 0.35) was higher than the mean scores of meeting the support needs (1.93 ± 0.34) (Table 1).

Three items had the same mean scores as the most important information needs. These items were “Information on how to talk with my relative about her experience with breast cancer”, “Information about ways I can help to decrease my relative's suffering from breast cancer”, and “Information about how to support my relative during her experience with breast cancer”.

Table 1. Item Mean Scores of Importance of ISNs and Meeting Needs Scales of the Women

	Importance of Needs		Meeting Needs	
	Information Needs	Support Needs	Information Needs	Support Needs
Item number	18	11	18	11
Levels of Importance of Information and Support Needs	3.68 ± 0.36	3.24 ± 0.58	2.28 ± 0.35	1.93 ± 0.34

Table 2. Information (1-18) and Support (19-29) Needs Questionnaire's Ranked Item Mean Scores (n = 110)

Item No	Needs	Importance	Needs Met
1*	Information on how to talk with my relative about	3.87 ± 0.43	1.81 ± 0.63
12*	Information about ways I can help to decrease my	3.87 ± 0.39	1.47 ± 0.66
13*	Information about how to support my relative	3.87 ± 0.41	1.50 ± 0.60
4*	Information about the emotional reactions of	3.86 ± 0.46	2.42 ± 0.60
5*	Information about the emotional reactions and	3.85 ± 0.54	2.59 ± 0.51
10*	Information about how to talk with my children	3.80 ± 0.59	1.64 ± 0.67
6*	Information about how to talk with my family (spouse/partner,children	3.78 ± 0.58	2.05 ± 0.71
9*	Information about my daughter's risk for breast	3.75 ± 0.72	2.07 ± 0.59
2*	Information about what causes breast cancer.	3.73 ± 0.62	2.45 ± 0.66
21**	Regular examinations of my breasts by a knowledgeable health	3.67 ± 0.65	2.52 ± 1.09
15*	Information and demonstration of breast self	3.65 ± 0.77	3.27 ± 0.90
7*	Information about my own personal risk for breast	3.63 ± 0.86	2.19 ± 0.57
23**	Support to help me deal with my worries about my	3.63 ± 0.70	2.45 ± 0.92
14*	Information about possible risk factors for breast cancer (e.g. high fat diet, hormone replacement therapy, etc.).	3.62 ± 0.70	2.75 ± 0.55
3*	Information about the treatments for breast cancer	3.61 ± 0.68	2.53 ± 0.57
24**	Have a knowledgeable health professional watch me do breast self-examination and check that I am doing it	3.59 ± 0.84	1.10 ± 0.33
26**	Have a group to attend for support.	3.56 ± 0.82	3.36 ± 0.75
16*	Information about mammography screening (i.e.	3.53 ± 0.81	3.15 ± 0.95
17*	Information about how to change my behaviour to	3.52 ± 0.83	3.12 ± 0.76
11*	Information about changes in my health habits	3.51 ± 0.79	2.83 ± 0.54
8*	Information about how to talk with my family about	3.50 ± 0.90	1.81 ± 0.68
28**	Support to help develop a "plan" if I should get	3.49 ± 0.88	2.39 ± 0.85
18*	Information about genetic counseling for myself and	3.44 ± 0.89	1.53 ± 0.69
27**	Support to help me "come to terms" with my	3.43 ± 0.96	2.37 ± 0.91

22**	Support to help me carry out breast self-examination	3.24 ± 0.93	2.88 ± 0.85
19**	Reminders for mammography appointments (i.e.	2.99 ± 1.03	1.00 ± 0.00
29**	Support to help me decrease my worries about	2.87 ± 1.28	1.15 ± 0.47
20**	Reminders for breast self-examinations (i.e. sent out	2.77 ± 1.06	1.00 ± 0.00
25**	Have someone to talk to about my worries about my	2.45 ± 1.20	1.01 ± 0.10

*Items of information needs **Items of support needs

Three most important support needs items were stated respectively as “Regular examinations of my breasts by a knowledgeable health professional” (3.67 ± 0.65), “Support to help me deal with my worries about my relative's illness” (3.63 ± 0.70) and “Have a knowledgeable health professional watch me do breast self-examination and check that I am doing it properly” (3.59 ± 0.84) (Table 2).

The first three items of information need to be stated as being met the most by the women were “Information and demonstration of breast self-examination” (3.27 ± 0.90), “Information about mammography screening” (3.15 ± 0.95), and “Information about how to change my behaviour to promote my health” (3.12 ± 0.76). The first three items of support need stated as being met the most by the women were stated respectively as “Support to help me carry out breast self-examination on a regular basis” (2.88 ± 0.85), and “Regular examinations of my breasts by a knowledgeable health professional (2.52 ± 1.09) (Table 2.).

Discussion

FDRs knowing what information and support they need will facilitate the approach of healthcare professionals. This study assessed the ISNs, and the needs met, of FDRs of women who had breast cancer. The mean scores of the importance of

information needs (3.68 ± 0.36) were higher than the mean scores of the importance of support needs (3.24 ± 0.58) (Table 1). The results of the study are similar to the literature⁶. In a study by Andiç and Karayurt (2012), the mean scores of the importance of information needs (3.72 ± 0.19) were higher than the mean scores of the importance of support needs (3.24 ± 0.41)²³. It should be borne in mind that FDRs of women with breast cancer are not only a source of support for their loved ones, but their health can be enhanced by providing early diagnosis.

The items of the importance of information needs stated as the most significant by the women had equal scores (3.87) and were “Information on how to talk with my relative about her experience with breast cancer”, “Information about ways I can help to decrease my relative's suffering from breast cancer”, and “Information about how to support my relative during her experience with breast cancer” (Table 2). The results of the study partially differ from the literature²⁴⁻²⁶. These behavioral differences may originate from ethnic background, and cultural structure of the society may result in not paying attention to their own risks, focusing on the relatives' disease instead. FDRs are interested in the psychological condition of the patient, and try to engage in beneficial communication with the patient. It is possible that the relatives of the patients are concerned about the psychological condition of the patient and try to engage in constructive

communication. In addition, the statements of the participants might indicate that the healthcare personnel do not assess the psychological conditions of the patients adequately during treatment and care.

Three of the most valued importance of support needs items were stated respectively as “Regular examinations of my breasts by a knowledgeable health professional” (3.67 ± 0.65), “Support to help me deal with my worries about my relative's illness” (3.63 ± 0.70) and “Have an expert health professional watch me do breast self-examination and check that I am doing it properly” (3.59 ± 0.84) (Table 2). Three of the most valued importance of support needs items in a study by Tunin et al. (2010) were stated as “Regular examinations of my breasts by an expert health professional”, “Have an expert health professional watch me do breast self-examination and check that I am doing it properly”, and “Have someone to talk to about my worries about my relative with breast cancer”²⁶. The support needs of the women taking part in this study are in accordance with the literature^{14,27}. This suggests that the participants need professional support and validating from the healthcare personnel. It is possible that the healthcare personnel do not allocate enough time to teach breast self-examination, explain the importance of breast self-examination, and have activities regarding the concerns related to the disease to the women who are at high danger of breast cancer.

The mean scores of meeting information needs were higher (2.28 ± 0.35) than the mean scores of meeting support needs (1.93 ± 0.34) (Table 1). These findings are in accordance with the literature^{14,26,28}.

The highest three items reported by the participants regarding meeting information needs were respectively “Information and demonstration of breast self-examination”, (3.27 ± 0.90), “Information about mammography screening (3.15 ± 0.95) and “Information about how to change my behaviour to promote my health” ($3.12 \pm$

0.76) (Table 2). The findings regarding meeting information needs reported by the participants are in accordance with the literature^{24,26,28}. The results demonstrate that women in the risk group receive sufficient information regarding mammography, and it is important to increase education provided on breast cancer screening^{29,30}. Advances in medical science, and specialization of health professionals in their own field may have contributed to the progress in this area. Information needs to be stated as being met the least in the participants were “Information about ways I can help to decrease my relative's suffering from breast cancer” (1.47 ± 0.66), “Information about how to support my relative during her experience with breast cancer” (1.50 ± 0.60), and “Information about genetic counselling for myself and my children” (1.53 ± 0.69). In a study these findings by Tunin et al. (2010), it shows parallelism with the research²⁶. These findings suggest that women who are at high risk do not have enough information on how to discuss the experienced sadness and how to support relatives with breast cancer. Not knowing how to discuss the risk of having breast cancer herself or the possibility of their children having it, and having information needs regarding genetic consulting been met very insufficiently might be an indication that the healthcare personnel give mainly information about the illness and the treatment, but do not meet the information needs regarding correct and helpful communication between the patients and their families. In addition, suggest that healthcare personnel do not carry out their role as a genetic consultant to meet the information needs of the patients. Different studies have demonstrated that measuring insufficiency in genetic risk knowledge is highly challenging, there is a lack of adequate counselling, and insufficient information regarding the issue³¹⁻³³.

The first three support needs items reported as being met the highest by the participants were “Reminders for breast self-

examinations” (3.36 ± 0.75), “Support to help me carry out breast self-examination on a regular basis” (2.88 ± 0.85) and “Regular examinations of my breasts by a knowledgeable health professional” (2.52 ± 1.09) (Table 1). Support needs items reported as not being met by the participants were “Reminders for mammography appointments” and “Reminders for breast self-examinations” (Table 1). The support needs of the participants in this study included reminders for mammography and for self-examinations, and although these results differ from the studies made outside of Turkey, they are in accordance with the studies conducted in Turkey²⁴⁻²⁶. The healthcare system in Turkey does not have practices reminding the women their mammography appointments and breast self-examinations, which might be the reason the findings differ in Turkey. Although the findings of the study partly differ from the literature conducted outside of Turkey due to cultural differences, technological advances, and the changes in the health system, the ISNs of women regarding breast cancer are similar in studies conducted in Turkey and in the world.

As a conclusion: the information needs were regarded as more significant than the support needs of the participants, and information needs were met more often than the support needs. As a member of a professional occupation, nurses should record the family histories of FDRs of breast cancer patients, assess these histories in light of the danger for breast cancer and meet the information needs of the relatives. In addition, conducting further studies investigating the ISNs of the FDRs of women with breast cancer is suggested.

Conflict of Interest

The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

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Ethical approval

Cukurova University’s Non-Invasive Clinic Research Ethics Committee. (Decision no:14 Date: 04.11.2016)

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RENAL PELVİSTEKİ İDRARIN ÜRETER TAŞININ İMPAKTASYONUNU BELİRLEMEDEKİ ROLÜ THE PREDICTIVE VALUE OF URINE IN RENAL PELVIS ON IMPACTION STATUS OF URETERAL STONE

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Öz

Giriş: Üreter taşının olduğu taraftaki renal pelvisin Hounsfield Ünitesi değerinin taşın impaktasyonu hakkında fikir verip veremeyeceğini değerlendirmek amaçlandı.

Gereç ve Yöntemler: Üreter taşı nedeniyle opere edilen hastaların, demografik verileri ile operasyon öncesi çekilen kontrastsız tomografi filmine göre hesaplanan, taşın transvers ve en uzun boyutu, üst üreterin çapı, üst üreterin alt üreter çapına oranı, taş dansitesi, renal pelvisin ön arka çapı ile renal pelvisteki idrarın ve mesanedeki idrarın HU değeri, taşın impakte olduğu ve olmadığı iki grup arasında karşılaştırıldı.

Bulgular: Hastaların ortanca yaşı 44 (37-53) yıl olup, %86,4'ü erkekti. Yaş, cinsiyet, komorbidite, taraf ve taş lokalizasyonu bakımından gruplar arasında fark yoktu ($p=0.067$, $p=0.073$, $p=0.093$, $p=0.0141$ ve $p=0.074$, sırasıyla). Renal pelvisteki idrarın HU değeri ile mesanedeki idrarın HU değeri gruplar arasında karşılaştırıldığında anlamlı farklılık görülmedi ($p=0.511$, $p=0.376$, sırasıyla). Mesanedeki idrar dansitesinin renal pelvis dansitesine oranına bakıldığında gruplar arasında anlamlı fark yoktu ($p=0.461$). Transvers taş uzunluğu, en uzun taş boyutu, üst üreter çapı ve üst üreter çapının alt üreter çapına oranı, taş dansitesi ve renal pelvis AP çapı, taş impaktasyonu olan grupta istatistiksel olarak anlamlı olacak şekilde daha büyüktü ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.025$, $p=0.016$ ve $p<0.001$ sırasıyla).

Sonuç: Transvers taş uzunluğunun, taşın en uzun boyutunun, üst üreter çapının, üst üreter çapının alt üreter çapına oranının, renal pelvis ön arka çapının ve taşın HU ünitesindeki artışın impaktasyonla ilişkisi gösterilmiştir. Renal pelvisin idrar HU değerinin impaktasyonla ilişkisi bulunamamıştır.

Anahtar Kelimeler: İmpaktasyon, üreter taşı, Hounsfield Ünitesi

Abstract

Introduction: To evaluate whether the Hounsfield Unit value of the renal pelvis on the side of the ureteral stone has any predictive value about the impaction of the stone.

Materials and Methods: Demographic data of the patients who were operated for ureteral stones and preoperative radiological parameters such as the transverse and longest size of the stone, the diameter of the upper ureter, the ratio of the upper ureter to the lower ureter diameter, the stone density, the anterior-posterior diameter of the renal pelvis, HU values of urine in the renal pelvis and urine in the bladder based on noncontrast computerized tomography were compared between the two groups with and without impacted stone.

Results: The median age of the patients was 44 (37-53) years, and 86.4% of patients were male. There was no difference between the groups in terms of age, gender, comorbidity, side and stone localization ($p=0.067$, $p=0.073$, $p=0.093$, $p=0.0141$ and $p=0.074$, respectively). When the HU value of urine in the renal pelvis and the HU of urine in the bladder were compared between the groups, no significant difference was observed ($p=0.511$, $p=0.376$, respectively). When the ratio of urinary density in the bladder to the renal pelvis density was analyzed, there was no significant difference between the groups ($p=0.461$). Transverse stone length, longest stone size, upper ureter diameter, and the ratio of upper ureter diameter to lower ureter diameter, stone density, and renal pelvis AP diameter were statistically significantly greater in the stone impaction group ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.025$, $p=0.016$, and $p<0.001$, respectively).

Conclusion: The significant relationship were found between the length of the transverse stone, the longest dimension of the stone, the diameter of the upper ureter, the ratio of the diameter of the upper ureter to the diameter of the lower ureter, the anterior-posterior diameter of the renal pelvis and the increase in the HU unit of the stone with impaction status. The urinary HU value of the renal pelvis was not found to be associated with impaction status.

Keywords: Ureteral stone, impaction, Hounsfield Unit

Giriş

Üreter taşlarına günlük üroloji pratiğinde oldukça sık rastlanır. Bu taşlar ağrı ve enfeksiyon riski yanında böbrek fonksiyonları üzerine olumsuz etkilerinden dolayı tedavi gerektirir¹. Üreter taşlarının bir kısmı spontan, bir kısmı medikal tedaviyle düşebilirken, bir kısmına da cerrahi müdahale gerekebilmektedir. Ses dalgasıyla kırma, retrograd veya antegrad üreteroskopi, laparoskopik veya açık yaklaşım cerrahi tedavi seçenekleridir². Tedavi seçiminde taşın yeri, boyutu, hastanın üriner sisteminin anatomisi gibi faktörler önemli olmakla birlikte taşın impakte olup olmadığı da dikkat edilmesi gereken bir parametredir. Taşın impakte olduğu olgularda, operasyon başarısının olumsuz etkilendiği, operasyon süresinin uzadığı ve üreter perforasyonu, avülziyonu ve üreterde darlık gelişimi gibi komplikasyon oranlarının daha yüksek olduğu bildirilmiştir^{3,4}. Taşın impakte olduğunun operasyon öncesi

belirlenebilmesi için hastanın yaşı, geçirilmiş taş cerrahisi öyküsü, operasyon öncesi C-reaktif protein değeri, eritrosit sedimentasyon hızı, hidronefroz derecesi, üreter duvar kalınlığı, taş boyutu gibi değerler önceki çalışmalarda değerlendirilmiştir^{1,5-8}. Obstrüksiyona yol açan üreter taşı renal pelvisteki idrar akımının yavaşlamasına veya durmasına neden olarak idrar retansiyonuna neden olur. Bu durum idrarın supersaturasyonuna neden olur. Süpersaturasyon çözücü sıvının içinde çözebileceğinden daha fazla çözülmemiş madde içermesi olarak tanımlanır. Süpersature idrarda çözünemeyen maddeler birikerek önce çekirdek sonrasında da kristallerin oluşumuna neden olur. Uzun dönemde bu durum taş oluşumuyla sonuçlanır⁹. Bu durumda yoğunlaşmış idrar bulunan renal pelvisten ölçülen Hounsfield Ünitesi değerinin yüksek olması beklenir. İmpakte olan bir taşın olmayan taşa göre daha fazla idrar retansiyonuna yol açması daha olasıdır. Bu çalışmada üreter taşının olduğu

taftaki renal pelvisin Hounsfield Ünitesi değerinin taşın impaktasyonu hakkında fikir verip veremeyeceği değerlendirildi. Ayrıca demografik verilerle birlikte transvers taş uzunluğu, en uzun taş boyutu, taşın üstündeki üreterin çapı, üst üreter çapının alt üreter çapına oranı, pelvisin ön arka çapı, taşın dansitesi gibi parametreleri de değerlendirildi.

Materyal ve Metot

2020 ile 2021 tarihleri arasında tek taraflı ve tek üreter taşı olan hastalara uygulanan üreteroskopik taş kırma operasyonları değerlendirildi. Operasyon verileri operasyon öncesi çekilen kontrastsız bilgisayarlı tomografi filmleri eşliğinde değerlendirildi. Hastalara operasyon öncesi operasyon ile ilgili bilgilendirme yapıp aydınlatılmış onam belgeleri imzalı olarak alındı. Operasyon öncesi tüm hastalara hemogram, biyokimya, kanama parametreleri ve idrar kültürü tetkikleri ile kontrastsız tomografi görüntüleme yöntemi rutin olarak uygulandı. Hastaların yaş, cinsiyet, boy, kilo, vücut kitle indeksi, taşın bulunduğu taraf, semptom süresi ve özgeçmiş gibi demografik verileri kaydedildi. Taşın transvers ve en uzun boyutu, üst üreterin çapı, üst üreterin alt üreter çapına oranı, taş dansitesi, renal pelvisin ön arka çapı ile renal pelvisteki idrarın ve mesanedeki idrarın HU değeri operasyon öncesi çekilen kontrastsız tomografi filmine göre hesaplandı. Operasyon sırasında veya sonrasında oluşan komplikasyonlar not edildi. Tüm operasyonlar aynı cerrah tarafından bir merkezde 7.5 F / 9.8 F üreterorenoskop (Karl Storz, Tutlingen, Germany) kullanılarak uygulandı. Taşın impaktasyon durumu operasyon sırasındaki endoskopik görünümüne göre belirlendi. Taş kırmada Holmium lazer litotriptör (Sphinx, Lisa laser, Germany) kullanıldı. Operasyon sonunda gerekli görülen hastalara üreteral çift J stent yerleştirildi.

Aynı taraf böbrekte taşı olan hastalarla opere edilen üreterde birden fazla taşı olan hastalar ve üreteral darlığı olan hastalar çalışmaya dahil edilmedi.

• İstatistiksel analiz

Veriler, Mac için SPSS sürüm 25.0 (SPSS Inc., Chicago, IL, ABD) kullanılarak analiz edildi. Normal dağılımı belirlemek için Shapiro-Wilk testi kullanıldı. Normal dağılmayan veriler medyan ve çeyrekler arası aralık (IQR) olarak verildi. İmpaktasyon olan ve olmayan grupları karşılaştırmak için Mann-Whitney U testi kullanıldı. Kategorik değişkenlerin karşılaştırılmasında ki-kare testi kullanıldı. İmpaktasyon öngörmede risk faktörleri belirlemek için regresyon analizi kullanıldı. Olasılık değerleri <0.05 anlamlı kabul edildi.

Bulgular

Hastaların ortanca yaşı 44 (37-53) yıl idi. Hastaların %86,4'ü erkekti ve hastaların %19,8'ine en az bir komorbidite eşlik ediyordu. Tablo 1'de hastaların demografik verileri sunulmuştur. Hastaların ortanca taş boyutu 9.00 (7.50-12.00) mm idi ve ortanca taş dansitesi 780.00 (641.00-1038.00) HU idi. Taşsızlık oranı %87,6 idi.

Veriler impaktasyon olan ve olmayan şeklinde ikiye ayrıldığında; yaş, cinsiyet, komorbidite, taraf ve taş lokalizasyonu bakımından gruplar arasında fark yoktu (Tablo 2). Ayrıca taşın olduğu taraftaki renal pelvisteki idrarın HU değeri ile mesanedeki idrarın HU değeri impaktasyon olan ve olmayan gruplar arasında karşılaştırıldığında anlamlı farklılık görülmedi (Tablo 2). Bunun yanında, mesanedeki idrar dansitesinin renal pelvis dansitesine oranı impaktasyon olan grupta daha yüksek olmakla birlikte gruplar arasında istatistiksel olarak anlamlı fark yoktu.

Tablo 1. Hastaların demografik verileri

		Değer
Yaş ^a		44.00 (37.00-53.00)
Cinsiyet ^b	Erkek	70 (%86.4)
	Kadın	11 (%13.6)
Taraf ^b	Sağ	38 (%46.9)
	Sol	43 (%53.1)
VKİ ^a		27.55 (24.59-29.41)
Ek hastalık ^b	Yok	65 (%80.2)
	Bir	14 (%17.2)
	Birden fazla	2 (%2.6)
Semptom süresi ^a (gün)		20.00 (12.00-30.00)
Taş boyutu ^a (mm)		9.00 (7.50-12.00)
Üst üreter çapı ^a (mm)		8.30 (6.00-10.20)
Alt üreter çapı ^a (mm)		3.70 (3.00-4.45)
Üst üreter çapı / Alt üreter çapı Oranı ^a		2.20 (1.62-2.78)
Renal pelvis AP çapı ^a		16.00 (11.57-21.00)
Taş dansitesi ^a (HU)		780.00 (641.00-1038.00)
Renal pelvis idrar dansitesi ^a (HU)		6.00 (2.00-12.00)
Mesane idrar dansitesi ^a (HU)		10.00 (6.00-15.00)
Üreteral stent ^b	Yok	47 (%58.0)
	Var	34 (%42.0)
Taşsızlık ^b	Başarılı	71 (%87.6)
	Başarısız	10 (%12.4)

^a Veriler ortanca ve çeyrekler arası aralık şeklinde sunulmuştur.

^b Veriler sayı ve yüzdelik olarak sunulmuştur.

VKİ: Vücut kitle indeksi, mm: Milimetre, HU: Hounsfield ünitesi,

Transvers taş uzunluğu, en uzun taş boyutu, üst üreter çapı ve üst üreter çapının alt üreter çapına oranı taş impaktasyonu olan grupta istatistiksel olarak anlamlı olacak şekilde daha büyüktü (Tablo 2). Ek olarak taş dansitesi ve renal pelvis AP çapı impaktasyon olan grupta istatistiksel olarak anlamlı olacak şekilde daha büyüktü. Taş migrasyonu impaktasyon olan grupta daha fazla görülürken taşsızlık oranı impaktasyon olmayan grupta istatistiksel olarak anlamlı daha fazla idi.

İmpaktasyonu öngörmeye yapılan çoklu değişken analizi sonucunda erkek cinsiyet taş impaktasyonu için bağımsız risk faktörü olarak bulunmuştur (r.0.114, %95 C.I.0.017-0.778, p=0.027). Ek olarak renal pelvis AP çapı impaktasyonu ön görmede bağımsız risk faktörü olarak saptanmıştır (r. 1.132, %95 C.I. 1.031-1.243, p=0.009). Bunun yanında taş boyutu ve taş dansitesi ile impaktasyon arasında çoklu analizde istatistiksel anlamlı ilişki saptanmamıştır (Tablo 3).

Tablo 2. Taş impaktasyonu olan grup verilerinin impaktasyon olmayan grupla karşılaştırılması

		İmpaktasyon olmayan	İmpaktasyon olan	p value
Yaş ^a		44.00 (36.00-53.00)	46.00 (41.00-59.00)	0.067
Cinsiyet ^b	Erkek	64 (%88.9)	6 (%66.7)	0.073
	Kadın	8 (%11.1)	3 (%33.3)	
Taraf ^b	Sağ	33 (%45.8)	5 (%55.6)	0.141
	Sol	39 (%54.2)	4 (%44.4)	
VKİ		27.50 (24.66-29.37)	29.30 (24.59-30.12)	0.017*
Taş lokalizasyonu ^b	Distal	34 (%47.2)	0	0.074
	Orta	14 (%19.4)	1 (%11.1)	
	Proksimal	24 (%33.3)	8 (%88.9)	
Ek Hastalık ^b	Yok	58 (%80.5)	7 (%77.7)	0.093
	Bir	12 (%16.6)	2 (%22.3)	
	Birden fazla	2 (%2.9)	0	
Semptom süresi ^a (gün)		20.00 (12.00-33.00)	15.00 (12.00-30.00)	0.314
Transvers taş uzunluğu ^a (mm)		6.70 (5.85-8.00)	9.00 (6.00-9.50)	<0.001*
En uzun taş boyutu ^a (mm)		9.00 (7.50-12.00)	10.00 (9.00-12.00)	<0.001*
Üst üreter çapı ^a (mm)		8.05 (5.85-10.15)	10.00 (8.30-11.00)	<0.001*
Alt üreter çapı ^a (mm)		3.70 (2.95-4.50)	3.65 (3.25-4.35)	0.055
Üst üreter / Alt üreter Oranı ^a		2.11 (1.59-2.73)	2.67 (2.36-3.15)	0.025*
Pelvis AP çapı ^a		14.65 (11.20-19.80)	21.00 (16.00-25.00)	<0.001*
Taş dansitesi ^a (HU)		752.00 (636.00-1038.00)	816.00 (755.00-1027.00)	0.016*
Renal pelvis idrar dansitesi ^a (HU)		5.50 (2.00-12.00)	6.00 (2.00-13.00)	0.511
Mesane idrar dansitesi ^a (HU)		10.00 (6.00-15.45)	10.00 (8.00-15.00)	0.376
Mesane/Renal pelvis idrar HU oranı ^a		1.50 (0.77-2.90)	2.50 (0.33-5.25)	0.431
Taş migrasyonu ^a	Yok	72 (%100)	0	0.022#
	Var	0	9 (%100)	
Taşsızlık ^b	Başarılı	70 (%97.2)	1 (%11.1)	<0.001#
	Başarısız	2 (%2.8)	8 (%88.9)	

^a Veriler ortanca ve çeyrekler arası aralık şeklinde sunulmuştur.

^b Veriler sayı ve yüzdelik olarak sunulmuştur.

VKİ: Vücut kitle indeksi, mm: Milimetre, HU: Hounsfield ünitesi,

Kalın gösterilen değerler istatistiksel olarak anlamlıdır.

* Mann Whitney U testi kullanılmıştır. # Fisher's exact testi kullanılmıştır.

Tablo 3. İmpaktasyonu belirlemede risk faktörleri

Değişkenler ^a	O.R.	95% C.I.		p.
		Lower	Upper	
Yaş	.964	.897	1.036	.323
Cinsiyet (Erkek)	.114	.017	.778	.027
VKİ	1.159	.968	1.388	.107
Semptom süresi (gün)	1.019	.997	1.042	.094
En uzun taş boyutu (mm)	1.069	.841	1.359	.584
Üst üreter çapı (mm)	1.227	.868	1.735	.247
Üst üreter / Alt üreter Oran	1.036	.580	1.851	.906
Pelvis AP çapı	1.132	1.031	1.243	.009
Taş dansitesi (HU)	1.001	.998	1.004	.483
Renal pelvis dansitesi (HU)	.966	.847	1.100	.598

^a: Değişkenler: Yaş, Cinsiyet (Erkek), VKİ, Semptom süresi (gün), Sagittal taş uzunluğu (mm), Üreter üst uç diameter (mm), Oran, Pelvis AP çapı, Taş dansitesi (HU), Renal pelvis dansitesi (HU)

Tartışma

Üreter taşlarında impaktasyonun tanımı üzerine tartışmalar devam etmektedir. Bazı yazarlar impaktasyonun tanımını üreteroskopi sırasında kılavuz telin taşın proksimaline geçirilememesi olarak tanımlamıştır^{10,11}.

Diğer bir tanım, kontrast maddenin taşın distaline geçememesi olarak tarif edilmiştir¹¹. Diğer bir impaktasyon kriteri, taşın aynı lokalizasyonda iki aydan uzun süre kalması olarak tanımlanmıştır¹². Taşın orta veya ileri derecede hidronefroza yol açması impaktasyon kriterlerinden biri olarak tarif edilmiştir. Taşın endoskopik olarak üreter mukozasına impakte olarak görülmesi de bir diğer tanımdır⁷. Görüldüğü üzere bu değerlendirmelerin bazıları operasyon öncesi dönemde yapılabilirken, bazıları operasyon sırasında yapılabilmektedir. Ayrıca bu tanımlamalar tartışmaya açıktır. Daha önce yapılan bir çalışmada sürenin impaktasyonu

belirlemede güvenilir bir parametre olmadığı bildirilmiştir¹³. Bu çalışmada da semptom süresinin impaktasyonla ilişkili olmadığını gözlemledik. Kontrast madde kullanılarak yapılan çekimler, kontrast madde alerjisi, uygulama güclüğü gibi nedenlerden dolayı günlük pratikte daha az sıklıkla tercih edilmektedir. Günlük pratikte görüntüleme yöntemi olarak kontrastsız bilgisayarlı tomografi en çok tercih edilen ve kılavuzlarda ilk yapılması önerilen tetkiktir. Bu yüzden bu tanımın her hastada uygulanması mümkün değildir. Kılavuz telin taşın proksimaline geçirilememesi ve taşın üreterdeki endoskopik görüntüsü impaktasyonun tanımlanması için uygun görülmektedir. Ancak bu yöntemler sadece operasyon sırasında kullanılabilir. Her hasta için taşın sebep olduğu hidronefrozun tespiti operasyon öncesi hem kolay hem de mümkündür. Yapılan çalışmalarda da artmış pelvis çapıyla taşın impaktasyonu arasında anlamlı sonuçlar bulunmuştur. Bu çalışmamızda da artmış renal pelvis ön arka çapının impaktasyonu tahmin etmede

önemli bir parametre olarak kullanılabileceğini belirledik. Hwang ve ark. impakte ureter taşlarının poliplerin oluşumuna ve ureterde darlık gelişimine neden olarak daha ileri seviyede hidronefroza yol açtığını bildirmişlerdir¹⁴. İmpakte olmuş ureter taşlarının tedavisinde hem başarı oranlarının göreceli olarak düşük olması hem de komplikasyon oranlarının daha yüksek görülmesi nedeniyle operasyon öncesi taşın impaktasyon durumunun tahmin edilmesi önemlidir. Hastanın operasyon sırasında ve sonrasında gelişebilecek olaylar konusunda bilgilendirilmesi ve uygun tedavi yönteminin seçilmesi açısından bu bilgi yol gösterici olacaktır. Günümüzde halen ureter taşlarının tedavisinin seçiminde taşın boyutuna ve lokalizasyonuna göre karar verilmesi önerilmektedir. Son yıllarda yapılan çalışmalarda boyut ve lokalizasyon dışındaki faktörlerin de operasyon başarısında etkili olduğu gösterilmiştir. Sarıca ve ark. impakte proksimal ureter taşlarında taşın bulunduğu bölgedeki ureter duvar kalınlığı arttıkça taşsızlık oranının azaldığını, rezidü fragman ve çift J stent yerleştirme ihtiyacının da arttığını göstermişlerdir¹. İleri seviyede hidronefroza sahip hastaların da operasyon sonrası taşsızlık oranlarının daha düşük olduğu rapor edilmiştir¹⁵. Bu çalışmamızda taşın böbreğe migrasyonunu, taşın impakte olduğu olgularda görüldüğünü gözlemledik. Ayrıca taşsızlık başarı oranları impaktasyon olmayan grupta anlamlı olarak daha yüksekti. Sonuçlarımız literatürle uyumlu olacak şekilde, taşın impakte oluşunun operasyon başarısını olumsuz etkilediğini göstermektedir. Üreter taşının impaktasyonunun operasyon öncesi tahmin edilebilmesi için çalışmalar yapılmış ve bazı kriterlere ulaşılmıştır. Elibol ve ark. ureter duvar kalınlığının, yaşın, taşın transvers boyutunun, taşın proksimalindeki ureter çapının, semptom süresinin ve renal pelvisin ön arka çapının artmasıyla taşın impakte olma riski arasında doğrusal bir ilişki olduğunu göstermişlerdir⁸. Başka bir çalışmada kadın

cinsiyetin, ASA skorunun yüksek olmasının, geçirilmiş taş operasyonu öyküsünün, operasyon öncesi idrar yolu enfeksiyonu varlığının ve artmış taş boyutunun impaktasyonla ilişkili olduğu rapor edilmiştir⁷. Sarıca ve ark. artmış C reaktif proteini, sedimantasyon hızı, hidronefroz derecesi ve ureter duvar kalınlığı değerinin taş impaktasyonu ile ilişkili olduğunu bildirmişlerdir⁵. Bu çalışmada transvers taş uzunluğunun, taşın en uzun boyutunun, üst ureter çapının, üst ureter çapının alt ureter çapına oranının, renal pelvis ön arka çapının ve taşın HU ünitesindeki artışın impaktasyonla ilişkili olabileceği gösterilmiştir. Taşın HU değeri ile taşın sertliği arasında doğrusal bir ilişki bulunduğundan dolayı daha sert taşlar impaktasyona daha çok sebep olabilir. Bu çalışmada erkek cinsiyet taş impaktasyonu için bağımsız risk faktörü olarak bulunmuştur. Ancak bu konu hakkında literatürde oldukça az veri mevcuttur. Bu konu hakkında yorum yapabilmek için başka çalışmalara ihtiyaç vardır.

Ancak bu çalışmamızda öngördüğümüz ureter taşının olduğu taraftaki renal pelvisin idrar HU değerinin impaktasyonla ilişkisini gösteremedik. Ayrıca mesanedeki idrar dansitesinin renal pelvis dansitesine oranında impaktasyonla ilişkili olmadığını gördük. Bunun bazı nedenleri olabilir. Örneğin idrarın süpersatüre olması için yeterince zaman geçmemiş olabilir. Ayrıca çekim yapılan hastanın hidrasyon durumu bu sonuçlarımızı etkileyebilir. Bu açıdan böyle bir çalışmanın planlanması sırasında aynı semptom sürelerine ve benzer hidrasyon oranlarına sahip hastalar üzerinde çalışma yapılması bu konuda bize daha güvenilir sonuçlar verebilir.

Çalışmamızın bazı kısıtlılıkları vardır. Birincisi ve en önemlisi hastalarla yapılan tek merkezli bir çalışma olmasıdır. Ancak bu aynı zamanda hastaların impaktasyon kriterlerinin ve tomografi verilerinin aynı hekimler tarafından standart bir şekilde değerlendirilmesine de sebep olmuştur. Bir diğeri ise hastaların semptom sürelerinin ve idrar dansitelerini etkileyecek tomografi

öncesi bir standart hidrasyon protokolünün bulunmamasıdır.

Sonuç

Üreter taşlarının tedavisi planlanırken taşın impaktasyon durumunun operasyon öncesi tahmin edilmesi tedavi başarısının ve olası komplikasyonların öngörülebilmesi açısından önemlidir. Operasyon öncesi çekilecek kontrastsız tomografi filmi ile belirlenecek transvers taş uzunluğunun, taşın en uzun boyutunun, üst üreter çapının, üst üreter çapının alt üreter çapına oranının, renal pelvis ön arka çapının ve taşın HU ünitesindeki artışın impaktasyonla ilişkili olabileceği gözönünde bulundurulmalıdır. Renal pelvisin idrar HU değerinin impaktasyonla ilişkisi bu çalışmada gösterilememekle birlikte benzer semptom sürelerine ve hidrasyon oranlarına sahip hastalar üzerinde çalışma yapılabilir.

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SECOND-LOOK LAPAROSCOPY CAN BE AN EARLY DIAGNOSTIC TECHNIQUE FOR ISCHEMIC COLITIS AFTER OPEN REPAIR OF RUPTURED ABDOMINAL AORTIC ANEURYSM RÜPTÜRE ABDOMİNAL AORT ANEVİZMA TAMİRİ SONRASI İSKEMİK KOLİT TANISINDA LAPAROSKOPİK İKİNCİL BAKI

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Abstract

Ischemic colitis following open repair of ruptured abdominal aortic aneurysm is an infrequent but severe complication and has high mortality rates. Colon ischemia or low perfusion can sometimes be detected intraoperatively or predicted by recognizing the high-risk patients. Since postoperative diagnosis of ischemic colitis requires early suspicion and timing is crucial for the management of ischemic colitis, rapid diagnostic tools are mandatory. In this context, second-look laparoscopy is a minimally invasive technique that is performed for diagnostic purposes and reduces negative laparotomies. Here, we describe a case of ruptured abdominal aortic aneurysm with ischemic colitis that was diagnosed via planned second-look laparoscopy.

Keywords: Ischemic colitis, ruptured abdominal aortic aneurysm, laparoscopy

Öz

Rüptüre abdominal aort anevrizmasının açık onarımını takiben iskemik kolit nadir görülen ancak ciddi bir komplikasyondur ve yüksek mortalite oranlarına sahiptir. Kolon iskemisi veya düşük perfüzyon bazen intraoperatif olarak tespit edilebilir veya yüksek riskli hastaların belirlenmesiyle önceden tahmin edilebilir. İskemik kolitin postoperatif tanısı erken şüphe gerektirdiği ve iskemik kolit tedavisinde zamanlama çok önemli olduğu için hızlı tanı araçlarının varlığı zorunludur. Bu bağlamda laparoskopik ikincil bakı, tanı amaçlı yapılan ve negatif laparotomileri azaltan minimal invaziv bir tekniktir. Bu çalışmada, rüptüre abdominal aort anevrizması sonrası planlı laparoskopik ikincil bakı ile teşhis edilen iskemik kolit olgusunu sunmayı amaçladık.

Anahtar Kelimeler: Rüptüre abdominal aort anevrizması, iskemik kolit, laparoskopi

Introduction

Ischemic colitis after ruptured abdominal aortic aneurysm (RAAA) repair is one of the major complications after these operations and may lead to perforation and then intra-abdominal sepsis, which makes early diagnosis very important in the postoperative period. Although the incidence of ischemic colitis has decreased after endovascular aneurysm repairs, the incidence after open repair of RAAA remains higher comparing the endoscopic interventions¹. Early diagnosis of ischemic colitis in postoperative intensive care conditions is crucial to conclude a decision about the appropriate time and type of the intervention.

We, herein, present the case of a patient who developed ischemic colitis after open repair of a RAAA and diagnosed with bedside laparoscopy in intensive care unit at postoperative 36th hour.

• Case

An 86-year-old male was admitted to the emergency department with sudden onset of abdominal pain. On history, the pain has started a couple of hours ago and did not relieve, and the patient denied any other gastrointestinal symptoms including diarrhea, constipation or hematochezia. His medical history was remarkable for cardiovascular disease with myocardial infarction 3 months ago, and he refused to undergo surgery for coronary artery bypass grafting. He has been under medication for 75 mg clopidogrel and 100 mg acetyl salicylic acid since the cardiac event. Other comorbidities were hypertension and diabetes. On presentation, general condition was poor, blood pressure was 60/30 mmHg and pulse rate was 86/min. Physical examination revealed tenderness in the middle region of the abdomen. Laboratory findings was unremarkable other than a mild metabolic acidosis.

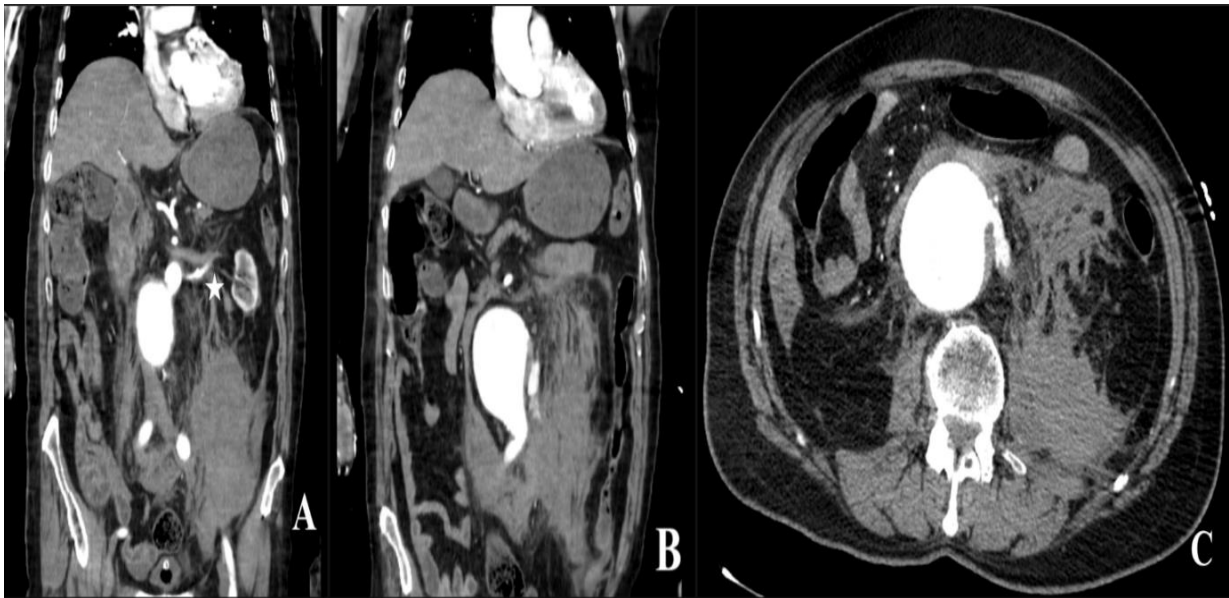


Image 1. Preoperative computed tomography angiogram images. The coronal images (A, B) show aortic abdominal aneurysm below the renal artery (star in A). Ruptured aneurysm at the left lateral wall in B and C.



Image 2. Sigmoid colon necrosis at second-look diagnostic laparoscopy in intensive care unit.

Computed tomography angiogram (CTA) showed a 6 cm diameter fusiform abdominal aortic aneurysm with ruptured left lateral wall, starting from the infrarenal level, continuing approximately 10 cm throughout to the proximal of the iliac bifurcation (Image 1). The patient was immediately brought to operating room and underwent surgery for an open repair. A tubular polytetrafluoroethylene (PTFE) graft, from the infrarenal level extending 1 cm proximal to the iliac bifurcation, was placed. During operation no gastrointestinal perfusion impairment was observed. A laparoscopic 12 mm trocar was placed in the right lower quadrant of the patient to perform second-look laparoscopy for a potential ischemic colitis. Patient was sent to intensive care unit after the surgery. During postoperative period he was treated with three types of inotropic agents, and he received low molecular weight heparin with treatment dosing of 1 mg/kg. In the 36th hour of post-surgery, he was still intubated

and due to its feasibility to perform, a bedside laparoscopy by using pre-existing trocar in intensive care unit was performed. On laparoscopy transmural necrosis of sigmoid colon was observed and patient was transferred to operating room for laparotomy (Image 2). Due to necrosis of sigmoid colon and distal descending colon, left hemicolectomy with an end colostomy was performed. There was no leakage or any other complication with the aortic graft. The patient who did not develop any complications in the postoperative period was discharged from the hospital 12 days following surgery with full recovery. Today, after two years, he is completely well and did not develop any other complications. Colostomy reversal was not planned for this patient due to his comorbidities and increased risk for general anesthesia.



Image 3. Preoperative computed tomography angiogram image. The branching of the inferior mesenteric artery (arrow) and complete filling of sigmoidal arteries.

Discussion

Ischemic colitis after ruptured abdominal aortic aneurysm (RAAA) repair is one of the major complications. Early diagnosis of ischemic colitis in postoperative intensive care conditions is crucial to conclude a decision about the appropriate time and type of the intervention. In this context, laparoscopy is a minimally invasive technique and easy to perform for a rapid and accurate diagnosis¹⁻³.

In preoperative period, demonstration of anomalies, such as absent middle colic

artery or incomplete marginal artery of Drummond or already existing arterial occlusions, with a detailed imaging study can provide to make predictions for the probability of ischemic colitis in RAAA with an impaired inferior mesenteric artery⁴. In our patient, preoperative CTA confirmed the complete and well patency of the superior mesenteric artery, and additionally inferior mesenteric artery was also patent in the initial CTA (Image 3). However, patients with renal failure is a diagnostic challenge because of the risk for developing contrast induced nephropathy. Even in postoperative newly developed renal failure, second-look laparoscopy can

replace CTA for the diagnosis of ischemic colitis and maintain renal safety of the patient⁵.

Early diagnosis of ischemic colitis is important due to high risk of mortality. Miller et al.⁶ reported high mortality rates as a result of severe colonic ischemia. In the same study bowel resections appear to be linked to late diagnosis of gastrointestinal ischemia. Authors suggest additional diagnostic work-up such as endoscopy or guaiac test for patients who have subtle signs and symptoms of ischemia.

In summary, laparoscopy as a second look procedure is a feasible technique to diagnose a possible gastrointestinal low perfusion or necrosis and it also aids surgeons to avoid unnecessary laparotomies. In RAAA, implementation of second-look laparoscopy as a step of open repair may facilitate early diagnosis of ischemic colitis.

Conflict of Interest

The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

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Ethical approval

Informed consent was obtained from the parents of the patient to publish this case in a medical journal.

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