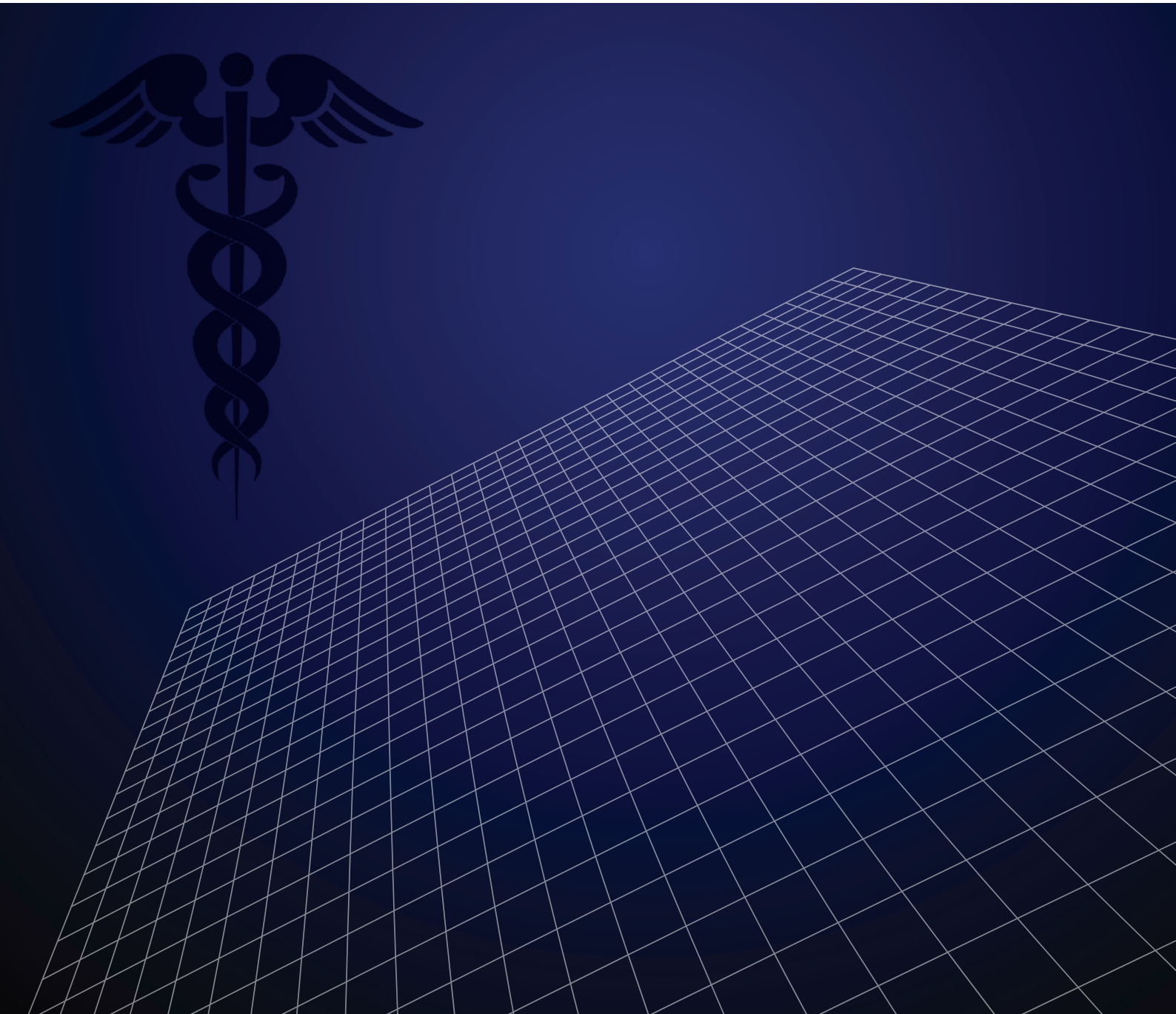
e-ISSN: 2149-8296

Turkish Journal of Clinics and Laboratory

Türk Klinik ve Laboratuvar Dergisi

Mart 2021, Cilt:12 Sayı:1



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BAŞ EDİTÖRDEN

Türk Klinik ve Laboratuvar Dergisi olarak zorlu bir yılı daha geride bırakıyoruz. COVID-19 pandemisi nedeniyle dünyanın her alanda büyük sıkıntılar yaşadığı bir yılda "uluslararası bir tabanda hastalıkların teşhis ve tedavisinde yenilikler içeren yüksek kalitede bilimsel makaleler yayınlamak" hedefimizde ilerlemeler kaydederek yolumuza devam ediyoruz.

2020 içinde planladığımız gibi 4 sayıyı zamanlamalara tam uyarak yayınladık. 4 derleme, 8 olgu sunumu, bir editöre mektuba ek olarak her bir sayıda 13, 13, 17 ve 15 olmak üzere 58 özgün makale eserler arasında yer aldı. Yüz güldürücü nokta ise bu 58 makalenin 40 tanesinin İngilizce olarak basılmasıydı. Böylece dergimizin içeriği yüzde 70 oranında yabancı dile dönüşmüş oldu. Yüksek uluslararası indekslere girmek açısından son derece önemli olan bu gelişmeyle birlikte atıf oranlarımız da çok yükseldi. Bulunduğumuz uluslararası indeksler ve başta Google Scholar içeriğinde İngilizce yayınlarla dikkat çeken dergimizin atıf oranı geçen yıla nazaran 3.2 kat yükseldi. Bu verilerle Index Medicus ön başvurusu gerçekleştirildi ve denetim süreci başladı.YÖK tarafından yakından takip edilen predatör/yağmacı dergilerin yarattığı güvensiz ortamda dergimiz en güvenli limanlardan biri olarak ön planda yer aldı.

Dergipark sisteminde yapılan düzenlemelerle online makale değerlendirme sistemi optimize edildi. Bu yenilik sayesinde hakem ekibimize, farklı branşlar/kurumlardan gelen bilim insanlarını eklemek çok daha kolaylaştı. Ayrıca değerlendirilecek makale ve hakem atama konusunda çok büyük kolaylık sağlanmış oldu. Böylece makale değerlendirme süreçlerini hızlandırabildik.

Daha önceki yıllarda kullanıma sunduğumuz sosyal medya hesaplarımız tanınırlığımıza artarak katkı sağlamaya devam etti. Gerek yayınlanan sayılarımızın duyurulması ve takibi gerekse doğrudan editöre yönelik sorulara olanak sağlaması okuyucularımıza güncel bir hizmet oldu.

2020 yılı içerisinde dergimizde bilimsel katkısı yüksek çok sayıda çalışma yayınlandı. Bizi seçen ve katkıda bulunan tüm bilim insanlarına teşekkür ediyoruz. Hepsi birbirinden değerli çalışmalar olan bu listede en çok atıf alanlar arasında diş hekimliği alanındaki ilk pilot çalışma (1), geniş bir pediyatrik hasta grubunda Çölyak hastalığında kemik dansitesini değerlendiren rapor (2), 225 hastada derin ven trombozunda farklı tedavileri karşılaştıran prospektif randomize klinik araştırma (3), Suriyeli mültecilerin doğum oranlarını inceleyen özgün karşılaştırmalı çalışma (4) ve 5000 e yakın hastada tiroid kanseri sıklığını ortaya koyan raporlar (5) sayılabilir.

Yeni yıla elbette ki yeni hedeflerle giriyoruz. Pandemi sürecini son derece olumlu sonuçlarla aşan dergimizin normalleşmenin başlamasıyla daha da ivmeleneceğine inanıyoruz. Dergimizin yapısının uluslararası yayınlara benzer şekilde kurumsallaşması değişmez çabamız olacak. Yayın içeriğimizin kalite standartlarının yükselmesi daha ileri indeks hedefimize ışık tutacak. Ulusal/uluslararası tanınırlığımızın artması, atıf sayımızın çoğalması saygınlığımızın daha da kabul görmesine destek olacak.

2020 yılı boyunca dergimize yayınlarıyla, fikirleriyle, önerileriyle katkı veren siz okuyucularımıza; desteklerini bizden esirgemeyen DNT Ortadoğu Yayıncılık Yönetim Kurulu'na ve birlikte çalışmaktan büyük mutluluk duyduğumuz yazı işlerindeki arkadaşlarımıza sonsuz teşekkür ediyoruz.

Doi: 10.18663/tjcl.903812

Saygılarımızla

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Turkish Journal of Clinics and Laboratory

To cite this article: Akkus M, Apaydin T. Clinical results of Nuss procedure for pectus excavatum in different age groups. Turk J Clin Lab 2021; 1: 1-6. [Article in Press]

Original Article

Clinical results of Nuss procedure for pectus excavatum in different age groups

Pektus ekskavatumda Nuss tekniğinin farklı yaş gruplarında klinik sonuçları

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Abstract

Aim: In 1998, Donald Nuss suggested the insertion of a metal bar behind the sternum for pectus excavatum as a minimally invasive technique. However, data regarding the relation between the age of the patient and clinical results of repair is limited. Aim of this study is to compare the clinical results of Nuss surgery for pectus excavatum in different age groups, to point out the optimal range of age for this procedure.

Material and Methods: From February 2012 to January 2020, data regarding 140 patients have been treated with Nuss surgery. We classified patients into three groups: patients younger than 15 years (group A), patients between 15 and 20 years (group B); and patients older than 20 years up to 40 years (group C) retrospectively. We evaluated patients' demographics, and compared results of surgery, duration of hospitalization and complication rates.

Results: One hundred ten patients were male and 30 were female. Male patients, clinical symptomatic patients with dyspnea in the preoperative period were seen more frequently in patients with older age, and each were statistically significant (p:0.003). In the early 30-day postoperative period, no mortality was observed. The most frequent postoperative complications were observed in group C (40,9%), followed by group B (18,2%) and group A (9,6%)(p:0.007). In logistic regression analysis, postoperative complications increased significantly in patients older than 20 years (p:0.003). Brace therapy was performed for 2 cases in Group A for recurrence after bar removal which occurred in adolescant period.

Conclusion: Nuss procedure can be recommended with low complication rates, short term hospitalization and high grade of success. Although the childhood period seems to be more suitable regarding the complications, surgery can be preferred with low recurrence rates in adolescant period.

Keywords: nuss procedure; pectus excavatum; minimally invasive repair of pectus excavatum

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Doi: 10.18663/tjcl.749597

Öz

Amaç: 1998 yılında Donald Nuss minimal invaziv teknik olarak pektus ekskavatumda sternum arkasına metal bar yerleştirilmesini önermiştir. Bununla beraber hastaların yaşları ve klinik sonuçları ile ilgili veriler sınırlıdır. Bu çalışmanın amacı, farklı yaş grupları arasında pektus ekskavatumda Nuss cerrahisinin klinik sonuçlarını karşılaştırmak, bu prosedür için en uygun yaş aralığını vurgulamaktır.

Gereç ve Yöntemler: Şubat 2012 ile Ocak 2020 yılları arasında Nuss operasyonu ile tedavi edilen 140 olgu çalışmaya alındı. Olgular 3 grup olarak sınıfandırıldı: 15 yaşından küçük olgular (grup A), 15-20 yaş aralığında olanlar (grup B), 20 yaşından büyük 40 yaşa kadar (grup C) olarak sıralandı. Hastaların, demografik yapıları, cerrahi sonuçları, hastanede yatış süreleri ve komplikasyon oranları değerlendirilerek karşılaştırıldı.

Bulgular: Yüz on hasta erkek, 30 hasta kadındı. Erkek olgular, solunum sıkıntısı klinik şikayeti olan olgular en sık ileri yaş grubunda görüldü ve istatistiksel olarak anlamlı idi (p:0.003). Erken postoperatif 30 gün ölüm izlenmedi. En sık komplikasyon grup C (%40,9), takiben grup B (%18,2) ve grup A (%9,7) görüldü (p:0.007). Lojistik regresyon analizinde 20 yaş üstü olan olgularda postoperatif komplikasyonlar anlamlı olarak yüksek bulundu (p:0.003). Ergenlik döneminde bar çıkarılması sonrası nüks gelişen 2 grup A olgusuna Brace tedavisi uygulandı.

Sonuç: Nuss tekniği, düşük komplikasyon oranı, kısa süreli hastanede yatış ve tatminkar sonuçları ile tavsiye edilebilir. Çocukluk dönemi, komplikasyonlara bağlı uygun gibi görülmesine rağmen cerrahi, nüks oranı düşüklüğü nedeniyle ergenlik döneminde tercih edilebilir.

Anahtar kelimeler: nuss tekniği; pektus ekskavatum; minimal invaziv onarım pektus cerrahisi

Introduction

In 1998, Donald Nuss suggested the insertion of a metal bar behind the sternum for pectus excavatum as a minimally invasive technique[1]. Since then, many articles have been published about this technique[2]. However, data regarding the relation between the age of the patient and clinical results of repair is limited. Optimal age reported in the literature is between 12 and 16 years [3].However, many clinicians perform this technique in both younger patients and adults [4-6]. Operations in adults have been reported to have higher rates of complication rates [3].

Aim of this study is to compare the clinical results of Nuss surgery for pectus excavatum between pediatric, adolescant and adult age groups, to point out the optimal range of age for this procedure.

Material and Methods

From February 2012 to January 2020, 140 patients have been treated with Nuss surgery in tertiary central hospital. We classified patients into three groups: patients younger than 15 years, patients between 15 and 20 years; and patients between 20 and 40 years. We evaluated patients' demographics, and compared results of surgery, duration of hospitalization and complication rates.

Degree of pectus excavatum was confirmed with computed tomography, in which the pectus index was determined by dividing the width of the chest wall at the widest point by the distance between the posterior side of sternum and anterior side of spine.

Three age groups were generated. Group A was composed of 52 patients between 3 and 14 years (mean11±3years). Group B composed of 66 patients between 15 and 20 years (mean 16.6±1.3 years). Group C composed of 22 patients between 21 and 40 years (mean 28,5±7,2 years). Ratio of males to females was 1.7(33/19) in Group A, 6.3(57/9) in Group B, 10(20/2) in Group C.

All patients were examined in the outpatient clinic in the preoperative period. Size of the chest wall was measured. Presence of asymmetry was checked. Depth of the sternal depression was also evaluated. Haller index was measured from computed tomography scans. Haller index was defined as the ratio of transverse diameter of the chest by the anterior posterior distance that shows the smallest distance between the anterior surface of the vertebra and posterior surface of the sternum.

All patients were examined with routine blood tests, pulmonary function tests, electrocardiogram, transthoracic echocardiography and thoracic computed tomography. Preoperative clinical data of patient groups is shown in Table 1. Bars composed of nickel, chromium and iron were implemented in all patient groups.

TABLE 1: PREOPERATİVE CLİNİCAL DATA OF PATİENT GROUPS					
	TOTAL (N:140)	GROUP A (N:52)	GROUP B (N:66)	GROUP C (N:22)	P
AGE	16,4±6,8 (3-40)	11±3 (3-14)	16,6±1,3 (15-20)	28,5±7,2 (21-40)	<0,001[cs]
SEX					
FEMALE	30 (21,4%)	19 (36,5%)	9 (13,6%)	2 (9,1%)	0,003[cs]
MALE	110 (78,6%)	33 (63,5%)	57 (86,4%)	20 (90,9%)	
SYMPTOMS	77 (55%)	19 (36,5%)	42 (63,6%)	16 (72,7%)	0,003k[w]
DYSPNEA	29 (20,7%)	4 (7,7%)	16 (24,2%)	9 (40,9%)	0,003k[w]
CHEST PAİN	41 (29,3%)	12 (23,1%)	23 (34,8%)	6 (27,3%)	0,368[kw]
FATİGUE	3 (2,1%)	1 (1,9%)	1 (1,5%)	1 (4,5%)	0,999[kw]
ARRHYTMİAS	4 (2,9%)	2 (3,8%)	2 (3%)	0	0,840[kw]
Data are presented as n (%) or mean±SD (range). Pearson chi-square test, Kruskall-Wallis test.					

Indications for surgery were cosmetic reasons, pectus index>3.25 or cardiac compression. Surgery was performed with general anesthesia and Nuss technique described by Donald Nuss in 1998[1]. Patients were followed at 1,3,6,12 and 24 months after the first operation and 1 and 12 months after removal of the bars.

Surgical Procedure

Two small incisions were made on each side of the chest wall on the midaxillary lines at the level of deepest chest wall depression. Introducer was placed into the right chest wall using videothoracoscopy and carbondioxide insufflation. After the introducer was passed from the right to the left chest wall from the highest hinge point, introducer was lifted and pressed the sternum to bring the proper shape to the sternum. A nylon tape was tied to the end of introducer and introducer was pulled from the contralateral side. Bent Nuss bars were binded to the end of the nylon tape, then bars were pulled with the help of the tape to the other side of chest wall. Bars were turned 180 degrees retrosternally to pick the sternum up. One fixation stabilizer were placed at the end of the bar on the right or left side to avoid bar dislocation.The number of the bars used is shown in Table 2. The bars implemented were removed 3 years after the first operation.

TABLE 2: PEROPERATİVE CLİNİCAL DATA OF PATİENT GROUPS					
	TOTAL (N:140) ±SD(MİNİMUM,MAXİMUM)	GROUP A (N:52)	GROUP B (N:66)	GROUP C (N:22)	P
HALLER İNDEX	2,9±0,4 (2,5-3,5)	2,9±0,4 (2,5-3,5)	2,8±0,4 (2,5-3,5)	2,8±0,4 (2,5-3,5)	0,481[kw]
NO. OF BARS İMPLEMENTED					
1	109 (77,9%)	47 (90,4%)	47 (71,2%)	15 (68,2%)	0,004[kw]
2	29 (20,7%)	5 (9,6%)	19 (28,8%)	5 (22,7%)	
3	2 (1,4%)	0	0	2 (9,1%)	
DURATİON OF OPERATİON(MİN.)	60,3±21,1 (15-120)	58,5±21,1 (15-120)	59,2±19,7 (30-120)	68,2±24,4 (30-120)	0,300[kw]
RECURRENCE	2	2	0	0	0.98[kw]
Data are presented as n (%) or mean±SD (range). Min: Minute, kw: Kruskall-Wallis test.					

Statistical Analyses

Statistical analysis was made using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). Pearson chi-square test was performed for categorical variables. The normality assumptions were controlled by the Shapiro-Wilk test. Kruskal Wallis test was used for comparison of non-parametric variables between groups and Bonferroni-Dunn test was used as a post-hoc test for significant cases. Binary logistic regression analysis was used to determine the effect of the study groups on postoperative complication. Data are expressed as n(%) or mean±SD (range), as appropriate. P values <0.05 were considered statistically significant.

Results

One hundred ten patients were male and 30 were female. Range of age was 3 and 40 years (mean, 16.4+-6.8 years). Male patients, symptomatic patients and dyspnea in the preoperative period were seen more frequently in patients with older age, each were statistically significant (p:0.003) (Table 1). Haller index isn't shown to have a relation with age (p:0,481). Duration of operation increased in patient groups with older age, but this wasn't statistically significant (p:0,300). In the patient groups with older age, number of bars implemented increased significantly (p:0.004) as shown in Table 2. In the early 30-day postoperative period, no mortality was observed.

The most frequent postoperative complications were observed in group C (40,9%), followed by group B (18,2%) and group A (9,6%), (p:0.007). There were no significant difference between postoperative complication rates of three groups shown in Table 3. Pleural catheter drainage was performed for pleural effusion and dyspnea for one patient from group B. Brace therapy was performed for 2 cases in Group A for recurrence after bar removal which occurred in adolescant period. Duration of hospitalization increased in older ages, but this wasn't statistically significant (p:0,552) (Table 3). In logistic regression analysis, postoperative complications increased significantly in patients older than 20 years (p:0.003) (Table 4).

TABLE 3: POSTOPERATİVE DATA OF PATİENT GROUPS

	TOTAL (N:140)	GROUP A (N:52)	GROUP B (N:66)	GROUP C (N:22)	P
COMPLİCATİONS (TOTAL)	26 (18,6%)	5 (9,6%)	12 (18,2%)	9 (40,9%)	0,007[cs]
PNEUMOTHORAX	10 (7,1%)	2 (3,8%)	4 (6,1%)	4 (18,2%)	0,096[cs]
PLEURAL EFFUSİON	4 (2,9%)	0	3 (4,5%)	1 (4,5%)	0,374[cs]
BAR DİSLOCATİON	5 (3,6%)	0	3 (4,5%)	2 (9,1%)	0,150[cs]
WOUND İNFECTİON	2 (1,4%)	0	1 (1,5%)	1 (4,5%)	0,647[cs]
BAR ALLERGY	7 (5%)	3 (5,8%)	2 (3%)	2 (9,1%)	0,610[cs]
COSTA FRACTURE	3 (2,1%)	0	1 (1,5%)	2 (9,1%)	0,064[cs]
HEMATOMA	2 (1,4%)	0	1 (1,5%)	1 (4,5%)	0,647[cs]
DURATİON OF HOSPİTALİZATİON	5,5±2,5 (2-18)	5,3±2,1 (2-14)	5,5±2,5 (2-18)	6,2±3 (3-14)	0,552

Data are presented as n (%). cs: Pearson chi-square test.

Tablo 4-Logistic regression analysis for postoperative complications

	OR (95%CI)	P
Group		
Group A	Reference	-
Group B	2,089(0,686-6,365)	0,195
Group C	6,508(1,857-22,804)	0,003

Discussion

Results of Nuss operation can vary between age groups. Data is less regarding the ideal age. In Donald Nuss' first original article, all cases were between 5 and 15 years [1]. Mean age for surgery progressed in the course of time. Etiology for this increment is reported as acquired thoracic dystrophy related with the prior radical excisional repairs of pectus [7]. Mean age has progressed to 14.4 years in USA in 2009 [8]. New data from South Korea reported that reconstruction can be performed in any age after 3 years [9]. The quantity of force needed for reconstruction at the younger age is less than half that of teens, and almost a third the force required compared to adult patients [10]. Besides, a trace of healing in scoliosis may be observed when done at a younger age [11]. Regarding the extended series from Korea, it's unnecessary to limit surgery to a specific age. On the other hand, adults have been successfully operated late in life [12].

In our study, we analyzed the results of Nuss surgery for pectus excavatum in different age groups. Group A composed of children, group B composed of adolescent patients until the completion of skeletal growth, and group C composed of adults. This classification is coherent with the consequtive phases of development and changes in the costal muscular chest wall architecture. A similar dispersion of study groups was used by Park and colleagues [9] and Kim and associates [13].

Referment with cosmetic complaints also increased significantly in other reports[2,3,4]. Zhang et al. [2] reported that usage of 2 and more than two bars increased significantly in adults. In our study, usage of 2 bars was much more in Group B and C although it was not statistically significant.

Postoperative morbidity was reported as %35 in 238 patients in the literature. In our study, its frequency increased with advancing patient age similiar to the literature [14]. Mean

number of postoperative complications of all groups was %18.6 and it increased significantly in adult group (%40.9) ($p<0.05$). The most frequent complication in the early postoperative period was pneumothorax, which was significantly more frequent in patients between 20 and 40 years of age. The occurrence of this complication varies widely up to %64 in the literature [15-18]. Surgical intervention is generally unnecessary for postoperative pneumothorax, it's prone to spontaneous recovery. The most frequent reason may be considered as insufficient implentation of reexpansion procedures during surgery.

Pleural effusion also may have occurred secondary to the increased space after reparation of the sternal position with a similiar consideration[18,19]. Thoracentesis or chest tube drainage was performed. Massive pleural effusion was drained with pleural catheter in one patient from Group B. In the literature, the reported complication rate requiring intervention is between 0.6% and 16.7% [4,20].

In several reports, it is pointed out that proper fixation of the bar is very essential. [21,22]. It's suggestted that at least 2 bars should be used in elderly patients [4]. Sliding of bars were much more in Group C in our study but this wasn't statistically significant.

Increment in bar allergies is reported in the last years' articles. Metal alloy bars were used generally. We used alloys composed of nickel, chromium and iron. Rate of metal alloy bar allergies is about %6.6 in several centers [23]. Rate of bar allergy was %5 in our series and any difference wasn't observed between age groups.

Recurrence due to rapid growth after bar removal in the adolescant period or pectus carinatum deformity may be observed although the complication rate was low during childhood [24]. Recurrence was seen in two cases in our series and they were treated via brace therapy. For this reason, repair in the adolescant period is preferred unless a serious cardiac and respiratory insufficiency is observed [25].

Limitation: Single centered cases and unequal dispersion of the groups limits the study.

Conclusion:

Nuss surgery can be recommended with low complication rates, short term hospitalization and high grade of success. Although complication rates increase at the age of 20 and above, the values are at an acceptable level. Although the childhood period seems to be more suitable regarding the complications, adolescant period can be preferred with low recurrence rates.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Nuss D, Kelly Jr RE, Croitoru DP, Katz ME. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. Journal of pediatric surgery 1998; 33: 545-52.
2. Zhang D, Tang J, Ben X et al. Surgical correction of 639 pectus excavatum cases via the Nuss procedure. Journal of Thoracic Disease 2015; 7: 1595-605.
3. Pawlak K, Gasiorowski L, Gabryel P, Galecki B, Zielinski P, Dyszkiewicz W. Early and late results of the Nuss Procedure in Surgical Treatment of Pectus Excavatum in different age groups. Annals of Thoracic Surgery 2016; 102: 1711-6.
4. Pilegaard HK. Extending the use of Nuss procedure in patients older than 30 years. Eur J Cardiothorac Surg 2011; 40: 334-7.
5. Aronson DC, Bosgraaf RP, van der Horst C, Ekkelkamp S. Nuss procedure: pediatric surgical solution for adults with pectus excavatum. World J surg 2007; 31: 26-9.
6. Coln D, Gunning T, Rmasay M, Swygert T, Vera R. Early experience with the Nuss minimally invasive correction of pectus excavatum in adults. World J Surg 2002; 26: 1217-21.
7. Haller JA, Jr., Scherer LR, Turner CS, Colombani PM. Evolving management of pectus excavatum based on a single institutional experience of 664 patients. Ann Surg 1989; 209: 578-82
8. Papandria D, Arlikar J, Sacco Casamassima MG et al. Increasing age at time of pectus excavatum repair in children: emerging consensus? J Pediatr Surg 2013; 48: 191-6
9. Park HJ, Sung SW, Park JK, Kim JJ, Jeon HW, Wang YP. How early can we repair pectus excavatum: the earlier the better? Eur J Cardiothorac Surg 2012; 42: 667-72.
10. Fonkalsrud EW, Reemtsen B. Force required to elevate the sternum of pectus excavatum patients. J Am Coll Surg 2002; 195: 575-7.
11. Park HJ, Kim JJ, Park JK, Moon SW. Effects of Nuss procedure on thoracic scoliosis in patients with pectus excavatum. Journal of thoracic disease 2017; 9: 3810-6.
12. Jaroszewski DE, Ewais MM, Chao CJ et al. Success of Minimally Invasive Pectus Excavatum Procedures (Modified Nuss) in Adult Patients (>/=30 Years). Ann Thorac Surg 2016. [9] Ewais MM, Chaparala S, Uhl R, Jaroszewski DE. Outcomes in adult pectus excavatum patients undergoing Nuss repair. Patient Relat Outcome Meas 2018; 9: 65-90

13. Kim DH, Hwang JJ, Lee MK, Lee DY, Paik HC. Analysis of the Nuss procedure for pectus excavatum in different age groups. The Annals of thoracic surgery 2005; 80: 1073-7.
14. Mao YZ, Tang ST, Wang Y, Tong QS, Ruan QL. Nuss operation for pectus excavatum: a single-institution experience. World Journal of Pediatrics 2009; 5: 292.
15. Shu Q, Shi Z, Xu WZ, Li JH, Zhang ZW, Lin R, Zhu XK, Yu JG. Experience in minimally invasive Nuss operation for 406 children with pectus excavatum. World Journal of Pediatrics 2011; 7: 257.
16. Aronson DC, Bosgraaf RP, van der Horst C, Ekkelkamp S. Nuss procedure: pediatric surgical solution for adults with pectus excavatum. World journal of surgery 2007; 31: 26-9.
17. Bosgraaf RP, van der Horst C, Ekkelkamp S. Nuss procedure: pediatric surgical solution for adults with pectus excavatum. World journal of surgery 2007; 31: 26-9
18. De Matos AC, Bernardo JE, Fernandes LE, Antunes MJ. Surgery of chest wall deformities. European Journal of Cardiothoracic Surgery 1997; 12: 345-50.
19. Cheng YL, Lee SC, Huang TW, Wu CT. Efficacy and safety of modified bilateral thoracoscopy-assisted Nuss procedure in adult patients with pectus excavatum. European journal of cardio-thoracic surgery 2008; 34: 1057-61.
20. Peter SD, Sharp SW, Ostlie DJ, Snyder CL, Holcomb III GW, Sharp RJ. Use of a subxiphoid incision for pectus bar placement in the repair of pectus excavatum. Journal of pediatric surgery 2010; 45: 1361-4
21. Park HJ, Chung WJ, Lee IS, Kim KT. Mechanism of bar displacement and corresponding bar fixation techniques in minimally invasive repair of pectus excavatum. Journal of pediatric surgery 2008; 43: 74-8.
22. Hebra A, Jacobs JP, Feliz A, Arenas J, Moore CB, Larson S. Minimally invasive repair of pectus excavatum in adult patients. The American Surgeon 2006; 72: 837-42.
23. Notrica DM. The Nuss procedure for repair of pectus excavatum: 20 error traps and a culture of safety. InSeminars in pediatric surgery 2019; 28: 72-77
24. Notrica DM. Modifications to the Nuss procedure for pectus excavatum repair: A 20-year review. InSeminars in pediatric surgery 2018; 27: 133
25. Nuss D. Minimally invasive surgical repair of pectus excavatum. InSeminars in pediatric surgery 2008; 17: 209-217

To cite this article: Altun E, Civan O, Urguden M. Tibial pilon fractures: Single center experience Turk J Clin Lab 2021; 1: 7-14.

Original Article

Tibial pilon fractures: Single center experience

Tibia pilon kırıkları: Tek merkez deneyimi

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ABSTRACT

Aim: This study aims to investigate the mid-term clinical outcomes of surgically treated Pilon Fractures (PF).

Material and Methods: Twenty patients, surgically treated for PF between 2002 and 2012 were included in the study. Patients were evaluated functionally based on the Weber and American Orthopaedic Foot & Ankle Society (AOFAS) protocols.

Results: Mean follow-up period was 31.55 (20–48) months. Nine (45%) of the 20 patients had open fractures. According to the Rüedi–Allgöwer Classification: type 1 in nine, type 2 in nine (45%) and type 3 fractures were observed in two patients. A comparison of the duration of union between closed and open fractures revealed that the union of open fractures took a significantly longer time (p= 0.004). Moreover, soft tissue complications developed to a proportionally lesser extent in patients who were applied staged fixation compared with those were applied direct fixation, although the difference was not statistically significant (p= 0.999).

Conclusion: The surgical treatment phase of PF should comply with maximum care provided and attention paid to soft tissue. It should be remembered that the fate/outcome of certain fractures is determined at the time of the incident and that certain negative outcomes are inevitable in some patients despite the best efforts.

Keywords: pilon fractures; tibial fractures; fractures; Weber and AOFAS; trauma

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Recevied: 07.11. 2020 accepted: 17.02.2021
Doi: 10.18663/tjcl.823018

Volume 12 Number 1 p: 7-14

ÖZ

Amaç: Bu çalışmanın amacı cerrahi tedavi uygulanan tibia pilon kırıklarının orta dönem klinik sonuçlarını incelemektir.

Gereç ve Yöntemler: 2002-2012 yılları arasında, tibia pilon kırığı nedeni ile cerrahi olarak tedavi edilmiş 20 hasta çalışmaya dahil edilmiştir. Çalışmaya dahil edilen hastalar fonksiyonel açıdan Weber ve Amerikan Ortopedik Ayak ve Ayak Bileği Derneği (AOFAS) protokolüne göre değerlendirildi.

Bulgular: Hastaların ortalama izlem süresi 31.55 (20-48 ay) aydı. Hastaların 9'u (%45) açık kırıktı. Ruedi Allgöwer Sınıflamasına gore 9 hastada tip 1, 9 hastada tip 2 (%45) ve 2 hastada tip 3 kırık mevcuttu. Kapalı kırıklar ile açık kırıkların kaynama süreleri karşılaştırıldığında, açık kırıklarda kaynama süreleri anlamlı bir şekilde uzun bulundu (p=0,004). Aşamalı tespit yaptığımız hasta grubunda yumuşak doku komplikasyonlarının direk tespit uygulanan hastalara göre oransal olarak daha az geliştiği görüldü ancak istatistiksel olarak anlamlı bir farka rastlanmadı (p=0,999).

Sonuç: Pilon kırıklarının cerrahi tedavi aşamasında, yumuşak dokuya maksimum saygı ve özen gösterilmelidir. Bazı kırıkların kaderinin olay anında çizildiği ve tüm çabalara rağmen bazı hastalarda kötü sonuçların kaçınılmaz olduğu unutulmamalıdır.

Anahtar kelimeler: pilon kırıkları, tibia kırıkları, kırıklar, Weber ve AOFAS, travma

Introduction

Pilon fractures (PF) are generally complex fractures caused by high-energy trauma, which are accompanied by major soft tissue injuries and involve the distal articular surface of the tibia and metaphysis. These account for 5%–7% of tibial fractures [1] and are gradually becoming more common due to widespread sports activities, increased lifespan and traffic accidents [2].

As PF are high-energy fractures, they are frequently accompanied by soft tissue injuries. In 10%–30% of the cases, it has been reported that even the tibia was exposed externally [3]. High-energy PF represent a great dilemma for the treating orthopaedist, and an appropriate soft tissue treatment constitutes the most important phase of the therapy [4].

The principles of Rüedi and Allgöwer, which classify the treatment into four main phases to deal with the soft tissue and joint damages, have become a milestone in the treatment of PF [5].

In this study, we aimed to present the mid-term outcomes of 20 patients with PF treated by following the principles of Rüedi and Allgöwer.

Material and Methods

Among 36 patients who were surgically treated for PF at a single centre by single surgeon (third author) between 2002 and 2012, we retrospectively evaluated the 20 PF of 20 patients who regularly visited for follow-up. Cases <18 years of age and with osteoporotic fractures were excluded. The study was approved by the local ethics committee (2015/124) and conducted in accordance with the principles of the Declaration of Helsinki.

Anteroposterior (AP) and lateral ankle radiography were performed as preoperative assessments. Fractures were classified according to Gustilo–Anderson Classification [6,7], Rüedi–Allgöwer classification [8], and AO classification [9].

The subluxated or dislocated ankles were reduced at emergency department. Afterwards, a short leg splint was applied to all patients. Patients who had open fractures underwent wound irrigation and debridement, and the fibula was identified through lateral incision. For the tibia, fixation with plates and screws were applied to those who received staged fixation after external fixator (EF) and to those who did not receive any in the same session, following the repair of the distal tibial articular surface. Following surgery, the limb was placed in a short leg splint and elevated. Cold compress was applied. Following the relief of the pain and oedema in patients whose drainages were pulled 48 hours after surgery, active and assisted ankle movements were initiated. Mobilisation was ensured using by crutches to prevent any load until bone consolidation was observed on radiographs.

The surgical treatment plan of the patients was developed based on soft tissue damage. We used the classification defined by Tscherne and Goetzen [10] to evaluate soft tissue damage.

Type of surgical incision was determined and modified according to the major fracture line revealed via radiography and the condition of the soft tissue. A distance of at least 7 cm was maintained between two incisions.

Statistical Analysis

Fisher's exact test was used for the analysis of categorical variable. Measured values of both groups were compared using the Mann–Whitney U Test. The analyses were performed using SPSS 22.0. A $P < 0.05$ was considered statistically significant.

Patient Evaluation:

Weber and AOFAS (hindfoot) protocols were performed in all patients who were admitted to outpatient clinic for follow-ups or examinations. In the Weber protocol, a healthy ankle was compared with a damaged ankle. A score of 0 is considered as a perfect outcome, scores of 1 and 2 as good and satisfying outcomes and scores of 3 and 4 as poor outcomes. In the AOFAS protocol, a score of ≥70 is considered as a good outcome, while a score <70 is considered a poor outcome.

Results

Eleven (55%) of the patients were males, while 9 (45%) were females; mean patient age was 48.60 (range 24–85) years. Eleven of the fractures were right and nine were left tibial fractures. Five patients had other organ and bone injuries. The accompanying injuries included lumbar vertebrae and contralateral lower extremity fractures in one patient; contralateral lower extremity fractures (tibia, talus and calcaneus) in two patients; ipsilateral neurovascular damage in one patient; and femur and tibial plateau fractures in the ipsilateral segment in one patient. The fractures of the lumbar vertebrae were treated conservatively, while other extremity fractures were treated surgically. Distribution of open and closed fractures according to aetiological factors and Gustilo–Anderson Classification [6,7] was reported in Table 1.

Table 1: Distribution of open and closed fractures according to aetiological factors

Aetiological Factors	Closed Fractures	Open Fractures (Gustillo-Anderson)				TOTAL
		Type1	Type 2	Type 3A	Type 3C	
Falling from a height	5(%25)	-	2(%10)	1(%5)	-	8(%40)
Falling down while walking	5(%25)	1(%5)	-	1(%5)	-	7(%35)
Motor-cycle accident	1(%5)	-	-	-	-	1(%5)
Fall of a heavy object	-	1(%5)	2(%10)	-	-	3(%15)
Gunshot Injury	-	-	-	-	1(%5)	1(%5)
TOTAL	11(%55)	2(%10	4(%20)	2(%10)	1(%5)	20(%100)

According to the Rüedi–Allgöwer classification [8], nine patients had type 1 fractures, nine patients had type 2 fractures and two patients had type 3 fractures. According to the AO classification [9], one patient had a 43B1 fracture, 13 patients had 43C1 fractures, five patients had 43C2 fractures and one patient had a 43B3 fracture. Six patients had grade 0, eight had grade 1, five had grade 2 and one had grade 3 soft tissue damage according to Tscherne and Goetzen classification [10].

The surgical intervention was delayed by an average of 13 (range 5–25) days in three patients to allow for the regression of oedema and the healing of soft tissue damage. In one of these patients, the calcaneal skeletal traction step was skipped and there was a 3-week waiting period before continuing the procedures. The remaining 17 patients received the first surgical intervention on the same or next day. Nine of the patients who received surgical intervention on the same day had open fractures.

EF was applied on the tibia of nine patients who received staged fixation. For fibula fractures, seven patients received semi-tubular plate fixation and two patients received intramedullary fixation. In these nine patients, the tibial distal medial anatomic plate was placed during the second session after an average of 41.8 (17–90) days. In three patients whose bones could be united via EF and who did not need any staged fixation as well as in one patient who had a Tscherne grade 3 soft tissue damage and tissue defect, the uniplanar EF was removed and the Ilizarov EF was applied once the soft tissue problems were solved with the EF (3 months later). In one patient, the Ilizarov EF was applied directly and the treatment was completed with this. In one patient, the treatment was completed with a short leg circular cast following the union achieved with the uniplanar EF.

Surgical incision was applied from the anteromedial in 15 patients, in two patients from the anterior and in one patient from the medial. In nine patients, the fixator was removed after soft tissue problems were solved, and the distal medial anatomic plate was used afterwards. Distal tibial medial anatomic plate was applied to 13 (65%) patients; T-L plate was applied to two of these for Tillaux fracture. Interfragmentary screw was applied in three (15%) patients, the DCP plate was applied in one (5%) patient and EF were applied in three (15%) patients (two Ilizarov types and one uniplanar).

Surgical fixation was applied to 14 of the 18 patients who had fibula fractures and conservative treatment was applied to four. The fibula of two patients was intact. Semi-tubular plate was applied in 11 (79%), intramedullary K wire in two (14%) patients and interfragmentary screw in one (7%) of the patients who had fibula fixation.

The mean preoperative period for the patients was 2.8 (0–25) days. In patients who waited for 25 days, the process was prolonged due to the delay in the regression of soft tissue lesions and oedema. The mean duration of surgery was 104.65 (range: 45–200) minutes.

The mean duration of postoperative parenteral antibiotic treatment was 6.4 (3–14) days. Cases in which the use of antibiotics lasted longer were those with open fracture and wound problems. Postoperative splinting was applied for an average of 7.4 (4–14) weeks.

Twelve (60%) of the patients received staged fixation (Figure 1), while eight (40%) of them directly received open reduction + internal fixation (Figure 2) (Table 2). In three of the patients in whom staged internal fixation was planned, the treatment was continued with an EF applied in the first session.

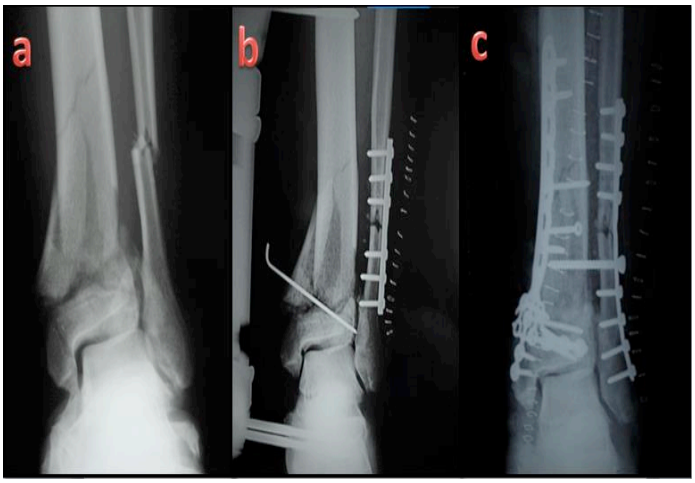

Figure 1: Staged fixation. a, Preoperative radiograph; b, First operation: EF+ Fibular plate; c, Early postoperative radiograph.

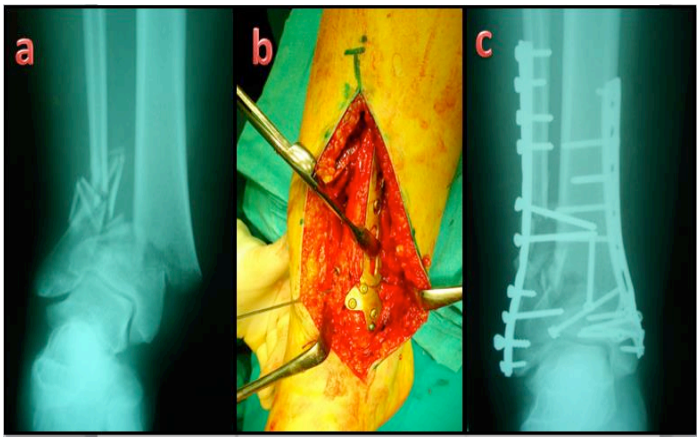

Figure 2: Patients who received direct fixation; a, preoperative radiograph; b, intraoperative imaging; c, postoperative radiograph

Table 2: Distribution of soft tissue complications after staged and direct fixations

Surgical Treatment	Soft Tissue Complication (+)	Soft tissue Complication (-)	TOTAL
Staged Fixation	5(%41,6)	7(58,4)	12(%60)
Directly Fixation	3(%37,5)	5(%62,5)	8(%40)
TOTAL	8(%40)	12(%60)	20(%100)

Nine (45%) of the patients had open fractures. The preoperative and postoperative follow-ups of the fractures varied depending on whether they were open or closed. The duration of union varied depending on the type of fracture (Table 3).

Table 3. Distribution of duration of union for the open and closed fractures

Fracture Type	Case	Union Time (week)		
		Average	Minimum	Maximum
Closed	11	10,18	7	14
Open	9	22,22	9	58
TOTAL	20	15,6	7	58

In the present study, mean patient follow-up period was 31.55 (20–48) months. The mean duration of union for the fractures was 15.6 (7–58) weeks. In statistical analysis using the Mann–Whitney U test for the duration of union of closed and open fractures, the duration of union for open fractures was significantly longer ($p = 0.004$).

When we compared the outcomes according to the AOFAS scale as good and poor outcomes, no significant difference was found across age groups ($p = 0.530$). There were no statistically significant difference across age groups ($p = 0.530$ and $p = 0.114$; respectively) of the AOFAS and Weber scores (Table 4). The distribution of the outcomes depending on the fracture classification according to the AOFAS and Weber score is summarised in Table 5.

Table 4. Distribution of the outcomes according to the Weber protocol by age groups

Result of Weber Protocol	Age Group (years)			TOTAL
	15-40	41-60	>60	
Perfect	2(%10)	1(%5)	-	3(%15)
Good/satisfying	3(%15)	5(%25)	2(%10)	10(%50)
Poor	-	5(%25)	2(%10)	7(%35)
TOTAL	5(%25)	11(%55)	4(%20)	20(%100)

When we examine the distribution of outcomes according to whether the fractures were open or closed, there were no statistically significant difference between each types for each groups according to the Weber and AOFAS protocol ($p = 0.362$ and $p = 0.285$; respectively). Moreover, RSD developed in three patients and deformity in two patients (Figure 3), (Table 6).

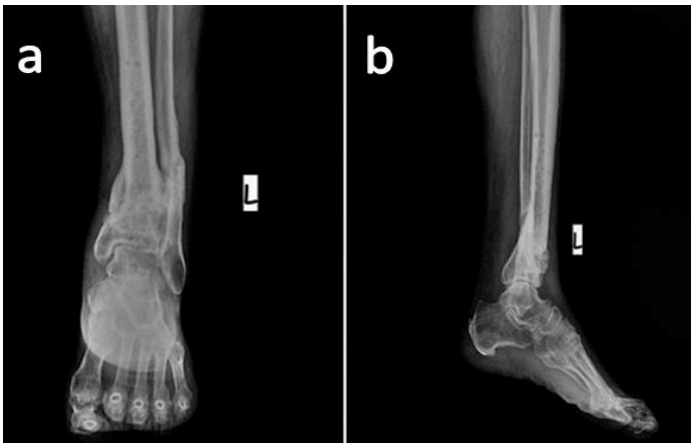

Figure 3. Final period radiographs of patient number 6 who had open fracture. a, varus deformity; b, tibia distal diaphyseal metaphyseal flexion

Four of the nine patients with open fractures had the history of smoking more than 10 packets per year. These four patients had delayed union but the statistical evaluation was not possible to declare the effect of smoking.

Discussion

The present study supported the proposal of the staged fixation principles if soft tissue conditions are not appropriate for direct fixation. The union time of the open fractures take longer than the closed ones.

There are many studies reporting the outcomes of different therapies in the literature. Kelam and Waddell [11] reported 94% good and perfect outcomes in PF developed due to rotational forces and stated that this rate decreased to 53% in fractures occurred due to high-energy trauma. In our study,

Table 5. Distribution of outcomes depending on the fracture classification according to the AOFAS and Weber score

Classification		RESULTS					TOTAL
		Weber			AOFAS		
		Perfect	Good/satisfy-ing	Poor	Good	Poor	
Ruedi-Allgöwer	Type 1	2(%10)	4(%20)	3(%15)	8(%40)	1(%5)	9(%45)
	Type 2	1(%5)	6(%30)	2(%10)	7(%35)	2(%10)	9(%45)
	Type 3	-	-	2(%10)	1(%5)	1(%5)	2(%10)
AO-Müller	43B1	1(%5)	-	-	1(%5)	-	1(%5)
	43B3	-	-	1(%5)	-	1(%5)	1(%5)
	43C1	2(%10)	8(%40)	3(%15)	12(%60)	1(%5)	13(%65)
	43C2	-	2(%10)	3(%15)	3(%15)	2(%10)	(%25)
TOTAL		3(%15)	10(%50)	7(%35)	16(%80)	4(%20)	20(%100)

the majority of our cases had PF that had resulted from high-energy trauma and that were accompanied by compression and disintegration of the limbs, and 45% of the patients in this study had open fractures. Based on the results of our study, the relatively low success rate compared to the one reported in the literature may be related to the fact that 40% of the patients had fallen from heights (vertical compression) and 15% of them had experienced trauma due to the falling of heavy objects, with majority of these fractures being open ones. However, these results may also have been due to the patient age of ≥40 years in 75% of the cohort.

Ganz evaluated the success rate of therapy with respect to the fracture type during the long-term follow-up of cases who received open reduction and internal fixation. He pointed out that the type 3 fractures that occur following high-energy traumas, soft tissue injuries and bone disintegration tend to be more severe. Therefore, outcomes of type 3 fracture tend to be worse [12]. Watson et al. applied different fixation methods depending on the severity of soft tissue injury and fracture types [13]. According to the AO classification, they reported that non-union and wound complications in type C fractures treated with open reduction were much frequent than in those treated with external fixation. Ovadia and Beals [14] have demonstrated that functional outcomes are related to fracture types and have drawn attention to the fact that outcomes become worse as the fractures become more complex. In agreement with the literature, the functional outcomes of complicated fractures in our study were proportionally poorer.

Bone and Stegemann [15] emphasised in their study on open PF that complication rates increased and the time required for union became longer. In our study, wound problems were observed in six (30%) cases. The duration of union of closed and open fractures, the time required for the union of open fractures was significantly longer ($p = 0.004$).

Table 6. Demographics and clinical outcomes of the cases

Patient	Gender	Age (years)	R-A	AO	G-A Type	Complication	Weber	AOFAS
1	M	52	Type 1	43C1	Type 1	No	Poor	Good
2	F	47	Type 2	43C2	Type 2	Delayed union, serous leakage, wound dehiscence arthritis,	Poor	Poor
3	F	51	Type 2	43C2	Closed	No	Poor	Poor
4	M	26	Type 1	43C1	Type 2	serous leakage	Perfect	Good
5	F	46	Type 1	43C1	Closed	serous leakage,	Good/satisfying	Good
6	M	67	Type 1	43C1	Type 3a	Varus deformity, non-union, deep infection, wound dehiscence, seropurulent leakage, arthritis	Poor	Poor
7	F	47	Type 1	43C1	Closed	No	Good/satisfying	Good
8	F	24	Type 1	43C1	Closed	No	Good/satisfying	Good
9	M	49	Type 1	43C1	Type 2	No	Poor	Good
10	M	54	Type 3	43C2	Closed	RSD, arthritis	Poor	Good
11	F	41	Type 2	43C1	Closed	No	Good/satisfying	Good
12	F	45	Type 2	43C2	Closed	RSD	Good/satisfying	Good
13	M	43	Type 2	43B1	Type 3a	No	Perfect	Good
14	F	45	Type 2	43C1	Type 1	No	Good/satisfying	Good
15	F	85	Type 1	43C1	Closed	Superficial infection	Good/satisfying	Good
16	M	80	Type 2	43C2	Closed	Peroneal nerve lesion, RSD	Good/satisfying	Good
17	M	65	Type 3	43B3	Type 3c	deep infection, , seropurulent leakage, arthritis, valgus deformity, shortening	Poor	Poor
18	M	36	Type 1	43C1	Closed	No	Perfect	Good
19	M	36	Type 2	43C1	Type 2	serous leakage	Good/satisfying	Good
20	M	33	Type 2	43C1	Closed	No	Good/satisfying	Good

M: Male, F: Female, R-A: Ruedi-Allgöwer Classification, AO: AO-Müller Classification, G-A: Gustillo-Anderson Type, RSD: Reflex Sympathetic Dystrophy

Among the methods used for treating PF, the "two-stage protocol" is the method that is presently drawing the most attention [16]. It gives time for the regression of soft tissue oedema before any open reduction and internal fixation is performed. Helfet et al. [17] previously evaluated 17 patients with PF in whom they applied the two-stage therapy. They obtained union in an average of 14.1 weeks in all cases, and they encountered superficial wound infections in only two cases, which recovered with local wound care. In a study conducted in 2001, Blauth et al. [18] evaluated, both functionally and radiographically, 51 of the 77 patients operated for PF over the last decade. They reported that compared with the other groups, range of motion was higher in the group in which the staged therapy was applied and that this group also had less pain, earlier return to work and faster improvement in activity levels. Moreover, there were no soft tissue complications and post-traumatic arthritis in this patient group. In our study, according to statistical analysis, there were no significant difference in terms of soft tissue complications between patients who had staged fixation and those who had direct fixation. This outcome was related to the insufficiency of the number of patients and the fact that 80% of the patients who developed complications had open fractures.

The incidence of various complications in PF treated with open reduction and internal fixation varies between 10% and 55% [14-18]. In a series prepared and studied by Teeny and Wiss [19], the ratio of wound problems was reported as 20.7% among those who received limited open reduction using only screws and then an EF and as 33.7% among those who underwent fixation with plate screws. The rate of deep tissue infection was 0% for Rüedi–Allgöwer types 1 and 2 fractures and 37% for type 3 fractures [5]. In our study, we observed wound problems in six cases (30%); these had open fractures, and wound problems were related to post-traumatic wounds in five of these six patients. Antibiotherapy and recurrent operations (debridement) were applied in two patients with seropurulent leakage.

Different success rates according to Rüedi–Allgöwer types have been reported in the literature [19,20]. In fractures accompanied by fibula fractures, the requirement of applying

plates to fibula remains debatable. Williams et al. argue that in the presence of segmented tibia fracture, the fibula plating may prevent broken pieces of the tibia from contacting each other, thereby delaying the progress of the union [21]. And also, there are some studies reporting delayed union of tibial diaphyseal fractures in the presence of associated fibular fractures [22]. In our case series, delayed union was observed in one patient, while deep infection and non-union were observed in one patient. Healing was achieved with recurrent surgical procedures in the patient with delayed union. In the other patient, healing of the deep infection was achieved through antibiotherapy and recurrent debridement.

Rüedi and Allgöwer reported that arthritis develops in the first two years in general after the injury [5]. Likewise, in their study reporting minimum 51 months follow-up outcomes of PF treated by ilizarov external fixator, Fırat et al. reported an arthritis ratio of minimum 31% [23]. In our series, four (20%) of the patients showed post-traumatic arthritis. It was observed that all patients who developed complications had complicated fractures or Gustilo type 3 fractures in which the reconstruction of the articular surface was anatomically difficult and which could result in the avascular necrosis of the subchondral bone.

We considered that the low success rate of our treatment compared to the one reported in the literature was due to the fact that majority of our cases had vertical compression due to falling from heights and most cases within the series had complicated fractures. The fact that 45% of the patients had open fractures effected the success rate of our study. It was observed that treatment become more difficult in patients with multipart articular surfaces, with cartilages that had collapsed towards the metaphysis, with bone loss and with prior exposure to high-energy traumas that increased the extent of soft tissue injury.

Limitations: Our study is retrospective and has no control group with a number of low patient number. Randomized controlled trials with large samples needed to determine the standard care.

Conclusion

The pilon fractures which requires highly orthopaedic fracture treatment experience was treated successfully by the leadership of a single surgeon with respect to the principles of Rüedi and Allgöwer.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Mauffrey C, Vasario G, Battiston B, Lewis C, Beazley J, Seligson D. Tibial pilon fractures: A review of incidence, diagnosis, treatment, and complications. Acta Orthop Belg 2011; 77: 432
2. Brumback RJ, McGarvey WC. Fractures of the tibial plafond. Evolving treatment concepts for the pilon fracture. Orthop Clin North Am 1995; 26: 273-285
3. Craig S, Bartlett C, Lon S. Fracture of the tibial pilon. In: Browner B, Jupiter J, Levine A, et al., eds. Skeletal Trauma, 3rd edn. Singapore: Elsevier, 2003; 2257.
4. Zelle BA, Dang KH, Ornell SS. High-energy tibial pilon fractures: an instructional review. Int Orthop 2019; 1-12.
5. Rüedi TP, Allgöwer M. Fractures of the lower end of the tibia into the ankle joint. Injury 1969; 1: 92-9.
6. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 1976; 58: 453–8
7. Gustilo RB, Mendoza RM, Williams DN. Problems in management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984; 24: 742–6
8. Ruedi TP, Allgöwer M. The operative treatment of intra-articular fractures of the lower end of the tibia. Clin Orthop Relat Res 1979; 138: 105-10.
9. Meinberg EG, Agel J, Roberts CS, Karam MD, Kellam JF. Fracture and Dislocation Classification Compendium- 2018. J Orthop Trauma 2018; 32: 1-10.
10. Tscheme H, Gotzen L. Fractures with soft tissue injuries. Berlin, Eieidelberg, Springer-Verlag, 1984.
11. Kellam JF, Waddel JP. Fractures of the distal tibial metaphysis with intraarticular extension-the distal tibial explosion fracture. J Trauma 1979; 19: 593-601.
12. Ganz R, Etter C. Long-term results of tibial plafond fractures treated with open reduction and internal fixation. Arch Orthop Trauma Surg 1991; 110: 277-283.
13. Watson JT, Moed BR, Karges DE, Cramer KE. Pilon fractures. Treatment protocol based on severity of soft tissue injury. Clin Orthop Relat Res 2000; 375: 78-90.

14. Ovadia DN, Beals RK. Fractures of the tibial plafond. J Bone Joint Surg Am 1986; 68: 543-51.
15. Bone L, Stegemann P, McNamara K, Siebel R. External fixation of severely communited and open tibial pilon fractures. Clin Orthop Relat Res 1993; 292: 101-7.
16. Patterson MJ, Cole JD. Two-staged delayed open reduction and internal fixation of severe pilon fractures. J Orthop Trauma 1999; 13: 85-91
17. Helfet DL, Suk M. Minimally invasive percutaneous plate osteosynthesis of fractures of the distal tibia. Instr Course Lect 2004; 53: 471-5.
18. Blauth M, Bastian L, Krettek C, Knop C, Evans S. Surgical options for the treatment of severe tibial pilon fractures: a study of three techniques. J Orthop Trauma 2001; 15: 153-60
19. Teeny SM, Wiss DA. Open reduction and internal fixation of tibial plafond fractures. Variables contributing to poor results and complications. Clin Orthop Relat Res 1993; 292: 108- 17.
20. Bourne RB, Rorabeck CH, Macnab J. Intra-articular fractures of the distal tibia: The pilon fracture. J Trauma 1983; 23: 591-6.
21. Williams TM, Marsh JL, Nepola JV, DeCoster TA, Hurwitz SR, Bonar SB. External fixation of tibial plafond fractures: is routine plating of the fibula necessary? J Orthop Trauma 1998; 12: 16-20.
22. Civan O, Alimoğlu B, İçen M, Taşkın S, Cavit A, Söyüncü Y, Ürgüden M. Pediatric tibial shaft and distal metaphyseal fractures. Jt Dis Relat Surg 2020; 31: 532-40.
23. Fırat A, Tecimel O, Işık Ç, Özdemir M, Öçgüder A, Bozkurt M. Ilizarov External Fixator in the Management of Tibial Pilon Fractures: Ankle Hinged vs Ankle Fixed Frame. Eklem Hastalik Cerrahisi 2013; 24: 133–8.

Turkish Journal of Clinics and Laboratory

To cite this article: Ozturk I. Fidancı H. Correlation of electrodiagnostic findings and the disabilities of arm, shoulder and hand questionnaire in ulnar neuropathy at the elbow. Turk J Clin Lab 2021; 1: 15-22.

Original Article

Correlation of electrodiagnostic findings and the disabilities of arm, shoulder and hand questionnaire in ulnar neuropathy at the elbow

Dirsekte ulnar nöropatide elektrodiagnostik bulgularla kol, omuz ve el sorunları anketinin korelasyonu

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Abstract

Aim: We aimed to find out whether there is a relationship between the electrodiagnostic findings and disabilities of arm, shoulder and hand (DASH) questionnaire in the ulnar neuropathy at the elbow (UNE).

Material and Methods: Patients whose clinical and electrodiagnostic findings were compatible with UNE were included in this retrospective cohort study. UNE patients were divided into mild, moderate and severe UNE according to the neurophysiological classification. DASH-disability / symptom (DASH-DS) scores of all patients were calculated. In addition, DASH work module (DASH-W) and DASH sports / performing arts module (DASH-SP) questionnaire were applied to some patients.

Results: Thirty-nine UNE patients were included in the study. There were 26 mild UNE patients, 8 moderate UNE patients, and 5 severe UNE patients. There was a positive correlation between neurophysiological classification of UNE and DASH-DS / DASH-W scores ($p = 0.002$ $r = 0.491$, $p = 0.012$ $r = 0.453$). An inverse correlation was found between DASH-W scores and ulnar nerve compound muscle action potential / sensory nerve action potential amplitudes ($p = 0.036$ $r = -0.413$, $p = 0.006$ $r = -0.492$). When the moderate and severe UNE group was evaluated as a single group, DASH-DS and DASH-W scores of mild UNE patients were low in those of moderate-severe UNE patients ($p = 0.001$, $p = 0.012$).

Conclusion: This study showed a positive correlation between the DASH scores and the neurophysiological classification in the UNE. In addition to the DASH-DS questionnaire, the use of the DASH-W questionnaire can be useful in UNE.

Keywords: DASH questionnaire; electrodiagnosis; ulnar neuropathy

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Recevied: 21.01.2020 accepted:18.12.2020
Doi: 10.18663/tjcl.679752

Öz

Amaç: Dirsekte ulnar nöropatide (DUN) elektrodiagnostik bulgular ile kol, omuz ve el sorunları (DASH) anketi arasında bir ilişki olup olmadığını bulmayı amaçladık.

Gereç ve Yöntemler: Klinik ve elektrodiagnostik bulguları DUN ile uyumlu olan hastalar bu retrospektif kohort çalışmasına dahil edildi. DUN hastaları nörofizyolojik sınıflandırmaya göre hafif, orta ve şiddetli DUN olarak ayrıldı. Tüm hastaların DASH-özürlülük / semptom (DASH-ÖS) skorları hesaplandı. Ayrıca bazı hastalara DASH iş modeli (DASH-İ) ve DASH yüksek performans sporları ve müzisyenler anketi uygulanmıştır.

Bulgular: Otuz dokuz DUN hastası çalışmaya dahil edildi. Yirmialtı hafif DUN, 8 orta DUN ve 5 şiddetli DUN hastası vardı. DUN'un nörofizyolojik sınıflandırması ile DASH-ÖS / DASH-İ skorları arasında pozitif bir korelasyon vardı ($p = 0.002$ $r = 0.491$, $p = 0.012$ $r = 0.453$). DASH-İ skorları ile ulnar sinir bileşik kas aksiyon potansiyeli / duyusal sinir aksiyon potansiyeli amplitüdleri arasında ters bir korelasyon bulundu ($p = 0.036$ $r = -0.413$, $p = 0.006$ $r = -0.492$). Orta ve şiddetli DUN grubu tek bir grup olarak değerlendirildiğinde, hafif DUN hastalarının DASH-ÖS ve DASH-İ skorları orta-şiddetli DUN hastalarının skorlarından daha düşük bulundu ($p = 0.001$, $p = 0.012$).

Sonuç: Bu çalışma DUN'da DASH skorları ile nörofizyolojik sınıflandırma arasında pozitif bir korelasyon olduğunu göstermiştir. DASH-ÖS anketine ek olarak, DASH-İ anketinin kullanımı DUN'da faydalı olabilir.

Anahtar kelimeler: DASH anketi; elektrodiagnoz; ulnar nöropati.

Introduction

Ulnar neuropathy at the elbow (UNE) is the second most common entrapment neuropathy. The diagnosis can be made by clinical features, electrodiagnostic tests and imaging methods. Sensory abnormalities in the ulnar nerve dermatome or weakness or atrophy in the muscles innervated by the ulnar nerve may be observed in UNE [1,2,3,4]. Although ultrasonography is also used in the diagnosis of UNE, nerve conduction studies have a more important place in the diagnosis of UNE [1,3,5]. In nerve conduction studies, the slowing of the ulnar motor nerve conduction velocity (NCV) across the above elbow-below elbow segment or the detection of a conduction block in this segment supports the diagnosis of UNE [1,6,7,8,9,10]. Within the electrodiagnostic tests, short segment motor nerve conduction studies across the elbow segment is considered as the gold standard [1,4,7,8,9]. With this method, UNE can be diagnosed and lesion localization can be found. UNE can be mild or moderate, or it can be severe enough to cause disability. Therefore, it is important to diagnose and follow up UNE. In addition to physical therapy, some patients with a lesion under the humeroulnar aponeurotic arcade (HUA) may be operated [1,5,11]. The upper limb disability can be evaluated with the disabilities of arm, shoulder and hand questionnaire (DASH) questionnaire [12,13]. The DASH questionnaire was used for postoperative evaluation in patients with UNE under HUA [14,15]. It was aimed to find the relationship between DASH questionnaire and electrodiagnostic findings of UNE. Thus, we also aimed to evaluate the use of DASH in UNE.

Material and Methods

Individuals who applied to the electromyography (EMG) laboratory between July 2018 and December 2019 and whose clinical and electrodiagnostic features were compatible with UNE were included in this retrospective cohort study. Patients were excluded from the study if they had polyneuropathy or a disease such as diabetes mellitus that would cause polyneuropathy, or a family history of hereditary polyneuropathy, or a history of surgery of the extremity, if there were findings compatible with polyneuropathy in nerve conduction studies. If the clinical and electrodiagnostic findings were compatible with UNE, the patient was considered to have UNE [3,4,16]. The patient was considered to have clinically UNE when one of the following criteria was: 1) Continuous paresthesia in the ulnar nerve dermatome 2) Hypoesthesia in the ulnar nerve dermatome 3) Weakness in the muscles innervated by the ulnar nerve. Turkish version of DASH questionnaire was applied to all patients. This questionnaire consisted of 30 questions [12,13]. DASH disability / symptom (DASH-DS) score was calculated in patients. If the patient did not answer more than 1 questions, the DASH-DS score was not calculated. DASH work module (DASH-W) and DASH sports /

performing arts module (DASH-SP) questionnaire was also applied to some patients, and in this optional questionnaire, the score was calculated if all questions were answered.

Cadwell Sierra Summit EMG unit (Cadwell laboratories, Kennewick, Washington, USA) was used for nerve conduction studies and needle EMG. Median, ulnar, peroneal, posterior tibial, sural nerve sensory and motor nerve conduction studies and needle EMG were applied to all patients. Electrodiagnostic tests were performed if the temperature of the extremities was above 32 degrees, otherwise the extremities were heated. Stimulation and recording were made using surface electrodes. Nerve stimulation was performed supramaximally. Low-high filters for sensory and motor nerve conduction studies were set at 20Hz-2kHz and 20Hz-10kHz, respectively. In motor and sensory nerve conduction studies, sweep speed and sensitivity were 5 ms / division, 1 ms / division and 2 mV / division and 10 µV / division, respectively. Compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitudes were obtained by measuring peak to peak. Ulnar nerve CMAP was obtained from the abductor digiti quinti (ADQ) and first dorsal interosseous (FDI) muscles, and the median nerve CMAP was obtained from the abductor pollicis brevis muscle. Median and ulnar nerves were stimulated at wrist, 5 cm proximal to the recording electrode. The stimulation site was 12 cm proximal from the recording electrode to obtain ulnar nerve CMAP recording from FDI muscle (the pathway of the ulnar nerve was taken into account). Ulnar motor nerve conduction was performed based on Buschbacher's method [17,18]. Kanakamedala's method was used for short segment motor nerve conduction in the elbow [8]. Short segment motor nerve conduction study across the elbow was performed at 2 cm intervals. The stimulation points were 2 cm (D2) and 4 cm (D4) distal to the medial epicondyle, medial epicondyle (ME), 2cm (P2), 4cm (P4) and 6 cm (P6) proximal to the medial epicondyle. Ulnar and median sensory nerve conduction studies were performed orthodromically. Peak latency was used in sensory nerve conduction studies. Sural nerve SNAP was obtained antidromically. The posterior tibial and peroneal nerve CMAPs were obtained using conventional methods. Stimulation points for obtaining the peroneal nerve CMAP were the ankle, below the head of the fibula, and the popliteal fossa. For reference values of nerve conduction studies, previous studies were considered [4,19]. For the diagnosis of UNE, it should have been one of the following electrodiagnostic criteria; 1) Ulnar motor NCV above elbow-below elbow segment <45 m/s, 2) In motor nerve conduction study, presence of conduction block across elbow segment (CMAP amplitude obtained by above elbow stimulation reduced by more than 50% compared to CMAP obtained by below elbow stimulation) 3) the velocity difference between motor NCV of the forearm and elbow segments (FEVD) > 14 m/s, 3) latency difference in the short segment motor nerve conduction study > 0.6 ms [4,16]. The lower reference limits of ulnar SNAP amplitude of 5th digit-wrist segment and distal ulnar nerve CMAP amplitude recorded from the ADQ muscle were considered as 7.5 µV and 7.0 mV, respectively [4,19]. UNE patients were divided into mild, moderate, severe and extreme UNE according to the classification proposed by Padua [2]. Extreme UNE patients were excluded from the study because ulnar CMAP could not be obtained in extreme UNE. Patients were considered to be mild UNE if there was a slowing of ulnar motor NCV across elbow segment, and a moderate UNE if SNAP amplitude was reduced in addition to slowing of ulnar motor NCV across elbow segment, and severe UNE if the ulnar SNAP could not be obtained in addition to slowing of ulnar motor NVC across elbow segment. Concentric needle electrodes were used for needle EMG. Positive sharp wave and fibrillation potentials were carefully examined. When the motor unit action potential amplitude was > 4 mV, it was considered neurogenic. This study was approved by institutional ethical committee (number 45/621). Informed consent was obtained from all patients and the principles of the Helsinki Declaration were followed.

Statistical Analysis

The Shapiro-Wilk test was used to determine the distribution of the data. Comparisons were made using Kruskal-wallis and Mann-Whitney u tests for independent samples. Tamhane's T2 test was used as post-hoc analysis. Pearson's Chi-squared test was used to analyze categorical variables. Spearman's test was used for correlation. Mean ± standard deviation (SD) and median of numeric data were calculated for descriptive statistics. Statistical Package for the Social Sciences (SPSS IBM Corp; Armonk, NY, USA) 22.0 was used to perform the statistical analysis.

Results

Forty-one UNE patients who met clinical and electrodiagnostic criteria were reviewed. Since 2 patients did not answer too many questions in the DASH questionnaire, these patients were excluded from the study. Thirty-nine patients were included in the study. 27 patients (69%) were male. The mean age of the patients was 42.5 ± 14.4 (range 18-77) years. The mean height,

weight and body mass index were 171.4 ± 8.5 cm, 76.9 ± 12.6 kg, 26.2 ± 4.0 kg/m2, respectively. The mean duration of the symptoms was 8.6 ±14.3 (1-60) months. The symptoms and neurological examination findings of the patients are shown in Table 1. The most common symptom was paresthesia in the 4th and/or 5th digits (100%), and the most common neurological examination finding was hypoesthesia in the 4th and/or 5th digits (95%). Electrodiagnostic findings of the patients are shown in table 1. The most abnormality in nerve conduction studies was in short segment motor nerve conduction studies. All patients had prolonged latency difference in the short segment motor nerve conduction study recorded from ADQ or FDI muscles. There were more neurogenic needle EMG findings in ADQ and FDI muscles than flexor carpi ulnaris and flexor digitorum profundus (ulnar nerve) muscles.

Table 1. Clinical features and electrodiagnostic findings of the UNE patients

	Number of patients with abnormal findings / total number of patients (%)
Symptoms	
Paresthesia of 4th / 5th digits	39 / 39 (100%)
Paresthesia of medial side of palm	26 / 39 (67%)
Wrist or forearm or elbow pain	15 / 39 (39%)
Weakness in hand	20 / 39 (51%)
Neurologic examination	
Hypoesthesia of the 4th and/or 5th digits	37 / 39 (95%)
Hypoesthesia of medial side of palm	28 / 39 (72%)
Weakness in ADQ muscle	16 / 39 (41%)
Weakness in FDI muscle	16 / 39 (41%)
Atrophy of ADQ muscle	4 / 39 (10%)
Atrophy of FDI muscle	6 / 39 (15%)
Tinel's sign	14 / 39 (36%)
Elbow flexion pressure test	23 / 39 (59%)
Ulnar nerve conduction studies	
5th-wrist segment SNAP amplitude	13 / 39 (33%)
Distal CMAP amplitude (recording from ADQ muscle)	7 / 39 (18%)
Motor NCV below elbow - above elbow segment m/s (recording from ADQ muscle)	20 / 39 (51%)
Motor NCV below elbow - above elbow segment m/s (recording from FDI) muscle)	19 / 33 (58%)
FEVD m/s (recording from ADQ muscle)	21 / 39 (54%)
FEVD m/s (recording from FDI muscle)	21 / 33 (64%)
Motor nerve conduction block across elbow segment	10 / 38 (26%)
Short segment ulnar motor nerve conduction studies	
Latency difference (recording from ADQ muscle)	33 / 39 (85%)
Latency difference (recording from FDI muscle)	29 / 33 (88%)
Latency difference (recording from ADQ or FDI)	39 / 39 (100%)
Latency difference at ME-P2 segment	31 / 39 (79%)
Latency difference at ME-D2 segment	7 / 39 (18%)
Latency difference at P2-P4 segment	1 / 39 (3%)
Needle EMG*	
ADQ	21 / 39 (54%)
FDI	23 / 39 (59%)
FDP (ulnar nerve)	9 / 37 (24%)
FCU	13 / 38 (34%)
ADQ or FDI or FDP or FCU	27 / 39 (69%)

ADQ: Abductor digiti quinti, FDI: first dorsal interosseous, FDP:flexor digitorum profundus (ulnar), FCU: flexor carpi ulnaris, EMG: electromyography, FEVD: the difference between the motor nerve conduction velocity of the forearm and elbow segments; CMAP: Compound muscle action potential, SNAP: sensory nerve action potential, NCV: nerve conduction velocity, ME: medial epicondyle, D2: 2 cm distal of ME, P2: 2 cm proximal to ME, P4: 4 cm proximal to ME. *:It was considered abnormal in the presence of active denervation finding or neurogenic motor unit action potential in the muscle examined with needle EMG.

According to the neurophysiological classification of UNE, 26 patients had mild UNE, 8 patients had moderate UNE, and 5 patients had severe UNE. Correlation of DASH scores and electrodiagnostic findings are shown in table 2. There was a positive correlation between neurophysiological classification of UNE and DASH-DS / DASH-W scores (p = 0.002 r = 0.491, p = 0.012 r = 0.453). In addition, an inverse correlation was found between DASH-W and ulnar nerve SNAP / CMAP amplitudes (p=0.036 r=-0.413, p=0.006 r=-0.492). Figure 1 shows the inverse correlation between distal ulnar nerve CMAP amplitude and DASH-W scores. DASH scores in the UNE groups are shown in table 3. DASH-DS scores of the moderate UNE group were significantly higher than the DASH-DS scores of the mild UNE group (Tamhane's T2 test was used for post-hoc analysis, p=0.020). When the UNE patients were divided into two groups as mild and moderate-severe UNE, the mean DASH-DS scores were obtained as 21.8 ± 17.0 (number=26, range 0-58) and 45.9 ± 20.7 (number=13, range 24-80) respectively in the mild and moderate-severe UNE group, and this difference was statistically significant (Mann-Whitney U test was used, p = 0.001). Similarly, the mean DASH-W scores were 20.7 ± 26.9 (number=19) and 43.2 ± 22.9 (number=11) respectively in mild UNE group and moderate-severe UNE group (p = 0.012). Figure 2 shows DASH-DS scores in the mild and moderate-severe UNE group.

Table 2. Correlation of electrodiagnostic findings and DASH scores

		DASH-DS	DASH-W	DASH-SP
Ulnar SNAP (5th-wrist segment)	P	0.056	0.036	0.645
	R	-0.330	-0.413	0.130
	Number	34	26	15
Ulnar CMAP amplitude	P	0.081	0.006	0.469
	R	-0.280	-0.492	-0.188
	Number	39	30	20
Ulnar motor NCV across elbow	P	0.132	0.842	0.150
	R	-0.245	-0.038	-0.315
	Number	39	30	17
Neurophysiological classification of UNE	P	0.002	0.012	0.641
	R	0.491	0.453	0.122
	Number	39	30	17

CMAP: Compound muscle action potential, SNAP: sensory nerve action potential, NCV: nerve conduction velocity, UNE: ulnar neuropathy at the elbow, DASH: The disabilities of arm, shoulder and hand questionnaire, DASH-DS: DASH disability / symptom, DASH-W: DASH-work module, DASH-SP: DASH sports / performing arts module. Spearman correlation test was used. P values < 0.05 were considered statistically significant.

Table 3. DASH scores in UNE groups based on neurophysiological classification

	DASH-DS scores mean ± SD (median)	DASH-W scores mean ± SD (median)	DASH-SP scores mean ± SD (median)
Mild UNE	21.8±17.0 (20.8) n=26	20.7±26.9 (12.3) n=19	24.4±31.7 (18.8) n=11
Moderate UNE	50.0±21.4 (52.9) n=8	44.6±26.4(43.8) n=7	29.7±47.7 (9.4) n=4
Severe UNE	39.5±19.9 (25.8) n=5	40.6±18.8(37.5) n=4	31.3±8.8 (31.3) n=2
p value	0.005	0.053	0.639

UNE: ulnar neuropathy at the elbow, DASH: The disabilities of arm, shoulder and hand questionnaire, DASH-DS: DASH disability / symptom, DASH-W: DASH-work module, DASH-SP: DASH sports / performing arts module. The DASH-DS score in the mild UNE group was significantly lower than the DASH-DS score in the moderate UNE group (p=0.020). Kruskal-wallis test was used. Tamhane's T2 test was used as post-hoc analysis. P values < 0.05 were considered statistically significant.

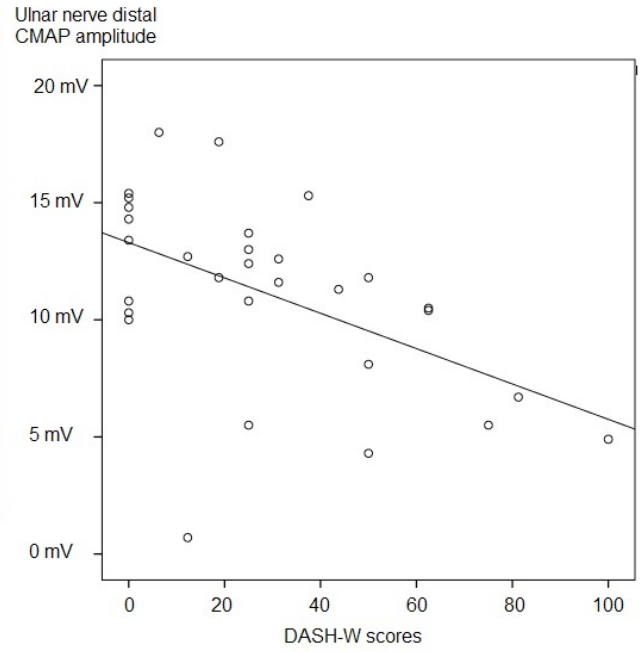

Figure 1. Correlation of ulnar nerve distal CMAP amplitude recording from ADQ muscle and DASH-W scores.

ADQ: Abductor digiti quinti, CMAP: compound muscle action potential, DASH-W: DASH-work module. There was an inverse correlation between the ulnar nerve distal CMAP amplitude and the DASH-W score (p=0.006 r=-0.492). Spearman correlation test was used. P values < 0.05 were considered statistically significant.

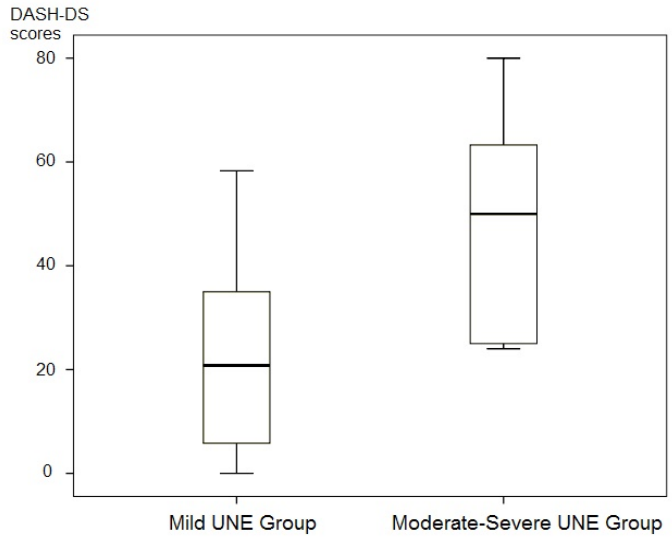

Figure 2. DASH-DS scores in mild UNE and moderate-severe UNE groups

DASH-DS: DASH disability / symptom, UNE: ulnar neuropathy at the elbow. Mean DASH-DS scores were 21.8 ± 17.0 (median 20.8, range 0-58) and 45.9 ± 20.7 (median 50.0, range 24-80) in the mild and moderate-severe UNE group, respectively. There was a statistically significant difference between the two groups (p = 0.001). Mann-Whitney u test was used. P values < 0.05 were considered statistically significant.

Discussion

UNE can cause mild to severe neuropathy. It may cause disability in some patients. In addition to physical therapy, surgical treatment is also a treatment option for some patients with lesions at HUA [11,14,15,20]. For this reason, it is important to diagnose and follow up UNE. Our primary goal in this study was to evaluate the correlation between electrodiagnostic findings and DASH questionnaire scores of UNE and to evaluate the use of the DASH questionnaire in the UNE.

The most common symptom in this study was paresthesia in 4th and/or 5th digits and the most frequent neurological examination finding was hypoesthesia in 4th and/or 5th digits. These findings were consistent with the literature [1,2,3,4]. Pain was a less common symptom. This finding was important because some of the questions in the DASH questionnaire were associated with pain. Tinel's sign and elbow flexion-pressure test were 36% and 59% positive, respectively, which supported the low diagnostic value of provocative tests reported in the literature [21]. The findings of nerve conduction studies in this study showed the importance of short segment motor nerve conduction studies in the diagnosis of UNE. All patients had abnormalities in the short segment motor nerve conduction study. This may be because the ulnar motor nerve conduction studies were performed by recording from both ADQ and FDI muscles. In previous studies, it was reported that ulnar motor nerve conduction studies performed by recording both muscles increased sensitivity for the diagnosis of UNE [1,3,4]. Consistent with the literature, in this study, ulnar nerve lesions at retroepicondylar groove were observed more than lesions at HUA in UNE [1,4,5]. Needle EMG findings were more abnormal in ADQ and FDI muscles than in proximal muscles innervated by ulnar nerve. These findings were consistent with the previous studies [4,22]. This can be explained by the topographic distribution of the ulnar nerve fascicles [23].

According to the Leeds assessment of neuropathic symptoms and signs (LANSS) pain scale, it was reported that electrodiagnostic findings did not differ in patients with and without neuropathic pain [24]. This may mean that the use of LANSS pain scale in UNE is limited. In addition, as we mentioned earlier in this study, pain was a less common symptom. In the DASH questionnaire, although there were questions about pain, the number of questions containing the word "pain" was less than five. The DASH questionnaire has been used in many studies related to UNE. DASH questionnaire is important in postoperative evaluation of patients operated

for UNE [14,15]. The DASH questionnaire was used in Padua's study for the neurophysiological UNE classification [2]. There was a positive correlation between DASH function scores and neurophysiological classification in that study. A similar positive correlation was found in this study. In this case, a positive correlation between neurophysiological classification and DASH scores can be mentioned. A significant difference was found in DASH scores between mild UNE and moderate UNE. Interestingly, while the DASH score of two severe UNE patients was 25, the DASH scores of some mild UNE patients were high (up to 58). It would be appropriate to interpret these findings as there may be mild UNE patients with high DASH scores as well as severe UNE patients with a low DASH scores. When UNE patients were divided into two groups, mild and moderate-severe, DASH-W scores were found to be significantly different in addition to DASH-DS scores. In this study, an inverse correlation was found between DASH-W and ulnar CMAP / SNAP amplitudes. Reduced CMAP or SNAP amplitudes are indicative of axonal degeneration. For this reason, it will be useful to use DASH-W in addition to DASH-DS in UNE. There was some limitations in this study. The low number of patients in the moderate and severe UNE group was one of the limitations of the study. The retrospective nature of the study was another limitation.

Conclusion

A positive correlation between DASH-DS / DASH-W scores and the neurophysiological classification of UNE, an inverse correlation between DASH-W and ulnar CMAP / SNAP amplitudes were found. In addition to DASH-DS, evaluation of UNE with DASH-W may increase the value of the DASH questionnaire. Some mild UNE patients may have high DASH scores, while some moderate and severe UNE patients may have low DASH scores.

Declaration of conflict of interest

No conflict of interest was declared by the authors. The authors declared that this study has received no financial support.

Acknowledgements

Part of this research was presented as an oral presentation at the 19th International Eastern Mediterranean Family Medicine Congress. We would like to thank Aslıhan Fidancı for her contribution to the Turkish abstract of this oral presentation.

References

1. Omejec G, Podnar S. Proposal for electrodiagnostic evaluation of patients with suspected ulnar neuropathy at the elbow. Clin Neurophysiol 2016; 127: 1961-7
2. Padua L, Aprile I, Mazza O et al. Neurophysiological classification of ulnar entrapment across the elbow. Neurol Sci 2001; 22: 11-6.
3. Beekman R, Van Der Plas JP, Uitdehaag BM, Schellens RL, Visser LH. Clinical, electrodiagnostic, and sonographic studies in ulnar neuropathy at the elbow. Muscle Nerve 2004; 30: 202-8.
4. Fidancı H, Savrun Y, Cengiz B, Kuruoğlu HR. The importance of arm-elbow velocity difference in the diagnosis of ulnar neuropathy at the elbow. Neurol Sci Neurophysiol 2019; 36: 16-21
5. Omejec G, Podnar S. Precise of ulnar neuropathy at the elbow. Clin Neurophysiol 2015; 126: 2390-6.
6. Campbell WW, American Association of Electrodiagnostic Medicine. Guidelines in electrodiagnostic medicine. Practice parameter for electrodiagnostic studies in ulnar neuropathy at the elbow. Muscle Nerve Suppl 1999; 8: 171-205.
7. Visser LH, Beekman R, Franssen H. Short-segment nerve conduction studies in ulnar neuropathy at the elbow. Muscle Nerve 2005; 31: 331-8.
8. Kanakamedala RV, Simons DG, Porter RW, Zucker RS. Ulnar nerve entrapment at the elbow localized by short segment stimulation. Arch Phys Med Rehabil 1988; 69: 959-63.
9. Azrieli Y, Weimer L, Lovelace R, Gooch C. The utility of segmental nerve conduction studies in ulnar mononeuropathy at the elbow. Muscle Nerve 2003; 27: 46-50.
10. Onar MK, Bayrak AO, Türker H, Kasım D. Electrophysiologic Findings of Ulnar Neuropathy at the Elbow. Journal of Experimental and Clinical Medicine 2006; 23: 91-4.
11. Allahverdi E, Allahverdi TD. The superiority of the Anterior Transposition Surgical Method to Decompression Procedures in a Case of Secondary Cubital Entrapment Neuropathy. Middle Black Sea Journal of Health Science 2017; 3: 26-31
12. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disability of the arm, shoulder and hand). Am J Ind Med 1996; 30:372.
13. Duger T, Yakut E, Oksuz C, Yorukan S, Bilgutay BS, et al. Reliability and validity of the Turkish version of the Disabilities of the Arm, Shoulder and Hand (DASH) Questionnaire. Fizyoterapi Rehabilitasyon 2006; 17: 99-107.
14. Ebersole GC, Davidge K, Damiano M, Mackinnon SE. Validity and responsiveness of the DASH questionnaire as an outcome measur following ulnar nerve transposition for cubital tunnel syndrome. Plast Reconstr Surg 2013; 142: 81-90.
15. Ido Y, Uchitama S, Nakamura K, Itsubo T, Hayashi M, Hata Y, Imaeda T, Kato H. Postoperative improvement in DASH score, clinical findings, and nerve conduction velocity in patients with cubital tunnel syndrome. Sci Rep 2016; 6: 27497.

16. Omejec G, Podnar S. Normative values for short-segment nerve conduction studies and ultrasonography of the ulnar nerve at the elbow. Muscle Nerve 2015; 51: 370-7
17. Buschbacher RM. Ulnar nerve motor conduction to the abductor digiti minimi. Am J Phys Med Rehabil 1999; 78: 9–14.
18. Oh S. Clinical Electromyography: Nerve Conduction Studies. 3rd Ed. Philadelphia: Lippincott Williams Wilkins 2003; 217-8.
19. Chen S, Andary M, Buschbacher R et al. Electrodiagnostic reference values for upper and lower limb nerve conduction studies in adult populations. Muscle Nerve 2016; 54: 371-7.
20. Altun G, Kurtulmus T, Oltulu İ, Sağlam N. In Situ Decompression in the Treatment of Cubital Tunnel Syndrome. SDÜ Tıp Fak Derg 2018; 25: 132-8.
21. Beekman R, Schreuder AH, Rozeman CA, Koehler PJ, Uitdehaag BM. The diagnostic value of provacative clinical tests in ulnar neuropathy at the elbow is marginal. J Neurol Neurosurg Psychiatry 2009; 80: 1369-74.
22. Eliaspour D, Sedighipour L, Hedayati-Moghaddam MR et al. The pattern of muscle involvement in ulnar neuropathy at the elbow. Neurol India 2012; 60: 36-9.
23. Jabaley ME, Wallace WH, Heckler FR. Internal topography of major nerves of the forearm and hand: a current view. J Hand Surg Am 1980; 5: 1-18.
24. Halac G, Topaloglu P, Demir S, Cıkrıkcıoglu MA, Karadeli HH, Ozcan ME, Asil T. Ulnar nerve entrapment neuropathy at the elbow: relation between the electrophysiological findings and neuropathic pain. J Phys Ther 2015; 27: 2213-6.

To cite this article: Ersoy O, Beyazpinar DS, Gunertem OE. Pump assisted beating heart coronary bypass in patients with renal dysfunction: can we prevent acute renal damage development? Turk J Clin Lab 2021; 1: 23-28.

Original Article

Pump assisted beating heart coronary bypass in patients with renal dysfunction: Can we prevent acute renal damage development?

Böbrek fonksiyonu bozuk hastalarda pompa destekli atan kalpte koroner bypass: Akut renal hasar gelişimini önleyebilir miyiz?

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Abstract

Aim: Different coronary bypass surgery techniques can be used to protect the kidneys in patients with impaired renal function. In conventional coronary artery bypass grafting technique, cardiopulmonary bypass (CPB) is established, hypothermia is performed, cardiac arrest is achieved by clamping the aorta. In the pump-assisted beating heart coronary bypass grafting technique, CPB is maintained for keeping the mean arterial pressure between certain levels. Hypothermia is avoided, aortic clamp and cardioplegia are not used. In this study, patients with impaired renal function were compared weather they had coronary artery bypass grafting in conventional or pump-assisted beating heart technique, in terms of acute renal damage and dialysis requirements in patients.

Material and Methods: Forty-eight patients who had coronary artery bypass graft surgery and whose serum creatinine level was higher than 1,3 mg / dl were included in the study. Twenty-four patients who underwent pump-assisted method were classified as Group I and 24 patients who underwent conventional method as Group II.

Results: There was no difference between the two groups in terms of renal function tests on preoperative evaluation. There were significant differences in urinary outputs before and during CPB, intensive care stays, acute renal damage and dialysis requirements ($p < 0.05$). Four out of 24 patients in group I (16.66%) and 18 patients of 24 patients in group 2 (75%) had acute renal failure (ARD). In group I patient dialysis was not required and in group II eight patients required dialysis ($p < 0.05$).

Conclusion: Different techniques have been developed due to increased mortality, morbidity and health expenditures in coronary artery bypass grafting in the presence of accompanying diseases. In our study, ARD and dialysis requirements were found to be higher by the conventional method in cases with serum creatinine level above 1.3 mg / dL. Pump-assisted beating heart coronary bypass surgery can be a good option in patients with high creatinine levels which we may encounter kidney problems in the postoperative period.

Keywords: coronary bypass; renal function; acute kidney injury

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Recevied: 09.01.2021 accepted: 07.03.2021
Doi: 10.18663/tjcl.893282

Volume 12 Number 1 p: 23-28

Öz

Amaç: Böbrek fonksiyonları bozuk olan olgularda böbrekleri korumak amacı ile farklı koroner bypass ameliyatı teknikleri kullanılabilir. Konvansiyonel koroner arter bypass greftleme tekniğinde kardiyopulmoner bypassa (KPB) girilerek, hipotermi uygulanmakta, aorta klemplenerek kardiyopleji ile kardiyak arrest sağlanmaktadir. Pompa destekli atan kalpte bypass greftleme tekniğinde ise ortalama arteriyel basıncı belli düzeyde tutmak amacıyla ihtiyaç duyulması halinde KPB'a girilmektedir. Hipotermiden kaçınılmakta, aorta klempi ve kardiyopleji kullanılmamaktadır. Bu çalışmamızda, böbrek fonksiyonları bozuk olan olgularda, konvansiyonel yöntem ile pompa destekli atan kalpte yapılan koroner bypass ameliyatı olan hastalarda gelişen akut renal hasarlanma ve diyaliz gereksinimi açısından karşılaştırdık.

Gereç ve Yöntemler: Klinigimizde 3 yıl içerisinde koroner arter hastalığı nedeniyle izole koroner arter bypass greft cerrahisi uygulanan ve serum kreatinin düzeyi 1,3 mg/dl'den yüksek olan 48 olgu çalışmaya dahil edildi. Atan kalpte pompa destekli yöntem uygulanan 24 olgu Grup I, konvansiyonel yöntem uygulanan 24 olgu Grup II olarak kabul edildi.

Bulgular: Preoperatif değerlendirmede böbrek fonksiyon testleri açısından her iki grup arasında farklılık yoktu. KPB öncesi ve KPB esnasında idrar outputları, yoğun bakım kalış süreleri, akut renal hasarlanma ve diyaliz gereksinimleri açısından anlamlı farklılık saptandı ($p<0.05$). Grup I'de 24 olgunun dördünde (%16,66); Grup 2'de ise 24 olgunun 18'inde (%75) akut böbrek hasarı saptandı. Grup I olgularında diyaliz ihtiyacı saptanmazken, Grup II'de sekiz hastada diyaliz ihtiyacı olduğu görüldü ($p<0.05$).

Sonuç: Eşlik eden hastalıkların varlığında koroner arter bypass greftleme de mortalite, morbidite ve sağlık harcamalarının artması sebebi ile farklı teknikler geliştirilmektedir. Çalışmamızda serum kreatinin düzeyi 1,3 mg/dl'nin üzerinde olan olgularda ABH ve diyaliz ihtiyaçları konvansiyonel yöntem ile daha fazla olduğu tespit edilmiştir. Kreatinin seviyeleri yüksek olan ve ameliyat sonrası dönemde böbrek problemleri ile karşılaşabileceğimizi düşündüğümüz olgularda pompa destekli atan kalpte bypass ameliyatı iyi bir seçenek olabilir.

Anahtar kelimeler: koroner bypass; renal fonksiyon; akut böbrek yetmezliği

Introduction

Coronary artery bypass grafting (CABG) is a common method used in the treatment of coronary artery disease. CABG surgeries are usually performed in two ways. The first is the conventional method that is using cardiopulmonary bypass (CPB) (on-pump CABG) and the second is of-pump CABG without CPB.[1] Although it is not used frequently, there is also a pump assisted beating heart bypass (PABHB) method in which both methods are used together if needed.

Acute renal damage (ARD) develops 10 to 60% after CABG surgery.[2,3] ARD, which developed in the postoperative period, prolongs hospital stay and intensive care stay. Renal replacement therapy is required in 1 to 5% of patients with ARD, and mortality is increased in these patients. In patients undergoing CABG surgery, the risk of developing ARD is higher in patients with impaired renal function before surgery.[4,5] Several consensus bodies have been set up to provide uniform criteria for the detection of ARD, to assist the comparisons during studies, and to facilitate the development of quantitative surveys. The Kidney Disease / Improving Global Outcomes criteria (KDIGO) is also one of the renal damage consensus.[6] KDIGO criteria are an evaluation method based on changes in serum creatinine levels and urine output.

In this study, we aimed to compare acute renal damage and the need for dialysis due to this caused by on-pump CABG and PABHB, in cases with preoperative impaired renal function tests.

Material and Methods

The studies were conducted between January 2012 and January 2015. Forty-eight patients who underwent isolated CABG for coronary artery disease within three years were implicated in the study. Twenty-four patients undergoing PABHB surgery were treated as Group I, and 24 patients undergoing conventional CABG were treated as Group II.

All operations were performed by the same surgeon. All cases underwent median sternotomy. The surgical method to be applied is planned randomly.

Patients were cooled to 30°C with CPB by aortocaval cannulation with conventional CABG technique. After clamping of the aorta, cardiac arrest was performed with cardioplegia. Following the completion of the distal

anastomoses, patients were heated and discharged from CPB. Aorta-valvular cannulation was performed in PABHB surgery to keep the mean arterial pressure at a certain level. When the mean arterial pressure dropped below 50 mmHg and / or during distal anastomosis on the posterior aspect of the heart, CPB was established. In all cases of PABHB operation, left ventricular sump was placed via right upper pulmonary vein. Sump was used to reduce left ventricular wall tension during distal anastomoses on the lateral and posterior sides of the heart during CPB. In PABHB surgery, all anastomoses were performed using an intracoronary shunt. Hypothermia was not performed and therefore rewarming was not needed.

Comorbid factors; hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), chronic obstructive pulmonary disease (COPD), compensated renal disease (CKD) and peripheral arterial disease (PAH) were recorded as demographic data. The European System for Cardiac Operative Risk Evaluation (Euroscore) scores were calculated.[6]

Ejection fractions (EF) were evaluated pre- and postoperatively. Urine outputs before and after CPB were recorded intraoperatively. Postoperative daily renal function tests (BFT) and hourly urine output were recorded.

For follow-up of renal function, serum creatinine levels and hourly urinary output were assessed according to the criteria of KDIGO (table 1). In our cases, we used KDIGO criteria only for the purpose of establishing the diagnosis of ARD and did not do any staging.

Table 1. The Kidney Disease / Improving Global Outcomes criteria

Stage	Serum creatinine level	Urine volume
1	1.5-2 times the baseline value within 7 days or ≥0.3 mg / dl increase within 48 hours	8 hours <0.5 ml / kg / hour
2	2.0-3 fold increase from baseline	16 hours <0.5 ml / kg / hour
3	Increase ≥ 3 times the baseline value Serum creatinine ≥4.0 mg / dL or Dialysis or <35 ml / min / 1.73 m2 reduction in eGFR in <18 years of age	≥ 24 hours <0.5 ml / kg / hour or 12 hour anuria

Patients requiring additional procedures, such as heart valve surgery, early mortality, patients with chronic renal failure, and patients with normal renal function (SCR <1.3 mg / dl) were considered exclusion criteria.

The obtained data was evaluated by SPSS (Statistical Package for the Social Sciences for Windows, version 20,0). We gave parametric values with mean and ± 2 standard deviations. We used Kolmogorov-Smirnov test for the normal distribution of data, Mann-Whitney U for parametric values and Chi-square tests for categorical values. The differences between the groups were compared with the One-Way ANOVA test. We considered p <0.05 as statistically significant.

This study was approved by the Baskent University Clinical Research Ethics Committee(94603339/18-050.01.08.01-779) and procedures were carried out in accordance with the 2013 Helsinki Declaration. Informed consents were obtained from all participants.

Results

The demographic characteristics of the patients are given in Table 2 and no statistical difference was found between the two groups.

Table 2. Demographic data

	Grup I	Grup II	p value
Average Age (years)	64.75 ± 11.76	68.00 ± 9.56	0.466
Weight (kg)	75.23 ± 9.45	77.49 ± 11.68	0.476
Length (cm)	168 ± 6.87	167.67 ± 9.59	0.255
Body Surface Area (m^2)	1.79 ± 0.154	1.78 ± 0.143	0.578
Male (n)	20	24	
Woman (n)	4	0	
Hypertension (n)	16	14	0.383
Diabetes mellitus (n)	6	10	0.249
Hyperlipidemia (n)	16	16	0.423
COPD (n)	6	4	0.381
Peripheric Arterial Disease (n)	4	6	0.451
Euroscore	5.27 ± 2.79	5.27±2.44	1.00
Preoperative EF (%)	47.25 ± 7.87	51.08 ± 10.41	0.32

*Abbreviations:COPD: Chronic obstructive pulmonary disease

The intraoperative and postoperative data of the patients are given in Table 3. There was no difference in terms of CPB durations, number of bypasses, patient temperature values, and duration of mechanical ventilation, while intensive care unit stay was found to be higher in patients treated with conventional methods (p = 0.011).

Compared with both groups before and after CPB, urine output was significantly lower in group II. According to the criteria of KDIGO ARD is developed in four (16.66%) of PABHB cases and 18 (75%) of conventional CABG cases (p <0.05). In the postoperative period, the PABHB group patients did not require dialysis whereas eight patients in the on-pump CABG group required dialysis (p <0.05).(Table 4)

Table 3. Postoperative characteristics of PABHB and CABG groups

	Grup I	Grup II	P value
Postoperative EF (%)	50.83± 7.18	49.66± 10.18	0.749
CPB Time (min)	79.83± 29.06	94.58± 23.59	0.186
Aortic clamp time (min)	0	50.41	
Temperature (° C)	33.84± 1.54	28.98± 1.89	0.488
Bypass Count (n)	4.08± 0.66	3.83± 0.83	0.427
Mechanical Ventilation Time (hour)	11.51±8.55	13.87±7.64	0.635
Intensive Care Time (days)	2.15±1.6	3.45±2.86	0.025
Time at the hospital (days)	9.77±4.45	10.15±3.47	0.412

*Abbreviations: PAHBB: Pump assisted beating heart bypass, EF: Ejection fraction, CPB: Cardiopulmonary bypass, min: minutes, °C: degree centigrade

Table 4. Intraoperative urine output, rate of ARD occurence and dialysis needs of patients

	Grup I	Grup II	p value
The volume of urine before CPB (ml)	658.33± 408.34	289.58± 188.73	0,01
Volume of urine during CPB (ml)	700.00± 380.19	239.58± 2210.93	0,002
Number of patients with ARD	4	18	0,003
Number of patients requiring dialysis	0	8	0,028

*Abbreviations: CPB: Cardiopulmonary bypass, ARD: Acute renal damage.

Discussion

When we compared PABHB and conventional CABG, we found that in the conventional method patients needed longer ICU care. Although there was no difference between the serum creatinine levels in both groups, postoperative ARD developed in 9% of the PABHB group and 75% of the conventional CABG group according to the KDIGO criteria. Again, the need for dialysis in these patient groups was 0 and 33.3%, respectively.

ARD is a complication frequently encountered after cardiac surgery, extending intensive care and hospital stay periods and increasing mortality seriously.[2,3,7] ARD and the need for postoperative renal replacement therapy increases the mortality rates from 25% to 50% .[8,9]

The development of ARD in CABG surgeries is multifactorial. Some of these risk factors are advanced age, female gender, DM, preoperative steroid use, past cardiac surgery, pre- and / or intraoperative mechanical support device use, and preoperative renal dysfunction.[10,11] Several studies have shown that a small change in preoperative renal function in patients undergoing cardiac surgery is an important effect on long- and mid-term outcomes.[12,13,14]

Another risk factor for ARD development is method of CABG surgery. While conventional CABG is still considered the gold standard method for coronary artery revascularization, this technique presents with a number of side effects including systemic inflammation, neurological and renal dysfunction. [15] The causes of ARD after cardiac surgery include ischemia - reperfusion, cytokine release, hemolysis and exposure to nephrotoxicity. CPB stimulates the systemic inflammatory response (SIRS) and SIRS has an adverse effect on renal blood flow.[16,17] Therefore, the duration of CPB is an important predictor of postoperative renal dysfunction.[18]

Conflicting results of renal dysfunction and mortality have been reported between the two groups in studies, while expecting the ARD is lower in the beating heart than conventional CABG, because of the absence of CPB.[19,20]

There is a very limited number of papers on the effect of PABHB technique on renal function. In a study conducted in patients with serum creatinine levels within the normal range (<1,3 mg / dl) in our clinic, there was no statistically significant difference between the two groups in terms of ARD development between the PABHB group and the conventional CABG groups.[21] In a study conducted by Chen et al., they found that the PABHB technique was superior to the conventional method.[22]

Prolonged CPB time is shown as a risk factor for ARD. In our study, there was no statistically significant difference between the two groups when the PAPHB and conventional CABG cases were compared in terms of CPB durations, but it was explicitly shorter in PABHB group (79.83 ± 29.06 minutes' vs 94.58 ± 23.59 minutes). The absence of difference in CPB duration between the two groups is due to multi-vessel bypass and complete revascularization desideration. We think that it is possible to explain ARD and dialysis requirements are less in the PABHB than the conventional method, the mean arterial pressure is not allowed to drop during the PABHB procedure, hypothermia is not applied, cardioplegia is not given.

Another effect on ARD is rewarming which is needed because of the hypothermia and CPB applied with organ protection purpose during CPB. Low CPB perfusion heat is associated with postoperative ARD.[23] In a study conducted by Boodhwani and colleagues, they found that the development

of postoperative renal dysfunction was higher in patients who underwent rewarming from 32°C to 37°C than those who rewarmed from 34°C during 10-15 minutes of rewarming.[24] We did not use hypothermia in the cases of PABHB and we did not need rewarming for this reason.

As a result; the PABHB technique is a good method to be applied in cases of impaired renal function. The advantage of the PABHB method over the conventional method is that the duration of CPB is short, it does not require hypothermia, and the aortic clamping is not used. At the same time, according to the on-pump CABG method, it provides advantages such as providing technical convenience and allowing complete revascularization because the hemodynamic stabilization can be kept for a long time.

Conclusion

The PABHB method is an important alternative to conventional CABG and on-pump CABG procedures in patients with impaired renal function tests. Hypothermia is not required, coronary perfusion is continued during bypass with the help of intracoronary shunt, hemodynamic problems are edged out by establishing CPB for keeping the mean arterial pressure above a certain level, the left ventricle can be decompressed during bypass procedure on the lateral and posterior surfaces of the heart and because of that possibility of total revascularization is increased. For these reasons we believe that the PABHB method is advantageous especially in patients with impaired renal function.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Thompson PD, Buchner D, Piña IL et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). Circulation 2003;107: 3109-3116.
2. Ornish D, Brown SE, Billings JH et al. Can lifestyle changes reverse coronary heart disease? : The Lifestyle Heart Trial. The Lancet 1990; 336: 129-133.
3. McFalls EO, Ward HB, Moritz TE et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med 2004; 351: 2795-2804.
4. Kervan Ü, Koç O, Özatik MA ve ark. Türkiye'deki kalp damar cerrahisi kliniklerinin dağılımı ve hizmetlerinin niteliği. Turk Gogus Kalp Dama 2011; 19: 483-489.
5. Hamulu A, Özbaran M, Atay Y, Pasacıoğlu H, Aras I, Buket S. Koroner bypass ameliyatında mortalite ve morbiditeye etki eden risk faktörlerinin belirlenmesi ve değerlendirilmesi. Turk Gogus Kalp Dama 1995; 3: 11-16.
6. Oğuş T, İpek G, Işık Ö, Berki T, Gürbüz A, Balkanay B. Yüksek risk taşıyan hastalarda kalp-akciğer makinası kullanılmaksızın çalışan kalpte koroner bypass yöntemi. Turk Gogus Kalp Dama 1996; 4: 9-14.
7. Şener T, Köprülü AŞ, Karpuzoğlu OE, Acar L, Temur B, Gerçekoğlu H. Kronik böbrek disfonksiyonu olan hastalarda atan kalpte koroner arter baypas cerrahisinin klinik sonuçları. Turk Gogus Kalp Dama 2013; 21: 918-923.
8. Fındık O, Haberal İ, Akyıldız M ve ark. EuroSCORE, Cleveland ve CABDEAL klinik risk sınıflama sistemlerinin Türk toplumu için duyarlılık ve özgüllüklerinin karşılaştırılması. Turk Gogus Kalp Dama 2012; 20: 458-466.
9. Bahar I, Akgul A, Ozatik ME et al. Acute renal failure following open heart surgery: risk factors and prognosis. Perfusion 2005; 20: 317-22.
10. Metha RH, Honeycutt E, Patel UD et al. Relationship of the time interval between cardiac catheterization and elective coronary artery surgery with postprocedural acute kidney injury. Circulation 2011; 124: 149-155.
11. Mangano CM, Diamondstone LS, Ramsay JG, Aggarwal A, Hersko A, Mangano DT. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. Multicenter Study of Perioperative Ischemia Research Group. Ann Intern Med. 1998; 128:194–203.
12. Dasta JF, Kane-Gill SL, Durtschi AJ, Pathak DS, Kellum JA. Cost and outcomes of acute kidney injury following cardiac surgery. Nephrol Dial Transplant 2008; 23: 1970- 4.
13. Rosner MH, Okusa MD: Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol 2006; 1: 19-32.
14. Lassnigg A, Schmidlin D, Mouhieddine M, Bachman LM, Druml W, Bauer P. Minimal changes of serum creatinine predict prognosis in patient after cardiothoracic surgery: A prospective cohort study. J Am Soc Nephrol 2004; 15: 1597-1605.
15. Thakar CV, Liangos O, Yared JP et al. ARF after open heart surgery: Influence of gender and race. Am J Kidney Dis 2003; 41: 742-51.
16. Karkouti K, Wijeysundera DN, Yau TM et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation 2009; 119: 495–502.

17. Park M, Coca SG, Nigwekar SU et al. Prevention and treatment of acute kidney injury in patients undergoing cardiac surgery: a systematic review. Am J Nephrol 2010; 31: 408–18.
18. Karkouti K, Beattie WS, Wijeysundera DN et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. J Thorac Cardiovasc Surg 2005; 129: 391-400.
19. Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: Pathophysiology and treatment: An update. Eur J Cardiothorac Surg 2002; 21: 232-244.
20. Chukwuemeka A, Weisel A, Maganti M et al. Renal dysfunction in high-risk patients after on-pump and off-pump coronary artery bypass surgery: A propensity score analysis. Ann Thorac Surg 2005; 80: 2148-2153.
21. Seabra VF, Alobaidi S, Balk EM, Poon AH, Jaber BL. Off-pump coronary artery bypass surgery and acute kidney injury: A meta-analysis of randomized controlled trials. Clin J Am Soc Nephrol 2010; 5: 1734-1744.
22. Palomba H, De Castro I, Neto ALC, Lage S, Yu L. Acute kidney injury prediction following elective cardiac surgery: AKICS score. Kidney Int 2007; 72: 624-31.
23. Kumar AB, Suneja M. Cardiopulmonary bypass-associated acute kidney injury. Anesthesiology 2011; 114: 964-970.
24. Salis S, Mazzanti VV, Merli G et al. Cardiopulmonary bypass duration is an independent predictor of mortality and morbidity after cardiac surgery. J Cardiothorac Vasc Anesth 2008; 22: 814–22.

To cite this article: Savas HB, Etli M. Paraoxonase 1 activity as a new biochemical marker in the diagnosis of peripheral arterial disease. Turk J Clin Lab 2021; 1: 29-32.

Original Article

Paraoxonase 1 activity as a new biochemical marker in the diagnosis of peripheral arterial disease

Periferik arter hastalığı tanısında yeni bir biyokimyasal gösterge olarak paraoksonaz 1 aktivitesi

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Abstract

Aim: Peripheral artery disease (PAD) is an atherosclerotic disease. It is seen in older ages. It causes cardiovascular morbidity and mortality. PAD may progress without any symptoms. Despite its high frequency, there is no laboratory parameter that directly indicates peripheral arterial disease in routine biochemical tests. The relationship between oxidative stress increase and PAD is known. In this study, it is aimed to show the possible usage of the activities of the antioxidant enzymes paraoxonase 1 and arylesterase as a new marker in the diagnosis of PAD.

Material and Methods: A total of 70 individuals, including 35 in the control group and 35 peripheral artery patients, were included in this study. The collected blood serums were separated and stored at -80 °C. Paraoxonase 1 and arylesterase activities were measured using the spectrophotometric method in the serum which was dissolved at room temperature. The results were subjected to statistical analysis. $P < 0.05$ was accepted as the level of significance.

Results: In the peripheral arterial disease group, the paraoxonase 1 and arylesterase activities were found to be significantly lower than those in the control group ($p < 0.05$). In peripheral arterial disease, paraoxonase 1 and arylesterase activities were shown to decrease.

Conclusion: In peripheral arterial disease, paraoxonase 1 and arylesterase activities were found to decrease significantly. The results of similar studies related to atherosclerosis in the literature were in line with our findings. It would be beneficial to support the results of this study with new studies and evaluate paraoxonase 1 and arylesterase activities in routine biochemistry laboratories for the diagnosis and follow-up of peripheral arterial disease.

Key words: Peripheral arterial disease; biochemical marker; paraoxonase 1.

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Recevied: 24.03.2020 accepted: 23.11.2020
Doi: 10.18663/tjcl.708810

Volume 12 Number 1 p: 29-32

Öz

Amaç: Periferik arter hastalığı (PAH) aterosklerotik bir hastalıktır. İleri yaşta görülür. Kardiyovasküler morbidite ve mortaliteye sebep olmaktadır. PAH, hiçbir belirti vermeden de seyredebilir. Sıklığı yüksek olmasına rağmen rutin biyokimyasal tetkiklerde direkt olarak periferik arter hastalığını gösteren bir laboratuvar parametresi bulunmamaktadır. Oksidatif stres artışı ile PAH arasındaki ilişki bilinmektedir. Bu çalışmada antioksidan enzimler olan paraoksonaz 1 ve arilesteraz aktivitelerinin PAH tanısında yeni bir marker olarak muhtemel kullanımının gösterilmesi amaçlanmıştır.

Gereç ve Yöntemler: 35 kontrol grubu ve 35 Periferik arter hastası olmak üzere toplam 70 bireyin olurları alınarak çalışmaya dâhil edilmiştir. Toplanan kanlar serumları ayrılarak -80 Co'de saklanmıştır. Oda ısısında çözünen serumlarda ticari kit kullanılarak, spektrofotometrik yöntem ile paraoksonaz 1 ve arilesteraz aktiviteleri ölçülmüştür. Sonuçlar istatistiksel analize tabi tutulmuştur. Anlamlılık düzeyi olarak $p<0,05$ kabul edilmiştir.

Bulgular: Periferik arter hastalığı grubunda, paraoksonaz 1 ve arilesteraz aktiviteleri, kontrol grubuna göre istatistiksel olarak anlamlı düzeyde düşük bulunmuştur ($p<0,05$). Periferik arter hastalığında paraoksonaz 1 ve arilesteraz aktivitelerinin azaldığı görülmüştür.

Sonuç: Periferik arter hastalığında paraoksonaz 1 ve arilesteraz aktivitelerinin istatistiksel olarak anlamlı düzeyde azaldığı görülmüştür. Literatürde ateroskleroz ile ilgili benzer çalışmaların sonuçları bulgularımız ile uyumludur. Yeni çalışmalarla desteklenmesi faydalı olmakla birlikte paraoksonaz 1 ve arilesteraz aktivitelerinin rutin biyokimya laboratuvarlarında bakılmasının periferik arter hastalığı tanısında ve takibinde değeri olabilecektir.

Anahtar kelimeler: Periferik arter hastalığı, biyokimyasal belirteç; paraoksonaz 1.

Introduction

Peripheral arterial disease (PAD) is an atherosclerotic disease. It is seen in older ages. It causes cardiovascular morbidity and mortality. PAD may progress without any symptoms [1]. Although its frequency is high, there is no laboratory parameter that directly indicates peripheral arterial disease in routine biochemical tests. The paraoxonase (PON1) enzyme is an esterase enzyme whose antioxidant aspect is evident. It is firmly attached to HDL. Thanks to the PON1 enzyme, it has been demonstrated in studies that HDL reduces lipid peroxides by various enzymatic mechanisms after accumulation of lipid peroxides forming as a result of oxidation of LDL [1]. Paraoxonase 1 activity is variable and affected by environmental factors. It differs based on communities. Paraoxonase 1 and Arylesterase (ARY) are enzymes in the esterase group that are encoded by the same gene whose active centers are similar. The primary importance of ARY is that it is an indicator of the actual protein that is not affected by changes in PON1. Disruption of the balance between oxidative stress and antioxidant capacity and formation of oxidative damage cause many serious diseases [2-8]. The relationship between oxidative stress increase and PAD is known [9]. In this study, it is aimed to show the possible usage of the activities of the antioxidant enzymes paraoxonase 1 and arylesterase as a new marker in the diagnosis of PAD.

Material and Methods

Ethical Considerations

The research was conducted with the approval of Alanya Alaaddin Keykubat University Clinical Research Ethics Committee (ALKÜ-KAEK) dated 26.09.2019 and numbered 10/14. The study was carried out in accordance with the ethical principles in the Declaration of Helsinki, which was adopted by the World Medical Association in 1964 and then updated continuously. All people included in the study signed an informed consent form.

Design

70 individuals, male and female, who visited the Alanya Research and Training Hospital of Alanya Alaaddin Keykubat University, including 35 healthy controls (10 women, 25 men) and 35 peripheral arterial disease patients (10 women, 25 men), were included in the study. The blood samples left over from routine examinations were collected. The collected blood was centrifuged in refrigeration, and its serum was separated and portioned in Eppendorf tubes and stored at -80 °C.

Measurement of Paraoxonase 1 (PON1) and Arylesterase (ARY) Activities

Paraoxonase 1 and arylesterase activities were measured by the spectrophotometric method in the serum using a commercial kit.

Paraoxonase 1 (PON1)

A fully automated and colorimetric commercial kit was used to measure paraoxonase 1 activity (Rel Assay Diagnostics, Gaziantep, Turkey). The basic principle of the measurement method of the kit is based on the measurement of basal paraoxonase 1 activity in the environment without NaCl and stimulated paraoxonase 1 activity in the environment containing NaCl. The absorbance change resulting from the hydrolysis of paraoxone was measured spectrophotometrically at 37 °C and 412 nm. The activity calculation was made by subtracting the basal PON1 activity from the stimulated PON1 activity. The results are given in U / l [10].

Arylesterase (ARY)

A fully automated and colorimetric commercial kit was used to measure arylesterase (ARY) activity (Rel Assay Diagnostics, Gaziantep, Turkey). The basic principle of the measurement method of the kit is the use of phenyl acetate as a substrate for the measurement of ARY activity. Phenol and acetic acid are formed as a result of the hydrolysis of phenyl acetate. The absorbance change resulting from the hydrolysis of phenyl acetate was measured spectrophotometrically. The results are given in U / l [11].

Statistical Analysis

The results were subjected to statistical analysis. ANOVA was applied with the SPSS package program. There were two groups in total, and for this reason, post-hoc tests were not needed. In the statistical analysis, $p<0.05$ was accepted as the level of significance in the comparison between the groups.

Results

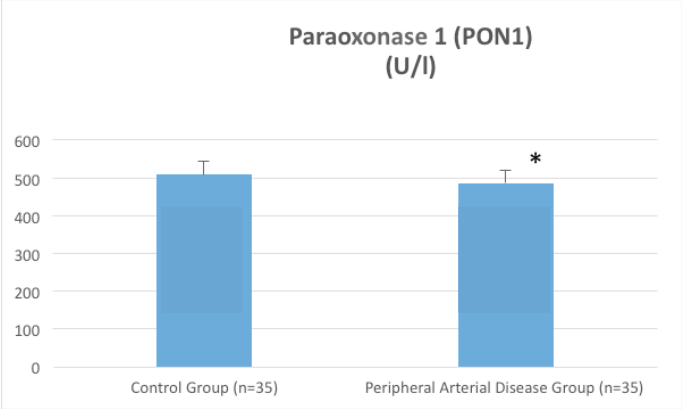
The mean age of the peripheral arterial disease group was 67.80 ± 8.70, whereas the mean age of the control group was 68.23 ± 7.80. In the peripheral arterial disease group, the paraoxonase 1 and arylesterase activities were significantly lower than those in the control group ($p<0.05$). The PON1 activity for the control (n = 35) and peripheral artery disease (n = 35) groups was found respectively as 509.54 ± 33.68 and 486.83 ± 30.93 ($p = 0.004$), while the ARY activity was respectively 612.17 ± 46.26 and 520.71 ± 52.63 ($p<0.001$). The results are shown in Table 1 and Graphic 1 and 2 below.

Table 1. Change in Paraoxonase 1 and Arylesterase Activity in Peripheral Arterial Disease

Parameter (Unit)	Control Group (n=35) (mean±SD)	Peripheral Arterial Disease Group (n=35) (mean±SD)	p
Paraoxonase 1 (PON1) (U/l)	509.54 ± 33.68	486.83 ± 30.93 *	0.004
Arylesterase (ARE) (U/l)	612.17 ± 46.26	520.71 ± 52.63 *	<0.001

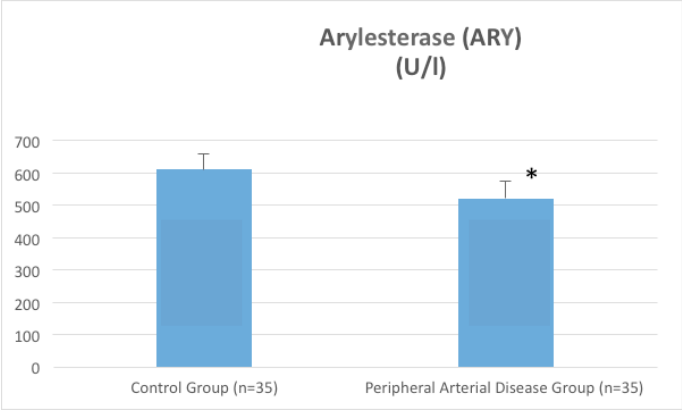
Explanation: *: For paraoxonase 1 and arylesterase activity, there was a statistically significant decrease in the peripheral artery disease group in comparison to the control group ($p<0.05$).

Graphic 1. Change in Paraoxonase 1 Activity in Peripheral Arterial Disease



Explanation: *: For paraoxonase 1 activity, there was a statistically significant decrease in the peripheral artery disease group in comparison to the control group ($p = 0.004$).

Graphic 2. Change in Arylesterase Activity in Peripheral Arterial Disease



Explanation: *: For arylesterase activity, there was a statistically significant decrease in the peripheral artery disease group in comparison to the control group ($p<0.001$).

Discussion

Peripheral arterial disease is a pathology that develops in the background of atherosclerosis. Atherosclerosis is an inflammatory disease caused by the combination of oxidized lipid accumulation in the intima layers of the vessels and immune cells. The most important step that initiates atherosclerosis is the migration of LDL cholesterol to the intima layer after its endothelial injury, oxidation and subsequent migration of monocytes and the formation of foam cells. The foam cells then become fat lines in the endothelial layer, and then, form atheromatous plaques [10-15]. An increase in oxidative stress increases foam cell formation and atherosclerosis. There is no parameter that is used in clinical biochemistry practice in the direct diagnosis of peripheral arterial disease. The activity of the paraoxonase 1 enzyme, which is an antioxidant enzyme and not only prevents LDL oxidation but also increases the activity of HDL, may be a biochemical marker in the diagnosis of peripheral arterial disease. According to the results of our study, paraoxonase 1 and arylesterase activities were decreased significantly in peripheral arterial disease ($p<0.05$). In a clinical study, it was previously shown that a decrease in PON1 activity increases carotid atherosclerosis and LDL oxidation [13]. In a study on experimental animal models, it was shown that increased PON1 activity decreased atherosclerosis [14]. The results of these studies on atherosclerosis in the literature were in line with our findings. While it would be beneficial to support this study with new studies, evaluation of the activities of the paraoxonase 1 and arylesterase enzymes in routine biochemistry laboratories may provide evidence for the diagnosis and follow-up of peripheral artery disease.

Conclusion

While deciding about the diagnosis and treatment of a patient, meticulous, clear, and accurate use of the information proven by scientific data is expressed as evidence-based medicine [15]. Therefore, a decrease in the activity of the paraoxonase 1 enzyme in peripheral arterial disease may be an important clinical biochemistry indicator in terms of evidence-based medicine.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. Savas HB. Klinik Biyokimyada kanıta dayalı yaklaşım. 1st ed. Ankara: Akademisyen Publishing; 2019.
2. Savran M, Aslankoc R, Ozmen O et al. Agomelatine could prevent brain and cerebellum injury against LPS-induced neuroinflammation in rats. Cytokine 2020; 127: 154957.
3. Savran M, Ozmen O, Erzurumlu Y, Savas HB, Asci S, Kaynak M. The Impact of Prophylactic Lacosamide on LPS-Induced Neuroinflammation in Aged Rats. Inflammation 2019; 42: 1913-24.
4. Seflek HN, Kalkan S, Cuce G, Kılınc I, Sozen ME. Effects of Nigella sativa oil on ovarian volume, oxidant systems, XIAP and NF-kB expression in an experimental model of diabetes. Biotech Histochem 2019; 94: 325-33.
5. Savas HB, Gultekin F, Ciris İM. Positive effects of meal frequency and calorie restriction on antioxidant systems in rats. North Clin Istanbul. 2017; 4(2): 109–116. doi: 10.14744/nci.2017.21548.
6. Gültekin F, Nazıroğlu M, Savaş HB, Çiğ B. Calorie restriction protects against apoptosis, mitochondrial oxidative stress and increased calcium signaling through inhibition of TRPV1 channel in the hippocampus and dorsal root ganglion of rats. Metab Brain Dis. 2018; 33(5): 1761-1774. doi: 10.1007/s11011-018-0289-0.
7. Savaş HB, Yüksel Ö, Şanlidere Aloğlu H, Öner Z, Demir Özer E, Gultekin F. Effects of food based yeast supplementation on oxidative stress in rats fed by high cholesterol diet. Cell Membranes and Free Radical Research. 2013; 5:3: 252-255.
8. Cankara FN, Özmen Ö, Savaş HB, Şahin Y, Günaydın C. Gastroprotective effect of tarantula cubensis extract in the indomethacin-induced peptic ulcer model in rats. Acta Med. Alanya 2020; 4(3): 278-284. doi:10.30565/medalanya.797406.
9. Koutakis P, Ismaeel A, Farmer P et al. Oxidative stress and antioxidant treatment in patients with peripheral arter disease. Physiol Rep 2018; 6: 13650.
10. Bednarz-Misa I, Berdowska I, Zboch M et al. Paraoxonase 1 decline and lipid peroxidation rise reflect a degree of brain atrophy and vascular impairment in dementia. Adv Clin Exp Med 2020; 29: 71-8.
11. Ayan D, Şeneş M, Çaycı AB et al. Evaluation of Paraoxonase, Arylesterase, and Homocysteine Thiolactonase Activities in Patients with Diabetes and Incipient Diabetes Nephropathy. J Med Biochem 2019; 38: 481-88.
12. Moore KJ, Sheedy FJ, Fisher EA. Macrophages in atherosclerosis: a dynamic balance. Nature Reviews Immunology 2013; 13: 709.
13. Tavori H, Aviram M, Khatib S et al. Human carotid atherosclerotic plaque increases oxidative state of macrophages and low-density lipoproteins, whereas paraoxonase 1 (PON1) decreases such atherogenic effects. Free Radical Biology and Medicine 2009; 46: 607-15.
14. Tward A, Xia Y-R, Wang X-P et al. Decreased atherosclerotic lesion formation in human serum paraoxonase transgenic mice. Circulation 2002; 106: 484-90.
15. Djulbegovic B, Guyatt GH. Progress in evidence-based medicine: a quarter century on. Lancet 2017: 390: 415-23.

To cite this article: Birben B, Gundogdu S B, Tikici D, Akkurt G, Akın M, Akın T, Er S, Berkem H. Tez M, External validation of the new prognostic western score in predicting survival after curative resection of gastric cancer. Turk J Clin Lab 2021; 1: 33-36.

Original Article

External validation of the new prognostic western score in predicting survival after curative resection of gastric cancer

Mide kanserinin küratif rezeksiyonundan sonra sağkalımı ön görmede new prognostic western score' un eksternal validasyonu

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Abstract

Aim: Gastric cancers may progress differently depending on the factors affecting the prognosis. In our study, we evaluated the external validation of the new prognostic western score used to predict the surveillance of gastric cancer patients undergoing curative resection.

Material and methods: The study included 139 patients over 18 years of age who underwent curative resection for gastric adenocarcinoma in our hospital between 2004 and 2015. The demographic characteristics of the patients and their albumin level, neutrophil lymphocyte ratio and pathological tumor-nodes-metastasis stage were evaluated.

Results: Fifty-nine (42.4%) of the patients were female and 80 (57.6%) were male. The mean albumin value was 39±7 mg/L, and the median value of the neutrophil/lymphocyte ratio was 2.5 (1.76-4). According to the pathological tumor-nodes-metastasis staging, 13 cases (9.4%) were stage 1, 21 (15.1%) stage 2, 99 (71.2%) stage 3, and 6 (4.3%) stage 4. The five-year median survival of the patients was 32.5 months. Age was significantly higher in the mortality group (P=.021). In the log-rank analysis, a low albumin level, a high neutrophil lymphocyte ratio, and a high tumor-nodes-metastasis stage were statistically significant in the mortality group (P=.001, .000 and .030 respectively). In the Cox regression analysis, the only significant variable was determined as pathological stage (P=.005).

Conclusion: The new prognostic western score was not significant in predicting the prognosis of gastric cancers.

Key words: albumin; neutrophil/lymphocyte ratio; survival; gastric cancer

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Volume 12 Number 1 p: 33-36

Öz

Amaç: Gastrik kanserlerde prognoz etki eden faktörlere bağlı olarak farklı seyredebilmektedir. Biz çalışmamızda küratif rezeksiyon yapılan gastrik kanserlerin sağkalımını ön görmede kullanılan new prognostic western score' un eksternal validasyonunu değerlendirdik.

Gereç ve Yöntemler: Hastanemizde 2004- 2015 yılları arasında gastrik adeno kanser nedeniyle küratif rezeksiyon yapılan 18 yaş üzeri 139 hasta çalışmaya dahil edildi. Hastaların demografik özellikleri albümin, nötrofil lenfosit oranı ve patolojik tümör-lenf nodu-metastaz evresi değerlendirildi.

Bulgular: Hastaların 59 (%42,4)' u kadın, 80 (%57,6)' i erkekti. Albümin ortalama değeri 39±7 mg/L, nötrofil lenfosit oranı medyan değeri 2,5 (1,76-4) idi. Hastaların patolojik tümör-lenf nodu-metastaz evrelemesine göre 13 (%9,4)' ü evre 1, 21 (%15,1)' i evre 2, 99 (%71,2)'u evre 3, ve 6 (%4,3)' sı evre 4 teydi. Hastaların 5 yıllık medyan sağkalımı 32,5 ay idi. Yaş mortalite grubunda anlamlı yüksek bulundu (P= 0,021). Log rank analizinde mortalite grubunda albümin düşüklüğü, nötrofil lenfosit oranı yüksekliği ve tümör-lenf nodu-metastaz evresi yüksekliği istatistiksel anlamlıydı (P= 0,001, 0,000 ve 0,030 sırasıyla). Cox regresyon analizinde anlamlı değişken sadece patolojik evre olarak belirlendi (P=0,005).

Sonuç: Mide kanserlerinde new prognostic western score prognozu göstermede anlamlı bulunmadı.

Anahtar kelimeler: albümin; nötrofil lenfosit oranı; sağkalım; mide kanseri

Introduction

Gastric cancer ranks third in cancer-related deaths worldwide [1]. Despite advances in gastric cancer treatment, the prognosis remains poor in advanced (locally advanced or metastatic) cases [2]. Although the tumor-nodes-metastasis (TNM) staging system is used in prognosis classification, the prognosis may differ among patients at the same stage and receiving the same treatment [3, 4]. Some inflammatory cells in the blood also negatively affect the prognosis with the proteins they secrete [5]. In this study, we aimed to validate the new prognostic western score in the prediction of survival in patients undergoing curative resection for gastric cancer.

Material and methods

Patients data

The study included 139 patients who underwent curative resection due to gastric adenocarcinoma between 2004 and 2015. The patients were retrospectively evaluated. The study was carried out in accordance with the Helsinki Declaration of Principles. The demographic characteristics of the patients and their albumin level, neutrophil/lymphocyte ratio (NLR) and pTNM results used in the new prognostic western score were examined. Patients younger than 18 years old, those with cancer other than gastric adenocarcinoma, and those receiving palliative treatment were excluded from the study. Based on the cut-off values in scoring, 1 point was given for albumin < 35 g/L, NLR > 2.62, and pTNM stage 3-4. The prognostic risk classification was made as Class 1 if the total number of points was 0, Class 2 if 1 point, Class 3 if 2 points, and Class 4 if 3 points in total. This study was approved by institutional ethical committee. Informed consent was obtained from all patients and the principles of the Helsinki Declaration were followed.

Statistical analysis

The basic patient demographic data were summarized as n (%) for categorical variables and mean with standard deviation (SD) or 95% confidence interval (CI) for continuous variables. Continuous variables were compared using Student's t-test or the Mann-Whitney U test as appropriate depending on the normality of their distribution. The differences between the categorical variables were assessed by Fisher's exact test or the $\chi 2$ test with Yeat's correction for continuity, when necessary. Receiver operating characteristic (ROC) curves and the area under the curve (c-statistic) for the outcome of overall mortality was calculated to determine the accuracy of the score.

Overall survival (OS) in the prognostic categories was calculated according to the Kaplan-Meier method. Log-rank tests were used to determine the significant differences between the survival curves. A multivariate Cox proportional hazard model with backward selection was performed to determine which factors were independently predictive of survival.

A P value of <0.05 was considered significant. Statistical analyses were conducted using SPSS v. 24.0.0.0 (SPSS IBM, New York, NY).

Results

Of the 139 patients included in the study, 59 (42.4%) were female and 80 (57.6%) were male, and the mean age value was 59 ± 13 (26-88) years. The mean albumin value was 39 ± 7 mg/L, and the median NLR value was 2.5 (1.76-4). According to the pTNM staging of the cases, 13 (9.4%) were stage 1, 21 (15.1%) were stage 2, 99 (71.2%) were stage 3, and 6 (4.3%) were stage 4. Among the prognostic factors for scoring, 11 patients had 0 risk factor while 67 patients had 1, 48 patients 2, and 13 patients 3 risk factors.

The five-year median survival of the patients was 32.5 months. When the mean age value was taken as cut-off, it was found to be significantly higher in the age mortality group in the log-rank analysis (P = .021). In the log-rank analysis, the decrease in albumin in the mortality group was statistically significant (P = .001), but when the cut-off value of albumin was taken as 3.5 mg/dl, it was not statistically significant (P = .650). The log-rank analysis also revealed that an elevated NLR was statistically significant in the mortality group (P = .000), but no statistical significance was observed at the NLR cut-off value of 2.62 (P = .612). In addition, in the same analysis, a significant difference was found in the mortality group as the stage increased both according to TNM and based on the cut-off value (P = .030 and .003, respectively) (Figure). There was no statistically significant difference in the log-rank analysis of the new prognostic western risk scoring (P = .065). In the Cox regression analysis, the only significant variable was found to be the pathological stage (P = .005). The data of the patients are given in the table.

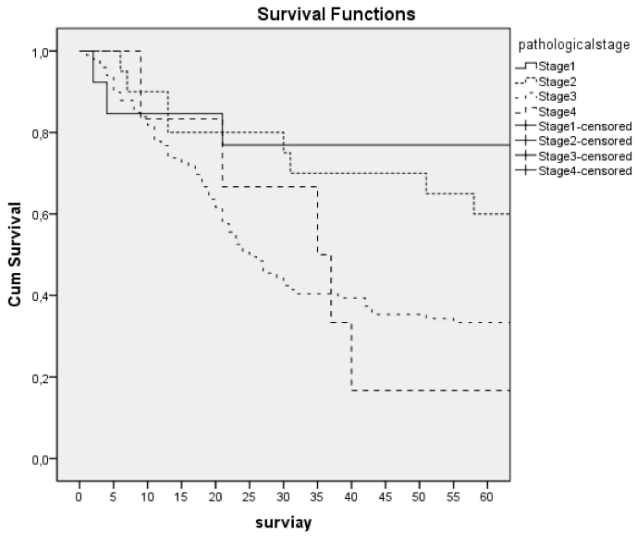

Figure: Statistical analysis of pathological stage in gastric cancer

Table: Demographic characteristics of the patients and statistical analysis results		
Variables	n = 139	p value
Gender F/M (%)	59/80(42.4/57.6)	=.157
Age (years) (m±sd)	59±13	=.021
Albumin g/L (m±sd)	39±7	=.001
Albumin at cut-off <3.5g/L		=.650
Median NLR	2.5 (1.76-4)	=.000
NLR at cut-off >2.62		=.612
TNM stage (%)		=.030
1	13 (9.4)	
2	21 (15.1)	
3	99 (71.2)	
4	6 (4.3)	
Stage at cut-off ≥3		=.003
Western score risk classification (n)		=.065
Risk class 1	11	
2	67	
3	48	
4	13	
TNM; Tumor-nodes-metastasis, NLR; neutrophil/lymphocyte ratio, F; Female, M; Male, m; mean, sd; standard deviation,		

Discussion

In addition to the late diagnosis and detection of gastric cancers in advanced stages, various markers have an important place in predicting prognosis [6]. This study is important in terms of being the first to attempt to validate the new prognostic western score in predicting the prognosis in gastric cancers.

Sun et al. [7] reported that the NLR-platelet/lymphocyte ratio combination was significant in showing prognosis in stage 1-2 gastric cancers, and in a similar study, Graziosi et al. [8] stated that an elevated NLR negatively affected OS. In the literature, it has been suggested that low albumin levels are effective in predicting OS [9, 10]. In the scoring system we validated, low albumin and high NLR values were found to be poor prognostic markers.

In studies conducted to date, Lu et al. [11] determined that lymphovascular invasion was a prognostic marker, and Graziosi et al. [6] also similarly found that an increase in the TNM stage, elevated NLR, and decreased albumin had a negative effect on OS. In the same study, the authors also suggested that the prognosis could be better predicted in gastric cancers with the new prognostic western score they developed using these prognostic markers [6]. In our study, it was seen that the TNM stage alone was significant in predicting the prognosis, but the new prognostic western score was not sufficient for this purpose.

The limitation of the study can be considered as the small number of patients and its retrospective nature.

Conclusion

External validation studies are one of the most reliable indicators for evaluating the accuracy of a system. In our study, the new prognostic western scoring system was not found significant in predicting prognosis in gastric cancer patients.

Funding

The author(s) received no finansial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer j Clin. 2018; 68: 394-424.
2. Digklia A, Wagner AD. Advanced gastric cancer: current treatment landscape and future perspectives. World J Gastroenterol. 2016; 22: 2403.
3. Amin MB, Edge SB. AJCC cancer staging manual. springer; 2017.
4. Shao Y, Geng Y, Gu W, et al. Assessment of lymph node ratio to replace the pN categories system of classification of the TNM system in esophageal squamous cell carcinoma. J Thorac Oncol. 2016; 11: 1774-84.
5. Cools-Lartigue J, Spicer J, McDonald B, et al. Neutrophil extracellular traps sequester circulating tumor cells and promote metastasis. J Clin Invest. 2013; 123: 3446-58.
6. Luigina G, Elisabetta M, Cristina VM, Annibale D. New prognostic western score predicting survival after curative resection of gastric cancer. Updates Surg. 2020: 1-8.
7. Sun X, Liu X, Liu J et al. Preoperative neutrophil-to-lymphocyte ratio plus platelet-to-lymphocyte ratio in predicting survival for patients with stage I–II gastric cancer. Chin J Cancer. 2016; 35: 57.
8. Graziosi L, Marino E, De Angelis V, Rebonato A, Cavazzoni E, Donini A. Prognostic value of preoperative neutrophils to lymphocytes ratio in patients resected for gastric cancer. Am J Surg. 2015; 209: 333-37.
9. Liu X, Sun X, Liu J et al. Preoperative C-reactive protein/albumin ratio predicts prognosis of patients after curative resection for gastric cancer. Transl Oncol. 2015; 8: 339-45.
10. Shen Q, Liu W, Quan H et al. Prealbumin and lymphocyte-based prognostic score, a new tool for predicting long-term survival after curative resection of stage II/III gastric cancer. Br J Nutr. 2018; 120: 1359-69.
11. Lu J, Dai Y, Xie J-W et al. Combination of lymphovascular invasion and the AJCC TNM staging system improves prediction of prognosis in N0 stage gastric cancer: results from a high-volume institution. BMC cancer. 2019; 19: 1-9.

To cite this article: Katar MK, Tikici D. Abdominal duvar endometriozisi; Retrospektif, gözlemsel bir çalışma. Turk J Clin Lab 2021; 1: 37-41.

Orjinal Makale

Abdominal duvar endometriozisi; Retrospektif, gözlemsel bir çalışma

Abdominal wall endometriosis; A retrospective, observational study

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ÖZ

Amaç: Bu çalışmanın amacı, abdominal duvar endometriozisi (ADE) olan hastalarda demografik ve klinik özellikleri, tanı araçlarını, cerrahi seçenekleri ve nüks oranlarını değerlendirmektir.

Gereç ve Yöntemler: Ocak 2015 ile Ocak 2020 tarihleri arasından kliniğimizde ADE nedeniyle opere edilen 44 hasta çalışmaya dahil edildi. Hastalara ait demografik veriler, operasyon geçmişi, klinik özellikler, tanı için kullanılan görüntüleme yöntemi, uygulanan operasyon tipi ve rekürrens durumu değerlendirildi.

Bulgular: Çalışmaya dahil edilen hastaların, yaşlarının median değeri 35 (26-48) olarak belirlendi. Hastalardan 1 (%2,3)'inin abdominal operasyon öyküsü bulunmazken; 39 (%88,6) hastanın cesarean section (C/S), 2 (%4,5) hastanın myomektomi ve 2 (%4,5) hastanın da histerektomi öyküsü bulunmaktadır. Çalışmaya dahil edilen hastalardan 2 (%4,5)'sinin herhangi bir şikayeti bulunmazken, 31 (%70,5) hastada karın ön duvarında kitle ve 39 (%88,6) hastada ise ağrı şikayeti bulunmaktaydı. ADE'nin 23 (%52,3) hastada pfannenstiel insizyonun sol lateralinde ve 17 (%38,6) hastada ise pfannenstiel insizyonun sağ lateralinde olmak üzere, büyük çoğunluğunun pfannenstiel insizyon hattında olduğu tespit edildi. Hastaların 34'ünde preoperatif tanı aracı olarak abdominal ultrasonografi (US) ve 10 hastada da abdominopelvik bilgisayarlı tomografi (BT) kullanılmıştır. Abdominal US'nin doğruluk oranının %85,2, abdominopelvik BT'nin doğruluk oranının ise %50 olduğu belirlenmiştir. Serimizdeki takip oranı %95,4 iken, takip süresi median değerinin 36,5 ay (13-57) olduğu gösterilmiştir. Ayrıca takipteki hastalardan birinde rekürrens geliştiği görülmüştür.

Sonuç: ADE, jinekolojik girişim öyküsü olan ve abdominal insizyon bölgesinde siklik ağrı ve şişlik ile gelen reprodüktif çağdaki tüm kadınlarda akla gelmelidir. Preoperatif tanı için, hastanın öyküsü ayrıntılı olarak sorgulanmalı; dikkatli bir fizik muayene yapılmalı ve tanı için abdominal US kullanılmalıdır. Tedavide cerrahi eksizyon tercih edilmelidir.

Anahtar kelimeler: Endometriozis; karın duvarı; siklik ağrı; kitle

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Doi: 10.18663/tjcl.859676

Volume 12 Number 1 p: 37-41

Abstract

Aim: The aim of this study is to evaluate demographic and clinical characteristics, diagnostic tools, surgical options and recurrence rates in patients with abdominal wall endometriosis (AWE).

Material and Methods: 44 patients who were operated for AWE in our clinic between January 2015 and January 2020 were included in the study. Demographic data of the patients, operation history, clinical features, imaging method used for diagnosis, type of operation performed and recurrence status were evaluated.

Results: The median age of the patients included in the study was determined as 35 (26-48). While 1 (2.3%) of the patients did not have a history of abdominal operation; 39 (88.6%) patients had cesarean section (C / S), 2 (4.5%) patients had myomectomy and 2 (4.5%) patients had hysterectomy history. In addition, 2 (4.5%) of the patients included in the study had no complaints, while 31 (70.5%) patients had a mass in the anterior abdominal wall and 39 (88.6%) patients had pain. AWE was in the left lateral of the pfannenstiel incision in 23 (52.3%) patients and in the right lateral of the pfannenstiel incision in 17 (38.6%) patients; the majority of them were found to be in the pfannenstiel incision. Abdominal ultrasonography (US) was used as a preoperative diagnostic tool in 34 of the patients and abdominapelvic computed tomography (CT) was used in 10 patients. It was determined that the accuracy rate of abdominal US was 85.2%, and the accuracy rate of abdominopelvic CT was 50%. While the follow-up rate in our series was 95.4%, the median value of follow-up period was 36.5 months (13-57). In addition, recurrence was observed in one of the patients followed up.

Conclusion: AWE should be considered in all women of reproductive age who have a history of gynecological intervention and present with cyclic pain and swelling at the abdominal incision. For preoperative diagnosis, the patient's history should be questioned in detail; a careful physical examination should be performed, and abdominal US should be used for diagnosis. Surgical excision should be preferred in treatment.

Keywords: Endometriosis; abdominal wall; cyclic pain; mass

Giriş

Endometriozis, endometrium dokusunun endometrial kavite dışında bulunması olarak tanımlanır.[1] Reprodüktif çağdaki kadınlarda insidansının %5-15 civarında olduğu bildirilmektedir.[2] Endopelvik alanda gelişebileceği gibi beyin, akciğer, umblikus, inguinal bölge veya insizyon skarı gibi ekstrapelvik alanda da gelişebildiği bildirilmiştir.[3,4] Abdominal duvar endometriozisi (ADE), subkutan adipoz dokuda veya karın duvarının muskuler tabakasında endometrium dokusunun varlığı ile karakterize nadir bir durumdur. İnsidansı % 0,03-3,5 arasında değişmektedir.[5,6] Genellikle cesarean section (C/S) gibi obstetrik veya jinekolojik cerrahi sırasında insizyon yerinde endometrial dokunun yayılmasından kaynaklanır.[5,7,8] En sık klinik bulgusu boyutları değişiklik gösterebilen ve menstruasyon sırasındaki siklik ağrı oluşturan kitledir.[9] ADE'nin klinik görünümü, ortaya çıkma zamanı ve yeri oldukça değişkendir ve bu durum çoğu zaman preoperatif tanı koymayı zorlaştırır. Ayrıca tanıda abdominal ultrasonografi (US) ve abdominopelvik bilgisayarlı tomografi (BT) kullanılmasına karşın, kesin tanı için hangi yöntemin kullanılacağı konusunda klinisyenler arasında fikir birliği bulunmamaktadır. Bu nedenlerden dolayı, ADE fıtık, lipom veya hematom ile karıştırılarak yanlış teşhis edilme riski taşımaktadır.[10]

Bu çalışmanın amacı, ADE olan hastalarda demografik ve klinik özellikleri, tanı araçlarını, cerrahi seçenekleri ve nüks oranlarını değerlendirmektir.

Gereç ve Yöntemler

Çalışma öncesinde etik kurul onayı, üniversitemiz Klinik Araştırmalar Etik Kurulu'ndan alındı. Bu çalışma tek merkezde, retrospektif ve gözlemsel bir çalışma olarak tasarlanmıştır ve Helsinki Deklarasyonu'na uygun olarak gerçekleştirilmiştir.

Ocak 2015 ile Ocak 2020 tarihleri arasından kliniğimizde ADE nedeniyle opere edilen (patolojik olarak da teyit edilen) 44 hasta çalışmaya dahil edildi. Hastanemiz veri tabanı incelenerek hastalara ait demografik veriler, operasyon geçmişi, klinik özellikler, tanı için kullanılan görüntüleme yöntemi, uygulanan operasyon tipi ve rekürrens durumu kayıt altına alındı.

Bulgular

Çalışmaya dahil edilen hastaların, yaşlarının median değeri 35 (26-48) olarak belirlendi. Hastaların doğum sayılarının ortanca değeri ise 1 (0-3)'di. Sadece 1 (%2,3) hastanın daha önce herhangi bir abdominal operasyon öyküsü bulunmazken; 39 (%88,6) hastanın C/S öyküsü bulunmaktadır. Diğer yandan geri

kalan 4 hastanın da C/S öyküsü bulunmasına karşın; hastalara en son uygulanan cerrahi işlemlerin 2 (%4,5) hastada myomektomi ve 2 (%4,5) hastada da histerektomi olduğu tespit edildi. C/S sayılarına bakıldığında 27 (%61,4) hastanın 1, 11 (%25) hastanın 2 ve 5 (%11,4) hastanın ise 3 C/S öyküsü bulunmaktadır.

Çalışmaya dahil edilen hastalardan 2 (%4,5)'sinin herhangi bir şikayeti bulunmazken, ADE insidental olarak tespit edilmiştir. Hastaların 31 (%70,5)'inde karın ön duvarında kitle şikayeti bulunurken, 39 (%88,6) hastanın ise ağrı şikayeti bulunmaktaydı. Ağrı, 25 (%64,1) hastada siklik, 14 (%35,9) hastada non-siklik karakterde olduğu belirlendi.

ADE'nin 23 (%52,3) hastada pfannenstiel insizyonun sol lateralinde, 17 (%38,6) hastada pfannenstiel insizyonun sağ lateralinde, 1 (%2,3) hastada median abdominal insizyon hattında, daha önce herhangi bir operasyon öyküsü olmayan 1 (%2,3) hastada sol rektus kasının lateralinde ve 2 (%4,5) hastada ise umblikusta yer aldığı tespit edildi. Ayrıca C/S öyküsü olan 1 (%2,3) hastanın ADE'ne pelvik endometriozisinde eşlik ettiği belirlendi. Hastalara ait demografik veriler Tablo 1'de verilmiştir.

Tablo 1: Demografik Özellikler

	n (%)
Yaş*	35 (26-48)
Doğum Sayısı*	1 (0-3)
Eski Operasyon Öyküsü	
Operasyon Öyküsü yok	1 (2,3)
Sezaryen	39 (88,6)
Myomektomi	2 (4,5)
Histerektomi	2 (4,5)
Sezaryen Sayısı	
0	1 (2,3)
1	27 (61,4)
2	11 (25)
3	5 (11,4)
Semptom	
Asemptomatik	2 (4,5)
Kitle	31 (70,5)
Ağrı	39 (88,6)
Ağrı Karakteri	
Siklik	25 (64,1)
Non-siklik	14 (35,9)
Kitle Yerleşim Yeri	
Pfannenstiel İnsizyon Sol	23 (52,3)
Pfannenstiel İnsizyon Sağ	17 (38,6)
Median Abdominal İnsizyon	1 (2,3)
Rektus Kasının Sol Laterali	1 (2,3)
Umblikus	2 (4,5)
Pelvik Endometriozis Birlikteliği	1 (2,3)
*Median (min-max).	

Hastaların 34'ünde preoperatif tanı aracı olarak abdominal US kullanılmış olup; bunlardan 29 (%85,2)'unda ADE, 2 hastada desmoid tümör, 2 hastada sütur granulomu ve 1 hastada da nörofibroma preoperatif tanı olarak bildirilmiştir. Hastaların 10'unda ise abdominopelvik BT preoperatif tanı aracı olarak kullanılmış olup; bunlardan 5 (%50)'inde ADE, 2 hastada desmoid tümör, 2 hastada inflamatuar granulom ve 1 hastada ise benign lipomatöz lezyon preoperatif tanı olarak belirlenmiştir. Ayrıca 3 hastanın preoperatif tanısında abdominal US'a ek olarak manyetik rezonans görüntüleme (MRI) kullanılmış olup, bu hastalarının tamamında preoperatif tanı olarak ADE bildirilmiştir. Preoperatif tanı araçlarına ait veriler Tablo 2'de verilmiştir.

Tablo 2: Preoperatif Tanı Doğruluğu

Preoperatif Tanı Aracı	Doğruluk (%)	Diğer Tanı
Abdominal US	29/34 (85,2)	Desmoid tümör 2 hasta, Nörofibroma 1 hasta, Sütur granulomu 2 hasta
Abdominopelvik BT	5/10 (50)	İnflamatuar granulom 2 hasta Desmoid tümör 2 hasta Benign lipomatöz lezyon 1 hasta
US ve MRI	3/3 (100)	

US: Ultrasonografi., BT: Bilgisayarlı Tomografi, MRI: Manyetik rezonans görüntüleme

Tedavi prosedürü olarak hastaların tamamına geniş eksizyon işlemi uygulanmıştır. Eksizyon işlemine ek olarak 2 (%4,5) hastada geniş fasya defekti oluşması nedeniyle mesh kullanılmıştır. ADE'e ek olarak pelvik endometriozis tespit edilen 1 (%2,3) hastaya da eksizyon işlemi ile birlikte sol salpingo-ooferektomi işlemi uygulanmıştır. Ayrıca 2 (%4,5) hastaya cerrahi tedaviye ek olarak medikal tedavi de (gonadotropin-releasing hormon) uygulandığı tespit edilmiştir. Tedavi prosedürü ve cerrahi tedavi ek medikal tedaviye ait veriler Tablo 3'te gösterilmiştir.

Tablo 3: Cerrahi Yönetim ve Rekürrens

	n (%)
Operasyon Prosedürü	
Eksiyon	41 (93,2)
Eksiyon+Mesh	2 (4,5)
Eksiyon+Sol SO	1 (2,3)
Tümör Boyutu (cm)*	3,5 (2-8,6)
Operasyon Sonrası Ek Medikal Tedavi	2 (4,5)
Takip Süresi (ay)	36,5 (13-57)
Rekürrens	1 (2,3)

* Median (min-max). SO: Salpingo-ooferektomi.

Hastalarımızdan 42 (%95,4)'sinin takiplerine devam ettiği tespit edilmiş olup, serimizdeki takip süresi median değerinin 36,5 ay (13-57) olduğu gösterilmiştir. Ayrıca 1(%2,3) hastanın takiplerinde rekürrens geliştiği belirlenmiştir. Bu hastaya reeksizyon önerilmiş fakat hastanın reoperasyonu reddetmesi nedeniyle uygulanamadığı tespit edilmiştir. Takip süresi ve rekürrense ait veriler Tablo 3'te verilmiştir.

Tartışma

ADE, oldukça nadir olmakla birlikte, pelvik veya jinekolojik operasyon öyküsü olan kadınlardaki prevelansı % 0,03-1,08 olarak bildirilmiştir.[11] Nadir olarak ortaya çıkmasına karşın, tespit edildiği takdirde derhal tedavi edilmesi gerekmektedir. Çünkü literatürde, ADE zemininde clear cell carcinoma and adenocarcinoma geliştiği bildirilmiştir.[12-14]

Patogenezi için çeşitli hipotezler ortaya atılmasına rağmen literatürde net bir fikir birliği bulunmamaktadır. En çok üzerinde durulan hipotez ise, C/S işlemi sırasında endometrial dokunun abdominal fasya ve subkutan dokuya iatrojenik implantasyonudur.[15] Ancak bu hipotezin aksine, ADE vakalarının %20'sinde cerrahi öyküsü olmadığı bildirilmiştir.[10] Cerrahi öyküsü olmayan bu hasta grubunda ise, ADE'nin endometriyal dokunun hematojen veya lenfatik yayılmasının bir sonucu olduğuna inanılmaktadır.[10] Gerçekleştirdiğimiz bu çalışmada, sadece bir hastanın operasyon öyküsü bulunmazken; kalan hastaların tamamında C/S başta olmak üzere en az bir operasyon öyküsü bulunmaktadır. Bu konunun aydınlatılması adına, ilerleyen zamanda yapılacak deneysel çalışmaların literatüre katkı sağlayacağına inanıyoruz.

Klinik olarak, ADE'n en sık görülen semptomları kitle ve ağrıdır.[10,16] Literatürle uyumlu olarak bizim serimizde de kitle ve ağrı semptomunun yoğunlukta olduğu belirlenmiştir. Ağrının ise ağırlıklı olarak siklik karakterde olduğu gösterilmiştir. Ayrıca 2 hastanın herhangi bir şikayeti bulunmamasına rağmen; başka bir neden için yapılan araştırmada, pfannenstiel insizyon hattında insidental olarak kitle tespit edilmiştir.

ADE'nin nadir olarak görülmesi ve sıklıkla sütur granülomu, yumuşak doku sarkomu, desmoid tümör gibi bazı hastalıklarla karışması, preoperatif tanıyı oldukça güçleştirmektedir. Şöyle ki; preoperatif klinik tanı doğruluğunun %26 ile %70 arasında değiştiği bildirilmiştir.[9,16,17] Preoperatif tanıda kullanılan en sık yöntemler arasında abdominal US, abdominopelvik BT, abdominapelvik MRI ve US klavuzluğunda ince iğne aspirasyon biyopsisi (İİAB) yer almaktadır.[18-19] Bizde literatürle uyumlu olarak preoperatif tanı aracı olarak çoğunlukla abdominal US ve daha az oranda abdominopelvik BT'yi kullandık. Serimizde, abdominal US'nin doğruluk oranı %85 üzerinde iken, BT'nin doğruluk oranının %50'de kaldığı tespit edilmiştir. Ortaya çıkan bu sonucun, abdominal US'nin avantajlarından biri olan radyologun US uygulaması sırasında karın duvarındaki hassas noktayı belirleyebilmesinden kaynaklanabileceğini düşünüyoruz.[20] Ayrıca çalışmamızda, US ve MRI'nin birlikte kullanıldığı 3 hastada doğruluk oranının %100 olması dikkat çekicidir. Öte yandan doğruluk oranının düşük olması nedeniyle hiçbir hastada preoperatif tanı aracı olarak İİAB'ni tercih etmedik.[16] Ancak Song HK ve arkadaşları, 38 hastanın dahil edildiği çalışmasında, preoperatif uygulanan görüntüleme yöntemlerinde hiçbir hastada malignite tespit edilmemesine rağmen, 3 hastanın postoperatif patolojisinde malignite tespit edilmesi nedeniyle, preoperatif dönemde ADE'nden şüphelenilen durumlarda İİAB önermektedir.[21] Diğer yandan İİAB işlemi, uygulama yerinde implantasyon için risk oluşturmaktadır.[22,23] Görünen o ki; bu konuda fikir birliği oluşabilmesi için geniş serili ve prospektif çalışmalara ihtiyaç vardır. Biz ise klinik tecrübemize dayanarak, preoperatif tanı aracı olarak öncelikle abdominal US'yi ve şüpheli bazı durumlarda ise abdominal US'ye ek olarak abdominopelvik MRI'yi öneriyoruz.

ADE'nin en yaygın tedavi seçenekleri medikal tedavi ve cerrahidir.[2,24] Medikal tedavide amaç, hormonların lezyon üzerindeki etkisini azaltarak semptomların giderilmesidir; ancak medikal tedavi uygulanan çoğu hastada cerrahi eksizyon gerekli olmaktadır.[18] Bu nedenle ADE tedavisinde cerrahi eksizyon, hem tanıda hem de tedavide en etkili seçenek olarak karşımıza çıkmaktadır. Çalışmamızdaki tüm hastalara, Kim SM ve arkadaşlarının çalışmasında önerildiği gibi en az 1 cm'lik temiz cerrahi sınırlar sağlanacak şekilde cerrahi eksizyon işlemi uygulanmıştır.[25] Fakat gerçekleştirdiğimiz literatür araştırmasında, temiz cerrahi sınır büyüklüğünün rekürrensdeki rolünü inceleyen çalışmaya rastlamadık. Ayrıca literatürde de önerildiği gibi, insizyonel herniyi önlemek adına 2 hastada cerrahi eksizyona ek olarak polipropilen mesh kullandık.[8,22,24] Takiplerimizde hastaların hiçbirinde insizyonel herni gelişmediğini belirledik. Diğer yandan ADE'ne ek olarak pelvik endometriozisi olan 1 hastada, ADE cerrahi olarak eksize edilirken pelvik endometriozis için ise salpingo-ooferektomi tercih edilmiştir. Ayrıca 2 hastaya ise cerrahi eksizyona ek olarak medikal tedavi de (gonadotropin-releasing hormon) verildiği belirlendi.

Gerçekleştirdiğimiz literatür incelemesinde, düşük rekürrens oranlarının (%4,5-9,1) olduğunu tespit ettik.[16,26] Çalışmamızda ise sadece 1 (%2,3)'inde rekürrens geliştiği tespit edildi. Hasta, ADE nedeniyle cerrahi işlem uygulanmasından 22 ay sonra aynı lokalizasyonda ağrılı şişlik nedeniyle tekrar başvuru yaptı. Abdominal US'de nüks ADE belirlenmesi üzerine tekrar operasyona alındı. Geniş eksizyonun yanı sıra mesh kullanıldı. Bu hastanın daha sonraki takiplerinde nüks tespit edilmedi.

Sonuç

ADE, jinekolojik girişim öyküsü olan ve abdominal insizyon bölgesinde siklik ağrı ve şişlik ile gelen reprodüktif çağdaki tüm kadınlarda akla gelmelidir. Preoperatif tanı için, hastanın öyküsü ayrıntılı olarak sorgulanmalı; dikkatli bir fizik muayene yapılmalı ve abdominal US ilk tercih edilecek görüntüleme yöntemi olarak kullanılmalıdır. Ayrıca ADE'nde tercih edilmesi gereken tedavi seçeneği cerrahi eksizyondur.

Çıkar çatışması / finansal destek beyanı

Bu yazıdaki yazarların herhangi bir çıkar çatışması yoktur. Yazının herhangi bir finansal desteği yoktur.

Kaynaklar

1. Nezhat FR, Shamshirsaz AA, Yildirim G. Pelvic pain, endometriosis, and the role of the gynecologist. Pediatric, Adolescent and Young Adult Gynecology. 1st ed. New Jersey: Wiley-Blackwell; 2009:174-94.
2. Alessandro P, Luigi N, Felice S, Maria PA, Benedetto MG, Stefano A. Research development of a new GnRH antagonist (Elagolix) for the treatment of endometriosis: A review of the literature. Arch Gynecol Obstet 2017; 295: 827-32.
3. Sarma D, terBrugge KG, Gentili F, Halliday W. Cerebellar Endometriosis. AJR Am J Roentgenol 2004; 182: 1543-6.
4. Huang H, Li C, Zarogoulidis P et al. Endometriosis of the lung: report of a case and liter- ature review. Eur J Med Res 2013; 18: 13.
5. Leite GKC, de Carvalho LFP, Korkes H et al. Scar endometrioma following obstetric surgical incisions: retrospective study on 33 cases and review of the literature. Sao Paulo Med J 2009; 127: 270–7.
6. Uçar MG, Şanlıkan F, Göçmen A. Surgical treatment of scar endometriosis following cesarean section, a series of 12 cases. Indian J Surg 2015; 77: 682–6.
7. Rindos NB, Mansuria S. Diagnosis and management of abdominal wall endometriosis: a systematic review and clinical recommendations. Obstet Gynecol Surv 2017; 72: 116-22.
8. Blanco RG, Parithivel VS, Shah AK, Gumbs MA, Schein M, Gerst PH. Abdominal wall endometriomas. Am J Surg 2003; 185: 596-8.
9. Chang Y, Tsai EM, Long CY, Chen YH, Kay N. Abdominal wall endometriomas. J Reprod Med 2009; 54: 155–9.
10. Horton JD, Dezee KJ, Ahnfeldt EP, Wagner M. Abdominal Wall endometriosis: A surgeon's perspective and review of 445 cases. Am J Surg 2008; 196: 207-12.
11. Nominato NS, Prates LF, Lauar I, Morais J, Maia L, Geber S. Caesarean section greatly increases risk of scar endome- triosis. Eur J Obstet Gynecol Reprod Biol 2010; 152: 83–5.
12. Taburiaux L, Pluchino N, Petignat P, Wenger JM. Endometriosis-associated abdominal wall cancer: a poor prognosis? Int J Gynecol Cancer 2015; 25: 1633-8.
13. Ferrandina G, Palluzzi E, Fanfani F et al. Endometriosis-associated clear cell carcinoma arising in caesarean section scar: a case report and review of the literature. World J Surg Oncol 2016; 14: 300.
14. Modesitt SC, Tortolero-Luna G, Robinson JB, Gershenson DM, Wolf JK. Ovarian and extraovarian endometriosis- associated cancer. Obstet Gynecol 2002; 100: 788-95.
15. Khachani I, Filali Adib A, Bezad R. Cesarean scar endometriosis: An uncommon surgical complication on the rise? Case report and literature review. Case Rep Obstet Gynecol 2017; 80: 629-24.
16. Bektas H, Bilsel Y, Sari YS et al. Abdominal wall endo- metrioma; a 10-year experience and brief review of the literature. J Surg Res 2010; 164: e77–e81.
17. Fernandez-Acenero MJ, Cordova S. Cutaneous endome- triosis: review of 15 cases diagnosed at a single institution. Arch Gynecol Obstet 2011; 283: 1041–4.
18. Oh EM, Lee WS, Kang JM, Choi ST, Kim KK, Lee WK. A surgeon's perspective of abdominal wall endometriosis at a caesarean section incision: Nine cases in a single institution. Surg Res Pract 2014; 2014: 765372.
19. Medeiros Fd, Cavalcante DI, Medeiros MA, Eleutério J Jr. Fine-needle aspiration cytology of scar endometriosis: Study of seven cases and literature review. Diagn Cytopathol 2011; 39: 18-21.
20. Savelli L, Manuzzi L, Donato ND et al. Endometriosis of the abdominal wall: ultrasonographic and doppler characteristics. Ultrasound Obstet Gynecol 2011; 10052: 132.
21. Song HK, Lee SH, Kim MJ, Shin JE, Lee DW, Lee HN. Abdominal wall mass suspected of endometriosis: clinical and pathologic features. Obstet Gynecol Sci 2020; 63: 357-62.
22. Patterson GK, Winburn GB. Abdominal wall endometriomas: Report of eight cases. Am Surg 1999; 65: 36-9.
23. Grigore M, Socolov D, Pavaleanu I, Scripcariu I, Grigore AM, Micu R. Abdominal wall endometriosis: an update in clinical, imagistic features, and management options. Med Ultrason 2017; 19: 430-7.
24. Purvis RS, Tyring SK. Cutaneous and subcutaneous endome- triosis. Surgical and hormonal therapy. J Derm Surg Oncol 1994; 20: 693-5.
25. Kim SM, Kim HK, Namkung J et al. A case of reconstruction of abdominal fascia using polypropylene mesh for patient of abdominal wall endometriosis after cesarean section. Korean J Obstet Gynecol 2012; 55: 517-21.
26. Khan Z, Zanfagnin V, El-Nashar SA, Famuyide AO, Daft- ary GS, Hopkins MR. Risk factors, clinical presentation, and outcomes for abdominal wall endometriosis. J Minim Invasive Gynecol 2017; 24: 478-84.

To cite this article: Kuscuoglu G, Damgaci L . Can carotid canal diameter be an indicator of anterior cerebral vascular variations and abnormalities? Turk J Clin Lab 2021; 1: 42-49.

Original Article

Can carotid canal diameter be an indicator of anterior cerebral vascular variations and abnormalities?

Karotid kanal çapı anterior serebral vasküler varyasyonların ve anomalilerin gösterilmesinde yol gösterici olabilir mi?

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Abstract

Aim: To measure the bony carotid canal diameters and to determine whether the variations of bony carotid canal width could be an indicator of cerebral vascular abnormalities and variations.

Material and Methods: Seven-hundred neck-brain CT angiographies were assessed retrospectively. Of the patients, 283 (40.4%) were women and 417 (59.6%) were men. Bilateral bony carotid canal diameter was measured. Cerebral vascular variations and aneurysms were recorded.

Results: Normal canal diameter on the right, in all patients was 5.631±0.502mm, in males 5.797±0.475mm and 5.388±0.441mm in females; on the left side, 5.666±0.512mm overall, 5.825±0.492mm in males and 5.432±04.49mm in females (p=0.039, <0.001 and <0.001 consequently).

In vascular hypoplasias, in all other vascular agenesias other than posterior communicating (Pcom) artery, in Moyamoya disease, in anterior and middle cerebral artery aneurysms the canal is narrow.

In the presence of fetal originated vessels, in dolichoectasias of vessels, except PCom, in all anterior communicating artery (ACom) variations and aneurysms, in internal cerebral artery aneurysm the canal is wide.

PCom agenesia, anterior cerebral artery A2 trifurcation and ACom fenestration is accompanied by narrow canal on the right and wide canal on the left.

Conclusion: Abnormal canal diameter may indicate to vascular variation or abnormaliti. The increased incidence of aneurysm in carotid canal anomalies implicates of the necessity of further studies with larger groups.

Keywords: cerebral; vascular; carotid; canal; CTA

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Recevied: 15/01/2021 accepted: 08/03/2021
Doi: 10.18663/tjcl.861566

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ÖZ

Amaç: Karotid kanal çapının ölçülmesi ve kanal çapındaki değişikliklerin serebral vasküler anomaliler ve varyasyonların göstergesi olup olamayacağının belirlenmesi amaçlandı.

Gereç ve Yöntemler: Yedi yüz beyin-boyun bilgisayarlı tomografi incelemesi retrospektif olarak değerlendirildi. Hastaların 283'ü (40.4%) kadın, 417'si (59.6%) erkekti. İki taraflı karotid kanal çapı ölçüldü. Serebral vasküler varyasyonlar ve anomaliler kaydedildi.

Bulgular: Sağ karotid kanal çapı tüm hastalarda 5.631±0.502mm, erkeklerde 5.797±0.475mm ve kadınlarda 5.388±0.441mm; sol karotid kanal çapı tüm hastalarda 5.666±0.512mm, erkeklerde 5.825±0.492mm ve kadınlarda 5.432±04.49mm bulundu (p=0.039, <0.001 ve<0.001).

Vasküler hipoplazilerde ve posterior komünikan arter (PCom) dışındaki diğer vasküler agenezilerde, Moyamoya hastalığında, anterior ve orta serebral arter anevrizmalarında karotid kanal dardır.

Fetal orjinli posterior serebral arter varlığında, PCom dışındaki dolikoektazilerde, anterior komünikan arter (ACom) varyasyon ve anevrizmalarında, internal serebral arter anevrizmasında karotid kanal geniştir.

PCom agenezisi, anterior serebral arter A2 trifukasyonu ve ACom fenestrasyonu sağda dar kanal solda geniş kanal ile birliktelik göstermektedir.

Sonuç: Karotid kanal çapındaki anormallikler, serebral vasküler varyasyon ve anevrizmaların göstergesi olabilir. Karotid kanal anormalliklerinde artan anevrizma insidansı daha geniş hasta gruplarında daha geniş çalışmaların gerekliliğini göstermektedir.

Anahtar kelimeler: serebral; vasküler; karotid; kanal; BTA

Introduction

In the absence of internal carotid artery (ICA), the bony carotid canal does not develop as well. In ICA hypoplasia, on the other hand, the canal is narrower than normal.[1] Other rare variations such as persistent stapedial artery and aberrant internal carotid artery also cause abnormalities in the carotid canal [2]. Moyamoya disease is characterized by ICA stenosis, carotid canal narrowing and increase in leptomeningeal vascularization secondary to ICA stenosis [3].

Starting from the effect of these variations and abnormalities on carotid canal, it does not seem extraordinary to think that changes in carotid canal diameter can provide clues about cerebral vascularization.

The objective of this study is to measure the bony carotid canal diameters and to determine whether the variations of bony carotid canal width could be an indicator of cerebral vascular abnormalities and variations.

Material and Methods

The research was reviewed and approved by the local ethics committee (Ankara Numune Educational and Research Hospital Ethics Committee) with the file number B.10.4.ISM.4.06.00.13/40045.

Images containing motion artifacts impairing the evaluation of the vascular tree or carotid canal, or metalic artefacts were excluded from the study. Cranial trauma and surgical history, malignities, acromegaly, fibrous displasia and all tumors and inflammatory disorders affecting the skull base were of the exclusion criterias.

Otherwise, patients older than 18 year of age with computerized tomography angiography (CTA) examinations done with different indications such as transient ischemic attack and stroke, vertigo, headache, or balance, movement, hearing and visual disorders between January 2013 and January 2014 were evaluated retrospectively. The study included 700 patients, of which 283 women (%40,4) and 417 men (%59,6).

CT Angiography Imaging Protocol:

Examinations were performed with 64-detector computerized tomography device (Aquilion 64, Toshiba Medical Systems, 2011, Japan). The parameters used in the examinations are as follows: collimation 64x0.5, gantry rotation time 0.5 sec, slice thickness 0.5 mm, pitch value 0.64 and X-ray tube 120kV & 450mA.

The patients were placed in supine position, their heads placed into a cranium headpiece in order to immobilize the head. Scanning in caudocranial direction was done after

determining localization on lateral topography and telling the patients to breathe shallow and not to swallow. Contrast material containing intravenous 100 ml non-ionic, high iodine concentration (350-400 mg/ml iodine concentration) was injected from an antecubital vein via 18-20 G catheter with 4 ml/sec speed using an automatic pump (Ulrich medicine technical version, 2004, Germany). After the contrast material, 40 cc of normal saline was administered. Bolus tracking technique was used during scannings. A cursor was placed on the aortic arch and the scan was started when density reached 130 Hounsfield Units (HU). Total scanning lasted approximately 9.6 seconds.

The obtained CTA images were examined using Aquarius® (iNtuition edition version, California, USA) software. After axial sections were examined, multi-planar reconstruction, volume rendering and maximum intensity projection reconstructions were used for assessement. HP ZR2440W (24", 1920x1200@60Hz) and ASUS PB278Q (27", 2560x1440@60Hz) monitors were used to assess the obtained images.

After the patient is layed on the table the head positioning may not always be symetrical. Furthermore, after being positioned the patient may disrupt his/her position. Therefore, prior to the measurements, sagittal plane adjustments of the hard palate, coronal plane adjustments parallel to the large sphenoid wings have been made and the measurements were obtained considering the internal acoustic canal symmetry (Fig. 1a, b.). All the measurements were made by the same radiologist experienced in head and neck radiology. Before the measurements were made, intraobserver reliability was calculated by obtaining double measurements of 30 carotid canals on images with optimized positions as described above (Intraclass correlation coefficient 0.999, p=<0.001), thus the measurements were found to be compatible.

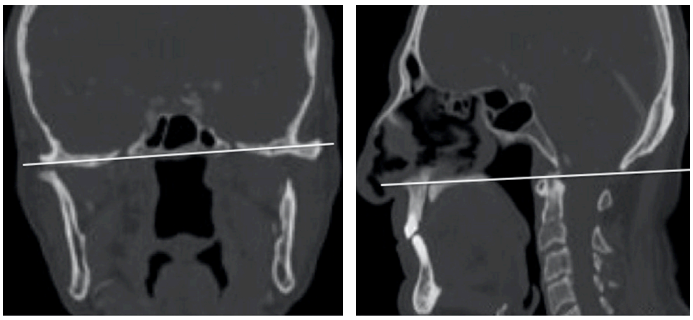

Figure 1a, b. Prior to measurement, symmetry was obtained to the large sphenoid wing on coronal plane, and parallel to the hard palate on sagittal plane.

Bone-to-bone measurements were done on axial sections, parallel to the skull base in CT bone window. Measurement was taken from the middle region of the transverse part of the petrous carotid canal (Fig. 2). Variations and abnormalities in anterior cerebral circulation were recorded. Since variations and anomalies of anterior communicating artery and anterior cerebral artery of A2 segment are in midline, they were accepted as bilateral because of affecting both ICAs.

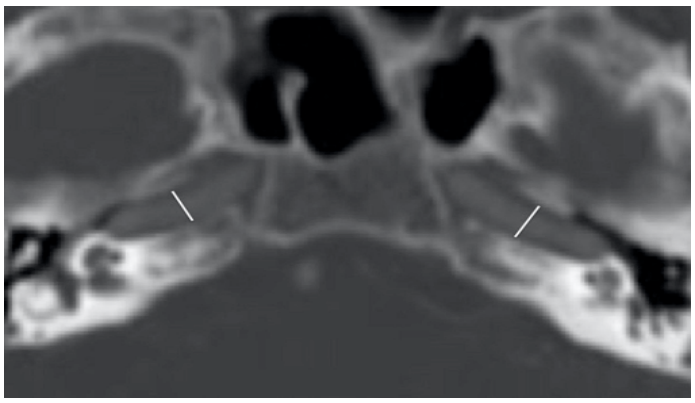

Figure 2. Measurement method of the carotid canal. Bone-to-bone measurement from the middle of the canal perpendicular to the canal wall was made.

Statistical Analysis

The data obtained at the end of the study were analyzed using SPSS 15.0 (Statistical Package for Social Sciences, 15.0, SPSS Inc., Chicago, USA) package software.

Intraclass correlation coefficient of 30 patients was calculated in order to evaluate the intraobserver reliability.

Continuous data distribution was heterogeneous, therefore non-parametric tests have been used. When comparing independent groups, Mann-Whitney U test was used for continuous variables, whereas Wilcoxon test was used when comparing dependent groups. Comparison of discrete variables between groups was assessed with Chi-square test.

Right-left canal diameters were compared with paired samples test, and canal diameters with respect to gender were compared with independent samples test.

P<0.05 value was accepted as significant. Descriptive statistic values were given as number and average percentage.

Results

The mean age of 700 cases assessed was 60.04 (19-89), 58.95 (24-89) for women and 60.79 (19-88) for men. In 345 (49.2%) (205 male (59.4%), 140 female (40.6 %) of these patients no variations or abnormalities have been detected. Normal canal diameters and gender distribution are presented on the Table. The canal is bilaterally more narrow in females (p<0.001). The canal diameter is more narrow on the right side of all patients (p=0.039).

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Variations or abnormalities were grouped as narrow compared to normal canal diameter or with wide canal diameter and presented on the Table. As a result of this classification, in ACA A2 trifurcation, ACom fenestration and PCom agenesia the canals were not bilaterally wide or narrow; narrow on the right and wide on the left. Others were found to be narrow or together with a wide canal.

Agenesia, hypoplasia and dolichoectasia were detected in the internal cerebral artery (ICA). Carotid canal diameter difference exists in hypoplasia (Figs. 3a and b) and dolichoectasia (Figs. 4a and b), but only the difference in hypoplasia was found significant ($p<0.05$). Both two carotid canals are also prominently narrow in Moyamoya case, which mainly affects the ICA (Figs. 5a and b). Agenesia, hypoplasia, dolichoectasia and fenestration were detected in anterior cerebral artery (ACA) A1 segment and anterior communicating artery, while hypoplasia, dolichoectasia, trifurcation and azygos were detected in A2 segment.

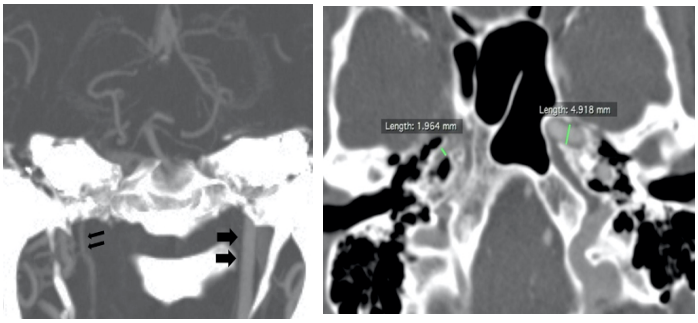

Figure 3a, b. 50-year-old man with internal cerebral artery (ICA) hypoplasia. Coronal maximum intensity projection CT image **(a)** shows right internal cerebral artery thinning (narrow arrows), the left is with normal calibration (wide arrows). On axial CT image **(b)**, right carotid canal is small, supporting ICA hypoplasia.

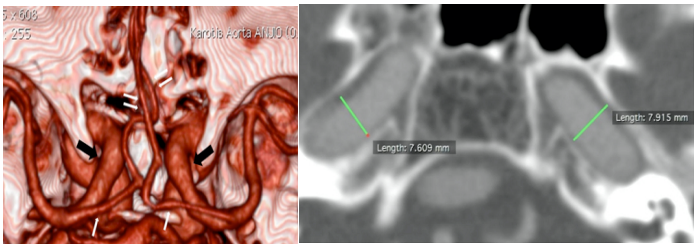

Figure 4a, b. 70-year-old woman with internal cerebral artery (ICA) and anterior cerebral artery (ACA) dolichoectasia. Volume rendering CT image **(a)** shows dolichoectasia both in ICA (wide black arrows) and ACA (narrow white arrows). On axial CT image **(b)** carotid canals are widened together with dolichoectasia.

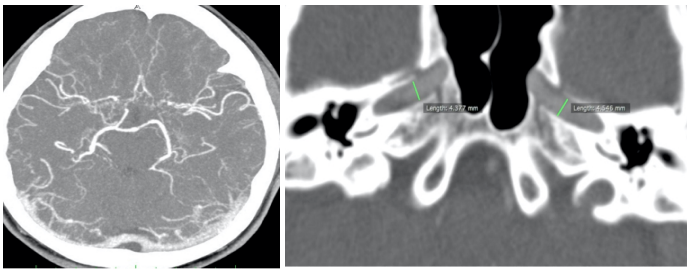

Figure 5a, b. 48-year-old woman with Moyamoya disease. Axial maximum intensity projection CT image of Moyamoya case **(a)** showing increased leptomeningeal vascularization secondary to anterior cerebral artery occlusion seen bilaterally. Axial CT image **(b)** shows bilaterally smaller carotid canals.

Ipsilateral carotid canal is narrow in cases of agenesia and hypoplasia at ACA A1 segment, while in fenestration and dolichoectasia the carotid canal is wider. Canal narrowness is significant in ACA A1 agenesia and right sided hypoplasias ($p<0.05$).

In ACA A2, hypoplasia and trifurcation are present with canal narrowness, while dolichoectasia and azygos A2 cases are present with expansion in canal (Figs. 6a, b and c).

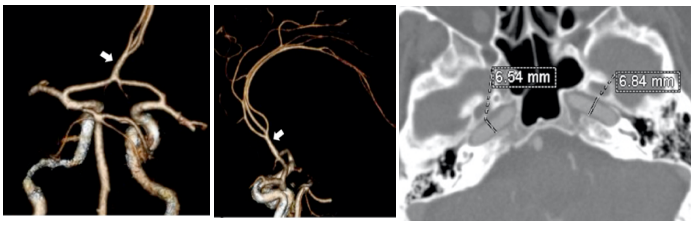

Figure 6a, b, c. 62-year-old man with azygos anterior cerebral artery. Volume rendering oblique axial **(a)** and sagittal **(b)** CT images show azygos anterior cerebral artery A2 segment. Axial CT image **(c)** shows widening of the carotid canal.

Anterior communicating artery agenesia, hypoplasia and dolichoectasia are present with expansion in canal, while fenestration does not fit any certain rule.

Carotid canal was observed narrower in middle cerebral artery (MCA) hypoplasia cases. MCA duplication did not affect carotid canal diameter.

Carotid canal is significantly wider in fetal origin of posterior cerebral artery cases ($p<0.05$). Carotid canal was detected minimally narrower in posterior communicating artery hypoplasia, and in agenesia cases wide at one side and narrow at the other side. All these differences were not found statistically significant.

The carotid canal was wider in the presence of persistent trigeminal artery and hypoglossal artery (Figs. 7a, b and c). However, statistical difference was not detected.

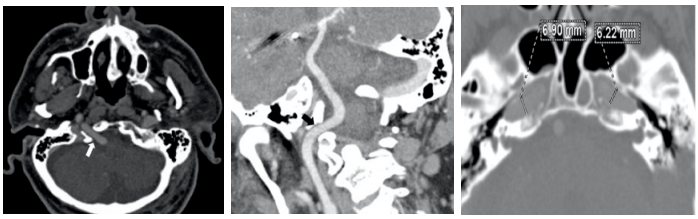

Figure 7a, b, c. 60-year-old man with persistent hypoglossal artery. On the axial **(a)** and oblique **(b)** reformatted CT images, persistent hypoglossal artery passes through the widened right hypoglossal canal. Axial CT image **(c)** shows widening of the carotid canal.

The carotid canal was observed wide in one of the cases of ICA clinoid segment aneurysm, while it was observed narrow in 4 cases. On the other hand, on left supraclinoid segment aneurysms, the carotid canal is narrow and the difference is significant (p=0.018).

The carotid canal was observed wide in anterior communicating artery aneurysms (Figs. 8a and b). In right-sided A1 and A2 aneurysms, the canal was observed narrow whereas it was observed wide in left-sided A2 aneurysms. But the difference is insignificant (p>0.05).

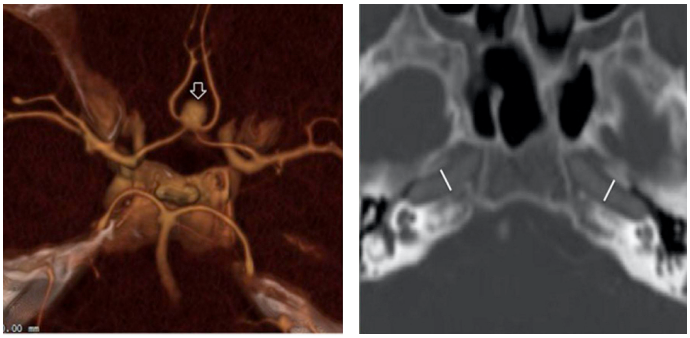

Figure 8a, b. 36-year-old man with anterior communicating artery aneurysm. Volume rendering image shows anterior communicating artery aneurysm **(a).** Axial CT image **(b)** shows widening of the carotid canal.

The carotid canal is generally narrower than normal in MCA aneurysms as well. The narrowing at right side in MCA bifurcation/trifurcation aneurysms is near to the significance limit (p=0.065), and significant at left side (p=0.019). Moreover, the difference in other segment aneurysms is not significant.

In posterior communicating artery aneurysms, one smaller and one wider carotid canal in comparison to normal were detected in two patients, which is insignificant.

When aneurysms are generally considered, carotid canal was found smaller in aneurysm cases.

Discussion

In medicine, particularly in radiology, there is an effort of clarifying of more complex diseases/issues using simple findings. An example for this effort is whether the abnormalities in bony carotid canal diameter would be a clue about cerebral circulation. Although partially, this subject is known. Indirect findings such as absence of bony carotid canal in ICA agenesia and bilateral small canal in Moyamoya disease are known [3-6]. However, variations in carotid canal diameter have not been verified in all cerebral arterial variations and abnormalities.

In this study, carried out for the reasons described above, the diagnosis was made with the absence of carotid canal in the case with ICA agenesia, thus it was distinguished from full occlusion [4,6]. Similarly, ICA hypoplasia was accompanied by small carotid canal and as a result a diagnosis was made [1]. This is because bony canal develops after ICA. Tanaka et al. [7] have found that the flow velocity in carotid and basilar artery changes significantly in the existence of Willis variations in 125 cases using cine phase-contrast magnetic resonance imaging. Besides, in an empirical study performed with three-dimensional phantom models, agenetic arteries have been found to alter the cerebral hemodynamics [8]. In the presented study, ICA and ACA A1 agenesia, ICA, ACA, MCA and PCom hypoplasias were accompanied by a narrow carotid canal; ACA A1 fenestration, azygos ACA A2, ACom agenesia and hypoplasia and MCA duplication were accompanied by a wide canal. ACA A2 trifurcation, ACom fenestration and PCom agenesia were accompanied by a narrow canal on the right and wide canal on the left. In a study of intracranial MR angiograms by Kane et al. [9] the correlation between ipsilateral absence or hypoplasia of the A1 segment and a reduced caliber of the ICA has been also reported. Similarly, the canal was also observed slightly smaller in posterior communicating artery hypoplasia.

Two of the very few studies done on carotid canal width are about Moyamoya disease. Bilateral bony carotid canal was revealed significantly small in Moyamoya cases according to the researches done in Japan, where the disease is frequently seen [3, 5]. In the study done by Watanabe et al. [3], carotid canal diameter was found as 5.27±0.62mm in the control group. The bony carotid canal diameter was measured as 3.31±0.44mm in 11 cases having Moyamoya disease. In another study, carotid canal diameter in the control group was 5.62±0.61mm, whereas it was measured as 4.70±0.61mm for 25 person group having Moyamoya disease.[5] Moyamoya disease, which is seen fairly seldom, is characterized by progressive stenosis of ICA's terminal segment and main branches. Its incidence is higher in East Asia[3]. In the presented study, it was seen that bilateral carotid canals in one case are smaller in comparison to the control group.

One of the abnormalities presented with the expansion of the canal is dolichoectasia. Dolichoectasia is characterized with arterial elongation and expansion. It is an arteriopathy apart from atherosclerosis and even if association is seen, there

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Table. Classification of normal carotid canal widths, variationts or abnormalities based on wide or narrow canal

	Right			Left	
Name of Variable	n	mean±SD (min-max)	p	n	mean±SD (min-max)
Normal canal diameters and gender distribution					
Normal diameter	345	5.631±0.502 (4.1-7.0)	0.039a	345	5.666±0.512 (4.4-7.2)
Men	205	5.797±0.475 (4.5-7)	<0.001	205	5.825±0.492(4.6-7.2)
Women	140	5.388±0.441 (4.1-6.9)	<0.001	140	5.432±04.49(4.4-6.9)
With narrow canal diameter					
ICA agenesia	1	∞	NA	1	∞
ICA hypoplasia	4	4.414±0.121 (2.4-5.6)	0.002*	4	5.275±0.340 (5.0-5.7)
Moyamoya disease	1	4.377	NA	1	4.546
ACA A1 agenesia	12	5.175±0.543 (4.2-6.5)	0.003*	3	5.500±0.435 (5.0-5.8)
ACA A1 hypoplasia	79	5.441±0.506 (3.6-6.6)	0.005*	34	5.603±0.532 (4.4-6.6)
ACA A2 hypoplasia	11	5.609±0.550 (5.0-6.5)	0.74	6	5.450±0.197 (5.3-5.7)
ACA aneurysm	9	5.400± 0.400 (5.0-6.0)	0.23	19	5325±0.472 (4.5-6.2)
ACA A2 trifurcationb	6	5.483±0.828 (4.4-6.7)	0.67	-	-
ACom Fenestrationb	2	5.550±0.156 (5.4-5.6)	NA	-	-
MCA aneurysm	24	5.344±0.439 (4.7-6.3)	0.004*	24	5.514±0.554 (4.3-6.7)
MCA hypoplasia	5	5.217±0.519 (4.5-6.1)	0.05	5	5.380±0.295 (5.0-5.8)
PCom agenesiab	14	5.414±0.704 (4.3-6.5)	0.24	-	-
PCom hypoplasia	33	5.564±0.476 (4.6-6.6)	0.40	29	5.628±0.390 (5.0-6.5)
PCom ectasia	3	5.433±0.493 (5.1-6.0)	0.47	1	5.200
TOTAL	204			127	
With wide canal diameter					
ICA ectasia	3	6.833±0.125 (5.4-7.7)	0.09	3	6.867±0.110 (5.8-8.0)
ICA aneurysm	7	5.783±0.560 (5.1-6.5)	0.52	0	-
ACA A1 ectasia	4	6.050±0.118 (4.9-7.7)	0.55	5	6.383±0.890 (5.7-8.0)
ACA A2 ectasia	2	6.300±0.198 (4.9-7.7)	NA	3	6.500±1.300 (5.7-8.0)
ACA A1 Fenestration	0	-	NA	1	5.700
Azygos ACA A2	7	6.043±0.591 (5.1-6.7)	0.06	7	6.090±0.414 (5.5-6.8)
ACA A2 trifurcationb	-	-	NA	6	5.650±0.852 (4.6-6.8)
ACom Fenestrationb	-	-	NA	2	5.750±0.354 (5.5-6.0)
ACom agenesia	5	5.820±0.572 (5.1-6.5)	0.44	5	6.160±0.487 (5.3-6.5)
ACom hypoplasia	8	5.800±0.462 (5.2-6.4)	0.36	8	5.938±0.489 (5.2-6.8)
ACom ectasia	1	6.000	NA	1	6.200
ACom aneurysm	16	5.733±0.613 (4.7-6.7)	0.51	16	5.794±0.446 (5.1-6.7)
MCA duplication	0	-	NA	2	5.700±0.707 (5.2-6.2)
PCom agenesiab	-	-	-	18	5.717±0.543 (5.0-6.9)
Fetal PCA	53	5.750±0.395 (5.0-6.5)	0.06	51	5.875±0.450 (4.6-7.0)
P. trigeminal arteryc	1	6.124	NA	1	5.700
P. hypoglossal arteryc	2	6.300±0.282 (6.1-6.5)	NA	0	-
TOTAL	109			129	

aComparison of left-right normal canal diameter. NA: Not available (No sufficient data for comparison).
bVariations with narrow carotid canal on one side and wide carotid canal on the other side.
c P=Persistent
Ectasia: is used to mean dolichoectasia.
ICA: Internal cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, MCA: Middle cerebral artery, AcomA: Anterior communicating artery, PcomA: Posterior communicating artery.
*p<0.05.

are proofs indicating them to be different entities [10,11]. In the present study, it was seen that the carotid canal was enlarged in dolichoectasia of ICA, ACA and ACom. It is claimed that dolichoectasia is a systemic pathology [10,11] and the reason for canal extension in ACA dolichoectasia is probably because of segmental dolichoectasia in concomitant ICA. The enlargement of left ICA and ACA A1 dolichoectasias were found to be statistically significant.

If an enlarged canal is accompanied by a variation, then it is fetal originated PCA, which is frequently encountered. It can be asumed that carotid canal diameter would also enlarge in persistent carotid-vertebrobasilar anastomosis. Because generally the posterior system is hypoplastic and it is supplied with a persistent artery extending from the anterior to the posterior. Enlargement in fetal originated PCA is near significance level (p=0.06) on one side, and significantly enlarged (p=0.004) on the other side. The canal is also enlarged in persistent trigeminal and hypoglossal artery cases, however the number of participants was insufficient for statistical evaluation.

Aneurysms affect carotid canal diameter as well. A high correlation was detected between the unilateral or bilateral internal carotid artery absence and Willis polygon aneurysm [12]. It is thought that Willis polygon variations affect hemodynamics and can cause aneurysm development. There are only few studies researching the correlation between Willis polygon variations and aneurysm [13-16]. In the study done by Krasny et al. [15] using digital subtraction angiography, ACA A1 segment variations were observed more frequently in aneurysm group compared to the control group. Besides, there are studies indicating the correlation between PcomA variations and aneurysm[13,17,18]. Lazzaro et al. [19] have detected that Willis polygon variations are more frequent in ruptured AComA and PComA aneurysms in comparison to the group without rupture. However, on contrary to all those studies no correlation was detected between variation existence and aneurysm in the presented study.

In the presented study, ACA and MCA aneurysms were accompanied by bilateral narrow carotid canals, the narrowness level was statistically significant on the right in ACA aneurysms and on the left in MCA aneurysm. The carotid canal is wide in ICA and ACom aneurysms. However, this findings was statistically insignificant probably because of the low number of participants. Similarly, in the study of Kim et al. [20] supraclinoid ICA was found wide in AcomA aneurysm cases. In two studies, the ACA A1 segment was found wider at the side of AComA aneurysm [20,21]. In one of those studies, it was reported that A1:A2 ratio increased, in other words A2 is thinner in comparison to A1[21]. In our study, parent artery diameter was not measured. In future studies, researching the correlation between parent artery diameter and same side carotid canal diameter could be instructive on aneurysm detection.

What is of importance in aneurysms is the time of occurrence. Congenital aneurysms may lead to changes in the carotid canal. However, aneurysms seen in most of the adults may not lead to any changes. Therefore, unless aneurysms are differentiated as congenital/acquired, a precise rule regarding the canal width might not be made. If we consider that the canal diameter affects the aneurysm, on contrary of the aneurysm affecting the canal, the increase of flow in a narrow canal might trigger an aneurysm distally to the narrowing. This should also be proved with larger series.

The width of carotid canal may be affected from reasons other than abnormalities such as aneurysm and Moyamoya disease, and variations of the circle of Willis. Therefore, disorders such as acromegaly, fibrous dysplasia, tumors and inflammatory diseases of the skull and the skull base, and due to the risk of metastasis all malignities are accepted as exclusion criteria. It should be kept in mind that extravascular factors may inhibit the fisibility of canal diameter measurement.

Normal carotid canal diameter values obtained from the presented study can be used in routine health screening. However, significant diameter difference was detected between right-left sides. Left carotid artery originates from the aortic arch. Therefore, left carotid artery might have wider diameter since it is exposed to higher pressure. The difference between men-women was found significant as well. Therefore, it should be known that the measurement alters with respect to gender and side.

This study has two important limitations. Firstly, there are relatively few cases per each abnormality when the cases are distributed, and secondly only CTA imaging was performed. Due to varying incidence of the mentioned abnormalities, homogeneous distribution was not observed in patient groups admitted to the study. Therefore, statistically significant result cannot be obtained. Multicentered studies including larger numbers of patients would be of benefit. CTA sensitivity decreases in very small aneurysms [22]. Thus, there is a probability of missing some aneurysms.

As a result, if we exclude extravascular reasons that may affect the canal, carotid canal diameter different than normal ranges

may indicate to abnormalities such as vascular variations or aneurysm. Variations are not very important alone, however some previous studies have shown their cooccurrence with increased aneurysm incidence. Although the relatively low number of patients in this study was an obstacle to create a rule, further multicentered larger studies may clarify this topic, and provide the premise of CTA use.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Bhat DI, Somanna S, Kovoor JME. Bilateral hypoplasia of the internal carotid artery. Indian J Radiol Imaging 2011; 21: 257–60.
2. Simon J. Dimmick, Kenneth C. Faulder. Normal Variants of the Cerebral Circulation at Multidetector CT Angiography. RadioGraphics 2009; 29: 1027-43
3. Watanabe A, Tomohiro O, Koizumi K et al. Bony carotid canal hypoplasia in patients with moyamoya disease. J Neurosurg Pediatrics 2010; 5: 591–4.
4. Dianbin Hou, Yu Mei, Yongqiang Ji et al. Congenital internal carotid artery hypoplasia Medicine (Baltimore) 2019; 98: 13986
5. Motoshima S, Noguchi T, Kawashima M et al. Narrowed petrous carotid canal detection for the early diagnosis of moyamoya disease. Fukuoka Igaku Zasshi 2012; 103: 206-14.
6. Porto FH, Silva MN, Domingues JR et al. Themissed missing hole. Arq Neuropsiquiatr 2012; 70: 467-9.
7. Tanaka H, Fujita N, Enoki T. Relationship between variations in the circle of Willis and flow rates in internal carotid and basilar arteries determined by means of magnetic resonance imaging with semi-automated lumen segmentation: Reference data from 125 healthy volunteers. AJNR 2006; 27: 1770-5.
8. Fahy P, McCarthy P, Sultan S et al. An experimental investigation of the hemodynamic variations due to aplastic vessels within three-dimensional phantom models of the circle of Willis. Ann Biomed Eng 2014; 42: 123-38.
9. Kane AG, Dillon W, Barkovich AJ. Reduced caliber of the internal carotid artery: a normal finding with ipsilateral absence or hypoplasia of the A1 segment. American Journal of Neuroradiology 1996; 17: 1295-301
10. Pico F, Labreuche J, Cohen A et al. GENIC Investigators. Intracranial arterial dolichoectasia is associated with enlarged descending thoracic aorta. Neurology 2004; 63: 2016-21.
11. Nakamura Y, Hirayama T, Ikeda K. Clinicoradiologic Features of Vertebrobasilar Dolichoectasia in Stroke PatientsJ. Stroke and Cerebrovascular Diseases 2010; 21: 5-10
12. Khan AA, Asari MA, Pasha MA. A case of bilateral absence of carotid canals in human skull. Bangladesh Journal of Medical Science 2016; 15: 275
13. Pascalau R, Padurean VA, Bartos D, Bartos A, Szabo AB. The Geometry of the Circle of Willis Anatomical Variants as a Potential Cerebrovascular Risk Factor. Turk Neurosurg 2018; 2: 1-8
14. Horikoshi T, Akiyama I, Yamagata Z et al. Magnetic resonance angiography evidence of sex linked variations in the circle of Willis and occurence of cerebral aneurysms. J Neurosurg 2002; 96: 697-703.
15. Krasny A, Nensa F, Sandalcıoglu IE et al. Association of aneurysms and variations of the A1 segment. J Neurointerv Surg 2014; 6: 178-183.
16. Swathan JP, Sani AF, Swatan E. Anatomical variations of circle of Willis is common in patients with intracranial aneurysm: Initial registry data from tertiary health center, Surabaya, Indonesia. JNeurological Sciencies 2017; 381: 953
17. Aktürk Y, Fırat MM, Güven ME, Beyhan M. Relation of the incidence of congenital variations and anomalies with intracranial aneurysms in intracranial arteries. Dicle Tıp Dergisi 2016; 43: 515-20
18. Bor AS, Velthius BK, Majoie CB, et al. Configuration of intracranial arteries and development of aneurysms: a follow-up study. Neurology 2008; 70: 700-5.
19. Lazzaro MA, Ouyang B, Chen M. The role of Willis anomalies in cerebral aneurysm rupture. J Neuro Interv Surg 2012; 4: 22-6.
20. Kim DW, Kim SD. Association between internal carotid artery morphometry and posterior communicating artery aneurysm. Yonsei Med J 2007; 48: 634–8.
21. Flores BC, Scott WW, Eddleman CS et al. The A1-A2 Diameter Ratio May Influence Formation and Rupture Potential of Anterior Communicating Artery Aneurysms Neurosurgery 2013; 73: 845–53.
22. Han A, Yoon DA, Kim ES, et al. Value of CT angiography for the detection of intracranial vascular lesions in patients with acute severe headache. Eur Radiol 2013; 23: 1443–9.

Turkish Journal of Clinics and Laboratory

To cite this article: Kuyumcu MS, Kuyumcu A. High fructose intake may be related to carotid artery stenosis.Turk J Clin Lab 2021; 1: 50-56.

Original Article

High fructose intake may be related to carotid artery stenosis

Fruktoz tüketimi karotis arter hastalığı ile ilişkili olabilir

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Abstract

Aim: It is known that high fructose intake is related to cardiovascular diseases but there is a limited number of researches in this era. The objective of this research is to evaluate the relation between Carotid Artery Stenosis (CAS) and high fructose intake.

Material And Methods: The patients are categorized into three groups: Patients with CAS≥60% (60 patients), patients with CAS<60% (60 patients) and patients with no carotid atherosclerosis (60 patients). Nutrient intake level of patients is observed and recorded by 24-Hour Dietary Recall Forms and the intake frequency of high-fructose dietary is enquired. Physical activity levels are also evaluated. All the collected data is compared among the groups.

Results: Fructose intake among ordinary people is found to be lower than the patients with CAS<60% ($p<0.001$). Besides, fructose intake of patients with CAS<60% is lower than fructose intake of patients with CAS≥60%. Multivariate regression analysis showed that high fructose intake is an independent risk factor for carotid stenosis over 60% ($p<0.001$). Fructose intake levels were higher in the calcific plaque group than in the non-calcific plaque group ($p<0.001$).

Conclusions: We determined a high fructose intake in patients with CAS. In light of our research data, we consider high fructose intake to have a potential role in the pathophysiology of CAS.

Keywords: Carotid artery stenosis; fructose; atherosclerosis

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Recevied: 18/01/2021 accepted: 03/03/2021
Doi: 10.18663/tjcl.864019

Öz

Amaç: Yüksek fruktoz tüketiminin kardiyovasküler hastalıklar ile ilişkili olduğu bilinmektedir, fakat çalışmalar sınırlıdır. Bu çalışmanın amacı, karotis arter darlığı (KAD) ile yüksek früktoz tüketimi arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: Hastalar, KAD>60% olan (60 hasta), KAD <60% olan (60 hasta) ve karotis aterosklereotik hastalığı bulunmayan (60 hasta) olarak üç gruba ayrılmıştır. Hastaların geriye dönük 3 günlük besin tüketim kayıtlar alınmıştır. Veriler gruplar arasında karşılaştırılmıştır.

Bulgular: Fruktoz tüketimi, KAD<%60 olan hastalara göre normal bireylerde daha düşük bulunmuştur (p<0.001). Ayrıca, KAD>60% olanlara göre KAD<60% olanlarda frukotz tüketimi daha düşüktür. Çok değişkenli regresyon analizinde yüksek früktoz tüketimi 60% üzeri karotis stenozu için bağımsız risk faktörü olarak saptanmıştır (p<0.001).

Sonuç: Çalışmamızda KAD olan bireylerde früktoz tüketimi yüksek saptanmıştır. Çalışmamız artmış Fruktoz tüketiminin KAD'a etkisi olabileceğini gösteren literatürde ki ilk çalışmadır.

Anahtar kelimeler: Karotis arter hastalığı; fruktoz; ateroskleroz.

Introduction

Atherosclerosis is a rapidly progressive disease characterized by the hardening and narrowing of the arteries due to the buildup of plaques inside the arteries [1]. The progress of atherosclerosis often causes adverse impacts such as apparent luminal stenosis due to the thickening of arteries and occasional occlusion of peripheral, coronary and carotid arteries [2, 3]. Most of the epidemiologic studies indicate that carotid artery stenosis may be related to ischemic stroke risk [4, 5]. Besides, plaque morphology and the state of the carotid artery lesions have also a significant role in stroke risk [4].

Fructose naturally occurs as a component of the whole fruit. The accompanying fiber which is metabolized as a part of a complete food naturally decelerates and modulates fructose release [6]. The overconsumption of either natural or refined fructose increases in recent years and this increase is believed to have a relation with some diseases such as insulin resistance, type-2 diabetes, hyperglycemia, cardiovascular diseases and especially obesity [7-9].

High fructose intake increases the number of low-density lipoprotein, decreases particle sizes with atherogenic effect, increases the expression of adhesion molecules in endothelial cells and triggers coronary pathophysiology and thus may cause atherosclerosis [10]. Some researches also show the relation between increased fructose intake and oxidative stress and inflammation which have a role in the pathophysiology of carotid artery atherosclerosis [11-14].

In light of these findings, this study aims to evaluate the relationship between fructose intake and CAS.

Material and Methods

We created three groups with the patients applying to our cardiology outpatient clinic between October 2016 and October 2017. Patients to whom were performed carotid ultrasonography for carotid artery stenosis or to assess cardiovascular risk were included in the study [15]. The patients having carotid ultrasound are categorized into three groups according to the level of stenosis: patients with C less than 60% (CAS<60), patients with carotid artery stenosis more than or equal to 60% (CAS≥60) and the patients without stenosis. The total number of evaluated patients was 543. The evaluation was completed after the number of each group reached 60. During the research, a dietitian surveyed the patients for 70 different types of fructose-rich nutrients (beverages and foods) to determine the intake frequency. The dietitian also recorded the nutrient intake of the patients with 24-hour Dietary Recall Forms. The records of dietary intake data were evaluated with Nutrient Information Systems (BeBIS 7.1) software.

The patients with symptomatic CAS, having cerebrovascular accident 6 months were excluded from this research. The patients with systemic inflammatory disease, acute coronary syndrome, cancer, previous myocardial infarction, congestive heart failure, serious valvular heart disease, chronic obstructive pulmonary disease, respiratory or kidney failure, hematologic disease and active infection were refused from this research. Local Ethical Committee reviewed and approved the research protocol of our study.

Definitions

Hypertension patients: patients with arterial blood pressure ≥140/90 mmHg or using antihypertensive drugs regularly. Diabetes mellitus patients: patients with fasting plasma glucose ≥126mg/dL and/or patients using anti-diabetics or insulin. Hyperglycemia is defined as total cholesterol level ≥200 mg/dL. Body Mass Index (BMI) is a person's weight in kilograms divided by the square of height in meters.

Doppler Ultrasonography Assessment

Esaote s.p.a MyLabClass C (Florence-Italy) and a linear 3-11MHz probe is used for Carotid artery examination. The stenosis classification is based on NASCET (The North American Symptomatic Carotid Endarterectomy Trial) [16].

Computed Tomography Angiography Assessment

Carotid Artery Stenosis was first examined with carotid artery Doppler ultrasound and then the computed tomography (CT). We CT scanned the patients with a CT device and a Philips Brilliance 64 detector.

Statistical Analysis

The collected data were analyzed using SPSS 18.0 statistics software (SPSS Inc., Chicago, IL, USA). Number of each group was adjusted as 60 patients. Because we calculated the minimum number of individuals that should be sampled with 90% power and 0.05 Type I error as at least 46 (R 3.0.1. open source program). The primary effect variable was determined as the QRS angle. 1% change in CAS rate was accepted as clinically relevant. Standard deviation of the primary effect variable was calculated as ± 0.15. The student's t-test was used to compare the normally distributed parameters. If there were two groups and the parameters were not normally distributed, we used the Mann-Whitney U test. One-way analysis of variance test was used to compare normally distributed variables between 3 groups. Tukey test was used for post-hoc analysis. Categorical variables were compared by the Chi-Squared test or Fischer's exact test. Major clinical factors and predictors of CAS≥60 as depicted in Table 1 and 2 were used in univariate and multivariate linear regression analysis. In all statistics $p<0.05$ was considered statistically significant.

Results

Baseline clinical characteristics and laboratory parameters of the study population are shown in Table 1. Smoking rates were found to be higher in the group of patients with CAS of 60% or more compared to other two groups (p=0.017). There was also no difference in terms of biochemical and hematological parameters between the 3 groups except white blood cell (WBC) (p=0.004) and platelet count (p=0.012).

Table 1. Baseline characteristics and laboratory parameters of groups.

Variables	Control (n=60)	Carotid artery stenosis <60 % (n=60)	Carotid artery stenosis ≥60% (n=60)	P Value			
				Difference between groups by ANOVA	CAS; <60% vs ≥60% CAS	Control vs ≥60% CAS	Control vs <60% CAS
Age,years	55,98 ±9,07	57,43 ± 9,75	59,48 ±10,27	0,143	-	-	-
Female, n(%)	27 (45,0%)	25 (41,7%)	27 (45,0%)	0,809	-	-	-
BMI, kg/m2	28,14 ± 2,80	28,26 ± 2,43	28,98 ±3 ,00	0,200	-	-	-
Diabetes mellitus, n(%)	51 (34,2)	47 (31,5)	51 (34,2)	0,536	-	-	-
Hypertension, n(%)	15 (25,0%)	21 (35,0%)	24 (40,0%)	0,207	-	-	-
Hyperlipidemia, n(%)	19 (29,2%)	24 (36,9%)	22 (33,8%)	0,633	-	-	-
Smoking, n(%)	15 (37,1%)	14 (22,2%)	27 (24,1%)	0,017	0,010	0,022	0,831
Coronary artery disease, n(%)	6 (10,0%)	6 (10,0%)	8 (13,3%)	0,799	-	-	-
Peripheral vascular disease, n(%)	3 (5,0%)	4 (6,7%)	8 (13,3%)	0,217	-	-	-
Grade of carotid artery stenosis, (%)	0 ± 0,00	30,17 ± 12,73	69,33± 10,53	<0,001	<0,001	<0,001	<0,001
Calcified plaque, n(%)	0 (0,0%)	34 (57,6%)	33 (55,0%)	<0,001	0,854	<0,001	<0,001
LVEF, %	58,0 ± 4,9	57,7 ± 5,9	58,4 ± 5,0	0,769	-	-	-
Glucose, mg/dL	115,4 ± 44,1	114,2 ± 44,8	129,3 ± 52,3	0,153	-	-	-
Creatinine, mg/dL	1,00 ± 0,16	1,05 ± 0,65	0,95 ± 0,21	0,403	-	-	-
Uric acid, mg/dL	5,78 ± 2,06	5,87 ± 2,06	5,98 ± 2,16	0,878	-	-	-
WBC,10^3/mm^3	8,4 ± 2,1	9,0 ± 2,2	9,8 ± 2,4	0,004	0,068	0,001	0,120
Hemoglobin, g/dL	13,4 ± 1,7	13,7 ± 1,6	14,1 ± 1,6	0,088	-	-	-
Platelets, 10^3/mm^3	236,5 ± 62,4	238,1 ± 70,0	270,5 ± 71,6	0,012	0,018	0,009	0,894
CRP,mg/L	3,7 ± 3,7	4,0 ± 3,6	4,9 ± 4,6	0,207	-	-	-
Total cholesterol, mg/dL	184,1 ± 79,6	190,4 ± 50,2	189,8 ± 46,7	0,812	-	-	-
LDL cholesterol, mg/dL	113,1 ± 57,3	114,3 ± 42,0	115,9 ± 38,2	0,947	-	-	-
HDL cholesterol, mg/dL	44,0 ± 24,2	45,3 ± 9,5	49,2 ± 13,1	0,206	-	-	-
Triglyceride, mg/dL	168,1± 145,0	167,1 ± 106,0	139,1 ± 89,0	0,391	-	-	-

Data are given as mean ± SD, n (%) or median (lower-upper limit). BMI body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; WBC, white blood cell. Carotid artery stenosis rate was calculated according to NASCET.

Macronutrient and fructose consumption is shown in table 2. Fructose consumption was lower in the control group than CAS<60 group and lower in CAS<60 group than CAS≥60 group (p<0.001). Total energy consumption also different between groups (p=0.011).

In order to determine the variables affecting CAS≥60, we applied multivariate and univariate regression analysis for the significant variables in Table 2 and major clinical factors (Table 3). In univariate regression analysis, CAS≥60% is associated with smoking (p=0.005), platelet (p=0.007) and WBC (p=0.004) count and fructose intake (p<0.001). In the multivariate regression analysis, higher platelet (p=0.007) and WBC level (p=0.001) and higher fructose intake (p<0.001) are determined as independent risk factors.

Patients with carotid artery stenosis were divided into 2 subgroups as patients with calcific (n=67) and non-calcific (n=53) carotid artery stenosis according to plaque morphological features (Table 4). No statistically significant difference was determined between these parameters except fructose intake (p<0.001).

Tablo 2. Evaluation of daily fructose and macronutrient consumption of groups.

				Difference between groups by ANOVA	CAS; <60% vs ≥60% CAS	Control vs ≥60% CAS	Control vs <60% CAS
Energy (kcal)	2522,2 ± 646,6	2673,7 ± 9,75	2877,0 ± 676,0	0,011	0.015	0.004	0.16
Carbohydrate (g)	266,2 ± 100,7	269,1 ± 89,6	300,0 ± 112,4	0,132		-	-
Protein (g)	85,2 ± 28,1	90,2 ± 24,4	93,2 ±27,7	0,260		-	-
Lipid (g)	119,5 ± 37,5	132,2 ± 38,7	139,9±39,9	0,058	-	-	-
Fiber (g)	27,1 ± 7,7	26,7 ± 7,9	27,7± 8,4	0,235		-	-
Fructose (g)	34,9 ± 12,7	37,9 ± 14,2	46,4 ± 16,4	<0,001	<0,001	<0,001	<0,001

Data are given as mean ± SD, n (%) or median (lower-upper limit). TE, total energy. Carotid artery stenosis rate was calculated according to NASCET.

Tablo 3. Multivariate logistic regression analysis showing the predictors for ≥60% carotid artery stenosis .

	Univariable		Multivariable	
Variables	Beta (95% CI)	p value	Beta (95% CI)	p value
Diabetes mellitus	0,786 (0,337-1,832)	0,577	-	-
Hypertension	1,556 (0,814-2,972)	0,181	-	-
Hyperlipidemia	1,037 (0,544-1,974)	0,913	-	-
Smoking	2,567 (1,329-4,959)	0,005	3,774 (1,740 -8,186)	0,059
Platelets	1,007 (1,002-1,011)	0,007	1,004 (1,002-1,012)	0,007
White blood cell	0,814 (0,701-0,944)	0,004	0,743 (0,623-0,887)	0,001
Energy consumption	1,005 (0,995-1,015)	0.069	-	-
Fructose consumption	1,045 (1,023-1,069)	<0,001	1,054 (1,027-1,082)	<0,001

CI, confidence interval

Discussion

This is one of the preliminary researches in the literature exploring the relationship between CAS and fructose intake. We determined in our research that patients with CAS have a high fructose intake. Also, this research shows that the overconsumption of fructose may be an independent risk factor for CAS.

While scientific researches in animals report that fructose affects the inflammatory processes and may be related to many diseases [17, 18], the researches in human bodies have not revealed the safe dose of fructose for human intake yet. The consumption of sugar and sweetened food increases every year and this increase is believed to be responsible for a series of emerging diseases. World Health Organization's (WHO) current suggestion is to decrease the energy from the added sugar below 5% and WHO states that the a decrease in the consumption of added sugar from the manufactured beverages and packaged food will also decrease the intake of fructose [19]. The mild level of intake was considered to be helpful in glycemic control but high and very high fructose intake was stated to have the risk of dysglycemia and dyslipidemia [20]. In this classification, the patients with CAS≥60 determined to have a fructose intake close to the upper limit of mild consumption. Although there is no certain medical treatment procedure developed for CAS today, the use of some therapeutic drugs such as statins, antiplatelet drugs, antihypertensive in combination with a healthy lifestyle will lead to the positive progress of the disease [15].

Table 4. Baseline characteristics and laboratory parameters of the patients according to plaque calcification.

Variables	Calcified plaque group (n=67)	Non-calcified plaque group (n=53)	p value
Age,years	59,62 ±9,94	57,57 ±10,06	0,259
Female, n(%)	29 (43,3%)	23 (43,4%)	0,990
BMI, kg/m2	28,36±2,85	28,97±2,58	0,254
Diabetes mellitus, n(%)	16 (23,9%)	6 (11,3%)	0,077
Hypertension, n(%)	27 (40,3%)	18 (34,0%)	0,570
Hyperlipidemia, n(%)	24 (35,8%)	22 (41,5%)	0,524
Smoking, n(%)	20 (28,9%)	21 (39,6%)	0,262
Coronary artery disease, n(%)	9 (13,4%)	5 (9,4%)	0,498
Peripheral vascular disease, n(%)	6 (9,0%)	6 (11,3%)	0,668
Grade of carotid artery stenosis, (%)	47,42 ± 22,70	53,04 ± 23,16	0,185
LVEF, %	58,0 ± 5,2	58,1± 5,8	0,841
Glucose, mg/dL	123,5 ± 55,1	119,6 ± 40,7	0,664
Creatinine, mg/dL	1,01 ± 0,26	0,99 ± 0,68	0,872
Uric acid, mg/dL	5,91 ± 2,10	5,93 ± 2,13	0,955
WBC,10^3/mm^3	8,5 ± 2,1	8,9 ± 2,7	0,274
Hemoglobin, g/dL	13,7 ± 1,5	14,0 ± 1,7	0,290
Platelets, 10^3/mm^3	255,1 ± 82,6	253,2 ± 65,6	0,890
CRP,mg/L	4,6 ± 3,5	4,3 ± 3,7	0,733
Total cholesterol, mg/dL	192,6 ± 43,5	187,0 ± 54,0	0,531
LDL cholesterol, mg/dL	114,8 ± 39,3	115,6 ± 41,2	0,913
HDL cholesterol, mg/dL	47,3 ± 10,7	47,3 ± 12,7	0,975
Triglyceride, mg/dL	147,2± 82,8	160,7± 117,0	0,464
Fructose (g)	36,56 ± 13,80	45,12 ± 16,24	<0,001

Data are given as mean ± SD, n (%) or median (lower-upper limit). BMI body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; WBC, white blood cell. Carotid artery stenosis rate was calculated according to NASCET

Oxidative stress has a significant role in endothelial dysfunction so in CAS pathogenesis [21-25]. Many researches state that high fructose intake induces oxidative stress by causing a decrease in the level of endogenous antioxidants and free radical production [12]. It is also reported that fructose increases the production speed of cardiac and vascular superoxide anions [26].

We have findings showing that high fructose intake is closely related to the inflammation that has a role in the pathophysiology of CAS [27]. Cigliano et al. determined in their research that the high fructose feeding in rats caused an increase in TNF- α levels which is an indication of systemic inflammation [28]. Another research determined that the high fructose diet in rats caused adipose tissue to express more immunosuppressive corticosteroids due to an increase in pro-inflammatory cytokines and macrophages. Besides, the TNF-α and other inflammatory cytokines increased in the liver and liver destruction was observed [29]. Another research stated that high fructose intake had a relationship with hypothalamic astrogliosis, neuroinflammation and high oxidative stress [30].

Limitations of the Study

The present study is a cross-sectional study with relatively small sample size. We don't have follow up on major adverse cardiovascular events data. So, our results should be verified in the multi-center prospective longitudinal studies with larger sample size. In addition, there is no evaluation system, which determines the diffuseness and severity of carotid artery disease, like SYNTAX score. The limitations of this study should be considered while interpreting the results.

Conclusion

This is one of the preliminary researches in the literature showing the the relationship between increased dietary fructose intake and CAS progress. Consequently, we can deduct that decreasing the consumption of high-fructose nutrients will have a constructive effect on the progress of atherosclerotic cardiovascular diseases. Additionally, this research will contribute to understand the pathophysiology of atherosclerosis and have the potential to enlighten new researches.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Touboul PJ, Hernández-Hernández R, Küçükoğlu S, Woo KS, Vicaut E, Labreuche J, et al. Carotid artery intima media thickness, plaque and Framingham cardiovascular score in Asia, Africa/Middle East and Latin America: the PARC-AALA study. The international journal of cardiovascular imaging 2007; 23: 557-67.
2. Köz C. Carotid intima-media thickness in type 1 diabetes mellitus. The Anatolian journal of cardiology 2010; 10: 59-60.
3. Güleç S. Global risk and objectives in cardiovascular disease. Archives of the Turkish Society of Cardiology 2009; 37: 1-10.
4. Ratchford EV, Evans NS. Carotid artery disease. Vascular medicine. 2014; 19: 512-5.
5. Franceschini N, Giambartolomei C, de Vries PS et al. GWAS and colocalization analyses implicate carotid intima-media thickness and carotid plaque loci in cardiovascular outcomes. Nature communications 2018; 9: 5141.
6. Jaffe R. Diabetes as an immune dysfunction syndrome. 1st ed Bioactive Food as Dietary Interventions for Diabetes 2013.
7. Tappy L, Lê KA, Tran C, Paquot N. Fructose and metabolic diseases: new findings, new questions. Nutrition (Burbank, Los Angeles County, Calif) 2010; 26: 1044-9.
8. Elitok A, Emet S, Bayramov F et al. Effect of bariatric surgery on flow-mediated dilation and carotid intima-media thickness in patients with morbid obesity: 1-year follow-up study. The Anatolian journal of cardiology 2020; 23: 218-22.
9. Akhavan-Khaleghi N, Hosseinsabet A. Evaluation of the longitudinal deformation of the left ventricular myocardium in subjects with impaired fasting glucose with and without increased glycated hemoglobin. The Anatolian journal of cardiology 2018; 19: 160-7.
10. Cirillo P, Pellegrino G, Conte S et al. Fructose induces prothrombotic phenotype in human endothelial cells : A new role for "added sugar" in cardio-metabolic risk. Journal of thrombosis and thrombolysis 2015; 40: 444-51.
11. Conti FF, Brito Jde O, Bernardes N et al. Cardiovascular autonomic dysfunction and oxidative stress induced by fructose overload in an experimental model of hypertension and menopause. BMC cardiovascular disorders 2014; 14: 185.
12. Jaiswal N, Maurya CK, Arha D et al. Fructose induces mitochondrial dysfunction and triggers apoptosis in skeletal muscle cells by provoking oxidative stress. Apoptosis : an international journal on programmed cell death 2015; 20: 930-47.
13. Celik A, Koç F, Kadi H, Ceyhan K, Erkorkmaz U. Inflammation is related to unbalanced cardiac autonomic functions in hypertension: an observational study. The Anatolian journal of cardiology 2012; 12: 233-40.
14. Tokgözoğlu L. Atherosclerosis and the role of inflammation. Archives of the Turkish Society of Cardiology 2009; 37: 1-6.
15. Piepoli MF, Hoes AW, Agewall S et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (EACPR). European heart journal 2016; 37: 2315-81.
16. Ferguson GG, Eliasziw M, Barr HW et al. The North American Symptomatic Carotid Endarterectomy Trial : surgical results in 1415 patients. Stroke 1999; 30: 1751-8
17. Cheng X, Qiu L, Wang F. 18α-Glycyrrhetinic acid (GA) ameliorates fructose-induced nephropathy in mice by suppressing oxidative stress, dyslipidemia and inflammation. Biomedicine & pharmacotherapy 2020; 125: 109702.
18. Zhao C, Zhang Y, Liu H, Li P, Zhang H, Cheng G. Fortunellin protects against high fructose-induced diabetic heart injury in mice by suppressing inflammation and oxidative stress via AMPK/Nrf-2 pathway regulation. Biochemical and biophysical research communications 2017; 490: 552-9.
19. Breda J, Jewell J, Keller A. The Importance of the World Health Organization Sugar Guidelines for Dental Health and Obesity Prevention. Caries research 2019; 53: 149-52.
20. Livesey G, Taylor R. Fructose consumption and consequences for glycation, plasma triacylglycerol, and body weight: meta-analyses and meta-regression models of intervention studies. The American journal of clinical nutrition 2008; 88: 1419-37.
21. Turan T, Menteşe Ü, Ağaç MT et al. The relation between intensity and complexity of coronary artery lesion and oxidative stress in patients with acute coronary syndrome. The Anatolian journal of cardiology 2015; 15: 795-800.
22. Gökdemir MT, Kaya H, Söğüt O, Kaya Z, Albayrak L, Taşkın A. The role of oxidative stress and inflammation in the early evaluation of acute non-ST-elevation myocardial infarction: an observational study. The Anatolian journal of cardiology 2013; 13: 131-6.

23. Lucas ML, Carraro CC, Belló-Klein A, Kalil AN, Aerts N. Oxidative stress in carotid arteries of patients submitted to carotid endarterectomy. The role of aging process. Acta cirurgica brasileira 2016; 31: 564-8.
24. Oktay V, Baydar O, Sinan Ü Y et al. The effect of oxidative stress related with ischemia-reperfusion damage on the pathogenesis of atrial fibrillation developing after coronary artery bypass graft surgery. Archives of the Turkish Society of Cardiology 2014; 42: 419-25.
25. Marchegiani F. Further evidence to support a role of oxidative stress and inflammation in myocardial infarction. The Anatolian journal of cardiology 2013; 13: 137-8.
26. Delbosc S, Paizanis E, Magous R et al. Involvement of oxidative stress and NADPH oxidase activation in the development of cardiovascular complications in a model of insulin resistance, the fructose-fed rat. Atherosclerosis 2005; 179: 43-9.
27. Ziyrek M, Tayyareci Y, Yurdakul S, Sahin ST, Yıldırımtürk O, Aytekin S. Association of mitral annular calcification with endothelial dysfunction, carotid intima-media thickness and serum fetuin-A: an observational study. The Anatolian journal of cardiology 2013; 13: 752-8.
28. Cigliano L, Spagnuolo MS, Crescenzo R et al. Short-Term Fructose Feeding Induces Inflammation and Oxidative Stress in the Hippocampus of Young and Adult Rats. Molecular neurobiology 2018; 55: 2869-83.
29. Veličković N, Djordjevic A, Vasiljević A, Bursać B, Milutinović DV, Matić G. Tissue-specific regulation of inflammation by macrophage migration inhibitory factor and glucocorticoids in fructose-fed Wistar rats. The British journal of nutrition 2013; 110: 456-65.
30. Li JM, Ge CX, Xu MX, Wang W, Yu R, Fan CY, et al. Betaine recovers hypothalamic neural injury by inhibiting astrogliosis and inflammation in fructose-fed rats. Molecular nutrition & food research 2015; 59: 189-202.

Turkish Journal of Clinics and Laboratory

To cite this article: Gurbuz T, Okcu NT, Gokmen O. Evaluating the sexual function differences among the infertile women. Turk J Clin Lab 2021; 1: 57-64.

Original Article

Evaluating the sexual function differences among the infertile women

İnfertil kadınların seksuel fonksiyon farklılıklarının değerlendirilmesi

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Abstract

Aim: This study aimed to investigate the frequency of sexual dysfunction among infertile women and evaluate the difference between the primary and secondary infertility groups in terms of menstrual pain, dyspareunia, smoking and night shift variables based on the Female Sexual Function Index (FSFI) score.

Material and Methods: Seventy women in the primary group and 29 women in the secondary group participated in this study. All participants were asked FSFI. The questionnaire containing duration of marriage, total FSFI score, menstrual pain, dyspareunia, smoking and night shift variables and also the demographic characteristics of patients such as age, infertility time and body mass index (BMI) was given to the subjects. SPSS 23.0 program was used for data statistical analysis. Pearson's Chi-squared test was used to compare categorical variables. Independent student t-test analysis was performed on binary variables to compare continuous variables between the groups.

Results: 19.2% of both groups had marriage duration of 1-3 years, 54.5% of them had marriage duration of 4-6 years and 26.3% of them had marriage duration of 7 years above. The mean age of the patients in the study was 34,58±4,25 years. The prevalence of sexual dysfunction among the women was 32.9 (n = 23 of 70) and 55.2% (n = 16 of 29) in primary infertile and secondary infertile women, respectively, but it did not show a statistically significant difference between the two groups.

Conclusion: There was no significant difference between both groups in terms of menstrual pain, dyspareunia, smoking and night shift variables but the difference was statistically significant in terms of marriage duration. The mean FSFI domains were not also significantly different between the two groups. There was also no significant relationship between age, infertility time and BMI of both groups and sexual dysfunction.

Keywords: infertility; female sexual function index; female sexual dysfunction

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Recevied: 11.06.2020 accepted: 15.10.2020
Doi: 10.18663/tjcl.751646

Öz

Amaç: Bu çalışmada, infertil kadınlar arasındaki cinsel işlev bozukluğu sıklığı araştırıldı ve Kadın Cinsel Fonksiyon İndeksi (KCFI) skoruna göre menstrüel ağrı, disparoni, sigara içme ve gece vardiyası değişkenleri açısından primer ve sekonder infertilite grupları arasındaki fark değerlendirildi.

Gereç ve Yöntemler: Çalışmanın primer grubuna 70 kadın ve sekonder grubuna 29 kadın katılmıştır. Tüm katılımcılardan geçerli ve güvenilir bir KCFI doldurmaları istendi. Katılımcılara evlilik süresi, toplam KCFI skoru, adet ağrısı, disparoni, sigara ve gece vardiyası değişkenlerinin yanı sıra hastaların yaş, kısırlık süresi ve vücut kitle indeksi (VKİ) gibi demografik özelliklerini içeren anket yapıldı. Veri istatistiksel analizi için SPSS 23.0 programı kullanıldı. Kategorik değişkenlerin karşılaştırılmasında Pearson ki-kare testi kullanıldı. Gruplar arası sürekli değişkenleri karşılaştırmak için ikili değişkenler üzerinde bağımsız t-testi analizi yapılmıştır.

Bulgular: Her iki grubun %19.2'si 1-3 yıl evlilik süresine, %54.5'i 4-6 yıl evlilik süresine ve % 26.3'ü 7 yıl yukarıda evlilik süresine sahiptir. Çalışmadaki hastaların yaş ortalaması 34,58 ± 4,25 idi. Primer infertil ve sekonder infertil kadınlarda kadınlar arasında cinsel işlev bozukluğu prevalansı sırasıyla %32.9 (n = 23/70) ve %55.2 (n = 16/29) idi, ancak iki grup arasında istatistiksel olarak anlamlı bir fark tespit edilmemiştir.

Sonuç: Her iki grup arasında menstrüel ağrı, disparoni, sigara içme ve gece vardiyası değişkenleri açısından anlamlı fark yoktu, ancak bu fark evlilik süresi açısından istatistiksel olarak anlamlı olarak tespit edildi. KCFI oranlarında iki grup arasında anlamlı olarak fark saptanmadı. Her iki grubun yaş, infertilite zamanı ve VKİ ile cinsel işlev bozukluğu arasında anlamlı bir ilişki saptanmadı.

Anahtar kelimeler: kısırlık; kadın cinsel fonksiyon ölçeği; kadın cinsel işlev bozukluğu

Introduction

Infertile women may experience higher sexual dysfunction than fertile women may. One of the main sources of anxiety, stress, and depression is infertility, which negatively affects sexual health [1]. Quality of life, emotional health, and sexual relationship of the couples are negatively affected by infertility [2,3]. Women may be more psychosexually affected by infertility than men [4]. One of the most important components of social health and quality of life is sexual function [5]. Daniluk et al. [6] defines dysfunctions as problems in case such problems disturb the partners. Infertility is defined as the women's inability to conceive one year after regular unprotected sexual activity [7,8].

There are different reasons particularly environmental changes for the decreasing rate of fertility rate all over the world [9]. Mascarenhas et al. [10] in a study conducted on global infertility rates in 190 countries from 1990 to 2010 showed that there were 48.5 million infertile couples among whom 19.2 million had primary infertility, and 29.3 million had secondary infertility and the research results show that the couples in developed countries had higher primary infertility while the couples in developing countries had higher secondary infertility. The inherent or acquired circumstances affecting illnesses such as extragenital etiology, the normal reproductive organs such as genital etiology or the psychological factors among the females can impair the women's reproductive function [11,12].

Smith et al. [13] states that infertility as prevalent health problems negatively affects about 20% of all couples and there is an association between infertility and significant psychosocial effect, which is regarded as a stressor [14]. Just a few studies have investigated the impact of infertility on sexual dysfunction of females, demonstrating that infertile women have sexual complaints and that depression, anxiety, and stress were more common among these women [15]. There are several domains for sexual dysfunction. Based on the diagnostic questionarre Female Sexual Function Index (FSFI) , there are six sexual dysfunctions sub types in females including desire (the interest to have sexual experience), arousal (having the interest to have sexual relation before stimulation), lubrication, orgasm (reaching organism after arousal and stimulation), sexual satisfaction, and pain which are measured based on the self-report of the patients.

The study aimed to investigate the frequency of sexual dysfunction among infertile women and evaluate the difference between the primary and secondary infertility groups in terms of menstrual pain, dyspareunia, smoking and night shift variables based on the FSFI score.

Material and Methods

This study was approved by Research Ethics Committee of Beykoz University (Permission granted /CAAE number: 2019/30.09, Decision no: 03) . And all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration

and its later amendments or comparable ethical standards. Informed consent was obtained from each patient. 99 women with primary infertility and secondary infertility participated in this study from October 2019 to February 2020. The participants were divided into two groups: primary group and secondary group. The women who were never able to conceive were regarded as primary infertility group and the women who had conceived before were regarded as secondary infertility group.

The primary group included 70 women and the secondary group included 29 infertile women. All participants presented the informed consent before enrolling in the study.

FSFI scale as a standardized and validated self-report was applied for measurement of the sexual dysfunction. Six domains including desire (the interest to have sexual experience), arousal (having a desire for sexual relation followed by stimulations), lubrication, orgasm (reaching orgasm after arousal and stimulation), satisfaction and pain measured based on patients' self-report were included in the FSFI score. Arousal (4 questions), desire (2 questions), orgasm (3 questions), satisfaction (3 questions), lubrication (4 questions), and pain (3 questions) are the six domains of the scale items. The sum of all scores obtained in all six domains was the total FSFI score. Better sexuality will result from a higher score. The total FSFI score is between 2 and 36. Female sexual dysfunction is a score below ≤26.5 [16].

Besides, the questionnaire containing the marriage duration of primary and secondary groups, total FSF1 score, menstrual pain, dyspareunia, smoking and night shift variables and also the demographic characteristics of patients in primary and secondary groups such as age, infertility time and body mass index (BMI) was given to the subjects.

Statistical Analysis

SPSS 23.0 program was used for data statistical analysis. Categorical measurements are summarized in numbers and percentages, average, deviation, and minimum to maximum for continuous variables. Categorical variables were compared using Pearson's Chi-squared test. Independent student t-test analysis was performed on binary variables by checking distributions to compare continuous variables between groups. Statistical significance was 0.05 in all tests. The initial result of this study was the dysfunction prevalence difference between the primary and secondary groups. Then, the sexual function subgroup scores were also included to evaluate all women's sexual function aspects.

Results

In this study, infertile women were divided into two groups. One group had primary fertility and another group has secondary infertility. Seventy women were included in the primary group, and 29 women were included in the secondary group. Table 1 shown that the difference between the primary and secondary groups in terms of marriage duration of primary and secondary groups, total FSFI score, menstrual pain, dyspareunia, smoking and night shift variables.

Table 1. Examination of the marriage duration of primary and secondary groups, total FSFI score, menstrual pain, dyspareunia, smoking and night shift variables (n: 99) *

		Infertility		Total(n:99)	p-value
		Primary (n: 70)	Secondary (n: 29)		
		n(%)	n(%)	n(%)	
Marriage Period	1-3 years	18 (25,7)	1 (3,4)	19 (19,2)	0,034*
	4-6 years	36 (51,4)	18 (62,1)	54 (54,5)	
	7 years above	16 (22,9)	10 (34,5)	26 (26,3)	
Total FSFI Score	Insufficient	23 (32,9)	16 (55,2)	39 (39,4)	0,109
	Moderate	32 (45,7)	8 (27,6)	40 (40,4)	
	Sufficient	15 (21,4)	5 (17,2)	20 (20,2)	
Menstrual Pain	Yes	34 (48,6)	13 (44,8)	47 (47,5)	0,454
	No	36 (51,4)	16 (55,2)	52 (52,5)	
Dyspareunia	Yes	36 (51,4)	10 (34,5)	46 (46,5)	0,093
	No	34 (48,6)	19 (65,5)	53 (53,5)	
Cigarette	Yes	37 (52,9)	12 (41,4)	49 (49,5)	0,207
	No	33 (47,1)	17 (58,6)	50 (50,5)	
Night Shift	Yes	20 (28,6)	5 (17,2)	25 (25,3)	0,178
		50 (71,4)	24 (82,8)	74 (74,7)	

* Pearson's Chi-squared

25.7% of the women in the primary group and 3.4% of the women in the secondary group had a marriage duration of 1-3 years, which was significantly different. 51.4% of the women in the primary group and 62.1% of the women in the secondary group had a marriage duration of 4-6 years. 22.9 % of the women in the primary group and 34.5% of the women in the secondary group had a marriage duration of 7 years above. There was a statistically significant difference between infertile patients in terms of their marital duration (p=0.034, p<0.05). Based on the bilateral comparisons, the number of those married for 4 to 6 years in the primary group was higher than that in the secondary group.

Total FSFI score was divided into three insufficient, moderate and sufficient scores. The insufficient, moderate and sufficient total FSFI scores in the primary group were 32.9%, 45.7%, and 21.4%, respectively while the insufficient, moderate and sufficient total FSFI scores in the secondary group were 55.2%, 27.6 and 17.2%, respectively. The mean insufficient, moderate and sufficient total FSFI scores in the primary group and the secondary group were 39.4%, 40.4%, and 20.2%, respectively. The primary group had a higher moderate and sufficient total FSFI score than that in the secondary group (p=0.109), though the difference between the primary group and secondary group in terms of sexual dysfunction was not statistically significant (p>0.05). In other words, the frequency of sexual dysfunction demonstrated no statistically significant difference between the two groups.

Figure 1 shows that the insufficient total FSFI score in the primary group was lower than that in the secondary group but the moderate and sufficient total FSFI scores in the primary group were higher than those in the secondary group. However, the difference between them is not significant. The moderate total FSFI score (40.4%) was the most frequent of the insufficient, and moderate total FSFI scores in both groups. The prevalence of sexual dysfunction among the women was 32.9 (n = 23 of 70) and 55.2% (n = 16 of 29) in primary infertile and secondary infertile women, respectively but the prevalence of sexual dysfunction did not show a statistically significant difference between the two groups.

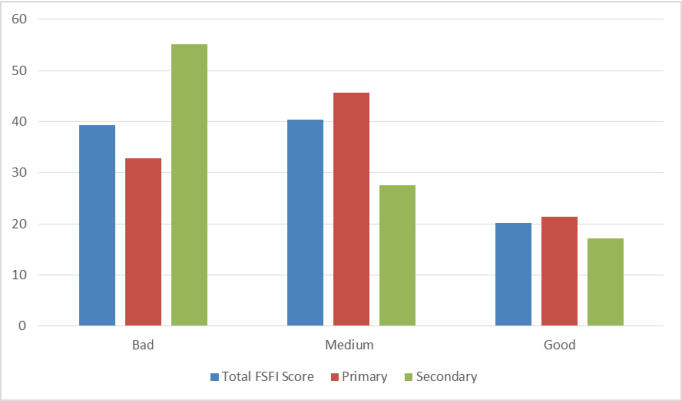

Figure 1. Frequency of sexual dysfunction in infertile patients

In terms of the menstrual pain, the primary group had higher menstrual pain than the secondary group had but these two groups showed no statistically significant difference (p>0.05). The menstrual pain in the primary group was 48.6% and in the secondary group 44.8% with the mean of 47.5%, which showed no statistically significant difference.

The primary group had higher dyspareunia than the secondary group, but these two groups showed no statistically significant difference (p>0.05). Dyspareunia rates in the primary and secondary groups were 51.4% and 34.5%, respectively, showing that there was dyspareunia in the primary group but this difference was not statistically significant.

The smoking rate of patients was 49.5%. Patients in the primary group were found to smoke more than the patients in the secondary group but these two groups showed no statistically significant difference (p>0.05).

25.3% of the patients were found to work at the night shift. Patients in the primary group were found to work at night shifts more than the patients in the secondary group. However, the difference between them was not statistically significant (p>0.05).

The demographic characteristics of the groups including age, infertility time and BMI are shown in Table 2.

The women's median age was 34,44 years (from 25 to 43 years) in the primary group and 34,90 years (from 28 to 45 years) in the secondary group. The patients' mean age was 34,58±4,25 years. The age distribution of patients in the primary and secondary groups was similar (p>0.05).

Infertility time was found to be shorter in the primary group than in the secondary group. However, the difference between them was not statistically significant (p>0.05).

The average BMI of the patients was 24.82. BMI of the patients in the primary group was lower than that of patients in the secondary group while they did not show a statistically significant difference (p>0.05). Table 3 shows the mean FSFI scores in primary and secondary infertile women.

The desire, orgasm and satisfaction scores of patients in the primary group were found to be lower than those of patients in the secondary group. However, the difference between them was not statistically significant (p>0.05).

The arousal and pain scores of the patients in the primary group were higher than those in the secondary group. However, the difference between them was not statistically significant(p>0.05).

The lubrication score was found to be similar in the primary and secondary groups (p>0.05). The total FSFI scores of orgasm, satisfaction, and pain were the lowest as the most prevalent sexual dysfunctions.

Table 2. Examination of the demographic characteristics of patients in primary and secondary groups				
	Infertility		Infertility	p-value
	Primary (n: 70)	Secondary (n: 29)		
	Mean±SD(Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Age	34,44±4,38 (25-43)	34,90±3,94 (28-45)	34,58±4,25 (25-45)	0,631
Infertility time	2,90±1,58 (1-9)	3,34±1,69 (1-8)	3,03±1,62 (1-9)	0,217
BMI	24,67±2,02 (21,6-30,1)	25,19±2,45 (21,3-31,2)	24,82±2,16 (21,3-31,2)	0,282
* Independent student t-test				

Table 2. Examination of the demographic characteristics of patients in primary and secondary groups				
	Infertility		Infertility	p-value
	Primary (n: 70)	Secondary (n: 29)		
	Mean±SD(Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Age	34,44±4,38 (25-43)	34,90±3,94 (28-45)	34,58±4,25 (25-45)	0,631
Infertility time	2,90±1,58 (1-9)	3,34±1,69 (1-8)	3,03±1,62 (1-9)	0,217
BMI	24,67±2,02 (21,6-30,1)	25,19±2,45 (21,3-31,2)	24,82±2,16 (21,3-31,2)	0,282
* Independent student t-test				

Table 3. Examination of patients in primary and secondary groups in terms of desire, arousal, lubrication, orgasm, satisfaction and pain score				
	Infertility		Total(n: 99)	P value
	Primary (n: 70)	Secondary (n: 29)		
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
FSFI desire score	3,52±1,36 (0,6-6,0)	3,69±1,07 (1,8-5,4)	3,57±1,28 (0,6-6,0)	0,550
FSFI arousal score	3,79±1,15 (0,3-6,0)	3,67±1,69 (0,9-6,0)	3,76±1,32 (0,3-6,0)	0,701
FSFI lubrication score	3,33±1,27 (0,9-6,0)	3,35±1,36 (1,5-6,0)	3,34±1,29 (0,9-6,0)	0,956
FSFI orgasm score	2,88±1,41 (0-6,0)	3,03±1,19 (0-5,6)	2,92±1,35 (0-6,0)	0,617
FSFI satisfaction score	2,77±1,31 (0-5,2)	3,22±1,27 (1,2-5,6)	2,90±1,31 (0-5,6)	0,117
FSFI pain score	1,11±1,05 (0-5,4)	1,02-1,0 (0-3,2)	1,09±1,03 (0-5,4)	0,698
* independent student t-test				

Discussion

Infertility is a problem which both partners face and couples undergo diagnostics, though the sexual function among the couples has been studied in only a few studies in the previous five years [17-19]. Most of the studies found that sexual dysfunction was prevalent among infertile women; a study which was published in 2014 used the FSFI to evaluate the sexual function of infertile women which was 25.7±4.6 [20].

Our study compares the two groups with primary infertility and secondary infertility in terms of frequency of sexual dysfunction. Our study shows that both groups with the statistically insignificant difference in insufficient total FSFI scores are at risk of sexual dysfunction and the desire, arousal, and the lubrication domains were the most affected domains of sexual function.

Our study showed that the marriage duration was longer in primary infertile women than in secondary infertile women,

which is not in line with the results of a study by [15] who found that the marriage duration was longer in the secondary group than in a primary group. Keskin et al. [15] also stated that there were significantly lower satisfaction and orgasm domains of FSFI and total FSFI scores in the secondary group and showed that 76.5% of the secondary group and 64.8% of the primary group had sexual dysfunction while our study shows that the primary group and the secondary group did not show a statistically significant difference.

Our study shows that the number of those married for 4 to 6 years in the primary group was higher than that in the secondary group. Therefore, a statistically significant difference was found between the primary and secondary in terms of their marital duration ($p=0.034$, $p<0.05$).

In terms of total FSFI score, the primary group was at a lower risk of sexual dysfunction than the secondary group was but the frequency of sexual dysfunction did not show a statistically significant difference between the two groups.

Jain et al. [21] showed that sexual problems in the primary and secondary groups including orgasmic failure, dyspareunia, and decreased libido were the most prevalent problems. Our study shows that the primary group had higher dyspareunia than the secondary group, but these two groups did not show any statistically significant difference. Patients in the primary group were found to smoke more than the patients in the secondary group but, these two groups showed no statistically significant difference ($p>0.05$). It is also found that the primary group works at night shifts than the secondary group does. Our study shows that the primary group was more affected by infertility than the secondary group in terms of duration of the marriage, dyspareunia, smoking and night shift work.

In our study, also the variables of age, infertility time and BMI as the risk factors which may affect the sexual function in infertile women were investigated to see the effect of such variables on the primary and secondary groups' sexual dysfunction. The patients' age in the study was 34.58 years. There was a similar age distribution of patients in the primary and secondary groups showing that age was not a significant factor affecting the sexual dysfunction. The primary group has shorter infertility time than the secondary group had but the difference was not statistically significant. BMI of the patients in the primary group was lower than that of patients in the secondary group but the difference was not statistically significant. Our findings of BMI scores are compatible with the findings of the study by Keskin et al. [15] that there was no statistical difference between two infertile groups in terms of BMI and also mentioned that independent predictors of FSFI score were age and income but they did not differ significantly in primary and secondary infertilities, which is in line with our study result.

Davari et al.[20] has compared the secondary and primary infertility women concluded that the women with secondary infertility were most seriously impaired, which is not in line with our study result showing that the secondary group and the primary group did not show a statistically significant difference.

Shahraki et al. [22] found that there was significantly higher sexual dysfunction among women with primary infertility than in the secondary group and healthy ones, which is not in line with our study results.

According to Benksim et al. [23] the intersection of several demographic characteristics and medical factors caused primary and secondary infertilities. However, socio-economic status, age, duration of marriage of women had a significant effect leading to increased severity of secondary infertility. This is not supported by our study results that there was a similar age distribution of patients in the primary and secondary groups showing that age was not a significant factor affecting the sexual dysfunction but it is in line with our finding that a statistically significant difference was between the infertile patients in their marital duration.

A study by [24] showed a significant relationship between duration of infertility and the sexual dysfunction but no significant correlation between the sexual dysfunction and type of infertility was found, while our study shows that the primary group has shorter infertility time than the secondary group had but there is no significant relationship between the sexual dysfunction and type of infertility.

Davari et al. [20] found a significant negative correlation between total FSFI score and age, marriage duration and partner age and showed high sexual dysfunction in primary and secondary infertile women, and that women in the secondary group experience more sexual dysfunction than those in the primary group while our study results showed that only marriage duration was significantly different in both primary and secondary groups and that the primary and secondary groups showed no significantly different sexual dysfunctions.

The study by Yousef et al. [25] showed that sexual dysfunction of the primary group was 78.9% and that of the secondary group was 74.7% which was not a statistically significant difference. This is consistent with our study results. This is also in line with the study by Jamali, et al. [24] who found the sexual dysfunction prevalence to be 100% in secondary group and 94.9% in primary group and reported female sexual dysfunction to be more prevalent in the women with secondary infertility than in those with primary infertility, but no statistically significant difference was found.

Yousef et al. [25] also indicated a highly statistically significant relationship between BMI and sexual function of the infertile women, which is not consistent with our study result.

Considering the above comparations, we can conclude that there is no significant difference between two primary and secondary groups in terms of secondary groups, total FSFI score, menstrual pain, dyspareunia, smoking and night shift variables but there is a significant difference between both groups in terms of marriage duration. In our study, the prevalence of sexual dysfunction among the women was 32.9 (n = 23 of 70) and 55.2% (n = 16 of 29) in primary infertile and secondary infertile women, respectively but the prevalence of sexual dysfunction did not show a statistically significant difference between the two groups. There was also no significant relationship between age, infertility time and BMI of both groups and sexual dysfunction. Some of the above results were consistent with our study results and some of them were not consistent with our study results but their studies and our study cannot conclude finally. The common point in all studies is that the prevalence of sexual dysfunction is quite high in women with primary infertility and secondary infertility.

Conclusion

The sexual dysfunction prevalence is quite high in women with primary infertility and secondary infertility and the insufficient total FSFI score of the primary was 55.2% and that of the secondary infertility was 32.9% but the primary and secondary groups showed no statistically significant difference. There was no statistically significant relationship between sexual dysfunction and the demographic characteristics of infertile women including age, infertility time and BMI. The desire, orgasm and satisfaction scores of patients in the primary group were lower than those of patients in the secondary group but they showed no statistically significant. Analyses of mean total FSFI and subgroup scores show that primary and secondary infertile women have no significant differences. It is also concluded that the primary group was more affected by infertility than the secondary group in terms of marriage duration, dyspareunia, smoking and night shift work but the difference between them was not statistically significant but in marriage duration. Therefore, it can be concluded that there is a significant association between marriage duration in both groups and sexual dysfunction.

This study can help evaluate infertile women's sexual function as a potential risk factor. Based on the infertility subtypes, we should carefully know the frequency of female sexual dysfunction and the difference between these two groups in terms of these subtypes. This study helps prevent sexual dysfunction development using psychological interventions and early screening. Preventive strategies can be adopted in case the risk factors are known. This subject needs further studies.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Omani-Samani R, Amini P, Navid B, Sepidarkish M, Maroufizadeh S, Almasi-Hashiani A. Prevalence of sexual dysfunction among infertile women in Iran: a systematic review and meta-analysis. Int J Fertil Steril 2019; 12: 278-83.
2. Iris A, Aydogan Kirmizi D, Taner CE. Effects of infertility and infertility duration on female sexual functions. Arch Gynecol Obstet 2013; 287: 809–12.
3. Monga M, Alexandrescu B, Katz SE, Stein M, Ganiats T. Impact of infertility on quality of life, marital adjustment, and sexual function. Urology 2004; 63: 126–30.
4. Aggarwal RS, Mishra VV, Jasani AF. Incidence and prevalence of sexual dysfunction in infertile females. Middle East Fertility Society Journal 2013; 18: 187–90.
5. Wischmann TH. Sexual disorders in infertile couples. J Sex Med. 2010; 7: 1868–76.
6. Daniluk JC, Koert E, Breckon E. Sexuality and infertility. In: Binik YM, Hall KSK, eds. Principles and Practice of Sex Therapy. 5th edn. New York: The Guilford Press, 2014; 419-36.
7. Vlaisavljević V. Neplodnost. In: Borko E, Takač I, eds. Ginekologija. 2nd edn. Maribor: Visoka zdravstvena šola; 2006;307-36.
8. Starc A, Trampus M, Pavan Jukić D, Grgas-Bile C, Jukić T, Polona Mivšek A. Infertility and Sexual Dysfunctions: A Systematic Literature Review. Acta clinica Croatica 2019; 58: 508-15.
9. Zegers-Hochschild F, Adamson GD et al. International Committee for Monitoring Assisted Reproductive Technology; World Health Organization, International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary of ART Terminology. Fertil Steril 2009; 92: 1520–4.
10. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med 2012; 9: 1001-356.
11. Vogler A. Obravnava neplodnega para. In: Vrtačnik Bokal E, Jančar N, eds. Sodobne oblike zdravljenja neplodnosti/IV spominski sestanek akad. prof. dr. Lidije Andolšek-Jeras. Ljubljana: Slovensko društvo za reproduktivno medicine, 2007; 10-4.
12. Zorn B. Moška neplodnost. In: Takač I, Geršak K, eds. Ginekologija in perinatologija. 1st edn. Maribor: Medicinska fakulteta. 2016; 206-16.

13. Smith JS. Couples undergoing infertility treatment: implications for counselors. Fam J 2003; 11: 383–74.
14. Meldrum DR. Infertility. In: Hacker NF, Moore JG, editors. Essentials of obstetrics and gynecology. Philadelphia: WB Saunders; 1998:610–20.
15. Keskin U, Coksuer H, Gungor S, Ercan CM, Karasahin KE, Baser I. Differences in prevalence of sexual dysfunction between primary and secondary infertile women. Fertil Steril 2011; 96: 1213–7.
16. Yaylali, G.F., Tekekoglu, S., Akin, F. Sexual dysfunction in obese and overweight women. Int J Impot Res 2010; 22: 220–6.
17. Bayar U, Basaran M, Atasoy N et al. Sexual dysfunction in infertile couples: evaluation and treatment of infertility. J Pak Med Assoc. 2014; 64: 138–45.
18. Masoumi SZ, Garousian M, Khani S, Oliaei SR, Shayan A. Comparison of quality of life, sexual satisfaction and marital satisfaction between fertile and infertile couples. Int J Fertil Steril 2016; 10: 290–6.
19. Yangin H, Kukulu K, Gulşen S, Aktaş M, Sever B. A survey on the correlation between sexual satisfaction and depressive symptoms during infertility. Health Care Women Int 2016; 37: 1082–95.
20. Davari Tanha F, Mohseni M, Ghajarzadeh M. Sexual function in women with primary and secondary infertility in comparison with controls. Int J Impot Res 2014; 26, 132–4.
21. Jain K, Radhakrishnan G, Agrawal P. Infertility and psychosexual disorders: relationship in infertile couples. Indian Journal of Medical Sciences 2000 ; 54: 1-7.
22. Shahraki Z, Tanha FD, Ghajarzadeh M. Depression, sexual dysfunction and sexual quality of life in women with infertility. BMC Womens Health 2018; 18: 92.
23. Benksim A, Elkhoudri N, Addi RA, Baali A, Cherkaoui M. Difference between Primary and Secondary Infertility in Morocco: Frequencies and Associated Factors. Int J Fertil Steril 2018; 12: 142-6.
24. Jamali S, Zarei H, Rasekh Jahromi A. The relationship between body mass index and sexual function in infertile women: A cross-sectional survey. Iran J Reprod Med 2014; 12: 189– 98.
25. Yousef, S., Mehasib, S., Ramadan, S., Saied, A. The Relationship between Sexual Function and Body Mass Index among Infertile Women. Egyptian Journal of Health Care 2017; 8: 29-42.

Turkish Journal of Clinics and Laboratory

To cite this article: Kirik S, Aslan M, Ozgor B, Gungor S. Evaluation of seizures and clinical features of pediatric patients diagnosed with Rett Syndrome who were detected to have MECP2 mutation. Turk J Clin Lab 2021; 1: 65-69.

Original Article

Evaluation of seizures and clinical features of pediatric patients diagnosed with Rett Syndrome who were detected to have MECP2 mutation

MECP2 mutasyonu saptanan Rett sendromu tanılı pediatrik hastalarin klinik ve nöbet özelliklerinin değerlendirilmesi

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Abstract

Aim: The aim of this study was to investigate the seizures and clinical characteristics of patients diagnosed with Rett syndrome with MECP2 mutation who were followed up in our tertiary pediatric neurology clinic.

Material and Methods: Patients who were admitted to the pediatric neurology clinic of Inonu University Faculty of Medicine between 2010 and 2015. The patients got MECP2 mutation and whose electronic medical datas were available, were included in our study. Electroencephalography (EEG) records of the patients and antiepileptic treatments they received were evaluated.

Results: The mean age of the patients was 10.2 (9.36 ± 2.75) and the mean age at onset of complaints was 15 months (12.1 ± 5.19). Six of 9 patients who had seizures had generalized tonic clonic seizures and three patients had focal seizures. The most preferred antiepileptic drug was valproic acid.

Conclusion: Rett syndrome characterized with cognitive detoration, epileptic seizures, and microcephaly. Increased awareness provides early diagnosis and suitable treatment for female patients applied with otism and microcephalia in particular, and it is also important for preventing unnecessary diagnostic tests.

Keywords: Rett syndrome, MECP2 mutation, pediatric, epilepsy

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Recevied: 16.06.2019 accepted: 15.10.2020
Doi: 10.18663/tjcl.578475

Öz

Amaç: Bu çalışmanın amacı üçüncü basamak pediatrik nöroloji kliniğimizde izlenen MECP2 mutasyonu saptanan Rett Sendromu tanılı hastaların nöbetlerini ve klinik özelliklerini araştırdık.

Gereç ve Yöntemler: Çalışmamıza İnönü Üniversitesi Tıp Fakültesi çocuk nöroloji kliniğine 2010-2015 yılları arasında başvuran ve MECP2 mutasyonu saptanan ve dosya verilerine ulaşılan hastalar dahil edildi. Hastaların elektroensefalografi (EEG) kayıtları, almış oldukları tedaviler değerlendirildi.

Bulgular: Hastaların yaş ortalaması 10,2 (9,36 ± 2,75) ve şikayete başlama yaşı ortalama 15 ay (12,1 ± 5,19) idi. Nöbet geçiren 9 hastanın altısında jeneralize tonik klonik nöbetler ve üç hastada fokal nöbetler vardı. En çok tercih edilen antiepileptic ise valproik asitti.

Sonuç: Rett sendromu bilişsel gerilik, epileptic nöbetler, mikrosefali ile karakterize bir durumdur. Artan farkındalık, özellikle otizm ve mikrosefali ile başvuran kız hastalara erken tanı ve uygun tedavi sağlarken, tanı için gereksiz testlerin yapılmasını da önler.

Anahtar kelimler: Rett sendromu, MECP2 Mutasyonu, Pediatrik

Introduction

Rett syndrome is a neurodevelopmental disorder identified with early neurological regression following normal development stages and nearly always seen on female patients. It was identified on 1966 by an Austrian pediatrician, Andreas Rett [1]. It is observed to have similar prevalence in all communities, which is approximately once in 15.000-20.000 live female births [2]. Patients are mostly born on time after a normal pregnancy. It is a genetic disease accompanied by loss of cognitive, verbal, fine-gross motor skills and communication, autonomic dysfunction, and frequent seizures [1].

Clinical course of Rett syndrome is examined in four phases [3]. The first phase, early-onset stagnation phase is observed between months 6-18, it is characterized with sudden changes in communication behavior of the infant and decrease in its interest to environment. Seizures are observed after year 1, especially around age 2 with the rapid destructive phase [3, 4]. Epileptic seizures have been reported on literature with various frequency between 60%-94%. In general, generalized tonic, tonic- clonic, and to a lesser extent, focal seizures are observed. Epileptic seizures may be confused with stereotypical movements frequently observed in patients and they may not be identified, for this reason electroencephalography (EEG) is an important tool on their distinction from non-epileptic behavioral movements. EEG findings of patients are often similar to four clinical phases of the disease. Nonetheless, EEG results are not characteristic for Rett syndrome [1, 4].

Mutations in MECP2 gene (OMIM#300005) are used the pathogenesis of Rett syndrome. MECP2 protein is present in high levels especially in the brain. Inactivation mutations in MECP2 gene results in improper and overexpression of genes that are not required to be expressed, and this causes negative effects on the maturation of central nervous system.

The purpose of this study was to contribute in literature by the evaluation 9 female patients diagnosed with Rett syndrome by detecting the mutation in MECP2 gene, with regard to the characteristics of epileptic seizures, EEG, treatment response and neuro-imaging methods.

Material and Methods

This study was performed by the retrospective evaluation of patients who have applied to Inonu University Faculty of Medicine Department of Pediatric Neurology Clinic between years 2010-2015. Genetic screening results for the MECP2 gene of 9 female patients living in the Eastern region of Turkey. Starting age of the stereotype, the frequency of seizures, types of seizures, mental retardation, head circumference and magnetic resonance imaging (MRI) results were reviewed in the study.

Peripheral blood samples were obtained from patients after they signed an informed consent forms for genetic investigation. Genomic DNA was isolated from venous blood by using kit (Qiagen, Germany) according to manufacturer's protocol. Direct sequencing of the coding exons of MECP2 gene was made for patients. An initial denaturating step of 95°C for 2 min. was performed, followed by 95°C for 30 sec,56°C for 30 sec. and 72°C for 50 sec, followed by 30 cycles at 95°C for 30 sec and 72°C for 50 sec .All reactions terminated by a final elongation step at 72°C for 5 min. The amplicons have been analyzed by direct sequencing with ABI Prism (Life Technologies, USA).

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We classified epileptic seizures according to the 2017 International Classification of Seizures, proposed by ILAE in 2017 [5].

This study was approved by local ethical committee. Informed consent was obtained from all patients and the principles of the Helsinki Declaration were followed.

Results

Average age of patients was 10,2 years old (9,36±2,75) and starting age for complaints was 15 months on average (12,1±5,19). Six of 9 patients with seizures had generalized tonic clonic seizures, and three patients had focal seizures. Patients who received two or more antiepileptic treatments were identified to have refractory epilepsy. Seizures were refractory in four of these 9 patients. Two of 4 patients with refractory seizures suffered seizures once a week, and other 2 patients had seizures once a month and/or more. Most commonly used anti-epileptic was valproic acid. Benzodiazepine was preferred in the combination therapy of all patients with refractory seizures. Most common anomaly in EEG was generalized epileptic anomalies (4 patients). Mutations, EEG results and used medications are presented in Table 1. This choice was due to clinician's preference according to clinical characteristics of patients.

Table 1. EEG, seizure pattern and antiepileptic drugs of patients

Patient	MECP2 Mutation	Type of seizure	Frequency of seizure	Drug resistant seizure	AED choice	EEG
1	R255X	GTC	4 in monthly	+	VPA-BZD	Multifocal
2	R255X	Focal	1-2 in monthly	+	VPA-BZD	Focal
3	R270X	Focal	1-2 in monthly	+	TPM-BZD-LAM	Focal
4	R168X	GTC	< 1 month	-	VPA	GED
5	R255X	Focal	< 1 month	-	VPA	Focal
6	R168X	GTC	4 > month	+	VPA-BZD-LEV	GED
7	T158M	GTC	1 in monthly	-	CBZ	GED
8	R133C	GTC	1 < month	-	LEV	GED
9	R168X	GTC	1 < month	-	VPA	GED

AE: Antiepileptic Drug GTC: Generalized tonic-clonic, VPA: Valproic acid, CBZ: Carbamezapine, BZD: Benzodiazepine, LEV: Levetiracetam, TPM: Topiramate, LAM: Lamotrigine, GED: Generalized epileptiform discharges

All patients had mental retardation and stereotype. While head circumference of 8 patients was ≤-2 SD, head circumference was in normal range in 1 patient. All patients underwent neuroradiological imaging. There were no pathological findings in the imaging of six patients. One patient had ischemic non-specific changes, and 2 patients had corpus callosum hypogenesis. Most common MECP2 mutations were R168X and R255X which were detected in three patients.

Discussion

After Rett syndrome was identified by Andreas Rett [1], mutations at Xq28 branch of MECP2 gene were described in detail on 1999. Its characteristics consist of stereotypes and epileptic clinical symptoms with early onset neuromotor development retardation. However, differentiation of stereotype and non-epileptic events from epileptic activities, and starting proper treatment on early period are important [1-3].

It was reported that seizures may lead to serious disturbance in hand skills, ambulation and verbal communication in Rett syndrome cases with epilepsy. According to normal population, seizures in early period are more common. While most commonly reported types of seizures are generalized tonic-clonic and partial seizures, tonic-myoclonic, absence and clonic seizures are observed to be more rare [6, 7]. Studies demonstrate that the frequency of focal seizures and generalized seizures varies. Seizures become more apparent in the third stage of the disease. Early stage EEG findings may be normal, but with advancing stages, focal epileptic, multifocal epileptic and generalized epileptic anomalies may be detected. There are articles reporting refractory seizures in nearly half of patients [8]. In many studies, valproic acid, benzodiazepines, carbamezapine and lamotrigine have been reported as most common treatment choices. While decreased frequency of seizures up to 75% has been reported with valproic acid, only 6% of patients has been reported to be seizure-free [9, 10]. In our study, valproic acid was the preferred antiepileptic in both patients with generalized seizures and patients with focal seizures. Seizure type was generalized tonic clonic seizures in six patients. Three patients had focal seizures. Patients who received two or more medical treatments were identified to have refractory epilepsy. Benzodiazepine was preferred in all patients with refractory seizures. Different from other studies, carbamezapine was preferred in 1 patient with focal seizures in

our study. Levetiracetam, a new generation antiepileptic, was preferred in 2 patients. Two patients were using 3 antiepileptics, two patients were using 2 antiepileptics, and 5 patients were using a single antiepileptic. No difference was determined in mutations with regard to seizure type and treatment response. In seven patients, number of seizures reduced below 50% after antiepileptic treatment. Two patients had at least 1 seizure in a week and they did not benefit from monotherapy.

Although sensitivity of electroencephalography (EEG) has been reported up to 80% in some articles, specificity is low. The common opinion on EEG is that it supports the diagnosis. Hipsarrhytmia and periodical pattern are very rare in EEG [9, 10]. EEG images performed before the start of seizures are generally normal. Electroencephalography results show similar properties in various stages [9]. Electrophysiological results are particularly important in Rett syndrome, in which stereotype and non-epileptic events are frequently observed [10, 17]. In our study, refractory seizures were present in 66,6% of patients with focal epileptic activity, 1 patient with multifocal epileptic activity, and 40% of patients with generalized epileptic activity. This was equal to 55.5% of all patients. Focal epileptic activities were common in central areas.

Tarquinio et al. [4] have stated in their study that there is a characteristic retardation in head circumference percentile of Rett syndrome patients that becomes apparent after age 1, and regular follow-up of head circumference is important. In our study, 8 of 9 patients had microcephalia (< -2SD).

From a clinical aspect, patients are divided in 4 clinical phases. Findings in Phase 1 are stagnation in head circumference and neuromotor development around 6 months. With advancing stages, clinical symptoms become worse. Phase 4 is late motor deterioration phase (starts after age 10, lasts for years); near to complete loss of speech, upper and lower motor neuron findings and Progressive scoliosis, muscle atrophy and rigidity, and decreased mobilization are observed. Stereotypical hand movements such as clapping, scrubbing, rubbing, washing, hitting, bringing hands into mouth, bending fingers and squeezing, which are performed particularly in the middle line, are one of the characteristics of the disease and they appear in phase 2 [2, 3]. All of the patients had the stereotype in our study. One of the patients was in phase 2, 5 patients were in phase 3, and 3 patients were in phase 4. Three patients underwent EEG in pre-seizure period, and only 1 patient had no additional pathology apart from paroxysmal anomaly.

Data on neuro-imaging results are limited in Rett syndrome. In addition, no disease-specific imaging results have been reported [1, 3]. Brain MRI results were normal in six patients, and 2 corpus callosum anomalies were detected in 2 patients (dysgenesis).

MECP2 mutations are detected at 95% rate in classic Rett syndrome, and at 75% in atypical Rett syndrome [11]. There are more than 1000 MECP2 mutations that may be associated with Rett syndrome [12]. However, R106W, R133C, T158M, R168X, R255X, R270X, R294X, R306C mutations are frequently detected in patients. These mutations are responsible for up to 70% of cases [13, 14, 16, 17]. In our study, GTC seizures were determined in 3 patients with R168X mutation. One of these patients was refractory to treatment, and seizures in other two patients were controlled with a single medication. R255X mutation was detected in 3 patients, and this corresponded to 2 of 3 patients with focal seizures. Two of patients with R255X mutation did not benefit from monotherapy. A patient with R255X mutation had refractory epilepsy.

Consequently, there is a small number of pediatric studies performed on Rett syndrome and EEG results. In particular, this study has the feature of being one of the first pediatric studies performed on seizures and electrophysiological characteristics by the identification of MECP2 mutations. Performance of future studies with a higher number of patients and clinical characteristics may present more information on electrophysiological results and mutations.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Dolce A, Ben-Zeev B, Naidu S, Kossoff EH. Rett syndrome and epilepsy: an update for child neurologists. Pediatr Neurol 2013; 48: 337-45.
2. Neul JL, Kaufmann WE, Glaze DG et al. Rett syndrome: revised diagnostic criteria and nomenclature. Ann Neurol 2010; 68: 944-50.
3. Smeets EE, Pelc K, Dan B. Rett Syndrome. Mol Syndromol 2012; 2: 113-27.
4. Tarquinio DC, Motil KJ, Hou W et al. Growth failure and outcome in Rett syndrome: specific growth references. Neurology 2012; 79: 1653-61.
5. Fisher RS, Cross JH, D'Souza C et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia 2017; 58: 531-42.
6. Chahrour M, Zoghbi HY. The story of Rett syndrome: From clinic to neurobiology. Neuron 2007; 56: 422-37.

7. Nissenkorn A, Gak E, Vecsler M, Reznik H, Menascu S, Ben Zeev B. Epilepsy in Rett syndromed-The experience of a National Rett Center. Epilepsia. 2010; 51: 1252-8.
8. Naidu S, Johnston MV. Neurodevelopmental disorders: Clinical criteria for Rett syndrome. Nat Rev Neurol 2011; 7: 312-4.
9. Glaze DG, Frost JD Jr, Zoghbi HY, Percy AK. Rett's syndrome. Correlation of electroencephalographic characteristics with clinical staging. Arch Neurol 1987; 44: 1053-6.
10. Glaze DG, Percy AK, Skinner S et al. Epilepsy and the natural history of Rett syndrome. Neurology 2010; 74: 909-12.
11. Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi HY. Rett syndrome is caused by mutation in X-linked MECP2, encoding methyl-CpG-binding protein 2. Nat Genet 1999; 23: 185-8.
12. Cuddapah VA, Pillai RB, Shekar KV et al. Methyl-CpG-binding protein 2 (MECP2) mutation type is associated with disease severity in Rett syndrome. J Med Genet 2014; 51: 152-8.
13. Adegbola AA, Gonzales ML, Chess A, LaSalle JM, Cox GF. A novel hypomorphic MECP2 point mutation is associated with a neuropsychiatric phenotype. Hum Genet 2009; 124: 615-23.
14. Artuso R, Mencarelli MA, Polli R et al. Early-onset seizure variant of Rett syndrome: definition of the clinical diagnostic criteria. Brain Dev 2010; 32: 17-24.
15. Krajnc N, Župančič N, Oražem J. Epilepsy treatment in Rett syndrome. J Child Neurol 2011; 26: 1429-33.
16. Vignoli A, Savini MN, Nowbut MS, Peron A, Turner K, La Briola F, Canevini MP. Effectiveness and tolerability of antiepileptic drugs in 104 girls with Rett syndrome. Epilepsy Behav 2017; 66: 27-33.
17. Tarquinio DC, Hou W, Berg A, Kaufmann WE, Lane JB, Skinner SA, Motil KJ, Neul JL, Percy AK, Glaze DG. Longitudinal course of epilepsy in Rett syndrome and related disorders. Brain 2017; 140: 306-18.

To cite this article: Akhanli P, Kayhan S, Imamoglu GI, Isak OA, Hepsen S. The determination of breast cancer risk factors: A single centre experience. Turk J Clin Lab 2021; 1: 70-76.

Original Article

The determination of breast cancer risk factors: A single centre experience

Meme kanseri risk faktörleri belirlenmesi: Tek merkez deneyimi

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Abstract

Aim: In developing countries like our country, the frequency of breast cancer is gradually increasing. There are several risk factors of breast cancer. Besides that there can be some unrevealed risk factors. The aim of our study is to reveal demographic data of patients with breast cancer followed up in our hospital and the risk factors of breast cancer.

Material and Methods: 237 female patients treated with the diagnosis of breast cancer between 2005 and 2015 were included in the study. Demographic information, familial features, type of breast cancer, histology, stage-grade, hormone receptor and human epidermal growth factor receptor 2 status of the patients were recorded from the files of the patients. The patients diagnosed with breast cancer were grouped in terms of risk factors, prognostic factors, and characteristics of breast cancer.

Results: A significant correlation was detected between early menarche and PR+ (p=0.034). It was observed that the disease occurred earlier in patients with early menarche (p=0.004). A high positive correlation was detected between triple negative breast cancer and tumor size (p=0.019 r=0.581). Breast cancer was occuring in early ages in nulliparous patients and there was a moderate positive correlation between them (p=0.024 r=0.284).

Conclusion: We revealed that breast cancer might occur in early ages in females with early menarche or both with early menarche and nulliparity. Understanding the etiopathogenesis of this common disease is necessary to determine the content of early diagnosis, treatment, and screening programs. Each society should have their unique screening programmes as distinct from Western societies.

Keywords: breast cancer; epidemiology; risk factors

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Recevied: 12.12.2020 accepted: 18.02.2021
Doi: 10.18663/tjcl.839811

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Öz

Amaç: Ülkemiz gibi gelişmekte olan ülkelerde ise meme kanseri sıklığı giderek artmaktadır. Meme kanserinin ortaya konulan birçok risk faktörleri bulunmakla birlikte, ortaya konmamış risk faktörleri de olabilir. Çalışmamızın amacı, merkezimizde takip ve tedavi edilen meme kanserli hastaların demografik verileri ve meme kanserine ait risk faktörlerini ortaya koymaktır.

Gereç ve Yöntemler: Çalışmaya 2005-2015 tarihleri arasında meme kanseri nedeni ile takip ve tedavi edilen 237 kadın hasta alındı. Hastaların demografik bilgileri, ailesel özellikleri, meme kanseri tipi, histolojisi, evresi ve derecesi, hormon reseptör ve epidermal büyüme faktör reseptör 2 durumu dosyalarından elde edilerek kaydedildi. Meme kanseri tanısı olan hastalar, kendi içinde risk faktörleri, prognostik faktörler ve meme kanseri özellikleri açısından gruplandırarak değerlendirildi.

Bulgular: Erken menarş ile progesteron reseptör pozitifliği arasında anlamlı bir ilişki bulundu (p=0,034). Erken menarş olanlarda, hastalığın daha erken ortaya çıktığı saptandı (p=0,004). TNBC ile tümör çapı ile pozitif yönde yüksek dereceli bir ilişki saptandı (p=0,019 r=0,581). Hiç doğum yapmayan hastalarda, meme kanseri daha erken yaşta ortaya çıkmaktaydı ve aralarında pozitif yönlü orta dereceli bir ilişki mevcuttu (p=0.024 r=0,284).

Sonuç: Çalışmamızda, erken menarş olan veya erken menarş olup hiç doğum yapmayan kadınlarda meme kanserinin daha erken ortaya çıkabileceği saptanmıştır. Yaygın görülen bu hastalığın etiyopatogenezini anlamak, erken teşhis, tedavi ve tarama programlarının içeriğinin belirlenmesi için gereklidir. Toplumumuzda, meme kanseri gelişiminde etkili risk faktörlerinin, batı toplumlarında olan risk faktörlerinden ne gibi farklılıklar gösterdiğini anlayabilmek ve ülkemize özgü tarama programlarını geliştirebilmek için daha büyük çaplı çalışmalara ihtiyaç vardır.

Anahtar kelimeler: meme kanseri; epidemiyoloji; risk faktörleri

Introduction

Breast cancer is the most common type of cancer among females in the world and comes after lung cancer in cancer-related deaths in females. It is the most frequent reason of cancer-related deaths in females between the ages of 15 and 49[1]. Breast cancer takes the lead at the rate of 45.9% within the type of cancer seen in females in our country. How women's health is affected in a society can be well comprehended when these rates are taken into consideration [2].

The frequency of breast cancer varies geographically worldwide. The incidence of breast cancer is greater in developed and industrialized countries. Food habits, industrialized modern life, early menarche, late delivery of a baby, oral contraceptive and hormone replacement therapy, late menopause, long life expectancy can be regarded as the reason of this situation [3]. We aimed to reveal demographic data of patients with breast cancer followed up in our hospital and the risk factors of breast cancer in our study.

Material and Methods

This study was designed as a retrospective, cross-sectional study. The Ethics Committee of our institute approved this study regarding the principles of the Declaration of Helsinki. Written informed consent was taken from subjects before taking part in the study.

The data of female patients followed up in Yildirim Beyazit Diskapi Training and Research Hospital Oncology Clinic between 2005 and 2015 were recorded retrospectively. Demographic information, familial features, type of breast cancer, histology, stage and grade, HR and HER2 status of the patients were recorded. Male patients and the patients with the diagnosis of carcinoma in situ were excluded from the study.

Data analysis was made in SPSS for Windows 21 Packet Programme. While descriptive statistics were stated as medium (min-max), categorical variables were stated as the number of case and in percentages (%) and frequency analyses were made. Whether potential risk factors have a statistically significant effect on breast cancer or not was evaluated by means of independent samples-T test, Chi-square test, and Bivariate method. 95% confidence interval of the effect of each risk factor on the development of breast cancer was calculated. The results for $p < 0.05$ were accepted as statistically significant.

Results

The data of 237 patients were recorded. 13.3±1.5 for menarche age, 48.5±4.4 for menopause age, 20.6 (±4.1) for maternal age at first delivery, 2.9±1.8 for parity, and 29.7±26.6 month for breast-feeding duration were detected. 209 (88.1%) patients gave birth but 27 (11.3%) patients. Early menarche was detected in 63 (26%) patients (age<12). Other demographic features of the patients with breast cancer were demonstrated in Table-1.

The most common histopathologic type was invasive ductal carcinoma observed in 162 (68.4%) patients. 78 (32.9%) of the cases were in Luminal A, 27 (11.4%) were in Luminal B, 84 (35.4%) were in human epidermal growth factor receptor 2 (HER2), and 48 (20.3%) were in triple-negative breast cancer (TNBC). Receptor distribution was as below: Estrogen receptor-positive (ER+) was 150 (63.3%), progesterone receptor-positive (PR+) was 114 (48.1%) and HER2+ was 85 (35.8%). Other histopathologic and hormone receptor features of the patients with breast cancer were demonstrated in Table-2.

The stages of breast cancer, operation types and other histopathologic features of the patients with breast cancer were demonstrated Table-3.

Table-1: Demographic features of the patients with breast cancer

Number	237
Age, year	54.95±13.1
Family history, n (%)	45 (19)
Breast cancer	42 (17.7)
Unknown	3 (1.3)
Menarche age, year	13.3±1.5
Maternal age at first delivery, year	20.6±4.1
Breastfeeding duration, month	29.7±26.6
Menopause age, year	48.5±4.4
Premenopausal, n (%)	89 (37.6)
Postmenopausal, n (%)	147 (62)
Menarche age, year	13.3±1.5
Early menarche, n (%)	63 (26)
Early menopause (age<40) , n (%)	5 (3.4)
Late menopause (age>55) , n (%)	11 (7.4)

Table- 3: The stages of breast cancer, operation types and histopathologic features of the patients with breast cancer

Stage, n (%)	
1 A	39 (16.5)
1 B	20 (8.4)
2 A	57 (24.1)
2 B	40 (16.9)
3 A	35 (14.8)
3 B	7 (3)
3 C	22 (9.3)
4	17 (7.2)
Metastasis Location, n (%)	
Bone	10 (4.2)
Lung	3 (1.3)
Liver	0 (0)
Others	2 (0.8)
Operation Type, n (%)	
Non-operated	6 (2.5)
MRM	203 (85.7)
BCS	28 (11.8)
Tumor size, mm	29.3±28.2
Number of removed lymph node, n	17.6±9.5
Number of metastatic lymph node, n	3.1±6.1
Perinodal involvement, n (%)	
Unknown	6 (2.5)
None available	179 (75.5)
Available	52 (21.9)
Perineural involvement, n (%)	
Unknown	5 (2.1)
None available	189 (79.7)
Available	43 (18.1)
Perivascular involvement, n (%)	
None available	176 (74.3)
Available	61 (25.7)
Grade, n (%)	
Grade 1	68 (28.7)
Grade 2	95 (40.1)
Grade 3	74 (31.2)

MRM: Modified Radical Mastectomy, BCS: Breast-conserving surgery

Table- 2: Histopathologic and hormone receptor features of the patients with breast cancer

Histology, n (%)	
Unknown	9 (3.8)
Ductal	162 (68.4)
Lobular	22 (9.3)
Medullar	8 (3.4)
Papillary	10 (4.2)
Others	26 (11)
Estrogen receptor, n (%)	
Negative	85 (35.9)
Positive	150 (63.3)
Unknown	2 (0.8)
Progesterone receptor, n (%)	
Negative	113 (47.7)
Positive	113 (47.7)
Unknown	11 (4.6)
HER2, n (%)	
Negative	146 (61.6)
Positive	82 (34.6)
FISH positive	4 (1.7)
Unknown	5 (2.1)
Surrogate definitions of intrinsic subtypes of breast cancer , n (%)	
Luminal A	78 (32.9)
Luminal B	27 (11.4)
HER2 +	84 (35.4)
TNBC	48 (20.3)

FISH: Fluorescence in situ hybridization HER2: human epidermal growth factor receptor 2 TNBC: triple-negative breast cancer

The patients were separated into two groups as below and above age 40. There were 34 patients under the age of 40 (age<40). The distribution for the patients under and above age 40 was as below respectively: 32.4% (11) / 33.0% (67) in Luminal A, 11.8% (4) / 11.3% (23) in Luminal B, and 26.5% (9) / 36.9% (75) in HER2+. TNBC was found as 29.4% (10) / 18.7% (48) respectively. Receptor positivity was found as ER+ 64.7% (22) /63.1% (128), PR+ 38.2% (13) /47.3% (101), HER2+ 26.5% (9) / 36.9% (76), TNBC 29.4% (10) / 16.7% (44). While perinodal involvement was found as 36.7% (11) / 21.7% (41), perivascular involvement was found as 38.2% (13) / 21.7% (44) respectively for the patients below and above age 40. A significant dominance was observed in ER+ and PR+ above age 40 (p=0.046, r=0.211). Histologic grade was found out worse with increasing age. There was not a significant difference between two groups in terms of family history and histologic grade (p=0.976). The rate of incidence of TNBC under age 40 was high.

A positive high correlation was observed between smoking and tumor size (p=0.0444, r=0.518).

A statistically significant difference was not found out in terms of tumor stage when compared the patients with a family history and not. Tumor size of the patients with a family history was found out bigger (p=0.004, r=0.694). HER2 showed an increase negatively (70.3%). TNBC was more common (r=0.132).

No statistically significant correlation was found out among early menarch and tumor stage, tumor size and grade, perinodal, perineural, and perivascular involvement, ER+ and HER2+. A significant correlation was detected in PR+ (p=0.034). The occurence of the disease was early in patients with early menarche with a 95% confidence level (p=0.004).

A statistically significant correlation was not found out in terms of tumor stage, tumor type, tumor grade, perinodal, perineural, and perivascular involvement when compared the patients giving birth to the nulliparous ones. No correlation was detected between nulliparity and HR+ and HER2+. A positive high correlation was detected between nulliparous patients and tumor size (r=0.492). Breast cancer was occuring in early ages in nulliparous patients and there was a moderate positive correlation between them (p=0.024 r=0.284).

No significant correlation was found out among advanced maternal age at first delivery (age >30) and tumor stage, perineural - perivascular involvement, histologic grade, type of breast cancer, HR+ and HER2+. A significant correlation was detected between advanced maternal age at first delivery and tumor size (p=0.0442 r=0.509). Tumor size was increasing in direct proportion to advanced maternal age at first delivery (p=0.016 r=0.163).

There was also no significant correlation detected between breastfeeding duration and tumor stage. Perivascular involvement rates were (48/193) 21.8% and (9/27) 33.3% respectively when compared the mothers who did not breast-feed to the breastfeeding ones. A low positive correlation with a 90% confidence level was observed between perinodal involvement and the patients who did not breast-feed. No significant correlation was detected between two groups in terms of tumor type, histologic grade, HR+ and HER2+. A moderate positive correlation was observed between the patients who did not breast-feed and show HER2 over expression (r=0.156).

Based on 50 as age limit, 61 patients within 147 patients diagnosed with postmenopausal went through menopause after the age of 50. A moderate positive correlation between these patients and tumor stage, and a positive correlation with a 90% confidence level between these patients and perinodal involvement were also detected. A moderate positive correlation was also observed between them and ER+ and PR+, which were 48.4% and 35.9% respectively (p=0.049 r=0.190, p=0.040 r=0.187) significant correlation was not detected among tumor type, histologic grade, perivascular involvement, tumor size, and HER2+.

We analysed TNBCs between each other due to the fact that they differ from the other types and 48 (20.3%) patients were with TNBC. While a significant correlation was not detected among tumor stage and perineural, perinodal and perivascular involvement and histologic grade, a high positive correlation was found out with tumor size (p=0.019 r=0.581).

Discussion

In our study, we revealed that breast cancer might occur in early ages in females with early menarche or both with early menarche and nulliparity. Demographic data of the patients diagnosed with breast cancer in our hospital were substantially compatible with literature.

That having a family history is one of the factors in the development of breast cancer [4]. A meta-analysis in which 52 epidemiologic studies were analysed revealed that 12% of the patients had one and 1% of the patients had one or more fam-

ily member with breast cancer [5]. We revealed in our study that 42 patients (17.7%) had a first degree relative with breast cancer. On the other hand, we detected that tumor size was bigger in the patients with a family history. A low positive correlation between family history and grade distribution was also detected and HER2 showed an increase negatively (70.3%). This correlation may depend on genetic differences but there is no knowledge related to this finding in literature.

That exposing to endogenous, estrogen and progesterone substantially increases breast cancer risk [5, 6]. Menarche age was 13.1±1.09 in 13,665 healthy females in a study conducted by Vicdan et al [7]. In accordance with the literature, mean menarche age was 13.3±1.5. While there was no significant correlation among early menarche and tumor stage, tumor size, perinodal, perineural and perivascular involvement, tumor grade, ER+ and HER2+, a significant correlation was found with PR+. A meta-analysis conducted by Abdulkareem, 10 studies within 19 showed that there was a positive correlation between early menarche and HR+ breast cancer [8]. We revealed a significant correlation between early menarche and PR+ not ER+ in our study. We detected that breast cancer occurs earlier in patients with early menarche. The correlation between early menarche and breast cancer, particularly HR+, is high but there is no information in literature in this direction. As a consequence, the screening programmes of the patients with breast cancer should be initiated earlier.

Compared the nulliparous patients to the ones giving birth, there was no significant correlation among tumor stage, perinodal, perineural and perivascular involvement, tumor grade, HR+ and HER2+. In the analysis of 36 studies conducted by Anderson et al., a high positive correlation was detected between nulliparity and HR+ breast cancer [9]. The reason why we did not acquire any data in this direction can be derived from the limited nulliparous patients in our study within the whole population. A high positive correlation was observed between nulliparity and tumor size. We found out that breast cancer occurs in early ages in the nulliparous patients and the ones with early menarche. There is no data in this direction in the studies. This situation can be related to the long-term estrogen exposition derived from early menarche and nulliparity.

No significant correlation was found out between advanced maternal age at first delivery, HR+ and HER2+. We detected that the tumor size of the patients having advanced maternal age was bigger and it increased in proportion to the age. We also determined that there is a correlation between advanced maternal age and perinodal involvement. According to a study of Bao et al., advanced maternal age was associated with both ER+/PR+ and ER-/PR- [10]. Besides, another study revealed that there was a positive correlation between advanced maternal age and HER2 breast cancer [11]. In accordance with literature, there was no correlation between advanced maternal age and HR+ and HER2 in our study. Perhaps this was because we had a small extent patient population. We could also add ethnic and genetic factors.

A significant correlation was not detected between the patients who did not breast-feed and HR+ and HER2+. The rate of the patients not showing HER2 over expression within the patients who did not breast-feed was 82.1%. According to a study conducted in China, a negative correlation was detected between breastfeeding duration and HER2 breast cancer [12]. In consequence of our study, similarly, we determined a moderate negative correlation between breastfeeding duration and HER2+. In spite of the data revealing that long-term breastfeeding decreases the development of breast cancer, it is not obvious whether breastfeeding duration has an effect on the development of breast cancer.

Mean menopause age was 48.5±4.4. It was 51 in western societies [13]. A study conducted by Sahin et al. revealed that mean menopause age for 729 females was 47±4.8 [14]. We revealed similar results in our study. It indicates that females in our society go through early menopause compared to the western societies. Due to the fact that the number of the patients in our study who were above 55 years of age was limited, we separated our patients into two groups considering late menopause age as above 50 (age>50), which was above 55 in western societies (age>55). A positive correlation between the patients going through late menopause and tumor stage and perinodal involvement was detected. ER+ in 48.4% and PR+ in 35.9% of the patients were determined and a significant correlation was found out. But there was no significant correlation with HER2+. Each one-year delay in menopause age causes an increase in breast cancer up to 3% [15]. In most of the studies, a positive correlation was determined between HER2 breast cancer and late menopause age. Similar results were detected

in 3 studies in literature review conducted by Anderson et al. [9]. We detected a significant correlation between related variables in a similar manner to literature. We also determined a significant correlation between perinodal involvement and tumor stage. This situation indicates that patients with late menopause are diagnosed at an advanced stage.

We also analysed TNBC because of the fact that it differs from the other types and detected that 48 (20.3%) patients were with TNBC. The mean age was 55.7±15.4 and 26 (54%) patients were under the age of 60. Between 10% and 20% of patients with breast cancer were with triple negative phenotype (TNBC) in different studies [16, 17]. TNBC was detected in 29.3% patients with family history of breast cancer and 16.2% patients without a family history. That detecting a high rate in patients with family history was also accordant with literature [18]. Besides that a significant correlation was detected between TNBC and tumor size. In a study conducted by Bauer et al., 92,358 patients were analysed in terms of TNBC and 6370 (12.5%) of them were detected with it. Median tumor size was 22 mm in the group of TNBC and 17 mm in the other group. The cancer cells were poorly differentiated or undifferentiated in 76% of TNBC cases and 28% in the other group. The stages of breast cancer differed in two groups based on the time of diagnosis. The patients in TNBC group were diagnosed at the advanced stage compared to the other one [19]. TNBC was at the rate of 20.3% in our patient group in accordance with literature and the mean age for TNBC was 55. Median tumor size of the patients with TNBC in our study was 34 mm in the first group and 28 mm in the other one. There was no significant correlation between histologic grade and TNBC. This situation may be derived from the limited patient included our study and/or multiple risk factors, which are effective on the development of breast cancer.

We revealed that breast cancer might occur in early ages in females with early menarche or both with early menarche and nulliparity. Understanding the etiopathogenesis of this common disease is necessary to determine the content of early diagnosis, treatment, and screening programs. Breast cancer screening for the patients with early menarche should be initiated in early ages for the diagnosis and treatment of the disease. Extended studies are required to comprehend how risk factors of breast cancer in our society differentiate from the others in western societies and to develop screening programmes.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Lozano R, Naghavi M, Foreman K et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2095–128.
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013; 63: 11–30.
3. Hortobagyi GN, Esserman L, Buchholz TA. Neoplasm of the breast. Cancer medicine. 7th ed. London: BC Decker Inc; 2006.
4. Russell RC, Bulstrode CJ, Williams NS. Bailey and Love's short practice of surgery. Chapter on Breast Cancer. 23rd ed. London: Hodder Arnold; 2000.
5. McPherson K, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. BMJ 2000; 9: 624–8.
6. Nelson HD, Zakher B, Cantor A et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med 2012; 156: 635–48.
7. Vicdan K, Kukner S, Dabakoglu T, Ergin T, Keles G, Gokmen O. Demographic and epidemiologic features of female adolescents in Turkey. J Adolesc Health 1996; 18: 54–8.
8. Abdulkareem IH. Aetio-pathogenesis of breast cancer. Niger Med J 2013; 54: 371–5.
9. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. Breast Cancer Res Treat 2014; 144: 1–10.
10. Bao P-P, Shu XO, Gao Y-T et al. Association of hormone-related characteristics and breast cancer risk by estrogen receptor/progesterone receptor status in the shanghai breast cancer study. Am J Epidemiol 2011; 174: 661–71.
11. Phipps AI, Buist DSM, Malone KE et al. Reproductive history and risk of three breast cancer subtypes defined by three biomarkers. Cancer Causes Control 201; 22: 399–405.

12. Xing P, Li J, Jin F. A case-control study of reproductive factors associated with subtypes of breast cancer in Northeast China. Med Oncol 2010; 27: 926–31.
13. McKinlay SM, Bifano NL, McKinlay JB. Smoking and age at menopause in women. Ann Intern Med 1985; 103: 350–6.
14. Sahin NH, Bal MD, Boğa NM, Gökdemirel S, Taşpınar A. Women's perception of the menopause and hormone treatment: barriers against hormone therapy. Climacteric 2011; 14: 152–6.
15. Ban KA, Godellas CV. Epidemiology of breast cancer. Surg Oncol Clin N Am 2014; 23: 409–22.
16. Perou CM, Sørlie T, Eisen MB et al. Molecular portraits of human breast tumours. Nature 2000; 406: 747–52.
17. Rakha EA, El-Rehim DA, Paish C et al. Basal phenotype identifies a poor prognostic subgroup of breast cancer of clinical importance. Eur J Cancer 2006; 42: 3149–56.
18. John EM, Hines LM, Phipps AI et al. Reproductive history, breastfeeding and risk of triple negative breast cancer: The Breast Cancer Etiology in Minorities (BEM) study. Int J Cancer 2018; 142: 2273–85.
19. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry. Cancer 2007; 109: 1721–8.

Turkish Journal of Clinics and Laboratory

To cite this article: Zor M., Küçükkelepçe Şimşek D., Gölbaşı Z., Türkiye'de aromaterapinin etkisine yönelik yapılan hemşirelik tezlerinin incelenmesi. Turk J Clin Lab 2021; 1: 77-94.

Orijinal Makale

Türkiye'de aromaterapinin etkisine yönelik yapılan hemşirelik tezlerinin incelenmesi

Investigation of nursing thesis about the effects of aromatherapy made in Turkey

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Öz

Amaç: Bu araştırma Türkiye'de aromaterapinin etkisini değerlendirmek üzere yapılmış hemşirelik lisansüstü tez çalışmalarının incelenmesi amacıyla yapılmıştır.

Gereç ve Yöntemler: Bu çalışma doküman analizi yöntemi kullanılarak yapılmıştır. Türkiye Ulusal Tez Veri Tabanı'nda "aromaterapi", "nonfarmakolojik yöntemler" ve "hemşirelik" kelimeleri kullanılarak tarama yapılmıştır. Tarama sonucu 66 teze ulaşılmıştır. Tezlerden ikisi tam erişime açık olmadığı, 13'ü hemşirelik tezi olmadığı ve yedisi aromaterapinin etkisini incelemediği için değerlendirme dışı bırakılmış, böylece çalışma 44 tez üzerinden yürütülmüştür.

Bulgular: Tezlerin 24'ü yüksek lisans ve 20'si doktora tezidir. Tezlerin tamamında aromaterapi olarak esansiyel yağ kullanılmıştır. Aromatik yağlar inhaler olarak ya da masaj yöntemiyle uygulanmıştır. Tezlerin 25'inde aromaterapinin kaygı/anksiyete/stres üzerindeki, 23 tezde uyku ve 19 tezde ise ağrı üzerindeki etkisi incelenmiştir. Çalışmaların tamamına yakınında kullanılan aromaterapinin incelenen değişken üzerinde etkili olduğu bulunmuştur.

Sonuç: Son on yılda hemşireler tarafından aromaterapinin etkisine yönelik yapılan lisansüstü tez çalışmalarının sayısı artmıştır. Çalışmaların sonuçları aromaterapinin ağrı, kaygı, anksiyete, stres ve uyku gibi değişkenler üzerinde olumlu etkileri olduğunu göstermektedir.

Anahtar kelimeler: Aromaterapi; lisansüstü tezler; hemşirelik

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Doi: 10.18663/tjcl. 856492

Abstract

Aim: This study was conducted to examine the nursing graduate thesis conducted to evaluate the effect of aromatherapy in Turkey.

Material and Methods: This study was conducted using the document analysis method. Aromatherapy, non-pharmacological methods and nursing words are used to reach the related theses at the Database of National Thesis Center of Turkey. As a result of the scanning, 66 theses were reached. Two of the theses were excluded because they were not open to full access, 13 were not nursing theses and seven theses did not examine the effect of aromatherapy, and the study was conducted over 44 theses.

Results: 24 of the theses are master's and 20 are doctoral dissertations. Essential oil was used as aromatherapy in all of the theses. Aromatic oils were applied as an inhaler or by massage method. While the effect of aromatherapy on anxiety / stress was examined in 25 theses, the effect on sleep was examined in 23 theses and its effect on pain was examined in 19 theses. It was found that aromatherapy used in almost all of the studies was effective on the variable studied.

Conclusion: In the last decade, the number of postgraduate thesis studies conducted by nurses on the effect of aromatherapy has increased. The results of the studies show that aromatherapy has positive effects on variables such as pain, anxiety, stress and sleep.

Keywords: Aromatherapy; postgraduate theses; nursing

Giriş

Aromaterapi, tamamlayıcı ve alternatif tedavi yöntemlerinden biri olup bitkilerin çeşitli bölümlerinden (yaprak, çiçek, kabuk, meyve, kök) elde edilen aromatik esansiyel yağların tedavi amaçlı kullanımı esasına dayanmaktadır. Yaygın kullanım alanı, kullanım kolaylığı, non invazif olması nedeni ile yaygın olarak kullanılmaktadır. Aromaterapi iyileşmeyi sağlamak için, inhaler ve/veya masaj gibi yöntemler şeklinde kullanılarak bazı hastalıklardan korumada, tedaviye destekleyici, fiziksel ve psikolojik iyilik halini yükseltmede kullanılan bir uygulamadır [1,2]. Aromaterapi, koku aracılığı ile limbik sistem ve hipotalamusa kadar uzanan bağlantılarla doğrudan beyin korteksine ulaşabilmektedir. Kortekse ulaşan koku birey üzerinde ruhsal, fiziksel ve davranışsal etkiler yaratmaktadır [2,3]. Aromatik yağların santral sinir sistemi üzerine oluşturduğu etki sonucunda rahatlama, sedasyon ve uyarıcı etkiler oluşmaktadır. Santral sinir sisteminin uyarısı ile beyne ulaşan bilgi akımı sayesinde vücuttaki enerji blokajı kırılmakta ve sonuçta enerji açığa çıkmaktadır. Açığa çıkan enerji akımının ilgili organlara dengeli bir biçimde yayılmasıyla iyileşme süreci desteklenmekte, fiziksel ve ruhsal iyilik hali ortaya çıkmaktadır. Aromaterapi, kadın doğum ve kadın sağlığı, nörolojik hastalıklar, kas-iskelet sistemi hastalıkları, otoimmun hastalıklar, sindirim sistemi hastalıkları, kanser ağrıları ve tedavilerinin yan etkilerini azaltma gibi iyilik halini ve yaşam kalitesini artırmada tercih edilmektedir [4-9].

Literatürde aromaterapinin başlıca olarak; doğum ağrısı [5,10], premenstrual sendrom [11], dismenore [12], bebeklerde koliğin giderilmesinde [13], fizyolojik parametreler [9,14], premenopozal dönem vazomotor yakınmalar [8,15], demans [7], osteoartrit [16,17], fibromiyalji [18] kabızlık [6], hipertansiyon [2,14], ağrı yönetimi [5,7,18], kemoterapiye ve gebeliğe bağlı bulantı ve kusma [19,20], yaşam kalitesini artırmada [7,8,15], uyku kalitesini artırmada [22], stres-anksiyeteyi azaltma veya giderme [3,23–25] gibi durumlarda yaygın olarak kullanıldığı görülmektedir. Sonuç olarak aromaterapi uygulamaları hastaların bedensel ve ruhsal sorunları dahil olmak üzere birçok tıbbi problemlerde kullanıldığı söylenebilir. Aromaterapi, bireyin sağlığını korumak, geliştirmek, hastalık anında bakım vermek ve rehabilitasyon sürecinde bireyi desteklemekte önemli sorumlulukları olan hemşirelikte de uzun yıllardır kullanılan bir uygulamadır. Florence Nightingale'in, hasta askerlerin alnını lavanta yağı ile ovduğu belirtilmektedir [26]. Son yıllarda ise geleneksel olarak kullanılan aromaterapinin bireyin sağlık sonuçları üzerindeki etkisini değerlendirmeye yönelik yapılan hemşirelik araştırmalarının sayısının arttığı görülmektedir. Bu çalışma sonuçlarının bir bütün olarak değerlendirilmesi aromaterapinin hemşirelik uygulamalarına entegre edilmesinin yolunu açacak ve uygulama alanı giderek genişleyen geleneksel ve tamamlayıcı tıp uygulamalarına sağlık çalışanlarının dikkatini çekecektir.

Gereç ve Yöntemler

Bu çalışma Türkiye'de hemşire ve ebeler tarafından aromaterapinin etkisini değerlendirmek üzere yapılmış lisansüstü tez çalışma-

larının incelenmesi amacıyla doküman analizi yöntemi kullanılarak yapılmıştır. Tezlerin taranması 15-24 Ağustos 2020 tarihleri arasında yapılmış olup, arama motoru olarak Türkiye Ulusal Tez Veri tabanı kullanılmıştır. Taramada yıl sınırlaması yapılmadan tüm lisansüstü tezler taranmıştır. Taramada kullanılan anahtar kelimeler Medical Subject Headings (MESH)'ten seçilmiştir. Kullanılan anahtar kelimeler "aromaterapi", "nonfarmakolojik yöntemler" ve "hemşirelik" kelimelerinin kombinasyonlarından oluşmuştur. İlgili anahtar kelimeler ile 66 teze ulaşılmıştır. Bu tezlerden tam metin erişime açık olmayan 2, hemşirelik çalışması olmayan 13 ve aromaterapinin etkisinin incelenmediği (girişimsel olmayan) 7 tez değerlendirme dışı bırakılmıştır. Kalan 44 tez doküman analizi yöntemi ile daha kapsamlı olarak incelenmiştir.

Bulgular

Bu araştırmada incelenen tezler 2007-2020 tarihleri arasında yürütülmüş olup 20'si yüksek lisans, 24'ü doktora tezidir. Tezlerin tamamında aromaterapi olarak esansiyel yağ kullanılmış olup büyük çoğunluğunda lavanta yağı kullanılmıştır. Aromaterapinin kullanılma yöntemine bakıldığında sıklıkla inhaler ve masaj yönteminin kullanıldığı görülmüştür. Tezlerin 25'inde aromaterapinin kaygı/anksiyete/stres üzerine, 23 tezde uyku ve 19 tezde ise ağrı üzerindeki etkisi incelenmiştir. Tezlerin 16'sı iç hastalıkları hemşireliği anabilim dalında, 11'i hemşirelik anabilim dalında yürütülmüştür (Tablo 1).

Yapılan yüksek lisans tezleri incelendiğinde sekiz tez çalışmasında aromaterapi uygulamada masaj yönteminin, 13'ünde inhalasyon yönteminin, bir çalışmada inhalasyon ve topikal birlikte ve bir çalışmada ise masaj, inhalasyon ve ayak banyosu şeklinde olduğu ve tamamında lavanta yağının kullanıldığı görülmüştür. Tezlerin tamamına yakınında kontrol grubu kullanılmış olup, yedi çalışmada aromaterapinin uyku üzerindeki etkisi, on çalışmada ağrı üzerindeki etkisi ve dokuz çalışmada da kaygı/stres üzerindeki etkisi incelenmiştir. Aromaterapinin uyku üzerine etkisinin incelendiği çalışmaların çoğunluğunda Pittsburgh Uyku Kalitesi İndeksi (PUKİ), ağrı üzerine etkisinin incelendiği çalışmaların çoğunluğunda Visuel Analog Skalası (VAS), kaygı üzerine etkisinin incelendiği çalışmalarda Durumluluk Kaygı Ölçeği (STAI FORM TX–I) kullanılmıştır. Yapılan çalışmaların sonuçlarına bakıldığında, uygulanan aromaterapinin uyku kalitesini arttırdığı, uygulanan işlemler sırasında, doğumda ağrı töleransını yükselttiği, hissedilen ağrı ve kaygı düzeyini azalttığı görülmüştür. Bunun yanı sıra aromaterapi uygulamasının yaşamsal bulguları olumlu yönde etkilediği ve konfor ve memnuniyet düzeyini arttırdığı bulunmuştur (Tablo 2).

Tablo 1. Aromaterapinin Etkisinin Değerlendiren Hemşirelik Tezlerinin Tanımlayıcı Bilgileri

Tezin yapıldığı tarih	2017-2020	21
	2012-2016	19
	2007-2011	5
Tezin türü	Yüksek lisans	20
	Doktora	24
Aromaterapi yöntemi	Esansiyel yağ	44
Aromaterapi ürünü	Lavanta	39
	Badem Yağı	7
	Nane Yağı	7
	Biberiye Yağı	6
	Papatya Yağı	6
	Portakal	3
	Limon	3
	Okaliptüs	3
	Zencefil	3
	Bergamot	2
	Karabiber Yağı	2
	Melekotu Yağı	1
Aromaterapi uygulama şekli	İnhaler	28
	Masaj	23
Değerlendirilen paramatre	Kaygı/anksiyete/stres	25
	Uyku	23
	Ağrı	19
	Yaşam kalitesi	5
	Yorgunluk	4
	Konfor	2
	Bulantı – kusma	2
	Memnuniyet	2
	Osteoartrit	2
Tezin Yapıldığı Hemşirelik Anabilim Dalı	İç Hastalıkları Hemşireliği Anabilim Dalı	16
	Hemşirelik Anabilim Dalı	11
	Hemşirelik Esasları Anabilim Dalı	5
	Çocuk Sağlığı ve Hastalıkları Hemşireliği Anabilim Dalı	4
	Cerrahi Hastalıkları Hemşireliği Anabilim Dalı	4
	Halk Sağlığı Hemşireliği Anabilim Dalı	2
	Ruh Sağlığı ve Psikiyatri Hemşireliği Anabilim Dalı	1
	Kadın Sağlığı ve Hastalıkları Hemşireliği Anabilim Dalı	1

Yapılan doktora tezleri incelendiğinde 13 tez çalışmasında aromaterapi uygulamada masaj yönteminin, 14'ünde inhalasyon yönteminin, dört çalışmada inhalasyon ve masaj yöntemi birlikte kullanılmıştır. Tez çalışmalarının tamamına yakınında lavanta yağı kullanıldığı ve yanı sıra lavanta ile birlikte badem, nane, biberiye, papatya, portakal, limon, okaliptüs, zencefil, bergamot, karabiber, melekotu, ylang-ylang, kakule, katı hindistan cevizi,

Tablo 2. Aromaterapinin Etkisini Değerlendiren Hemşirelik Yüksek Lisans Tezleri

Yazar/ Yılı	Tez Adı	Çalışmanın Tipi	Örneklem Sayısı	Aromaterapi yöntemi/ ürünü/ uygulama şekli	Kullanılan ölçüm aracı	Sonuç
Yaman[27] S./2011	Lavanta yağıyla uygulanan sırt masajının yaşlıların uyku kalitesine etkisinin incelenmesi	Ön Test-Son Test Deneme Modeli Yarı Deneysel Çalışma	60 kişi Masaj grubu: 34 Aromaterapi + Masajı grubu: 34	Esansiyel Yağ / Lavanta/ Masaj	Pittsburg Uyku Kalitesi İndeksi (PUKİ), Pittsburg Uyku Kalitesi İndeksinin 3 günlük versiyonu (PUKİ-3)	Araştırmada her iki grubun PUKİ puan ortalamalarının masaj sonrasında anlamlı olarak düşüş gösterdiği saptanmıştır. Grupların masaj sonrası PUKİ puan ortalamaları karşılaştırıldığında ise aromaterapi grubundaki düşüşün masaj grubundan daha fazla olduğu ve aradaki farkın istatistiksel olarak anlamlı olduğu belirlenmiştir (p<0.001).
Karabulut[28] H. /2014	Doğum eyleminde aromaterapinin etkileri	Randomize kontrollü çalışma	60 gebe Deney Grubu:30 Kontrol Grubu:30	Esansiyel Yağ /Lavanta/ Masaj, inhaler ve ayak banyosu	Visuel Analog Skala (VAS), Durumluluk Kaygı Ölçeği (STAI FORM TX–I)	Aromaterapi uygulanan gruptaki kadınlar, kontrol grubundaki kadınlara göre aktif fazda doğum ağrısını daha az algılamıştır. Geçiş fazında, deney grubundaki kadınlar, kontrol grubundaki kadınlara göre doğum ağrısını daha az algıladıkları bulunmuştur. Deney gurubundaki kadınların kontrol grubundaki kadınlara göre latent fazda ve geçiş fazında yaşadıkları kaygı ve anksiyete düzeylerinin daha düşük olduğu saptandı. Deney grubundaki kadınlarda doğum eyleminin ikinci ve üçüncü evrelerinin süreleri kontrol grubuna göre daha kısa sürdüğü gözlenmiştir. Deney grubundaki yenidoğanların birinci dakika APGAR skor ortalaması kontrol grubundakilere göre daha yüksek bulundu.
Şentürk[29] A. /2015	Hemodiyaliz hastalarına inhalasyon yolu ile lavanta yağı uygulamasının anksiyete düzeyi ve uyku kalitesine etkisi	Deneysel çalışma	34 kişi Deney Grubu:17 Kontrol Grubu:17	Esansiyel Yağ /Lavanta/ İnhaler	Pittsburgh Uyku Kalitesi İndeksi (PUKİ), Visüel Analog Uyku Skalası (VAS)- Gündüz Uykululuk Düzeyi Hamilton Anksiyete Değerlendirme Ölçeği(HAM-A)	Müdahale grubundaki bireylerin kontrol grubundaki bireylere göre öznel uyku kalitesinin daha yüksek olduğu, VAS gündüz uykululuk puan ortalamalarının düştüğü (p<0.05) saptanmıştır. Müdahale grubundaki bireylerin kontrol grubundaki bireylere göre Hamilton Anksiyete Ölçeği tüm alt boyut ve toplam puan ortalamaları arasındaki farkın istatistiksel olarak ileri derecede anlamlı olduğu bulunmuştur (p<0.001).
Barış[30] N./2015	Aromaterapinin yoğun bakım ünitesinde çalışan hemşirelerin stres ve anksiyeteleri üzerine etkisi	Kendinden Kontrollü, Yarı Deneysel Klinik Çalışma	45 kişi Deney Grubu:28 Kontrol Grubu:17	Esansiyel Yağ /Lavanta/ İnhaler	Algılanan Stres Ölçeği, Durumluk Kaygı Ölçeği, Sürekli Kaygı Ölçeği, Visuel Analog Scale	Araştırmanın sonunda hemşirelere uygulanan lavantanın stres ve anksiyete düzeyi ile yaşam bulguları üzerine etkisi olmadığı saptanmıştır (p>0.05). Ancak kontrol ve deney grubunda yer alan hemşirelerin uygulama öncesine göre uygulama sonrasında durumluk kaygı skorlarında istatistiksel olarak anlamlı olacak şekilde düşüş görülmüştür (deney grubu için p<0.001).

İlter [31] M.S./2016	Onkoloji hastalarına port kateterizasyonu işlemi sırasında uygulanan inhaler aromaterapinin ağrıya etkisi	Randomize kontrollü çalışma	60 kişi Deney Grubu:30 Kontrol Grubu:30	Esansiyel Yağ / Portakal, lavanta ve papatya yağı, / İnhaler	Visuel Analog Scale-VAS	Müdahale grubunun işlem öncesi 6,2±1,6 olan ağrı puan ortalamasının, işlem sırasında 5,0±1,2'ye düştüğü, işlem sonrasında tekrar 5,5±1,2'ye yükseldiği, kontrol grubunun ise; işlem öncesi 6,0±0,9 olan ağrı puan ortalamasının, işlem sırasında 7,4±1,4'e yükseldiği ve işlem sonrasında 6,5±1,6'ya düştüğü belirlenmiştir (p<0.05).
Ayik [32] C./2016	Ameliyat öncesi dönemde aromaterapi masajının anksiyete ve uyku kalitesine etkisinin incelenmesi	Randomize kontrollü çalışma	80 kişi Deney Grubu:40 Kontrol Grubu:40	Esansiyel Yağ / Lavanta/ Masaj	Richard Campbell Uyku Ölçeği (RCUÖ), Durumluk Kaygı Ölçeği (DKÖ)	Çalışma grubu ile kontrol grubu arasında ameliyat sabahı DKÖ ve RCUÖ puan ortalaması bakımından istatistiksel olarak anlamlı bir fark olduğu (p<0.05) saptanmıştır. Çalışma grubunda aromaterapi masajından sonra ameliyat sabahı DKÖ puan ortalamasının ameliyat öncesi akşama göre düştüğü, aradaki farkın istatistiksel olarak anlamlı olduğu (p<0.05) saptanmıştır.
Gürakan[33] G./2016	Palyatif bakım alan kanser hastalarında aromaterapi sırt masajının ağrı şiddeti ve plazma beta endorfin düzeyine etkisi	Deneysel araştırma	31 kişi Aromaterapi:11Masaj: 10 Kontrol:10	Esansiyel Yağ / Lavanta/ Masaj	Sayısal Ağrı Skalası, Ecog Performans Durumu Skalası, Brief Ağrı Envanteri	Aromaterapi, masaj ve kontrol grubunda bulunan hastaların; ikinci, üçüncü ve dördüncü uygulamadan sonra ölçülen ağrı şiddeti puanları ve ECOG performans durumu puanları arasında istatistiksel olarak anlamlı bir fark bulunmuştur (p<0.05). Aromaterapi ve masaj grubundaki hastaların en şiddetli ağrı, en hafif ağrı ve ortalama ağrı puanlarında zamanla anlamlı bir azalma olduğu saptandı (p<0.05). Ayrıca aromaterapi ve masaj grubundaki hastaların plazma-beta endorfin düzeylerinde ikinci ölçümde anlamlı bir artış olduğu saptandı (p<0.05).
Dalkıran[34] S.S/2017	Preoperatif dönemdeki kanser hastalarında lavanta yağı ile yapılan sırt masajının uykuya etkisi	Ön test – son test deneme modeli ile yarı deneysel çalışma	80 kişi Deney Grubu:40 Kontrol Grubu:40	Esansiyel Yağ / Lavanta/ Masaj	Pittsburg Uyku Kalitesi İndeksinin 3 günlük versiyonu (PUKİ-3)	Öntest deney grubunda uyku kalitesinin kontrol grubuna göre daha düşük olduğu saptanmıştır. Uygulanan lavanta yağı girişimi sonrasında deney grubunda uyku kalitesinin önemsenecek düzeyde arttığı, kontrol grubunda ise uyku kalitesinin aradan geçen zamanda azaldığı saptanmıştır. Deney grubunun uyku kalitesinin başlangıçta kontrol grubuna göre düşük olmasına rağmen girişim sonrasında kontrol grubundan daha iyi bir uyku kalitesine ulaştığı belirlenmiştir.
Gürler[35] M./2017	Menopozal dönemdeki kadınlara uygulanan aromaterapinin uyku ve yaşam kalitesine etkisi	Ön test ve son test düzende, kontrol gruplu deneysel çalışma	50 kişi Deney Grubu:27 Kontrol Grubu:30	Esansiyel Yağ /Lavanta, Limon/ İnhaler	Pittsburg Uyku Kalitesi İndeksi (PUKİ) ve Menopoza Özgü Yaşam Kalitesi Ölçeği (MÖYKÖ)	Müdahale grubunun aromaterapi öncesi PUKİ toplam puanı 14.85±1.23 iken, kontrol grubunun uygulama öncesi PUKİ toplam puanı 15.20±0.92 bulunmuştur. Aromaterapi sonrası müdahale grubunun PUKİ toplam puanı 9.74±2.12, kontrol grubunun PUKİ toplam puanı 14.60±1.10 olup gruplar arasında istatistiksel olarak anlamlı bir fark bulunmuştur (p<0.001).

Cenkci[36] Z. /2017	Aromaterapinin doğum eylemindeki ağrı, konfor ve memnuniyet üzerine etkisi	Randomize kontrollü, yarı deneme modeli çalışma	60 gebe Deney Grubu:30 Kontrol Grubu:30	Esansiyel Yağ / Lavanta/ İnhaler	Visual Analog Scale (VAS), Doğum Konforu Ölçeği (DKÖ), Postpartum Kendini Değerlendirme Ölçeğinin "Doğum Deneyiminden Memnuniyet" alt boyutu	Doğumun Latent fazında VAS ortalaması deney grubunda 3,4±2,1, kontrol grubunda 6,6±2,0, Aktif fazında deney grubunda 6,1±1,7, kontrol grubunda 8,7±1,0, Geçiş fazında deney grubunda 8,3±0,9, kontrol grubunda ise 9,8±0,5 olarak belirlenmiş ve gruplar arasındaki farkın tüm fazlarda anlamlı olduğu saptanmıştır (p=0,000). Doğumun Latent fazında DKÖ puan ortalaması deney grubunda 37,1±4,4, kontrol grubunda 30,2±4,4, Aktif fazında deney grubunda 36,3±3,2, kontrol grubunda 25,3±4,6, Geçiş fazında deney grubunda 33,6±3,9 kontrol grubunda ise 21,1±4,7 olarak belirlenmiş ve gruplar arasındaki farkın tüm fazlarda anlamlı olduğu saptanmıştır (p=0,000). Deney grubunun Doğum Deneyiminden Memnuniyet Ölçeği puan ortalamasının 30,03±2,53, kontrol grubunun 27,6±3,6 olduğu ve aradaki farkın istatistiksel olarak anlamlı olduğu bulunmuştur (p=0,000).
Beyliklioğlu[37] A./2017	Aromaterapinin mastektomi öncesi hastaların anksiyeteleri üzerine etkisi	kontrol gruplu ön test-son test yarı deneme modeli çalışma	80 kişi Deney grubu:40 Kontrol grubu:40	Esansiyel Yağ / Lavanta/ İnhaler	Durumluk-Sürekli Anksiyete Envanteri'	Deney grubundaki hastaların ön-test durumluk anksiyete puan ortalamasının 43,00±11,48, son-test durumluk anksiyete puan ortalamasının 37,28±9,93 olduğu ve aradaki farkın istatistiksel olarak anlamlı olduğu saptanmıştır (p=0,003).
Genç[38] H. /2017	Lavanta yağının benign prostat hiperplazili hastaların ameliyat öncesi yaşam bulguları ve kaygı düzeyine etkisi	Ön test-son test kontrol gruplu yarı deneme modeli çalışma	110 kişi Deney Grubu:55 Kontrol Grubu:55	Esansiyel Yağ / Lavanta/ İnhaler	Hasta İzlem Formu (yaşamsal bulgular) Durumluluk Kaygı Ölçeği	Araştırma kapsamında; deney grubunun durumluk kaygı ön test puan ortalaması 65.07±6.24 iken aromaterapi sonrası 26.60±7.47'e düşmüştür. Kontrol grubunda ise durumluk kaygı ön test puan ortalaması 66.29±4.20 iken aromaterapi sonrası 63.50±2.94'e düşmüştür. Deney grubu ile kontrol grubu karşılaştırıldığında fark istatistiksel olarak önemli bulunmuştur. Aromaterapi öncesi ve sonrası yaşam bulgularındaki değişim incelendiğinde ise deney grubundaki bireylerin sistolik kan basıncı ortalaması 127.54±20.27 iken, aromaterapi sonrası 124.36±16.27'ye solunum sayısı ortalaması 21.85±2.51 iken, aromaterapi sonrası 20.54±3.09'a düşmüş, SPO2 ortalaması ise 93.63±1.89 iken aromaterapi sonrası 94.09±1.54'e yükselmiş ve ölçümler arasındaki fark istatistiksel olarak önemli bulunmuştur.
Taşan[39] E./2018	İnhaler lavantanın hemodiyaliz hastalarında damara ulaşım sırasında oluşan ağrıya etkisi	Randomize, kontrollü, deneysel çalışma	60 kişi Deney Grubu:30 Kontrol Grubu:30	Esansiyel Yağ / Lavanta/ İnhaler	Visuel Analog Skala (VAS)	Müdahale grubunun inhaler lavanta uygulaması öncesi 3.8±0.3 olan ağrı puan ortalamasının uygulama sonrası 3.0±0.2'ye düştüğü ($p<0.05$), kontrol grubunun ise ağrı puan ortalamasının 5.4±0.3'den, 5.6±0.6'ya yükseldiği ve inhaler lavantanın herhangi bir olumsuz etki yaratmadığı saptandı ($p>0.05$).

Gülşen[40] G./2018	Üst gastrointestinal endoskopi işlemi uygulanan hastalara müzik eşliğinde uygulanan inhaler aromaterapinin vital bulgulara etkisi	Randomize, kontrollü, deneysel çalışma	90 kişi Müzik Grubu:30 Aromaterapi: Grubu:30 Müzik+aromatepi grubu:30	Esansiyel Yağ / Lavanta, Papatya, Neroli/ İnhaler	Endoskopi işlemi sonrası işlem ile ilgili memniyet sorularını içeren form, Vital bulgu takip formu	Araştırmada tüm gruplarda işlem öncesine göre işlem sırasında nabız değerlerinin arttığı, fakat en az artışın grubu ile müzik eşliğinde aromaterapi uygulanan grupta en çok artışın ise kontrol grubunda olduğu görüldü(p<0.05).
Kanca[41] C./2019	Diz osteoartriti olan hastalarda, ısırgan-zencefil esansiyel yağlarıyla yapılan masajın ve buz uygulamasının ağrı üzerine etkinliğinin değerlendirilmesi	Ön test son test tasarımlı girişimsel, randomize kontrollü çalışma	66 kişi Aromaterapi grubu:30 Buz uygulaması grubu:22 Kontrol grubu : 22	Esansiyel Yağ / Lavanta, Isırgan, zencefil / Masaj	Sayısal Derecelendirme Ölçeği (NRS) Olgu Rapor Formu(ORF)	Masaj grubunun %63,6'sının, buz grubunun %36,4'ünün ve kontrol grubunun %40,9'unun hikayesinde operasyon geçirdiği saptanmıştır. NRS 1.seans değeri masaj grubunda en yüksek değerde iken, NRS 8.seans değeri en düşük masaj grubunda olmuştur. Her üç grupta da NRS 8.seans değerlerinin anlamlı derecede düştüğü görülmekle beraber, en fazla düşüşün masaj grubunda olduğu görülmektedir.
Özdemir[42] T.S./2019	Hemodiyaliz hastalarında av fistül uygulaması sırasında oluşan ağrıyı gidermede lavanta aromaterapinin etkisi	Randomize kontrollü, deneysel çalışma	90 kişi İnhaler Aromaterapi grubu:30 Topikal Aromaterapi grubu:30 Kontrol grubu: 30	Esansiyel Yağ / Lavanta/ İnhaler, Topikal	Sözel Kategori Ölçeği (SKÖ), Visuel Analog Skala(VAS)	Çalışmaya katılan hemodiyaliz hastalarının uygulama öncesi ağrı puan ortalamaları uygulama grubunda, 57,58 ± 20,28, kontrol grubunun 48,53 ± 20,23 olduğu, uygulama sonrası uygulama grubunda 19,49 ± 15,66 ve kontrol grubunda 45,33 ± 25,52, olduğu belirlendi (p<0,005). Lavanta yağı uygulaması sonrası ağrı puan ortalamaları inhaler lavanta grubunda 22,66 ± 15,35, topikal lavanta grubunda 16,33 ± 15,97, kontrol grubunda 45,33 ± 25,52, plasebo ilk uygulaması sonrası inhaler lavanta grubunda 24 ± 15,16, topikal lavanta grubunda 41,16 ± 16,27, kontrol grubunda 45,33 ± 25,52 olduğu saptandı.
Koç[43] E./2019	Lavanta yağının kronik otitis media hastalarının ameliyat öncesi yaşam bulguları ve kaygı düzeyine etkisi	Ön test-son test kontrol gruplu yarı deneysel çalışma	88 kişi Deney grubu:44 Kontrol grubu:44	Esansiyel Yağ / Lavanta/ İnhaler	Hasta Yaşam Bulguları Formu Durumluk Kaygı Ölçeği (DKÖ)	Deney ve kontrol grubunda lavanta yağı inhalasyonunun etkisine bakıldığında yaşam bulgularında aromaterapi sonrası önemli farklılığın olduğu saptanmıştır (p<0,005). Aromaterapi öncesi SKB ortalaması 118.30±12.39 iken aromaterapi sonrası 107.50±11.44'e, DKB ortalaması 74.09±9.96 iken 67.95±8.79'a, nabız ortalaması 82.55±9.68 iken 72.18±7.46'ya, solunum sayısı ortalaması 20.95±1.26 iken 19.32±1.49'a düşmüştür. Gruplar arasındaki fark; Nabız, SKB, DKB ve solunum sayısı yönünden istatistiksel olarak anlamlı bulunmuştur (p<0,005).
Coşar[44] B.F./ 2019	Aromaterapi masajının kronik nonmalign ağrısı olan hastalarda ağrı, anksiyete ve uyku kalitesi üzerine etkisinin incelenmesi	Randomize kontrollü çalışma	40 kişi Aromaterapi grubu:20 Kontrol grubu:20	Esansiyel Yağ / Lavanta/ Masaj	Görsel Değerlendirme Skalası, Kısa Ağrı Envanteri, Durumluk-Sürekli Kaygı Envanteri Pittsburgh Uyku Kalitesi İndeksi (PUKİ)	İkinci hafta VAS ağrı şiddetinde (VAS2) ve ikinci hafta ve dördüncü hafta ağrı giderme yüzdesinde gruplar arasında anlamlı bir fark saptanmıştır. Aromaterapi grubunda hem ağrı şiddetinde hem de ağrı giderme yüzdesinde anlamlı bir azalma saptanmıştır. Aromaterapi ve kontrol grupları durumluluk-süreklilik kaygı ölçeği puanları açısından kıyaslandığında; her iki grupta da istatistiksel olarak anlamlı fark saptanmıştır. Durumluk sürekli kaygı puanındaki azalma aromaterapi grubunda kontrol grubuna göre daha fazladır. Gruplar uyku kalitesi açısından değerlendirildiğinde ise; hem aromaterapi hem de kontrol grubunda global PUKI uyku kalitesi puanında anlamlı bir azalma olduğu; aromaterapi grubundaki puan azalmasının kontrol grubuna daha fazla olduğu saptanmıştır.

Öz[45] M./2019	Yaşlılarda aromaterapi masajının uyku kalitesi ve uykululuk düzeyine etkisi	Ön test-son test yarı deneysel çalışma	15 kişi Aromaterapi grubu:15	Esansiyel Yağ / Lavanta/ Masaj	Pittssburg Uyku Kalitesi İndeksi (PUKİ) Epworth Uykululuk Skalası	Aromaterapi masajını uygulamadan önce Pittsburgh uyku kalitesi ölçek değerinin ortalama 15,93+4,11 olduğu, aromaterapi uyguladıktan sonra yapılan ölçümlerde ise ölçek değerinin ortalama 4,93+2,05 olduğu ve aralarında istatistiksel olarak anlamlı farklılıklar olduğu saptandı (p=0,001, p<0,05). Aromaterapi masajı uygulama öncesinde Epworth uykululuk skalası ölçek değerinin (12,13+2,44), uygulanan aromaterapiden sonra yapılan ölçümlerde (2,06+1,70) daha düşük olduğu ve aralarında istatistiksel olarak anlamlı farklılıklar olduğu saptandı (p=0,001, p<0,05).
Sezgin[46] Y./2020	Arterio-venöz fistül kanülasyonu öncesi uygulanan aromaterapi ve el masajının ağrı ve stres düzeylerine etkisi	Randomize kontrollü, deneysel çalışma	159 kişi Aromaterapi grubu:53 El masajı grubu:53 Kontrol grubu:53	Esansiyel Yağ / Lavanta/ İnhaler	Visuel Analog Skala (VAS) Hemodiyaliz Stresör Ölçeği (HSÖ)	Araştırma sonucunda AVF kanülasyonu öncesi aromaterapi uygulanan hastaların işlemden sonraki ağrı ve düzeylerinin kontrol grubuna göre daha fazla düştüğü, benzer şekilde el masajı uygulanan hastalarda VAS ve HSÖ değerlerinin kontrol grubuna göre daha fazla düştüğü, gruplar arasındaki farkın ileri derecede anlamlı olduğu (p <0.001), seanslar ilerledikçe girişimlerin etkinliğinin arttığı belirlendi. Aromaterapiyle el masajı girişimleri karşılaştırıldığında, AVF kanülasyonunun ağrısını gidermede etkilerinin benzer olduğu, hemodiyaliz fizyolojik stresörleri azaltmada aromaterapinin, psikolojik ve toplam hemohiyaliz stresörlerini azaltmada el masajının daha etkili olduğu ve gruplar arasındaki farkın istatistiksel olarak anlamlı olduğu belirlendi.

jojoba, yasemin, gül ve menekşe yağının kullanıldığı görülmüştür. Tezlerin tamamına yakınında kontrol grubu kullanılmış olup, iki çalışma tek grup üzerinden yürütülmüştür. Yapılan doktora tezlerine bakıldığında çalışmada aromaterapinin klasik masaj, refleksoloji, müzikterapi, vibrasyon, gevşeme tekniği ve dokunma gibi farklı tamamlayıcı tedavilere birlikte kullanıldığı görülmüştür. Doktora tezleri incelendiğinde, kaygı/anksiyete, ağrı, bulantı-kusma, konfor, kortizol düzeyi, yaşam kalitesi, yorgunluk, bilişsel fonksiyonlar, gündüz uykululuk durumu, uyku kalitesi, bakım yükü, premenstrual semptomlar, yorgunluk, konstipasyon, yaşamsal bulgular, kaşıntı, sigara içme alışkanlıkları ve bebeklerde koliğin üzerindeki etkisi gibi birbirinden farklı pek çok alanda kullanıldığı saptanmıştır. Tezlerde kullanılan ölçüm araçlarına bakıldığında; İnfant Kolik Ölçeği,, Durumluluk Süreksli Kaygı Envanteri, Çok Boyutlu Algılanan Sosyal Destek Ölçeği, Yorgunluk Şiddet Ölçeği, Pittsburg Uyku Kalitesi İndeksi(PUKİ), Fibromiyalji Etki Düzeyi ölçeği, Yaşam Kalitesi Ölçeği Rotterdam Semptom Kontrol Listesi, Visuel Analog Scale (VAS), Brazelton Yenidoğan Davranış Değerlendirilme Ölçeği, Günlük Konstipasyon İzlem Formu, Yorgunluk Ciddiyet Skalası, Romatoid Artrit Hastalık Aktivite Değerlendirme formu, WOMAC Diz Osteoartrit Değerlendirme Ölçeği, Alt Bacaklardaki Artroz ve Yaşam Kalitesi Ölçeği, Piper Yorgunluk Ölçeği, Premenstrual Sendrom Ölçeği, Nöropsikiyatrik Envanter (NPE), Cohen-Mansfield Ajitasyon Envanteri (CMAE), Zarit Bakım Verme Yükü Ölçeği (ZYBÖ), The Western Ontario and McMaster Üniversitesi (WOMAC) Osteoartrit İndeksi, Bulantı Kusma-Öğürmeye İlişkin Hasta Günlüğü Formu, Blessed Oryantasyon Bellek Konsantrasyon Testi, Epworth Uykululuk Ölçeği, Douleur Neuropathique 4 Questions (DN4), Genel Konfor Ölçeği, Hasta ve Hekim Memnuniyet Skalası, Rhodes Bulantı, Kusma ve Öğürme İndeksi, Fagerström Nikotin Bağımlılığı Testi, Ulusal Acil Servisler Kalabalıklaşma Çalışması ölçeği gibi duruma özgü ölçüm araçlarının kullanıldığı görülmektedir. Yapılan çalışmaların sonuçlarına bakıldığında, uygulanan aromaterapinin hissedilen ağrı ve kaygı/anksiyete düzeyini, bulantı- kusma ve öğürmeyi, yorgunluk düzeyi ve şiddetini, ajitasyonu ve bakım verenlerinin bakım yükünü, premenstrual semptomları, konstipasyon şikayetlerini, bebeklerde koliği azalttığı uyku kalitesini, yaşam kalitesini, konfor düzeyini, memnuniyet düzeyini arttırdığı ve fiziksel fonksiyonları, yaşamsal bulguları olumlu yönde etkilediği bulunmuştur (Tablo 3).

Tartışma

Tamamlayıcı ve alternatif tedavi yöntemlerinin güvenli olduğu inancı ve sağlığa olumlu katkılarının bulunması bu yöntemlerin yaygın olarak kullanılmasını sağlamaktadır. Kullanılan bu yöntemlerden bir de bitkisel ürünlerin kullanımı esasına dayanan aromaterapidir. Aromaterapide kullanılan bitkisel ürünlerin doğal kaynaklı olduğunun bilinmesi, reçete edilmeden rahatlıkla ulaşılabilmesi, ekonomik olması, invazif girişim gerektirmemesi bireyin sağlığı için risk teşkil etmemesi bitkisel

Tablo 3. Aromaterapinin Etkisini Değerlendiren Hemşirelik Doktora Tezleri

Yazar/ Yılı	Tez Adı	Çalışmanın Tipi	Örneklem Sayısı	Aromaterapi yöntemi/ ürünü/ uygulama şekli	Kullanılan ölçüm aracı	Sonuç
Çetinkaya[47] B./2007	Aromaterapi Masajının Bebeklerde Koliğin Giderilmesi Üzerine Etkisinin İncelenmesi	Girişim uygulanmayan kontrol grubu ile zaman dizisi modelinde yarı deneysel çalışma	40 kişi Deney grubu: 20 Kontrol grubu: 20	Esansiyel Yağ / Lavanta, Badem yağı/ Masaj	İnfant Kolik Ölçeği, Durumluluk Sürekli Kaygı Envanteri Çok Boyutlu Algılanan Sosyal Destek Ölçeği,	Aromaterapi masajı uygulaması öncesinde, deney ve kontrol grubu kolikli bebekler arasında kolik durumu ve haftalık ağlama süreleri açısından anlamlı bir fark saptanmamıştır (p>0.05). Ön izlemde, deney ve kontrol grubu annelerin durumluluk kaygı durumları arasında istatistiksel olarak anlamlı bir fark saptanmamıştır (p>0.05). Deney ve kontrol grubu bebeklerin, izlemlere göre infant kolik ölçeği puan ortalamaları ve haftalık ağlama süreleri incelendiğinde, iki grup arasında izlemlere göre anlamlı bir ilişki saptanmıştır (p<0,005).
Arslan [48] S./2007	Dokunma, Müzikterapi ve Aromaterapinin Yoğun Bakım Hastalarının Fizyolojik Durumlarına Etkisi	Randomize kontrollü çalışma	72 kişi Deney Grubu:36 Kontrol Grubu:36	Esansiyel Yağ /Lavanta/ İnhaler	Araştırmacılar tarafından iki bölümden oluşturulan ve ikinci bölümünde girişim öncesi ve sonrası fizyolojik ölçümlerinin kaydedildiği 3 günlük kayıt formu	Dokunma sonrası hemoglobin ortalaması; kontrol grubunda 11.94 (SS=3.16), deney grubunda 13.10 (SS=2.54) olarak saptanmış ve aradaki fark istatistiksel olarak anlamlı bulunmuştur. (p= 0.05). VII Müzik terapi sonrası nabız ortalaması; kontrol grubunda 104.58 (SS=27.46), deney grubunda 93.11 (SS=17.99) olarak belirlenmiş ve aradaki fark istatistiksel olarak anlamlı bulunmuştur (p=0.040). Deney ve kontrol grubu arasında aromaterapi öncesi nabız ortalaması; kontrol grubunda 103.83 (SS= 25.02), deney grubunda 97.13 (SS= 21.85) saptanmış ve aradaki fark istatistiksel olarak anlamsız bulunmuştur (p= 0.231). Aromaterapi sonrası kontrol grubunda 102.41 (SS= 25.26), deney grubunda 91.86 (SS=15.35) olarak belirlenen nabız ortalamaları arasındaki fark istatistiksel olarak anlamlı saptanmıştır (p=0.036).

Demirbağ[49] C. B./2011	Müzik ve Aromaterapi Eşliğinde Yapılan Uyku ve Dokunmanın Fibromiyalji Hastalarında Fibromiyaljinin Etki Düzeyi İle Yorgunluk ve Uyku Kalitesine Etkisi	Kontrol gruplu öntest-sontest deneme modeli çalışma	162 kişi Dokunma+Müzik+Aroma Grubu:54 Uyku+Müzik+Aroma grubu: 54 Kontrol Grubu:54	Esansiyel Yağ / Lavanta, nane, portakal, gül, papatya, asya çiçeği, biberiye, ateş çiçeği, ıhlamur / Masaj, İnhaler	Yorgunluk Şiddet Ölçeği, Pittsburg Uyku Kalitesi İndeksi Fibromiyalji Etki Düzeyi ölçeği	Girişim grubu hastalarında fibromiyalji semptom sorgulaması son-test semptom bulguların da istatistiksel olarak önemli fark olması (p<0,05) girişimin hastaların semptomlarını azaltmada etkili olduğunu göstermektedir. Yorgunluk Şiddeti Ölçeğinin girişim gruplarında son-test puan ortalamalarında önemli düşüşün olması (p<0.05), müdahale sonrası hastaların yorgunluklarının azaldığını ifade etmektedir. Fibromiyalji Etki Düzeyi Ölçeği ölçeği puan ortalaması her iki girişim grubunda sontestte önemli düşüşü(p<0,05) hastaların hastalık durumlarının, hastalığın gidişinin olumlu yönde değiştiğini göstermektedir. Pittsburgh Uyku Kalitesi İndeksi son-test toplam puanlarının ortalamalarında her iki girişim grubunda da önemli farklılık (p<0.05), olması uyku kalitesi ve uyku bozukluğunda iyileşme olduğunu ispatlamaktadır.
Ovayolu[50] Ö./2011	Kemoterapi Alan Meme Kanserli Kadınlara Uygulanan Aromaterapinin Semptomlara ve Yaşam Kalitesi Etkisi	Randomize kontrollü deneysel çalışma	280 kişi Aromaterapi masajı grubu:70 Aromaterapi inhaler grubu: 70 Masaj grubu: 70 Kontrol Grubu:70	Esansiyel Yağ /Lavanta, nane, biberiye, papatya, yasemin, menekşe, okaliptüs, tatlı badem/ Masaj, İnhaler	Yaşam Kalitesi Ölçeği Rotterdam Semptom Kontrol Listesi	Uygulama öncesi koku ve aromaterapi masajı grubunun yaşam kalitesi genel toplam puanının düşük, kontrol ve masaj grubunun ise orta düzeyde olduğu ve tüm hasta gruplarının hem psikolojik hem de fiziksel semptomları yoğun olarak yaşadıkları saptandı. Uygulama sonrası altıncı ve 10. haftalarda; yaşam kalitesi toplam ve alt boyut puanları kontrol grubunda düşerken, koku, masaj ve aromaterapi masajı grubunda yükseldiği, özellikle aromaterapi masajı grubunda yer alan hastalarda bu artışın daha belirgin olduğu tespit edildi (p<0.05). Benzer şekilde Rotterdam semptom kontrol listesi genel toplam, psikolojik ve fiziksel semptom alt boyut puan ortalamalarının kontrol grubunda artarken, diğer üç grupta özellikle aromaterapi masajı grubunda uygulama öncesine göre anlamlı şekilde düştüğü, yani hastaların yaşadığı semptomların ve şiddetinin azaldığı belirlendi (p<0.05).

Cürcani [51] M./2012	Hemodiyaliz Hastalarına Uygulanan Aromaterapinin Kaşıntı Üzerine Etkisi	Ön test ve son test kontrol gruplu deneysel çalışma	80 kişi Deney Grubu:40 Kontrol Grubu:40	Esansiyel Yağ / Lavanta, çay ağacı, tatlı badem yağı, jojoba yağı ve papatya yağı, / Masajı	Visuel Analog Scale-VAS	Deney ve kontrol grubunda yer alan hastaların kaşıntı skorlarının gruplar arası karşılaştırılmasında; deney grubundaki hastaların kaşıntı skorları son-test puan VI ortalamalarının (7.20±3.14), kontrol grubundaki hastaların son-test puan ortalamalarına göre (10.00±2.47) düşük olduğu ve gruplar arasındaki farkın istatistiksel yönden çok önemli olduğu bulundu (p<0.001). Deney ve kontrol grubunda yer alan hastaların laboratuar parametrelerinin gruplar arası karşılaştırmalarında; deney grubundaki hastaların kan üre azotu sontest düzeylerinin (118.26±36.76), kontrol grubunda bulunan hastaların kan üre azotu sontest düzeylerine göre (138.80±48.69) düşük olduğu belirlendi ve gruplar arasındaki fark istatistiksel yönden önemli bulundu (p<0.05).
Taşdemir[52] N./2012	Gevşeme Tekniği, Aromaterapi ve Her İki Yöntemin Birlikte Uygulanmasının Ameliyat Sonrası Ağrıya Etkisi	Deneysel çalışma	100 kişi Gevşeme Grubu:25 Aromaterapi grubu:25 Gevşeme ve Aromaterapi grubu: 25 Kontrol Grubu:25	Esansiyel Yağ / Lavanta/ Masaj	Visual Analog Skala (VAS),	Araştırmanın verilere göre, kontrol ve girişim grubu hastalar arasında cerrahi işlem öncesi bireysel özellikleri, ameliyat sonrası ağrı şiddetleri ve yaşam bulguları arasında istatistiksel olarak anlamlı bir fark yoktur. Ameliyat sonrası analjezik gereksinimleri açısından istatistiksel olarak anlamlı fark (p<0.05) olduğu 81 belirlendi. Girişim gruplarındaki hastaların daha düşük analjezik gereksimi olduğu saptandı (p<0.05).
Özdemir [53] H./2012	Esansiyel Hipertansiyonlu Kadınlara İnhalasyon Yoluyla Uygulanan Aromaterapinin Arteriyel Kan Basıncı, Nabız ve Kaygı Düzeyine Etkisi	Çapraz gruplu tek kör deneysel çalışma	40 kişi Aromaterapi: 20 Kontrol:10	Esansiyel Yağ / Lavanta, bergamot, ylang-ylang/ İnhaler	Durumluk ve Sürekli Kaygı Ölçeği	Çalışmada aromaterapinin ilk haftasında sistolik kan basıncı(p<0.001), diastolik kan basıncı (p<0.001), nabız hızı (p<0.001) ve durumluluk kaygı puanının azaldığı (p<0.001), biopac parametrelerinde yalnızca galvanik deri direncinde anlamlı azalma (p=0.038) sağladığı saptanmıştır.
Tosun [54] Ö./2013	Aromaterapi, Müzikterapi ve Vibrasyon Uygulamalarının Yenidoğanın Stres ve Davranışları Üzerine Etkisi	Randomize kontrollü çalışma	80 kişi Aromaterapi grubu:20 Müzik terapi grubu: 20 Vibrasyon uygulama grubu: 20 Kontrol Grubu:20	Esansiyel Yağ / Lavanta, Tatlı badem yağı/ Masaj	Brazelton Yenidoğan Davranış Değerlendirilme Ölçeği, Yenidoğan Stres Değerlendirme Formu	Araştırmanın birinci aşamasında, yapılan faktör analizi sonrasında, BYDDÖ'nin orjinalinden 5 madde çıkartılmış. Cronbach alfa değeri 0.974 (30 madde) olarak bulunmuş. "Davranış Alt Boyutu" 23 madde, "Destek Alt Boyutu" 7 maddeden oluşmuştur. Tekrar test güvenirliğinde korelasyon katsayısının yüksek olduğu belirlenmiştir (p<0.001). Preterm yenidoğanların çalışma öncesi ve sonrası BYDDÖ ve YSDF puanları arasındaki fark ortalamalarının kontrol grubuna göre fazla olduğu (p=0.001, (p=0.040) ve farkın kontrol grubundan kaynaklandığı saptanmıştır (p<0.05).

Lafcı [55] D./2014	Aroma Masajının Yaşlılardaki Konstipasyona Etkisi	Girişim-kontrol deseninde yarı deneysel çalışma	48 kişi Deney Grubu:24 Kontrol Grubu:24	Esansiyel Yağ / biberiye, zencefil, karabiber, badem yağı/ Masaj	Visual Analog Skala (VAS), Günlük Konstipasyon İzlem Formu	Aroma masajı sırası ve sonrası girişim grubunda, "dışkılama sayısı" "dışkı miktarı" ve "dışkı kıvamı" puan ortalamalarının istatistiksel olarak anlamlı düzeyde arttığı, "dışkılama sırasında ıkınma" ve "dışkılama sonrası tam boşalamama hissi" puan ortalamalarının ise azaldığı belirlenmiştir. Kontrol grubunda ise "dışkılama sayısı" ve "dışkı miktarı" puan ortalamalarının arttığı, "dışkılama sırasında ıkınma" puan ortalamasının ise azaldığı belirlenmiştir
Metin [56] G.Z./2015	Romatoid Artritli Hastalarda Aromaterapi Masajı ve Refleksoloji Uygulamalarının Ağrı Ve Yorgunluğa Etkileri	Randomize kontrollü, yarı deneme modeli çalışma	51 kişi Aromaterapi masajı grubu:17 Refleksoloji:17 Kontrol grubu:17	Esansiyel Yağ / Lavanta/ masaj	Visual Analog Skala (VAS), Yorgunluk Ciddiyet Skalası, Romatoid Artrit Hastalık Aktivite Değerlendirme formu	Aromaterapi grubunda ağrı skorları, araştırmanın ikinci ve altıncı haftaları arasında, yorgunluk dördüncü ve altıncı haftalar arasında azalmıştır (p<0,05). Refleksoloji grubunda ise ağrı ve yorgunluk uygulama boyunca azalmıştır (p<0,05). Aromaterapi masajı, sabah tutukluğu üzerine herhangi bir etkide bulunmamasına rağmen, refleksoloji sabah tutukluğunu dördüncü haftadan itibaren kısaltmıştır (p<0,05). Her iki yöntem de, hastaların sağlık algısını arttırmıştır (p<0,05).
Pehlivan [57] S./2015	Diz Osteoartritli Yaşlı Bireylere Uygulanan Aromaterapi Masajının Ağrı, Fonksiyonel Durum Ve Yaşam Kalitesine Etkisi	Randomize ön test – son test kontrollü deneysel çalışma	Aromaterapi masaj grubu:30, Plasebo masaj grubu: 30 Kontrol grubu:30	Esansiyel Yağ / Lavanta/ Masaj	WOMAC Diz Osteoartrit Değerlendirme Ölçeği, Alt Bacaklardaki Artroz ve Yaşam Kalitesi Ölçeği	Aromaterapi grubunda uygulama sonrası WOMAC ağrı, tutukluk, günlük aktivitelerde yaşanan zorluklar anlamlı olarak azaldığı ve yaşam kalitesi fiziksel aktivite, ağrı, zihinsel sağlık, sosyal destek düzeylerinin anlamlı olarak yükseldiği belirlendi (p<0.001). Sekizinci hafta değerlendirmesinde sosyal destek dışındaki tüm parametrelerde öncesine göre farklılığın anlamlı olarak devam ettiği saptandı (p<0.05). Ancak 4. hafta ile karşılaştırıldığında, 8. hafta değerlerinde anlamlı olarak bir düşme saptandı (p<0.05). Masaj grubunda uygulama sonrası WOMAC ağrı, tutukluğun anlamlı olarak azaldığı ve yaşam kalitesi fiziksel aktivite, ağrı, zihinsel sağlık düzeylerinin anlamlı olarak yükseldiği belirlendi (p>0.05)
Muz [58] G./2015	Hemodiyaliz Tedavisi Alan Bireylerde İnhalasyon Yoluyla Uygulanan Aromaterapinin Uyku Kalitesi ve Yorgunluk Düzeyine Etkisi	Randomize, kontrollü, çalışma	62 kişi Deney Grubu:27 Kontrol Grubu:35	Esansiyel Yağ /Lavanta, Tatlı portakal/ İnhaler	Visuel Analog Skala (VAS) Pittsburg Uyku Kalitesi İndeksi (PUKİ) Piper Yorgunluk Ölçeği	Müdahale ve kontrol grubundaki bireylerin başlangıç izlemlerinde VAS yorgunluğu, Piper Yorgunluk Ölçeği ve PUKİ ölçeği gündüz uyku işlev bozukluğu alt boyutu hariç diğer tüm alt boyut ve toplam puan ortalamalarında almış oldukları puanlar arasında fark olmadığı (p>0,05), müdahale grubunun kontrol grubuna göre diğer izlemlerde VAS yorgunluk, Piper Yorgunluk Ölçeği ve PUKİ tüm alt boyut ve toplam puanlarının anlamlı derecede düştüğü belirlenmiştir(p<0.05)

Yayla [59] M.E./2016	İnhaler Yolla Uygulanan Aromaterapinin İmplante Edilebilir Venöz Port Kateter İğne Girişine Bağlı Prosedürel Ağrı ve Anksiyete Üzerine Etkisi	Randomize, kontrollü, deneysel çalışma	123 kişi lavanta müdahale grubu:41, okaliptüs müdahale grubu: 41 Kontrol grubun: 41	Esansiyel Yağ / Lavanta, Okliptus/ İnhaler	Visuel Analog Skala (VAS) Durumluk Kaygı Ölçeği	Araştırma bulguları lavanta müdahale grubunda kontrol grubuna göre VAS puan ortalamalarının anlamlı derecede düştüğünü göstermiştir (p<0,05). Okaliptüs müdahale ve kontrol grubundaki bireylerin VAS puan ortalamaları arasında anlamlı bir fark bulunmamıştır (p>0,05). Ayrıca araştırmada lavanta müdahale, okaliptüs müdahale ve kontrol grubundaki bireylerin STAI-I puan ortalamalarında almış oldukları puanlar arasında anlamlı bir fark olmadığı bulunmuştur (p>0,05).
Uzunçakmak[60] T./ 2016	Üniversite Öğrencilerine Uygulanan Aromaterapinin Premenstruel Sendrom İle Baş Etmeye Etkisi	Randomize kontrollü deneysel tasarım çalışma	77 Kişi Deney grubu:40 Kontrol grubu:37	Esansiyel Yağ / Lavanta/ İnhaler	Premenstrual Sendrom Ölçeği	Araştırmada deney ve kontrol grubunun 3 izlem süresince PMS ölçeği ortalama puanları karşılaştırıldığında, gruplar arasında istatistiksel olarak anlamlı bir farklılık olduğu belirlenmiştir (p<0.05) saptanmıştır. Deney ve kontrol grupları arasında PMS ölçeği ve anksiyete, depresif duygulanım, yorgunluk, sinirlilik, ağrı, şişkinlik, depresif düşünceler alt boyutları ön test ve 3. izlem ortalama puanları açısından istatistiksel olarak anlamlı bir farklılık olduğu (p<0.05), iştah ve uyku değişimleri alt boyutlarında anlamlı bir farklılık olmadığı (p>0.05) saptanmıştır.
Kaymaz[61] T. T./2016	Orta Ve İleri Evre Demans Hastalarına Uygulanan Aromaterapinin Ajitasyon Ve Bakım Verenin Yüküne Etkisi	Randomize kontrollü, araştırma	28 kişi Müdahale grubu:14 Kontrol grubu:14	Esansiyel Yağ /Lavanta, limon çimeni/ İnhaler, Masaj	Nöropsikiyatrik Envanter (NPE) Cohen-Mansfield Ajitasyon Envanteri (CMAE) Zarit Bakım Verme Yükü Ölçeği (ZYBÖ)	Aromaterapi grubunda, CMAE ve NPE skorları, araştırmanın başlangıcına göre ikinci ve dördüncü haftalarda azalmıştır (p<0,05). Aromaterapi sonunda, müdahale ve kontrol grupları ZBYÖ skoru arasındaki fark istatistiksel olarak anlamlı bulunmuştur (p<0,05). Müdahale grubundaki kişilerin aromaterapi uygulama sonrasındaki bakım yükü, kontrol grubundaki kişilerden anlamlı derecede daha düşüktür (p<0.05).
Arslan[62] D./2016	Osteoartritli Bireylerde Aromaterapi Masajının Diz Ağrısı Ve Fonksiyonel Duruma Etkisi	Non-randomize girişimsel çalışma	92 kişi Aromaterapi masaj grubu:33, Klasik masaj grubu: 30 Kontrol grubu:32	Esansiyel Yağ / tatlı badem yağı, kayısı çekirdeği yağı, lavanta, okaliptus, zencefil yağı/ Masaj	Vizüel Analog Skala (VAS), The Western Ontario and McMaster Üniversitesi (WOMAC) Osteoartrit İndeksi	Aromaterapi masajı, klasik masaj ve kontrol gruplarında bireylerin izlem haftalarına göre değerlendirilmesinde ise; tekrarlı ölçümlerde anova kullanılmıştır. İleri analizinde ise bonfferroni testinden yararlanılmıştır. Araştırma kapsamına alınan bireylerin, başlangıç GKÖ ve WOMAC puan özelliklerine göre gruplar arasındaki fark istatistiksel olarak anlamlı olmadığı bulunmuştur (p>0,05). Aromaterapi masaj grubunun GKÖ (istirahat-aktivite) ve WOMAC indeksinden alınan puanları klasik masaj ve kontrol grubundaki bireylere göre daha fazla azaldığı ve bu farkın istatiksel olarak anlamlı olduğu bulunmuştur (p<0,001).

Zorba[63] P./2016	Masaj Ve İnhaler Yollarla Uygulanan Aromaterapinin Kemoterapiye Bağlı Akut Bulantı Kusmaya Etkisinin Karşılaştırılması	Randomize kontrollü araştırma	40 kişi Aromaterapi grubu:20 Kontrol grubu:20	Esansiyel Yağ / İngiliz nanesi, bergamot, kakule / İnhaler, Masaj	Vizüel Analog Skala (VAS), Bulantı Kusma-Öğürmeye İlişkin Hasta Günlüğü Formu	Aromatik masaj gurubunun 3. ve 4. kemoterapi kürlerinde bulantı-öğürme yaşama durumu inhalasyon ve kontrol grubundakilere göre anlamlı şekilde daha düşüktür (p<0,001). Araştırmamızda, masaj ve inhaler aromaterapi gruplarındaki bireylerde izlenen tüm kürlerde bulantı şiddeti kontrol grubundakilere göre anlamlı derecede azaldığı saptanmıştır (p<0.001).
Yıldırım[64] A.T./2017	Huzurevinde Yaşayan Yaşlılarda Aromaterapi Uygulamasının Bilişsel Fonksiyonlar Ve Gündüz Uykululuk Durumuna Etkisi	Kontrol grupsuz ön test-son test yarı deneysel çalışma	15 kişi Aromaterapi grubu:15	Esansiyel Yağ / Biberiye, limon, lavanta yağ/ İnhaler	Blessed Oryantasyon Bellek Konsantrasyon Testi, Epworth Uykululuk Ölçeği	İşlem öncesinde katılımcıların ortalama 8,51±2,33 olan gündüz uykululuk puanı biberiye-limon yağı karışımı uygulaması sonrası 8,13±2,54 (p>0,05), lavanta yağı uygulaması sonrası 5,56±4,02 (p<0,001) bulunmuştur. Gündüz uykululuk puan ortalamasındaki bu anlamlı düşüş lavanta yağının gündüz uykululuk durumunu azalttığını göstermektedir. Uygulama öncesi 14,69±7,35 olan bilişsel fonksiyon puan ortalaması biberiye-limon yağı karışımı uygulaması sonrası 11,26±7,76 (p<0,001); lavanta yağı uygulaması sonrası 11,41±7,78 (p<0.001) bulunmuştur.
İzgü [65] N./2017	El ve Ayağa Uygulanan Aromaterapi Masajının Kemoterapi İlişkili Periferal Nöropatik Ağrı ve Yorgunluk Üzerine Etkisi	Randomize kontrollü, deneysel çalışma	40 kişi Deney grubu:20 Kontrol grubu:20	Esansiyel Yağ /ingiliz nanesi, papatya, biberiye, katı hindistan cevizi/ Masaj	Douleur Neuropathique 4 Questions (DN4), Visuel Analog Scale-VAS, Piper Yorgunluk Ölçeği	Araştırmada, müdahale grubundaki hastaların 4. ve 6. hafta DN4 ağrı anketi puan ortancası kontrol grubuna göre anlamlı derecede düşük bulunmuş, 6. haftada kontrol grubunda nöropatik ağrısı olan hasta oranının müdahale grubuna göre anlamlı düzeyde daha yüksek olduğu belirlenmiştir (p<0,05). 2., 4. ve 6. hafta VAS puan ortancası müdahale grubunda kontrol grubuna göre anlamlı düzeyde daha düşük bulunmuştur (p>0,05).
Kasar[66] S.K./2018	Miyofasiyal Ağrı Sendromu Olan Bireylerde Tetik Nokta Enjeksiyonu Sırasında Uygulanan İnhaler Aromaterapinin Ağrı, Anksiyete, Konfor ve Kortizol Düzeyine Etkisi	Plasebo-randomize kontrollü çalışma	66 kişi Aromaterapi grubu:22 plasebo grubu: 22 kontrol grubu:22	Esansiyel Yağ/Lavanta/ İnhaler	Visuel Analog Scale-VAS), Durumluk Kaygı Envanteri, Genel Konfor Ölçeği, Hasta ve Hekim Memnuniyet Skalası	Çalışma sonunda; örneklemi oluşturan hastaların yaş ortalaması 48.8±11.35 olup, %78.8'i kadındır. Hastaların ağrı puan ortalamaları incelendiğinde; aromaterapi grubunda plasebo ve kontrol grubuna göre işlem ortası ve işlem sonrası anlamlı şekilde azalmakta iken plasebo ve kontrol grubunda artmaktadır (p<0.05). Hastaların anksiyete düzeyleri incelendiğinde, aromaterapi grubundaki hastaların işlem sonrası ölçüm medyanının, işlem öncesi ölçüm medyanından anlamlı olarak düşük olduğu (p>0.05). Ayrıca aromaterapi grubundaki bireylerin distress termometresi işlem sonrası ölçüm medyan değeri anlamlı olarak düşerken, plasebo ve kontrol grubundaki bireylerin anlamlı olarak artmaktadır. Aromaterapi, plasebo ve kontrol gruplarında genel konfor ölçeği işlem öncesi ve sonrası ölçüm ortalamaları karşılaştırıldığında aromaterapi grubunda işlem sonrası toplam ortalaması anlamlı olarak yüksek iken plasebo ve kontrol gruplarında anlamlı derece düşüktür (p<0,05).

Ertürk [67] E.N./2019	Kemoterapi Alan Hastalara Uygulanan Nane Yağının Bulantı Kusma ve Öğürme Üzerine Etkisi	Kalitatif (bireysel derinlemesine görüşme) ve kantitatif (randomize kontrollü) çalışma	80 kişi müdahale grubu:36 kontrol grubu: 44	Esansiyel Yağ / Nane, Tatlı badem yağı / İnhaler	Visüel Analog Skala (VAS) Rhodes Bulantı, Kusma ve Öğürme İndeksi	Müdahale grubundaki bireylerin kontrol grubundaki bireylere göre nane yağı uygulaması sonrası bulantı şiddeti, bulantı, kusma ve öğürme semptomlarında anlamlı derecede ($p<0.05$) azalma olduğu ve daha az antiemetik ilaç kullandıkları belirlenmiştir.
Işık [68] A.I./2019	Üniversite Öğrencilerinin Sigara İçme Alışkanlıkları Üzerinde Aromaterapinin Etkisi	Kontrol gruplu, yarı deneysel araştırma	58 kişi Karabiber grubu:21 melekotu grubu:18 Kontrol grubu:19	Esansiyel Yağ /Karabiber, melekotu yağı / İnhaler	Fagerström Nikotin Bağımlılığı Testi	Araştırmadan elde edilen bulgulara göre, grup içi karşılaştırmada karabiber ve melekotu yağı uygulayan öğrencilerin uygulama sonrası sigara içme isteği puan ortalamaları azalmıştır. Kontrol grubunda anlamlı bir değişiklik olmamıştır. Gruplararası karşılaştırmada deney grubunda (karabiber ve melekotu yağı) yer alan öğrencilerin uygulama sonrası sigara içme isteğinde azalma olduğu tespit edilmiştir.
Şimşek [69] P./2019	Lavanta Yağı Aromaterapisinin Acil Servis Sağlık Çalışanlarında Kalabalıklaşmayla İlişkili Anksiyete Düzeyi Üzerindeki Etkisinin Değerlendirilmesi	Girişimsel çalışma	35 kişi Girişim grubu:35	Esansiyel Yağ/Lavanta/ İnhaler	Durumluk Anksiyete Ölçeği, Ulusal Acil Servisler Kalabalıklaşma Çalışması ölçeği	Aromaterapi öncesinde ve sonrasında acil servis sağlık çalışanlarının anksiyete düzeyi Durumluk Anksiyete Ölçeği kullanılarak değerlendirildi. Durumluk anksiyete düzeyi ile kalabalıklaşma arasında pozitif yönde orta düzeyde anlamlı bir ilişki olduğu belirlendi ($r=0.415$, $p<0.001$). Lavanta yağı aromaterapisinin acil servis sağlık çalışanlarında kalabalıklaşma ile ilişkili anksiyete düzeyinin azaltılmasında istatistiksel olarak anlamlı bir etkiye sahip olduğu saptandı ($p<0.05$).
Karaaslan[70] M.M./2020	Bebeklere Uygulanan Aromaterapi ve Abdominal Masajın Konstipasyon ve Annenin Kaygı Düzeyine Etkisi	Yarı Deneysel Çalışma	69 bebek Aromaterapi masaj grubu, 23 klasik masaj grubu: 23 kontrol grubu: 23	Esansiyel Yağ / Lavanta, tatlı badem / Masaj	Durumluk Kaygı Envanteri	Aromaterapi masaj grubu ve klasik masaj grubunda bebeğin kaka miktarı, bebeğin kaka yaparken ağlama durumu ve bebeğin gaz çıkartma durumunun istatistiksel olarak anlamlı olduğu, aromaterapi masaj grubunda etkinin daha fazla olduğu saptandı ($p<0.05$). Aromaterapi masaj uygulanan gruptaki annelerin, diğer gruplardaki annelere göre daha düşük kaygı ortalama değerine sahip olduğu saptandı. En düşük durumluluk kaygı envanteri ortalama değeri masajdan 4 hafta sonra aromaterapi grubunda elde edildi ($p<0.05$).

ürünlerin farmakolojik ajanlara oranla daha uygun ve güvenilir alternatifler olarak kabul edilmesine ve kullanımının artmasına neden olmaktadır [2, 25,26]. Aromaterapinin bu şekilde yaygın kullanımından dolayı, sağlık hizmetlerinin her basamağında görev alan hemşireler tarafından aromaterapi ile ilgili çalışmaların yürütülmesi ihtiyacı doğmuştur. Ülkemizde konu ile ilgili yürütülen tezlere bakıldığında ilk uygulamaların 2007 yılında Çocuk Sağlığı ve Hastalıkları Hemşireliği ve Cerrahi Hastalıkları Hemşireliği anabilim dallarında doktora tezi olarak yürütüldüğü görülmektedir (Tablo 1). Bu konudaki çalışmaların son on yılda arttığı da dikkati çekmektedir. Yürütülen tezlere bakıldığında, 20'sinin yüksek lisans 24'ünün doktora tezi olduğu ve çoğunluğunun İç Hastalıkları Hemşireliği Anabilim Dalında yürütüldüğü saptanmıştır. Bunun yanı sıra hemşireliğin tüm anabilim dallarında da aromaterapi ile ilgili çalışmalar yürütülmüştür (Tablo 1). Aromaterapide kullanılan uçucu yağların bireyler üzerinde fiziksel, psikolojik ve ruhsal olarak birçok etkisi mevcuttur [2, 25]. Aromatik yağlar etkilerini sinir sistemine veya kan dolaşımına katılarak bütün vücut sistemleri üzerinde gösterebilirler. Bu etkilere baktığımızda, analjezik etki, antienflamatuvar etki, duyusal öğrenme, bilinçli algılama ve zedelenmiş dokunun onarımında kullanılan uçucu yağların, bitkilerin kendisinden 100 kat daha yoğun etkiye sahiptir [26, 71]. Aromaterapik uygulamalar hastalığın yalnızca tedavisinde etkili olmayıp aynı zamanda vücut ve ruh sağlığı için geniş kapsamlı bir etkileşim üzerinden tedavi öngören uygulamalardır. Bu bilgiler ışığında aromaterapinin etkisini inceleyen tezlerin 25'inde aromaterapinin kaygı/anksiyete/stres üzerine, 23'ünde uyku ve 19'unda ise ağrı üzerindeki etkisi incelenmiş ve hissedilen ağrı ve kaygı/anksiyete düzeyini, bulantı- kusma ve öğürmeyi, yorgunluk düzeyi ve şiddetini, ajitasyonu ve bakım verenlerinin bakım yükünü, premenstrual semptomları, konstipasyon şikayetlerini, bebeklerde koliği azalttığı uyku kalitesini, yaşam kalitesini, konfor düzeyini, memnuniyet düzeyini arttırdığı ve fiziksel fonksiyonları, yaşamsal bulguları olumlu yönde etkilediği görülmüştür (Tablo 2, Tablo 3). Ayrıca aromaterapinin etkisinin incelendiği sayısız çalışma, güvenlik sınırları içerisinde yapılan aromaterapi uygulamalarının ne kadar yararlı olabileceği gerçeğini kanıtlanmıştır. Aromaterapinin kullanımı ile hemşirelik bakımının kalitesini artacağı ve hemşire ile hastası arasında güvenli bir ilişki sağlayarak tedavi edici yönü ile beraber hemşire ile hasta arasında güçlü bir terapötik etkisi olduğu düşünülmektedir.

Sonuç olarak, hemşirelik alanında aromaterapinin etkisinin incelendiği pek çok çalışma bulunmaktadır. Ancak buna rağmen hemşireliğin tüm anabilim dallarında kullanımının sağlanması için daha fazla çalışmaya ihtiyaç duyulmakta ve bu alanda çalışacak hemşirelere verilecek eğitimlerle kontrollü uygulamaları artırılması önerilmektedir.

Çıkar çatışması/finansal destek beyanı

Bu yazıdaki hiçbir yazarın herhangi bir çıkar çatışması yoktur. Yazının herhangi bir finansal desteği yoktur.

KAYNAKLAR

1. Gültekin E. Ethical ıssues in aromatherapy courses in Turkey, Turkiye Klin. J. Med. Ethics-Law Hist. 2020; 28: 273–278.
2. Kanat T. Aromaterapi. Journal of Biotechnology and Strategic Health Research, 2019; 3: 67-73.
3. Barış EN, Öztunç G. Sağlık çalışanlarında aromaterapı<nı<n stres ve anksı<yete üzerı<ne etkı<sı<. 2016; 5: 107–11.
4. Farahani MA, Afsargharehbagh R., Marandi F, Moradi M, Hashemi SM, Moghadam MP, Balouchi A. Effect of aromatherapy on cancer complications: A systematic review. Complementary therapies in medicine, 2019; 47: 102169.
5. Tanvisut R, Traisrisilp K. And Tongsong T. Efficacy of aromatherapy for reducing pain during labor: a randomized controlled trial, Arch. Gynecol. Obstet. 2018; 297: 1145–50.
6. Lai et al. Effectiveness of aroma massage on advanced cancer patients with constipation: A pilot study, Complement. Ther. Clin. Pract. 2011; 17: 37–43.
7. Scuteri D. et al. Aromatherapy and aromatic plants for the treatment of behavioural and psychological symptoms of dementia in patients with alzheimer's disease: clinical evidence and possible mechanisms, Evidence-based Complement. Altern. Med. 2017.
8. Nikjou R, Kazemzadeh R, Asadzadeh F, Fathi R. And Mostafazadeh F. The effect of lavender aromatherapy on the symptoms of menopause, J. Natl. Med. Assoc., 2018; 110: 265–69.
9. Olapour A, Behaeen K, Akhondzadeh R, Soltani F, Razavi FAS, Bekhradi R. The effect of inhalation of aromatherapy blend containing lavender essential oil on cesarean postoperative pain, Anesthesiol. Pain Med., 2013; 3: 203–7.
10. Mansour Lamadah S. The effect of aromatherapy massage using lavender oil on the level of pain and anxiety during labour among primigravida women, Am. J. Nurs. Sci. 2016; 5: 37-41.
11. Uzunçakmak, T. Ayaz Alkaya S., Effect of aromatherapy on coping with premenstrual syndrome: A randomized controlled trial, Complement. Ther. Med., 2017; 36: 63–7.
12. Apay SE., Arslan S, Akpinar RB, Celebioglu A. Effect of Aromatherapy Massage on Dysmenorrhea in Turkish Students, Pain Manag. Nurs., 2012; I: 236–40.
13. Çetinkaya B, Başbakkal Z. The effectiveness of aromatherapy massage using lavender oil as a treatment for infantile colic Int. J. Nurs. Pract., 2012; 18: 164–69.
14. Nategh M, Heidari MR, Ebadi A, Kazemnejad A, Beigi MAB, Effect of lavender aromatherapy on hemodynamic indices among patients with acute coronary syndrome: a randomized clinical trial, Iran J. Crit. Care Nurs. 2015; 7: 201–8.
15. Taavoni, S., Darsareh, F., Joolaee, S. And Haghani, H. The effect of aromatherapy massage on the psychological symptoms of postmenopausal Iranian women, Complement. Ther. Med. 2013; 21: 158–63.

16. Pehlivan S, Karadakovan A. Effects of aromatherapy massage on pain, functional state, and quality of life in an elderly individual with knee osteoarthritis, Japan J. Nurs. Sci. 2019; 16: 450–8.
17. Efe Arslan,D, Kutlutürkan S, Korkmaz M. The effect of aromatherapy massage on knee pain and functional status in participants with osteoarthritis, Pain Manag. Nurs., 2019; 20: 62–9.
18. Demirbağ BC, Erc B. The effects of sleep and touch therapy on symptoms of fibromyalgia and depression. Iranian journal of public health, 2012; 41: 44.
19. Vaziri,F, Khosropoor M, Hidari M, Pourahmad S, Morshed Behbahani B, Saki F. The effect of aromatherapy by lavender oil on ınfant vaccination pain: a double blind randomized controlled trial, J. Caring Sci. 2019; 8: 17–21.
20. Joulaeerad N, Ozgoli G, Hajimehdipoor H, Ghasem E, and Salehimoghaddam F. Effect of aromatherapy with peppermint oil on the severity of nausea and vomiting in pregnancy: A single-blind, randomized, placebo-controlled trial, J. Reprod. Infertil., 2018; 19: 32–8.
21. Farahani MA. Et al., Effect of aromatherapy on cancer complications: A systematic review, Complement. Ther. Med. 2019; 47: 102169.
22. Genç F, Karada< S, Kiliç AN, Tan M, Cerit D. The effect of aromatherapy on sleep quality and fatigue level of the elderly: A randomized controlled study, Holist. Nurs. Pract. 2020; 34: 155–62
23. Barati F, Nasiri A, Akbari N, Sharifzadeh G. The effect of aromatherapy on anxiety in patients, Nephrourol. Mon., 2016; 8.
24. Rezaie-Keikhaie K.et al. Effect of aromatherapy on post-partum complications: A systematic review, Complement. Ther. Clin. Pract., 2019; 35: 290–95.
25. Rajai,N, Sajadi SA, Teymouri,F, Zareiyan A, Siavoshi S, Malmir M. The effect of aromatherapy with lavender essential oil on anxiety and stress in patients undergoing coronary artery bypass graft surgery, Jundishapur J. Chronic Dis. Care, 2016; 5.
26. Özdemir H, Öztunç G. Hemşirelik uygulamalarında aromaterapi. Turkiye Klinikleri Hemsirelik Bilimleri, 2013; 5.
27. Yaman S. (2011),Lavanta yağıyla uygulanan sırt masajının yaşlıların uyku kalitesine etkisinin incelenmesi, Yüksek Lisans Tezi, Fırat Üniversitesi, Sağlık Bilimleri Enstitiüsü, Elazığ.
28. Karabulut H. (2014), Doğum eyleminde aromaterapinin etkileri, Yüksek Lisans Tezi, İstanbul Üniversitesi, Sağlık Bilimleri Enstitüsü, Kadın Sağlığı ve Hastalıkları Hemşireliği, İstanbul.
29. Şentürk A. (2015), Hemodiyaliz hastalarına inhalasyon yolu ile lavanta yağı uygulamasının anksiyete düzeyi ve uyku kalitesine etkisi, Yüksek Lisans Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
30. Barış N. (2015), Aromaterapinin yoğun bakım ünitesinde çalışan hemşirelerin stres ve anksiyeteleri üzerine etkisi, Yüksek Lisans Tezi, Çukurova Üniversitesi, Sağlık Bilimleri Enstitüsü, Adana.
31. İlter M.S. (2016) Onkoloji hastalarına port kateterizasyonu işlemi sırasında uygulanan inhaler aromaterapinin ağrıya etkisi, Yüksek Lisans Tezi, Gaziantep Üniversitesi, Sağlık Bilimleri Enstitüsü, Gaziantep.
32. Ayik C. (2016) Ameliyat öncesi dönemde aromaterapi masajının anksiyete ve uyku kalitesine etkisinin incelenmesi, Yüksek Lisans Tezi, Dokuz Eylül Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
33. Gürakan G. (2016), Palyatif bakım alan kanser hastalarında aromaterapi sırt masajının ağrı şiddeti ve plazma beta endorfin düzeyine etkisi, Yüksek Lisans Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
34. Dalkıran S.S (2017), Preoperatif dönemdeki kanser hastalarında lavanta yağı ile yapılan sırt masajının uykuya etkisi, Yüksek Lisans Tezi, Marmara Üniversitesi, Sağlık Bilimleri Enstitüsü, İstanbul.
35. Gürler M. (2017), Menopozal dönemdeki kadınlara uygulanan aromaterapinin uyku ve yaşam kalitesine etkisi, Yüksek Lisans Tezi, Nevşehir Hacı Bektaş Veli Üniversitesi, Fen Bilimleri Enstitüsü, Nevşehir.
36. Cenkci Z. (2017), Aromaterapinin doğum eylemindeki ağrı, konfor ve memnuniyet üzerine etkisi, Yüksek Lisans Tezi, Çukurova Üniversitesi, Sağlık Bilimleri Enstitüsü, Adana.
37. Beyliklioğlu A. (2017), Aromaterapinin mastektomi öncesi hastaların anksiyeteleri üzerine etkisi, Yüksek Lisans Tezi, Çukurova Üniversitesi, Sağlık Bilimleri Enstitüsü, Adana.
38. Genç H. (2017), Lavanta yağının benign prostat hiperplazili hastaların ameliyat öncesi yaşam bulguları ve kaygı düzeyine etkisi, Yüksek Lisans Tezi, İnönü Üniversitesi, Sağlık Bilimleri Enstitüsü, Malatya.
39. Taşan E. (2018), İnhaler lavantanın hemodiyaliz hastalarında damara ulaşım sırasında oluşan ağrıya etkisi, Yüksek Lisans Tezi, Gaziantep Üniversitesi, Sağlık Bilimleri Enstitüsü, Gaziantep.
40. Gülşen G. (2018), Üst gastrointestinal endoskopi işlemi uygulanan hastalara müzik eşliğinde uygulanan inhaler aromaterapinin vital bulgulara etkisi, Yüksek Lisans Tezi, Gaziantep Üniversitesi, Sağlık Bilimleri Enstitüsü, Gaziantep.
41. Sert C. (2019), Diz osteoartriti olan hastalarda, ısırgan-zencefil esansiyel yağlarıyla yapılan masajın ve buz uygulamasının ağrı üzerine etkinliğinin değerlendirilmesi, Yüksek Lisans Tezi, Düzce Üniversitesi, Sağlık Bilimleri Enstitüsü, Düzce.
42. Özdemir T.S. (2019), Hemodiyaliz hastalarında av fistül uygulaması sırasında oluşan ağrıyı gidermede lavanta aromaterapinin etkisi, Yüksek Lisans Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
43. Koç E. (2019), Lavanta yağının kronik otitis media hastalarının ameliyat öncesi yaşam bulguları ve kaygı düzeyine etkisi, Yüksek Lisans Tezi, İnönü Üniversitesi, Sağlık Bilimleri Enstitüsü, Malatya.
44. Coşar B.F. (2019), Aromaterapi masajının kronik nonmalign ağrısı olan hastalarda ağrı, anksiyete ve uyku kalitesi üzerine etkisinin incelenmesi, Yüksek Lisans Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
45. Öz M. (2019), Yaşlılarda aromaterapi masajının uyku kalitesi ve uykululuk düzeyine etkisi, Yüksek Lisans Tezi, Üsküdar Üniversitesi, Sağlık Bilimleri Enstitüsü, İstanbul.

46. Sezgin Y. (2020), Arterio-venöz fistül kanülasyonu öncesi uygulanan aromaterapi ve el masajının ağrı ve stres düzeylerine etkisi, Yüksek Lisans Tezi, Düzce Üniversitesi, Sağlık Bilimleri Enstitüsü, Düzce.
47. Çetinkaya B. (2007), Aromaterapi masajının bebeklerde koliğin giderilmesi üzerine etkisinin incelenmesi, Doktora Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
48. Arslan S. (2007), Dokunma, müzikterapi ve aromaterapinin yoğun bakım hastalarının fizyolojik durumlarına etkisi, Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Erzurum.
49. Demirbağ C. B. (2011), Müzik ve aromaterapi eşliğinde yapılan uyku ve dokunmanın fibromiyalji hastalarında fibromiyaljinin etki düzeyi ile yorgunluk ve uyku kalitesine etkisi, Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Erzurum.
50. Ovayolu Ö. (2011), Kemoterapi alan meme kanserli kadınlara uygulanan aromaterapinin semptomlara ve yaşam kalitesi etkisi, Doktora Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
51. Cürcani M. (2012), Hemodiyaliz hastalarına uygulanan aromaterapinin kaşıntı üzerine etkisi, Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Erzurum.
52. Taşdemir N. (2012), Gevşeme tekniği, aromaterapi ve her iki yöntemin birlikte uygulanmasının ameliyat sonrası ağrıya etkisi, Doktora Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
53. Özdemir H. (2012), Esansiyel hipertansiyonlu kadınlara inhalasyon yoluyla uygulanan aromaterapinin arteriyel kan basıncı, nabız ve kaygı düzeyine etkisi, Doktora Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
54. Tosun Ö. (2013), Aromaterapi, müzikterapi ve vibrasyon uygulamalarının yenidoğanın stres ve davranışları üzerine etkisi, Doktora Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
55. Lafcı D. (2014), Aroma masajının yaşlılardaki konstipasyona etkisi, Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Erzurum.
56. Metin G.Z. (2015), Romatoid artritli hastalarda aromaterapi masajı ve refleksoloji uygulamalarının ağrı ve yorgunluğa etkileri, Doktora Tezi, Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
57. Pehlivan S. (2015), Diz osteoartritli yaşlı bireylere uygulanan aromaterapi masajının ağrı, fonksiyonel durum ve yaşam kalitesine etkisi, Doktora Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
58. Muz G. (2015), Hemodiyaliz tedavisi alan bireylerde inhalasyon yoluyla uygulanan aromaterapinin uyku kalitesi ve yorgunluk düzeyine etkisi, Doktora Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
59. Yayla M.E. (2016), İnhaler yolla uygulanan aromaterapinin implante edilebilir venöz port kateter iğne girişine bağlı prosedürel ağrı ve anksiyete üzerine etkisi, Doktora Tezi, Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
60. Uzunçakmak T. (2016), Üniversite öğrencilerine uygulanan aromaterapinin premenstruel sendrom ile baş etmeye etkisi, Doktora Tezi, Gazi Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
61. Kaymaz T. T. (2016), Orta ve ileri evre demans hastalarına uygulanan aromaterapinin ajitasyon ve bakım verenin yüküne etkisi, Doktora Tezi, Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
62. Arslan D. (2016), Osteoartritli bireylerde aromaterapi masajının diz ağrısı ve fonksiyonel duruma etkisi, Doktora Tezi, Gazi Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
63. Zorba P. (2016), Masaj ve inhaler yollarla uygulanan aromaterapinin kemoterapiye bağlı akut bulantı kusmaya etkisinin karşılaştırılması, Doktora Tezi, Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara
64. Yıldırım A.T. (2017), Huzurevinde yaşayan yaşlılarda aromaterapi uygulamasının bilişsel fonksiyonlar ve gündüz uykululuk durumuna etkisi, Doktora Tezi, Gazi Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
65. İzgü N. (2017), El ve ayağa uygulanan aromaterapi masajının kemoterapi ilişkili periferal nöropatik ağrı ve yorgunluk üzerine etkisi, Doktora Tezi, Hacettepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Ankara.
66. Kasar S.K.(2018), Miyofasiyal Ağrı sendromu olan bireylerde tetik nokta enjeksiyonu sırasında uygulanan inhaler aromaterapinin ağrı, anksiyete, konfor ve kortizol düzeyine etkisi, Doktora Tezi, Ege Üniversitesi, Sağlık Bilimleri Enstitüsü, İzmir.
67. Ertürk E.N. (2019), Kemoterapi alan hastalara uygulanan nane yağının bulantı kusma ve öğürme üzerine etkisi, Doktora Tezi, Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Kayseri.
68. Işık A.I. (2019), Üniversite Öğrencilerinin Sigara İçme Alışkanlıkları Üzerinde Aromaterapinin Etkisi, Doktora Tezi, İstanbul Üniversitesi-Cerrahpaşa, Lisansüstü Eğitim Enstitüsü, İstanbul.
69. Şimşek P. (2019), Lavanta yağı aromaterapisinin acil servis sağlık çalışanlarında kalabalıklaşmayla ilişkili anksiyete düzeyi üzerindeki etkisinin değerlendirilmesi, Doktora Tezi, İstanbul Karadeniz Teknik Üniversitesi, Sağlık Bilimleri Enstitüsü, Trabzon.
70. Karaaslan M.M. (2020), Bebeklere uygulanan aromaterapi ve abdominal masajın konstipasyon ve annenin kaygı düzeyine etkisi, Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Erzurum.
71. Watt G., and Janca, A. Aromatherapy in nursing and mental health care, Contemp. Nurse, 2008;30:(1), 69–75, , doi: 10.5172/conu.673.30.1.69.

Turkish Journal of Clinics and Laboratory

To cite this article: Sendur HN, Cerit MH, Cindil E. Evaluation of performance of chest x-ray in distinguishing intensive care unit need among COVID-19 patients. Turk J Clin Lab 2021; 1: 95-101.

Original Article

Evaluation of performance of chest x-ray in distinguishing intensive care unit need among COVID-19 patients

Yoğun bakım ihtiyacı olan COVID-19 hastalarını ayırt etmede akciğer grafisinin performansının değerlendirilmesi

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Abstract

Aim: To investigate the performance of chest X-ray (CXR) in distinguishing the patients who necessitate intensive care unit (ICU) admission among COVID-19 patients.

Material and Methods: Between April to August 2020, 166 consecutive hospitalized COVID-19 patients who underwent acquisition of CXR within 24 hours of hospital admission were included in the study. Age, gender, number of comorbidities, smoking status and duration of symptoms for all patients were noted. Observer 1 interpreted the radiographic findings of CXRs of all patients. Distribution of radiographic findings were noted. Afterwards, Observer 1 and observer 2 assigned radiographic assessment of lung edema (RALE) score for each CXR independently. Sensitivity, specificity values in distinguishing COVID-19 patients who require ICU for each observer were calculated. Intraclass Correlation Coefficient (ICC) test was used to assess interobserver agreement levels.

Results: Of the included patients, 128 (77.1%) patients were hospitalized only whereas 38 (22.9%) patients had necessity for ICU admission. Using 7.5 for RALE score as a cut-off point in distinguishing COVID-19 patients who need ICU admission Observer 1 had 89.5% and 93% for sensitivity and specificity, respectively; and Observer 2 had 89.5% and 91.4% for sensitivity and specificity, respectively. The ICC value for the interobserver agreement in RALE scores was 0.988 (95% confidence interval: 0.983 – 0.991).

Conclusion: CXR can be helpful in distinguishing COVID-19 patients who necessitates ICU admission and a RALE score higher than 7.5 is indicative for ICU requirement.

Keywords: COVID-19; chest x-ray; intensive care unit

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Recevied: 17.12.2020 accepted: 15.03.2021
Doi: 10.18663/tjcl.842478

Öz

Amaç: COVID-19 hastalarından yoğun bakım ünitesi (YBÜ) ihtiyacı olanları ayırt etmede akciğer grafisinin performansının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Nisan ve Ağustos 2020 tarihleri arasında, hastaneye yatırılan ve 24 saat içinde akciğer grafisi elde olunan ardışık 166 COVID-19 hastası çalışmaya dahil edildi. Tüm hastaların yaş, cinsiyet, eşlik eden hastalık, sigara içme durumu ve semptom süresi kaydedildi. Birinci gözlemci tüm hastaların akciğer grafilerinde radyolojik bulguları değerlendirdi. Radyografik bulguların dağılımı not edildi. Daha sonra iki gözlemci birbirinden bağımsız olarak tüm akciğer grafilerine akciğer ödemi radyografik değerlendirme (AÖRD) skoru verdi. Her iki gözlemci için COVID-19 hastalarından YBÜ ihtiyacı olanları belirlemede duyarlılık ve özgüllük değerleri hesaplandı. Intraclass Correlation Coefficient (ICC) testi gözlemciler arası uyumluluğu değerlendirmek için kullanıldı.

Bulgular: Hastaların 128'i (%77.1) sadece hastaneye yatırılırken, 38'i (%22.9) YBÜ'ne ihtiyaç duydu. AÖRD skoru için 7.5 eşik değeri olarak kullanıldığında YBÜ gereksinimi olan COVID-19 hastalarını ayırt etmede birinci gözlemci için %89.5 ve %93 duyarlılık ve özgüllük değerleri; ikinci gözlemci için %89.5 ve %91.4 duyarlılık ve özgüllük değerleri bulundu. Gözlemciler arası uyumluluk için ICC değeri 0.988 (%95 güven aralığı: 0.983 – 0.991) olarak bulundu.

Sonuç: Akciğer grafisi YBÜ ihtiyacı olan COVID-19 hastalarını belirlemede yardımcı olabilir ve 7.5'ten büyük AÖRD skoru YBÜ gereksinimini gösterir.

Anahtar kelimeler: COVID-19; akciğer grafisi; yoğun bakım ünitesi

Introduction

Undisputedly, the coronavirus disease 2019 (COVID-19) pandemic has had unprecedented effects on global healthcare systems in 2020 and the exact end of this pandemic is still unpredictable. Almost all countries attempted to develop strategies in their healthcare organizations for potential patient surges and maintaining the quality of patient care. The COVID-19 disease mainly affects the respiratory tract. Symptoms of the disease may vary in range of asymptomatic to fatal and it can progress rapidly [1-3]. The severity of the disease may cause admission to intensive care unit (ICU) which ordinarily has limited numbers of beds in healthcare systems. In this context, as the magnitude of the pandemic can demonstrate spikes, ICU management comprises one of the key points of the healthcare strategies developed for COVID-19 pandemic [4]. Therefore, detecting the COVID-19 patients who need ICU admission in a timely manner has paramount importance.

Although the reference standard for the diagnosis of COVID-19 infection is reverse transcription polymerase chain reaction (RT-PCR) test imaging, particularly chest CT, can play a pivotal role in containment of the disease especially in regions where testing kits are in short supply or turnaround times are lengthy [5-7]. Furthermore, it has been reported that features extracted from radiologic examinations can be helpful in predicting prognosis and clinical outcome of the disease [8-11]. Due to its high sensitivity CT scans were in focus of vast majority of the studies which investigated the role of imaging in COVID-19 pandemic. However, despite its lower sensitivity in comparison to CT scans, chest X-ray (CXR) has advantages of low radiation dose to patients and portability which can limit disease transmission [7]. Several studies also demonstrated that CXR can be helpful in the setting of pandemic [12,13]. Moreover, one recent study reported that CXR is a reproducible imaging tool to evaluate COVID-19 infection and can be useful in predicting clinical outcome of the patients [11]. Therefore, in the current study, we aimed to investigate the performance of CXR in distinguishing the patients who necessitate ICU admission among COVID-19 patients.

Material and methods

The institutional ethics committee approved this retrospective study. The requirement for the written informed consent was waived by institutional ethics committee. Between April to August 2020, our hospital database was searched for all hospitalized COVID-19 patients who underwent acquisition of CXR within 24 hours of hospital admission. Negative RT-PCR test, no available CXR within 24 hours of hospital admission and unavailability of complete demographic data were used as exclusion criteria. 174 consecutive laboratorially confirmed and hospitalized COVID-19 patients were included in the study.

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8 patients were excluded from the study due to poor diagnostic CXR image quality. Therefore, final study cohort consisted of 166 laboratorially confirmed COVID-19 patients. Age, gender, number of comorbidities, smoking status and duration of symptoms (time interval between symptom onset and hospital admission) for all patients were noted. Patients were divided into subgroups according to their ages (<65 years and ≥65 years), smoking status (never smoked, active smoker, former smoker), and number of comorbidities (none, 1, and ≥2).

A radiologist (Observer 1) who had 10 years of experience in CXR interpretation assessed all CXRs of the included patients. The radiologist was aware that patients were laboratorially confirmed COVID-19 patients, however was blinded to all other demographic and clinical data of the patients. Observer 1 determined the distribution patterns of the lung abnormalities were as follows: a.) unilateral or bilateral; b.) upper zone, lower zone or both zones; c.) central, peripheral or both areas. Presence of pleural effusion was also noted. Afterwards, the Observer 1 used a radiographic assessment of lung edema (RALE) score [14-16] for each CXR in range of 0 (no pathological abnormality) to 48 (complete pathological involvement of both lungs) to assess the disease severity quantitatively (Figures 1 and 2). To assess the reproducibility of the RALE scores, a second radiologist (Observer 2) who had 9 years of experience in CXR interpretation evaluated all CXRs for only RALE score assessment in a separate session independently. Observer 2 was also blinded to all demographic and clinical data of the patients except COVID-19 positivity.

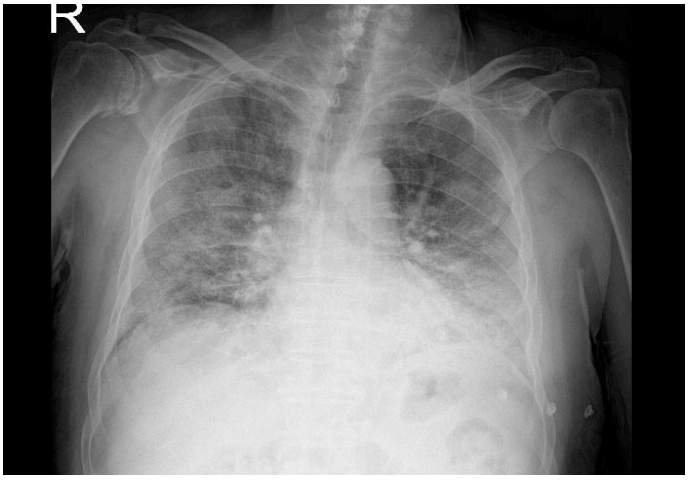

Figure 1. Chest X-ray (CXR) of a 75 years old male COVID-19 patient who admitted to intensive care unit. CXR demonstrates bilateral patchy ground glass opacities with accompanying consolidation at left lower zone. Radiographic assessment of lung edema score was assigned as 20 and 21 for Observer 1 and observer 2, respectively.

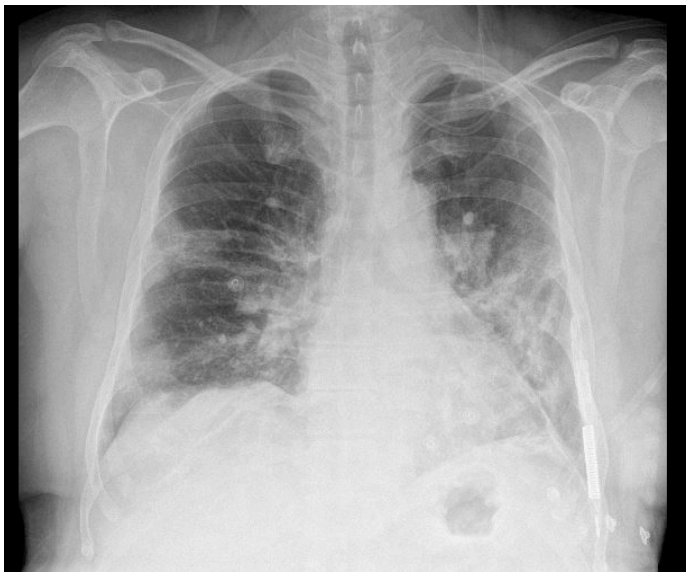

Figure 2. Chest X-ray (CXR) of a 64 years old male COVID-19 patient who admitted to intensive care unit. CXR demonstrates bilateral consolidations. Radiographic assessment of lung edema score was assigned as 27 and 24 for Observer 1 and observer 2, respectively.

Statistical Analysis

All statistical analyses were performed using SPSS software version 22.0 (IBM Corp, Armonk, NY). Continuous variables were presented as mean ± SD whereas categorical variables were presented as percentage values. Kolmogorov-Smirnov test was used to assess the normality of data distribution. Mann Whitney U test was used to compare differences between groups. Pearson Chi-Square test was used to compare categorical variables of independent groups. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) in distinguishing patients who need ICU admission were calculated for RALE scores of each observer. Area under the receiver operating characteristic curve (AUROC) for each observer and 95% confidence intervals (CI) were calculated. Intraclass Correlation Coefficient (ICC) test was used to assess interobserver agreement levels. The ICC test results was interpreted as poor for values less than 0.5; moderate for values between 0.5 and 0.75; good for values between 0.75 and 0.9; excellent for values higher than 0.9 [17]. A P value of 0.05 was used as treshold for statistical significance.

Results

A total of 166 laboratorially confirmed COVID-19 patients were included in the study. The mean age of the patients was 48.37 ± 17.91 years (range: 19-89 years). Of these patients, 128 (77.1%) patients were hospitalized only whereas 38 (22.9%) patients had necessity for ICU admission. The mean

of symptom duration was 4.57 ± 3.61 days (median: 4 days, range: 1-20 days). The most of the patients (73/166, 44%) had no pre-existing comorbidities whereas 44 (26.5%) patients had ≥2 pre-existing comorbities. The most of the patients (85/166, 51.2%) were never smoked. Table 1 represents the demographic data of the included COVID-19 patients. Age (P <0.001), pre-existing comorbidities (P <0.001) and smoking status (P = 0.001) had significant associations with ICU admission. Table 2 represents the distribution of patients according to subgroups and ICU admission.

Table 1. Demographic data of the included COVID-19 patients

Patient Characteristics	Value
Age (years)	48.37 ± 17.91 (range: 19-89 years)
Gender	
Male	92 (55.4%)
Female	74 (44.6%)
Number of pre-existing comorbidities	
0	73 (44%)
1	49 (29.5%)
≥2	44 (26.5%)
Smoking status	
Never smoked	85 (51.2%)
Active smoker	59 (35.5%)
Former smoker	22 (13.3%)
Symptom duration (days)	4.57 ± 3.61 (range: 1-20 days)

Of the included COVID-19 patients, radiographic abnormalities was found in CXRs of 100 (60.2%) patients whereas CXRs of 66 (39.8%) patients demonstrated no abnormality and were interpreted as normal. There was significant difference in duration of symptoms between the CXR normal (median: 3 days) and CXR abnormal (median: 5 days) groups (P = 0.001). The type of main abnormal finding was ground glass opacity (74/100, 74%) and it was followed by consolidation (26/100, 26%). Among the patients whose CXRs revealed abnormalities, lung involvements demonstrated unilateral and bilateral findings in 19 and 81 patients, respectively. Lung involvements were detected in upper zones, lower zones and both zones in 6, 59, and 35 patients respectively. Distribution patterns of the abnormal findings were in central, peripheral, and both areas in 18, 32, and 50 patients, respectively. Pleural effusion was observed in only 11 patients. Table 3 represents the distribution of the radiographic findings of the included COVID-19 patients.

Table 2. Distribution of patients according to subgroups and intensive care unit (ICU) admission.

Patient Characteristics	Hospitalized (n=128)	ICU (n=38)	P value
Age			
<65	117	15	<0.001
≥65	11	23	
Gender			
Male	72	20	0.694
Female	56	18	
Comorbidities			
None	71	2	<0.001
1	42	7	
≥2	15	29	
Smoking status			
Never	69	16	0.001
Former	10	12	
Active	49	10	

Table 3. Distribution of radiographic findings in COVID-19 patients with abnormal chest X-rays (n=100)

Radiographic finding	Number of patients
Type of main parenchymal abnormality	
Ground glass opacity	74 (74%)
Consolidation	26 (26%)
Affected lungs	
Unilateral	19 (19%)
Bilateral	81 (81%)
Distribution	
Upper	6 (6%)
Lower	59 (59%)
Both	35 (35%)
Distribution	
Central	18 (18%)
Peripheral	32 (32%)
Both	50 (50%)
Pleural effusion	
Yes	89 (89%)
No	11 (11%)

The means of RALE scores were 5.83 ± 8.41 (range: 0-36) and 5.69 ± 8.58 (range: 0-32) for Observer 1 and 2, respectively. If cut-off point was determined as 7.5 for RALE score, in distinguishing COVID-19 patients who need ICU admission the Observer 1 had 89.5%, 93%, 79.1% and 96.7% for sensitivity, specificity, PPV and NPV, respectively; and the Observer 2 had 89.5%, 91.4%, 75.6% and 96.7% for sensitivity, specificity, PPV and NPV, respectively. AUROC values for Observer 1 and Observer 2 were 0.947 (95% CI: 0.899 – 0.995) and 0.938 (95% CI: 0.883 – 0.992), respectively. The ICC value for the interobserver agreement in RALE scores was 0.988 (95% CI: 0.983 – 0.991).

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Discussion

The COVID-19 pandemic has spread all across the world and healthcare systems encountered overwhelming workload. Due to potential patient surges it is extremely important to render quick and accurate decisions in the battle with this pandemic. Because ICU resources are scarce critical care triage is one of the main goal for the management of this outbreak. In this study we found that RALE score assigned based on CXRs obtained within 24 hours of hospital admission can accurately distinguish COVID-19 patients who need admission to ICU. As the results of the current study can be helpful in determining the COVID-19 patients who require ICU admission it may play an important role in critical care triage for clinicians and ICU practitioners.

In the current study we found that older age (≥65 years) and pre-existing comorbidities had significant associations with ICU requirement. These findings are in line with the previous studies [18-21]. There are controversial results in the literature about the association between smoking status and severity of the disease. Zhao et al [22] reported that smoking increases the risk of severe COVID-19 approximately by twofolds. However, Lippi et al [23] reported that active smoking is not associated with severity of the disease. In the current study we found a significant association with the smoking status of the patients and ICU requirement. Interestingly, our findings revealed that 54.5% (12/22) of former smokers admitted to ICU whereas only 16.9% (10%59) of active smokers admitted to ICU. However, former smokers were older (median: 68 years) than the active smokers (median: 46 years) in this study cohort and age may be confounding factor for these results. Future studies are necessary to investigate the complex relationship between the disease severity and smoking status.

CXR is relatively low cost imaging technique which is widely used in the evaluation of pneumonias. Although, most of the studies which assess imaging features of COVID-19 pneumonia focused on CT imaging, several studies also reported the radiographic findings of COVID-19 patients. Bilateral consolidations and/or ground glass opacities with a predilection for peripheral and lower zones are the most common findings detected on CXRs of patients with COVID-19 pneumonia [6,10-13]. In the current study the most of the CXRs with abnormal findings demonstrated bilateral lung involvement, and we found that the majority of the CXRs with abnormal findings demonstrated radiographic abnormalities in lower zones (59%); and in both central and peripheral areas (50%). Notably, although all included COVID-19 patients were hospitalized, CXRs of 39.2% (66/166) patients were interpreted as normal. A study which included CXR examinations of 636 symptomatic patients with COVID-19 who admitted to urgent care centers revealed that 58.3% of CXRs were interpreted as normal [24]. On the other hand, Stephanie et. al [12] reported that the sensitivity of CXR in COVID-19 patients increases with symptom duration. In our study symptom duration of patients with normal CXRs (median: 3 days) are significantly shorter than symptom duration of patients with abnormal CXRs (median: 5 days). Although CXRs of symptomatic COVID-19 patients can be normal the difference in symptom duration between patients normal and abnormal CXRs also had potential influence on these results.

It has been demonstrated that CT findings can be helpful to predict critical disease or ICU requirement in COVID-19 patients. Balbi et al [11] reported that CXR also can be helpful to predict the need for ventilatory support or mortality. Cozzi et al [15] investigated the correlation between radiographic findings with clinical outcomes. They interpreted CXRs of 234 COVID-19 patients and reported that RALE score higher than 15 had a correlation with increasing risk of being admitted to ICU. In our study a RALE score higher than 7.5 had high sensitivity (89.5%) and specificity (91.4% - 93%) for both observers in distinguishing COVID-19 patients who need ICU admission. Differences in study cohorts or potential differences in ICU admission criteria between institutions may lead discordant results. Future multinational and multicentric studies may allow us to better understand the role of RALE scores in predicting ICU need.

In the study of Cozzi et al [15] two independent reader assigned RALE scores in COVID-19 patients and found that inter-reader agreement in the assignment of RALE scores was very good (ICC value 0.92). Moreover, Balbi et al [11] reported that another scoring system [25] which was experimentally developed to assess the severity of COVID-19 pneumonia based on CXR findings also demonstrated almost perfect inter-rater agreement (ICC value 0.91) . These results indicate that CXR scoring systems in COVID-19 patients are reproducible. Similarly, in the current study we found an excellent (ICC value

0.988) interobserver agreement for RALE scores. Therefore, our findings are in line with the previous studies.

This study has several limitations. The main limitations of the current study are retrospective design and lack of comparison with CT scans. Moreover, number of included patients is relatively small. As the sensitivity of CT imaging is superior to CXR in COVID-19 patients future studies with a larger number of patients in prospective design which also compare CXRs and CT imaging may be more valuable. Additionally, this study does not provide information about the final outcome (recovery or death) of the patients who admitted to ICU. Therefore, investigations that also provide information about the final outcome of these patients can ensure better understanding of the role of CXR in this pandemic.

Conclusion

The current study revealed that CXR can be helpful in distinguishing COVID-19 patients who necessitates ICU admission and a RALE score higher than 7.5 is indicative for ICU requirement.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Guan WJ, Ni ZY, Hu Y et al. China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020; 382: 1708-20.
2. Chen N, Zhou M, Dong X et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507–13.
3. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China JAMA 2020; 323: 1061-9.
4. Phua J, Weng L, Ling L et al. Asian Critical Care Clinical Trials Group. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med 2020; 8: 506-17.
5. Huang G, Gong T, Wang G et al. Timely Diagnosis and Treatment Shortens the Time to Resolution of Coronavirus Disease (COVID-19) Pneumonia and Lowers the Highest and Last CT Scores From Sequential Chest CT. AJR Am J Roentgenol 2020; 215: 367-73.
6. Wong HYF, Lam HYS, Fong AH et al. Frequency and Distribution of Chest Radiographic Findings in Patients Positive for COVID-19. Radiology 2020; 296: 72-8.
7. Rubin GD, Ryerson CJ, Haramati LB et al. The Role of Chest Imaging in Patient Management during the COVID-19 Pandemic: A Multinational Consensus Statement from the Fleischner Society. Radiology 2020; 296: 172-80.
8. Tekcan Sanli DE, Yildirim D, Sanli AN et al. Predictive value of CT imaging findings in COVID-19 pneumonia at the time of first-screen regarding the need for hospitalization or intensive care unit. Diagn Interv Radiol 2 December 2020 10.5152/dir.2020.20421 [Epub Ahead of Print]
9. Colombi D, Bodini FC, Petrini M et al. Well-aerated Lung on Admitting Chest CT to Predict Adverse Outcome in COVID-19 Pneumonia. Radiology 2020; 296: 86-96.
10. Toussie D, Voutsinas N, Finkelstein M et al. Clinical and Chest Radiography Features Determine Patient Outcomes in Young and Middle-aged Adults with COVID-19. Radiology 2020; 297: 197-206.
11. Balbi M, Caroli A, Corsi A et al. Chest X-ray for predicting mortality and the need for ventilatory support in COVID-19 patients presenting to the emergency department. Eur Radiol 2020; 8: 1–14.
12. Stephanie S, Shum T, Cleveland H et al. Determinants of Chest X-Ray Sensitivity for COVID- 19: A Multi-Institutional Study in the United States. Radiology: Cardiothoracic Imaging Sep 24 2020. doi:10.1148/ryct.2020200337
13. Smith DL, Grenier JP, Batte C, Spieler B Characteristic Chest Radiographic Pattern in the Setting of COVID-19 Pandemic. Radiology: Cardiothoracic Imaging Sep 3 2020. doi:10.1148/ryct.2020200280.
14. Warren MA, Zhao Z, Koyama T et al. Severity scoring of lung oedema on the chest radiograph is associated with clinical outcomes in ARDS. Thorax 2018; 73: 840-6.

15. Cozzi D, Albanesi M, Cavigli E et al. Chest X-ray in new Coronavirus Disease 2019 (COVID-19) infection: findings and correlation with clinical outcome. Radiol Med 2020; 125: 730-7.
16. Homayounieh F, Zhang EW, Babaei R et al. Clinical and imaging features predict mortality in COVID-19 infection in Iran. PLoS One. 2020; 15: 239519
17. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016; 15: 155-63.
18. CDC COVID-19 Response Team. Severe outcomes among patients with Coronavirus Disease 2019 (COVID-19) – United States, February 12- March 16, 2020. MMWR Morb Mortal Wkly Rep 2020; 69: 343-6.
19. Zhou F, Yu T, Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395: 1054-62.
20. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020; 323: 1239-42.
21. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA 2020; 323: 1775-6.
22. Zhao Q, Meng M, Kumar R et al. The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. J Med Virol 2020; 92: 1915-21.
23. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). Eur J Intern Med 2020; 75: 107-8.
24. Weinstock MB, Echenique A, Russell JW et al. Chest x-ray findings in 636 ambulatory patients with COVID-19 presenting to an urgent care center: a normal chest x-ray is no guarantee. J Urgent Care Med 2020; 14: 13-8
25. Borghesi A, Maroldi R. COVID-19 outbreak in Italy: experimental chest X-ray scoring system for quantifying and monitoring disease progression. Radiol Med 2020; 125: 509-13.

Turkish Journal of Clinics and Laboratory

To cite this article: Sarı R , Buldanlı MZ. Lenfoproliferatif hastalıklarda splenektomi endikasyonları ve klinik sonuçlarımız. Turk J Clin Lab 2021; 1: 102-106.

Orjinal Makale

Lenfoproliferatif hastalıklarda splenektomi endikasyonları ve klinik sonuçlarımız

Splenectomy indications and clinical results in lymphoproliferative diseases

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Öz

Amaç: Hematolojik malignitelerde sistemik tutulum nedeniyle cerrahinin faydası oldukça sınırlıdır. Splenektomi özellikle izole dalak lenfomalarında kimi zaman hem tanı hem de tedavi amaçlı gerekir. Bu çalışmanın amacı lenfoma tanısıyla takip edilen hastalarda splenektominin endikasyon ve yararlarını incelemek, operasyon sonrasındaki klinik sonuçlarımızı tartışmaktır.

Gereç ve Yöntemler: Çalışmamıza Ocak 2012 ve Aralık 2019 tarihleri arasında lenfoid malignite nedeniyle hematoloji bölümünce takip edilen ve splenektomi endikasyonuyla tarafımıza yönlendirilen hastalar dahil edildi. Hastalara ait demografik ve klinik veriler ile tedavi sonuçları geriye dönük olarak incelendi.

Bulgular: Çalışmaya toplam 44 hasta dahil edildi. Hastaların splenektomi zamanındaki yaş ortalaması 58,2 (±12.4) idi. Hastaların %63,6'sı erkekti. Splenektomi sonrası ortalama takip süresi 12,3 (3-94) aydı. 26 hasta semptomatik splenomegali, 18 hasta medikal tedaviyle düzeltilemeyen trombositopeni ve anemi gibi endikasyonlarla opere edildi. Tedavi sonrası klinik iyileşme splenik marjinal zon lenfomasında diğer lenfoma tiplerine göre daha yüksekti.

Sonuç: Son yıllarda özellikle monoklonal antikorlarla yapılan medikal tedaviler sayesinde lenfoma tedavisinde cerrahi ihtiyacı giderek azalmaktadır. Verilerimiz dalak tutulumu olan lenfoid malignitelerde ve özellikle splenik marjinal zon lenfomasında splenektominin etkili ve güvenli bir tedavi seçeneği olduğunu göstermektedir.

Anahtar Sözcükler: lenfoma; marjinal zon lenfoma; splenektomi

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Doi: 10.18663/tjcl.822973

Abstract

Aim: The benefits of surgery are very limited in hematological malignancies due to systemic involvement. Splenectomy is sometimes required for both diagnosis and treatment, especially in isolated splenic lymphomas. The aim of this study is to examine the indications and benefits of splenectomy in patients with lymphoma diagnosis and to discuss our postoperative clinical results.

Material and Methods: Patients who were followed up by the hematology department for lymphoid malignancy between January 2012 and December 2019 and referred to us with the indication of splenectomy were included in our study. The demographic and clinical data of the patients and the treatment results were analyzed retrospectively.

Results: A total of 44 patients were included in the study. The mean age of the patients at the time of splenectomy was 58.2 (± 12.4). Sixty three percent of the patients were male. The mean follow-up time after splenectomy was 12.3 (3-94) months. Twenty six patients were operated due to symptomatic splenomegaly, 18 patients were operated due to thrombocytopenia and anemia that could not be corrected by medical therapy. Clinical improvement after treatment was higher in splenic marginal zone lymphoma than in other types of lymphoma.

Conclusion: In recent years, the need for surgery in the treatment of lymphoma has been decreasing, especially through medical treatments with monoclonal antibodies. Our data show that splenectomy is an effective and safe treatment option in lymphoid malignancies and especially in splenic marginal zone lymphoma.

Keywords: lymphoma; marginal zone lymphoma; splenectomy

Giriş

Dalak hematopoetik ve immünolojik fonksiyonları nedeniyle oldukça önemli bir organdır. Her ne kadar korunması amaçlansa da hematolojik ve lenfoproliferatif hastalıkların tanı veya tedavisinde bazen splenektomi kaçınılmazdır. Elektif splenektominin en temel endikasyonu benign veya malign hematolojik bozukluklardır [1].

Hematolojik hastalıklarda medikal tedaviye yanıtsız olgularda veya başarısızlık durumunda sık başvurulan etkili bir tedavi yöntemidir [2]. Lenfoproliferatif hastalıklarda ise medikal tedavi alternatiflerinin artması ve dalağın immün sistemdeki önemli rolü nedeniyle splenektomi uygulamaları azalmaktadır. Ayrıca bu hastalıklarda sistemik tutulum nedeniyle splenektominin faydası da oldukça sınırlıdır. Önceleri tanı amaçlı yapılan operasyonlar yerini daha minimal invaziv bir yaklaşım olan görüntüleme eşliğindeki biyopsilere bırakmıştır [3]. Son yıllarda gelişen modern tedavi alternatifleri ve monoklonal antikorlar sayesinde splenektomi gerekliliği daha da azalmıştır. Genellikle masif splenomegaliye bağlı gastrointestinal ya da solunum sistemi ile ilgili klinik belirtiler oluştuğunda veya hipersplenizm nedenli düzeltilmesi mümkün olmayan anemi, trombositopeni varlığında alternatif tedavi olarak başvurulur. Sadece primer dalak lenfomalarında küratif amaçlı splenektominin yeri vardır. Masif splenomegaliyle seyreden diğer lenfoproliferatif bozukluklarda ise debulking prosedürünün bir bileşeni olarak uygulanabilir [4].

Gelişen biyomedikal teknoloji ve minimal invaziv cerrahinin artan önemi ile birlikte laparoskopik splenektomi dalak boyutlarının normal olduğu birçok hastalıkta standart tedavi haline gelmiştir [5]. Masif veya ultra masif dalak varlığında ise Avrupa Endoskopik Cerrahi Derneği (EAES) tarafından el yardımlı laparoskopik splenektomi ya da açık splenektomi önerilmektedir [6]. Altta yatan hastalığa bağlı oluşabilecek morbidite, mortalite ve medikal tedavinin yan etkileri düşünüldüğünde gittikçe karmaşıklaşan tedavi ortamında splenektominin faydaları oldukça fazladır [7]. Fakat splenektominin de invaziv bir girişim olduğu unutulmamalı multidisipliner değerlendirme ile kar/zarar analizi yapılarak cerrahi kararı en doğru şekilde verilmeye çalışılmalıdır.

Bu çalışmadaki amacımız lenfoma tanısıyla takip edilen hastalardaki splenektomi endikasyonlarını incelemek, operasyon sonrasında düzelen klinik bulguları tartışmaktır.

Gereç ve Yöntemler

Bu çalışma için Ocak 2012 ile Aralık 2019 tarihleri arasında kliniğimizde splenektomi uygulanan toplam 274 hastaya ait veriler geriye dönük incelendi. Çalışmaya bu hastalar içerisinden sadece lenfoid malignite nedenli hematoloji kliniğince takibi sırasında splenektomi endikasyonuyla polikliniğimize konsülte edilen ve elektif koşullarda opere edilen 44 hasta dahil edildi. Diğer nedenlerle opere edilen ve acil cerrahi uygulanan hastalar çalışma dışı bırakıldı. Çalışma Helsinki bildirgesine uygun olarak yapıldı ve yerel etik kurul

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tarafından onaylandı (Proje no:514/188/8). Veriler doğrudan hastane elektronik veri tabanı ve matbu hasta dosyaları retrospektif olarak taranarak elde edildi.

Hastalara ait demografik verilerin yanı sıra, operasyon öncesi ve sonrasındaki klinik, laboratuvar bulgular, cerrahi öncesi uygulanan medikal tedaviler, splenektomi endikasyonları, operasyon sonrası gelişen komplikasyonlar ve cerrahinin sağladığı fayda analiz edildi. Lenfoma tipini belirlemek için Dünya Sağlık Örgütü (WHO) 2016 sınıflandırılması kullanıldı ve splenik marjinal zon lenfoma (SMZL) tanılı hastalar Grup 1 diğer Hodgkin dışı lenfoma (NHL) tanılı hastalar ise Grup 2 olarak tanımlandı. Hastalara elektif operasyonun 2 hafta öncesinde pnömokok, meningokok ve hemofilus influenza tip B aşıları uygulandı. Tüm hastalar açık cerrahi teknikle opere edildi. Hastalara operasyon sonrası 1 hafta boyunca profilaktik oral antibiyotik ve tromboemboli profilaksisi için düşük molekül ağırlıklı heparin verildi. Takiplerde platelet sayısı 1 milyon üstünde ölçülen hastalara asetil salisik asit başlandı.

İstatistiksel analizler için Statistical Package for Social Scienses (SPSS) 21.0 programı kullanıldı. Sürekli değişkenlerin değerlendirilmesinde normal dağılım gösteren veriler ortalama±SD, normal dağılım göstermeyenler ortanca (min-max) olarak belirtildi. Kategorik değişkenler frekans (%) olarak sunuldu.

Bulgular

Çalışma için belirlenen periyotta splenektomi yapılan 274 hastadan lenfoproliferatif malignite tanısı olan 44 (%16) hasta çalışmaya dahil edildi. Bu hastaların operasyon zamanındaki yaş ortalaması 58,2 (±12,4) idi ve hastaların çoğunluğunu (%65,9) erkek hastalar oluşturmaktaydı. Tüm hastalar NHL tanılıydı ve baskın histolojik tip 28 (%63,6) hasta ile SMZL idi. Splenektomi endikasyonları incelendiğinde 26 (%59) hasta semptomatik splenomegali, 18 (%41) hasta medikal tedaviyle düzeltilemeyen anemi ve trombositopeni nedeniyle opere edildi. Operasyon öncesi dönemde SMZL tanı hastalarda anemi daha sıktı, trombositopeni oranı ise her iki grupta benzerdi. Hastaların %72'sine ilk tedavi olarak kemoterapi başlanmıştı. Hastalara ait detaylı demografik ve klinik veriler tablo-1'de sunuldu.

Preoperatif değerlendirmede Grup 1'deki hastaların ortalama hemoglobin ve platelet değerleri daha düşüktü. Splenektomi sonrası bu parametrelerin her iki grupta da yükseldiği gözlendi. (Tablo 2) Splenektomi sonrası ortalama takip süremiz 12,3 (3-94) aydı.

İki gruptaki morbidite oranı eşitti. Grup 1'de 7 (%25) Grup 2'de 4 (%25) hasta olmak üzere toplam 11 (%25) hastada çeşitli komplikasyonlar gözlendi. Peroperatif 3 hastanın kanama nedenli transfüzyon ihtiyacı oldu. Postoperatif dönemde ise sadece 1 hastada transfüzyon gerektirecek kadar kanama gözlendi. Operasyon sonrası takiplerde 3 hastada subfrenik apse, 2 hastada atelektazi, 1 hastada derin ven trombozu ve 1 hastada akut pankreatit saptandı. Bir hastada post-splenektomi sepsise bağlı mortalite görüldü ve mortalite oranı %2,2 olarak saptandı. Operatif komplikasyonlara ait veriler ayrıntılı olarak tablo 3'de gösterildi.

Tablo 1. Demografik ve klinik veriler

	Grup 1 (n:28)	Grup 2 (n:16)	Toplam (n:44)
Yaş ortalaması	59,5 (±12,6)	56,1 (±10,2)	58,2 (±12,4)
Cinsiyet Erkek Kadın	 17 (%61) 11 (%39)	 12 (%75) 4 (%25)	 29 15
Splenektomi endikasyonu Splenomegali Sitopeni	 20 (%71) 8 (%29)	 6 (%37) 10 (%63)	 26 18
Anemi (Hb<12g/dl)	21 (%75)	9 (%56)	30
Trombositopeni (plt<150x10^3/µL)	12 (%43)	6 (%37)	18
Kemoterapi başlanan	18 (%64)	14 (%87)	32

* Hb: Hemoglobin, Plt: Platelet.

Tablo 2. Splenektomi öncesi ve sonrasına ait ortalama laboratuvar değerleri

	Grup 1	Grup 2
Ortalama Hemoglobin (g/dL) Preoperatif Postoperatif	 10,4±2,3 11,5±2,6	 11,1±1,9 11,9±2,1
Ortalama Platelet (10^3/uL) Preoperatif Postoperatif	 212±94 470±251	 266±124 493±283

Tablo 3: Postoperatif komplikasyonlar

	Grup 1	Grup 2	Toplam
Kanama • Peroperatif • Postoperatif	 2 1	 1 0	 3 (%6,8) 1 (%2,2)
Subfrenik apse	2	1	3 (%6,8)
Atelektazi	1	1	2 (%4,5)
Tromboemboli	0	1	1 (%2,2)
Akut Pankreatit	1	0	1 (%2,2)
Sepsise bağlı mortalite	0	1	1 (%2,2)

Tartışma

Lenfoma genellikle sistemik tutulum gösteren bir hastalık olduğundan tedavisinde cerrahi uygulama oldukça sınırlıdır. Splenektomi lenfoma tanısı olan hastalarda genellikle splenomegaliye bağlı gelişen klinik semptomları gidermek, sitopeniyi düzeltmek veya tedavide kür sağlamak amacıyla

uygulanabilir. Dünya Sağlık Örgütü (DSÖ) tarafından 2001 yılından beri farklı bir kategoride sınıflandırılan splenik marjinal zon lenfoması (SMZL) izole dalak tutulumu ile seyreden nadir görülen bir non-Hodgkin lenfoma türüdür [8]. Hastalığın seyrinde genellikle masif izole splenomegali ve hipersplenizme bağlı ciddi sitopeni görülmekte olup splenomegali ve sitopeni görülme oranı diğer lenfomalara kıyasla daha yüksektir [9]. Bu nedenle tedavisinde ilk basamak yaklaşım splenektomi veya rituksimabla uygulanan immünoterapidir. Rituksimab tedavisinin düşük toksisite ile yüksek yanıt (%88-95) sağladığı yönünde yayınlar mevcuttur [10,11]. Fakat uygun tedavi rejimi ve ne kadar süre devam edeceği henüz açıklığa kavuşmamıştır. Ayrıca literatürde splenektomiyi rituksimab veya kemoterapi ile karşılaştıran bir çalışma bulunmamaktadır. SMZL tanılı hastalarda splenektomi sıklıkla gerekmekte ve cerrahi tedavi kimi zaman ilk seçenek olarak önerilmektedir [12]. Bizim çalışmamızda da literatüre benzer şekilde lenfoma nedenli splenektomi yapılan hastaların %63,6'sını SMZL tanılı hastalar oluşturmaktadır.

Splenektomi için seçilen hastalar immün süpresyonu ve genel anestezi altında abdominal cerrahiyi tolere edebilecek performansta olmalıdır. Hematolojik hastalıklarda splenektomi sonrası düşük oranlarda morbidite ve mortalite gözlenir. Splenektomi sonrası komplikasyon görülme oranı % 8-52 arasında değişmekte olup malignite nedenli yapılan ameliyatlarda bu oran yüksektir [13]. Bagradio ve arkadaşlarının hematolojik hastalıklar nedenli splenektomi yapılan 1715 vakayı içeren çalışmasında morbidite %17 ve mortalite %1,6 oranında saptanmıştır [14]. Aynı çalışmada splenektomi nedenleri benign ve malign olarak ayrıldığında ise malign hasta grubunda bu oranın %27,2 olduğu raporlanmıştır. Bizim çalışmamızdaki morbidite ve mortalite oranları sırasıyla %25 ve %2,2'dir.

Kanama ve enfeksiyon en sık görülen komplikasyonlardır. Musallam ve arkadaşlarının yaptığı bir çalışmada splenektomi sonrası transfüzyon oranını %29,4 (laparoskopi sonrası %11,2 açık cerrahi sonrası %47) olarak bulmuştur [15]. Splenektomi sonrası gelişen enfeksiyon tablosunda etkeni tanımlamak oldukça zordur. Bu nedenle elektif operasyondan en az 2 hafta önce kapsüllü bakterilere karşı aşılama önerilmektedir. Yapılan çalışmalar benign ve malign koşullara göre değişmekle birlikte splenektomi sonrası enfeksiyon görülme oranlarını %1 ile %6,3 arasında bildirmiştir [14-18]. Çalışmamızda enfektif komplikasyonu olan 3 (%6,8) hastamız vardı ve bu hastalardan 1'inde (%2,2) sepsis nedenli mortalite gözlendi. Trombotik komplikasyonların (derin ven trombozu, pulmoner emboli vs.) görülme sıklığı 3812 hastayı içeren geniş bir kohort çalışmasında değerlendirildi ve splenektomiden sonraki 90 gün içinde 71 (%1,9) hastada venöz tromboemboli saptandı ve bu oran hem genel popülasyondan (%0,06) ve hem de appendektomi sonrası (%0,6) görülen oranlardan belirgin yüksekti [19]. Literatürde yer alan diğer çalışmalar da benzer şekilde splenektomiyi takiben venöz tromboemboli görülme oranının %1,8-%3,3 arasında değiştiğini bildirmiştir [14,15,20]. Çalışmamızda bu oran %2,2 olarak bulundu.

Postoperatif enfeksiyöz komplikasyonlar; antibiyotik profilaksisi, uygun intraoperatif ısı kontrolü, kateter (nazogastrik, üriner ve santral venöz gibi) ve drenlerin erken çekilmesi gibi birkaç basit önlemle azaltılabilir [21]. Operasyon öncesi ve sonrası erken dönemde tromboemboli profilaksisi özellikle malign hastalarda oldukça kritiktir. Preoperatif anemi, koagülopati ve kanama riski yüksek operasyon nedeniyle transfüzyon ihtiyacının arttığı aşikardır. Splenektomi de dahil olmak üzere cerrahi uygulamalarda 1 ünite kan transfüzyonun artmış enfeksiyöz komplikasyon ve mortalite oranlarıyla ilişkili olduğu saptanmıştır [22].

Çalışmamızın retrospektif olması ve literatüre kıyasla nispeten az sayıda hasta içermesi başlıca kısıtlılıklarıdır.

Sonuç

Medikal tedaviler ve özellikle de monoklonal antikorlardaki gelişmeler hematolojik hastalıklarda splenektomi endikasyonlarını oldukça azaltmıştır. Yine de lenfoid malignitelerde splenomegaliye bağlı klinik semptomlar ve tedaviye bağlı sitopeni varlığında splenektomi düşük morbidite ve mortalite oranlarıyla güvenle uygulanabilmesi nedeniyle tedavi alternatifi olarak önemini korumaktadır.

Çıkar çatışması / finansal destek beyanı

Bu yazıdaki yazarların herhangi bir çıkar çatışması yoktur. Yazının herhangi bir finansal desteği yoktur.

Kaynaklar

1. Bonnet S, Guedon A, Ribeil J-A, Suarez F, Tamburini J, Gaujoux S. Indications and outcome of splenectomy in hematologic disease. Journal of visceral surgery 2017; 154: 421-9
2. Ciftciler R, Pasayeva A, Aksu S bet al. Indications and Outcomes of Splenectomy for Hematological Disorders. Open Med (Wars) 2019; 14: 491-6.
3. Tokue H, Hirasawa S, Morita H et al. Percutaneous image-guided biopsy for non-mass-forming isolated splenomegaly and suspected malignant lymphoma. PLoS One 2014; 9: 111657.

4. Onisâi M, Vlădăreanu AM, Nica A et al. Splenectomy in Lymphoproliferative Disorders: A Single Eastern European Center Experience. Medicina (Kaunas) 2019; 56: 12.
5. Uranüs S, Dorr K. Laparoscopy in Abdominal Trauma. Eur J Trauma Emerg Surg 2010; 36: 19-24.
6. Habermalz B, Sauerland S, Decker G et al. Laparoscopic splenectomy: the clinical practice guidelines of the European Association for Endoscopic Surgery (EAES). Surg Endosc 2008; 22: 821-48.
7. Alobuia WM, Perrone K, Iberri DJ, Brar RS, Spain DA, Forrester JD. Splenectomy for benign and malignant hematologic pathology: Modern morbidity, mortality, and long-term outcomes. Surg Open Sci 2020; 2: 19-24.
8. Swerdlow SH, Campo E, Harris NL, et al, eds. WHO Classification of Tumors of the Haematopoietic and Lymphoid Tissues. IARC Press; 2017.
9. Rodgers, G. Thrombocytopenia: Pathophysiology and classification. In Wintrobe's Clinical Haematology, 12th ed.; Greer, J., Foerster, J., Lukens, J., Rodgers, G., Paraskevas, F., Glader, B., Eds.; Lippincott Williams & Wilkins: Philadelphia, PA, USA, 2009; pp. 1289–91.
10. Kalpadakis, C, Pangalis GA, Vassilakopoulos, TP, Sachanas S, Angelopoulou MK. Treatment of splenic marginal zone lymphoma: should splenectomy be abandoned? Leukemia & Lymphoma 2013; 55: 1463–70.
11. Bennett M, Schechter GP. Treatment of splenic marginal zone lymphoma: splenectomy versus rituximab. Semin Hematol 2010; 47: 143-7.
12. Lenglet J, Traullé C, Mounier N et al. Long-term follow-up analysis of 100 patients with splenic marginal zone lymphoma treated with splenectomy as first-line treatment. Leuk Lymphoma 2014; 55: 1854-60.
13. Cadiere B, Grilli A, Bron D. Comparison of Laparoscopic Splenectomy Outcomes for Benign and Malignant Hemopathies. J Laparoendosc Adv Surg Tech A 2020; 30: 1172-6.
14. Bagrodia N, Button AM, Spanheimer PM, Belding-Schmitt ME, Rosenstein LJ, Mezhir JJ. Morbidity and Mortality Following Elective Splenectomy for Benign and Malignant Hematologic Conditions: Analysis of the American College of Surgeons National Surgical Quality Improvement Program Data. JAMA Surg 2014; 149: 1022-9.
15. Musallam KM, Khalife M, Sfeir PM et al. Postoperative outcomes after laparoscopic splenectomy compared with open splenectomy. Ann Surg 2013; 257: 1116-23.
16. Winslow ER, Brunt LM. Perioperative outcomes of laparoscopic versus open splenectomy: a meta-analysis with an emphasis on complications. Surgery 2003; 134: 647-53.
17. Rosen M, Brody F, Walsh RM, Tarnoff M, Malm J, Ponsky J. Outcome of laparoscopic splenectomy based on hematologic indication. Surg Endosc 2002; 16: 272-9.
18. Balague C, Targarona EM, Cerdan G, et al. Long-term outcome after laparoscopic splenectomy related to hematological diagnosis. Surg Endosc 2004; 18: 1283–7.
19. Thomsen RW, Schoonen WM, Farkas DK, Riis A, Fryzek JP, Sørensen HT. Risk of venous thromboembolism in splenectomized patients compared with the general population and appendectomized patients: a 10-year nationwide cohort study. J Thromb Haemost 2010; 8: 1413-6.
20. Taner T, Nagorney DM, Tefferi A et al. Splenectomy for massive splenomegaly: long-term results and risks for mortality. Ann Surg 2013; 258: 1034-9.
21. Berenguer CM, Ochsner MG Jr, Lord SA, Senkowski CK. Improving surgical site infections: using National Surgical Quality Improvement Program data to institute Surgical Care Improvement Project protocols in improving surgical outcomes. J Am Coll Surg 2010; 210: 737-41.
22. Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. J Am Coll Surg 2009; 208: 931-7.

To cite this article: McCusker K, Czaplicka C, McCusker R, Gunaydin S. Efficacy of theories related to extracorporeal life support specialist assisting client during the COVID-19 pandemic. Turk J Clin Lab 2021; 1: 107-112.

Review

Efficacy of theories related to extracorporeal life support specialist assisting client during the COVID-19 pandemic

COVID-19 pandemisindeki vücutdışı yaşam desteğinde uygulayıcıların hastalara destek olma teorilerinin etkinliği

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Abstract

As the wave of respiratory and cardiac failure due to an unprecedented pandemic hits our medical centers, extracorporeal life support (ECLS) specialists have become more involved with long term intensive care; our relationship to patient care has been altered. ECLS and Ventricular Assist Devices have become essential tools in the care of critically ill patients with respiratory failure, post-cardiotomy failure, and viral infection. During this pandemic, there have been many advancements and rapid growth towards options of long term mechanical cardiopulmonary support, especially in the adult patient population. ECLS cases reported to the International Extracorporeal Life Support Organization registry, showing >73,000 patients. With the growth of this patient population and the changing "ECLS specialist-Patient" family relationship, it is essential to explore handling the grief of the patients. Individuals dealing with pain demonstrate a variety of reactions as they adjust to a life without a loved one. This review examines the efficacy of theories related to ECLS specialists, assisting a client, and families grieving the loss of a significant person in their life.

Keywords: extracorporeal life support; extracorporeal membrane oxygenation; cardiopulmonary bypass

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Recevied:14.02.2021 accepted: 18.02.2021
Doi: 10.18663/tjcl.880106

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Öz

Pandeminin beklenmedik şiddetiyle sarsılan hastanelerimizde vücutdışı yaşam desteği (VDYD) uygulayıcıları hastaların uzun süreli bakımlarında daha çok yer almakta ve hastalar ve aileleriyle daha yoğun iletişime girmektedir. VDYD ve ventrikül destek cihazları ileri derecede hasta olan bu grupta solunum desteği, kardiyotomi sonrası yetmezlik ve viral enfeksiyon tedavisinde ön plana çıkmaktadır. VDYD kullanımıyla ilgili olarak da pandemic döneminde uzun süreli destek özellikle erişkin hastalar için yaygınlaşmıştır. Uluslararası VDYD Derneği verilerine göre uygulama sayıları 73.000 leri geçmiştir. Sayıların bu denli artmasıyla hasta ve hasta ailesiyle olan ilişkilerin optimumda yürütülmesi de önem kazanmıştır. Sevenlerinin hasta olması veya kaybedilmesi yoğun bir hüzün ve acı oluşturmaktadır. Bu derleme VDYD uygulayıcılarının hastalara veya ailelerine yönelik destekleri üzerine geliştirilmiş teorilerin etkinliğine açıklık getirmek üzerine hazırlanmıştır.

Anahtar kelimeler: ekstrakorporeal yaşam desteği; ekstrakorporeal membran oksijenasyonu; kardiyopulmoner bypass

Introduction

Background

There is no one definitive way for extracorporeal life support (ECLS) specialists to comfort families as they grieve, endure, and witness this critical experience. Every individual is uniquely different in how they attempt to manage the loss of a mechanically supported patient. Historically, many researchers and scholars have contributed ideas and theories examining methodologies that may assist in the grief process. This review examines several methods utilized to enable the grieving person to cope and recover from the effects of bereavement and subsequent grief. One theory looks at the concept of grief within a psychosocial transition context [1], including aspects such disposition and active participation in personal growth, thereby enabling a positive outcome.

A second theory under investigation relates to the viability of collaboration between family and other care support, creating a systematic step by step approach that facilitates recovery from bereavement [2]. This second theory is further defined by Shapiro when stating, "the family's priority will be to bring overwhelming experiences back to a manageable level and restore routines of everyday life". This implies that a concerted effort is focused by the family to enable 'return to normality,' aided and supported by the collaboration between the immediate family and external assistance. Set against this background, sources such as the National Cancer Institute point out that questions are posed by some researchers, regarding if outside assistance is required by these determined to be suffering from the 'normal' reaction when faced with bereavement [3]. Within their study, it is noted that further questions are raised by researchers regarding the credibility of providing additional counseling; maintaining that time in itself acts as a 'healer.' Thereby allowing the inference that 'normally' such persons experiencing bereavement will adapt to a changed 'environment' over a given period. They also raise the question of available resources, suggesting that supporting care should be allocated to thee who may not be experiencing the process of 'normal grief.'

Countering NCI's theory, such external resources, by acting in an appropriate supporting role, "may alleviate the probability of future ill-health and complications" [4]. Nevertheless, the author also agrees in part with [5], further questioning the viability of support from health care professionals, due to issues such as their lack of knowledge or understanding pertaining to a case. Dent defends the sustainability of the professional's personal experience but maintains that their 'understanding' may be limited by experience.

Moreover, personal bias or subjective perceptions may interfere with the process of fully understanding each patient's situation and circumstance due to the possibility that the professional's understanding may be "colored by subjective values and prejudices". Notwithstanding, this does not negate support from family members in close friends, perhaps in part supporting Shapiro's [2] thesis regarding collaboration between perfusionists and family members. Logically such support by professionals can be seen as indirectly connected to the bereaved person, yet directly assisting the family

members. Riley et al. [1] pursue a different perspective in which a process is enabled that allows the bereaved to develop a positive mindset, thereby revising their viewpoint of the new psychological environment in which they find themselves. This theory lends to promote an attitude of 'self-support' and perhaps by inference, a' survivalist' approach.

Research Problem and Findings

Normal Grief

According to [6], normal grief is a process that is "self-limiting", enabling the operation of emotions that eventually result in recovery. Additionally, Woof et al. maintain that most of those suffering from grief have the wherewithal to adapt. This process of adaption can be likened to a form of transition. A viewpoint offered by Wortman & Boerner [7], expands on Riley et al. 's theory regarding coming to terms with psychosocial development and the bereaved person's ability to accept and play a role in the healing process Wortman et al. maintain that "personal loss is considered to be an important part of successful adult development". Based on this thesis, an inference can be drawn, or assumption can be made that without the 'bereavement' experience, an individual's personal development is incomplete. Therefore, leading from this notion, such an experience is 'part of life'; thereby, a natural process.

Added to this, is the ability of the bereaved to develop a "sense of coherence construct"[8], thereby including personality characteristics such as "resilience and hardiness." Almedom further expands by suggesting that both "positive and negative aftermaths, "recovery" and "chronic trauma," respectively, are necessarily two sides of the same coin". This further adds weight to the notion that both outcomes, be it temporary or prolonged, be part of a natural process, therefore, be allowed to evolve over a period of time. This again asks the question regarding the viability of intervention by health care personnel or specialist professionals, while seeking to assist the bereaved.

As the spread of cardiac and respiratory collapse continues to grow in numbers, perfusionists are being utilized in these forums at increasing rates. A further recent study looks at the possibility in which persons experiencing trauma may emerge from a "traumatic event in a better psychological state" after coming to terms with the "adversity" of the event [9]; thereby supporting Riley et al., Wortman et al. & Almedom's theory discussed earlier. When referring to a bereaved child, Pasternak points out the necessity for adaption, both from the child's viewpoint and the surrounding environment. In addition, Pasternak claims that the purpose of enabling the adaption process is to discover alternative ways to meet the child's requirements while completing the "developmental roles of the child".

In an interesting development, a study conducted in both the United States of America and China depicted the influence of culture within a 'normal grief' scenario [10]. In this study, they attempted to measure grief processing and deliberate grief avoidance in two different cultures. Although their attempt to establish a definitive pattern to this management of grief was inconclusive, evidence supported the importance of ritual, especially in China. The study showed how rituals offered "comforting guidelines" that enabled clarity and support to the bereaved. Bonanno et al. continue to note that such Chinese rituals include communal aspects that benefit from "interpersonal connectedness", which is essentially part of Chinese social culture.

Furthermore, it would appear that emotional bonds between the 'departed' and the bereaved are encouraged as part of the process of 'healing,' thereby perhaps lessening the impact of grief. This inclusion of communal support lends credibility to Shapiro's thesis in which the theory of cultural and developmental systems is discussed. Here the similarity between the construction of "collaborations between care providers and families" and communal "interpersonal connectedness". This supports the theory of a supportive environment rather than the method Riley et al. leans toward, a process of psychosocial transition leading a positive outcome. The individual disposition to achieve such a result enables the bereaved individual is regarded as an "active participant"; and to acquire resilience and hardiness.

Doren et al. [11] notes how the bereaved focus on how their loved one had lived, rather than on their' passing.' This adds another viewpoint in how identifying with family or extended family positively can facilitate relief when faced with the prospect of bereavement, further validating Shapiro's theory. Doren et al. also suggest that external support, such as specialist, should consider assisting the bereaved by encouraging ways in which they can remember the 'departed.' This is enabled through "displaying pictures or commemorating special days such as birthdays and death anniversaries". Also, this allows the bereaved to allow the 'past' (death) to be connected with the future [12].

Perhaps this practice goes against beliefs and cultures, which may focus more on enabling the bereaved ability to forget and to 'resume' their daily lifestyle; therein more biased towards Riley et al. 's thesis. Regarding a psychosocial transition in which, the bereaved are more likely to independently 'work' through the grief process, and proceed to a sustainable outcome and a sense of finality or resolution. Another methodology encouraged by healthcare professionals incorporates the bereaved undergoing 'grief work' to enable recovery from losing a loved one. Bonanno [13] illustrating this process by describing it as "a period of working through the thoughts, memories, and emotions associated with the lost relationship…". Furthermore, another viewpoint maintains that this is "a way of neutralizing the stimuli" [14], which leads to reduced distress.

Associated with 'grief work' [15], further expand on this theory by defining stressors that are biased towards loss, thereby allowing the bereaved to primarily connect to feelings and emotions are associated with death. However, their study looks at "restoration-oriented stressors", in which focus is targeted at more secondary or perhaps less subjective viewpoints in which the bereaved can establish a path towards rebuilding their life without the deceased, and also establishing new relationships within the family environment and circles of friends.

Perhaps this viewpoint can be seen as a combination of both Riley et al. 's and Shapiro's theories relating to overcoming the loss of a loved one. First, the act of rebuilding tends to lean towards Riley et al., by enabling a psychosocial transition in which the 'patient' or bereaved actively participates in a personal growth program incorporating a positive disposition. Also seen within this 'restoration-orientated' stressor is the potential to renew or further relationships with family and friends, thereby perhaps facilitating their support as an added benefit to the recovery process. By alternatively shifting the 'grief work' between a focus that is both loss-orientated and restoration-orientated, such a process is seen as a viable and natural process which has a potentially positive outcome.

According to [16], by enabling the bereaved to enact such variation of 'grief' work facilitates temporary denial of the more 'extremity' or 'low point' encountered within the grieving process. Moreover, by shifting such orientation, the bereaved can view the bereavement experience from a more objective viewpoint [17], rather than allocating blame or 'self-pity' to their situation and loss. Following, this paper looks deeper into Riley et al. 's and Shapiro's theories by analyzing grief from a parent/child perspective.

Parental and Family Loss

While discussing the above two theories, attention deserves to be directed at research that was conducted to ascertain the relevance of a deceased child and its implication for the parents. First, it is stated that there are significant differences between how a mother and father react [18]. The author goes on to maintain that a mother's reactions "being stronger and more prolonged". Where studies have been enacted utilizing 'depression inventories,' mother's bereaved by the loss of their child "has been shown to have higher depression scores than mothers of living children [19]. Perhaps this emphasis on the mother's loss attributes a greater severity being derived from the maternal aspect within the issue of parental grief.

Pre-Existing Relationships

ECLS specialists should be aware of another concept related to the ability of the bereaved to process loss is based on relationships formed between the deceased and the bereaved before death. Moffitt [20] discusses in-depth the critical influence of the 'quality' of the relationship when the bereaved seeks to secure a measure of 'closure.' A secure connection can enable the bereaved to process their loss by internalizing past experiences that occurred before the death of a loved one. On the other hand, a situation in which the relationship between the deceased and bereaved was compromised, a longer-term inability to effectively process grief can be a reality. Such compromise is created by either the lack of possible weakness of 'attachment,' thereby creating an uneasy relationship before bereavement.

Social Issues Derived from Bereavement

Bereavement, either in the short or long term, inevitably isolates the individual from their typical day to day social environment, creating stress like the reasonable security provided by a circle of friends and the local community can be temporarily withdrawn. Added to this, legal issues about the deceased, including medical and legal documentation, inheritance issues, lack of income can contribute to an overwhelming sense of isolation [21]. The authors also point out that this deprivation can develop new growth in order to combat the 'threat' and stress of social isolation and that "post-traumatic growth is both a process and an outcome", further

validating Riley et al. in their espousal of an individual's natural ability to successfully work through the grieving process.

Impact of Grief

Resid [22] also confirm quantitative evidence suggesting that such a loss can enable the security of the marriage relationship to be maintained, and "the ability to maintain marital closeness over time might be a key to well-being for most parents". Another variable found within the context of a marriage relationship pertains to the aspect of personal resources [23]. In their qualitative study titled 'Living after Loss' identified such resources as 'self-competence,' which can affect competency in "daily life tasks. These personal resources are primarily attributed to both financial status and health. Mrazek et al. further suggest that despite evidence pointing to non-contributing factors of "death forewarning" and "marital quality," higher competency did contribute to "more positive mental health outcomes." Inference derived from this suggestion, allows their thesis to infer that the bereaved couple's possession of more significant resources is more enabled to process their grief, thereby creating an environment favorable to recovery.

Intense or Complicated Grief

As ECLS specialist, the area of intense and complicated grief is especially a concern. According to [24], not all bereavement can be processed through 'normal grief.' Their study suggests that "others deviate from this norm", thereby allowing or initiating the "concept of abnormality and possibility the attention of health professionals".

Conclusion

This review submits that based on the above definition, normal grief can be better addressed by ECLS specialist towards being viewed and supported by Riley et al. 's theory in which a transitional psychosocial process can be found. This process utilizes qualities that include an individual's disposition towards a self-help program resulting in a positive outcome. Logical assumption leads this discussion to verify that 'normal grief' is presupposed on the outcome of the bereavement grief process, whereby abnormal grief is similarity closely connected to an unfavorable or negative result.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Riley LP, LaMontagne LL, Hepworth JT, Murphy BA. Parental grief responses and personal growth following the death of a child. Death Studies 2007; 31: 277- 99.
2. Shapiro, E. Whose recovery, of what? Relationships and environment promoting grief and growth. Death Studies 2008; 32: 40-58.
3. Nolen AL, Putten JV. Action Research in Education: Addressing Gaps in Ethical Principles and Practices. Educational Researcher 2007; 36: 401-7.
4. Dent A. Supporting the bereaved: theory and practice. Healthcare Counseling and Psychotherapy Journal 2005, Ingram Publishing/Alamy.
5. Baruch Y. Response Role in Academic Studies-A Comparative Analysis Human Relations 1999; 52(4):421-438.
6. Woof WR., Carter YH. The grieving adult and the general practitioner: a literature review in two parts (part 2). British Journal of General Practice 1997; 47: 509-14.
7. Wortman CB, Boerner K. Beyond the Myths of Coping with Loss: Prevailing Assumptions Versus Scientific Evidence, 2006.
8. Almedom AM. Towards Light at the End of the Tunnel. Journal of Loss and trauma 2005; 10: 253-65.
9. Pasternak RE, Reynolds CF 3rd, Schlernitzauer M, et al. Acute open-trial nortriptyline therapy of bereavement-related depression in late life. J Clin Psychiatry 1991; 52: 307-10.
10. Bonnano GA, Papa A, LaLande K et al. Grief Processing and Deliberate Grief Avoidance. Journal of Consulting and Clinical Psychology 2005; 73: 86-98.
11. Doren G, Hansen ND. Constructions of Mexican American Family. Cultural Diversity and Ethnic Minority Psychology 2010; 12: 199-211.
12. Kissane DW, McKenzie M, Bloch S, et al.: Family-focused grief therapy: a randomized, controlled trial in palliative care and bereavement. Am J Psychiatry 2006; 163: 1208-18.
13. Bonanno GA, Lilienfield SO. Let's be realistic; when grief counseling is effective and when it's not. Prof Psychol Res Pr 2008; 39: 377-8.
14. Doughty EA, Wissel A, Glorfield C. Current trends in grief counseling. Article 94. New Orleans, LA, United States of America, 2018.

15. Stroebe M, Schut H. The dual-process model of coping with bereavement; rationale and description. Death Studies 1999; 23: 197-224.
16. Shear K, Frank E, Houck PR, et al.: Treatment of complicated grief: a randomized controlled trial. JAMA 2005; 293: 2601-8.
17. Steidl S, Mohi-uddin S, Anderson AK. Effects of emotional arousal on multiple systems: evidence from declarative and procedural learning. Learn. Mem 2006; 13: 650-8.
18. Dyregov A. Parental reactions to the loss of an infant child: A review. Scandinavian Journal of Psychology 1990; 31: 266-80.
19. Clark JP. Balancing Qualitative & Quantitative methodology in Health Services Research: How can qualitative research methods best complement administrative data analysis. CEHIP, Ontario, Canada, 2000.
20. Moffitt TE. The New Look of Behavioral genetics in Developmental Psychopathology: Gene-Environment Interplay in Antisocial Behaviors. Psychological Bulletin 2005; 131: 533-54.
21. Roberts LW, Geppert C, Connor R et al. An Invitation for Medical Educators to Focus on Ethical and Policy Issues in Research and Scholarly Practice. Acad med. 2001; 76: 876-85
22. Resid, W. Research in social work. Encyclopedia of social work. 18th ed., Vol 2, pp.487. Silver Spring, MD: National Association of Social Workers, 1989.
23. Mrazek PJ, Haggerty RJ, eds: Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research. Washington, DC: National Academy Press, 1994.
24. Woof WR, Carter YH. The grieving adult and the general practitioner: a literature review in two parts (part 2). British Journal of General Practice 1997; 47: 509-14.

To cite this article: Tanriverdi O, Askin L. Sağ sinüs valsalva kökenli sol koroner sistemin göğüs ağrısı ile prezentasyonu. Turk J Clin Lab 2021; 1: 113-115.

Olgu Sunumu

Sağ sinüs valsalva kökenli sol koroner sistemin göğüs ağrısı ile prezentasyonu

Presentation of left coronary system originating with right sinus valsalva with angina pectoris

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Öz

Her üç koroner arterin sağ sinüs valsalvadan çıkması oldukça nadirdir. Koroner anomaliler ateroskleroz nedeniyle iskemiye neden olabilir. Ekokardiyografi, koroner anjiyografi, bilgisayarlı tomografi (BT) ve manyetik rezonans görüntüleme (MRG) gibi yöntemler koroner arterlerin anormal kökenini ve seyrini teşhis etmek için kullanılır. Bizim çalışmamızda sadece koroner anjiografi ve ekokardiyografik görüntülemeler yapılabildi. Akut koroner sendrom (AKS) tanılı tıkayıcı koroner lezyonları olmayan ve her üç koroner arterin de sağ sinüs valsalvadan kaynaklandığı bir vakayı sunmayı amaçladık.

Anahtar Kelimeler: Akut koroner sendrom; Bilgisayarlı tomografi; Manyetik rezonans görüntüleme

Abstract

All three coronary arteries originate from the right sinus valsalva is rarely. Coronary anomalies can cause ischemia due to atherosclerosis. Echocardiography, coronary angiography, computed tomography (CT), and magnetic resonance imaging (MRI) have been used to diagnose the origin and course of abnormal coronary arteries. In our study, only coronary angiography and echocardiographic imaging were performed. We aimed to present a case with acute coronary syndrome (AKS) have not obstructive lesions and all three coronary arteries originated from the right sinus valsalva.

Keywords: Acute coronary syndrome; Computed tomography; Magnetic resonance imaging

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Doi: 10.18663/tjcl. 843776

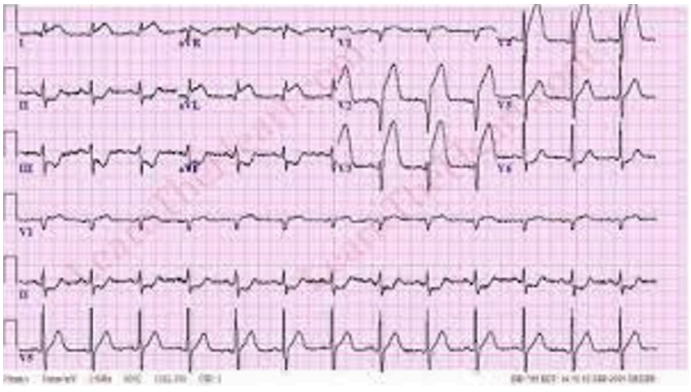
Volume 12 Number 1 p: 113-115

Giriş

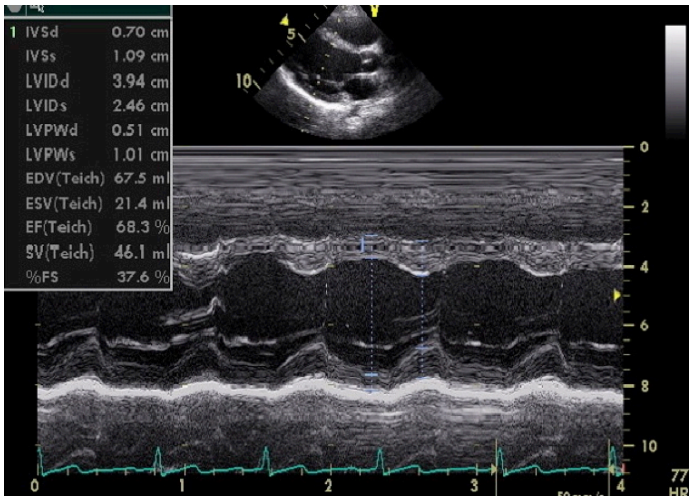
Anormal sinüs kökenli koroner arterler miyokard iskemisi ve ani kardiyak ölüme yol açabilecek nadir koroner arter anormalileridir. Sağ sinüs valsalva kökenli ayrı çıkışlı sol ön inen (LAD) ve sol sirkumfleks (LCx) koroner arter oldukça nadirdir ve literatürde çok az vaka bildirilmiştir. Bu yazıda, akut koroner sendrom (AKS) ile prezente sağ sinüs kökenli ayrı ayrı çıkışlı koronerleri olan vakayı sunmayı amaçladık.

Olgu

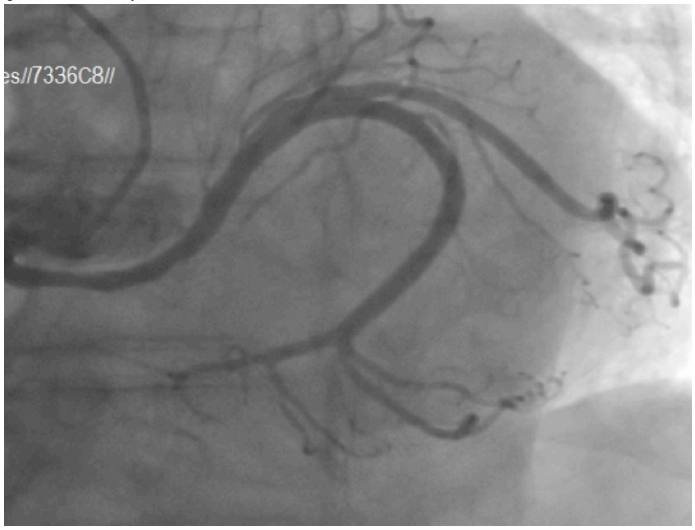
Sigara içicisi, dislipidemik, diyabeti olmayan, normotansif 84 yaşında erkek hasta acil servise 6 saat süre ile sol kola yayılan retrosternal göğüs ağrısı ile başvurdu. 12 derivasyonlu elektrokardiyogramda (EKG) anterior derivasyonda ST segment yükselmesi olup normal sinüs ritminde idi (şekil 1). Hastanın kanda bakılan troponin değeri 12 ng/mL olup pozitifti. Hasta AKS ön tanısı ile koroner yoğun bakıma alındı. Hastanın bakılan ekokardiyografi parametrelerinde M-mod ile EF' si % 68 olup, kardiyak ventrikül fonsiyonları normal gözlendi (Şekil 2). Yoğun bakım yatışının 2. gününde, devam eden göğüs ağrısı nedeniyle, sağ femoral arterden koroner anjiyografi yapıldı. 6F JL 4.0 tanı kateteri ile seçici koroner arter kanülasyonu denendi; bununla birlikte, sol koroner küspis kökenli koroner arterler görüntülenemedi. 6F JR4.0 tanı kateteri ile sağ koroner arter kanülasyonunda sağ koroner kuspisten ayrı olarak ortaya çıkan sol koroner arterler saptandı (Şekil 3). Aynı katater ile manipülasyon yapıldıktan sonra sağ koroner arter görüntülenebildi. Sağ koroner arter (RCA) normal olarak gözlendi (şekil 4). Hastanın koronerlerinde tıkanıklık yapıcı lezyona rastlanmayıp plak lezyonlar saptandı ve medikal tedavi kararı alındı. Hastanın kendi rızasıyla çok kesitli kardiyak tomografi çekilememesi nedeniyle tomografi görüntüleri elde edilemedi. Hastanın takiplerinde komplikasyon görülmedi ve medikal tedavisi düzenlenerek 1 ay sonra kardiyoloji poliklinik kontrolü önerildi.



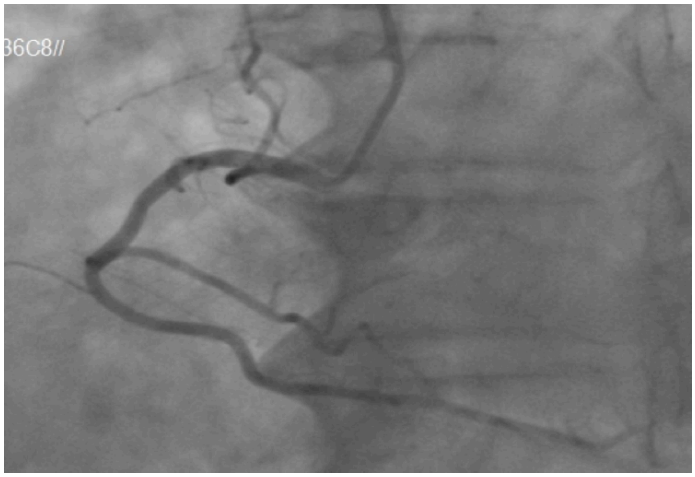
Şekil-1. 12 derivasyonlu elektrokardiyogram



Şekil-2. Eko parametreleri



Şekil-3. Koroner anjiografi görüntülemesi



Şekil-4. Koroner anjiografi görüntülemesi

Tartışma

Koroner arter anomalileri nadir olarak otopsi serilerinde % 0.3, anjiyografik serilerde ise % 1.3 oranında görülmektedir. İzole bir anomali olarak ya da diğer konjenital kardiyak defektlerle birlikte görülebilir [1,2]. Koroner anomalinin en yaygın şekli, sağ koroner sinüsten veya proksimal RCA'dan LCX anormal kökenidir. Sağ sinüs valsalva kökenli sol ana koroner arter iyi bilinen bir koroner anormalidir ve ani kardiyak ölümle ilişkilidir, ancak hem LAD hem de LCx'in zıt sinüsten kökenli olması oldukça nadirdir. Koroner anjiyografik ve manyetik rezonans görüntüleme çalışmasında bu anormali insidansının %3,1 olduğu bildirilmektedir [3]. Engel ve diğ. [4] bununla ilgili dört vaka bildirmiş ve Click ve ark. [5] ise koroner anormaliler ile ilgili üç olgu bildirmiştir.

Koroner arter anormalisi kökenini ve seyrini tespit etmek için ekokardiyografi, koroner anjiyografi, bilgisayarlı tomografi ve manyetik rezonans görüntüleme gibi çeşitli görüntüleme yöntemleri kullanılır. LAD çıkış anormalisinin en sık görülen seyri pulmoner gövdenin önü ve aortun arka tarafında anormal LCX' tir [5]. Ancak bizim vakamızda, anormal kökenli LAD büyük damarlar arasında seyretmektedir. Bu anormal koronerlere sahip hastalarda aterosklerotik hastalık veya anormal çıkış açısı, yarık benzeri veya daralmış ostium, intramural seyir veya aort kökü ve pulmoner gövde arasındaki kompresyon nedeniyle iskemi gelişebilir. İntravasküler ultrason (İVUS) çalışmaları ile iskeminin önemli bir patofizyolojik mekanizması olan koroner segmental hipoplazi ve lateral luminal kompresyon ile intususepsiyon olduğu keşfedilmiştir [6].

CASS çalışmasından elde edilen bir analiz, anormal LCx dışında diğer koroner anormalilerin ateroskleroz için yüksek risk oluşturmadığını göstermiştir [7]. Anormal LCx'de artmış ateroskleroz riski, genişleyen aort tarafından koroner arter duvarında artan strese bağlı olabilir [8]. Anormal koronerleri olan hastaların tedavisi medikal, PKG veya cerrahi olabilir. İnterarterial seyirli LAD' si olan asemptomatik hastalar iskemi belirtileri açısından dikkatle değerlendirilmeli ve ağır egzersizden kaçınmaları tavsiye edilmelidir. Bu koroner çıkış anormalilerine perkütan koroner girişim (PKG), değişen ostial konfigürasyon, aort çıkış açıları, arter trasesi ve aterosklerotik lezyonun yeri nedeniyle teknik olarak zorlayıcıdır.

Klavuz kateter, hem aort başlangıç açısı hem de çıkan aortun genişliğine göre ayarlanmalıdır. Yatay bir çıkışa sahip RCA için standart Judkins genelde iyi bir tercihtir. Daha düşük çıkışlı RCA' da Judkins ilk tercih judkins katater olmakla beraber, çıkan aort dilate ise çok amaçlı kateter de kullanılabilir. Ostium (Shepard'ın Crook RCA) yönünün yukarı yönlü olduğu RCA için sol Amplatz kateterler tercih edilir. Kavisli ve kalsifiye RCA lezyonları için klavuz kateterin derin angajmanı veya 1 veya 2 solunda sol Amplatz 1 veya 2 kateterler tercih edilmelidir [9]. Başarılı PKG için kılavuz kateter seçimi oldukça önemlidir. Klavuz tel ve balon desteği lezyonu geçmek için önemlidir ve işlem süresini önemli ölçüde azalttığı gösterilmiştir [10].

Sonuç olarak, sol koroner sistem görüntülemesinde koronerlerin görülememesi şüphe uyandırmalıdır. Sağ koroner sinüsten kökenli üç koroner arter son derece nadir konjenital bir anormalidir. Bu koroner çıkış anormalisi ateroskleroz veya anormal anatomi nedeniyle anjinaya sahip olabilir. Bizim vakamızda EKG' de ST elevasyonu olmasına rağmen koronerlerde darlık gözlenmedi. Koroner çıkış anormalileri için kılavuz kateterlerin seçimi, manipülasyonu ve operatörün dikkati bu vakanın vurgulanması gereken noktalarıdır.

Kaynaklar

1. Askin L, Demırelli S, Ermis E. Successful percutaneous coronary ıntervention of a stenotic aberrant circumflex artery: a rare cause of acute coronary syndrome. Int J Cardiovasc Res 2015; 4: 2.
2. Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. Cathet Cardiovasc Diagn 1990; 21: 28–40.
3. Kashyap BP, Himanshu G, Hrudaya N et al. Origin of all three major coronary arteries from the right sinüs of valsalva: clinical, angiographic, and magnetic resonance imaging findings and incidence in a select referral population. Catheter Cardiovasc Interv 2007; 69: 711–8.
4. Engel HJ, Torres C, Page HL. Major variations in anatomical origin of the coronary arteries: angiographic observations in 4,250 patients without associated congenital heart disease. Cathet Cardiovasc Diagn 1975; 1: 157–69.
5. Click RL, Holmes DRJ, Vlietstra RE et al. Anomalous coronary arteries:location, degree of atherosclerosis and effect on survival. A report from the Coronary Artery Surgery Study. J Am Coll Cardiol 1989; 13: 531–7.
6. Angelini P, Walmsley RP, Libreros A et al. Symptomatic anomalous origination of the left coronary artery from the opposite sinus of valsalva. Clinical presentations, diagnosis and surgical repair. Tex Heart Inst J 2006; 33: 171–9.
7. Bartorelli AL, Capacchione V, Ravagnani P et al. Anomalous origin of the left anterior descending and circumflex coronary arteries by two separate ostia from the right sinus of valsalva. Int J Cardiol 1994; 44: 294–8.
8. Wilkins CE, Betancourt B, Mathur VS et al. Coronary artery anomalies. Tex Heart Inst J 1988; 15: 166–73.
9. Ikari Y, Masuda N, Matsukage T et al. Backup force of guiding catheters for the right coronary artery in transfemoral and transradial intervention. J Invasive Cardiol 2009; 21: 570–4.
10. Topaz O, Di Sciascio G et al. Coronary angioplasty of anomalous coronary arteries. Notes on technical aspects. Cathet Cardiovasc Diagn 1990; 21: 106–11.

To cite this article: Cesur S, Siyah ÜÖ, Kılıç EK, Sarı M, Hatipoğlu ÇA, Kınıklı S. Covid-19 pandemisi döneminde tanı konulan bir toplum kaynaklı Legionella pneumophila pnömonisi olgusu. Turk J Clin Lab 2021; 1: 116-119.

Olgu Sunumu

Covid-19 pandemisi döneminde tanı konulan bir toplum kaynaklı *Legionella pneumophila* pnömonisi olgusu

A community-acquired pneumonia case due to Legionella pneumophila diagnosed during the Covid-19 pandemic period

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Öz

Legionella pneumophila, hafif seyirli pnömoniden, ağır seyirli pnömoni ve çoklu organ yetmezliğine kadar değişebilen klinik seyir gösteren, toplum ve hastane kaynaklı pnömonilere neden olabilen, sporadik veya salgınlar şeklinde ortaya çıkabilen bir bakteriyel pnömoni etkenidir. Legionella pneumophila, akla getirilmezse ve tanıya yönelik testler istenmezse gözden kaçabilir. Burada, Covid -19 pandemisi döneminde acil servise yüksek ateş, öksürük, nefes darlığı şikayetleri ile başvuran ve idrarda Legionella antijen pozitifliği ile Legionelloz tanısı konulan bir olgu sunuldu. Olguda Covid-19 infeksiyonu bilgisayarlı tomografide tipik tutulum saptanmaması ve Covid-19 polimeraz zincir reaksiyonu testinin negatif saptanması ile ekarte edildi. Olguya Legionella pneumophila'ya yönelik levofloksasin tedavisi 14 güne tamamlandı. Klinik ve laboratuvar bulguları düzelen hasta taburcu edildi.

Sonuç olarak, Covid-19 pandemi döneminde Legionella pneumophila pnömonisinin Covid-19 pnömonisi ile karışabileceği, anamnez ve klinik bulguları legionella ile uyumlu hastalarda akılda tutulması gerektiği görüşündeyiz.

Anahtar kelimeler: Atipik pnömoni; Covid-19; Legionella pneumophila; ayırıcı tanı

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Volume 12 Number 1 p: 116-119

Abstract

Legionella pneumophila is a bacterial pneumonia agent ranging from mild pneumonia to severe pneumonia and multi-organ failure, which can cause community and hospital-acquired pneumonia, sporadic or outbreaks. If Legionella pneumophila is not considered and diagnostic tests are not requested, it can be overlooked. Here, we present a case who was admitted to the emergency room with high fever, cough, and shortness of breath during the Covid-19 pandemic and was diagnosed with Legionellosis with Legionella antigen positivity in the urine. In the case, Covid-19 infection was ruled out by the absence of typical involvement in computed tomography and the negative detection of the Covid-19 polymerase chain reaction test. Levofloxacin treatment for Legionella pneumophila was applied to the patient for a period of 21 days. The patient, whose clinical and laboratory findings improved, was discharged.

In conclusion, we conclude that Legionella pneumophila pneumonia can be confused with Covid-19 pneumonia during the Covid-19 pandemic period and should be kept in mind in patients whose anamnesis and clinical findings are compatible with legionella.

Key words: Atypical pneumonia; Covid-19; Legionella pneumophila; differential diagnosis

Giriş

Lejyonella pneumophila, doğadaki sıcak veya soğuk çeşitli su kaynaklarında, şehir su şebekelerinde ve klima sistemlerinde, solunum cihazları, soğutma kulelerindeki sularda bulunabilen, fakültatif intrasellüler yerleşim gösteren Gram negatif bir bakteridir. İmmun yetmezlik, maligniteler, diabetes mellitus, kronik akciğer hastalığı, immunsüpresif ilaçlar (kortikosteroid vb.) sigara kullanımı, yaşlılık ve erkek cinsiyet Legionella infeksiyonu için risk faktörleri arasında yer alır [1-5]. Bulaş, kontamine suların bulunduğu çeşitli gereçlerden (duş başlıkları, solunum terapi cihazları, nemlendiriciler vb.) kaynaklanan aerosollerin solunum yoluyla alınmasıyla gerçekleşir [1,3,4,5].

Bu yazıda, Covid-19 pandemisi sırasında anamnez,muayene bulguları ve görüntüleme yöntemleri ile Legionella pneumophila (L.pneumophila) pnömonisi düşünülen ve idrarda Legionella antijen testi pozitifliği ve balgamda polimeraz zincir reaksiyonu (PZR) pozitifliği ile kesin tanı konulan bir olgu sunularak literatür gözden geçirildi.

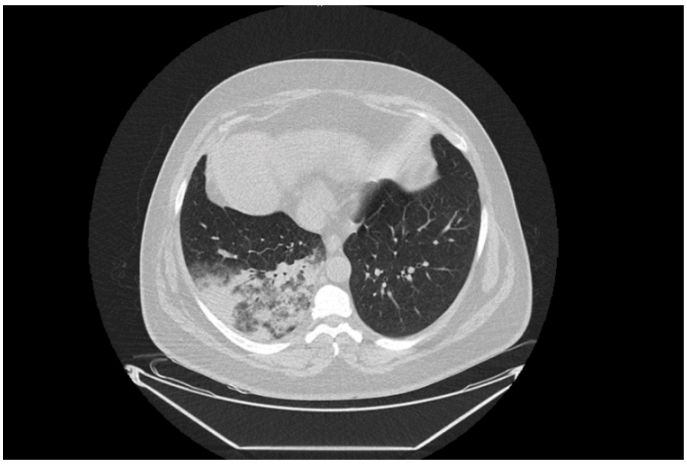
Olgu

Ankara ilinde ikamet etmekte olan 41 yaşında erkek hasta yeni başlayan yüksek ateş öksürük nefes darlığı şikayeti ile acile başvurmuştu. Anamnezinden 3 gün önce Antalya'da bir otelde klimalı ortamda kaldığı ve duş aldığı, şikayetlerinin Ankara'ya döndükten sonraki gün başladığı öğrenildi. Özgeçmişinde ek hastalığı olmadığı, 20 paket/yıl sigara tükettiği öğrenildi. Fizik muayenesinde; ateş 39°C, nabzı 100/dakika, kan basıncı 110/75 mm/Hg, solunum sayısı 27/ dakika, O2 saturasyonu %90 idi. Genel durumu orta, bilinci açık ve oryante idi. Solunum sistemi muayenesinde, takipneik olan hastanın akciğer muayenesinde sağ akciğer bazalinde kaba raller mevcuttu. Diğer muayeneleri doğaldı. Laboratuvar testlerinde; lökosit sayısı 13.970 /mm3, hemoglobin 13.6 gr/dl, trombosit 182 000/mm 3 lenfosit sayısı 1480 /mm3 eritrosit sedimantasyon hızı 48 mm/saat, C-reaktif protein 281 mg/dl, üre 19 mg/dl, kreatinin 0,9 mg/dl, sodyum 136 mmol/L, potasyum 4,5 mmol/L, aspartat aminotransferaz (AST) 39 U/L, alanin aminotransferaz 38 U/L, laktik dehidrogenaz (LDH) 417 U/L (normali <232 U/L), total bilirübin 0.3 mg/dl idi. Hastadan kan ve idrar kültürleri alındı. Toraks bilgisayarlı tomografisinde 'Sağ akciğer alt lobda konsolidasyon ve buzlu cam tarzında dansite artımı gösteren infiltrasyon alanı' olarak rapor edildi. Hastadan alınan kan ve idrar kültürlerinde üreme olmadı. Balgamdan solunum yolu etkenlerine yönelik multiplex PZR testi (Bosphore solunum yolu patojenleri panel kiti V4, Anatolia geneworks,Türkiye) ve Covid-19 infeksiyonuna yönelik nazofarenks sürüntü örneğinde PZR testi (Bioeksen, Türkiye) istendi.

Hastanın anamnezinde uzun süre sigara kullanması, otelde duş alma öyküsü olması, klinik ve radyolojik olarak pnömoni bulgularının olması nedeniyle idrar örneği Legionella antijeni

araştırılmak üzere Türkiye Halk Sağlığı Kurumu Mikrobiyoloji Referans Laboratuvarı'na gönderildi. Hastaya seftriakson 1×2 gr /gün intravenöz (I.V) ve levofloksasin 750 mg/gün IV başlandı.

Covid-19 PZR testi negatif saptandı. İmmünokromatografik yöntemle araştırılan idrarda L. pneumophila serogrup 1 antijeni pozitif sonuçlandı. Balgam örneğinden gönderilen multiplex PZR testinde de Legionella pneumophila pozitif saptandı, hastanın Sağlık Müdürlüğüne bildirimi yapıldı. Genel durumu düzelen, oksijen satürasyonu normal değerlerine dönen hastada levofloksasin tedavisi 14 güne tamamlamak üzere taburcu edildi.



Resim. Hastanın yatış esnasında çekilen Toraks BT'sinde sağ akciğer alt lobda konsolidasyon ve buzlu cam tarzında dansite artımı

Tartışma

Pnömoni, Legionella infeksiyonunun en yaygın olarak tanımlanan bulgusudur ve Lejyoner hastalığı olarak da isimlendirilir [6]. Legionella pneumophila (L. pneumophila) insidansı toplumdan edinilmiş pnömonilerde %1-30 bildirilmektedir [7,8].

L. pneumophila pnömonisinde klinik bulgular; hafif öksürük ve ateşten, yaygın pulmoner tutulumla karakterize pnömoni, akut respiratuvar distress sendromu ve çoklu organ yetersizliğine kadar değişen bir spektruma sahiptir [1-3,6,7].

L. pneumophila pnömonisinde hastalarda ateş, halsizlik, baş ağrısı, myalji, prodüktif olmayan öksürük gibi nonspesifik bulgular görülebilir. İshal olguların %25-50'sinde görülür. Nörolojik semptomlar, baş ağrısı, letarji ve ileri evrede ensefalopatidir [1-3,5,6].

Sunduğumuz olguda fizik muayenede yüksek ateş (39°C), öksürük, nefes darlığı, takipne ve sağ akciğer bazalde raller mevcuttu,ishal ve nörolojik semptomlar yoktu. Legionella pnömonisinde laboratuvar testlerinde transaminazlar, kreatinin fosfokinaz ve LDH yüksekliğiyle hiponatremi ve hipofosfatemi görülebilir [1,3,4,6,7]. Sunduğumuz hastada laboratuar değerlerinde LDH değerlerinde artış, lökositoz, CRP değeri ve sedimentasyon hızında yükseklik mevcuttu.

L. pneumophila tanısında, balgam, bronkoalveoler lavaj gibi alt solunum yolu örneklerinde kültür, direkt floresan antikor testi (DFA), serumda indirekt floresan antikor testi ya da ELISA testi, idrarda antijen testi veya polimeraz zincir reaksiyonu (PZR) testi kullanılmaktadır. [1,2,4,6]. Tanıda idrarda antijen testi, sadece L. pneumophila serogrup 1'i gösterir ve pnömoni olgularının %85'inde serogrup 1'e bağlı gelişir. Bu testin duyarlılığı %70, özgüllüğü ise %100'dür [3,9]. Sunduğumuz hastada Legionella pnömonisi kesin tanısı idrarda Legionella antijen testinin pozitifliği ve balgamda multipleks PZR yöntemiyle Legionella pneumophila'nın saptanmasıyla kondu.

L. pneumophila'da akciğer grafisi bulguları genellikle nonspesifiktir. Kavitasyon ve apse oluşumu nadirdir. Sıklıkla hızla progresyon gösteren asimetrik yamalı infiltrasyonlar gözlenir. Akciğer tomografisinde L.pneomophila pnömonisinde sıklıkla perihiler bölgelerde, sınırları belirli, demarkasyon hatları oluşturan buzlu cam dansitesi şeklinde görülebilir [10].

Covid-19 infeksiyonuna bağlı akciğer tutulumunda BT'de farklı tutulum şekilleri görülebilmekle birlikte genellikle viral pnömoniyi düşündüren iki taraflı, periferik dağılıma sahip ve alt lobları tutan buzlu cam görüntüsü (opasiteleri) görülebilir. Buzlu cam görüntülerine konsolidasyon anormallikleri eşlik edebilir veya eşlik etmeyebilir [11].

Sunduğumuz olguda, Covid-19 pandemisi döneminde gelmesi, Covid-19 infeksiyonunda görülebilen yüksek ateş, öksürük ve nefes darlığı semptomlarının olması ve toraks BT'de sağ akciğer alt lobda konsolidasyon ve buzlu cam tarzında dansite artımı gösteren infiltrasyon alanı saptanması nedeniyle kesin tanı için Covid-19 PZR testi istendi.

Legionella infeksiyonunun tedavisinde levofloksasin, veya azitromisin tedavide ilk tercih ilaçlardır [12,13]. Legionella pnömonisi alternatif ilaçlar moksifloksasin, siprofloksasin , makrolidler ve tetrasiklinlerdir [13]. Cecci ve ark. [12] Legionella pnömonisinde mortalite oranını florokinolon bazlı tedavi alan hastalarda, florokinolon dışı tedavi alan hastalara göre daha düşük oranda bildirmişlerdir.

L. pneumophila pnömonisinde tedavi süresi ortalama 7-14 gün arasında önerilmektedir [1,10,13]. Ağır olgularda tedavi süresi 21 güne kadar uzatılabilir [1].

Sunduğumuz hastada tedavide başlangıçta pnömoniye yönelik ampirik olarak seftriakson ve levofloksasin tedavisi başlandı, idrarda Legionella antijen testi ve balgamda Legionella PZR testi pozitif saptanınca tedavi levofloksasinle 14 güne tamamlandı.

Akıncı ve ark. [4] ateş, kuru öksürük ve konuşma bozukluğu şikayetleri ile başvuran, şikayetlerinden bir hafta önce otelde konaklama öyküsü olan ve 4 gün süreyle amoksisilin/klavulonat kullanmasına rağmen şikayetleri geçmeyen 56 yaşında bir erkek hastada idrarda Legionella antijeninin pozitif saptanması ile tanı koymuşlardır. Hastanın kaldığı otelden alınan su örneklerinden yapılan kültürde Legionella pneumophila serogrup 1 üretilmiştir. Hastaya klaritromisin ve rifampisin kombinasyonu 21 gün süreyle uygulanmıştır.

Özyürek ve ark. [7] öksürük, ateş, halsizlik ve bir haftadır süren ishal yakınmaları olan 18 yaşında erkek hastada L.pneumophila'ya bağlı olarak gelişen pnömoni bildirmişlerdir. Hastada klinik ve radyolojik olarak pnömoni bulgularının saptanması, pnömoniye ishalin eşlik etmesi, transaminaz yüksekliği (AST 143 IU/L, ALT 104 U/L), hiponatremi (126 mEq/L) varlığı ve daha önceden kullanılan beta laktam antibiyotik tedavisine yanıt alınamaması nedeniyle L.pneumophila pnömonisi ön tanısı konulmuştur. Hastada kesin tanı indirekt fluoresan antikor (IFA) testi pozitifliği ile konmuştur.

Sunduğumuz olguda, anamnezde sigara kullanımı ve otelde duş alma öyküsü olması, klinik ve radyolojik olarak pnömoni bulgularının olması nedeniyle hastada Legionella pnömonisi olabileceği düşünüldü. Kesin tanı, idrar örneği Legionella antijeni pozitifliği ve balgam örneğinde multiplex PZR testinde de Legionella pneumophila pozitif saptanması ile konuldu. Hastaya levofloksasin tedavisinin 14 gün süreyle uygulanması planlandı.

Sonuç olarak, Covid-19 pandemi döneminde Legionella pneumophila pnömonisinin Covid-19 pnömonisi ile karışabileceği ve anamnez ve klinik bulguları legionella ile uyumlu hastalarda legionellozun akılda tutulması gerektiği görüşündeyiz

Kaynaklar

1. Siyah ÜÖ, Arslan K, Cesur S, Hatipoğlu ÇA, Sevim Ş, Kınıklı S. Akut Solunum Sıkıntısı Sendromuna İlerleyen Toplum Kaynaklı Legionella pneumophila Pnömonisi: Bir Olgu Sunumu. Klimik Dergisi 2020; 33: 95-99.
2. Mülazimoglu L, Yu VL. Can legionnaires' disease be diagnosed by clinical criteria?: a critical review. Chest 2001; 120: 1049-53.
3. Edelstein PH, Roy CR. Legionnaires' disease and Pontiac fever. In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th ed. Philadelphia, PA: Elsevier Saunders, 2015: 234, 2633-44.
4. Akıncı E, Baran G, Erbay A, Çolpan A, Afacan G, Bodur H. Lejyoner Hastalığı: Bir Olgu Nedeniyle. T Klin J Microbiol-Infec 2003; 2: 28-31.
5. Stout JE, Yu VL. Legionellosis. New Engl J Med 1997; 337: 682-87.
6. Murdoch D, Chambers ST, Priest P. Clinical manifestations and diagnosis of Legionella infection. UptoDate 2020.
7. Özyürek S, Şimşek S, Hocaoğlu B, Hitit G, Göktaş P. Toplumdan Edinilmiş Bir Legionella pneumophila Pnömonisi Olgusu. Flora 1997; 3: 212-15.
8. Torres A, Serra-Batlles. Severe Community-acquired Pneumonia. Am Rev Respir Dis 1991; 144: 312-8.
9. Erdogan H, Erdogan A, Lakamdayali H, Yilmaz A, Arslan H. Travel-associated Legionnaires disease: Clinical features of 17 cases and a review of the literature. Diagn Microbiol Infect Dis. 2010; 68: 297-303.
10. Küpeli E. Atipik pnömoniler. Şen N, Özhan MH (Editör) Pnömoni. Türkiye Solunum Araştırmaları Derneği, Eğitim Kitapları Serisi yayınları, 2017: 83-111.
11. McIntosh K. Coronavirus disease 2019 (COVID-19): Clinical features. UptoDate 2021.
12. Cecchini J, Tuffet S, Sonneville R et al. Antimicrobial strategy for severe community-acquired legionnaires' disease: A multicentre retrospective observational study. J Antimicrob Chemother. 2017; 72: 1502-9.
13. Murdoch D, Chambers ST, Priest P. Treatment and prevention of Legionella infection. UptoDate 2020.

To cite this article: Bozdogan D, Caliskan A. Repair of recurrent upper extremity pseudoaneurysm secondary to glass laceration in 4 years old girl. Turk J Clin Lab 2021; 1: 120-122.

Case Report

Repair of A recurrent upper extremity pseudoaneurysm secondary to glass laceration in a 4 years old girl

4 yaşında bir kız çocuğunda cam kesisi sonrası oluşan rekürren üst ekstremite psödoanevrizmasının onarımı

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Abstract

Pseudoaneurysm (PA) of radial artery is rare especially in the children. The real incidence is unknown, probably because these lesions are seldom reported, especially in children. In this case report, we aimed to share our experience on this subject.

Keywords: pseudoaneurysm; false aneurysm; radial artery injury

ÖZ

Radyal arter psödoanevrizması çocuk yaş gruplarında nadir rastlanan bir durumdur. Gerçek insidans bilinmemektedir çünkü özellikle çocuk yaş grubunda rapor edilen olgu sayısı oldukça azdır. Bu olgu sunumda konu ile ilgili tecrübemizi paylaşmak istedik

Anahtar kelimeler: psödoanevrizma; yalancı anevrizma; radyal arter hasarı

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Recevied: 08.12.2020 accepted: 16.02.2021
Doi: 10.18663/tjcl.893297

Volume 12 Number 1 p: 120-122

Introduction

In childhood, pseudoaneurysm (PA) of upper ekstremity is rare and even less common in radial artery.[1] The most common causes of radial PA in children are penetrating trauma and iatrogenic arterial injury.[2] Symptoms and signs of a PA are almost always associated with its size and localization.[3] Diagnosis can be confirmed by color Doppler utrasonography. Early intervention is recommended when it is diagnosed. [4,5] Conservative or Surgical/Endovascular treatments should be performed as soon as possible to prevent possible complications, such as rupture, hemorrhage, thromboembolism, ischemia, venous compression, neurologic complications, and cutaneous erosions.[6] In children, the treatment that protects the blood flow of the hand should be chosen primarily, so as not to disrupt the development of the limb.

Case

A 4 year old girl presented with sudden onset of a swelling in her left wrist. Five days before the appearance of this lump, she sustained a glass laceration of her left wrist which was sutured in an other hospital's emergency room. Two days after that, pseudoaneurysm was diagnosed and treated with ultrasound guided compression therapy in the same hospital. 3 days after that, she admited our hospital with increased pain and swelling . On examination, a 11x7,5 mm diameter expansile mass at the radial aspect of the volar surface of the left wrist was found. (Figure I) The lesion was tender, round shaped, and semicontiguous to the wound site A thrill was palpable and auscultation revealed a bruit. Motor and sensory examinations were unremarkable. The patient underwent to colour duplex ultrasound that showed the presence of PA arising from the main left radial artery, continuous bidirectional blood flow in the neck of the pseudoaneurysm and a turbulent blood flow within the lesion and in the radial artery which was patent. Ulnar artery and palmar arch integrity were also confirmed. Therefore, we decided to perform a surgical exploration of the radial artery. under sedation and local anesthesia. Longitidunal disection was made. Radial artery was reached and secured proximaly and distally. After that, aneurismatic sac was opened. (Figure-II). After the sac had extracted, both ends of the radial artery were identified and oversaw. End to end reconstruction was performed via 8-0 prolene sutures (Figure-III) The child was discharged from the hospital on day 2, with no postoperative complications. Asetilsalisilic asit 3mg/kg/day was recommended.

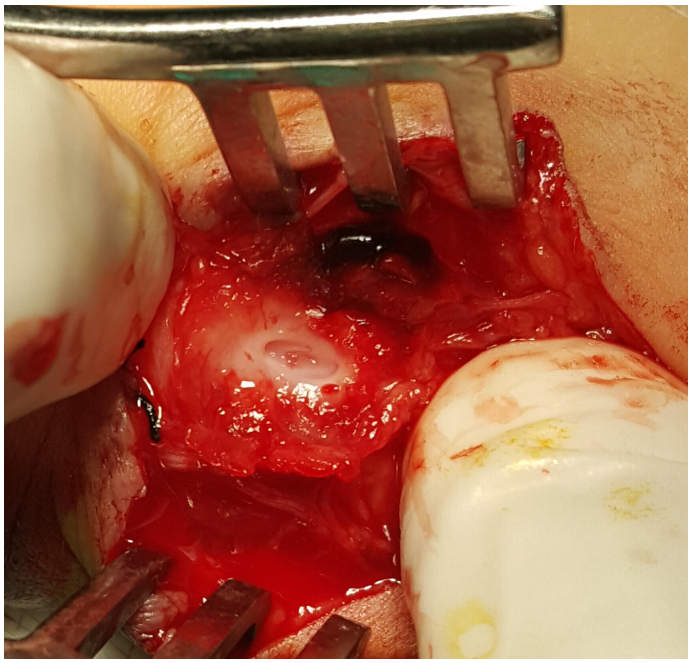

Figure: I

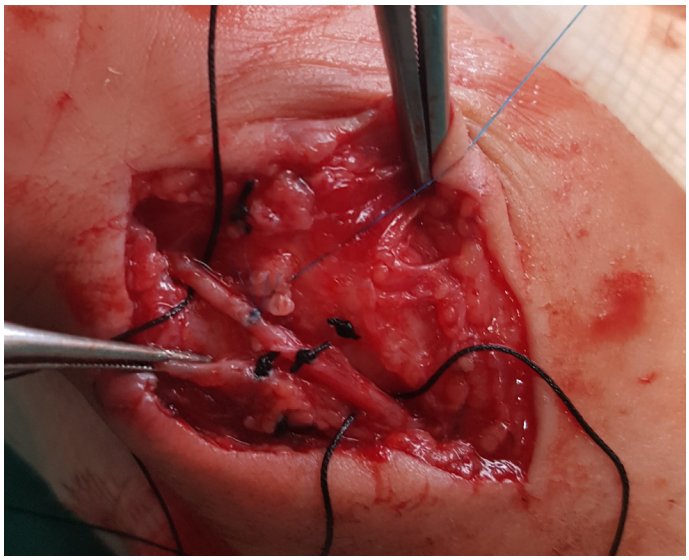

Figure: II

Figure: III

In the repeated follow-ups in the 3rd and 6th months, 1st and 3rd years Doppler usg performed while applying pressure to the ulnar artery did not show any deterioration in the radial artery flow. However, the child hand's development delay and loss of function were not observed.

Discussion

A review of the literature from 2000 to 2018 undertaken on PubMed showed that overall incidence of upper extremity PA was about less than 0.04% in all age.[7] Most common localization of upper extremity PA's is brachial artery.[3] In addition, PA of the distal upper extremity may mimic many other soft tissue masses in the children.[8] Therefore, true incidence of distal radial artery PA are not known, precisely.

Early identification and prompt treatment of radial PA are crucial because they have severe potential complications, such as upper limb, hand and finger losses.[3]

There are various treatment options in the treatment of brachial artery pseudoaneurysms including ultrasound-guided compression, percutaneous thrombin injection, endovascular stenting, aneurysmectomy, surgical repair, and artery ligation.[9]

Ultrasound-guided compression therapy is a non-invasive treatment option. Ceccanti et al. It recommends compression therapy as the first option for upper limb distal pseudoaneurysms, regardless of the the size of the aneurysms. If the pseudoaneurysm is not thrombosed after 4 weeks of compression treatment and / or aneurysm grows, interventional treatments are recommended.[8]

thrombin injection is another recommended treatment. It has been shown to be used effectively in radial and brachial artery pseudoaneurysms. It can be applied safely in all age groups. A disadvantage of the procedure is that it requires experienced hands. Nerve damage due to the procedure has been reported. Hematoma, new pseudoaneurysm and intravascular thrombosis may develop at the sheat intervention site placed during the procedure.[10]

Surgical intervention is needed in complicated situations; such as symptomatic, expanding, and with large haematomas, and in patients with failed conservative management. such as ultrasound-guided compression, percutaneous, thrombin injection.[11]

Prompt surgical treatment options which is include ligation of the artery if distal circulation is not compromised, excision of the pseudoaneurysm, and anastomosis using patch graft or end to end anastomosis are asociated with satisfactory results. However, current operative management after excision of radial pseudoaneurysm remains controversial, with some authors advising vascular reconstruction, and others opting for arterial ligation.[11]

In order to prevent delay in limb growth with complete restoration of hand blood circulation in children, we chosen the method including pseudoaneurysm excision and radial artery reconstruction.[3]

Conclusion

Pseudoaneurysm of radial artery in the childhood is rare. The real incidence is unknown. Prompt treatment ıs mandatory. Surgical treatment is the most prefered option for patient with distal upper ekstremity pseudoaneurysm. Long term results of surgical or non-surgical treatments is not clear. Our case is very rare due to its location. The method to be used in the treatment of recurrent pseudoaneurysms is still controversial. we believe that; Surgical treatment should be the first choice in recurrent pseudoaneurysms. The technique to be chosen, if possible, is vascular repair, especially for the purpose of preserving limb development in pediatric patients.

*Local Ethical Committee reviewed and approved the research protocol of our study. Informed constent was obtained from parents of the patient and the principles of the Helsinki Declaration were followed.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

References

1. Coşkunfirat OK, Özgentaş HE. True aneurysm of the radial artery after iatrogenic injury and successful reconstruction with an interposition vein graft. J Reconstr Microsurg. 2003; 19: 143-6
2. Levis JT, Garmel GM. Radial Artery Pseudoaneurysm Formation After Cat Bite to the Wrist. Ann Emerg Med 2008; 51: 668–70.
3. Yuksel A, Nas OF, Kan II, Tok M, Erdogan C. Percutaneous Coil Embolization for the Treatment of a Giant Brachial Artery Pseudoaneurym in a Child. Ann Vasc Surg 2017; 45: 56-8.
4. Turowski GA, Amjadi N, Sterling A, Grant Thomson J. Aneurysm of the radial artery following blunt trauma to the wrist. Ann Plast Surg. 1997; 23: 527-30
5. Kara H. Surgical treatment of iatrogenic pseudoaneurysms. Turkish J Vasc Surg 2019; 28: 174–9.
6. Sarkar R, Coran AG, Cilley RE, Lindenauer SM, Stanley JC. Arterial aneurysms in children: Clinicopathologic classification. J Vasc Surg 1991; 13: 47-56
7. Sheiman RG, Brophy DP, Perry LJ, Akbari C. Thrombin injection for the repair of brachial artery pseudoaneurysms. Am J Roentgenol 1999; 173: 1029-30
8. Ceccanti S, Frediani S, Andreoli GM, Giannini L, Ferro R, Cozzi DA. Effective compression bandage for repair of a complicated radial artery pseudoaneurysm. Ann Vasc Surg 2014; 28: 9-12
9. Brophy DP, Sheiman RG, Amatulle P, Akbari CM. Iatrogenic femoral pseudoaneurysms: Thrombin injection after failed US-guided compression. Radiology. 2000; 214: 278-82
10. Garvin RP, Ryer EJ, Yoon HR et al. Ultrasound-guided percutaneous thrombin injection of iatrogenic upper extremity pseudoaneurysms. J Vasc Surg 2012; 59: 1664–9.
11. Leone V, Misuri D, Console N. Radial artery pseudoaneurysm after a single arterial puncture for blood-gas analysis: A case report Cases J. 2009; 2: 1–3.

Turkish Journal of Clinics and Laboratory

To cite this article: Erratum: Cakmak HSG, Akdemir N. Knowledge and implication about oral antineoplastics drugs use of cancer patient. Turk J Clin Lab 2020; 5: 387-392.

Original Article

Knowledge and implication about oral antineoplastics drugs use of cancer patients

Kanser hastalarının oral antineoplastik ilaç kullanımına ilişkin bilgi ve uygulamaları

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2020 ARALIK (2020-11-5) SAYISINDA YAYINLANAN YUKARIDA BELİRTİLEN YAZIDA KURUM İSİMLERİ HATALI OLMUŞTUR. DÜZELTİLMİŞ HALİ 2021 MART SAYISINDA DÜZELTİLMİŞ VE SON HALİ BU ŞEKİLDERDİR.

TJCL EDİTÖR KURULU

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Recevied: 13/01/2020 accepted: 09/03/2020
Doi: 10.18663/tjcl.674152

TURKISH JOURNAL of CLINICS and LABORATORY

Türk Klinik ve Laboratuvar Dergisi

Turkish Journal of Clinics and Laboratory - Türk Klinik ve Laboratuvar Dergisi

Tıp dergilerine gönderilecek makalelerin standart gereksinmeleri ile ilgili tüm bilgileri www.icmje.org internet adresinde bulabilirsiniz

Amaç ve kapsam: "Turkish Journal of Clinics and Laboratory", hakemli, açık erişimli ve periyodik olarak çıkan, DNT Ortadoğu Yayıncılık A.Ş. ye ait bir dergidir. Hedefimiz uluslararası bir tabanda hastalıkların teşhis ve tedavisinde yenilikler içeren yüksek kalitede bilimsel makaleler yayınlamaktır. Yılda dört kez çıkan bir bilimsel bir tıp dergisidir. Hakemli bir dergi olarak gelen yazılar konsültanlar tarafından, öncelikle, biyomedikal makalelere ait Uluslararası Tıp Dergileri Editörleri Komitesi (www.icmje.org adresinden ulaşılabilir) tarafından tanımlanan standart gereksinimler ile ilgili ortak kurallara uygunluğu açısından değerlendirilir. Tıbbın her dalı ile ilgili retrospektif/prospektif klinik ve laboratuar çalışmalar, ilginç olgu sunumları, davet üzerine yazılan derlemeler, editöre mektuplar, orijinal görüntüler, kısa raporlar ve cerrahi teknik yazılarıları yayımlayan bilimsel, uluslar arası hakemli bir dergidir. Başka bir dergide yayımlanmış veya değerlendirilmek üzere gönderilmiş yazılar veya dergi kurallarına göre hazırlanmamış yazılar değerlendirme için kabul edilmez.

On-line makale gönderimi: Tüm yazışmalar ve yazı gönderimleri dergipark üzerinden http://dergipark.gov.tr/tjcl yapılmalıdır. Yazı gönderimi için detaylı bilgi bu internet adresinden edinilebilir. Gönderilen her yazı için özel bir numara verilecek ve yazının alındığı e-posta yolu ile teyid edilecektir. Makalelerin "full-text" pdf formuna http://dergipark.gov.tr/tjcl linkinden ulaşılabilir.

Açık erişim politikası: Turkish Journal of Clinics and Laboratory açık erişimi olan bir dergidir. Kullanıcı lar yazıların tam metnine ulaşabilir, kaynak gösterilerek tüm makaleler bilimsel çalışmalarda kullanılabilir.

Aşağıdaki rehber dergiye gönderilen makalelerde aranan standartları göstermektedir. Bu uluslararası format, makale değerlendirme ve basım aşamalarının hızla yapılmasını sağlayacaktır.

Yazarlara Bilgi: Yazıların tüm bilimsel sorumluluğunu yazar(lar)a aittir. Editör, yardımcı editör ve yayıncı dergide yayınlanan yazılar için herhangi bir sorumluluk kabul etmez.

Dergi adının kısaltması: Turk J Clin Lab

Yazışma adresi: Yazılar e-mail yoluyla sorumlu yazar tarafından, Dergipark ta yer alan Turkish Journal of Clinics and Laboratory linkine girip kayıt olduktan sonra gönderilmelidir.

Makale dili: Makale dili Türkçe ve İngilizcedir. İngilizce makaleler gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanı tarafından düzeltilebilir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu amaçla, Türk Dil Kurumu Sözlük ve Yazım Kılavuzu yazım dilinde esas alınmalıdır.

Makalenin başka bir yerde yayımlanmamıştır ibaresi: Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. 400 kelimeden az özetler kapsam dışıdır. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

Değerlendirme: Dergiye gönderilen yazılar format ve plagiarism açısından değerlendirilir. Formata uygun olmayan yazılar değerlendirilmeden sorumlu yazara geri gönderilir. Bu tarz bir zaman kaybının olmaması için yazım kuralları gözden geçirilmelidir. Basım için gönderilen tüm yazılar iki veya daha fazla yerli/yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayıma kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir. Makalenin dergiye gönderilmesi veya basıma kabul edilmesi sonrası isim sırası değiştirilemez, yazar ismi eklenip çıkartılamaz.

Basıma kabul edilmesi: Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak basım sırasına alınır. Her yazı için bir doi numarası alınır.

Yayın hakları devri: http:/www.dergipark.ulakbim.gov.tr/tjclinlab adresi üzerinden online olarak gönderilmelidir. 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.

Etik kurallar: Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. Turkish Journal of Clinics and Laboratory gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Teşekkür yazısı: Varsa kaynaklardan sonra yazılmalıdır.

Maddi destek ve çıkar ilişkisi: Makale sonunda varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmelidir. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları "Cumulated Index Medicus" ta kullanılan stile uymalıdır. Kaynak sayısının araştırmalarda 25 ve derlemelerde 60, olgu sunumlarında 10, editöre mektupta 5 ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce köşeli parantez kullanılarak belirtilmelidir. Örneğin [4,5]. Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

Şekil ve tablo başlıkları: Başlıklar kaynaklardan sonra yazılmalıdır.

4. Şekiller: Her biri ayrı bir görüntü dosyası (jpg) olarak gönderilmelidir.

Makalenin basıma kabulünden sonra "Dizginin ilk düzeltme nüshası" sorumlu yazara e-mail yoluyla gönderilecektir. Bu metinde sadece yazım hataları düzeltilecek, ekleme çıkartma yapılmayacaktır. Sorumlu yazar düzeltmeleri 2 gün içinde bir dosya halinde e-mail ile yayın idare merkezine bildirecektir.

Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

Özpolat B, Gürpınar ÖA, Ayva EŞ, Gazyağcı S, Niyaz M. The effect of Basic Fibroblast Growth Factor and adipose tissue derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end to end anastomosis rat model. Turk Gogus Kalp Dama 2013; 21: 1010-19.

Kitaptan yapılan alıntı;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Tek yazar ve editörü olan kitaptan alıntı;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams&Wilkins; 1996: 46-60.

Çoklu yazar ve editörü olan kitaptan alıntı;

Schulz JE, Parran T Jr: Principles of identification and intervention. In:Principles of Addicton Medicine, Graham AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams&Wilkins; 1998:1-10.

Eğer editör aynı zamanda kitap içinde bölüm yazarı ise;

Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag;1988:45-67.

Doktora/Lisans Tezinden alıntı;

Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

Sitenin adı, URL adresi, yazar adları, ulaşım tarihi detaylı olarak verilmelidir.

DOI numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of Complementary and Alternative Medicine into Family Practice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

Diğer referans stilleri için "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References" sayfasını ziyaret ediniz.

Bilimsel sorumluluk beyanı: Kabul edilen bir makalenin yayınlanmasından önce her yazar, araştırmaya, içeriğinin sorumluluğunu paylaşmaya yetecek boyutta katıldığını beyan etmelidir. Bu katılım şu konularda olabilir:

a. Deneylerin konsept ve dizaynlarının oluşturulması, veya verilerin toplanması, analizi ya da ifade edilmesi;

b. Makalenin taslağının hazırlanması veya bilimsel içeriğinin gözden geçirilmesi

c. Makalenin basılmaya hazır son halinin onaylanması.

Yazının bir başka yere yayın için gönderilmediğinin beyanı: "Bu çalışmanın içindeki materyalin tamamı ya da bir kısmının daha önce herhangi bir yerde yayınlanmadığını, ve halihazırda da yayın için başka bir yerde değerlendirilmede olmadığını beyan ederim. Bu, 400 kelimeye kadar olan özetler hariç, sempozyumlar, bilgi aktarımları, kitaplar, davet üzerine yazılan makaleler, elektronik formatta gönderimler ve her türden ön bildirileri içerir."

Sponsorluk beyanı: Yazarlar aşağıda belirtilen alanlarda, varsa çalışmaya sponsorluk edenlerin rollerini beyan etmelidirler:

1. Çalışmanın dizaynı

2. Veri toplanması, analizi ve sonuçların yorumlanması

3. Raporun yazılması

Kontrol listesi:

1. Editöre sunum sayfası (Sorumlu yazar tarafından yazılmış olmalıdır)

2. Başlık sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Yazarlar, kurumları, sorumlu yazar posta adresi, tüm yazarların e-mail adresleri, sorumlu yazarın telefon numarası)

3. Makalenin metin sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Özet/anahtar kelimeler, Summary/keywords, makale metni, kaynaklar, tablo ve şekil başlıkları, tablolar, şekiller)

4. Tablo ve grafikler metin içinde olmalıdır.

5. Şekiller (En az 300 dpi çözünürlükte) ayrı bir veya daha fazla dosya halinde gönderilmelidir.