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Journal article on the Internet Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm Website Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

An organization as an author The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

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CONTENTS

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ORIGINAL ARTICLE

Comparison of Pet Owners and Non-Pet Owners in Terms of Depression, Anxiety and Quality of Life

Evcil Hayvan Sahibi Olanlar ve Olmayanların Depresyon, Anksiyete ve Yaşam Kalitesi Açısından Karşılaştırılması

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ABSTRACT

Objective: In this study, it was aimed to compare pet owners and non-pet owners in terms of depression, anxiety and quality of life.
Methods: A total of 397 healthy volunteers over the age of 18, 192 pet owners, and 205 non-pet owners were included in our study. Sociodemographic data form, World Health Organization Quality of Life Scale-Short Form (SF-36), and Hospital Anxiety and Depression Scale (HADS) were administered to all participants.
Results: Of all participants, 60.2% (n=239) were female and 39.8% (n=158) were male. The mean age of pet owners (36.74±9.56) was similar to non-pet owners (35.52±9.16) (p=0.194). The mean depression scores of pet owners (4.39±3.37) were significantly lower than non-pet owners (6.02±3.72) (p<0.001). The mean anxiety scores of pet owners (5.82±3.49) were significantly lower than non-pet owners (7.24±4.07) (p<0.001). Physical function, emotional role function, energy vitality, mental health and pain mean scores of SF-36 subscales were found to be significantly higher in pet owners (respectively; p=0.020, p=0.020, p=0.039, p=0.031, p=0.025).
Conclusion: It can be said that pet owners have a lower risk of depression and anxiety, and in many fields have a better quality of life.

Keywords: Pet, Cat, Dog, Depression, Anxiety, Quality of Life

ÖZ

Amaç: Bu çalışmada, evcil hayvan sahibi olan kişilerle evcil hayvan sahibi olmayan kişilerin depresyon, anksiyete ve yaşam kalitesi açısından karşılaştırılması amaçlanmıştır.
Yöntem: Çalışmamıza, 192 evcil hayvan sahibi olan ve 205 evcil hayvan sahibi olmayan 18 yaş üstü toplam 397 sağlıklı gönüllü dahil edilmiştir. Tüm katılımcılara sosyodemografik veri formu, Dünya Sağlık Örgütü Yaşam Kalitesi Ölçeği-Kısa Formu (SF-36) ve Hastane Anksiyete ve Depresyon Ölçeği (HADÖ) uygulanmıştır.
Bulgular: Tüm katılımcıların %60.2'si (n=239) kadın, %39.8'i (n=158) erkekti. Evcil hayvan sahibi olanların yaş ortalaması (36.74±9.56), evcil hayvan sahibi olmayanların yaş ortalaması (35.52±9.16) ile benzerdi (p=0.194). Evcil hayvan sahibi olanların depresyon puan ortalamaları (4.39±3.37) evcil hayvan sahibi olmayanlardan (6.02±3.72) anlamlı derecede düşüktü (p<0.001). Evcil hayvan sahibi olanların anksiyete puan ortalamaları (5.82±3.49) evcil hayvan sahibi olmayanlardan (7.24±4.07) anlamlı derecede düşüktü (p<0.001). Evcil hayvan sahibi olanlarda SF-36 alt ölçeklerinden fiziksel fonksiyon, emosyonel rol güçlüğü, enerji canlılık, ruhsal sağlık ve ağrı puan ortalamaları anlamlı olarak daha yüksek saptanmıştır (sırayla; p=0.020, p=0.020, p=0.039, p=0.031, p=0.025).
Sonuç: Evcil hayvan sahibi olanların depresyon ve anksiyete açısından daha düşük riske sahip olduğu ve birçok alanda daha iyi bir yaşam kalitesine sahip olduğu söylenebilir.

Anahtar Kelimeler: Evcil hayvan, Kedi, Köpek, Depresyon, Anksiyete, Yaşam kalitesi

Introduction

The number of people who own pets all over the world has been increasing rapidly in recent years (1). Pets play important roles in people's lives, providing companionship and entertainment to people. There is evidence that owning a pet can improve human psychological health through the development of strong emotional bonds (2). Having a pet has many benefits in terms of mental health, such as reducing stress, increasing the quality of life, and supporting social interaction (3, 4). In a cross-sectional study of pet owners over the age of 13 living in Bangladesh, 140 pet owners and 140 non-pet owners were compared. It has been reported that pet owners are 41% less depressed than non-pet owners (5). In another study, it was shown that people with Acquired Immunodeficiency Syndrome (AIDS) who own a pet report less depression than people with AIDS who do not own a pet (6). One study evaluated whether owning a pet contributes to long-term survival, independent of depression and anxiety, in patients who survived at least 6 months after myocardial infarction. In conclusion, not having a pet has been reported as the only significant independent predictor of mortality (7). The type of pet was also evaluated in studies. A Norwegian study reported that owning a dog showed better health outcomes than a cat or not pet owners. Cat owners reported worse general health (8). The number of studies evaluating the quality of life in pet owners is limited, and in a study evaluating the quality of life in pet owners in New Zealand, dog ownership was associated with significantly higher scores on physical quality of life only (9). The effect of owning a cat and/or dog on

quality of life was investigated during a strict lockdown period in Victoria, Australia, during the coronavirus 19 (COVID-19) pandemic. Pet ownership has been found to be significantly associated with lower quality of life (10).

Studies evaluating depression, anxiety, and quality of life together on this subject are rare. In this respect, our study can contribute to the literature. In this study, it was aimed to investigate whether there is a difference in depression, anxiety and quality of life between pet owners and non-pet owners.

Materials And Methods

Sample

Our study is a cross-sectional study conducted between 20 August 2021 and 20 September 2021. A total of 397 healthy volunteers, 192 people with pets and 205 people without pets, were included in the study. Sociodemographic data form, Hospital Anxiety and Depression Scale (11), World Health Organization Quality of Life Scale-Short Form (SF-36) (12) were administered to all participants. The surveys were created using Google Docs. We sent all participants an introductory note detailing the purpose of the study and an assurance that the confidentiality of the data would be preserved. A confirmation tab was added stating that participation in the survey was on a voluntary basis, and online consent was obtained from those who voluntarily agreed to participate in the study. After obtaining informed consent, those who agreed to participate in the study were able to continue to fill out the scales. This questionnaire was sent to all researchers' contacts using WhatsApp Messenger, an American free software owned by Facebook Inc., a cross-platform messaging service. The criteria for inclusion in the study were to be over the age of 18 and to be at least a primary school graduate. Exclusion criteria from the study were determined as having a severe internal disease that may affect the quality of life and having an active psychiatric disease. All stages of this study were carried out in accordance with the rules of the Declaration of Helsinki. Written ethics committee approval was obtained from XXXXX University Faculty of Medicine Clinical Research Ethics Committee with the decision number KAEK-602 on 18.08.2021.

Statistical analysis

SPSS 23.0 program was used for analysis. Kolmogorov Smirnov test was used for the assumption of normality. Descriptive variables are given as median, 25% and 75% quartiles (Q1-Q3), mean ± standard deviation, minimum, maximum, percentage and number. Chi-square test was used in the analysis of categorical data. In the comparison of the two groups, the T-test was used when the data were normally distributed, and the Mann-Whitney U test was used when the data were not normally distributed. The Kruskal Wallis H Test was used when the data were not normally distributed in the analysis of the difference between the numerical values of the three or more groups. Spearman correlation analysis was used for correlation analysis. $p<0.05$ was considered statistically significant.

Results

239 (60.2%) of the participants were female and 158 (39.8%) were male. While 192 (48.4%) people had a pet, 205 (51.6%) people did not have any pets. Sociodemographic characteristics of pet owners and non-pet owners are summarized in Table 1.

Table 1. Comparison of sociodemographic characteristics of pet owners and non-pet owners.

		Pet owner (n=192)		Non-pet owner (n=205)		χ2	z	p
		n	%	n	%			
Gender	Female	111	57.8	128	62.4	0.886		0.347
	Male	81	42.2	77	37.6			
Marital status	Married	62	32.3	78	38.0			
	Single	122	63.5	114	55.6	2.868		0.238
	Married	8	4.2	13	6.3			
Educational status	Primary school	1	0.5	1	0.5			
	High school	10	5.2	14	6.8	0.460		0.574
	University	181	94.3	190	92.7			
Pet type	Cat	128	66.7					
	Dog	38	19.8					
	Bird	21	10.9					
	Others	5	2.6					
Age (Year) (Median) (Q1-Q3)		36 (29-43)		34 (29.50-41)			-1.299	0.194
Duration (months) (mean±SD) (min-max)		45.27±59.09 (1-420)						
Number of pets (median) (min-max)		1 (1-40)						

Depression and anxiety mean scores of pet owners were found to be significantly lower than non-pet owners (respectively; $p<0.001$, $p<0.001$). SF-36 physical function, emotional role difficulty, energy vitality, mental health, and pain mean scores of those who own pets were found to be significantly higher (respectively; $p=0.020$, $p=0.020$, $p=0.039$, $p=0.031$, $p=0.025$). No significant difference was found in the mean scores of physical role difficulty, social functionality and general health (respectively; $p=0.443$, $p=0.070$, $p=0.211$).

Negative and significant correlations were found between depression and anxiety scores and SF-36 subscale scores (all p values < 0.001). When a comparison was made according to the pet type (cat, dog, bird, other), no significant difference was found

Table 2. Comparison of the quality of life scale (SF-36) and hospital anxiety and depression scale scores of pet owners and non-pet owners.

	Pet owner (n=192)	Non-pet owner (n=205)	z	t	p
Depression (mean±SD) (min-max)	4.39±3.37 (0-15)	6.02±3.72 (0-17)	-4.588		***<0.001***
Median (Q1-Q3)	3.50 (2-7)	6 (3-9)			
Anxiety (mean±SD) (min-max)	5.82±3.49 (0-16)	7.24±4.07 (0-20)	-3.550		***<0.001***
Median (Q1-Q3)	6 (3-8)	7 (4-10)			
Physical function (mean±SD)	90.47±13.66	85.98±19.07	-2.330		***0.020***
Median (Q1-Q3)	95 (86.25-100)	95 (80-100)			
Physical role function (mean±SD)	84.24±30.63	81.10±33.39	-0.767		0.443
Median (Q1-Q3)	100 (75-100)	100 (75-100)			
Emotional role function (mean±SD)	77.43±35.12	67.48±41.28	-2.320		***0.020***
Median (Q1-Q3)	100 (66.66-100)	100 (33.33-100)			
Energy vitality (mean±SD)	57.14±19.55	52.93±20.83		-2.072	***0.039***
Mental health (mean±SD)	65.29±16.60	61.35±18.05	-2.157		***0.031***
Median (Q1-Q3)	64 (52-80)	60 (48-76)			
Social function (mean±SD)	73.89±18.08	70.43±18.56	-1.809		0.070
Median (Q1-Q3)	75 (62.50-87.50)	75 (62.50-87.50)			
Pain (mean±SD)	83.83±16.93	79.68±18.94	-2.234		***0.025***
Median (Q1-Q3)	90 (77.50-100)	87.50 (67.50-90)			
General health (mean±SD)	66.80±14.72	64.87±15.79		-1.253	0.211

in terms of depression and anxiety scores (respectively; p=0.221, p=0.144). In addition, no significant difference was found in terms of quality of life according to the type of pet (p>0.05 was found in all subscales when comparing the SF-36 subscale scores).

Discussion

In our study, it was determined that the average score of depression and anxiety was lower in those who owned a pet. Pet owners were found to have a better quality of life in the areas of physical function, emotional role functioning, energy vitality, mental health, and pain.

In a study, it was reported that pet owners had lower depression scores compared to non-pet owners (5). In a meta-analysis to determine the effectiveness of animal-assisted activities and animal-assisted therapy to reduce depressive symptoms in humans, it was shown that animal-assisted activities and animal-assisted therapy were associated with fewer depressive symptoms (13). In another study, it was shown that even a short 20-minute session with a therapy dog can be an effective alternative intervention to reduce anxiety in students (14). In a study conducted in our country, 87 people who own pets and 68 people who do not have pets were compared. As a result of the study, the depression scale scores of those who did not own a pet were found to be significantly higher, but the anxiety scale scores were found to be similar in both groups (15). In a study by Bolstad et al., it was shown that owning a pet was associated with fewer anxiety symptoms, even after calculating various demographic and economic variables (16). In our study, having a pet was associated with less depression and anxiety. It has been reported that there is a significant relationship between different social isolation indicators and loneliness and depressive symptoms in adults (17). Researchers have reported that living with animals has psychological benefits. These benefits have been reported as higher self-esteem, more positive mood, greater life satisfaction, and lower levels of loneliness (18). We think that the lower depression and anxiety levels in pet owners in our study may be related to these conditions.

In our study, depression, anxiety, and quality of life were found to be similar when compared according to the type of pet. There are different results in the literature on this subject, and there are studies reporting that cat owners have significantly lower levels of depressive symptoms than dog owners (19). In another study, it was found that the rates of depression in cat owners were higher than in dog owners and those who did not have pets (8). It has been reported that there is a significant relationship between the level of attachment to pets and mental health (20). The lack of difference between pet types in our study suggested that the levels of attachment to animals might be similar regardless of the pet type.

In our study, it was found that pet owners have a better quality of life in many areas than non-pet owners. In a

study, owning a dog was associated with significantly higher scores in physical quality of life. Having a pet other than a dog or cat was associated with significantly higher social scores. No difference was found in other quality of life domains (9). In another study, it was found that having a pet was significantly associated with lower quality of life (10). It has been reported that attachment styles to pets can affect the quality of life (21). We think that the different quality of life outcomes between studies may be related to this. In addition, studies have reported that anxiety and depression are independent predictors of poor quality of life (22, 23). In our study, significant relationships were found between quality of life and anxiety and depression. We think that a better quality of life in many areas may be associated with lower depression and anxiety levels in pet owners.

Our study is one of the limited numbers of studies conducted in our country on this subject and has a high sample size. These are the strengths of our study. The limitations of our study are that it is cross-sectional, based on self-report, and the pet attachment style was not evaluated. The fact that the number of samples was not determined by power analysis is another limitation of our study.

Conclusion

We can say that having a pet may be associated with better mental health outcomes and better quality of life in many areas. Having a pet can have protective effects, given that mental health problems are on the rise around the world. Our study is one of the rare studies that found lower depression and anxiety levels and higher quality of life in pet owners together. We think that prospective studies with a larger sample size should be conducted on this subject.

Conflict of Interest

None declared by the authors.

Financial Disclosure

None declared by the authors.

References

1.https://www.economist.com/international/2019/06/22/pet-ownership-is-booming-across-the-world.

2.Wells, D. The effects of animals on human health and well-being. Journal of social issues 2009; 65(3): 523.

3.Bakerjian D. Pets impact on quality of life, a case study. Geriatr Nurs 2014; 35(2): 160-163.

4.Koohsari MJ, Yasunaga A, Shibata A, et al. Dog ownership, dog walking, and social capital. Humanities and Social Sciences Communications 2021; 8(1):1-6.

5.Chakma SK, Islam TT, Shahjalal M, Mitra DK. Depression among pet owners and non-pet owners: a comparative cross-sectional study in Dhaka, Bangladesh. F1000Res 2021; 10:574. https://doi.org/10.12688/f1000research.53276.1.

6.Siegel JM, Angulo FJ, Detels R, Wesch J, Mullen A. AIDS diagnosis and depression in the Multicenter AIDS Cohort Study: the ameliorating impact of pet ownership. AIDS Care 1999; 11(2): 157-170.

7.Friedmann E, Thomas SA, Son H. Pets, depression and long term survival in community living patients following myocardial infarction. Anthrozoos 2011; 24(3): 273-285.

8.Enmarker I, Hellzén O, Ekker K, Berg AG. Health in older cat and dog owners: The Nord-Trondelag Health Study (HUNT)-3 study. Scand J Public Health 2012; 40(8): 718-724.

9.Lewis A, Krägeloh CU, Shepherd D. Pet ownership, attachment and health-rated quality of life in New Zealand. Electronic Journal of Applied Psychology: General Articles 2009; 5(1): 96-101.

10.Phillipou A, Tan EJ, Toh WL, et al. Pet ownership and mental health during COVID-19 lockdown. Aust Vet J 2021; 99(10): 423-426.

11.Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67(6): 361-70.

12.Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30(6): 473-83.

13.Souter MA, Miller MD. Do animal-assisted activities effectively treat depression? A meta-analysis. Anthrozoös 2007; 20(2): 167-180.

14.Grajfoner D, Harte E, Potter LM, McGuigan N. The Effect of Dog-Assisted Intervention on Student Well-Being, Mood, and Anxiety. Int J Environ Res Public Health 2017; 14(5): 483.

15.Şan MA. Evcil hayvan sahiplerinde depresyon ve anksiyete düzeylerinin incelenmesi. Master's thesis, Bursa Uludağ Üniversitesi 2020.

16.Bolstad CJ, Porter B, Brown CJ, Kennedy RE, Nadorff MR. The Relation Between Pet Ownership, Anxiety, and Depressive Symptoms in Late Life: Propensity Score Matched Analyses. Anthrozoos 2021; 34(5): 671-684.

17.Ge L, Yap CW, Ong R, Heng BH. Social isolation, loneliness and their relationships with depressive symptoms: A population-based study. PLoS One 2017; 12(8): e0182145.

18.El-Alayli A, Lystad AL, Webb SR, Hollingsworth SL, Ciolli JL. Reigning cats and dogs: A pet-enhancement bias and its link to pet attachment, pet-self similarity, self-enhancement, and well-being. Basic and Applied Social Psychology 2006; 28(2): 131-143.

19.Branson SM, Boss L, Cron S, Turner DC. Depression, loneliness, and pet attachment in homebound older adult cat and dog owners. Journal of Mind and Medical Sciences 2017; 4(1): 38-48.

20.McDonald SE, O'Connor KE, Matijczak A, et al. Attachment to Pets Moderates Transitions in Latent Patterns of Mental Health Following the Onset of the COVID-19 Pandemic: Results of a Survey of U.S. Adults. Animals (Basel) 2021; 11(3): 895.

21.White N, Mills D, Hall S. Attachment Style Is Related to Quality of Life for Assistance Dog Owners. Int J Environ Res Public Health 2017;14(6):658.

22.AbuRuz ME. Anxiety and depression predicted quality of life among patients with heart failure. J Multidiscip Healthc 2018; 11: 367-373.

23.Cakmak S, Gen E. Relationship between quality of life, depression and anxiety in type 1 and type 2 diabetes. Dusunen Adam: Journal of Psychiatry & Neurological Sciences 2020; 33: 155-169.

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ORIGINAL ARTICLE

Does Serum R-Spondin-1 Play a Role in Pathophysiology of Polycystic Ovary Syndrome?

PCOS Patofizyolojisinde Serum R-Spondin-1'in Bir Rolü Var mıdır?

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ABSTRACT

Objective: It has been thought that many novel metabolic and inflammatory markers are involved in the etiology of Polycystic ovary syndrome (PCOS). R-spondin-1 (Rspo1) is a member of the roof plate-specific spondin protein family. Rspo1 levels have been associated to obesity and insulin resistance. In this study, it was aimed to investigate whether the Rspo1 plays role in the PCOS pathophysiology.
Materials and methods: This cross-sectional study included newly diagnosed, treatment-naïve PCOS patients and healthy controls. The Rspo1 levels were compared between PCOS patients and healthy controls. In addition, the Rspo1 levels were compared within PCOSS group according to body mass index (BMI) and Ferriman Gallwey (FG) score.
Results: verall, 83 subjects (47 patients with PCOS and 36 healthy controls) were included in the study. TheO PCOS and control groups were comparable regarding age and BMI. However, FG score, homeostasis model assessment of insulin resistance score, Rspo1 and total testosterone levels were significantly higher in patients with PCOS when compared to controls (p<0.001, p=0.01, p=0.02, p=0.001 respectively). In the PCOS group, there was no significant difference in the Rspo1 levels among BMI and FG scores subgroups It was also found that the Rspo1 had a significant positive correlation with total testosterone and dehydroepiandrosterone sulfate levels (p=0.03, r=0.23; p=0.08, r=0.30, respectively).
Conclusion: The Rspo-1 may be associated with PCOS pathophysiology through total testosterone and dehydroepiandrosterone sulfate. Further molecular and genetic studies are needed to support this hypothesis.

Keywords: R-spondin-1, Polycystic ovary syndrome, Ferriman Gallwey scores

ÖZ

Amaç: Pek çok yeni inflamatuar ve metabolik belirtecin Polikistik Over Sendromu (PCOS) etiyolojisinde rol oynadığı düşünülmektedir. R-spondin-1 (Rspo1), tepe tabakaya özgü spondin protein ailesinin bir üyesidir. Rspo1 seviyeleri obezite ve insülin direnci ile ilişkilendirilmiştir. Rspo1'in PCOS patofizyolojisinde rolü olup olmadığını araştırmayı amaçladık.
Gereç ve Yöntem: Bu kesitsel çalışma, yeni tanı konmuş ve tedavi edilmemiş PCOS olguları ve PCOS'u olmayan bir kontrol grubu ile planlandı. PCOS'lu hastalar ve sağlıklı katılımcılar, Rspo1 seviyeleri için karşılaştırıldı. Ayrıca PCOS grubu vücut kitle indeksi (VKİ) ve Ferriman Gallwey skorlarına (FGS) göre de gruplandırılarak Rsop1 düzeyleri açısından karşılaştırıldı.
Bulgular: PCOS grubunda 47, kontrol grubunda 36 olmak üzere toplam 83 katılımcı çalışmaya dahil edildi. PCOS ve kontrol grupları benzer yaş ve VKİ'ye sahipti. Kontrol grubu ile karşılaştırıldığında, PCOS hastalarının FGS, insülin direnci skorlarının homeostaz modeli değerlendirmesi, Rspo1 ve toplam testosteron düzeyleri anlamlı olarak daha yüksekti (sırasıyla p<0,001, p=0.01, p=0.02, p=0.001). PCOS hastaları BMI ve FGS değerlerine göre alt sınıflara ayrıldığında, hem BMI hem de FGS değerleri açısından Rspo1 seviyeleri arasında istatistiksel olarak anlamlı bir fark yoktu. Ayrıca, Rspo1, toplam testosteron ve dehidroepiandrosteron sülfat seviyeleri ile anlamlı bir pozitif korelasyon gösterdi (sırasıyla p=0.03, r=0.23; p=0.08, r=0.30).
Sonuç: Rspo-1, toplam testosteron ve dehidroepiandrosteron sülfat yoluyla PCOS patofizyolojisi ile ilişkilendirilebilir. Bu hipotezi desteklemek için daha fazla moleküler ve genetik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: R-spondin-1, Polikistik over sendromu, Ferriman Gallwey skorları

Introduction

Polycystic ovary syndrome (PCOS) is a clinical syndrome associated with menstrual irregularity and androgen excess, which is seen in 6-20% of women reproductive age (1). It is characterized by chronic anovulation, infertility, hyperandrogenaemia, obesity, dyslipidemia, and chronic low-intensity inflammation (2). The PCOS has a complex, multifactorial etiology including genetic, environmental, and inflammatory factor or their combination (3,4). Some inflammatory markers such as serum C-reactive protein, tumor necrosis factor-a and interleukin-6 have been linked to hyperandrogenism and PCOS (5,6). The serum markers for inflammation have become increasingly important as markers of atherosclerosis and cardiovascular disorders. In many studies, it was found that increased inflammatory marker concentrations are associated with traditional cardiovascular risk factors such as obesity, dyslipidemia, glucose intolerance, type 2 diabetes and hypertension. In fact, it has been suggested that chronic low-grade inflammation is involved in the pathogenesis of insulin resistance and later in the development of cardiovascular disease (7-9). Given that the frequencies of insulin resistance, cardiovascular events, type II diabetes mellitus and hypertension in

patients with PCOS, it was shown that there is a close relationship between chronic inflammation and PCOS etiology (10).

The R-spondin is a member of the specific spondin protein family of the roof plate involving four members. It is structurally related to the cysteine-rich furin-like and thrombospondin domains. R-spondin-1 (Rspo1) is an intestinal growth factor known to exert its effects through activation of the Wnt signaling pathway, which, in turn, results in expression of Wnt target genes (11). The Wnt signaling has been proven to play important roles in the development and pathogenesis of various diseases including diabetes mellitus (12). In addition, the R-spondin-1 levels have been shown to be associated with obesity and insulin resistance, and are significantly increased compared to the healthy population in both clinical conditions (13).

Given that the insulin resistance and obesity are common comorbid conditions in PCOS, it was aimed to investigate whether the Rspo1 has a role in the pathophysiology of PCOS in this study.

Materials and Methods

The study included 83 subjects (47 patients with PCOS and 36 healthy controls) among patients presented to endocrinology and metabolism disorders outpatient clinic of Kayseri City Hospital between 2019 and 2021. The inclusion criteria were: subjects aged >18 years without clinical signs of infection or inflammation, alcohol or drug use, history of chronic diseases such as diabetes mellitus, chronic kidney disease, and heart disease, or pregnancy. The exclusion criteria included: smoking, pregnancy, breastfeeding and presence of an endocrine disorders including congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome, hyperprolactinemia, thyroid dysfunction and adrenal disorders. The diagnosis of PCOS was made based on the European Society of Human Reproduction and Embryology / American Society of Reproductive Medicine (ESHRE / ASRM) criteria: the presence of two of the three features of hyperandrogenism (hirsutism, high testosterone or free androgen index, oligo or amenorrhea and the presence of polycystic ovary on sonography) (14). All patients had newly diagnosed PCOS and were treatment naive. The height and body weight measurements were made after an overnight fasting and BMI was calculated according to these measurements. Based on the World Health Organization (WHO) classification, the patients with BMI≥30.0 kg/m^2 were defined as obese (15). In the study, all patients were evaluated for hirsutism by a trained staff member using modified Ferriman-Gallwey (FG) score (16). All pelvic sonography studies were performed by same radiologist.

The blood samples were drawn following 12-hours fasting after 20 minutes resting in sitting position. The sera were stored -80°C until assays. The serum Rspo1 concentration was evaluated by Enzyme-Linked Immunosorbent Assay (ELISA) using a commercial kit (Limit of Quantification: 3.62 pg/mL, Assay Range: 10-1000 pg/mL, YL Biont, Shanghai, China). The Rspo1 level was analyzed according to the manufacturer's instructions and expressed as pg/mL. The concentrations of the samples were calculated through calibration curves obtained from study standards with known levels. The regression coefficient of our calibration curve was 0.991. The intra-assay and inter-assay coefficient of variation (CV) is <8% and <10%, respectively.

Statistical Analysis

Statistical analyses were performed using the 22.0 SPSS statistical program. Parametric variables are presented as mean ±standard deviations while non-parametric variables are presented as median (min.-max). Shapiro-Wilks test and histograms were used to determine whether continuous variables were normally distributed. Two independent groups of parametric variables were compared using Student's t test. Mann Whitney U test was administered to non-parametric variables The relationship correlation among non-parametric variables were analyzed using Spearman correlation tests. Pearson's correlation tests were used for parametric variables. Qualitative data was defined as %. A Chi-square test was applied to look for differences between groups. A *p* value of < 0.05 was considered to indicate statistically significant differences.

Ethical Consideration

The study was conducted in accordance to tenets of the Declaration of Helsinki. The was approved by Kayseri City Hospital Ethics Committee (approval number: 2019/391, date: 22.05.2019). With the principle of voluntarism, written and verbal information was provided, and the data was collected by filling out the forms by the participants who gave informed consent. The authors expressed no conflict of interest.

Results

Overall, 83 subjects (47 patients with PCOS and 36 healthy controls) were included in the study. The mean age was 24.7±5.7 years in the PCOS group and 25.3±5.1 years in the control group, indicating no significant difference (p=0.26). Again, there was no significant difference in BMI between PCOS and control groups (29.3±4.9 kg/m2 vs. 27.0±6.0 kg/m2, respectively). It was found that the FG score, homeostasis model assessment of insulin resistance score, Rspo1 and total testosterone levels were significantly higher in patients with PCOS when compared to controls (p<0.001, p=0.01, p=0.02, p=0.001 respectively). However, there was no significant difference in fasting and postprandial plasma glucose, thyroid stimulating hormone, free thyroxin, white blood cells, leukocyte, lymphocyte, dehydroepiandrosterone sulfate, low-density lipoprotein, high-density lipoprotein values between groups (Table 1). The Rspo1 had a significant positive correlation with total testosterone and

dehydroepiandrosterone sulfate levels (p=0.03, r=0.23; p=0.08, r=0.30, respectively).

The patients with PCOS were classified into 3 subgroups according to FG scores: group 1, patients with FG score<8; group 2, patients with FG score of 8-13; and group 3, patients with FG score>13. No significant difference was found in the Rspo1 levels among 3 groups (p=0.31). Again, the patients with PCOS were classified into 3 subgroups according to BMI: obese patients, BMI≥30 kg/m2 and non-obese patients, BMI<30 kg/m2. When the Rspo1 levels were compared obese and non-obese patients, no significant difference was found (422.7±287.4 vs. 413.0±283.7, respectively; p=0.48)

Discussion

The Rspo1 is a new marker shown to play a role in many events in the body such as gut epithelium regeneration, diabetes mellitus in recent studies (12,17). In PCOS and diabetes mellitus, there are many common metabolic abnormalities including obesity and insulin resistance (18). The Rspo1 was also detected in the human pancreas, but its role is not known clearly (19). In a cellular study, it was shown that the Rspo1 activates Wnt signaling in MIN6 β-cells cells and that Rspo1 not only promotes cell growth and survival, but is also an insulin secretagogue (19). Interestingly, in the cell study, the highest dose of Rspo1 failed to induce proliferation in MIN6 β-cells and it was though that this cell line is desensitized by a recombinant protein (20).

In our study, it was found that the PCOS patients had higher Rspo1 and HOMA-IR levels than healthy controls. As expected, insulin resistance was higher in PCOS patients compared to the healthy controls in our study. It was considered that the significant Rspo1 elevation in PCOS patients might be related to the finding of higher insulin resistance in PCOS patients in our study. Studies have shown that the Wnt pathway and Rspo1 may also affect the glucagon-like peptide-1 (GLP-1) pathway (21,22). The anti-obesity effect of GLP-1 is well- known and is used in the treatment (23). Again it was thought that the reason underlying higher frequency of obesity among PCOS patients may be abnormalities in Wnt pathway and their effects on GLP-1, although it was not statistically significant in our study.

The Rspo1 also has significant effects on the reproductive system. In a previous study on Rspo1 knockout female mice, it was found that there was masculinization in the reproductive system. Therefore, the Rspo1 may be required for activation of the Wnt signaling pathway in female gonadal differentiation (24). Many mutations have been identified in the Rspogen family. For example, Parma and colleagues describe a recessive mutation in the gene encoding Rspo1; by addition of a single nucleotide, this recessive mutation resulted in a frameshift and a new stop codon, leading removal of Rspo1 (25). Although the Rspo-1 values were higher in PCOS patients in our study, the presence of masculinizing findings such as increased FG score and hair loss suggests that there may be a mutation in the Rspo-1 gene in these patients.

The Rspo1 is required for female sex development in pregnancy. It activates the WNT/β catenin pathway to inhibit development towards male sex development. During the critical gonadal stages, including 6 to 9 weeks after fertilization, their production decreases in the testes and increases in the ovaries (26). Decreasing of Rspo1 function can cause female-to-male gender reversal (27). The Rspo1 is one of the most important factors for ovarian differentiation in XX gonads (28). Due to difference in R-spondin levels between PCOS and control groups in our study, it may be suggested that there may be mutations in R-spondin genes in patients with PCOS.

The study has some limitations. Firstly, the study should be evaluated with more different markers and genetic parameters. Secondly, further studies are needed in groups with higher patient numbers.

Conclusion

We found that the Rspo-1 levels were significantly higher in PCOS patients compared to the healthy controls. In addition, the HOMA-IR values and FG scores were higher in the PCOS group than the healthy controls. The Rspo1 had a significant positive correlation with total testosterone and dehydroepiandrosterone sulfate levels

Table 1. Clinical and laboratory data of the patients

	PCOS Group (n=47)	Control Group (n=40)	p
Age (year)	26 (18-38)	24 (18-37)	0.260
BMI (kg/m^2)	30.1 (17.9-43.2)	28.5 (18.0-38.5)	0.060
White blood cells (10^3/μL)	7.8 (5.6-11.4)	7.8 (4.7-13.4)	0.830
Neutrophil (10^3/μL)	4.7 (2.6-6.6)	4.8 (1.9-9.6)	0.500
Lymphocyte (10^3/μL)	2.5 (1.6-3.5)	2.3 (1.3-3.4)	0.160
Fasting plasma glucose (mg/dL)	89.4±8.2	87.9±6.7	0.370
Postprandial plasma glucose (mg/dL)	109.9±7.8	103.8±15.0	0.640
HOMA-IR	5.4±2.4	2.9±1.4	**0.010**
Low-density lipoprotein (mg/dL)	101.3±27.9	92.6±27.5	0.170
High-density lipoprotein (mg/dL)	52.2±14.6	53.9±12.3	0.590
Thyroid stimulating hormone (mU/L)	2.2±0.84	2.1±0.9	0.720
Free thyroxine (ng/L)	12.2 (9.6-15.3)	12.2 (9.7-16.4)	0.650
Total Testosteron (μg/L)	0.5 (0.1-0.8)	0.3 (0.09-0.7)	**0.001**
Dehydroepiandrosterone sulphate (μg/L)	1554.4±229.1	982.6±173.7	0.350
Ferriman Gallwey scores	12 (7-21)	8 (2-12)	**<0.001**
Rspo-1 (pg/mL)	342.9 (55-904)	147.8 (70-564)	**0.002**

BMI: Body mass index, HOMA-IR: Homeostasis model assessment of insulin resistance, Rspo-1: R-spondin-1.

Data were expressed as mean±standard deviations or median (min.-max.) according to parametric or non-parametric distribution.

References

1. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril. 2012;97(1):28-38. e25.

2. Tsilchorozidou T, Overton C, Conway GS. The pathophysiology of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2004;60(1):1-17.

3. Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. Nat Rev Endocrinol. 2011;7(4):219-31.

4. Escobar-Morreale HF, Luque-Ramirez M, San Millan JL. The molecular-genetic basis of functional hyperandrogenism and the polycystic ovary syndrome. Endocr Rev. 2005;26(2):251-82.

5. Kelly CC, Lyall H, Petrie JR, Gould GW, Connell JM, Sattar N. Low grade chronic inflammation in women with polycystic ovarian syndrome. J Clin Endocrinol Metab. 2001;86(6):2453-5.

6. Escobar-Morreale HF, Calvo RM, Villuendas G, Sancho J, San Millan JL. Association of polymorphisms in the interleukin 6 receptor complex with obesity and hyperandrogenism. Obes Res. 2003;11(8):987-96.

7. Frishman WH. Biologic markers as predictors of cardiovascular disease. Am J Med. 1998;104(6A):18S-27S.

8. Fernandez-Real JM, Ricart W. Insulin resistance and chronic cardiovascular inflammatory syndrome. Endocr Rev. 2003;24(3):278-301.

9. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation. 2005;111(11):1448-54.

10. Usta A, Avci E, Bulbul CB, Kadi H, Adali E. The monocyte counts to HDL cholesterol ratio in obese and lean patients with polycystic ovary syndrome. Reprod Biol Endocrinol. 2018;16(1):34.

11. Kim KA, Wagle M, Tran K, Zhan X, Dixon MA, Liu S, et al.R-Spondin family members regulate the Wnt pathway by a common mechanism. Mol Biol Cell. 2008;19(6):2588-96.

12. Welters HJ, Kulkarni RN. Wnt signaling: relevance to beta-cell biology and diabetes. Trends Endocrinol Metab. 2008;19(10):349-55.

13. Kang YE, Kim JM, Yi HS, Joung KH, Lee JH, Kim HJ, et al.Serum R-Spondin 1 Is a New Surrogate Marker for Obesity and Insulin Resistance. Diabetes Metab J. 2019;43(3):368-76.

14. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-7.

15. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii, 1-253.

16. Hatch R, Rosenfield RL, Kim MH, Tredway D. Hirsutism: implications, etiology, and management. Am J Obstet Gynecol. 1981;140(7):815-30.

17. Qu M, Xiong L, Lyu Y, Zhang X, Shen J, Guan J, et al.Establishment of intestinal organoid cultures modeling injury-associated epithelial regeneration. Cell Res. 2021;31(3):259-71.

18. Moran LJ, Misso ML, Wild RA, Norman RJ. Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod Update. 2010;16(4):347-63.

19. Kim KA, Kakitani M, Zhao J, Oshima T, Tang T, Binnerts M, et al.Mitogenic influence of human R-spondin1 on the intestinal epithelium. Science. 2005;309(5738):1256-9.

20. Kim KA, Zhao J, Andarmani S, Kakitani M, Oshima T, Binnerts ME, et al.R-Spondin proteins: a novel link to beta-catenin activation. Cell Cycle. 2006;5(1):23-6.

21. Nam JS, Turcotte TJ, Yoon JK. Dynamic expression of R-spondin family genes in mouse development. Gene Expr Patterns. 2007;7(3):306-12.

22. Wong VSC. Role of R-Spondin-1 in the Regulation of Pancreatic β-Cell Behaviour. University of Toronto. 2011.

23. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020;43(Suppl 1):S98-S110.

24. Chassot AA, Ranc F, Gregoire EP, Roepers-Gajadien HL, Taketo MM, Camerino G, et al.Activation of beta-catenin signaling by Rspo1 controls differentiation of the mammalian ovary. Hum Mol Genet. 2008;17(9):1264-77.

25. Parma P, Radi O, Vidal V, Chaboissier MC, Dellambra E, Valentini S, et al.R-spondin1 is essential in sex determination, skin differentiation and malignancy. Nat Genet. 2006;38(11):1304-9.

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ORIGINAL ARTICLE

Sexual Lives of Hemodialysis Patients: A Phenomenological Approach

Hemodiyaliz Hastalarının Cinsel Yaşamları: Fenomenolojik Bir Yaklaşım

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ABSTRACT

Objective: This study aims to analyze the effect of the hemodialysis practice on the patients' sexual functions and sexual experiences.
Materials and Methods: Designed as phenomenological research, the study was performed with 19 patients who had hemodialysis treatment from 20 January 2021 to 20 February 2021 and agreed to participate in the study. The research data were collected by using individual in-depth interviews, the researchers' notes, and patients' personal notes. The 'Patient Information Form' and the semi-structured 'Interview Form' were used as the data collection tools. The research data were examined thematically by using the content analysis method. Two main and eight sub-themes were determined.
Results: The hemodialysis patients included in the study said that sexuality is an indispensable part of their life, they cannot enjoy sexual intercourse due to hemodialysis, they have fear of damaging the fistula or catheter during sexual intercourse, the frequency of sexual intercourse decreases and/or their sexual life ends, they experience erectile dysfunction due to additional diseases, It was determined that they 'refused to have sexual intercourse due to fatigue due to hemodialysis and experienced problems in their family relations', 'do not want to have intercourse due to religious obligations that must be fulfilled after sexual intercourse, and 'avoid sexual intercourse due to contamination during the COVID-19 pandemic.
Conclusion: In our study, it was found that the sexual functions of the patients who had chronic renal failure and underwent hemodialysis deteriorated. So that the patients will develop positive coping mechanisms against the burden imposed on them by hemodialysis, it is recommended that these patients be oriented toward receiving professional psychological support and be educated about sexuality.

Keywords: Hemodialysis, sexual function, phenomenological approach, Turkey

ÖZ

Amaç: Bu çalışma, hemodiyaliz uygulamasının hastaların cinsel işlevlerine ve cinsel deneyimlerine etkisini incelemeyi amaçlamaktadır.
Gereç ve Yöntemler: Fenomenolojik araştırma olarak tasarlanan çalışma, 20 Ocak 2021 - 20 Şubat 2021 tarihleri arasında hemodiyaliz tedavisi gören ve araştırmaya katılmayı kabul eden 19 hasta ile gerçekleştirildi. Araştırma verileri; bireysel derinlemesine görüşmeler, araştırmacıların notları ve hastaların kişisel notları kullanılarak toplandı. Veri toplama aracı olarak "Hasta Bilgi Formu" ve yarı yapılandırılmış "Görüşme Formu" kullanıldı. Araştırma verileri içerik analizi yöntemi kullanılarak tematik olarak incelenmiş olup 2 ana ve 8 alt tema belirlendi.
Bulgular: Çalışmada yer alan hemodiyaliz hastaları cinselliğin hayatın vazgeçilmez bir parçası olduğunu, hemodiyaliz nedeniyle cinsel ilişkiden zevk alamadıklarını, cinsel ilişki sırasında fistül veya katetere zarar verme korkusu yaşadıklarını, cinsel ilişki sıklığının azaldığını ve/veya cinsel yaşamlarının bittiğini, ek hastalıklara bağlı olarak sertleşme sorunları yaşadıklarını, hemodiyaliz kaynaklı yorgunluk nedeniyle cinsel ilişkiye girmeyi reddettiklerini ve aile içi ilişkilerinde problemler yaşadıklarını, cinsel ilişki sonrası yerine getirilmesi gereken dini yükümlülükler nedeniyle ilişkiye girmek istemediklerini ve COVID-19 pandemisi sırasında bulaş nedeniyle cinsel ilişkiden kaçındıkları belirlenmiştir.
Sonuç: Çalışmamızda, hemodiyaliz uygulanan hastaların cinsel fonksiyonlarının bozulduğu belirlendi. Hemodiyalizin getirdiği yüke karşı hastaların olumlu baş etme mekanizmaları geliştirebilmeleri için bu hastaların profesyonel psikolojik destek almaya yönlendirilmesi ve cinsellik konusunda eğitilmesi önerilmektedir.

Anahtar Kelimeler: Hemodiyaliz, cinsel fonksiyon, fenomenolojik yaklaşım, Türkiye.

Introduction

Chronic renal failure is the progressive and irreversible loss of kidney function, during which the glomerular filtration rate falls below 60 ml/min as a consequence of the kidney damage persisting for a minimum of three months on the basis of different etiologies (1). The renal replacement therapy (RRT) method applied mostly to patients with chronic renal failure is the hemodialysis program. According to 2020 data released by the Turkish Society of Nephrology, the RRT point prevalence was 1007.6 per million, the RRT incidence was 150.5, the hemodialysis incidence was 9.645, and the hemodialysis prevalence was 61.341 in Turkey (2).

The patients with chronic renal failure have physiological (1, 3), psychological, and economic problems (4-8) during the disease and treatment processes, and the loss of sexual functions comes at the top of the most important problems experienced by the patients (3). It is asserted that the factors such as endocrinologic problems, diabetes, hypertension, glomerular and vascular diseases, medications, psychosocial factors, and depression are among the causes of the loss of sexual functions in patients with chronic renal failure (3, 5). In the relevant literature, it is discerned that the number

of sexual dysfunctions increased in the hemodialysis patients and the prevalence of sexual dysfunctions was 60-80% among the hemodialysis patients (4,6,7), the prevalence of sexual dysfunctions was 60-70% among the women (8), and the prevalence of erectile dysfunction was 58-88% among the men (9-11).
Sexual dysfunction is a multifaceted health problem and requires a multidisciplinary team approach (3,8-11). Having information about the sexual dysfunction and the factors giving rise to it is of extreme importance to the nurses as the members of this team to ensure the early diagnosis and treatment of sexual dysfunction, to enhance the quality of patient's life (12-14), and also, to protect and develop sexual health (15-19). Upon the review of the relevant literature, it was ascertained that there were a limited number of quantitative studies (7, 20) and qualitative studies (21-23) that analyzed the sexual functions of the patients who had chronic renal failure and had hemodialysis treatment. Therefore, this study aimed to phenomenologically examine the effects of hemodialysis practice on the patients' sexual functions.

Methods

Study Design

This study was performed on the basis of the descriptive phenomenological approach.

Research Setting and Sample

The research population was comprised of 35 hemodialysis patients who had treatment at the hemodialysis unit of a public hospital in Konya province of Turkey from 20 January 2021 to 20 February 2021. The purposive sampling method was used in the research. In this sampling method, the researcher first selects a sample group from the population, and then, a sub-group that the researcher thinks will make the largest contribution to the research is created from the selected sample group (24). It is asserted that the qualitative studies in which in-depth interviews are held can be conducted with small sample groups limited to 5-25 participants (25). When the answers given by the research participants to the questions begin to be similar to each other, it is deemed that the saturation criterion is satisfied and the data collection process is stopped (26, 27). The criteria to be met by the patients to be included in the research were (a) to be aged 18 years or above, (b) to have no communication or perception problem, (c) to undergo hemodialysis for a minimum of one year, (d) to have no psychiatric problem, (e) to speak and understand Turkish, and (f) to volunteer to take part in the study. Four patients who had hemodialysis for a period shorter than one year, seven patients who did not agree to participate in the research, two patients with psychiatric diseases, and three old patients who had trouble understanding the questions were left out of the research. The study was completed with 19 hemodialysis patients who met the criteria for being included in the research and agreed to participate in the research.

Data Collection Tools

The research data were collected by using the 'Patient Information Form' and the semi-structured 'Interview Form', both of which were prepared by the researchers in light of the relevant literature (21,22,28,29).
The 'Patient Information Form' had a total of 20 questions. In this form, 11 questions were designed to identify the hemodialysis patients' sociodemographic characteristics (age, gender, marital status, education level, and so on), 9 questions found out about the patients' chronic diseases ("For how long have you had chronic renal failure?", "For how long have you undergone hemodialysis?", and so on), and 1 question pertained to the patients' sexual intercourse frequencies.

The semi-structured 'Interview Form' contained five open-ended questions. These questions were as below:

1. How do you define sexuality?
2. How does the hemodialysis treatment affect your sex life?
3. How does a fistula/catheter connected to your body along with hemodialysis treatment affect your sex life?
4. What were the changes you had to make in your sex life along with hemodialysis treatment before COVID-19?
5. What were the changes that took place in your sex life during the COVID-19 pandemic?

Data Collection

As the pandemic continued during the research, the researchers collected the research data by using the face-to-face in-depth interview method upon putting on masks, aprons, gloves, and face visors and in full compliance with the social distancing and hygiene rules in the interviews. If the patients agreed that their statements could be recorded during the interview, the statements were audio-recorded. At the same time, the patients' statements were written down by the researchers during interviews. All participants were interviewed by the researchers themselves. The interviews were held in three stages with each participant. In the first stage, the participant patients were informed about the research purpose and its coverage, and accordingly, a work plan was produced. In the second stage, the individual interviews were held with the participant patients, and each interview took 35-45 minutes on average. If a question was not fully understood by a participant patient due to the barriers created by the protective equipment utilized for preventing the spread of the COVID-19 pandemic, the question was repeated by the researchers. In the third stage, the interview reports written by the researchers were examined, and the accuracy of data in the interview reports was checked and confirmed by the participants.

Data Analysis

The 'Content Analysis' was used as the method in the process of analysis of the data that were collected under the research. The collected data were first conceptualized, and then the themes were identified by organizing the data logically. After the content analysis was conducted for the data, the data were coded by naming the sections of the data (a word, a sentence, a paragraph, and so on). As per the participants' views, the classifications were created in the context of sub-problems. The answers given by the participants to a question were classified as themes, sub-themes, and codes. Next, the collected data were transferred to the computer platform. Expert opinions about the themes, sub-themes, and codes were received from one faculty member from the department of sociology and two faculty members from the department of nursing.

Results

Participants' Descriptive Characteristics

Table 1 displayed the participant patients' descriptive characteristics. It was discerned that 57.9% of the participant hemodialysis patients were male, their mean age was 54.31±15.21 years, 36.8% of them were housewives and did not work, 63.2% of them were primary school graduates, and 52.6% had medium-level income (Table 1).

Table 2 exhibited the participant hemodialysis patients' features in relation to chronic diseases and COVID-19. It was identified that the participant hemodialysis patients' disease duration and hemodialysis duration ranged from 1 to 23 years, all of them underwent hemodialysis three times a week, 31.6% of them tested positive for COVID-19, 42.1% of them had a sex life that ended, and 36.8% of them had sexual intercourse once a month and 21.1% of them had sexual intercourse twice a month (Table 2).

Thematic Results

Two themes and eight sub-themes were produced from the analysis of patients' data. The themes were 'the meaning of sexuality' and 'the effects of hemodialysis on sex life'. Certain citations made from the face-to-face interviews and the patients' written accounts about the themes were presented in this part and Table 3.

Theme 1: The meaning of sexuality

Sub-theme 1.1: Integral part of life

The participant hemodialysis patients stated that sexuality was an indispensable part of life, and the intra-family relations deteriorated and their psychological state was negatively affected when no sexual relationship was present between the couples. Some patients' views about this sub-theme were presented below:

- Sexuality is a part of life, it is like eating and drinking. However, these chronic diseases put an end to everything in life. I have no sex life, the quality of my life fell considerably. (P1)
- Sexuality seemed insignificant initially, however, along with this treatment process, I eventually understood how significant it was. Without sexuality, family life was also not in place. (P16)

Theme 2: The effects of hemodialysis on sex life

Sub-theme 2.1. The loss of sexual drive and the sexual dissatisfaction/failure to have pleasure in sex

In this study, some patients said that they lost their sexual drive and failed to take pleasure in sex while some patients stated that they could not be satisfied. Some patients' statements about this sub-theme are as follows:

- Before I had this disease, we used to have higher levels of sexual drive and have sexual intercourse more frequently. Since I got the disease, I can never have sexual satisfaction. (P3)
- My spouse was getting angry initially, he/she did not want to understand me, he/she was forcing me to have sexual intercourse. Sexual reluctance and dissatisfaction come into play in the sexual intercourse that takes place forcibly. Over time, my spouse also understood that, and he/she does not force me to have it any longer. (P14)

Sub-theme 2.2. The fear of damaging the fistula or catheter during sexual intercourse

The patients who underwent hemodialysis with the fistula/catheter reported that this situation affected their sex lives negatively and restricted their positions during sexual activity. Moreover, the participant patients told that they prevent the catheter from getting wet/being dislocated/causing infection/being damaged and so they did not want to have sexual activity. Some patients' statements about this sub-theme are as follows:

- When the catheter was first installed, my spouse and I never had sexual intercourse for three months because of the challenge of having a bath following the intercourse and because my spouse feared harming me. Until the catheter was removed from my neck and the fistula was inserted into my body, I experienced a sexually challenging process. (P4)

- Initially, when the catheter was installed, it was difficult to move and have a bath. I had pain in the body part where the catheter was installed, and even if the tip of the catheter was covered, it would swing back and forth. When the fistula

was inserted, I could not move due to the fear of damaging the fistula. (P17)

Sub-theme 2.3. The fall in the frequency of sexual intercourse and the end of sex life

In this study, the participating patients stated that the frequency of sexual intercourse decreased and/or ended due to the changes in the symptoms and moods during the treatment process.

- Initially, we used to have sexual intercourse once or twice a week. At present, the sexual drive and the frequency of sexual intercourse are low. We have sexual intercourse once a month. (P5)
- My spouse never approached me for the last two years, this disease put an end to my sex life. (P7)
- Together with the dialysis treatment, the frequency of sexual intercourse diminished. I have a sex life as tiny as to be deemed inexistent. (P3)

Sub-theme 2.4. The erection problems due to additional diseases

In this study, the participant hemodialysis patients said that some chronic diseases (diabetes, heart diseases, and so on), and the advanced age gave rise to erection problem over time and hence, and their sex lives were negatively affected.

- Additionally, I had diabetes, and it also affected my sex life very negatively. I had trouble in the sexual sense, and my sexual drive and the frequency of sexual intercourse declined by 60%. I had an erection problem in my penis. (P9)
- Together with the dialysis treatment, sexual drive decreased, and eventually, it disappeared. I think that age also has an effect. I also have no erection. (P12)

Sub-theme 2.5. The refusal to have sexual intercourse due to the hemodialysis-based fatigue

In this study, the participant hemodialysis patients told that, after the hemodialysis therapy, they felt very tired in general due to the dialysis, they could not compose themselves during the entire they did not want to perform any sexual activity. Some patients' statements about this sub-theme are as follows:

- Together with the dialysis treatment, I began to feel weak and tired. Especially during the day on which I have dialysis, I cannot do anything. On that day, my spouse does not also disturb me for sex. (P2)
- As I felt very tired, feeble, and weak in general following the dialysis, my spouse distanced herself/himself from me and did not approach me. This situation affected our sex life adversely. (P11)

Sub-theme 2.6. The religious requirements to be met following the sexual intercourse

In this study, the participant hemodialysis patients stated that they did not want to have sexual activities as they were supposed to have a bath to perform the ritual ablution of the whole body following each sexual intercourse and this situation affected their sex lives negatively. Some patients' statements about this sub-theme are as follows:

- When the catheter is attached to me, even if we have sexual intercourse the next day after I undergo hemodialysis, having a bath becomes a problem. It is necessary not to make the catheter wet. Frequently having sexual intercourse requires that the ritual ablution of the whole body be frequently performed. (P13)
- The need to have a bath following sexual intercourse reduces the frequency of having sexual intercourse. (P15)

Sub-theme 2.7. The sexual avoidance during the COVID-19 pandemic

In this study, the participant patients who had contact with a COVID-19 patient or tested positive for COVID-19 asserted that their sex lives were negatively affected, they had fears and had no sexual activity due to thinking that they would infect their partners. Some patients' statements about this sub-theme are as follows:

- When I had COVID-19, I did not have sexual intercourse with my spouse so that my spouse would not be infected with COVID-19. (P2, P13, P15)
- Sexual reluctance was in place during the pandemic, there was a decrease in sexual drive. (P11, P12)

Table 1. Sociodemographic characteristics of the hemodialysis patients (n = 19)

Code	Age	Sex	Marital Status	Education	Working	Income Status
P1	60	Female	Married	Primary education	Half day	Bad
P2	47	Female	Married	Primary education	Housewife	Middle
P3	52	Female	Married	Primary education	Housewife	Bad
P4	30	Female	Married	Primary education	Housewife	Middle
P5	44	Male	Married	Primary education	Half day	Good
P6	32	Female	Married	Primary education	Housewife	Good
P7	56	Female	Married	Primary education	Housewife	Good
P8	82	Male	Married	Primary education	Not working	Middle
P9	60	Male	Married	Primary education	Not working	Bad
P10	65	Male	Married	Primary education	Not working	Middle
P11	41	Male	Married	Secondary education	Not working	Middle
P12	75	Male	Married	High education	Not working	Middle
P13	45	Male	Married	Primary education	Not working	Bad
P14	67	Female	Married	Secondary education	Housewife	Middle
P15	40	Male	Married	High education	Not working	Middle
P16	49	Male	Married	Secondary education	Not working	Middle
P17	62	Female	Married	Primary education	Housewife	Middle
P18	81	Male	Married	High education	Not working	Good
P19	44	Male	Married	Secondary education	Not working	Bad
The Average Age: 54.31±15.21 (Min: 30: Max: 82)						

Min: Minimum, Max: Maximum

Table 2. Characteristics of Hemodialysis Patients Related to COVID-19 and Other Chronic Illness (n=19)

Patient code	Duration illness	Hemodialysis time	Hemodialysis frequency	Covid-19	Frequency of sexual intercourse
P1	11	11	3/week	No	-
P2	7	7	3/week	Yes	1/moon
P3	6	6	3/week	No	2/moon
P4	9	1	3/week	No	2/moon
P5	23	23	3/week	No	1/moon
P6	20	18	3/week	No	1/moon
P7	2	2	3/week	No	-
P8	1	1	3/week	Yes	-
P9	9	7	3/week	No	1/moon
P10	4	4	3/week	Yes	-
P11	11	11	3/week	Yes	1/moon
P12	3	2	3/week	No	-
P13	15	15	3/week	Yes	1/moon
P14	6	6	3/week	No -	-
P15	1	1	3/week	Yes	1/moon
P16	16	16	3/week	No	-
P17	4	4	3/week	No	2/moon
P18	5	5	3/week	No	1/moon
P19	11	11	3/week	No	2/moon

Table 3. Themes and sub-themes created from the sexual experiences of hemodialysis patients

Themes	Sub-Themes
1. The meaning of sexuality	1.1. Integral part of life
2. Effects of hemodialysis on sexual life	2.1. Loss of sexual desire and dissatisfaction-inability to enjoy
	2.2. Fear of damaging the fistula or catheter during sexual intercourse
	2.3. Decrease in frequency of sexual intercourse and end of intercourse
	2.4. Having erection problems due to additional diseases
	2.5. Refusal of sexuality due to fatigue from hemodialysis
	2.6. Religious requirements after sexual intercourse
	2.7. Avoiding sex during the COVID-19 pandemic

Discussion

In the current study, the hemodialysis patients said that the sexuality was like eating and drinking, and their daily life activities were disrupted and intra-family relations deteriorated, they had problems with their spouses, and their psychological state was negatively affected when their sex lives were disturbed by the disease. Upon the review of the relevant literature, it is discerned that there are studies in support of the findings of this current study (4,22,29). In the current study, even if the participant hemodialysis patients have sexual problems with their partners, they consider this situation as a part of life, and so this situation can be associated with the low-level sexual drive. These results showed that offering psychological guidance was important to the development of effective coping methods by talking about hemodialysis patients' sexual problems.

In the current study, it was identified that the hemodialysis patients suffered from the loss of sexual drive and could not be satisfied and take pleasure in sex. As per

the review of the relevant literature, it is discerned that the previous studies performed with the hemodialysis patients obtained results similar to the findings of this current study and found that the patients' satisfaction with the sexual intercourse decreased (21,23,29) and the women had more problems than men in relation to sexual drive, satisfaction, and romanticism. As the reason for these problems, it is stated that the patients were urged to have sexual intercourse following the hemodialysis and they suffered from the loss of sexual drive, dissatisfaction, and the inability to have pleasure (21,28,30-32). Upon the review of the relevant literature, it was found that the women who underwent hemodialysis had no sexual activity at all or had low-level sexual functionalities (orgasm 75.1%, arousal 64.0%, lubrication 63.3%, pain 60.7%, satisfaction 60.1%, and sexual drive 58%) (20). Along with these results, it is supposed that the female and male hemodialysis patients who had sexual problems suffered from the fall in self-respect, the feeling of inadequacy, and the negative body image over time. The reasons behind this situation are considered to be the factors such as being sexually restricted and not having a proper sexual education.

In the relevant literature, a large majority of the patients undergoing hemodialysis therapy feared damaging the fistula/catheter accidentally due to the positions taken during the sexual intercourse, and thus, their sex lives were restricted. Certain patients stated that their spouses were more considerate about having sexual intercourse than them whereas some patients asserted that they were forced by their spouses to have sexual intercourse even if they did not want to do so (21, 29). These results are in a similar vein to the findings of the current study. Along with these results, it was thought that the fistula affected the sexuality less even if it affected the body image negatively while the presence of the catheter affected the patients' sex lives more.

In the relevant literature, the studies conducted with the hemodialysis patients stated that changes in the body image, and the fall in the men's testosterone hormones and the women's estrogen hormones made the patients sexually inactive (21,29,33,34), the patients had sexual problems in terms of romanticism, anorgasmia, avoidance, and communication, and they should be supported psychologically (29). The study results indicated that the sexual health of the patients with chronic renal failure was negatively affected by the symptoms and intensive treatments that they had. Therefore, the hemodialysis patients' sexual health should be examined regularly, the hemodialysis patients should be evaluated routinely for sexual dysfunction, and sexual health education should be offered to these patients.

In the current study, it was found that some male patients, who had hemodialysis treatment, experienced erection problems, and according to these patients, this problem was associated with age and comorbidities. In the relevant literature, the quantitative studies performed with the hemodialysis patients set forth that the hemodialysis patients' age and sexual functionality were negatively associated, the erection problem increased as the age, depression level, and comorbidities increased (3,7,9,29,35), and the characteristics related to the state of health affected the sexual dysfunction (11). It is discerned that the findings of this current study are akin to the study results in the relevant literature. Along with the results of this current study, it is important that the sexual consultancy in the form of training be offered to them by providing them with andrology consultations to male patients in order to get rid of erectile dysfunction. In the current study, most hemodialysis patients asserted that the fall in sexual drive and sexual intercourse or the refusal to have sexual intercourse was associated with fatigue. In the relevant literature, some female patients did not desire any sexual activity and refused to have sexual intercourse as they felt tired (21,32,36,37). It is important that the treatment programs for reducing/eliminating this fatigue be reviewed, necessary initiatives in this direction be put in place, and treatment protocols for dealing with fatigue be created.

In the current study, it was identified that most patients said that, following each sexual intercourse, they were supposed to perform the ritual ablution of the whole body while having a bath as required by the religious rituals, and this situation affected their sex lives negatively. In the relevant literature, it was found that there was no study about the religious requirements in terms of fistula and catheter use. These results demonstrated that it was an overlooked issue that the hemodialysis patients were supposed to have a shower as required by the religious rituals. Along with these results, it was considered that, while catheter or fistula was being connected to the Muslim patients, it should be remembered and taken into account that the Muslim patients were supposed to have a shower as required by the religious rituals.

To reduce the risk of infection during the COVID-19 pandemic, people are expected to have a social distance from each other. It is asserted that sexual activity is one of the daily life activities likely to be affected by social distancing (38). In the relevant literature, there are compilations of studies that indicate that the social isolation and physical distancing measures implemented due to the COVID-19 pandemic had effects on sexual behavior (38, 39). It is discerned that the findings of this current study are in a similar vein to the relevant literature. Along with these results, it is considered that protecting and improving sexual health through sexual training during the pandemics such as COVID-19 is of importance.

Conclusion

In conclusion, it was found that the sexual functions of the patients who had chronic renal failure and

underwent hemodialysis deteriorated. So that the patients will develop positive coping mechanisms against the burden imposed on them by chronic renal failure and hemodialysis, it is recommended that these patients be oriented toward receiving professional psychological support and be educated about sexuality.

Ethical Aspect of Research

Before the study data was collected, the approval of the Ethics Committee of the Burdur Mehmet Akif Ersoy University Non-Interventional Clinical Research Ethics Committee (Decision No: GO 2021/32) and the approval of the Ministry of Health (2020-12-08T11_48_14) was taken; Verbal and written informed consent was obtained from the hemodialysis patients. Assurance was given about the confidentiality of the information and sound recordings used in the study. In the study, code names P1, P2, P3 ..., P19 were given to the questionnaires instead of the names of the participants. This study was conducted in accordance with the Good Clinical Practice and Reporting Standards of Qualitative Researches of the Declaration of Helsinki.

Limitations of the Study

The results of this study are limited to the patient population of the hospital where the study was conducted. Therefore, the results may not be generalizable. In addition, the fact that the study was conducted with 19 hemodialysis patients who participated voluntarily, that there was no gender discrimination and that patients who could not have sexual intercourse were not excluded can be counted among the limitations.

Declaration of Conflicting Interests

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

Financial Disclosure

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

References

1.Pakyüz ÇS. Böbrek Hastalıklarında Hemşirelik Bakımı (Thomas N., Çeviri Editörü: Karadakovan A.) Bölüm: 6, Kronik Böbrek Hastalığı. Nobel Akademik Yayıncılık Eğitim Danışmanlık Tic.Ltd.Şti., 4. Basımdan Çeviri, İstanbul, 2016: s.117.

2.Türk Nefroloji Derneği (TND, Registry Report). Regıstry of The Nephrology, Dıalysıs And Transplantatıon In Turkey (2020). https://www.nefroloji.org.tr/folders/file/registry_2019.pdf. Accessed 12 May 2021.

3.Göriş S, Bilgi N. Sexual dysfunction and nursing care in patients with end-stage renal disease. Journal of Nephrology Nursing. 2015; 10(1): 68-74.

4.Esen B, Kahvecioğlu S, Atay AE, ve ark. Evaluation of relationship between sexual functions, depression and quality of life in patients with chronic kidney disease at predialysis stage. Renal Failure. 2015;37(2): 262-267.

5.Özyalvaçlı EM, Metin A. Kronik böbrek yetmezlikli erkek hastalarda cinsel sağlık. Androloji Bülteni. https://www.journalagent.com/androloji/pdfs/AND_17_61_112_117.pdf. Erişim Tarihi: 04.07.2022.

6.Hekmat R, Maghsudloo F, Mohebi M, et al. A study of the main determinants of sexual dysfunction in women aged 15-45 years on chronic hemodialysis. Saudi Journal of Kidney Diseases and Transplantation. 2016; 27(5): 916-920.

7.Savadi H, Khaki M, Javnbakht M, Pourrafiee H. The ımpact of hemodialysis on sexual function in male patients using the ınternational ındex of erectile function questionnaire (IIEF). Electronic Physician. 2016;8(5):2371-2377

8.Kim HJ, Doo WS, Kazandı YJ, et al. Association between the hemodialysis adequacy and sexual dysfunction in chronic renal failure: a preliminary study. BMC Urol. 2014; 8:14,4.

9.Gorsane I, Amri N, Younsi F, Helal I, Kheder A. Erectile dysfunction in hemodialysis patients. Saudi Journal of Kidney Diseases and Transplantation. 2016;27(1): 23-28.

10.Sarı E, Usta MF. The relationship between erectile dysfunction and hyperhomocysteinemia in patients with chronic renal failure. Androl Bul. 2017;19(2): 33-39.

11.Lau LC, Adaikan PG, Vathsala A, et al. Clinical prevalence and associated factors of erectile dysfunction in patients undergoing haemodialysis. Ann Acad Med Singapore. 2018;47(2): 78-81.

12.Günalay S, Taşkıran E, Mergen H. Evaluation of non-compliance with diet and fluid restriction in hemodialysis patients. Istanbul Bilim University Florence Nightingale Medical Journal. 2017;3(1):9-14

13.Özyalvaçlı ME, Metin A. Sexual health in male patients with chronic renal failure. Andrology Bulletin.2015;17(61): 112-117.

14.Oliveira APB, Schmidt DB, Amatneeks TM, et al. Quality of life in hemodialysis patients and the relationship with mortality, hospitalizations and poor treatment adherence. Brazilian Journal of Nephrology. 2016;38(4): 411-420.

15.Akyol AD. Investigation of factors affecting quality of life in hemodialysis patients. Journal of Nephrology Nursing. 2016;11(1):17-33.

16.Çiçek AU, Fettahoğlu EÇ, Özatala E, Sarı SA. Evaluation of sexually abused adolescents with repertory grid technique: A cross-sectional study. Cukurova Medical Journal. 2019;44(3):1007-1016.

17.Aker S, Yüksel S. Determination of factors affecting treatment compliance of hypertensive hemodialysis patients: Qualitative study. Journal of Human Sciences. 2016;13(3): 4389-4404.

18.Varol E, Sivrikaya SK. Quality of life and nursing in chronic renal failure. Journal of Duzce University Institute of Health Sciences. 2018;8(2): 89-96.

19.Oskay Ü. Sexual problems in gynecological cancer patients and the models and approaches used to solve these problems. Journal of Ege University Faculty of Nursing. 2019;31(1): 108-119.

20.Saglimbene V, Natale P, Palmer S, et al. The prevalence and correlates of low sexual functioning in women on hemodialysis: A multinational, cross-sectional study. PLoS One. 2017;12(6): e0179511.

21.Villarreal-Alvarez M, Garcia VFJ, Gonzalez CL, et al. Body Changes and Decreased Sexual Drive after Dialysis: A Qualitative Study on the Experiences of Women at an Ambulatory Dialysis Unit in Spain. Int J Environ Res Public Health. 2019;16(17): 3086.

22.Chiaranai C. The Lived Experience of Patients Receiving Hemodialysis Treatment for End-Stage Renal Disease: A Qualitative Study. J Nurs Res. 2016;24(2): 101-8.

23.Valsaraj PB, Bhat MS, Prabhu R, Dinesh N. A Qualitative Research on the Experience of Haemodialysis in South Karnataka: Lived Experience of Persons undergoing Haemodialysis. JKIMSU. 2014;3(2): 90-100.

24.Yıldırım A, Şimşek H. Qualitative research methods in the social sciences. 11th Edition, Seçkin Publishing.2018;100-427.

25.Wang W, Tang J., Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. Journal of Medical Virology. 2020;92(4): 441–447.

26.Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579: 270-273.

27.Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet, 2020;395(10223): 497–506.

28.Chaiviboontham S, Phinitkhajorndech N, Tiansaard J. Symptom Clusters in Patients with End-Stage Renal Disease Undergoing Hemodialysis. Int J Nephrol Renovasc Dis. 2020;13:297–305.

29.Kenkin G, Gümüş BA, Yiğitoğlu TG. Sexual dysfunctions and related variables with sexual function in patients who undergo dialysis for chronic renal failure. Journal of Clinical Nursing.2018; 28(1-2): 257-269.

30.Palmer BF, Clegg DJ. Gonadal dysfunction in chronic kidney disease. Reviews in Endocrine and Metabolic Disorders. 2017;18 (1): 117 – 130.

31.Almutary H, Bonner A, Douglas C. Which patients with chronic kidney disease have a greater symptom burden? A comparative study of advanced CKD stage and dialysis modality. J Ren Care. 2016; 42 (2): 73-82.

32.Fleishman TT, Dreiher J, Shvartzman P. Patient-reported outcomes in maintenance hemodialysis: a cross-sectional, multicenter study Qual Life Res. 2020; 29(9): 2345-2354.

33.Aribi L, Masmoudi R, Ben Houidi A, et al. Sexual disorder in hemodialysis patients. La tunisie Medicale. 2015;93(2): 79– 84.

34.Ören M, Kızıltepe R, Özekes BÇ. Sexuality in old age. Ege Medical Journal. 2016; 55:38-44.

35.Antonucci M, Palermo G, Recupero SM, et al. Male sexual dysfunction in patients with chronic end-stage renal insufficiency and in renal transplant recipients. Archivio Italiano di Urologia e Andrologia. 2015;87(4): 299-305.

36.McCabe PM, Sharlip DI, Lewis R, et al. Risk Factors for Sexual Dysfunction Among Women and Men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015 The Journal of Sexual Medicine. 2016;13(2): 153-167.

37.Kurtuluş FO, Salman MY, Fazlıoğlu A, Fazlıoğlu B. Effects of Renal Transplantation on Female Sexual Dysfunction: Comparative Study With Hemodialysis and a Control Group. Transplant Proc. 2017;49(9): 2099-210.

38.Şahin E, Satılmış Gİ. COVID-19 pandemisinde cinsellik ve cinsel sağlık. Androl Bul. 2020;22:249−253.

39.Tetik S, Alkar YÖ. Sexual Health During the Corona Pandemic. Turkey Clinics Pandemic Pacicology. 2020;8-16.

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ORIGINAL ARTICLE

Pediatric Angiography: Single Center Experience

Pediatrik Anjiolar: Tek Merkez Deneyimi

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ABSTRACT

Objective: Congenital heart disease is the most common congenital anomaly. Early diagnosis and timely intervention are important in congenital heart disease. The aim of this study to share our experience and follow-up results of diagnostic and interventional angiography procedures performed in our center.
Materials and Methods: The retrospective study included patients who underwent catheter angiography in our clinic between July 2018 and October 2021.
Results: This study included 47 children with a mean age of 5.7 (SD, 2.9) years (0-17 years) who underwent catheter angiography. 47% of study population was girls. Diagnostic catheter angiography was performed in 29 patients. Successful interventional catheter angiography was performed in 18 patients. No significant complications were observed during or after diagnostic and interventional catheter angiography.
Conclusion: Diagnostic and interventional angiography procedures can be performed successfully in our clinic. In recent years, interventional angiography procedure has been preferred more because it shortens the hospital stay and does not create surgical scar tissue.

Keywords: children, congenital heart defects, angiography, cardiac catheterization

ÖZ

Amaç: Doğuştan kalp hastalığı en sık görülen doğumsal anomalidir. Doğuştan kalp hastalıklarında erken tanı ve zamanında müdahale önemlidir. Bu çalışmanın amacı merkezimizde yapılan tanısal ve girişimsel anjiyografi işlemleri deneyimlerimizi ve takip sonuçlarını paylaşmaktır.
Gereç ve Yönfem: Retrospektif çalışmaya kliniğimizde Temmuz 2018-Ekim 2021 tarihleri arasında kateter anjiyografi yapılan hastalar dahil edildi.
Bulgular: Bu çalışmaya, ortalama yaşı 5.7 (SD, 2.9) yıl (0-17 yaş) olan ve kateter anjiyografisi yapılan 47 çocuk dahil edildi. Çalışma popülasyonunun %47' si kızlardan oluşuyordu. 29 hastaya tanısal kateter anjiyografi yapıldı. Onsekiz hastaya başarılı girişimsel kateter anjiyografi yapıldı. Tanısal ve girişimsel kateter anjiyografi sırasında veya sonrasında önemli bir komplikasyon gözlenmedi.
Sonuç: Kliniğimizde tanısal ve girişimsel anjiyografi işlemleri başarı ile yapılabilmektedir. Son yıllarda hastanede kalış süresini kısaltması ve cerrahi skar dokusu oluşturmaması nedeniyle girişimsel anjiyografi işlemi daha çok tercih edilmektedir.

Anahtar Kelimeler: çocuklar, doğumsal kalp kusurları, anjiyografi, kardiyak kateterizasyon

Introduction

Congenital heart disease (CHD) refers to structural, functional, or metabolic abnormalities of the heart or major blood vessels that occur during embryogenesis. CHD is the most common congenital anomaly in newborns (1). CHD rate is approximately 5-8 per 1.000 live births (2). Cardiovascular abnormalities are still the most common cause of infant mortality today (3). Therefore, early diagnosis and timely intervention are important in terms of reducing the morbidity, mortality rate and health care costs related to CHD.

The specialty of pediatric interventional cardiology has grown significantly over the last three decades. Treatment of cardiovascular diseases in children with congenital heart disease has substantially advanced because to technological advancements. Interventional therapy has become an acceptable alternative treatment for many CHD, including closure of atrial septal defects (ASD), patent ductus arteriosus (PDA), dilation of stenotic valves (aortic and pulmonary), and dilation of stenotic vessels (coarctation of the aorta).

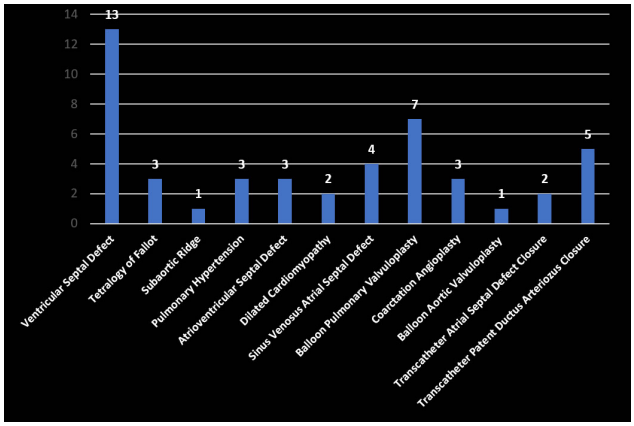
In this article, we planned to share our experience and follow-up results of diagnostic and interventional angiography procedures performed in our center.

Materials and Methods

Forty-seven patients who underwent catheter angiography in our clinic between July 2018 and October 2021 were reviewed retrospectively. All patients underwent detailed physical examination before catheter angiography. Electrocardiograms of the patients were taken and evaluated in terms of arrhythmia. Echocardiographic examinations of the patients were performed and their intracardiac morphologies were evaluated. The preoperative examinations of the patients were evaluated and consulted with the anesthesia department. Before catheter angiography, detailed information about the procedure was given to both parents. Signed consent forms were obtained from both parents before the procedure. The procedures were performed under general anesthesia. All patients underwent detailed physical examination and echocardiographic examinations 24 hours after the catheter angiography procedure. Angiography was performed on children using the femoral artery and femoral vein. Pressure recordings from the entered heart chambers, arteries and veins and blood samples were taken for oximetric study. Vasoreactivity test was performed on necessary patients.

Results

We retrospectively analysed 47 children with a mean age of 5.7 (SD, 2.9) years (0-17 years) who underwent catheter angiography. Also, 47% of study population was girls. Diagnostic catheter angiography was performed in 29 patients. Graphic 1 shows that angiography distribution.



Graph 1: Angiograpy Distribution

Diagnostic catheter angiography was performed on 13 patients with ventricular septal defect (VSD). Hemodynamic parameters were measured. Contrast injections were performed as necessary for PDA, coarctation or any other additional defect. The patients were referred to Pediatric cardiac surgery in terms of operation. Catheter angiography was performed to evaluate the coronary arteries of 2 patients with a diagnosis of dilated cardiomyopathy. Coronary anatomy was found to be normal. Hemodynamic parameters were measured. The patients were referred to the heart transplant center. Catheter angiography was performed in 3 patients with tetralogy of Fallot (TOF) in order to visualize the pulmonary vascular bed and to detect the presence of coronary anomaly. Coronary anatomy of the patients was normal. One patient had a right arcus aorta. Because the pulmonary vessels of 1 patient were extremely narrow, Blalock-Taussig shunt was planned. Catheter angiography was performed in 1 patient with the diagnosis of subaortic ridge. Moderate aortic regurgitation and significant aortic stenosis were detected. The patient was referred to the surgical department for ridge resection. Catheter angiography was performed in 3 primary pulmonary hypertension patients and their hemodynamic parameters were measured. Appropriate pulmonary hypertension drugs were started for the patients whose vasoreactivity test was found to be negative. Catheter angiography was performed in the patient with a diagnosis of 4 sinus venosus ASD. It was observed that the right upper pulmonary vein drained into the right atrium in 3 of them. The patients whose hemodynamic parameters were studied were referred to the surgical department for operation. Catheter angiography was performed in 3 patients with atrioventricular septal defect (AVSD) diagnosis. Gooseneck deformity was observed in left ventricular contrast injection. Hemodynamic parameters were studied. Pulmonary hypertension was not detected. The patients were referred for surgery. Interventional catheter angiography was performed on a total of 18 (38%) patients. Seven patients with valvular pulmonary stenosis underwent pulmonary balloon valvuloplasty. Coarctation angioplasty was performed in 3 patients with aortic coarctation (figure 1).

Aortic balloon valvuloplasty was performed in 1 patient. After the balloon valvuloplasty procedure, there was a significant decrease in the gradient taken from the aortic valve level; In addition, minimal aortic regurgitation was detected. Transcatheter ASD closure was performed in 2 patients with a diagnosis of secundum ASD (figure 2). No residual migration through the device was observed. It was seen that the distance of the device to the anatomical structures in the heart was appropriate. No regurgitation was observed in the atrioventricular valves. There was no sign of compression on the aorta.

Transcatheter PDA closure was performed in 5 patients with a diagnosis of PDA (figure 3). No residual migration through the device was observed. No stenosis was found in the descending aorta and left pulmonary artery. No complications were observed during or after the procedure in any of our patients.

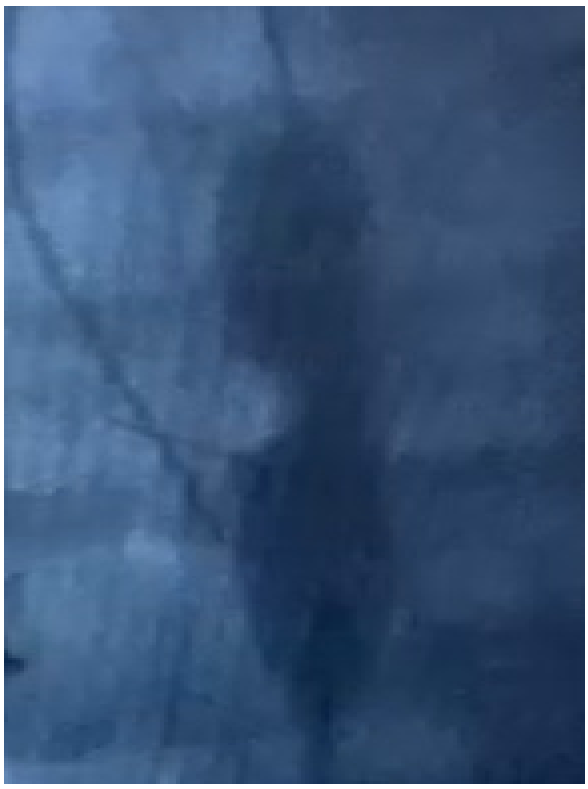


Figure 1: Coarctation angioplasty

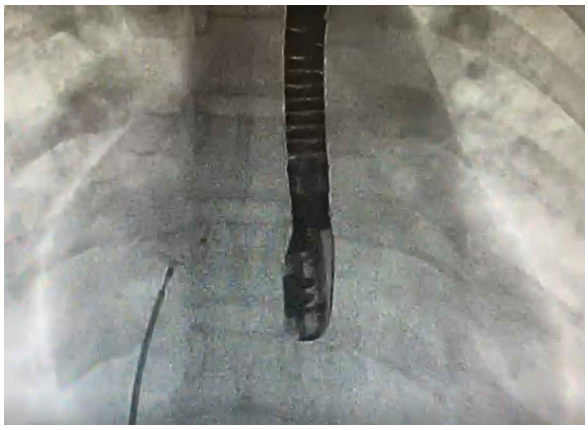


Figure 2: Transcatheter ASD closure

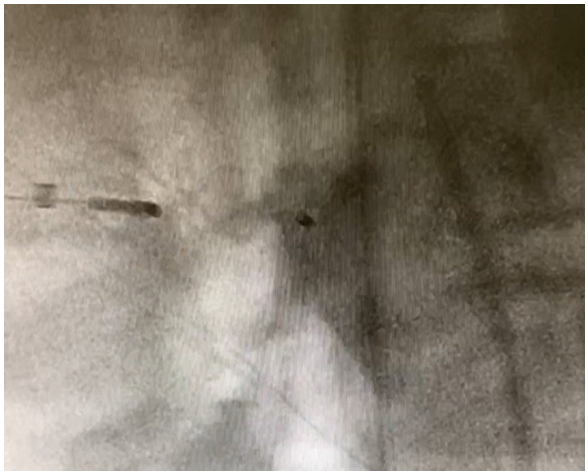


Figure 3: Transcatheter PDA closure

Discussion

The most common cardiac anomalies in children are VSD, which account for about 30% of all CHD (4). Large VSDs are unlikely to close, and patients with VSD will experience symptoms of congestive heart failure. We plan to perform catheter angiography to detect the presence of pulmonary hypertension, the presence of additional congenital heart diseases such as PDA, aortic coarctation, and to measure the amount of shunt after VSD closure indication is established. Catheter angiography was performed on 13 patients with a diagnosis of VSD, and there were no complications during or after the procedure.
All patients who underwent diagnostic angiography were discussed in the cardiac surgery council, and it was decided to perform surgical procedure (AVSD, TOF, Subaortic ridge, Sinus venosus ASD) on patients with indications.

Approximately 19% of all CHDs are caused by ASD (4). When compared to previous reports, the incidence of several of the abnormalities has increased due to developments in diagnostic techniques for CHD (5). If ASD is not closed, in later ages development of right ventricular volume overload and later dysfunction, progressive pulmonary vascular disease carries the risk of developing atrial arrhythmias and paradoxical embolism. Transcatheter ASD closure compared to surgical ASD closure, it has advantages such as shortening the hospital stay, no cardiac bypass and no scarring of thoracotomy. For these reasons, we used the ASD closure device to close the hemodynamically significant ASDs of our patients who were diagnosed with ASD and whose rims were judged to be adequate by transoesophageal echocardiography. Although it is a safe and effective treatment method, air embolism of device closure, device embolization, device dislocation, arrhythmia, cardiac perforation, and tamponade has complications. No complications developed during or after ASD closure.
The presence of the normal fetal structure frequently connecting the left pulmonary artery and the descending aorta beyond 2 to 3 weeks of life is known as PDA, and it accounts for 5% to 10% of all CHD, excluding those in premature newborns (6). PDAs that are large and cause significant shunting are left untreated, Eisenmenger syndrome may develop. Hemodynamically important and significant duct surgery or should be closed by interventional methods. In our clinic, we closed PDAs with systole-diastolic murmur, hemodynamically significant, and heart failure findings, with the appropriate device selection. No device embolization, protrusion into the aorta or pulmonary artery was observed.

Pulmonary balloon valvuloplasty is used safely in the treatment of pulmonary stenosis. In children the results of balloon pulmonary valvuloplasty are successful. It was observed that these patients did not have residual stenosis after the procedure and in the controls. Moderate to severe pulmonary regurgitation did not develop in any of the patients.

Coarctation of the aorta is the common anomaly among all congenital heart lesions (7). The clinical picture is mostly dependent on left ventricular systolic load. Angiography is the gold standard for the evaluation of coarctation. Percutaneous balloon angioplasty is an alternative treatment method to surgery in the treatment of coarctation. It can be applied at any age. Complications such as bleeding in the femoral artery, loss of femoral pulse, hematoma, hemiparesis, aneurysm, and arrhythmia may develop (8). No complications were observed during and after balloon angioplasty for aortic coarctation. Re-coarctation did not develop in the follow-up of the patients.

Valvular aortic valve stenosis (AS) occurs in approximately 3% to 6% of patients with CHD (9). Aortic valvuloplasty for congenital AS is a safe technique with a reported incidence of complications of 3% (10,11). The initial balloon chosen for the valvuloplasty should be 85% to 90% of the aortic valve annulus measured via aortic angiography. Our patient underwent valvuloplasty with a balloon with a length of 85% of the aortic valve annulus measured in angiography. Significant decrease in gradient was detected; however, mild moderate aortic regurgitation was detected.

In conclusion diagnostic and interventional angiography procedures can be performed successfully in our clinic. In recent years, interventional angiography procedure has been preferred more because it shortens the hospital stay and does not create surgical scar tissue.

Ethics Committee Approval

Approval for this study was obtained from the Local Ethics Committee of Selçuk Medical Faculty Ethics Committee (2022/352).

Conflict of Interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding Source Declaration

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

References

1.Van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol 2011;58:2241-7.

2.Bernstein D. Congenital heart disease. In: Behrman RE, Kliegman RM, Jenson HB, (eds). Nelson textbook of pediatrics. 21th ed. Philadelphia: Saunders; 2019:1878-1942.

3.Pinto Júnior VC, Branco KM, Cavalcante RC, Carvalho Junior W, Lima JR, de Freitas SM, et al. Epidemiology of congenital heart disease in Brazil. Rev Bras Cir Cardiovasc 2015;30:219-24.

4.Miyague NI, Cardoso SM, Meyer F, et al. Epidemiological study of congenital heart defects in children and adolescents. Analysis of 4,538cases. Arq Bras Cardiol 2003;80:269 –78.

5.Carlgren LE. The incidence of congenital heart disease in childrenborn in Gothenburg 1941–1950. Br Heart J 1959;21:40 –50.

6.Moore P, Brook MM, Heymann MA. Patent ductus arteriosus. In: Allen HD, Gutgesell HP, Clark EB, and Driscoll DJ, editors. Moss and Adams' Heart Disease in Infants, Children, and Adolescents. Philadelphia, PA: Lippincott, Williams & Wilkins, 2001:652– 69.

7.Miyague NI, Cardoso SM, Meyer F, et al. Epidemiological study of congenital heart defects in children and adolescents. Analysis of 4,538 cases. Arq Bras Cardiol 2003;80:269 –78.

8.Forbes TJ, Kim DW, Du W, et al. Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). J Am Coll Cardiol 2011; 58:2664-74.

9.Roberts WC. Anatomically isolated aortic valvular disease. The case against its being of rheumatic etiology. Am J Med 1970;49:151–9.

10.Moore P, Egito E, Mowrey H, Perry SB, Lock JE, Keane JF. Midterm results of balloon dilation of congenital aortic stenosis: predictors of success. J Am Coll Cardiol 1996;27:1257– 63.

11.Pedra CA, Sidhu R, McCrindle BW, et al. Outcomes after balloon dilation of congenital aortic stenosis in children and adolescents. Cardiol Young 2004;14:315–21.

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ORIGINAL ARTICLE

Being a Nursing Student in a Pandemic: Fear of COVID-19 and Clinical Practice

Pandemide Hemşirelik Öğrencisi Olmak: COVİD-19 Korkusu ve Klinik Uygulama

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ABSTRACT

Aim: This research was conducted to examine the views of nursing students on fear of COVID-19 and clinical practice training during the pandemic process.
Methods: It is a descriptive study. Students studying in the 2nd, 3rd and 4th grades of a university providing undergraduate nursing education in Turkey were included in the study. Subjects were recruited from a population of 235 students. The data of the research; the data were collected using the Introductory Information Form prepared by the researchers by scanning the literature and the "COVID-19 Fear Scale". Number, percentage, and Kruskal Wallis H test were used to evaluate the data.
Results: The mean age of the students participating in the study was found to be 20.65 ± 1.36. Students; a significant difference was found between their attitudes towards patient care in clinical practice, their thoughts on the impact of their clinical practice on their social lives, students' thoughts about going to clinical practice, and their thoughts about experiencing pain, and their COVID-19 fear levels $p<0.05$.
Conclusion: It was concluded that students with high COVID-19 fear levels did not want to take part in patient care in clinical practice, were afraid of being excluded from social life, and preferred school practice instead of clinical practice. In line with these results, it may be recommended to provide psychological support to eliminate fears of COVID-19 to encourage students to clinical practice.

Keywords: clinical practice, COVID 19, fear, nursing, pandemic

ÖZ

Amaç: Bu araştırma, hemşirelik öğrencilerinin pandemi sürecinde COVID-19 korkusu ve klinik uygulama eğitimine ilişkin görüşlerini incelemek amacıyla yapılmıştır.
Yöntem: Tanımlayıcı bir çalışmadır. Araştırmaya Türkiye'de hemşirelik lisans eğitimi veren bir üniversitenin 2., 3. ve 4. sınıflarında öğrenim gören öğrenciler dahil edilmiştir. Katılımcılar 235 öğrencilik bir popülasyondan seçilmiştir. Araştırmanın verileri; veriler, araştırmacılar tarafından literatür taranarak hazırlanan Tanıtıcı Bilgi Formu ve "COVID-19 Korku Ölçeği" kullanılarak toplanmıştır. Verilerin değerlendirilmesinde sayı, yüzde ve Kruskal Wallis H testi kullanıldı.
Bulgular: Araştırmaya katılan öğrencilerin yaş ortalaması 20.65 ± 1.36 olarak bulundu. Öğrenciler; klinik uygulamada hasta bakımına yönelik tutumları, klinik uygulamalarının sosyal yaşamlarına etkisine ilişkin düşünceleri, öğrencilerin klinik uygulamaya gitmeye ilişkin düşünceleri, korku seviyeleri ve ağrı hissetmeye ilişkin düşünceleri ile COVID-19 durumları arasında anlamlı bir fark bulundu. $p<0.05$.
Sonuç: COVID-19 korku düzeyi yüksek öğrencilerin klinik uygulamada hasta bakımında yer almak istemedikleri, sosyal hayattan dışlanmaktan korktukları ve klinik uygulama yerine okul uygulamasını tercih ettikleri sonucuna varıldı. Bu sonuçlar doğrultusunda öğrencileri klinik uygulamaya teşvik etmek için COVID-19 korkularını ortadan kaldırmak için psikolojik destek verilmesi önerilebilir.

Anahtar kelimeler: Klinik uygulama, COVID 19, korku, hemşirelik, pandemi

Introduction

Nursing education is a clinical practice-oriented education. Clinical practice provides the student with the opportunity to cope with the patient and the patient's problems develop the skills of synthesizing the knowledge learned in the lessons and practice patient care. In addition, the psychomotor and intellectual skills of the student can be improved with clinical practice. However, clinical practice is also important in terms of preparing students for future nursing roles (1,2). However, facing uncertain infectious disease threats during clinical practice during the pandemic period will increase the psychological pressure on students (3).

Extraordinary situations such as epidemics can arouse fear in many people (4,5). The fact that students who practice clinical practice during the pandemic period are in the same environment as people who are likely to be infected or carriers and face the risk of COVID-19 transmission will create more stress on students compared to other segments of society (6).

This suggests that this situation will increase students' fear levels. In studies from different countries examining the stress level of nursing students during the pandemic period, it was found that the stress levels of nursing students were high (7-9). It has been concluded that negativities such as the fact that healthcare professionals are at the forefront during the pandemic period and the possibility of disease transmission to themselves and

their families will affect nursing students' perceptions of the profession (8). Stress is a particularly important issue in education as it has the potential to inhibit learning and performance (2). The high level of fear related to COVID-19 suggests that nursing students will increase their occupational stress levels and they may be reluctant to learn in the field of clinical practice. In line with all this information, this study was conducted to examine the views of nursing students on fear of COVID-19 and clinical practice training during the pandemic process.

Research Questions

1. Does fear of COVID-19 affect attitudes towards clinical practice?

2. What are the psychosocial concerns of the students due to COVID-19 regarding their attitudes towards clinical practice?

Methods

Design

This research was conducted in a descriptive type to examine the views of nursing students about the fear of COVID-19 and clinical practice training during the pandemic process.

Sample and setting

The recommended sample size was calculated as 147, based on the 95% confidence interval, 5% margin of error, and the expected 50% response distribution according to the sample calculation of the known universe. The sample of the study consisted of 201 students (n=235) who were studying in the 2nd, 3rd, and 4th grades of the nursing department and agreed to participate in the research. It was aimed to reach the whole population without using the sample selection method. 22 students who did not want to participate in the research, 6 students who filled in the forms incompletely, and 6 students who were absent at the time of the research were excluded from the study. First-year students in the nursing department were not included in the study due to the lack of clinical practice during the course periods. The participation rate of nursing students in the research is 85.5%. The research was conducted with 2nd, 3rd, and 4th-year nursing students enrolled in the fall semester at the university between November 1, 2021, and November 15, 2021. At that time, the number of daily cases in our country was between 20 thousand and 30 thousand.
All students studying in the 2nd, 3rd, and 4th grades of nursing and who agreed to participate in the research were included in the study.

Data collection

The data were prepared by the researchers by scanning the literature (6,8,10,11); It was collected with the "Introductory Information Form" and the COVID-19 Fear Scale, which includes the descriptive characteristics of the students and their thoughts on clinical practice in the hospital during the pandemic period.

The questionnaire

Information Form: The introductory information form was prepared by the researchers in line with the relevant literature (6,8,10,11). The form consists of a total of 24 questions, including the socio-demographic characteristics of the students (10 questions) and the questions containing the students' thoughts on clinical practice (9 questions).

Questions about the difficulties experienced by students in clinical practice (9 questions).

In hospital practice, I do not want to collect data from the patient because of the fear that the patient may have COVID-19.
During the COVID-19 period, I do not want to touch the patient in the hospital application.
During the COVID-19 period, I do not want to spend a lot of time in hospital practice to support patients psychologically and socially.
During the COVID-19 period, I do not want to do invasive procedures (such as injecting, and drawing blood) in hospital practice.
If I catch COVID-19 in the hospital application during the COVID-19 period, I do not want to go to the hospital practises because I am afraid of being away from my family.
I am afraid of the possibility of infecting people (family, friends, etc.) with whom they share the same place when returning to my living place at the end of the hospital application during the COVID-19 period.
I am afraid of being excluded from the place where I live (dormitory, apartment, etc.) because I went to the hospital during the COVID-19 period.
In the COVID-19 era, I would prefer the school application instead of the hospital application.
The thought of going to the hospital practice during the COVID-19 period causes pain in my body.

COVID-19 Fear Scale: COVID-19 Fear Scale, Ahorsu et al. (2020) (12). Seller et al. (2020) have adapted it into Turkish. The scale is a one-dimensional 7-item 5-point Likert type scale. The Cronbach's alpha internal consistency coefficient of the scale was found to be 0.84. CFA analyzes of the scale showed that all fit indices were within acceptable limits ($\chi 2$ (13, N = 1304) = 299.47, $p < .05$; SRMR = .061; GFI = .936; NFI = .912; IFI = .915; CFI = .915). The scale consists of one dimension and there is no reverse item. A score between 7 and 35 is taken from the scale. A high score indicates that the COVID-19 pandemic fears level is 'high' (13). The Cronbach alpha value of our research is 0.78.

Application of research

Research forms were prepared in Google Docs online surveys. Oral information about the research was

given to the students who agreed to participate in the research to collect the data. Informed consent text explaining the purpose and information of the study and a consent box declaring their participation in the study were placed at the beginning of the questionnaire. Written consent was obtained with the consent box. The survey link was distributed to the students through social media groups where general announcements were made. Feedback was collected online during the research period via Google Docs.

Analysis of data

Data analysis was done with SPSS 23.0. Explanatory data were presented as number (n), mean, and percentage (%). Mann Whitney U test "Z" table value was used to compare the scale scores of the independent group. Obtained results were evaluated at a $p<0.05$ significance level.

Ethics

To implement the research and collect data, permissions were obtained from the school where the research was conducted (permission numbered 19581359-605.01/04.12.2020), Selcuk University the Local Ethics Committee (decision permission numbered 2021/448), the scale permission used in data collection, and the students who agreed to participate in the research. This study was conducted by the Helsinki Declaration of Good Clinical Practice Principles.

Results

The mean age of the students participating in the study was 20.65 ± 1.36 and the mean score of COVID-19 was 15.43 ± 16.14 (Table 1).

The comparison of the difficulties experienced by the students in clinical practice with the COVID 19 fear scale score is given in Table 2. In clinical practice, for students with a high fear of COVID-19; It was determined that they did not want to fulfill the practices of collecting data from the patient, performing invasive interventions on the patient, and caring for the patient ($p<0.05$). It was determined that students with a high fear of COVID-19 did not want to go to the clinic because they were afraid of being away from their families if they caught COVID-19 in the hospital practice, and they were afraid of infecting the people with whom they shared the same place and being ostracized by these people ($p<0.05$). Finally, students with high COVID-19 fear scale scores reported that the thought of going to the hospital during the COVID-19 period caused pain in their bodies ($p<0.05$).

Table 2. Comparison of the difficulties experienced by students in clinical practice and the COVID-19 fear scale

		Yes Median [IQR]	No Median [IQR]	Test and p value
Students' attitudes towards patient care in clinical practice	In hospital practice, I do not want to collect data from the patient because of the fear that the patient may have COVID-19.	18 [13Q22]	13 [9Q16]	Z=-5.618 p<0.001
	During the COVID-19 period, I do not want to touch the patient in the hospital application.	17 [14Q21]	13 [9Q17]	Z=-5.001 p<0.001
	During the COVID-19 period, I do not want to spend a lot of time in hospital practice to support patients psychologically and socially.	17 [12.5Q22]	14 [11Q18]	Z=-3.141 p=0.002
	During the COVID-19 period, I do not want to do invasive procedures (such as injecting, and drawing blood) in hospital practice.	18 [14Q22]	14 [10Q18.5]	Z=-3.01 p=0.002
	If I catch COVID-19 in the hospital application during the COVID-19 period, I do not want to go to the hospital practices because I am afraid of being away from my family.	18 [14Q23]	14 [10Q17.25]	Z=-4.382 p<0.001
Findings on the students thoughts on the impact of their clinical practice on their social lives	I am afraid of the possibility of infecting people (family, friends, etc.) with whom they share the same place when returning to my living place at the end of the hospital application during the COVID-19 period.	18 [12.5Q22]	14 [1025Q18]	Z=--3.096 p=0.002
	I am afraid of being excluded from the place where I live (dormitory, apartment, etc.) because I went to the hospital during the COVID-19 period.	20 [12.75Q23.25]	14 [11Q18]	Z=--3.431 p=0.001
Students' thoughts on clinical practice	In the COVID-19 era, I would prefer the school application instead of the hospital application.	16.5 [13 Q21]	12 [7Q15]	Z=-5.257 p>0.001
Students' thoughts on clinical practice and pain	The thought of going to the hospital practice during the COVID-19 period causes pain in my body.	19 [14Q21.75]	14 [10 Q18]	Z=-3.46.2 p=0.001

IQR: 25th percentile, 75th percentile

Z: Mann-Whitney U

Table 1. Data on students' sociodemographic characteristics and covid-19 fear scores n=201

		n	%
Sex	Female	135	67.2
	Male	66	32.8
Class	2. years	77	38.3
	3. years	71	35.3
	4. years	53	26.4
Income rate	Income less than expenses	66	32.8
	Income equals expense	119	59.2
	Income more than expenses	16	8.0
University stay	Dormitory	182	90.5
	Home	8	4.0
	Homestay	11	5.5
Place of residence	Rural	35	17.4
	Town	109	54.2
	Province	57	28.4
Chronic disease status	Available	7	3.5
	Unavailable	194	96.5
A psychiatric illness for which medication is used	Available	3	1.5
	Unavailable	198	98.5
Smoking status	Yes	29	14.4
	No	172	85.6
Alcohol use status	Yes	12	6.0
	No	186	94.0
Age	20,65 ± 1,36 (min: 18, max:25)		
COVID-19 fear score	15.43 ± 16.14 (min: 7, max:35)		

Discussion

In this study, the attitudes of nursing students, who are the health personnel of the future, towards clinical practice during the pandemic period were examined. Our findings show that students' fears of COVID-19 negatively affect their desire for clinical practice. It has been found that students with high fear of COVID-19 have a lower desire for patient care in clinical practice. In this study, students' fears of COVID-19 were moderate. De Los Santos, Labrague, & Falguera (2021) reported that students' COVID-19 fear levels were moderate (14). In another similar study, Elsharkawy & Abdelaziz (2021) found university students to have a high level of fear of COVID-19 (15). It is stated that fear is an expected and justified emotion in a negative or unexpected situation (16,17). Moderate fears of nursing students who will practice in the hospital, which is a risky environment during the pandemic period; Considering the pandemic process, it can be interpreted as experiencing health anxiety as an expected and justified emotion. In addition, it is considered proof that nursing students take the global problem of the COVID-19 pandemic seriously.

In this study, the opinions of nursing students, who are health professionals of the future, about clinical practice during the pandemic period; we presented the thoughts on patient care in the clinic, the impact of their clinical practice on their social lives, their views on clinical practice, and their views on experiencing pain.

Students' attitudes towards patient care in clinical practice;

In this study, it was found that students with a high level of fear of COVID-19 did not want to collect data from the patient, touch the patient, provide psychosocial support to the patient, and engage in invasive interventions. In terms of Aldwin's stress theory, such crises caused by natural or technological disasters, also called focal stressful events, emerge suddenly and threaten people's mental and/or physical integrity to a significant extent (18). Personal control over such situations is reported to be very weak (17). In this study, we think that students' avoidance of contact with patients in the clinical setting may be due to the possible change in personal control of students during the pandemic, which is a stressful situation. In addition, we can say that students avoid contact with the patient because they are afraid of contagion.
Findings on the students thoughts on the impact of their clinical practice on their social lives;
Students with a high level of fear of COVID-19; It has been determined that he is afraid of infecting the people he lives with. In a qualitative study with nursing students, it is stated that students are afraid of transmitting COVID-19 to their families (17). In addition, it is stated that healthcare workers who are at the forefront of the COVID-19 epidemic are afraid of carrying diseases to their families and this is among the difficulties they experience (19). This study finding is similar to the literature found. These results make us think that nursing students may have had a fear of contracting the virus because they were in the hospital environment.

In this study, it was found that students with a high level of fear of COVID-19 were afraid of being excluded by the people they lived with due to their clinical practice. It has been reported that healthcare workers are exposed to stigma because of working with patients infected with COVID-19. Healthcare workers have been exposed to the most obvious forms of stigmatization as "disease carriers/spreaders" (20). We think that students are badly affected by this stigmatized news through social media. As a result, we think that students' fear of exclusion increases their COVID-19 fear levels.

Students' thoughts on clinical practice

In this study, students with high COVID-19 fear levels; It has been found that if COVID-19 is infected in practice, he does not want to go to the hospital practice because he is afraid of being away from their family and they want to practice at school. It has been reported that nursing students have a low level of fear

of COVID-19 in theoretical education, and higher fear of contracting COVID-19 in clinical education (17). In similar studies, it was found that students did not want to go to clinical training because they were afraid of contagion (21,22). This finding may be explained by students' thinking that COVID-19 is more likely to be transmitted from the hospital than from the school.
Students' thoughts on clinical practice and their thoughts on experiencing pain

The COVID-19 fear level of the students who said that the thought of going to the hospital practice during the COVID-19 period causes pain in their body was found to be higher. In the study of Ciftci and Demir (2020), it was found that there was no difference between individuals' fear levels and perceived stress levels (23). In a study, it was determined that there is a positive relationship between increased stress levels and pain (24). Students think they are more likely to be infected with COVID-19 from the hospital. We think that these unpleasant feelings increase the stress of the students and cause pain.

Limitations

As it is a descriptive study, we cannot determine its causality. In a study with an online survey, duplicate entries could not be controlled. Students nursing reading motivations were not questioned. It has not been questioned whether they or their relatives have had COVID-19, whether they have relatives who died from COVID-19, whether they are anti-vaccine, etc.

Conclusion

It has been determined that there is a relationship between the fear of COVID-19 and the problems experienced by the students in the clinic. It was determined that the students avoided contact with the patient because they were afraid of contagion and they were afraid of transmitting the disease to their families. In addition, students reported that COVID-19 infection may be more contagious in the hospital, that they can be excluded from social life if they get COVID-19, and that their fears about COVID-19 cause pain to them. The result of the students' reluctance toward clinical applications is interesting. We recommend that studies be conducted on the methods that can be applied to reduce the fear of COVID-19 in nursing students, who will be at the forefront during the pandemic period. In addition, it is recommended to add theoretical and laboratory practice to the education processes so that students are ready for COVID-19 and similar pandemic processes.

Conflict of Interest: None

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References

1.Duruk N. Evaluation of nursing first year students' level of satisfaction with clinical practice and perceived stress. Turkish Journal of Research & Development in Nursing 2019;21(3):1-13.

2.Jimenez C, Navia□Osorio PM, Diaz CV. Stress and health in novice and experienced nursing students. Journal of Advanced Nursing 2010;66(2):442-455.

3.Tsamakis K, Rizos E, Manolis AJ, Chaidou S, Kympouropoulos S, Spartalis E, Spandidos DA, Tsiptsios D, Triantafyllis AS. COVID-19 pandemic and its impact on mental health of healthcare professionals. Experimental and Therapeutic Medicine 2020;19(6):3451-3453.

4.Goyal K, Chauhan P, Chhikara K, Gupta P, Singh MP. Fear of COVID 2019: First suicidal case in India!. Asian Journal of Psychiatry 2020;49(2020).

5.Mamun MA, Griffiths MD. First COVID-19 suicide case in Bangladesh due to fear of COVID-19 and xenophobia: Possible suicide prevention strategies. Asian Journal of Psychiatry 2020;51:102073.

6.Arpacioglu S, Baltali Z, Unubol B. Burnout, fear of COVID, depression, occupational satisfaction levels and related factors in healthcare workers in the COVID-19 pandemic. Cukurova Medical Journal 2021;46(1):88-100.

7.Savitsky B, Findling Y, Ereli A, Hendel T. Anxiety and coping strategies among nursing students during the COVID-19 pandemic. Nurse Education in Practice 2020;46:102809.

8.Cici R, Yilmazel G. Determination of anxiety levels and perspectives on the nursing profession among candidate nurses with relation to the COVID□19 pandemic. Perspectives in Psychiatric Care 2021;57(1):358-62.

9.Sun Y, Wang D, Han Z, Gao J, Zhu S, Zhang H. Disease prevention knowledge, anxiety, and professional identity during COVID-19 pandemic in nursing students in Zhengzhou, China. Journal of Korean Academy of Nursing 2020;50(4):533-40.

10.Ozgunay SE, Akca F, Karasu D, Eminoglu S, Gamli M. Evaluation of Anesthesiologists' Fear Levels and Prophylaxis Practices During the Coronavirus (COVID-19) Pandemic Process. JARSS 2021;29(1):25-31.

11.Dewart G, Corcoran L, Thirsk L, Petrovic K. Nursing education in a pandemic: Academic challenges in response to COVID-19. Nurse Education Today 2020;92:104471.

12.Ahorsu DK, Lin C-Y, Imani V, Saffari M, Griffiths MD, Pakpour AH. The fear of COVID-19 scale: development and initial validation. International Journal of Mental Health and Addiction 2020:1-9.

13.Satici B, Gocet-Tekin E, Deniz ME, Satici SA. Adaptation of the fear of COVID-19 scale: Its association with psychological distress and life satisfaction in Turkey. International Journal of Mental Health and Addiction 2020:1-9.

14.De Los Santos JAA, Labrague LJ, Falguera CC. Fear of COVID□19, poor quality of sleep, irritability, and intention to quit school among nursing students: A cross□sectional study. Perspectives in Psychiatric Care 2021:1-8.

15.Elsharkawy NB, Abdelaziz EM. Levels of fear and uncertainty regarding the spread of coronavirus disease (COVID□19) among university students. Perspectives in Psychiatric Care 2021;57(3):1356-1364.

16.Steimer T. The biology of fear-and anxiety-related behaviors. Dialogues in Clinical Neuroscience 2002;4(3):231.

17.Lovric R, Farcic N, Miksic S, Vcev A. Studying during the COVID-19 pandemic: A qualitative inductive content analysis of nursing students' perceptions and experiences. Education Sciences 2020;10(7):188.

18.Aldwin CM. Stress, coping, and development: An integrative perspective. Second Edition. New York: Guilford Press; 2007.

19.Karasu F. An intensive care nurse at the forefront of the epidemic as coronavirus (COVID-19) cases increase: "Heroes Standing on the Front". Journal of Intensive Care Nursing 2020;24(1):11-4.

20.Demir SA. Social exclusion and epidemics in the framework of labeling theory: The COVID-19 process and stigma. Yalova Journal of Social Sciences 2021;11(2):13-25.

21.Elrggal ME, Karami NA, Rafea B, Alahmadi L, Al Shehri A, Alamoudi R, Koshak H, Alkahtani S, Cheema E. Evaluation of preparedness of healthcare student volunteers against middle east respiratory syndrome coronavirus (MERS-CoV) in Makkah, Saudi Arabia: A cross-sectional study. Journal of Public Health 2018;26(6):607-612.

22.Al-Hazmi A, Gosadi I, Somily A, Alsubaie S, Saeed AB. Knowledge, attitude and practice of secondary schools and university students toward Middle East Respiratory Syndrome epidemic in Saudi Arabia: A cross-sectional study. Saudi Journal of Biological Sciences 2018;25(3):572-7.

23.Ciftci F, Demir A. Investigation of COVID-19 fear and anxiety levels of Turkish professional football players in the COVID-19 pandemic. Journal of Sports and Recreation Research 2020;2:26-38.

24.Shevlin M, Nolan E, Owczarek M, McBride O, Murphy J, Gibson Miller J, Hartman TK, Levita L, Mason L, Martinez AP, McKay R, Stocks TVA, Bennett KM, Hyland P, Bentall RP. COVID□19□related anxiety predicts somatic symptoms in the UK population. British Journal of Health Psychology 2020;25(4):875-82.

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ORIGINAL ARTICLE

Investigation of Depression and Anxiety Symptoms and Associated Factors in Children with Cerebral Palsy in the COVID-19 Pandemic: Parents' Perceived Social Support, Depression and Corona Anxiety

COVID-19 Pandemisinde Serebral Palsili Çocuklarda Depresyon ve Anksiyete Belirtileri ve İlişkili Faktörlerin İncelenmesi: Ebeveynlerin Algılanan Sosyal Destek, Depresyon ve Korona Kaygısı Düzeyleri

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ABSTRACT

Objective: There is little research on the impact of the COVID-19 pandemic on the mental health of children with cerebral palsy (CP). The primary aim of this study is to determine the level of anxiety and depression in children with CP during the COVID-19 pandemic. The secondary aim is to examine the relationship between perceived social support, depression and COVID-19 anxiety levels of parents of children with CP and anxiety and depression symptoms in children with CP.
Material and Methods: Data were gathered by snowball sampling method using an online survey. Depression and anxiety levels of children with CP were evaluated via Revised Child Anxiety and Depression Scale-Parent (RCADS-P). Depression, corona anxiety, and perceived social support levels of parents of children with CP were evaluated with Beck Depression Scale for Primary Care, Corona Anxiety Scale (CAS), and Multidimensional Scale of Perceived Social Support, respectively. The Pearson correlation test was employed to assess whether or not there was an interconnection amongst continuous variables and different independent samples under consideration. Total Anxiety Scale, Major Depressive Disorder and Total Internalizing Scale sub-dimension scores of the RCADS-P were evaluated as dependent variables according to the groups in the multiple linear regression analysis.
Results: The sample covered 102 children (61, %59.8 boys) with CP and their parents (67, %65.8 mothers). Predictors of the anxiety symptoms of children with CP, in order of importance, were the parents' corona anxiety total score (β=0.324, p=0.003) and the parents' depression total score (β=0.266, p=0.025). Only the parent' CAS total score predicted the depressive symptoms of children with CP (β=0.365, p=0.001).
Conclusion: Coronavirus anxiety of the parents was found to be the strongest predictor of anxiety and depression symptoms in children with CP. These results suggest that the COVID-19 pandemic has increased the mental health needs of both children with CP and their parents.

Keywords: cerebral palsy; children; anxiety; depression; parents; COVID-19

ÖZ

Amaç: COVID-19 pandemisinin Serebral palsili (SP) çocukların ruh sağlığı üzerindeki etkisi hakkında çok az araştırma bulunmaktadır. COVID-19 pandemisinin SP'li çocukların ruh sağlığı üzerindeki etkisi hakkında çok az araştırma bulunmaktadır. Bu çalışmanın birincil amacı, COVID-19 pandemisinde SP'li çocuklarda anksiyete ve depresyon düzeyinin belirlenmesidir. Bu çalışmanın ikincil amacı ise SP'li çocukların ebeveynlerinin algılanan sosyal destek, depresyon ve COVID-19 anksiyetesi düzeyleriyle SP'li çocuklardaki anksiyete ve depresyon belirtileri arasındaki ilişkinin incelenmesidir.
Gereç ve Yöntem: Veriler kartopu örneklem yöntemiyle çevrimiçi anketler kullanılarak toplanmıştır. SP'li çocukların depresyon ve anksiyete düzeyleri Çocuklarda Anksiyete ve Depresyon Ölçeği-Yenilenmiş Ebeveyn formuyla (ÇADÖ-YE) değerlendirilmiştir. SP'li çocukların ebeveynlerinin depresyon, korona kaygısı ve algılanan sosyal destek düzeyleri sırasıyla Birinci Basamak İçin Beck Depresyon Ölçeği, Corona Anksiyete Ölçeği (KAÖ) ve Çok Boyutlu Algılanan Sosyal Destek Ölçeği ile değerlendirilmiştir. Sürekli değişkenler ve incelenen farklı bağımsız örnekler arasında bir bağlantı olup olmadığını değerlendirmek için Pearson korelasyon testi kullanılmıştır. Çoklu doğrusal regresyon analizinde, ÇADÖ-YE'nin Toplam Kaygı, Majör Depresif Bozukluk ve Toplam İçselleştirme Ölçeği alt boyut puanları gruplara göre bağımlı değişken olarak değerlendirilmiştir.
Bulgular: Örneklemi SP'li 102 çocuk (61, %59.8 erkek) ve ebeveynleri (67, %65.8 anne) oluşturmuştur. SP'li çocukların anksiyete belirtilerinin yordayıcıları önem sırasına göre ebeveynlerin korona kaygısı toplam puanı (β=0.324, p=0.003) ve ebeveynlerin depresyon toplam puanı (β=0.266, p=0.025) olmuştur. CP'li çocuklardaki depresif belirtileri yalnızca ebeveynin KAÖ toplam puanı yordamıştır (β=0.365, p=0.001).
Sonuç: Ebeveynlerin koronavirüs kaygısının, SP'li çocuklarda anksiyete ve depresyon belirtilerinin en güçlü yordayıcısı olduğu bulundu. Bu sonuçlar, COVID-19 pandemisinin hem SP'li çocukların hem de ebeveynlerinin ruh sağlığı ihtiyaçlarını artırdığını göstermektedir.

Anahtar Kelimeler: serebral palsi; çocuklar; anksiyete; depresyon; ebeveynler; COVID-19

Introduction

In recent times, cerebral palsy (CP), a neurodevelopmental disorder, has become prevalent in children. The conditions are caused by injury to a developing brain that does not culminate in further deterioration and is characterized by cognitive, communication, perception, and behavior difficulties

(1). As a result of the associated social and physical risk factors, children with CP are at an increased risk of mental health problems (2). Recent researches have elucidated that children and adolescents with CP experience stress, anxiety, and depression because of their difficulty integrating into their communities (3). Furthermore, research has revealed that children with CP were not the only ones who suffer from depression and anxiety as these problems are also present among their parents (4). The problem stems from the fact that parents are typically the primary caregivers, responsible for caring for and assisting their children with CP, culminating in negative emotions including anxiety and distress (5). Consequently, it is ostensible that caring for a child with CP exposes parents to psychological issues, even under normal circumstances.

During the pandemic, those with special educational needs, including those with autism spectrum disorder (ASD), intellectual disability, and CP, were considered more susceptible to mental health problems than their typically developing peers (6). Compared to the period before the outbreak of the COVID-19 pandemic, more severe and frequent behavioral problems were detected in children with attention deficit hyperactivity disorder (ADHD) and ASD (7). Notably, countless families with children with ASD had inadequate education options during the pandemic, if any, as special remote education was limited, and most faced disruptions in behavioral, speech, and occupational therapy (8-10). As such, it has been shown that the closure of special education institutions due to the government's measures to curtail the virus' contagion had prevented children with CP from accessing requisite intervention essential for their physical and emotional health (11). However, the ramification of the pandemic on the accessibility of special education and the subsequent mental health status of children with CP remains elusive.

Along with the adverse repercussions attributed to the advent of the pandemic on children, governments' efforts to contain the virus' spread had a substantial negative impact on parents and other primary caregivers (12, 13). According to the findings of scholarly discourse in England, COVID-19 is correlated with an upsurge in anxiety and fear among households with children relying on special education (14). Furthermore, parents with children with disabilities who receive social support have been shown to experience less depression; as a result, social support for parents of these children is deemed invaluable (15). As per Fontanesi et al. (2020), parents of children with disabilities exhibited a higher probability of experiencing parental fatigue and perceived low social support (16). In general, studies have found that the pandemic has hampered the mental health of parents of these children. However, the effect of the decrease in social support resources in the COVID-19 pandemic on the depression and anxiety levels of the caregivers of children with CP is unknown.

In the literature, although there are studies investigating the mental health of caregivers of children with CP during the COVID-19 pandemic, a few studies has been found on the mental health of children with CP, which is a vulnerable group against mental diseases (17). Determining factors influencing anxiety and depression levels of children with CP is crucial to prepare appropriate intervention programs aiming to reduce anxiety and depression symptoms in COVID-19 pandemic. The first aim of this study is to determine the level of anxiety and depression symptoms in children with CP during the COVID-19 pandemic. The secondary aim is that to examine the relationship between perceived social support, depression and COVID-19 anxiety levels of parents of children with CP and anxiety and depression symptoms in children with CP. We generated several hypotheses; first, we hypothesized that there would be significant positive relationships between the anxiety and depression levels of children with CP and both depression and corona anxiety levels of parents. Second, Perceived social support level of parents has a significantly negative correlation with the corona anxiety and depression levels of parents. Third, the corona anxiety levels of parents would significantly predict depression and anxiety levels of children with CP.

Material and Methods

An observational and cross-sectional clinical trial was undertaken between May 2020 and June 2020. The data was gathered using an online survey developed through Google forms software. The survey was first distributed to parents of children with CP; these participants were retrieved from Gazi Universityıs Child Neurology Department database and were contacted via social networking sites (e.g., WhatsApp) and requested to forward the survey to other caregivers. The inclusion criteria for caregivers were as follows: They had to be 18 years or older, had a child with CP aged 8 to 18 years, had primary responsibility for the child with CP, shared a residence with the child, and were at least a primary school graduate. Participants in this study gave their informed permission (online) after being fully informed of the study's objectives and procedures. Demographic information of the children with CP and their parents was recorded in the sociodemographic data form. Depression and anxiety levels of children with CP were evaluated via Revised Child Anxiety and Depression Scale-Parent (RCADS-P). Depression, corona anxiety, and perceived social support levels of parents of children with CP were evaluated with Beck Depression Scale for Primary Care, Corona Anxiety Scale (CAS), and Multidimensional Scale of Perceived Social Support, respectively.

Measures

Revised Child Anxiety and Depression Scale (RCADS-P)

Children and adolescents with anxiety and depression can be assessed using this instrument as it conforms

with the requirements of the DSM-IV diagnostic manual. Forms for both parents and children are available. Six subscales and 47 items are used to diagnose anxiety disorders, with six focusing on general anxiety disorder, seven on separation anxiety disorder, nine on panic disorder, six on obsessive-compulsive disorder (OCD), nine on social anxiety disorder, and ten on major depressive disorder (10 items). Higher scores obtained RCADS-P indicate high anxiety, depression and total internalizing symptoms. It has been shown by Görmez et al. to be a valid and reliable tool for children and adolescents aged 8-17 years with anxiety and depression in Turkey. (18). All subscales of the RCADS-P except the OCD subscale were used to determine the anxiety and depression levels of children with CP.

Beck Depression Scale for Primary Care (BDI-PC)

The tool was transcribed into Turkish by Aktürk et al. and was leveraged to ascertain depressive symptoms through its seven through seven constructs: sadness, pessimism, past failures, self-loathing, self-blame, loss of interest, and suicidal ideation or desire. To meet the maximal criterion for depression diagnosis, the study participants were asked about their emotions in the "last two weeks, including today." The constructs of the scales each encompass four-digit ratings from 1 to 3.The final score is computed by summing up each construct's score, and a maximum of 21 points can be obtained in total. Despite the lack of a cutoff point, scores of 4 and higher are 90% likely to result in depression. (19). BDI-PC was used to determine depression levels of the parents of children with CP.

Coronavirus Anxiety Scale (CAS)

Another important scale used during the study is the CAS, which is the brainchild of Lee (2020). The foundation of the scale is to ascertain the levels of anxiety towards COVID-19 in adults (30). The elements in the scale are scored in a 5-point Likert-type scale, with values spanning from 0 to 4. CAS has been deemed effective in detecting physical symptoms concerning COVID-19 fear and anxiety (Cronbach's alpha coefficient: 0.95) (20). The higher the ratings on scale are displayed the person feels more corona anxiety and fear. Significantly, it is worth noting that the scale was translated into Turkish by Bicer et al. (2020), and it has been proved to be credible and accurate among adults (21). CAS was used to determine the corona anxiety levels of parents.

Multidimensional Scale of Perceived Social Support (MSPSS)

The MSPSS, which is the development of Zimet et al. (1988), was deployed in the work to assess how much people feel supported by their family members, friends, and other significant persons in their lives, through 12-items (22). The items on the scale were responded to on a 7-point Likert scale, with 1 denoting strong disagreement and 7 signaling strong agreement. The higher the ratings on each component, the more social support one feels from family, friends, and other important individuals. The MSPSS scale was reworked with adults to reflect the Turkish cultural context by Eker and Arkar (1995) (23). All of the subscales of MSPSS were applied to evaluate perceived social support levels of parents.

Statistical Analysis

SPSS version 23.0, which was leveraged to analyze data that was collected from the investigation, was used in this study. Descriptive statistics were expressed in terms of percentages, the mean, and the standard deviation. Because the numerical variables' skewness and kurtosis values fluctuated between ±1, it was presumed that the data were distributed normally. The Pearson correlation test was employed to assess whether or not there was an interconnection amongst continuous variables and different independent samples under consideration. To compare continuous variables amongst groups, the t-test was used. The Total Anxiety Scale, Major Depressive Disorder, and Total Internalizing Scale sub-dimension scores of the RCADS were evaluated as dependent variables according to the groups in the multiple linear regression analysis. Considering the Durbin-Watson, Condition index, VIP, and Tolerance values observed while using this method, it was determined that no multicollinearity problem was observed in the analysis. Internal reliability coefficients (Cronbach's alpha) were used for the reliability analysis of the scale. The level of statistical significance was accepted as $p<0.05$.

Results

In the present study the sample comprised 102 children (61, %59.8 male) with CP aged 8 to 18 years and their parents (67, %65.8 mother). The parents were between the ages 27 to 61 (M age = 39.60 ± 8.01). Most of the parents recruited in the study were married (91.10 %), had at least a high school degree (53.06%), and did not suffer from chronic disease such as diabetes or cancer (68.71%). The sociodemographic characteristics of the children and their parents, who are the primary caregiver, in the sample are shown in Table 1. 40.2% (n=41) of the children were girls, 30.4% (n=31) were in the 5th grade, and their mean age was 11.39±2.48 years. While 45.1% (n=46) of the parents reported that their children received special education during the pandemic period, 39.6% (n=17) stated that the special education period was less than two hours a week and this period was less than the pre-pandemic period.

The distribution of psychiatric disorders in children with CP according to RCADS is shown in Figure 1. Accordingly, the most common psychiatric disorder among children with CP was separation anxiety disorder (SAD) (55.9%), while the least common psychiatric disorder was Obsessive Compulsive Disorder (OCD) (12.7%). The results show that one out of two (55.9%) children with CP had SAD, one out of four (27.5%) had panic disorder (PD), and one out of five (19.6%) had major depressive disorder (MDD).

Table 1. Sociodemographic characteristics of parents and children in the sample

Variables	n	%
Primary Caregiver		
Mother	67	65.7
Father	35	34.3
Parent marital status		
Married	93	91.2
Divorced/Widowed	9	8.8
Parent education status		
Middle school and below	22	21.6
High school	49	48.0
College education	31	30.4
Parent' chronic disease status		
Yes	32	31.3
No	70	68.7
Number of children in the family		
1	29	28.4
2	40	39.2
3	25	24.5
≥ 4	8	7.9
Gender of the child		
Girls	41	40.2
Boys	61	59.8
Child's class		
3rd grade	12	11.8
4th grade	16	15.7
5th grade	31	30.4
6th grade	10	9.8
7th grade	20	19.6
8th grade	10	9.8
10th grade	3	2.9
Status of receiving special education during the pandemic period		
Yes	46	45.1
No	56	54.9
Duration of special education received during the pandemic period (n=46)		
≤ 2 hours per week	17	36.9
3-5 hours per week	15	32.6
≥ 6 hours per week	14	30.5
Parent age		
Mother (mean ± sd)	37.91	7.59
Father (mean ± sd)	42.85	7.89
Whole sample (mean ± sd)	39.60	8.01
Child's age		
Girls (mean ± sd)	11.78	2.30
Boys (mean ± sd)	11.13	2.58
Whole sample (mean ± sd)	11.39	2.48

sd: standard deviation

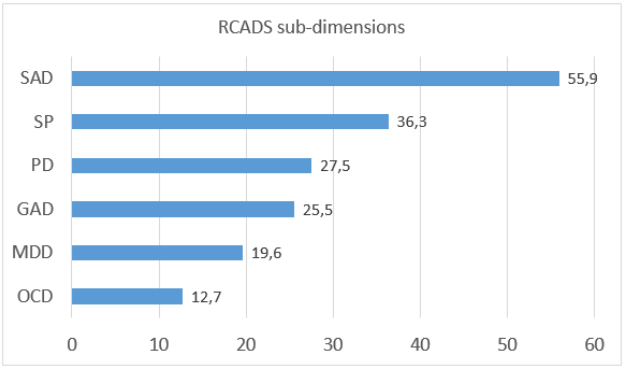

Figure 1. Distribution of Internalizing Disorders by RCADS

RCADS: Revised Child Anxiety and Depression Scale, Separation anxiety disorder: SAD, SP: Social phobia, PD: Panic disorder, GAD: Generalized anxiety disorder, MDD: Major Depressive Disorder, OCD: Obsessive compulsive disorder

Table 2. Comparison of children who received and did not receive special education during the pandemic period in terms of total scores of RCADS, BDI, CAS and MSPSS

RCADS sub-dimensions	Special Education Yes (n=46)		Special Education No (n=56)		Statistical analysis		
	M	SD	M	SD	t	p	Cohen's d
Separation anxiety disorder	66.91	11.17	60.71	13.58	2.480	**0.015**	0.49
Social phobia	54.15	12.69	46.62	12.40	3.018	**0.003**	0.60
Generalized anxiety disorder	59.89	12.10	53.41	12.66	2.623	**0.010**	0.52
Panic disorder	62.58	14.85	58.10	13.64	1.585	0.116	0.31
Obsessive compulsive disorder	58.95	13.26	54.50	11.88	1.788	0.077	0.35
Total Anxiety Scale	62.80	12.39	54.94	13.87	2.984	**0.004**	0.59
Major depressive disorder	64.93	10.59	58.55	12.82	2.701	**0.008**	0.54
Total Internalizing Scale	64.00	11.35	56.03	13.63	3.161	**0.002**	0.63
BDI	4,52	4,37	2,78	3,75	2.155	**0.034**	0.42
CAS	5,08	4,98	2,85	2,93	2.810	**0.006**	0.54
MSPSS sub-dimensions							
Family	20,47	5,79	21,03	6,65	-0.446	0.657	-0.08
Friends	20,36	5,40	19,51	6,00	0.745	0.458	0.14
Significant Order	17,65	7,08	17,32	7,06	0.235	0.815	0.04

M: Mean, SD: Standard Deviation, RCADS: Revised Child Anxiety and Depression Scale

Table 3. Evaluation of the relationships between the scales applied in the study

Variable	M	SD	BDI	CAS	MSPSS		
					Fam	Fri	SO
RCADS- SAD	63.50	12.87	0.315**	0.438**	-0.103	-0.321**	-0.221*
RCADS- SP	50.01	13.02	0.417**	0.497**	-0.054	-0.099	-0.080
RCADS- GAD	56.33	12.77	0.473**	0.416**	-0.160	-0.113	-0.068
RCADS- PD	60.12	14.30	0.272**	0.361**	-0.078	-0.161	-0.159
RCADS- OCD	56.50	12.65	0.435**	0.358**	-0.011	-0.111	-0.042
RCADS- TAS	58.49	13.73	0.439**	0.468**	-0.096	-0.188	-0.126
RCADS- MDD	61.43	12.23	0.304**	0.415**	-0.213*	-0.285**	-0.225*
RCADS- TIS	59.62	13.21	0.431**	0.479**	-0.137	-0.228*	-0.156
BDI	3.56	4.12	1	-	-	-	-
CAS	3.86	4.12	0.582**	1	-	-	-
MSPSS- Fam	20.78	6.25	-0.348**	-0.205*	1	-	-
MSPSS- Fri	19.90	5.72	-0.430**	-0.256**	0.441**	1	-
MSPSS- SO	17.47	7.04	-0.275**	-0.126	0.259**	0.577**	1

M: Mean, SD: Standard Deviation, BDI: Beck Depression Inventory, CAS: Coronavirus Anxiety Scale, RCADS: Revised Child Anxiety and Depression Scale, Separation anxiety disorder: SAD, SP: Social phobia, GAD: Generalized anxiety disorder, PD: Panic disorder, OCD: Obsessive compulsive disorder, TAS: Total Anxiety Scale, MDD: Major depressive disorder, TIS: Total Internalizing Scale, MSPSS: Multidimensional Scale of Perceived Social Support, Fam: Family, Fri: Friends, SO: Significant Order

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Table 4. Evaluation of RCADS scale sub-dimensions with multiple linear regression analysis

	Unstandardized Coefficients		95% CI		Standardized Coefficients		
	Estimate	SE	LL	UL	Beta (β)	t	*p*
Total Anxiety Scale[a]							
BDI	0,887	0,390	0,113	1,661	0,266	2,274	**0,025**
CAS	1,079	0,359	0,366	1,791	0,324	3,005	**0,003**
MSPSS- Fam	0,161	0,218	-0,272	0,594	0,073	0,738	0,463
MSPSS- Fri	-0,018	0,287	-0,587	0,551	-0,008	-0,063	0,950
MSPSS- SO	-0,052	0,209	-0,467	0,364	-0,027	-0,247	0,805
Major Depressive Disorder[b]							
BDI	-0,016	0,359	-0,728	0,696	-0,005	-0,045	0,964
CAS	1,082	0,330	0,427	1,738	0,365	3,279	**0,001**
MSPSS- Fam	-0,130	0,201	-0,529	0,268	-0,067	-0,650	0,517
MSPSS- Fri	-0,227	0,264	-0,751	0,296	-0,106	-0,862	0,391
MSPSS- SO	-0,176	0,193	-0,558	0,206	-0,101	-0,915	0,362
Total Internalizing Scale[c]							
BDI	0,682	0,374	-0,061	1,425	0,213	1,821	0,072
CAS	1,113	0,345	0,429	1,797	0,347	3,229	**0,002**
MSPSS- Fam	0,078	0,209	-0,338	0,493	0,037	0,370	0,712
MSPSS- Fri	-0,097	0,275	-0,644	0,449	-0,042	-0,353	0,725
MSPSS- SO	-0,072	0,201	-0,471	0,327	-0,038	-0,358	0,721

CI = Confidence Interval; *LL* = Lower Limit; *UL* = Upper Limit, BDI: Beck Depression Inventory, CAS: Coronavirus Anxiety Scale, RCADS: Revised Child Anxiety and Depression Scale, MSPSS: Multidimensional Scale of Perceived Social Support, Fam: Family, Fri: Friends, SO: Significant Order

a Durbin-Watson=1.916, Condition Index=13.778, Tolerance=0.535-0.775, VIF=1.291-1.870
b Durbin-Watson=2.262, Condition Index=13.778, Tolerance=0.535-0.775, VIF=1.291-1.870
c Durbin-Watson=1.960, Condition Index=13.778, Tolerance=0.535-0.775, VIF=1.291-1.870

The distribution of internalizing disorders in children with CP according to RCADS is shown in Figure 1. Accordingly, the most common psychiatric disorder was separation anxiety disorder (SAD) (55.9%), while the least common psychiatric disorder was obsessive compulsive disorder (OCD) (12.7%). The results show that one out of two (55.9%) children have SAD one out of four (27.5%) have panic disorder (PD), and one out of five (19.6%) have major depressive disorder (MDD).

The comparison of children who received and did not receive special education during the pandemic period in terms of RCADS sub-dimensions is shown in Table 2. It was determined that the RCADS Separation anxiety disorder (t(100)=2.480, p=0.015), Social phobia (t(100)=3.018, p=0.003), Generalized anxiety disorder (t(100)=2.623, p=0.010), Total Anxiety Scale (t(100)=2.984, p=0.004), Major depressive disorder (t(100)=2.701, p=0.008), and Total Internalizing Scale (t(100)=3.161, p=0.002) sub-dimension scores of the children who received special education during the pandemic period were higher than the children who did not receive special education. While no significant difference was found between the groups in terms of MSPSS sub-dimension total scores, BDI-PC (t(100)=2.155, p=0.034) and CAS scores (t(100)=2.810, p=0.006) were found to be significantly higher in parents of children who received special education during the pandemic period.

The evaluation of the relationships between the scales applied in the study is shown in Table 3. There was a significant positive correlation between all RCADS sub-dimensions and BDI-PC and CAS scale (p<0.01 for each). It was determined that there was a significant negative correlation between the MSPSS all sub-dimension scores and BDI-PC total scores (p<0.01 for each). In addition, it was observed that there was a negative significant relationship between the CAS scores and the family (r=-0.205, p=0.038) and friend (r=-0.256, p=0.009) sub-dimension scores of the MSPSS.

Predictors of the RCADS total anxiety sub-dimension, in order of importance, were the CAS total score (β=0.324, p=0.003) and the BDI-PC total score (β=0.266, p=0.025). In this model, while the predictors explained 26% of the variance, the created model was significant (F(101)=6.962, p<0.001). Only the CAS total score predicted the major depressive disorder subscale of the RCADS. (β=0.365, p=0.001). In this model, the predictors explained 21% of the variance, and the forming model was significant (F(101)=5.322, p<0.001). Similarly, only the CAS total score predicted the total anxiety and depression score of the RCADS. (β=0.347, p=0.002). The predictors in this model explained 26%, and the forming model was significant (F(101)=7.043, p<0.001). Evaluation of RCADS sub-dimensions by multiple linear regression analysis is shown in Table 4.

Discussion

In this study, it was found that the children who received special education during the COVID-19 pandemic had higher separation anxiety, social phobia, generalized anxiety, depression, and total internalizing symptoms than those who did not. While the parent's coronavirus anxiety level was a predictor of the child's anxiety, depression, and internalizing symptoms, the parent's depressive symptoms were found to be the predictor of the anxiety symptoms in the children.

In our study, we found separation anxiety in 55.9%, social anxiety in 36.3%, a panic disorder in 27.5%, generalized anxiety in 25.5%, and depression symptoms in 19.6% of children with CP during the COVID-19 pandemic. In a study conducted before the pandemic, it was reported that 43.7% of children with CP had separation anxiety, 35% had social phobia, and 42.5% had generalized anxiety symptoms (24). In a study during the COVID-19 pandemic, it was shown that both children with special needs and their parents experienced anxiety associated with the negative effects of the pandemic (25). The fact that anxiety disorder symptoms were higher in our results compared to pre-pandemic studies supports the studies showing the negative effects of the pandemic on the mental health of children with neurodevelopmental disorders (6, 17).

In a study examining the impact of COVID-19 on the families of children with special educational needs, parents stated that they were worried about the continuity of their children's education, their future, and the problems that social changes would bring (26). In our study, it was determined that half of the children with CP did not go to special education, and the children who received special education had higher separation anxiety, social phobia, generalized anxiety, total anxiety scores, depressive symptoms, and total internalizing symptoms compared to those who did not. The depressive symptoms and coronavirus anxiety of the parents of the children who went to special education were found to be higher than the parents of the children who did not. These results can be interpreted in several different ways. The decrease in stress factors such as performance expected situations and peer bullying when educational institutions are not attended may explain the lower anxiety and internalizing symptoms in children with CP who do not attend special education. The fact that parents of children with CP who attend special education have more depressive and coronavirus anxiety symptoms than those who do not attend may have led to a biased evaluation of anxiety, depression, and total internalizing symptoms of children with CP attending special education.

In our study, negative correlations were found between depression symptoms in children with CP and all sub-dimensions of their parents' perceived social support. In addition, a negative correlation was found between parents' coronavirus anxiety levels and perceived social support from friends and significant people. Parallel to our study, it was reported that the perceived social support level of parents of children with special needs was a protective factor for

excessive anxiety during the COVID-19 pandemic (27). These results suggest that improving the social support systems of the parents of children with CP may have a positive effect on both the depression, anxiety, and internalizing symptoms of the children with CP, as well as the coronavirus anxiety and depressive symptoms of the parents.

In a study that evaluated the relationship between parents' worry and children's internalizing and externalizing symptoms during the COVID-19 pandemic in 2021, a positive correlation was shown between the worry of parents and their children's internalizing symptoms (28). In line with the results of previous studies conducted during the pandemic period, our results show that parents' depressive symptoms and coronavirus anxiety are the predictors of anxiety symptoms in children with CP. In addition, it was determined that the coronavirus anxiety of the parents was the strongest predictor of the depressive symptoms and total internalizing symptoms of children with CP. These results indicate that mental health professionals who deal with children with CP who have high anxiety, depression and internalizing symptoms during the pandemic should keep in mind that the parents of these children may also have high coronavirus anxiety and/or depressive symptoms.

The results of this study should be evaluated in the light of several methodological limitations that should be addressed for future research. First limitation is the cross-sectional design of the study and therefore the inability to establish a cause-effect relationship between the findings. Although the descriptive features such as type of CP, verbalization skills, and mental capacity of the patients with follow-up in our clinics were recorded, the descriptive features of the children with CP reached by snowball sampling method were obtained only from the statements of the parents. In this study, due to the differences in data sources, the variables of the study were not evaluated according to types of CP, verbalization skills, and mental capacities, which is considered as a major limitation. Although CP is frequently seen together with both psychiatric and other medical diseases, the lack of data on the medical diseases or psychiatric disorders of the children with CP in the sample is another limitation of the study. The last of our limitations is that the data of the study were obtained from a single source and with self-report scales. It is recommended that future studies be planned using different data collection approaches and structured psychiatric assessment to minimize the limitations mentioned above and biases that may have affected the current findings.

Despite the above-mentioned limitations, the present findings offer important implications for research and practices. The results of this study are valuable as it is the first study to our knowledge that examines the relationship between anxiety and depression symptoms of children with CP and aforementioned factors in the COVID-19 pandemic. In this study, the detection of higher anxiety and depression symptoms in children with CP compared to pre-pandemic studies highlights the negative impact of the COVID-19 pandemic on the mental health of children with CP. It is claimed that tele-psychiatry practices are very effective in meeting the increased mental health needs of children with special needs in the COVID-19 pandemic (29). In addition, the fact that the coronavirus anxiety and depression levels of the parents of children with CP who attend special education are higher than the parents of those who do not attend special education shows that additional precautions should be taken for this population. For instance, planning online psychological training in special education institutions to help both children with CP and parents of children with CP to protect their mental health can be considered as the first step. It is very important in clinical practice to consider that parents of children with CP who have high anxiety and depression symptoms may have high depressive symptoms as well as coronavirus anxiety because the mental health of the parents of children with CP is directly related to the quality of care for these children (30). In this pandemic, parents of children with CP should be encouraged to use psychological help resources provided by the government and non-governmental organizations that aim to alleviate the symptoms of coronavirus anxiety and depression.

Conclusion

Coronavirus anxiety of the parents was found to be the strongest predictor of anxiety and depression symptoms in children with CP. These results suggest that the COVID-19 pandemic has increased the mental health needs of both children with CP and their parents. Assessing both children with CP and their parents' mental health and their associated factors should be a focal point of any evaluation.

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References

1.Bax M, Goldstein M, Rosenbaum P, et al. Proposed definition and classification of cerebral palsy, April 2005. Developmental medicine and child neurology. 2005;47:571-6.

2.Bjorgaas H, Hysing M, Elgen I. Psychiatric disorders among children with cerebral palsy at school starting age. Research in developmental disabilities. 2012;33:1287-93.

3.Lindsay S. Child and youth experiences and perspectives of cerebral palsy: a qualitative systematic review. Child: care, health and development. 2016;42:153-75.

4.Scherer N, Verhey I, Kuper H. Depression and anxiety in parents of children with intellectual and developmental disabilities: A systematic review and meta-analysis. PLOS ONE. 2019;14:e0219888.

5.Farajzadeh A, Maroufizadeh S, Amini M. Factors associated with quality of life among mothers of children with cerebral palsy. International journal of nursing practice. 2020;26:e12811.

6.Aishworiya R, Kang YQ. Including children with developmental disabilities in the equation during this COVID-19 pandemic. Journal of autism and developmental disorders. 2021;51:2155-8.

7.Pecor KW, Barbyannis G, Yang M, et al. Quality of Life Changes during the COVID-19 Pandemic for Caregivers of Children with ADHD and/or ASD. International journal of environmental research and public health. 2021;18:3667.

8.Eshraghi AA, Li C, Alessandri M, et al. COVID-19: overcoming the challenges faced by individuals with autism and their families. Lancet Psychiatry. 2020;7:481-3.

9.Manning J, Billian J, Matson J, Allen C, Soares N. Perceptions of Families of Individuals with Autism Spectrum Disorder during the COVID-19 Crisis. J Autism Dev Disord. 2021;51:2920-8.

10.Mutluer T, Doenyas C, Genc HA. Behavioral implications of the Covid-19 process for Autism Spectrum Disorder, and individuals' comprehension of and reactions to the pandemic conditions. Frontiers in psychiatry. 2020;11.

11.Cankurtaran D, Tezel N, Yildiz SY, Celik G, Akyuz EU. Evaluation of the effects of the COVID-19 pandemic on children with cerebral palsy, caregivers' quality of life, and caregivers' fear of COVID-19 with telemedicine. Irish Journal of Medical Science (1971-). 2021:1-8.

12.Gassman-Pines A, Ananat EO, Fitz-Henley J. COVID-19 and parent-child psychological well-being. Pediatrics. 2020;146.

13.Patrick SW, Henkhaus LE, Zickafoose JS, et al. Well-being of parents and children during the COVID-19 pandemic: a national survey. Pediatrics. 2020;146.

14.Asbury K, Fox L, Deniz E, Code A, Toseeb U. How is COVID-19 affecting the mental health of children with special educational needs and disabilities and their families? Journal of Autism and Developmental Disorders. 2021;51:1772-80.

15.Sipal RF, Sayin U. Impact of perceived social support and depression on the parental attitudes of mothers of children who are deaf. Journal of Child and Family Studies. 2013;22:1103-11.

16.Fontanesi L, Marchetti D, Mazza C, et al. The effect of the COVID-19 lockdown on parents: A call to adopt urgent measures. Psychological Trauma: Theory, Research, Practice, and Policy. 2020;12:S79.

17.Lai B, Wen H, Sinha T, et al. The impact of COVID-19 on the lifestyles of adolescents with cerebral palsy in the Southeast United States. Disability and Health Journal. 2021:101263.

18.Gormez V, Kılınçaslan A, Orengul AC, et al. Psychometric properties of the Turkish version of the Revised Child Anxiety and Depression Scale–Child Version in a clinical sample. Psychiatry and Clinical Psychopharmacology. 2017;27:84-92.

19.Aktürk Z, Dağdeviren N, Türe M, Tuğlu C. Birinci Basamak İçin Beck Depresyon Tarama Ölçeği'nin Türkçe Çeviriminin Geçerlik ve Güvenirliği. Türkiye Aile Hekimliği Dergisi. 2005;9:117-22.

20.Lee SA. Coronavirus anxiety scale: A brief mental health screener for COVID-19 related anxiety. Death Studies. 2020:1-9.

21.BİÇER İ, ÇAKMAK C, DEMİR H, KURT ME. Koronavirüs anksiyete ölçeği kısa formu: Türkçe geçerlik ve güvenirlik çalışması. Anatolian Clinic the Journal of Medical Sciences. 2020;25:216-25.

22.Zimet GD, Dahlem NW, Zimet SG, Farley GK. The multidimensional scale of perceived social support. Journal of personality assessment. 1988;52:30-41.

23.Eker D, Arkar H. Çok boyutlu algılanan sosyal destek ölçeğinin faktör yapısı, geçerlik ve güvenirliği. Türk Psikoloji Dergisi. 1995;10:45-55.

24.McMahon J, Harvey A, Reid SM, May T, Antolovich G. Anxiety in children and adolescents with cerebral palsy. Journal of paediatrics and child health. 2020;56:1194-200.

25.Lee SJ, Ward KP, Chang OD, Downing KM. Parenting activities and the transition to home-based education during the COVID-19 pandemic. Children and Youth Services Review. 2021;122:105585.

26.Neece C, McIntyre LL, Fenning R. Examining the impact of COVID-19 in ethnically diverse families with young children with intellectual and developmental disabilities. Journal of Intellectual Disability Research. 2020;64:739-49.

27.Ren J, Li X, Chen S, Chen S, Nie Y. The influence of factors such as parenting stress and social support on the state anxiety in parents of special needs children during the COVID-19 epidemic. Frontiers in Psychology. 2020;11.

28.Li X, Zhou S. Parental worry, family-based disaster education and children's internalizing and externalizing problems during the COVID-19 pandemic. Psychological trauma: theory, research, practice, and policy. 2021.

29.Ben-Pazi H, Beni-Adani L, Lamdan R. Accelerating Telemedicine for Cerebral Palsy During the COVID-19 Pandemic and Beyond. Frontiers in Neurology. 2020;11.

30.Farajzadeh A, Dehghanizadeh M, Maroufizadeh S, Amini M, Shamili A. Predictors of mental health among parents of children with cerebral palsy during the COVID-19 pandemic in Iran: A web-based cross-sectional study. Research in Developmental Disabilities. 2021;112:103890.

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ORIGINAL ARTICLE

Comparison of Culture, Direct Microscopy, and Polymerase Chain Reaction Results for Detection of Mycobacterium Tuberculosis Complex in Clinical Specimens

Klinik Örneklerde Mycobacterium Tuberculosis Kompleksi'nin Saptanması İçin Kültür, Direkt Mikroskopi Ve Polimeraz Zincir Reaksiyon Sonuçlarının Karşılaştırılması

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ABSTRACT

Aim: Tuberculosis is a chronic, necrotizing disease known since prehistoric times. The most important stage of the tuberculosis control program is the microbiological identification, typing and detection of drug resistance of the Mycobacterium tuberculosis complex for the detection of active cases. The aim of this study is to compare the results of the methods used in the detection of M.tuberculosis complex in clinical samples.
Materials and Methods: The results of the samples sent to the laboratory for the purpose of investigating M. tuberculosis complex between January 2016 and January 2022 from patients with pre-diagnosis of tuberculosis were evaluated retrospectively. In microbiological diagnosis, Ehrlich-Ziehl-Neelsen (EZN) staining method, culture (BACTEC MGIT 320 automated system and Löwenstein Jensen (LJ) medium, and polymerase chain reaction (PCR) tests were used.
Results: A total of 1706 samples with all three requests (EZN, culture and TB-DNA) were included in the study. The mean age of the patients was 46.49±25.77 years and 1025 (60.1%) were male. Culture in 48 (2.8%) samples, PCR positivity in 40 (2.3%) and EZN positivity in 32 (1.9%) samples were mostly sent from the departments of chest diseases (52.8%) and pediatrics (24.1%).
Conclusion: It was determined that the culture method gave more reliable results than PCR and EZN in demonstrating the presence of M. tuberculosis complex. As a result, since the culture method, gives late results, extensive routine use of molecular tests such as PCR is needed for accurate diagnosis of tuberculosis in a short time and to detect drug resistance.

Keywords: Mycobacterium tuberculosis, EZN, Löwenstein Jensen medium, TB-DNA

ÖZ

Amaç: Tüberküloz insanlık tarihi kadar eski bir geçmişe sahip olan kronik, nekrotizan bir hastalıktır. Tüberküloz kontrol programının en önemli aşaması olan aktif olguların tespiti için Mycobacterium tuberculosis kompleksin mikrobiyolojik yöntemlerle tanımlanması, tiplendirilmesi ve ilaç direncinin saptanması gerekmektedir. Bu çalışmanın amacı klinik örneklerde M.tuberculosis kompleksin tespitinde kullanılan yöntemlerin sonuçlarının karşılaştırılmasıdır.
Gereç ve yöntem: Tüberküloz ön tanılı hastalardan Ocak 2016 - Ocak 2022 tarihleri arasında M. tuberculosis kompleks araştırılması amacıyla laboratuvara gönderilen örneklerin sonuçları rektospektif olarak değerlendirildi. Mikrobiyolojik tanıda; Ehrlich-Ziehl-Neelsen (EZN) boyama, kültür (BACTEC MGIT 320 otomatize sistemi ve Löwenstein Jensen (LJ) besiyeri ve polimeraz zincir reaksiyonu (PZR) testi kullanıldı.
Bulgular: Çalışmaya her üç istemi olan (EZN, kültür ve TB-DNA) toplam 1706 örnek alındı. Hastaların yaş ortalaması 46,49±25,77 olarak saptanmıştır ve 1025'i (%60,1) erkektir. Örneklerin 48'inde (%2,8) kültür, 40'ında (%2,3) PZR ve 32'sinde (%1,9) EZN pozitifliği saptandı. Örnekler en çok göğüs hastalıkları (%52,8) ve pediatri (%24,1) kliniklerinden gönderilmiştir.
Sonuç: M. tuberculosis kompleks varlığının gösterilmesinde kültür yönteminin PZR ve EZN'ye göre daha güvenilir sonuç verdiği saptandı. Sonuç olarak kültür yöntemi geç sonuç verdiğinden tüberkülozun kısa sürede doğru tanısı ve ilaç direnci tespiti için PCR gibi moleküler testlerin geniş rutin kullanımına ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Mycobacterium tuberculosis, EZN, Löwenstein Jensen besiyeri, TB-DNA

Introduction

Tuberculosis (TB) is one of the most important fatal diseases caused by a single infectious agent. According to the World Health Organization (WHO) 2019 Global TB Report; approximately 10 million people were infected with TB in 2018 (1). Neglect and rejection of treatment by the patients increases the Multi-Drug Resistant Tuberculosis (MDR-TB) rate. In addition, increasing anti-TB drug resistance has become an important problem due to travel and migration (2,3). Along with the developments in molecular diagnostic methods, around 200 Mycobacterium species have been identified recently, and most of them are disease agents in humans (4). The most isolated mycobacterium species in TB cases is Mycobacterium tuberculosis (5). Since tuberculosis is one of the diseases that cause the highest mortality and morbidity in the world, epidemiological studies should be reported regularly. It is extremely important to identify M. tuberculosis as

soon as possible in order to prevent the spread of the infection and to start specific treatment. Examples of traditional approaches used in the diagnosis of tuberculosis are microscopic examination by staining with acid-resistant staining (ARB) and identification of the agent by culture (6).

The diagnosis of TB is made by detecting the agent in respiratory tract samples such as sputum, bronchoalveolar lavage (BAL) or body fluids such as urine, blood, sterile body fluids (pleura, peritoneum, pericardium, joint, cerebrospinal fluid). Although new molecular diagnostic methods continue to develop in recent years, culture method maintains its importance as the "gold standard" in the diagnosis of Mycobacterium spp. (7).

There are three types of media used in the culture. Hard-boiled eggs [eg Löwenstein Jensen (LJ)], solid agar (eg. Middlebrook 7H11), liquid broth (eg. Middlebrook 7H12). Incubation in liquid broth requires 1-3 weeks, while solid media requires 3-8 weeks. 5-10% carbon dioxide accelerates reproduction. Among the automated rapid culture methods, commercial systems such as "Mycobacterium growth indicator tube" (MGIT) 960 system, BACTEC 460 TB system, BACTEC 9000 MB system, BACTEC MGIT 320, ACT Myco E SP 2 system can be counted. With these methods, rapid primary isolation of mycobacteria, differentiation of "Mycobacterium tuberculosis complex (MTC)" and non-TB mycobacteria and detection of susceptibility of mycobacteria to anti-tuberculosis drugs are performed (8).

Culture method takes 3-4 weeks for the bacilli to reproduce and form a visible colony. In addition to traditional methods in the diagnosis of tuberculosis, molecular diagnostic methods have been developed with high sensitivity and specificity (6). Molecular methods are useful to identify mycobacteria grown in culture at the species level in a short time, to investigate their susceptibility to tuberculosis drugs, to detect drug-resistant cases, and to detect mutations related to resistance (9).

In this study, it was aimed to investigate and compare the results of culture, direct microscopy and PCR methods in the detection of Mycobacterium tuberculosis complex strains in various clinical samples. In addition, it was aimed to investigate the distribution of tuberculosis positivity according to hospital units.

Materials and Methods

In the study, 1706 clinical samples that EZN staining, culture and PCR methods were performed in Selçuk University Medical Faculty Hospital Microbiology Laboratory from various clinics between 01.01.2016-01.01.2022 were analyzed retrospectively. Culture, EZN stain, and TBC DNA results of the patients were evaluated and compared.

Samples such as sputum, bronchoalveolar lavage (BAL), abscess, joint fluid, biopsy, fine needle aspiration were subjected to pre-treatment (homogenization, decontamination, concentration). Homogenization-NALC (N-Acetyl-LCysteine+Sodium) method was performed with glass beads and vortex. Decontamination was done with sodium buffer. Concentration was done by centrifugation (15 min at 3000 g). After the pre-treatment EZN stain was applied for the presence of bacilli.

Sample (0.5 ml) was inoculated into LJ medium and BACTEC MGIT 320 liquid culture bottle (BD BBL™ MGIT™, Ireland). The remaining samples were stored in a -20˚C refrigerator. If there was growth in media, positivity was seen within one week (standard deviation 10 days). Culture positivity was determined by both automated system and visual evaluation. In addition to routine EZN staining, positive culture samples were also stained to determine mycobacterial species.If 6-6'-dimicolate-a-D-trehalose (KORD) factor was seen in microscopy, the bacteria grown in the medium was accepted as TB (Tuberculosis Complex Bacteria). After full proof of TB positivity, mycobacterial susceptibility tests was performed. Tuberculosis culture extended to six weeks in the absence of signal (20).

Samples were given to the molecular unit for TB-DNA study after pre-treatment. DNA extraction was carried out in accordance with the protocol using a DNA isolation kit (Artus® M. tuberculosis RG PCR Kit, QIAGEN, Germany).The primers used in the PCR test are specific for M. tuberculosis (TB-DNA target site). All operations before and after extraction were carried out in a biological safety cabinet. The isolated samples were amplified on the Rotor-Gene RT-PCR (QIAGEN, Germany). M. tuberculosis complex was considered positive when the targeted DNA region was detected.

Statistical Analysis

The results obtained in the study were analyzed with the SPSS 21.0 package program. Frequency and percentages were given as descriptive statistics. Roc Curve was used to determine the reliability of the tests in diagnosis. Sensitivity, specificity, positive and negative predictive values of EZN, Culture and PCR tests were calculated manually. Culture was accepted as the gold standard method.

Ethics Approval

For this research; Selcuk University Faculty of Medicine Local Ethics Committee approval was obtained (Date: 21.06.2022; number: 2022/13).

Results

The results of 1706 samples from various clinical samples were scanned in order to detect the presence of M. tuberculosis complex. The mean age of the patients was 46.49±25.77 years. Of the patients, 1025 (60.1%) were male and 681 (39.9%) were female. Culture, PCR, and EZN positivity rates were; 48 (2.8%) , 40 (2.3%)

and 32 (1.9%) respectively (Table 1). Repeated results of the same patients were not included in the study. TB-DNA in 10 patients (0.58%) with negative culture results and EZN staining test in five patients (0.29%) were positive. In addition, 30 (1.8%) patients with positive culture results had positive TB-DNA tests and 27 (1.6%) had positive EZN results. 52.8% (n = 900) of the samples were sent from chest diseases clinics and 24.1% (n = 412) from pediatrics (Table 2). Sputum samples constitute the majority of the samples (n = 1169; 68.5%) and followed by bronchoalveolar lavage samples with a rate of 17.7% (Figure 2).

Table 1. Positivity rates of the methods

Methods	Positive		Negative	
	n	%	N	%
Culture	48	2.8	1658	97.2
TB-DNA	40	2.3	1666	97.7
EZN	32	1.9	1674	98.1
Total			1706	100

TB DNA* Tuberculosis complex Deoxyribo nucleic acid

EZN* Ehrlich-Ziehl-Neelsen

As a result of the evaluation made by accepting the culture method as the gold standard, the sensitivity of the PCR and EZN methods was calculated as 60.4% and 41.6%, and the specificity as 99.3% and 99.2%, respectively. The positive predictive value of the PCR test was 81.3%, the negative predictive value was 99.3%; the positive predictive value of EZN was 70% and the negative predictive value was 99.2%.

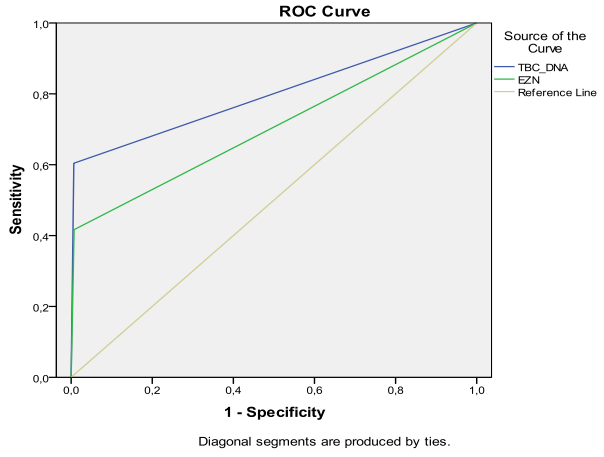

Figure 1. Roc Curve

In our study the area under the curve (AUC) for TBC DNA was 0.79 for EZN, and 1.00 for Culture as a result of ROC analysis when culture was taken as a reference test.

Other*= Nephrology, Orthopedics and Traumatology, Urology, Hematology, Palliative Care Center, Dermatology, Rheumatology, General Surgery, Gynecology and Obstetrics, Anesthesia and Reanimation, Medical Oncology, Plastic, Reconstructive and Aesthetic Surgery, Infectious Diseases .

Table 2. Distribution of clinical samples by hospital units

Hospital Units	N	%
Chest diseases	900	52.8
Pediatric	412	24.1
Cardiology	6	0. 4
Thoracic surgery	19	1.1
Neurology	23	1.4
Gastroenterology	44	2.6
Internal diseases	18	1
Other	284	16.6
Total	1706	100.0

According to the results of the research, more than half of the samples (52.8% (n=900)) were sent from the chest diseases unit.

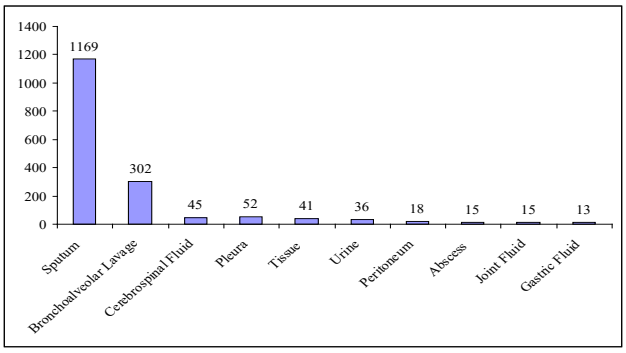

Figure 2. Distribution of clinical samples

Most of the clinical samples examined were sputum samples (n = 1169; 68.5%), followed by bronchoalveolar lavage samples with 17.7%.

Discussion and Conclusion

Tuberculosis maintains its importance as public health problems. Diagnosis and control of tuberculosis is extremely important in terms of protecting public health as it is an airborne disease (10). EZN staining is a rapid test used in the early diagnosis of tuberculosis. Even if the initial diagnosis of pulmonary and extra-pulmonary tuberculosis is made with clinical data, it is essential for the definitive diagnosis to be detected by laboratory tests (11).

Prior to the introduction of molecular methods into diagnostic mycobacteriology, the only way for rapid diagnosis of tuberculosis was the evaluation of EZN smears, preferably prepared from sputum, by direct microscopy. In microscopic examination, 5,000-10,000

bacilli per milliliter must be present in the patient sample (12). Although it is an inexpensive test and results can be obtained within one day, the staining technique applied to the samples of culture-confirmed tuberculosis cases, the low sensitivity (45-80%), which varies depending on the speed of the centrifugation process, the experience of the person evaluating the smear preparation, and the prevalence of tuberculosis in the studied population. Since it cannot be excluded and has a low positive predictive value (50-80%), microscopy is insufficient in the diagnosis of TB (13, 14).

In our study, EZN positivity was detected in 32 (1.9%) of 1706 samples. The sensitivity and specificity of EZN were found to be 41.6% and 99.2 respectively. Since M.tuberculosis and non-tuberculosis Mycobacteria cannot be distinguished by microscopic examination, culture is still considered as the gold standard (Table 1). If ≥10 live tuberculosis bacilli are found in the clinical sample, it can be demonstrated in culture. It is a conventional method with a sensitivity of 80-85% and a specificity of approximately 98%. Since M. tuberculosis divides and reproduces approximately every 18 hours, an average of 2-8 weeks is required for the agent to be identified in culture media (10,11,14).

Efforts are made around the world to make the routine use of rapid and reliable diagnostic tests with high specificity and sensitivity, at certain standards on which intensive research has been carried out. Many diagnostic systems and test techniques have been developed and put into use by the manufacturers, especially in the last 20 years that can be applied directly from patient samples and/or culture environments, and can provide fast results for the diagnosis of tuberculosis. Among these, molecular genetic techniques are promising (10, 15,16).

Nucleic acid amplification based molecular diagnostic tests are still being developed to support clinical and laboratory diagnosis, and research on their study performance continues uninterruptedly (13). Parallel with our results Malburny et al (17) conducted a study for the detection of M.tuberculosis by PCR (Xpert MTB/RIF) from a total of 180 samples, 91 of which were respiratory and 89 were non-respiratory, taken from 132 patients with suspected tuberculosis. PCR sensitivity and specificity were 100% and 100% and 85.7% and 97.3% for respiratory and non-respiratory samples, respectively. Kit-based commercial tests are used in the rapid diagnosis of tuberculosis. In a meta-analysis of sixty studies, the mean sensitivity and specificity of these tests were 96% and 85% in smear-positive samples, respectively; it was found to be 66% and 98% in smear-negative respiratory samples (18).

In our study the area under the curve (AUC) for TBC DNA was 0.79 for EZN, and 1.00 for Culture as a result of ROC analysis when culture was taken as a reference test (Figure 1). In addition, according to the results of the research, 52.8% (n = 900) of the samples were sent from the chest diseases unit (Table 2).The majority of clinical samples studied were sputum samples (n = 1169; 68.5%), followed by bronchoalveolar lavage samples with 17.7% (Figure 2).

In the study conducted by Kivihya-Ndgugga et al (19), the effectiveness of the PCR method and the routine procedures used in the diagnosis of tuberculosis were compared. As a result of the study, it was reported that the PCR method is superior to the routine procedures in the diagnosis of tuberculosis.

As a result, a test that can diagnose and detect drug resistance in a short time is needed for the effective and accurate treatment of tuberculosis , which causes approximately two million deaths each year. Microscopy cannot meet this need due to its low sensitivity despite its high specificity values. PCR method is reliable, fast and superior to the routine procedures in the diagnosis of tuberculosis but in the same time it is very expensive. Culture methods, which are still used as the gold standard, cause delays in diagnosis and treatment due to their high sensitivity and high specificity. Considering the samples with EZN (+) and culture (–),Non-M.tuberculosis mycobacteria (MOTT) was not determined in the study. Finally, it should be emphasized that the use of culture, PCR and EZN staining methods together in the microbiological diagnosis of tuberculosis is very important for early diagnosis and diagnosis of the disease all over the world.

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Declaration Of Interest Statement: All authors declare that they have no conflict of interest.

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References

1.World Health Organization. Global tuberculosis report https://www.who.int/tb/publications/global_report/en/. Accessed 15 October 2019.

2.Tomioka H, Namba K. Development of antituberculous drugs. current status and future prospects. Kekkaku 2006;81(12):753-74.

3.Baylan O. Tensively drug resistant and extremely drug resistant tuberculosis forms after multi-drug resistant tuberculosis: new faces of the old disease. Mikrobiyol Bul 2011;45(1):181-95.

4.Colonel A. Mycobacterium: General Characteristics, Laboratory Diagnosis and Staining Procedures. In: Başustaoğlu A. Clinical Microbiology. 1st ed.Atlas Bookstore, Ankara. 2009:543-72.

5.Yaman G, Parlak M, Demirol M, Güdücüoğlu H, Berktaş M. Evaluation of EZN Staining and Tuberculosis Culture Results of Various Clinical Samples. Ortadogu Med J 2012;4(1):19-22.

6.Ozkara SV. Tuberculosis Laboratory Diagnostic Methods. V

Tuberculosis Symposium and VI. Tuberculosis Laboratory Diagnostic Methods Applied Course; 18-21 October 2007; Ankara, Turkey.

7.Ceyhan İ, Şimşek H, Tarhan G. Comparison and evaluation of Lowenstein-Jensen medium and 2% Ogawa medium for the diagnosis of tuberculosis. Mikrobiyol Bul 2012;46(1):33-8.

8.Pfyffer G, Brown-Elliott BA, Wallace RJ. Mycobacterium: General characteristic, isolation, and staining procedures. Murray PR, Baron EJ, Jorgensen JH (Eds). Manuel of Clinical Microbiology. 8th ed. Washington: ASM Pres, 2003; 532-60.

9.Bulut Y. Molecular diagnostic Methods and Innovations. Trabzon mycobacteria days; 2009; Trabzon, Turkey.

10.Moore DF, Curry JI. Detection and identification of Mycobacterium tuberculosis directly from sputum sediments by ligase chain reaction. J Clin Microbiol 1998; 36:1028-31.

11.Cheng VC, Yew WW, Yuen KY. Molecular diagnostics in tuberculosis. Eur J Clin Microbiol Infect Dis 2005; 24:711-20.

12.Alp A. Current status in laboratory diagnosis of tuberculosis. Hacettepe Med J 2011; 42:28-33.

13.Centers for Disease Control and Prevention. Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. Morb Mortal Wkly Rep 2009;58: 7-10.

14.Zeka AN, Tasbakan S, Cavusoglu C. Evaluation of the GeneXpert MTB/RIF assay for rapid diagnosis of tuberculosis and detection of rifampin resistance in pulmonary and extrapulmonary specimens. J Clin Microbiol 2011; 49: 4138-41

15.Köksalan OK. Tuberculosis diagnosis and its weaknesses today. ANKEM 2010;24:61-3.

16.Nyendak MR, Lewinsohn DA, Lewinsohn DM.New diagnostic methods for tuberculosis. Curr Opin Infect Dis 2009;22:174-82.

17.Malbruny B, Le Marrec G, Courageux K, Leclercq R, Cattoir V. Rapid and efficient detection of Mycobacterium tuberculosis in respiratory and non-respiratory samples. Int J Tuberc Lung Dis 2011;15:553–55.

18.Greco S, Girardi E, Navarra A, Saltini C. Current evidence on diagnostic accuracy of commercially based nucleic acid amplifi cation tests for the diagnosis of pulmonary tuberculosis. Thorax 2006; 61:783–90.

19.Kivihya-Ndugga L, van Cleeff M, Juma E, Kimwomi J, Githui W, Oskam L, and Klatser P. Comparison of PCR with the routine procedure for diagnosis of tuberculosis in a population with high prevalences of tuberculosis and human immunodeficiency virus. J Clin Microbiol, 2004;42(3):1012-15.

20.T.R. Ministry of Health ''Tuberculosis Diagnosis and Treatment Guidelines''. 2019; 2.Print: Ankara.

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ORIGINAL ARTICLE

Increased Serum Kynurenine/Tryptophan Ratio in Rats Fed Added Sugar

İlave Şekerlerle Beslenen Ratlarda Artmış Serum Kinürenin/Triptofan Oranı

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ABSTRACT

Aim: The consumption of added sugars containing fructose has increased dramatically. Various studies have revealed that added sugar consumption may be involved in the pathogenesis of cardiovascular, metabolic, and neurocognitive disorders by triggering subclinical inflammation. The imbalance in the kynurenine pathway metabolites may be associated with inflammation and oxidative stress. This study aims to investigate the effect of high-fructose corn syrup-55 (HFCS-55), invert sugar and sucrose intervention on the kynurenine pathway metabolite levels (tryptophan, kynurenine, 3-hydroxykynurenine, 3-hydroxyanthranilic acid, quinolinic acid, and kynurenic acid) in Wistar rats.
Material and Methods: Twenty-four Wistar male rats (8-12 weeks old, weighing 300-350 g) were included in the study. After one week of conditioning, the animals were randomly divided into four groups: chow diet and tap water (control, n = 6), chow diet and tap water including 10% HFCS-55 (55% sucrose, 45% glucose), chow diet and tap water including 10% sucrose, chow diet and tap water including 10% invert sugar (33% sucrose, 66% glucose and fructose). At the end of the 3-month experimental period, serum kynurenine metabolites levels were measured by tandem mass spectrometry.
Results: Serum kynurenine levels and kynurenine/tryptophan ratio were significantly higher ($p<0.05$) and serum kynurenic acid levels were significantly lower ($p<0.05$) in rats fed with HFCS, sucrose and invert sugar compared to the control group.
Conclusion: Our findings suggest that consumption of added sugar may lead to an imbalance in the kynurenine pathway metabolites. The altered kynurenine metabolism may trigger inflammation and oxidative damage, and may predispose to chronic diseases.

Keywords: Tryptophan; kynurenine; HFCS; sucrose; inflammation.

ÖZ

Amaç: Fruktoz içeren ilave şekerlerin tüketimi önemli ölçüde artmıştır. Çeşitli çalışmalar, ilave şeker tüketiminin subklinik inflamasyonu tetikleyerek kardiyovasküler, metabolik ve nörobilişsel bozuklukların patogenezinde rol oynayabileceğini ortaya koymuştur. Kinürenin yolağı metabolitlerindeki dengesizlik, inflamasyon ve oksidatif stres ile ilişkili olabilir. Bu çalışmanın amacı, Wistar ratlarda yüksek fruktozlu mısır şurubu-55 (YFMŞ-55), invert şeker ve sukroz müdahalesinin kinurenin yolağı metabolit seviyeleri (triptofan, kinürenin, 3-hidroksikinürenin, 3-hidroksiantranilik asit, quinolinik asit ve kinürenik asit) üzerindeki etkisini araştırmaktır.
Gereç ve Yöntem: Yirmi dört Wistar erkek rat (8-12 haftalık, 300-350 g ağırlığında) çalışmaya dahil edildi. Bir haftalık koşullandırmadan sonra, hayvanlar rastgele dört gruba ayrıldı: normal besin ve musluk suyu (kontrol, n = 6), normal besin ve %10 HFCS-55 (%55 sakaroz, %45 glikoz) içeren musluk suyu, normal besin ve %10 sakaroz içeren musluk suyu, normal besin ve %10 invert şeker içeren musluk suyu (%33 sakaroz, %66 glikoz ve fruktoz). 3 aylık deney süresinin sonunda, tandem kütle spektrometrisi ile serum kinurenin seviyeleri ölçüldü.
Bulgular: Kontrol grubuna göre HFCS, sakkaroz ve invert şeker ile beslenen ratlarda serum kinurenin düzeyleri ve kinurenin/triptofan oranı anlamlı olarak daha yüksek ($p<0.05$) ve serum kinurenik asit düzeyleri anlamlı olarak daha düşük ($p<0.05$) bulundu.
Sonuç: Bulgularımız, ilave şeker tüketiminin kinurenin yolu metabolitlerinde bir dengesizliğe yol açabileceğini düşündürmektedir. Değişen kinurenin metabolizması, inflamasyonu ve oksidatif hasarı tetikleyebilir ve kronik hastalıklara zemin hazırlayabilir.

Anahtar Kelimeler: Triptofan; kinürenin; HFCS; sakkaroz; iltihap

Introduction

Intake of added sugars such as sucrose, invert sugar, and high-fructose corn syrup (HFCS) has increased dramatically in the last century. A growing body of evidence suggests that consumption of added sugars might have adverse health effects (1). Fructose is the main component of added sugars. Fructose metabolism is distinct from other sugars in that it causes a decrease in intracellular ATP levels, nucleotide turnover, and stimulation in uric acid production (2). This biochemical pathway is associated with mitochondrial oxidative stress leading to the blockade of fatty acid oxidation and stimulation in lipogenesis and gluconeogenesis (3).

The main added sugars in the human diet are HFCS and sucrose. HFCS forms are classified according to their fructose content as HFCS-55 (55% fructose and 45% glucose), HFCS-42 (42% fructose and 58% glucose) and HFCS-90 (90% fructose and 10% glucose) (4, 5). Invert sugar is another of the most used sweeteners by the industries in sugary foods and beverages. It is obtained by acid or enzymatic hydrolysis of sucrose and glucose, fructose and sucrose content varies depending on the degree of hydrolysis (6). Intake of added sugar is related to many diseases such as diabetes, obesity, cardiovascular diseases, liver diseases, cancer, cognitive disorders, and rodent models have characterized

various aspects of the resulting disease phenotypes (7). Chronic, low-grade inflammation is a key factor in the pathogenesis of these chronic diseases (8-10). Therefore, identifying modifiable risk factors that can reduce chronic inflammation is essential to prevent chronic diseases. According to observational studies, added sugar consumption may stimulate subclinical inflammation. At the center of the potential related mechanisms is that added sugar consumption increases de novo free fatty acid synthesis in the liver and these fatty acids trigger the production of reactive oxygen species, oxidative stress, and inflammatory processes (11). However, there is controversy and confusion regarding the metabolism and health effects of fructose, sucrose, and HFCS, and further studies are needed (12).

Recently, an increasing number of studies have demonstrated the relationship of the kynurenine pathway with inflammation, immune system activation, and neurodegeneration. It is the primary metabolic route of tryptophan and is responsible for approximately 99% of tryptophan catabolism, which is not used for protein synthesis (13). The metabolism of tryptophan via the kynurenine pathway is initiated by the enzymes tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO1 and IDO2) (14). IDO1 plays a minor role in tryptophan catabolism under physiological conditions, while the IDO1-dependent metabolism is strongly stimulated by interferons and other cytokines in inflammatory conditions (15). Kynurenine pathway has two main branches. Under physiological conditions, kynurenine is preferably converted into 3-hydroxykynurenine, 3-hydroxyanthranilic acid, quinolinic acid, and NAD+, these reactions are catalyzed by the enzymes kynurenine 3-monooxygenase (KMO), kynureninase (KYNU), 3-hydroxyanthranilic acid dioxygenase (3HAO) and quinolinate phosphoribosyl transferase (QPRT), respectively. The remaining kynurenine is converted to kynurenic acid by the kynurenine amino transferases (KATs) (16). Inflammation leads to alterations in the balance of the kynurenine pathway metabolites (15). It has been shown that imbalances in the kynurenine pathway may be involved in the pathogenesis of many diseases or disorders such as Alzheimer's, multiple sclerosis, amyotrophic lateral sclerosis, schizophrenia, bipolar disorder, depression, cancer, diabetes, cardiovascular diseases, rheumatoid arthritis (17-19).

In summary, although the consumption of added sugar is thought to be a risk factor for various chronic diseases through oxidative stress and inflammation-mediated mechanisms, there are conflicting findings on this subject, and more studies are needed. Therefore, in our study, we aimed to contribute to the elucidation of the effects of added sugar consumption on health by measuring the metabolites of the kynurenine pathway (tryptophan, kynurenine, 3-hydroxykynurenine, 3-hydroxyanthranilic acid, quinolinic acid, and kynurenic acid), which are markers associated with inflammation and oxidative stress, in Wistar rats administered added sugar.

Material and methods

Animals

Wistar Albino male rats, 8-12 weeks old (n = 24), weighting 300-350 g, were housed in their cages at constant temperature (24 ± 2 ° C), humidity (60%), 12-hour light / dark cycle and with free access to food and water. During the study, rats were housed in polycarbonate thermoregulated cages with 6 rats per cage in the Animal House of ……. University Experimental Medicine Research and Application Center (……..), ……., Turkey. After one week of conditioning, the animals were randomly divided into four groups: chow diet (Bil Yem, Turkey) and tap water (control, n = 6), chow diet (Bil Yem, Turkey) and tap water including 10% HFCS-55 (Cargill, U.S.A., 55% sucrose, 45% glucose), chow diet (Bil Yem, Turkey) and tap water including 10% sucrose (Konya Seker, Turkey, 50% sucrose, 50% glucose), chow diet (Bil Yem, Turkey) and tap water including 10% invert sugar (Torku, Turkey, 33% sucrose, 66% glucose and fructose). Ethical approval was obtained from ……Local Ethics Committee. The solid and liquid diet compositions are detailed in Table 1.

Table 1. Composition of the solid and liquid diets administered during the study to the different groups.

	Basal Diets	Sugar Solutions		
Composition	Chow diet	10% HFCS-55 Solution	10% Sucrose Solution	10% Invert Sugar Solution
Carbohydrate, %	62	10	10	10
of which sugars, %	-	10	10	10
Protein, %	23	-	-	-
Fat, %	4	-	-	-
Fiber, %	7	-	-	-
Minerals, %	5	-	-	-
Moisture, %	12	90	90	90

At the end of the 3-month experimental period, the rats have fasted for 12 hours and then the animals were anesthetized by intraperitoneal injection of ketamine (87 mg/kg) and xylazine (13 mg / kg), and body weights were recorded.

Sample Collection

Approximately 1 mL blood sample was taken into the serum separator gel tubes from the tail vein of Wistar rats between 8.00 and 10.00 AM. The blood samples in serum separator gel tubes were centrifuged at 2000 x g for 10 min and the serum samples were separated, portioned into eppendorf tubes, and stored at -80° C until analysis.

Tandem Mass Spectrometric Analysis

Chemicals

L-Tryptophan (CAS Number: 73-22-3), L-kynurenine (CAS Number 2922-83-0), Kynurenic acid (CAS Number 492-27-3), 3-Hydroxyanthranilic acid (CAS Number 548-93-6), 3-Hydroxy-DL-kynurenine (CAS Number 484-78-6), Quinolinic acid (CAS Number 89-00-9), HPLC grade water (CAS Number: 7732-18-5), acetonitrile (CAS Number 75-05-8), formic acid (CAS Number: 64-18-6) and L-Kynurenine- d4 Trifluoroacetic Acid Salt (Catalog No: K661007) were obtained from Sigma Aldrich and Toronto Research Chemicals (North York, ON, Canada), respectively.

Instrumentation

Chromatographic separation was performed using a Shimadzu HPLC system (Kyoto, Japan) and Phenomenex C18 HPLC column (50 mm x 4.6 mm). API 3200 triple quadrupole mass spectrometer equipped with an electrospray ionization interface was used (Applied Biosystems/MDS Sciex) as the detector. The mobile phase A and B consisted of 0.1% formic acid/water (v/v%) and 0.1% formic acid/acetonitrile (v/v%), respectively. The total run time was 5 minutes. The Q1 to Q3 ion transitions were 205.2/146.2, 209.1/94.1, 190.2/144.0, 154.0/136.0, 225.1/110.0, 168.0/124.0, and 213.1/140.1 for tryptophan, kynurenine, kynurenic acid, 3-hydroxyanthranilic acid, 3-hydroxykynurenine, quinolinic acid, and kynurenine-d4, respectively. Ionspray voltage, source temperature, curtain, ion source (GS1), and ion source (GS2) gas values were adjusted to 5000 V, 350 °C, 20, 50, 50 psi, respectively. Intra and inter-assay CV% values were lower than 7% and recovery values were higher than 96% for all metabolites.

Sample Preparation

Serum tryptophan, kynurenine, kynurenic acid, 3-hydroxyanthranilic acid, 3-hydroxykynurenine, and quinolinic acid concentrations were measured with the modification of the method developed by Tong et al (20). Briefly; 300 µL of serum sample was taken into eppendorf tubes and 100 µL of kynurenine-d4 was added. To precipitate proteins, the mixture was vortexed with 1000 µL acetonitrile containing 1% formic acid (v/v%) for 30 seconds and centrifuged at 15000 rpm for 10 minutes. The supernatants were evaporated under nitrogen gas at 40°C. The residues were dissolved in 200 µL acetonitrile containing 0.1% formic acid: water (25:75, v/v%) mixture. 30 µL was injected into LC-MS/MS system.

Statistical Analysis

Statistical analysis was performed with SPSS statistical software package version 21.0. Shapiro-Wilk test was performed to find out the distribution. One-way ANOVA analysis (post-hoc analysis with LSD or Games-Howell) was performed to compare more than two groups. $p<0.05$ was considered as statistically significant.

Results

The initial weights of the HFCS, sucrose, invert sugar, and control groups were 374.66±20.15, 381.83±19.47, 376.66±17.90, and 381.50±14.81 g, respectively, and there was no statistically significant difference between the groups (p = 0.875). After the 3-month added sugar intervention, weights of the HFCS, sucrose, invert sugar, and control groups were 539.10±54.19, 540.66±50.68, 517.33±66.82 and 490.83±40.93 g, respectively, and there was no statistically significant difference between the groups (p = 0.365).

Serum kynurenine levels and kynurenine/tryptophan ratio were significantly higher ($p<0.05$) and serum kynurenic acid levels were significantly lower ($p<0.05$) in rats fed with HFCS, sucrose, and invert sugar compared to the control group. Serum quinolinic acid ($p<0.001$), 3-hydroxyanthranilic acid (p=0.025), and 3-hydroxykynurenine (p=0.022) levels in rats fed with HFCS were significantly higher than the control group. Moreover, serum 3-hydroxykynurenine (p=0.042), quinolinic acid (p=0.034), and kynurenine/tryptophan ratio (p=0.023) were significantly higher in rats fed with HFCS compared to the invert sugar group (Table 2 and Figure 1).

Table 2. Kynurenine pathway metabolite levels of rats fed added sugars.

	HFCS	Sucrose	Invert sugar	Control	p
					a:0.064
Tryptophan (ng/mL)	15860±932	13160±725	14985±760	15349±854	b:0.128
					c:0.795
					a:0.007
Kynurenine (ng/mL)	372.34±93.52	264.92±22.90	260.42±35.44	161.64±64.95	**b:0.037**
					c:0.047
					a:<0.001
Kynurenine/Tryptophan	0.0233±0.0045**	0.0206±0.0042	0.0174±0.0041	0.0106±0.0035	**b:<0.001**
					c:0.010
					a:0.022
3-hydroxykynurenine (ng/mL)	11.99±4.35**	9.57±6.09	6.38±2.34	5.58±2.32	b:0.138
					c:0.758
					a:0.025
3-hydroxyanthranilic acid (ng/mL)	62.95±19.95	45.39±11.41	55.81±15.10	41.76±12.55	b:0.682
					c:0.123
					a:<0.001
Quinolinic acid (ng/mL)	6.63±0.70**	6.20±1.18	4.17±0.91	2.67±0.81	b:0.288
					c:0.256
					a:0.019
Kynurenic acid (ng/mL)	84.98±8.18	92.86±10.77	96.13±11.46	142.26±30.43	**b:0.034**
					c:0.048

a: HFCS vs control, b: Sucrose vs control, c: Invert vs control, **: statistically significant difference between HFCS and invert sugar groups.

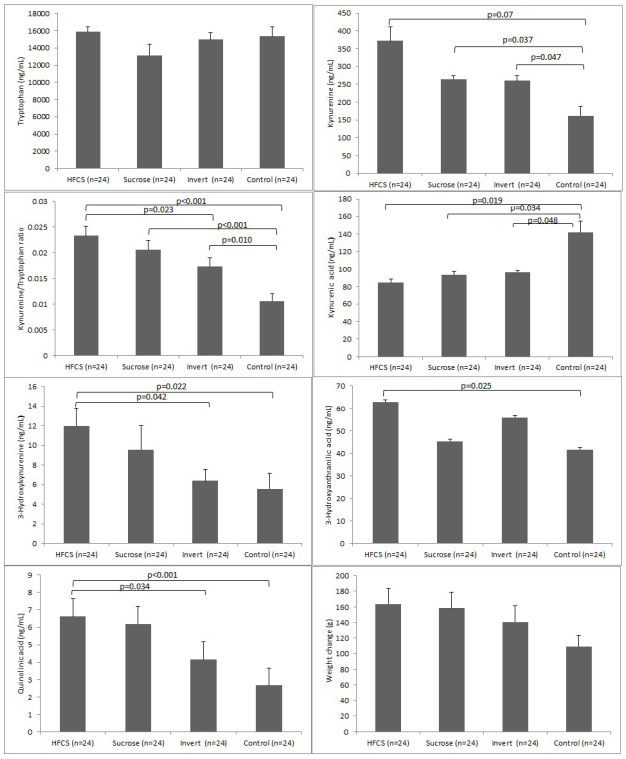

Figure 1. The change of tryptophan-kynurenine pathway metabolite levels and weight in rats fed with added sugars.

Discussion

The health effects of added sugars have become one of the most debated topics in all nutrition. Overconsumption of added sugars has been associated with an increased risk of diabetes, obesity, cardiovascular disease, dyslipidemia, liver disease, cognitive decline, and even cancer (7). However, data to support these claims have been consistently challenged and many contradictory studies have been shown (21-24). Chronic, low-grade inflammation plays a key role in the pathogenesis of all these diseases. According to observational studies, dietary added sugar intake may induce subclinical inflammation (11).

Aeberli et al. investigated the effects of sugar-sweetened beverages (SSBs) consumed in small to medium amounts for 3 weeks in twenty-nine healthy young men subjects (age: 20–50 years, BMI: 19–25 kg/m2). Six 3-week interventions were designed in random order as follows: 600 mL SSBs containing 1) 40 g fructose / d [medium fructose (MF)], 2) 80 g fructose / d [high fructose (HF)], 3) 40 g glucose / d [medium glucose (MG)], 4) 80 g glucose / d [high glucose (HG)], 5) 80 g sucrose / d [high sucrose (HS)], or 6) dietary advice to consume low fructose. As a result of the study, it was shown that high-sensitivity C-reactive protein (hs-CRP) levels increased significantly after all interventions (60-109%, $p < 0.05$) (25). Jin et al conducted 4-week double-blind, randomized controlled intervention study with 24 overweight Hispanic-American adolescents (hepatic fat> 8%, age 11–18 years, BMI> 85th percentile). Intervention groups were as follows: fructose-sweetened beverage (n = 11) (99 g / day) and glucose-sweetened beverage (n = 13) (99 g / day). As a result of the study, a statistically significant change was observed between the hs-CRP levels among the groups ($p = 0.019$). After the 4-week intervention, subjects receiving glucose drinks showed significant improvement in plasma hs-CRP levels, adipose insulin sensitivity, and LDL oxidation (26).

A randomized, single-blind study involving healthy subjects (n = 14) was conducted by Jameel et al. after an overnight fast, participants were given one of 3 different isocaloric drinks containing 50 g of fructose or glucose or sucrose dissolved water. 30, 6, and 120 minutes after the intervention, blood samples of the participants were collected and their plasma lipid, insulin, and hs-CRP levels were measured. The changes in plasma cholesterol, LDL, and HDL levels (expressed as area under curve, AUC) were found higher in fructose-consuming participants than others. The change in hs-CRP levels was higher in participants consuming fructose than those consuming glucose ($p<0.05$), while no statistically significant difference was found with the sucrose group ($p=0.07$) (27).

However, studies are showing that there is no significant difference in the levels of inflammation markers such as hs-CRP, interleukin-6, and TNF-a in the fructose and glucose intervention groups (28-31).

Increased inflammatory signals induce IDO-1 activity, leading to an imbalance in the kynurenine pathway metabolite levels (32). For example, in a study conducted with rheumatoid arthritis patients, it was reported that serum tryptophan, 3-hydroxykynurenine, and 3-hydroxyanthranilic acid levels decreased while kynurenine, kynurenic acid, and xanthurenic acid concentrations were increased compared to healthy controls (19). Our findings show that serum kynurenine levels and kynurenine/tryptophan ratio were significantly higher in rats fed with HFCS, sucrose, and invert sugar compared to the control group, and the levels of kynurenic acid were significantly lower. Moreover, serum quinolinic acid, 3-hydroxyanthranilic acid, and 3-hydroxykynurenine levels of rats fed with HFCS were significantly higher than the control group. Our findings suggested that the balance between kynurenine pathway metabolite levels was disturbed in rats consuming added sugar and this may be associated with increased inflammation or oxidative stress.

This study indicates that the consumption of added sugar, especially HFCS, may trigger chronic diseases by triggering metabolic events related to inflammatory response and oxidant-antioxidant balance in the organism. Since the consumption of added sugar is a preventable risk factor, studies that reveal the effects of added sugar consumption on health are clinically very important. However, the lack of measurements

of other parameters related to inflammation and oxidant-antioxidant balance, and the limited number of experimental animals are the main limitations of the study.

Conclusions

To our best knowledge, this is the first study to comprehensively investigate the kynurenine pathway metabolite (tryptophan, kynurenine, 3-hydroxykynurenine, 3-hydroxyanthranilic acid, quinolinic acid, and kynurenic acid) levels in rats fed different added sugars (HFCS-55, invert sugar, sucrose). Our findings provide new evidence that the balance between kynurenine pathway metabolite levels is disrupted in rats consuming added sugar and that this may be a risk factor for cardiovascular diseases, neurocognitive disorders, and metabolic diseases through increased inflammation or oxidative stress. Dietary habits are one of the most easily modifiable risk factors. Given the dramatic increase in added sugar intake and potential adverse health effects, it is essential to identify the biochemical and pathological pathways involved in added sugar consumption, and further studies are needed.

Conflict of Interest

The authors declare that they have no conflict of interest relevant to the content of this manuscript.

References

1.Heidari-Beni M, Kelishadi R. The Role of dietary sugars and sweeteners in metabolic disorders and diabetes. In: Mérillon J-M, Ramawat KG, eds. Sweeteners: Pharmacology, Biotechnology, and Applications. Cham: Springer International Publishing 2018:225-243.

2.Johnson RJ, Nakagawa T, Sanchez-Lozada LG, et al. Sugar, uric acid, and the etiology of diabetes and obesity. Diabetes 2013;62(10):3307-3315.

3.Johnson RJ, Sánchez-Lozada LG, Andrews P, Lanaspa MA. Perspective: A historical and scientific perspective of sugar and its relation with obesity and diabetes. Adv Nutr 2017;8(3):412-422.

4.Rippe JM, Angelopoulos TJ. Added sugars and risk factors for obesity, diabetes and heart disease. Int J Obes (Lond) 2016;40 Suppl 1:S22-27.

5.Parker K, Salas M, Nwosu V. High fructose corn syrup: production, uses and public health concerns Biotechnol Mol Biol Rev 2011;5:71-8.

6.Molz P, Molz W, Dallemole D, et al. Invert sugar induces glucose intolerance but does not cause injury to the pancreas nor permanent DNA damage in rats. Anais da Academia Brasileira de Ciências 2020;92.

7.Rippe JM, Angelopoulos TJ. Relationship between Added Sugars Consumption and Chronic Disease Risk Factors: Current Understanding. Nutrients 2016;8(11):697.

8.Pereira SS, Alvarez-Leite JI. Low-Grade Inflammation, Obesity, and Diabetes. Curr Obes Rep 2014;3(4):422-431.

9.Lopez-Candales A, Hernández Burgos PM, Hernandez-Suarez DF, et al. Linking Chronic Inflammation with Cardiovascular Disease: From Normal Aging to the Metabolic Syndrome. J Nat Sci 2017;3(4).

10.Minihane AM, Vinoy S, Russell WR, et al. Low-grade inflammation, diet composition and health: current research evidence and its translation. Br J Nutr 2015;114(7):999-1012.

11.Della Corte KW, Perrar I, Penczynski KJ, et al. Effect of dietary sugar intake on biomarkers of subclinical inflammation: a systematic review and meta-analysis of intervention studies. Nutrients 2018;10(5).

12.Ruff JS, Hugentobler SA, Suchy AK, et al. Compared to sucrose, previous consumption of fructose and glucose monosaccharides reduces survival and fitness of female mice. The Journal of nutrition 2015;145(3):434-441.

13.Davis I, Liu A. What is the tryptophan kynurenine pathway and why is it important to neurotherapeutics? Expert Rev Neurother 2015;15(7):719-721.

14.Larkin PB, Sathyasaikumar KV, Notarangelo FM, et al. Tryptophan 2,3-dioxygenase and indoleamine 2,3-dioxygenase 1 make separate, tissue-specific contributions to basal and inflammation-induced kynurenine pathway metabolism in mice. Biochim Biophys Acta 2016;1860(11):2345-2354.

15.Sorgdrager FJH, Naudé PJW, Kema IP, et al. Tryptophan Metabolism in Inflammaging: From Biomarker to Therapeutic Target. Front Immunol 2019;10(2565).

16.Savitz J. The kynurenine pathway: a finger in every pie. Mol Psychiatry 2020;25(1):131-147.

17.Chen Y, Guillemin GJ. Kynurenine pathway metabolites in humans: disease and healthy States. Int J Tryptophan Res 2009;2:1-19.

18.Song P, Ramprasath T, Wang H, et al. Abnormal kynurenine pathway of tryptophan catabolism in cardiovascular diseases. Cell Mol Life Sci 2017;74(16):2899-2916.

19.Forrest CM, Kennedy A, Stone TW, et al. Kynurenine and neopterin levels in patients with rheumatoid arthritis and osteoporosis during drug treatment. Adv Exp Med Biol 2003;527:287-295.

20.Tong Q, Song J, Yang G, et al. Simultaneous determination of tryptophan, kynurenine, kynurenic acid, xanthurenic acid and 5-hydroxytryptamine in human plasma by LC-MS/MS and its application to acute myocardial infarction monitoring. Biomedical chromatography: BMC 2018;32(4).

21.Lowndes J, Sinnett S, Pardo S, et al. The effect of normally consumed amounts of sucrose or high fructose corn syrup on lipid profiles, body composition and related parameters in overweight/obese subjects. Nutrients 2014;6(3):1128-1144.

22.Hodge AM, English DR, O'Dea K, et al. Glycemic index and dietary fiber and the risk of type 2 diabetes. Diabetes Care 2004;27(11):2701-2706.

23.Sievenpiper JL, de Souza RJ, Mirrahimi A, et al. Effect of fructose on body weight in controlled feeding trials: a systematic review and meta-analysis. Ann Intern Med 2012;156(4):291-304.

24.Jacobs DR, Jr., Meyer KA, Kushi LH, et al. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. Am J Clin Nutr 1998;68(2):248-257.

25.Aeberli I, Gerber PA, Hochuli M, et al. Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. Am J Clin Nutr 2011;94(2):479-485.

26.Jin R, Welsh JA, Le NA, et al. Dietary fructose reduction improves markers of cardiovascular disease risk in Hispanic-American adolescents with NAFLD. Nutrients 2014;6(8):3187-3201.

27.Jameel F, Phang M, Wood LG, et al. Acute effects of feeding fructose, glucose and sucrose on blood lipid levels and systemic inflammation. Lipids Health Dis 2014;13:195.

28.Angelopoulos TJ, Lowndes J, Sinnett S, et al. Fructose Containing Sugars at Normal Levels of Consumption Do Not Effect Adversely Components of the Metabolic Syndrome and Risk Factors for Cardiovascular Disease. Nutrient 2016;8(4):179.

29.Johnston RD, Stephenson MC, Crossland H, et al. No difference between high-fructose and high-glucose diets on liver triacylglycerol or biochemistry in healthy overweight men. Gastroenterology 2013;145(5):1016-1025.e1012.

30.Silbernagel G, Machann J, Häring HU, et al. Plasminogen activator inhibitor-1, monocyte chemoattractant protein-1, e-selectin and C-reactive protein levels in response to 4-week very-high-fructose or -glucose diets. Eur J Clin Nutr 2014;68(1):97-100.

31.Raatz SK, Johnson LK, Picklo MJ. Consumption of Honey, Sucrose, and High-Fructose Corn Syrup Produces Similar Metabolic Effects in Glucose-Tolerant and -Intolerant Individuals. J Nutr 2015;145(10):2265-2272.

32.Huang YS, Ogbechi J, Clanchy FI, et al. IDO and Kynurenine Metabolites in Peripheral and CNS Disorders. Front Immunol 2020;11(388).

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ORIGINAL ARTICLE

Neonatal Jaundice: Knowledge, Practice, And Attitude Among Primigravida Women

Yenidoğan Sarılığı: Primigravid Kadınlarda Bilgi, Uygulama ve Tutumlar

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ABSTRACT

Objective: Neonatal jaundice is characterized by a yellowish coloration of the skin and sclera of newborn infants and elevated serum bilirubin levels.
In this study, it was aimed to evaluate the knowledge, practices and attitudes of primigravidas in Diyala province of Iraq regarding neonatal jaundice.
Material and Methods: A questionnaire was applied to 165 women who were primigravidas between January 1, 2022 and March 31, 2022 in hospitals and health centers to evaluate their knowledge, practices and attitudes about neonatal jaundice.
Results: Although 71.4% of the women knew the two signs of neonatal jaundice, 78.8% of them did not know any of the dangerous signs of neonatal jaundice. 28.4% of women knew that there are two effective treatment methods for the treatment of neonatal jaundice. 57.6% of the women were not aware of any of the severe complications of neonatal jaundice.
Conclusion: Most of the primigravida in this study decided to visit physicians when their babies have jaundice without using traditional treatment.

Keywords: Neonatal jaundice, knowledge, practice, and attitudes

ÖZ

Amaç: Yenidoğan sarılığı, yenidoğan bebeklerin cilt ve skleralarının sarımsı bir renk alması ve serum bilirubin düzeylerinin yükselmesi ile karakterizedir.
Bu çalışmada Irak'ın Diyala ilindeki primigravidlerin yenidoğan sarılığı ile ilgili bilgi, uygulama ve tutumlarının değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntemler: 1 Ocak 2022-31 Mart 2022 tarihleri arasında hastane ve sağlık ocaklarında primigravid 165 kadına yenidoğan sarılığı ile ilgili bilgi, uygulama ve tutumlarını değerlendirmek için anket uygulandı.
Bulgular: Kadınların %71.4'ü yenidoğan sarılığının iki belirtisini bilse de %78.8'i yenidoğan sarılığının tehlikeli belirtilerinden hiçbirini bilmiyordu. Kadınların %28.4'ü yenidoğan sarılığının tedavisi için iki etkili tedavi yöntemi olduğunu biliyordu. Kadınların %57.6'sı yenidoğan sarılığının ciddi komplikasyonlarından habersizdi.
Sonuç: Bu çalışmadaki primigravidlerin çoğu, bebekleri sarılık olduğunda geleneksel tedaviyi kullanmadan doktorları ziyaret etmeye karar verdi

Anahtar kelimeler: Yenidoğan sarılığı, bilgi, uygulama ve tutumlar

Introduction

Neonatal jaundice (NNJ) is a yellowish coloration of the skin and sclera of newborns, and it is mediated by the elevation of bilirubin in the blood (1).

The imbalance between production and excretion of bilirubin leads to increased bilirubin levels in the blood and discoloration of the skin and other membranes. (2,3)also have positive attitudes, and are not guided by outmoded socio-cultural beliefs and practices are more likely to seek early care and treatment for neonatal jaundice. Objective: This study investigated caregivers' knowledge, attitude and practices regarding neonatal jaundice in a tertiary health facility in the Volta region of Ghana. Methods: This was a descriptive cross-sectional study that employed a quantitative approach for data collection. A total of 202 caregivers from the Ho Teaching Hospital in the Volta region of Ghana were sampled using a systematic random sampling strategy where quantitative data was collected using a questionnaire and analyzed with STATA version 14.0. Ordered logistic regression was used to determine the factors that were associated with caregivers' knowledge regarding neonatal jaundice and attitude after controlling for relevant covariates. Results: Less than half of the caregivers demonstrated good knowledge (45.5%.

Neonatal jaundice may be physiological due to the inability of the immature newborn's liver to convert unconjugated bilirubin for execration. (4,5).

Pathological jaundice may be due to ABO and Rh incompatibility prematurity, infections, and septicemia (6,7). If a high level of neonatal bilirubin is not detected

and treated can result in lethargy, poor feeding, acute and chronic encephalopathy, and significant disability such as mental retardation and deafness (8,9).

Earlier studies showed that mothers have inadequate knowledge about causes, signs and symptoms, and prevention of NNJ complications. Approximately 35% of mothers identified jaundice from discoloration of skin and eyes(10). Another study found that approximately 70% of women with infants had moderate knowledge about NNJ. Approximately 30% of them consulted a physician after the onset of neonatal jaundice, while 14% of them used traditional medicines before seeking medical advice (11,12).

African pregnant women have a high awareness of the signs and symptoms of NNJ while having poor knowledge of its causes and complications (13-16). This knowledge was different from one country to another, such as in Iran (77%), Iraq (80.2%), Ethiopia (63.5%), and Malaysia (70%) (11,14,16-18)yet preventable health problem, particularly in low-and middle-income countries (LMICs.

Several harmful practices are applied for the treatment of NNJ, such as cutting of post auricular area of an infant, using herbal treatment, exposure of neonate to sunshine, and giving glucose water to the infant (12,15-19). Therefore, this study aims to determine primigravida women's knowledge, practice, and attitude to neonatal jaundice in Diyala governorate.

Material and Methods

This is a descriptive-analytical hospital-based study to evaluate the knowledge background of primigravida women of reproductive age toward neonatal jaundice regarding causes, clinical manifestation, complications, mode of treatment, and other aspects, in addition to their practice and attitude regarding conventional medical approaches. From 1 January 2022 – to 31 March 2022, a sample of pregnant women attending AL- Batool Teaching hospital and five primary health care centers in Baqubah city/ Diyala Governorate/Iraq was selected randomly. At the end of the study, we collected information from 165 pregnant women. We included the following variables in the questionnaire: Demographic characteristics including age, residency, age of current pregnancy, education level, and occupation, knowledge domain included symptoms of jaundice, dangerous symptoms of jaundice, causes of neonatal jaundice, effective treatment, and the complications of severe jaundice. The practice and attitude domains included direct questions with yes or no responses. These questions were about using medical herbs, fluorescent use at home, using sunlight, referring to a physician, or referring to traditional healers. The ethics committee at the college of medicine /university of Diyala approved this study, and We took verbal consent from primigravida women involved in the study. The data were processed and analyzed using the Statistical Package for Social Sciences version 21 (SPSS Inc., Chicago, IL, USA. Multivariate logistic regression test was used to analyze risk factors. A p-value <0.05 was considered significant, and the confidence interval was set at 95%.

Results

Table 1 shows the maternal variables, where the common age of the respondents was 53.33% between 18-25 years old, and 69.09% were from urban areas. In comparison, the women in the second trimester of pregnancy constituted (n= 94, 56.96% of the respondents. About half of them (n= 84, 50.90%) have a secondary level of education.

Table 1. The characteristics of the study group

Variables	No.	(%)
Respondents' age (in years)		
18 – 25	88	53.33%
26 – 35	53	32.12%
36 – 45	24	14.54%
Total	165	100%
Age of present pregnancy		
First trimester	35	21.20%
Second trimester	94	57.00 %
Third trimester	36	21.80%
Total	165	100%
levels of education		
Primary	46	27.90%
Secondary	84	50.90%
Tertiary (University, Institute)	35	21.20%
Total	165	100%
Kind of residency		
Rural	51	30.90%
Urban	114	69.10%
Total	165	100%
Employment		
Housewife	103	62.42%
Private sector employee	10	6.06%
Governmental sector	52	31.51%
Total	165	100%

Table (2) shows the frequency distribution of primigravida mothers according to the knowledge domain. Low education level of the mothers lead to knowledge level being insufficient by 2.01 folds in comparison to educated women (OR 2.1, 95% CI 1.3-3.4; p = 0.003). Primigravida women employed in public and private sectors were twice likelier to have a good attitude about jaundice than housewives [AOR = 2.07, (95%CI: 1.03-4.20), *P* = 0.041]. A high proportion of mothers knew two or more symptoms of jaundice 71.4%, and a few knew only one sign of jaundice 21.9%. Eleven women 6.7% said they know none of the symptoms of jaundice. About dangerous features of jaundice, 130 primigravidas 78.8 % know none of the symptoms, and a small proportion of them 21.2% especially those in the third trimester knew one sign. [AOR = 2.07, (95%CI: 1.03-4.20), *P* = 0.041]. Rural residence women had low level of knowledge

of jaundice in comparison to urban women (OR 2.1, 95% CI 1.3-3.4; p = 0.004). A high number of mothers do not know/ or had no information about the causes of neonatal jaundice (n=74), only 50 women could know a single cause, and 41 24.8% knew two or more causes of jaundice. A high number of mothers knew one effective mode of therapy 57%, 28.4 % knew two effective ways, and 14.6 % knew a non-effective therapy mode. Most participants knew nothing about complications of neonatal jaundice 57.6%. Women who know one complication accounted for 28.5%, while those who know two or more complications accounted for 13.9%.

Table 2: Frequency distribution of the study group according to knowledge domain questions:

Knowledge domain response	No.	%	P value
Symptoms of jaundice(Yellowish discoloration of the eyes, skin, other membranes and Pallor)			
0	11	6.7	
1	36	21.9	
≥2	118	71.4	0.0451
Dangerous features of jaundice (Refusal of feeds, fever, lethargy, and convulsion)			
0	130	78.8	0.0532
1	35	21.2	
≥2	0	----	
Causes of neonatal jaundice (infection, blood incompatibility, and prematurity)			
0	74	44.8	0.0894
1	50	30.4	
≥2	41	24.8	
Effective treatment (phototherapy, blood transfusion)			
0	24	14.6	
1	94	57	0.05
2	47	28.4	
The complication of severe jaundice (brain damage, deafness, mental handicap, and death)			
0	95	57.6	
1	47	28. 5	
≥2	23	13.9	*0.097158*

The frequency of mothers according to practice domain is demonstrated in table 3. Regarding the first question, "Using medical herbs," the yes response was 79.4 %, and the no response was 20.6 %. Regarding the second question, "Fluorescent use at home," the yes answer accounted for 86.1%, whereas the no response accounted for 13.9 %. Yes, the response regarding the third question, "Using sunlight," was 6.7 %, whereas no response accounted for 93.3%. Regarding the fourth question, "Referring to physician," a yes response accounted for 93.3%, whereas a no response accounted for 6.7%. Regarding the fifth question, "Referring to traditional healers," a yes response accounted for 0.0 %, whereas a no response accounted for 100%.

Table 3: Frequency distribution of the study group according to practice &attitude domains questions

Question	**Response**				
	Yes		No		P value
	No.	%	No.	%	
1. Using medical herbs	131	79.4	34	20.6	0.0895
2. Fluorescent use at home	142	86.1	23	13.9	0.05
3. Using sunlight	11	6.7	154	93.3	0.045
4. Referring to the physician	154	93.3	11	6.7	0.035
5. Referring to traditional healers	0	0.0	165	100.0	0.001
6. Nothing	0	0.0	165	100.0	0.001

Discussion

This study reveals that participants have some knowledge of various aspects of neonatal jaundice. More than half (53.03%) of the primigravida women were aged between 18-25 years old. Pregnant women in the third trimester were two times more likely to have a good attitude about jaundice than those in the first and second trimesters, which is similar to Ethiopian and Ghana studies (16,20) this may be related that women in third trimester have more chance and time to learn about jaundice etiology and complications from other people or their families. Women in the rural residence had low knowledge level by 2.1 folds in comparison to urban women, as well as low education level of the mothers lead to knowledge level being insufficient by 2.01 folds in comparison to educated women which is similar to other studies (17,19,21). Primigravida women employed in public and private sectors were twice likelier to have a good attitude about jaundice than housewives which may be related to increased awareness about NNJ from other women in the field of work. In this study, mothers' awareness of neonatal jaundice symptoms is high; 71% knew two signs, while 21.9 % knew one symptom. It is near the rate reported by an earlier study in Iraq, where 81% knew two symptoms of NNJ) [14yet preventable health problem, particularly in low-and middle-income countries (LMICs]. Despite the high knowledge of women about the symptoms of jaundice, the knowledge was low in many aspects, such as the dangerous features and complications of NNJ. Most women knew nothing about dangerous features of jaundice; they accounted for about 78.8 %, and 21.2% knew one perilous symptom. Also 57.6% of women knew nothing about complications of severe jaundice. This finding indicates the proper knowledge of women in our community about dangerous symptoms and complications of severe NNJ is low. This study agrees with former studies, (14, 17,19,21). More than half of mothers in this study know one or more causes of NNJ while 44.8% did not know any possible cause of NNJ, however, 24.8% of them know more than two possible causes of NNJ, which is a promising result, these findings are similar to a previous study

(14). Many mothers in this study are more likely to use good practices such as referring to a physician and use of fluorescent light; at home. The use of traditional medicine to treat NNJ is common in underdeveloped countries (14,17-19). All participants in this study did not attend traditional, healers (that =165, 100%). Using medical herbs is a common practice in our community to treat NNJ, however we found 20.6% dislike using such herbs. While using sunlight is an uncommon practice in this study, 93.3% said it is an ineffective practice to treat NNJ ,however 85.4% of studied women know two effective modes of treating NNJ (phototherapy and blood transfusion , similar results were obtained in previous studies (12,13,20).

Conclusion

One of the promising approaches practiced by primigravida in this study was a positive response to visit physicians when facing problems with neonatal jaundice without using traditional treatment. Maternal education level and urban residence are essential factors affecting mothers' knowledge about neonatal jaundice.

Recommendations: to change malpractices with NNJ in the community, the level of education of women in the community should be increased, especially in primary health centers, and invested in social media to correct how to deal with neonatal jaundice.

References

1. Abbey P, Kandasamy D, Naranje P. Neonatal jaundice. Indian J Pediatr 2019;86:830–41.

2. Khan RS, Houlihan DD, Newsome PN. Investigation of jaundice. Medicine (Baltimore) 2015;43:573–6.

3. Salia SM, Avaya A, Wuni A, et al. Knowledge, attitudes, and practices regarding neonatal jaundice among caregivers in a tertiary health facility in Ghana. PLoS One 2021;16:1–20.

4. Anderson CM, Kandasamy Y, Kilcullen M. The efficacy of home phototherapy for physiological and non-physiological neonatal jaundice: A systematic review. J Neonatal Nurs 2021;28;,312-26

5. Olusanya BO, Teeple S, Kassebaum NJ. The Contribution of Neonatal Jaundice to Global Child Mortality: Findings From the GBD 2016 Study. Pediatrics 2018;141: e20171471

6. Aggarwal B, Agrawal A, Chaudhary P, Gupta G, Rana S, Gupta S. Neonatal Jaundice: Knowledge, attitude beliefs, and practices of postnatal mothers in a tertiary care hospital in Uttarakhand, India. Indian J Child Health 2017;4:603–8.

7. Padidar P, Shaker M, Amoozgar H, et al. Detection of neonatal jaundice by using an android OS-based smartphone application. Iran J Pediatr 2019;29, e84397.

8. Christensen RD, Agarwal AM, George TI, Bhutani VK, Yaish HM. Acute neonatal bilirubin encephalopathy in the State of Utah 2009–2018. Blood Cells, Mol Dis 2018;72:10–3.

9. Mojtahedi SY, Izadi A, Seirafi G, Khedmat L, Tavakolizadeh R. Risk factors associated with neonatal jaundice: A cross-sectional study from Iran. Open Access Maced J Med Sci 2018;6:1387.

10. Khalesi N, Rakhshani F. Knowledge, attitude and behavior of mothers on neonatal jaundice. Seizure 2008;95:23–7.

11. Amirshaghaghi A, Ghibli K, Shoja MM, Kooshavar H. Neonatal jaundice: knowledge and practice of Iranian mothers with icteric newborns. Pak J Biol Sci 2008;11:942–5.

12. Goodman OO, Kehinde OA, Odugbemi BA, Femi-Adebayo TT, Odusanya OO. Neonatal Jaundice: Knowledge, Attitude and practices of mothers in Mosan-Okunola community, Lagos, Nigeria. Niger Postgrad Med J 2015,22:158-63.

13. Egube BA, Ofili AN, Isara AR, Onakewhor JU. Neonatal jaundice and its management: knowledge, attitude, and practice among expectant mothers attending antenatal clinic at University of Benin Teaching Hospital, Benin City, Nigeria. Niger J Clin Pract 2013;16:188–94.

14. Aalan Hadi Al-Zamili, Zainab Allawi Saadoon. Knowledge, Attitude and Practice of Mothers to Neonatal Jaundice. *Medico-Legal Update* 2020;*20*,1065–70.

15. Ogunlesi TA, Abdul AR. Maternal knowledge and care. Seeking behaviors for newborn jaundice in Sagamu, Southwest Nigeria. Niger J Clin Pract 2015;18:33–40.

16. Adeeb MNA, Kumarasamy K, Hamid SA, Mahat N, Arumugam K, Shukor SA. Knowledge and Attitude of Neonatal Jaundice–Orang Asli Perspective. J Sains Kesihat Malaysia 2016;14:65–8.

17. Adebami OJ. Appraisal of maternal knowledge of neonatal jaundice in Ilesa, Southwestern Nigeria: implications for the persistence of acute bilirubin encephalopathy in developing countries. Basic Res J Med Clin Sci 2015;4:156–63.

18. Shrestha S, Maharjan S, Shrestha S, Petrini MA. Knowledge about neonatal jaundice among Nepalese mothers. J BP Koirala Inst Heal Sci 2019;2:34–42.

19. Amegan-Aho KH, Segbefia CI, Glover NDO, Ansa GA, Afaa TJ. Neonatal Jaundice: awareness, perception and preventive practices in expectant mothers. *Ghana Med J*. 2019;53:267-72.

20. Seneadza NAH, Insaidoo G, Boye H, et al. Neonatal jaundice in Ghanaian children: Assessing maternal knowledge, attitude, and perceptions. PLoS One 2022; 17:1-13

21. Sutcuoglu S, Dursun S, Halicioglu O, et al. Evaluation of maternal knowledge level about neonatal jaundice. J Matern Fetal Neonatal Med 2012; 25:1387-9

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ORIGINAL ARTICLE

Comparison of Sinus Tarsi and Extensile Lateral Approach in Intra-articular Calcaneus Fractures

Eklem İçi Kalkaneus Kırıklarında Sinüs Tarsi ve Ekstensil Lateral Yaklaşımın Karşılaştırılması

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ABSTRACT

Objective: In this study, we aimed to compare the clinical and radiological results of the extensile lateral (EL) approach and sinus tarsi (ST) approach in calcaneal fracture surgery.
Materyal-Metod: A total of 40 patients with Sanders II-III calcaneal fractures, including 22 patients in the EL group and 18 patients in the ST group, were included in this retrospective study. In the radiological evaluation, changes in the calcaneus Bohler and Gissane angle, length, width, and height were measured during the preoperative and postoperative period. Clinically, American Orthopedic Foot and Ankle Society (AOFAS) and the visual analog scale (VAS) were evaluated. In addition, postoperative complications were also evaluated.
Results: In terms of demographic data, the results of both groups were similar. Both the length of hospital stay and the time to surgery were shorter in the ST group (p=0.019, p=0.02, respectively). There was no significant difference between the groups regarding radiological, clinical AOFAS and VAS scores. 13.6% superficial infection was seen in the EL group, and no wound problems were encountered in the ST group (p=0.102). The rate of sural nerve injury was 36.4% in the EL group and 5.6% in the ST group (p =0.003).
Conclusion: Both approaches clinical and radiological outcomes were similar. However, the advantages of the ST approach were shorter hospital stays, lower rate wound infections, and sural nerve injury problems.

Keywords: Calcaneus fracture, extensile lateral, sinus tarsi, minimally invasive

ÖZ

Amaç: Bu çalışmada kalkaneus kırığı cerrahisinde ekstansil lateral (EL) yaklaşım ile sinüs tarsi (ST) yaklaşımının klinik ve radyolojik sonuçlarını karşılaştırmayı amaçladık.
Gereç ve yöntem: Bu retrospektif çalışmaya, EL grupta 22 hasta ve sinüs tarsi grubunda 18 hasta olmak üzere Sanders II-III kalkaneus kırığı olan toplam 40 hasta dahil edildi. Radyolojik değerlendirmede, preoperative ve postoperative dönemde Bohler ve Gissane açısı, kalkaneusun uzunluğu, genişliği ve yüksekliğindeki değişiklikler ölçüldü. Klinik olarak ise Amerikan Ortopedik Ayak ve Ayak Bileği Derneği (AOFAS) ve görsel analog skalası (VAS) değerlendirildi. Ayrıca postoperative komplikasyonlar da değerlendirildi.
Bulgular: Demografik veriler açısından her iki grubun sonuçları benzerdi. ST grubundaki hastaların lateral ekstensil grubuna göre ameliyata alınma ve hastane kalış süresi açısından istatistiksel olarak anlamlı bir şekilde daha kısaydı (p=0.019, p=0.02, sırasıyla). Gruplar arasında radyolojik, klinik AOFAS ve VAS skorları açısından anlamlı fark bulunmadı. Ekstensile lateral grubunda %13,6 yüzeyel enfeksiyon görüldü ve sinüs tarsi grubunda herhangi bir yara sorununa rastlanmadı (p=0,102). Sural sinir yaralanması extensil lateral grupta 36.4% oranında, sinüs tarsi grubunda ise 5.6% oranında görüldü (p=0.003).
Sonuç: Her iki yaklaşımın klinik ve radyolojik sonuçları benzerdi. Ancak hastanede kısa yatış süresi, yara yeri enfeksiyon problemlerinin ve sural sinir yaralanmasının az olması ST yaklaşımının avantajıydı.

Anahtar kelimeler: Kalkaneus kırığı, ekstensil lateral, sinus tarsi, minival invaziv

Introduction

Calcaneus fractures constitute a significant portion of lower extremity fractures, and most of them are intra-articular fractures (1). Intra-articular calcaneal fractures are not just a subtalar joint problem. At the same time, the loss of height in the calcaneus affects the talus and impairs the biomechanics of the talonavicular and ankle joints. In order to reconstruct the foot biomechanics, the calcaneal articular surface, calcaneus width, length and height must be restored (2,3).

Intra-articular fractures of the calcaneus are treated conservatively and surgically but debate remains about the ideal treatment. Some authors emphasize conservative treatment due to wound site problems and infection development in surgically treated calcaneal fractures (4,5). However, long-term immobilization and the possibility of developing early subtalar arthritis stand out as disadvantages of conservative treatment (6). In recent years, the tendency for surgery has increased to prevent intra-articular displacement and reduce the possibility of developing arthrosis (7-10).

Different open surgical techniques have been described for calcaneus fractures, with the EL approach being the most commonly used technique (7,11). An important advantage of this approach is the wide surgical approach of view, facilitating direct reduction of the articular surface and the lateral calcaneal wall. However, wound site problems have

been reported with an average rate of 14-18% in patients operated with this approach (12,13). Various minimally invasive techniques, including mini-incision technique, percutaneous fixation, and arthroscopic assisted fixation, have been reported to reduce the risk of complications (8,14). With the ST approach, one of these techniques, in addition to providing joint restoration by directly seeing the subtalar joint, a rigid fracture fixation can be provided without causing soft tissue damage (15). In recent years, comparative studies have become popular with the application of the ST approach in calcaneal fracture surgery (6,8,16).

It is aimed to compare the results of the recently popular ST approach and the classical EL approach in calcaneus fractures.

Material and Methods

Our study evaluated 65 patients who were opereted for calcaneal fractures in our center between May 2018 and March 2022.

Study,Van Yuzuncu Yıl University Non-invasive Ethics committee approval numbered 2022/04-14 was obtained by the ethics committee. Patients aged 18-65 years who were operated on for calcaneal fracture in our clinic and who had Sanders type II and III fractures detected with preoperative computed tomography (CT) were included. Talus, navicular, etc., accompanying the calcaneal fractures and those with a history of bilateral calcaneal fractures, patients treated for osteoporosis and rheumatic disease were excluded. Forty patients (22 EL, 18 ST) were included in the study. Data such as age, gender, smoking, diabetes history, side of injury, time to surgery, length of hospital stay, and follow-up time were collected for all patients.

Surgical Technique

Sinus tarsi approach

Surgery was performed with tourniquet in the lateral decubitus position. A 3-5 cm oblique incision was made, extending from 1 cm posterior to the lateral malleolus to the metatarsals. After the sural nerve and peroneal tendons were preserved, the calcaneofibular ligament was dissected and the posterior facet, anterior process and calcaneocuboid joint were visualized. In order to correct the calcaneus length, height, and varus deformity, a kirschner (K) wire was inserted retrograde from the calcaneal tubercle. Then, after the reduction of the posterior facet fracture, a fixation was provided with one screw. The other fracture fragments were reduced and they were fixed with temporary K wires. One or two cannulated screws were inserted percutaneously from the posterior to the anterior aspect of the calcaneus. For patients with insufficient posterior facet support, additional fixation was performed with a small-sized plate. Fluoroscopy was used for all procedures. After providing rigid fixation, the incision site was closed with sutures. The drain was not used (Figure 1).

Figure 1: A) Preoperative lateral view of the intra-articular calcaneal fracture in which the posterior facet collapsed. **B)** Intraoperative view of the surgery with the ST approach **C,D)** postoperative radiological images

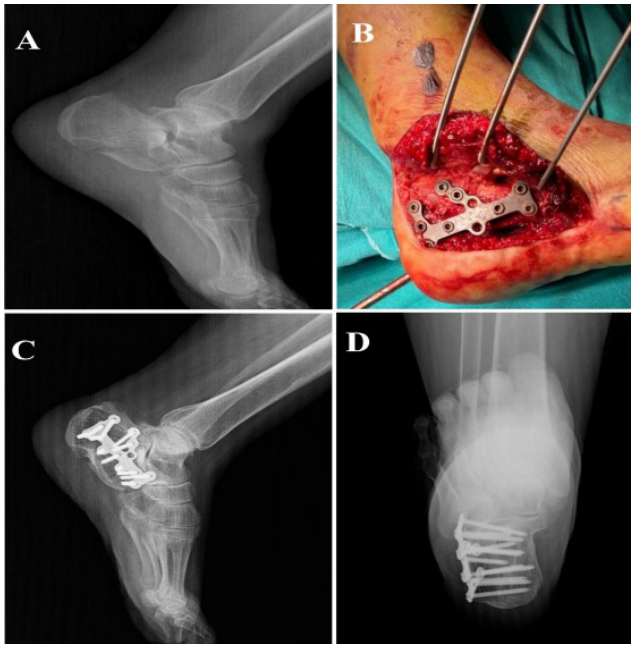

Figure 2: A) Preoperative lateral view of the intra-articular calcaneal fracture in which the posterior facet collapsed. **B)** Intraoperative view of the surgery with the EL approach **C,D)** postoperative radiological images

Lateral Extensile Approach

Surgery was performed with tourniquet in the lateral decubitus position. For the EL approach, an L-shaped incision was made extending from the 5 cm proximal

posterior of the lateral malleolus to the fifth metatarsal. After the full-thickness flap was seperated from the bone, it was temporarily fixed with K-wires. Articular surface was restored, all fragments were reduced and checked with fluoroscopy. Fracture fixation of the calcaneus was performed with an anatomical locking plate. After controlling the bleeding, a hemovac drain was placed.

Bone grafting was not required in both approach. All procedures were performed by 2 surgeons with at least 5 years of experience. The patients in both groups were followed for two or three weeks in a short leg splint, active movement was initiated when the wound healed. Weight-bearing was allowed at 10 to 12 weeks. Lateral and axial radiographic images were taken to evaluate the calcaneal fracture preoperatively. Computed tomography was taken to confirm the Sanders (11) classification, which evaluated the intra-articular condition of the fracture before surgery. In addition to the Bohler and Gissane angle, the height, length and width of the calcaneus were also evaluated radiologically (17).

The American Orthopedic Foot and Ankle Association ankle-posterior foot score was used to evaluate the function in the postoperative period (15). A visual analog score was used to evaluate pre-and postoperative pain scores. The pain score consists of a scale ranging from 0 (no pain) to 10 (unbearable pain) (18).

In the postoperative period, wound complications, deep infection, sural nerve injury, nonunion, revision surgery, and subtalar arthritis were evaluated.

Statistical analysis

The study's sample size was calculated using the G*Power statistical program (ver.3.1.9.7). Accordingly, the sample size was determined as 40 samples in two groups, with a Power (test power) of 0.90, an effect size of 0.9, and a Type-1 error (α) of 0.05. Descriptive statistics for variables; expressed as mean (mean ± standard deviation), median (min-max), number (n), and percent (%). Shapiro-Wilk (n<50) and Skewness-Kurtosis tests were used to ensure that the continuous measurements in the study conformed to the normal distribution. For normally distributed measurements, the Independent T-test was used to compare continuous measurements Mann-Whitney U test was used for non-normally distributed measurements. Chi- square test and Binary Z-ratio test were used to determine the relationships between categorical variables. The statistical significance level was taken as 5% in the study and SPSS (IBM SPSS for Windows, ver.26) program was used for analysis.

Results

Eighteen patients were operated on with the ST approach and 22 with the EL approach. The EL group consisted of 17 men (77.3%) and five women (22.7%) with a mean age of 40.6±13.7 years. There were 15 men (83.3%) and 3 (16.7%) women in the ST group with a mean age of 38.9±12.9 years. The results of the two groups were similar in terms of age and gender. (p=0.698, p= 0.634, respectively). According to the Sanders classification, seven patients (31.8%) had type II fractures and 15 weeks (68.2%) type III fractures in the EL group. In the ST group, type II fractures were observed in 9 patients (50%), and type III fractures were observed in 9 patients. There was no significant difference between the two groups regarding Sanders fracture classification (p=0.243). In addition, there was no statistically significant difference between the two groups in terms of extremity sides, follow-up time, and presence of diabetes mellitus (p=0.822, p= 0.597, p=0.083, respectively). The mean time to surgery was 6.1±4.3 days in the ST group and 11.1±6.6 days in the EL group. Regarding time to surgery and hospital stay, patients in the ST group had significantly shorter periods than the EL group (p=0.019, p=0.02, respectively). In addition, the extensil lateral group was significantly higher than the ST group in terms of smoking (p=0.013).

Table.1: Demographic data of the patients.

n		EL group		ST group		*p.
		%	n	%		
Sex male/ female	E	17	77.3%	15	83.3%	0.634
	K	5	22.7%	3	16.7%	
Sanders classification	II	7	31.8%	9	50.0%	0.243
	III	15	68.2%	9	50.0%	
Side of injury	Right	9	40.9%	8	44.4%	0.822
	Left	13	59.1%	10	55.6%	
Tobacco		8	36.4%	6	33.3%	***0.013***
DM		1	4.5%	0	0.0%	0.083
		Mean ± SD		Mean ± SD		**p.
Age, years		40.6 ± 3.7		38.9 ± 2.9		0.698
Follow-up duration, months		25.4 ± 3.6		23.0 ± 1.1		0.597
Time to surgery, days		11.1 ± 6.6		6.1 ± 4.3		***0.019***
Length of stay in hospital, days		13.4 ± 5.4		9.0 ± 4.5		***0.021***

SD: Standard deviation, **DM:** Diabetes mellitus; *Chi-square test **Independent T-test.

A satisfactory postoperative fracture reduction was achieved in both groups compared to preoperatively. There was no significant difference between the groups in the radiological evaluation (Table 2).

In both groups, the postoperative VAS scores at the last follow-up were statistically significantly lower than those during the preoperative period (P=0.001, P=0.001, respectively). There was no statistically significant difference between the groups in terms of preoperative and postoperative VAS scores (P=0.268, P=0.299, respectively). Although the AOFAS clinical

Table 2: Preoperative and postoperative X-ray measurements of the EL and ST groups

		EL group	ST group	
		Mean±SD Median (min-max)	Mean±SD Median (min-max)	*p.
Bohler angle preoperative		8.0 (2-26)	7.5 (3-28)	*0.742*
Bohler angle postoperative		22.9±10.0	26.1±9.8	*0.428*
	**p.	***0.001***	***0.001***	
Gıssane angle preoperative		104.6±22.4	113.8±11.9	*0.243*
Gıssane angle postoperative		117.4±9.5	120.9±9.1	*0.353*
	**p.	*0.059*	*0.243*	
Length preoperative		76.9±5.1	74.6±7.3	*0.370*
Length postoperative		81.5±5.5	79.1±6.9	*0.395*
	**p.	***0.005***	*0.176*	
Width preoperative		48.5±6.0	48.4±7.8	*0.973*
Width postoperative		43.0±8.6	42.0±6.0	*0.783*
	**p.	***0.011***	***0.009***	
Height preoperative		44.8±6.3	45.7±9.8	*0.791*
Height postoperative		51.9±4.9	46.9±9.7	*0.101*
	**p.	***0.002***	*0.736*	

SD: Standart deviation;, ***** Independant T-test / Mann- Whitney U test ****** Dependent (paired) T-test

score of the ST group was slightly higher than the EL group (p=0.585) (Table 3).

Table 3: Functional evaluation results of the EL and ST groups.

	EL group	ST group	
	Median (min-max)	Median (min-max)	*p.
VAS preoperative	8.0 (6-10)	9.0 (8-10)	*0.268*
VAS postoperative	5.0 (2-8)	3.5 (3-5)	*0.299*
***p.**	***0.001***	***0.001***	
AOFAS score	64.5 (27-100)	84.5 (26-88)	*0.585*

***** *Independant T-test/ Mann- Whitney U test*

Table 4: Postoperative complications

n	EL group		ST group		
	%	n	%	*p.	
Superficial infection	3	13.6%	0	0.0%	*0.102*
Deep infection	0	0.0%	0	0.0%	
Sural nerve injury	8	36.4%	1	5.6%	***0.003***
Nonunion	0	0.0%	0	0.0%	
Revision surgery	0	0.0%	0	0.0%	
Subtalar arthritis	6	27.3%	4	22.2%	*0.656*

*Binary Z-ratio test

Superficial infection was observed in 3 cases in the EL group (13.6%), and no wound site problems were encountered in the ST group. Sural nerve injury was seen in 8 cases (36.4%) in the EL group and 1 case (5.6%) in the ST group (p=0.003). Sural nerve injury was not observed visually in any of the cases during the operations. The diagnosis was made by sensory examination performed in the postoperative period. There was no case of nonunion or revision in both groups. Subtalar arthritis was observed in 6 cases (27.3%) in the EL group and 4 cases (22.2%) in the ST group on the last follow-up radiographs (p=0.656) (Table 4).

Discussion

Our study aimed to retrospectively compare the results of intra-articular calcaneal fractures in a group of patients treated with ST or EL approach. Our results showed that the reduction quality, stability of internal fixation, and functional results were similar in both surgical approaches. There were more wound complications in the EL group, but there was no statistically significant difference. The sural nerve injury was significantly higher in the EL group. The hospital discharge time was shorter in the ST group. In addition, the time to surgery after injury was shorter in the ST group.

It has been reported that adequate radiological improvement was achieved with the EL and ST approach in the surgery of calcaneus fractures, and the postoperative VAS score and AOFAS clinical results were also good. It has been shown that these two approaches are not superior to each other in terms of radiological and clinical results (8,16,17,19). In our

study, it was observed that radiological improvement was sufficient in both EL and ST groups, but there was no statistically significant difference between them. There was a similar significant improvement in VAS scores in both groups in the postoperative period. The AOFAS clinical scores of the ST group were slightly higher than the EL group, although it was not statistically significant. According to the results of our study, radiological and clinical similar results were obtained in both surgical approaches.

A literature review examining calcaneus fractures report that there are generally more wound site problems in patient groups operated with the EL approach compared to the ST approach. Ma et al. (15) found the complication rate related to wound healing to be 14.75% in the EL approach and 5.36% in the ST approach, and they reported that the difference was statistically significant. Lin et al. (20) found that the wound infection rate was higher in Sanders type IV fractures, which were 34.04% in the EL approach and 14.28% in the ST approach. In another study comparing both methods, the infection rate was 13.3% in the EL approach and 5% in the ST approach (8). In our study, the infection rate was 13.6% in the EL approach. No wound site problem was observed in the ST approach.

One of the critical complications in calcaneus fracture surgery is sural nerve injury. Weber et al. (21) reported the rate of sural nerve injury as 7.7% in their patients treated with the EL approach. Yeo et al.(8) reported sural nerve injury at a rate of 6.6% in the EL group and 5% in the ST group in their comparative study. A study on Sanders type IV fractures observed 14.89% sural nerve injury in the EL group. It was not seen in the ST group (20). In a cadaveric study, it was reported that sural nerve injury developed in the ST approach at a relatively lower rate compared to the EL approach, but the approach should be modified to minimize this complication (22). In our study, complications related to the sural nerve were reported at a higher rate (36.4%) in the EL group than in the literature. In the ST group, it was seen with a rate of 5.6%. The difference was statistically significant.

One of the complications after intra-articular calcaneal fracture surgery is subtalar arthritis seen during follow-up. Despite the anatomic reconstruction, many patients treated with open reduction and internal fixation progress to painful posttraumatic subtalar arthritis and required subtalar fusion in the late stage (23). Problems related to the subtalar joint have been reported, especially in publications on the EL approach (24). In a large-series study with a mean follow-up of 91 months, the rate of subtalar arthritis was found to be 77%, and it was reported that fusion was required in 18% of them (25). Lin et al.(20) found subtalar arthritis with a rate of 31.43% in the ST group and 27.66% in the EL group in Sanders type IV fractures. In our study, subtalar arthritis findings were observed in 27.3% of the EL group and 22.2% of the ST group. The difference was not statistically significant. Most of our patients did not have enough clinical findings to require fusion.

In the EL approach, it is necessary to wait for the foot edema to regress and skin lines to appear to avoid complications related to the surgical area. In the ST approach, surgery can be performed without waiting, even when there are blisters on the skin. It may enable the patient to undergo surgery earlier. However, Shuler et al. (26) showed that the longer the time between injury and surgery, the higher the wound healing complications. On the other hand, Kwon et al. (27) found that postponing surgery did not reduce the wound complication rates when the EL approach was used, while the wound complication rate increased when minimally invasive approaches were used. Ma et al. (15) reported that the patients in the ST group had a significantly shorter waiting time from injury to surgery than the EL group and that the wound site problem was less in the ST group. They stated that this resulted in a shorter hospital stay and lower costs in the ST group. Patients in the ST group were discharged from the hospital earlier than the EL group, and this time was significantly shorter.

Our study has some limitations: The most important of these can be considered operations by more than one surgeon. Another significant limitation is the small number of patients and the retrospective study. The strength of our study is the patient population with similar age and gender groups, follow-up periods.

Conclusion

Many methods have been described in the literature for the surgery of intra-articular calcaneal fractures. It was observed that the clinical and radiological results of the minimally invasive ST approach, which has become popular recently, and the EL approach was similar. However, the advantages of the ST approach were short hospital stays, lower rate wound infection problems, and sural nerve injury. Furter studies are recommended large series and prospective studies for both approaches.

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References

1. Buzzi R, Sermi N, Soviero F, Bianco S, Campanacci DA. Displaced intra-articular fractures of the calcaneus: ORIF through an extended lateral approach. Injury 2019 Jul;50 Suppl 2:2-7.

2. Khazen G, Rassi CK. Sinus Tarsi Approach for Calcaneal Fractures: The New Gold Standard? Foot Ankle Clin 2020 Dec;25(4):667-81.

3. Sharr PJ, Mangupli MM, Winson IG, Buckley RE. Current management options for displaced intra-articular calcaneal fractures: Non-operative, ORIF, minimally invasive reduction and fixation or primary ORIF and subtalar arthrodesis. A contemporary review. Foot Ankle Surg 2016 Mar;22(1):1-8.

4. Griffin D, Parsons N, Shaw E, et al. Operative versus non-operative treatment for closed, displaced, intra-articular fractures of the calcaneus: randomised controlled trial. BMJ 2014 Jul 24;349:g4483.

5. Dickenson EJ, Parsons N, Griffin DR. Open reduction and internal fixation versus nonoperative treatment for closed, displaced, intra-articular fractures of the calcaneus: long-term follow-up from the HeFT randomized controlled trial. Bone Joint J 2021 Jun;103-B(6):1040-6.

6. Zhou HC, Yu T, Ren HY, et al. Clinical Comparison of Extensile Lateral Approach and Sinus Tarsi Approach Combined with Medial Distraction Technique for Intra-Articular Calcaneal Fractures. Orthop Surg 2017 Feb;9(1):77-85.

7. Schepers T. The sinus tarsi approach in displaced intra-articular calcaneal fractures: a systemic review. Int Orthop 2011; 35:697-703.

8. Yeo JH, Cho HJ, Lee KB. Comparison of two surgical approaches for displaced intra-articular calcaneal fractures: sinus tarsi versus extensile lateral approach. BMC Musculoskelet Disord 2015 Mar 19;16:63.

9. Konya MN, Sargın S. Effect of Treatment Modality on Clinical Results of Calcaneal Fractures: A Retrospective Comparative Study. Acta Med. Alanya 2017;1(2):23-8 [Turkish].

10. Aslan A, Sargın S, Gülcü A, Konya MN. Clinical, radiological and patient-reported outcomes in intra-articular calcaneal fractures: Comparison of conservative and surgical treatment. Eklem Hastalik Cerrahisi 2019;30(2):143-148.

11. Sanders R. Displaced intra-articular fractures of the calcaneus. J Bone Joint Surg Am 2000; 82:225-50.

12. Maskill JD, Bohay DR, Anderson JG. Calcaneus fractures: a review article. Foot Ankle Clin 2005;10:463–89.

13. Seat A, Seat C. Lateral Extensile Approach Versus Minimal Incision Approach for Open Reduction and Internal Fixation of Displaced Intra-articular Calcaneal Fractures: A Meta-analysis. J Foot Ankle Surg 2020 Mar-Apr;59(2):356-66.

14. Kline AJ, Anderson RB, Davis WH, Jones CP, Cohen BE. Minimally invasive technique versus an extensile lateral approach for intra-articular calcaneal fractures. Foot Ankle Int 2013; 34:773–80.

15. Ma C, Zhao J, Zhang Y, et al. Comparison of the modified sinus tarsi approach versus the extensile lateral approach for displaced intra-articular calcaneal fractures. Ann Transl Med 2021 Apr;9(8):695.

16. Xia S, Lu Y, Wang H, Wu Z, Wang Z. Open reduction and internal fixation with conventional plate via L-shaped lateral approach versus internal fixation with percutaneous plate via a sinus tarsi approach for calcaneal fractures - a randomized controlled trial. Int J Surg 2014;12(5):475-80.

17. Basile A, Albo F, Via AG. Comparison Between Sinus Tarsi Approach and Extensile Lateral Approach for Treatment of Closed Displaced Intra-Articular Calcaneal Fractures: A Multicenter Prospective Study. J Foot Ankle Surg 2016 May-Jun;55(3):513-21.

18. Hildebrand KA, Buckley RE, Mohtadi NG, Faris P. Functional outcome measures after displaced intra-articular calcaneal fractures. J Bone Joint Surg Br 1996 Jan;78(1):119-23.

19. Kline AJ, Anderson RB, Davis WH, Jones CP, Cohen BE. Minimally invasive technique versus an extensile lateral approach for intra-articular calcaneal fractures. Foot Ankle Int 2013 Jun;34(6):773-80.

20. Lin J, Xie C, Chen K, et al. Comparison of sinus tarsi approach versus extensile lateral approach for displaced intra-articular calcaneal fractures Sanders type IV. Int Orthop 2019 Sep;43(9):2141-9.

21. Weber M, Lehmann O, Sagesser D, Krause F. Limited open reduction and internal fixation of displaced intra-articular fractures of the calcaneum. J Bone Joint Surg Br 2008; 90:1608-16.

22. Park JH, Chun DI, Park KR, et al. Can sural nerve injury be avoided in the sinus tarsi approach for calcaneal fracture?: A cadaveric study. Medicine (Baltimore) 2019 Oct;98(42): e17611.

23. Csizy M, Buckley R, Tough S, et al. Displaced intra-articular calcaneal fractures: variables predicting late subtalar fusion. J Orthop Trauma 2003 Feb;17(2):106-12.

24. Harvey EJ, Grujic L, Early JS, Benirschke SK, Sangeorzan BJ. Morbidity associated with ORIF of intra-articular calcaneus fractures using a lateral approach. Foot Ankle Int 2001; 11:868-73.

25. Schindler C, Schirm A, Zdravkovic V, Potocnik P, Jost B, Toepfer A. Outcomes of intra-articular calcaneal fractures: surgical treatment of 114 consecutive cases at a maximum care trauma center. BMC Musculoskelet Disord 2021 Mar 1;22(1):234.

26. Shuler FD, Conti SF, Gruen GS, Abidi NA. Wound-healing risk factors after open reduction and internal fixation of calcaneal fractures: does correction of Bohler's angle alter outcomes? Orthop Clin North Am 2001 Jan;32(1):187-92.

27. Kwon JY, Guss D, Lin DE, et al. Effect of Delay to Definitive Surgical Fixation on Wound Complications in the Treatment of Closed, Intra-articular Calcaneus Fractures. Foot Ankle Int 2015; 36:508-17.

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ORIGINAL ARTICLE

The Effect of Continuing Nursing Care Applied with a Coaching Strategy for Patients with Total Knee Replacement on Some Patient Outcomes: A Randomized Controlled Study Protocol

Total Diz Protezli Hastalara Koçluk Stratejisi ile Uygulanan Sürekli Hemşirelik Bakımının Bazı Hasta Sonuçlarına Etkisi: Randomize Kontrollü Çalışma Protokolü

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ABSTRACT

Aim: This study aims to determine the effects of continuous nursing care applied with a pre- and postoperative coaching strategy to patients with total knee replacement on some patient outcomes (pain control, anxiety level, self-care power, activities of daily living, patient satisfaction, hospital readmission status, and use of painkillers).
Materials and methods: This research was a parallel group (experiment-control) randomized controlled clinical trial. Data were obtained from patients who underwent 72 knee replacement surgeries between January 20, 2021, and October 28, 2021, using the Patient Identification Form, the Visual Analog Scale, the Self-Care Scale, the Newcastle Nursing Satisfaction Scale, the State Anxiety Inventory, and the Barthel Daily Living Activity Index. The patients were followed up preoperatively and postoperatively. This study is registered in the Clinical Trials database (NCT04683588).
Results: Statistical analysis of the data obtained from this research was calculated using the SPSS 25 package program in the computer environment. Number, percentage, mean and standard deviation were used for descriptive statistics, and chi-square analysis was used to compare the similarity/homogeneity of the groups regarding descriptive characteristics. Obtained results were evaluated at a $p<0.05$ significance level.
Conclusion: As a result of the research, it was concluded that the patients in the experimental group had a positive effect on pain, analgesic use, anxiety, self-care power, activities of daily living and patient satisfaction compared to the patients in the control group.

Keywords: Total knee replacement; coaching; nurse coaching strategy; nursing care; randomized controlled trial.

ÖZ

Amaç: Bu araştırmanın amacı, total diz protezli hastalara ameliyat öncesi ve sonrası koçluk stratejisiyle uygulanan sürekli hemşirelik bakımının bazı hasta sonuçları üzerine etkisini belirlemektir.
Gereç- Yöntem: Araştırma, paralel grup (deney-kontrol) randomize kontrollü klinik araştırma özelliğindedir. Veriler 20 Ocak 2021- 28 Ekim 2021 tarihleri arasında 72 diz protez ameliyatı yapılan hastalardan elde edilmiştir. Deney grubunda yer alan hastalar koçluk stratejisi ile hemşirelik bakımı, kontrol grubu ise; hastaları ise rutin hemşirelik bakımı almıştır. Veriler; Hasta Tanılama Formu, Vizuel Analog Skala, Öz Bakım Gücü Ölçeği, Newcastle Hemşirelik Bakımından Memnuniyet Ölçeği, Durumluk Anksiyete Envanteri ve Barthel Günlük Yaşam Aktivite İndeksi kullanılarak elde edilmiştir. Hastalar ameliyat öncesi ve ameliyat sonrası süreçte takip edilmiştir. Bu çalışma Clinical Trials veri tabanına (NCT04683588) kayıtlıdır.
Bulgular: Araştırma sonucunda elde edilen verilerin istatistiksel analizi, bilgisayar ortamında SPSS 25 paket programı kullanılarak hesaplanmıştır. Tanımlayıcı istatistikler için sayı, yüzde, ortalama ve standart sapma, grupların tanımlayıcı özellikler yönünden benzerliğinin/homojenliğinin karşılaştırılmasında ki-kare analizi kullanılmıştır. Elde edilen sonuçlar $p<0,05$ anlamlılık düzeyinde değerlendirilmiştir.
Sonuç: Araştırma sonucunda deney grubu hastalarının kontrol gruba hastalarına göre ağrı, analjezik kullanımı, anksiyete, öz-bakım gücü, günlük yaşam aktiviteleri ve hasta memnuniyeti üzerine olumlu yönde etkisi olduğunu göstermektedir.

Anahtar kelimeler: Total diz protezi; koçluk; hemşire koçluk stratejisi; hemşirelik bakımı; randomize kontrollü çalışma.

Introduction

Total knee arthroplasty (TKA) is the process of reshaping the articular surface (femoral, tibial, and patellar surfaces) that has deteriorated due to arthritis, trauma, congenital and tumoral factors, with a prosthesis made of metal or plastic raw materials (1,2). TKA is applied more to adults, especially to individuals over the age of 55 (2,3). Although TKA surgery is among the surgeries with a high patient satisfaction rate, some

complications may develop, and the rate varies between 1.65% and 11.3%. (2,4). These complications include delayed wound healing, nerve (peroneal) damage, stress fractures (patella, femur, and tibia), prosthesis instability, subluxation, dislocation, infection, and urinary infection. Nursing care and follow-up have a privileged place, especially in preventing problems and complications that may occur, early diagnosis, and treatment of them in the fastest time. In addition, coping with these difficulties and problems requires the patient to provide their own care and rehabilitation and to take on more responsibility. Active involvement of the patient is required (5). Qualified nursing care applied with the patient' active participation before, during, and after TKA surgery is crucial in preventing complications, increasing functional results, quality of life, and patient satisfaction (6,7).

The nurse is the professional member who interacts with the patient the most and spends a long time with the patient than the other members of the team (1,8,9). In this context, the training, information, skill acquisition, counseling, and care practice that the nurse will provide to the patient will contribute to the desired results by positively affecting both the success of the surgery and the recovery process of the patient (9,10,11). Many models/theories/approaches/methods/strategies are used in nursing process practices. One of them is the nurse coaching strategy (12,13). Nurse coaching is the entire supportive, guiding, and motivating dynamic process for the patient to reach their goals in a shorter time by sharing patient experiences with the nurse (9,14).

In the postoperative period, it is expected that the physiological and psychological problems of the patient will be resolved, self-care should be provided, and the patient will be able to cope with pain, adapt to his new situation, and complete the process with the least possible complication/uncomplicated. To achieve these, it is very important for the patient to have knowledge about the process and to be involved in the process. This can be done by providing active patient participation with a nurse coaching strategy (14). The nurse coaching strategy has been used by many researchers in different patient groups and has been reported to have many advantages (14,15,16). Although the coaching strategy has been studied many times in the literature in different diseases and patient follow-ups, it is seen that there is a limited number of studies in the postoperative patient group (16,19). To our knowledge, there is no study in which the coaching strategy covering the pre-and post-operative care process and follow-up for TKA was used. It was assumed that this was a significant deficiency. In this study, it was thought that the nurse coaching strategy would have significant effects on patient outcomes in patients with TKA.

Aim of the study: This study is an experimental type of research conducted to determine the effects of continuous nursing care administered with a nurse coaching strategy to patients who are planning to have TKA surgery on pain, anxiety, self-care agency, activities of daily living, patient satisfaction, hospital readmission rates and use of pain medication.

Material Method

Design

This study was planned as a parallel group randomized controlled clinical trial with repeated measurements.

Participants

The study population consisted of patients who were examined between January 2021 and October 2021 in the Orthopedics and Traumatology outpatient clinic of the hospital where this study was conducted and decided to have knee prosthesis surgery. Patients (N=165) who had knee prosthesis surgery between the specified dates constituted the population of this study.

Inclusion criteria

- Willingness to participate in this research,
- Being literate,
- Ability to speak Turkish and verbal communication,
- Not having a primary psychiatric diagnosis,
- No vision and hearing problems,
- No cognitive and mental problems,
- Not having trauma,
- Being 18 years or older,
- Living in the city center of Konya.

Exclusion criteria

- Having undergone revision knee prosthesis operation,
- Application of analgesic drugs to the knee joint space during the operation,
- Application of patient-controlled analgesia for postoperative pain control,
- Having difficulty in understanding the content of this research,
- Having a health problem that prevents exercise or evaluation.

Variables of this Study

Independent variables

- Continuous nursing care applied with the coaching strategy

Dependent variables

- Pain Control (intensity)
- State Anxiety Inventory score
- Self-Care Agency Scale score
- Daily Living Activity Index score
- Nursing Satisfaction Scale score
- Re-admission status
- Pain medication use status

Study Group and Power Analysis

The sample of this study consisted of 72 patients who had knee arthroplasty surgery between January 2021 and November 2021 and who met the criteria of the present study and agreed to participate in this study. The patients were divided into two groups as experimental and control groups. Continuous nursing care covering pre- and post-operative processes was applied to the patients in the experimental group using the nurse coaching strategy. Patients in the control group received routine nursing care, along with the patient education booklet. In this study, five repeated measurements were made in two groups. In calculating the sample size of this study, the G*Power statistical analysis program with a Type I error of 0.05 and a Type II error of 0.5 (based on 95% power) and a medium effect size value was used and the sample size was 66 patients for the 33 experimental and 33 control groups. Given that losses might occur for both groups, 72 patients were included in this study, 10% more for both groups (Figure 1).

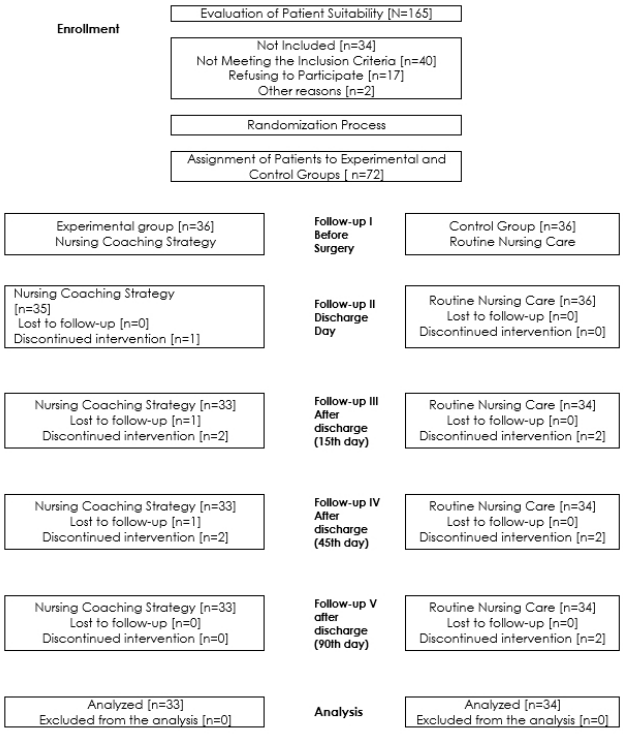

Figure 1. CONSORT chart

Randomization and Blinding

Randomization

Patients were assigned to the experimental and control groups using the "simple randomization" method to prevent selection bias and control the variables that may affect the difference in outcome parameters in the present study. Randomization was carried out by a statistician other than the researchers, using a computer program. Patients who applied to the orthopedics and traumatology outpatient clinic before randomization, who decided to have TKA surgery and were accepted to have surgery, were included in this study. Patients who met the inclusion criteria of this study were informed about this study and their verbal and written consent were obtained. Patients were assigned to the experimental and control groups according to the list prepared by the statistician according to the simple randomization method.

Blinding: No blinding was performed in the present study. Since the researcher managed the implementation process of this study, researcher blinding could not be done. The information about which group the patients belonged to was given by an independent person to the researcher, who collected the data of this study and carried out the application, after obtaining the verbal and written consent of the patients and collecting the initial data. On the other hand, the patients in the experimental and control groups were hospitalized in different rooms since randomization would be disrupted if the patients in the sample group and their relatives interacted in the service. Because the researcher directed the process, the researcher could not be blinded. The information about which patients will be assigned to the experimental and control groups was told to the researcher by another neutral person, in the order of the list determined by the statistician. Thus, the internal validity of this research was ensured. Experimental and control group data were recorded on the computer by the researcher without specifying the data, and data analyses were performed by an expert statistician. In this way, the blind technique method was also performed regarding statistical analysis. The randomization process of this study was planned according to the CONSORT 2017 (Updated Guidelines for Reporting Randomized Parallel Group Studies).

Data Collection Tools

Data were collected using the Patient Identification Form, the Visual Analogue Scale (VAS), the Self-Care Agency Scale (SCA), the Newcastle Satisfaction with Nursing Scale (NSNS), State-Trait Anxiety Inventory (STAI), and the Barthel Index for Activities of Daily Living (ADL). The motivational support interview technique was used in the application of the coaching strategy to the experimental group of patients. The Motivational Interview Form was used for the follow-up of the experimental group patients who were given nursing

care with the coaching strategy, and the Control Group Follow-up Form was used for the follow-up of the control group patients.

Creation and Evaluation of Patient Education Booklet

The booklet to be used in patient education is prepared in line with the current literature and evidence-based practices. In the booklet, pre-operative practices (including period preparations, practices during the surgery, post-operative care and problems that may be encountered, and home care after discharge) are included for patients who are planned for TKA.

The education booklet prepared by the researchers was submitted for expert opinion, and content validity was performed. The booklet was sent to the experts using e-mail. The experts evaluated the patient education booklet with the "Assessment Form for the Appropriateness of Written Educational Materials" and "DISCERN Written Material Evaluation Tool." The training booklet was given its final shape by the researchers according to the suggestions from the experts. The "Multiple Peer-Reviewed Content Validity" method was used in the evaluation of the patient education booklet. Kendall's Coefficient of Concordance test was used to analyze the data obtained from the assessment tools. It was concluded that there was a statistical agreement between the expert opinions for both the "Evaluation Form of Written Educational Materials" and "Discern Form" tools (for the Written Material Evaluation Tool; W=0.044, p=0.266>0.050, for the DISCERN form; W=0.080, p=0.152>0.050).

Pilot Study

The pilot study of this study was carried out in the institution where this study was conducted between September 24 and December 30, 2020, to evaluate the intelligibility of the data collection forms by the patients. After the approval of the ethics committee and the institution, this pilot study was carried out between these dates with the patients who met the study criteria and were accepted to participate in this study. Pilot study was completed with eight patients, four from the experimental group and four from the control group.

Procedures

The implementation process of the research consisted of three stages and a total of 11 steps. The stages are indicated in Table 1.

Stage 1=Preparation Stage: It consists of two simultaneous steps.

First step

By reviewing the literature and evaluating the methods used in patient education, the nurse coaching strategy planned to be used in this study was decided.

Second step

As a result of the literature review, the appropriate measurement tools (VAS, State-Trait Anxiety Inventory, Self-Care Agency Scale, Barthel Index for Activities of Daily Living and Newcastle Satisfaction with Nursing Scale) were decided for the hypotheses of this research.

Stage 2 = Application Stage: It consisted of eight consecutive steps.

First step – surgery decision stage in the outpatient clinic (pre-operative process I)

This step began with the decision on the surgical process after patients applied to the outpatient clinic. Patients admitted to the orthopedics and traumatology clinic for planned TKA surgery and planned to be hospitalized were evaluated whether they met the inclusion criteria, and the patients who met the inclusion criteria were informed about this research process. The patients who agreed to participate in this study were provided to read the Minimum Informed Voluntary Consent Form (BIGOF) and their written consent was obtained. The patients whose consent was obtained were assigned to the experimental and control groups according to the randomization list created by the statistician. In this step, both the socio-demographic characteristics of the patients (Patient Diagnosis Form) were filled in by the researcher in the outpatient clinic, the patient was informed before hospitalization, and the training booklet prepared by the researcher was given to the patient. A coaching interview on pain, anxiety, self-care, and daily life activities was conducted with the patients in the experimental group using the coaching strategy method.

Second step – Time to hospitalization (pre-operative period II)

This step includes the operation day, which is included in the pre-operative period, and the period immediately before the operation (the day of admission to the ward). At this stage, carried out by the researcher, a coaching interview was conducted in the patient's room using the coaching strategy method for the patient's anxiety state. In addition, the physiological preparation of the patients was carried out by the researcher. Here, training was given on the practices that the patients are expected to do after the surgery (extremity strengthening exercises, breathing and coughing exercises, in-bed exercises, sitting in the bed, getting out of bed after the surgery, and the positions to be careful). In addition, it covers the presentation of the clinic, the operation of the service, the introduction of the orthopedics and traumatology service team, and informing the patient and the companion to meet their needs regarding the service and treatment process.

Third step – 0th day after surgery

It covers the post-operative period (0th day of post-operative) of the patients who underwent surgery. This step includes the post-operative nursing care practices of the patient determined by the researcher (e.g., transferring the patients from the surgery to the clinic, pain control and monitoring, monitoring of vital signs, controlling the wound area, hemovac drain control, transition to oral feeding, nausea control, evacuation, wound care, prevention of complications, providing comfort and rehabilitation exercises). The pain status of the patients was evaluated with VAS by the researcher. A coaching session was held to increase the power of coping with pain using the coaching strategy method for the patient whose pain status was evaluated.

Fourth step – 1st day after surgery

This stage covers the period between 24 and 26 hours after surgery. It covers the period after the routine drug treatments of the patients completed 24 hours after the surgery. After removing the elastic bandage and dressing the patient, whose leg was fully wrapped with an elastic bandage in the operating room, the incision site was evaluated regarding heat, redness, edema, and tenderness. The dressing of the incision area of the patient whose drain was removed was renewed, and anti-embolism socks were put on, and the patient was mobilized by taking the necessary precautions. A coaching session for the daily life activities (feeding, dressing, walking, changing in-bed position, transfer, using the toilet) of the patient whose pain was evaluated was carried out using the coaching strategy method.

Fifth step- 2nd day after surgery

It covers the period after the 48th hour after the surgery. A coaching session was held for self-care behaviors. The pain status of the patient was evaluated with VAS by the researcher.

Sixth step- Post-operative (Discharge day)

It covers the 24-48 hours before the discharge of patients scheduled to be discharged. The patients were given discharge training (possible complications, wound care, conditions requiring emergency treatment and care, exercises, physical restrictions, methods for pain reduction and coping, and drug use information) by the researcher with a nurse coaching strategy.

Seventh step- I. control after discharge (15th day)

It covers 14-17 days when the patients come to the first polyclinic for control after discharge. In the interview conducted by the researcher with the patients, the problems they had difficulty in daily life were questioned after discharge. Re-informing, training, and counseling were provided about the completion of the deficiencies in the knowledge and practice regarding the problems (e.g., about nutrition, activity, exercise, drug use, and issues to be careful about) encountered by the patients, and about the correction of the mistakes if any.

Eighth step- II. control after discharge (45th day)

It is the time when the patients come to the outpatient clinic for the second time after discharge, that is, the 45th day after the surgery. In the interview made by the researcher with the patients, the situations they had difficulties in daily life after discharge were questioned, and information, training, and counseling were provided about the completion of the deficiencies regarding these problems (e.g., about nutrition, activity, exercise, drug use and issues to be careful about) and about the correction of the mistakes, if any.

Ninth step- III. control after discharge (90th day)

It is the time when the patients come to the outpatient clinic for the third time after discharge, that is, the 90th day after the surgery. In this interview, the researcher asked the patients about the situations they had difficulties in daily life after discharge and provided information, training, and counseling about the completion of the deficiencies regarding these problems (about (e.g., nutrition, activity, exercise, drug use, and issues that need attention) and the correction of the mistakes if any.

***Stage 3 = Reporting Stage*:** At this stage, the last follow-up data of the patients were completed on October 28, 2021. Data were entered in a computer environment using SPSS 24 package program (Table 2).

Flow Chart of the Research

Data Analysis

Statistical analyses were performed using the SPSS [IBM SPSS Statistics 24] package program. "Frequency tables" and "descriptive statistics" were used to interpret statistical findings. Obtained results were evaluated at $p<0.05$ significance level. Parametric methods were used for measurement values suitable for normal distribution. Shapiro-Wilk tests were performed according to the number of samples in accordance with the normal distribution values. In addition, Q-Q plots, kurtosis, and skewness coefficients were examined. In this study, modified intention to treat (MoITT) and intention to treat (ITT) analyses for attenuation bias and treatment purpose were applied in the data analysis phase. Since it was not possible to reach the data of the patients who were excluded from the present study after randomization, the missing data were filled in in the computer environment (Table 2).

Table 1. Application Chart of the Research

1.Stage: Prepatation Stage	1.Step	Literature Review Deciding on the Appropriate Nursing Strategy Determining the Sample Appropriate for the Criteria
	2.Step	Deciding on Appropriate Measurement Tools
2. Stage: Application Stage	1.Step	**Deciding on surgery in the outpatient clinic** Randomization and assignment to the appropriate group, Obtaining patient consent, Implementation of patient diagnosis form and pre-hospitalization information training for patients planned for surgery by the researcher and giving the training booklet to them, Conducting a coaching interview on pain, anxiety, self-care, and daily living activities using the coaching strategy method for the experimental group, Application of VAS, State-Trait Anxiety Inventory, Self-Care Agency Scale, Barthel Index for Activities of Daily Living measurement tools by the researcher
	2.Step	**Day of hospitalization of the patient (just before surgery)** It includes the introduction of the service, the introduction of the operation of the service, the introduction of the orthopedics and traumatology clinic team, and the information of the patient to meet the service and process-related needs by the researcher. The coaching interview was held in the patient's room with the anxiety-oriented coaching strategy method for the experimental group.
	3. Step	**Surgery day (post-op day 0)** It covers the post-operative nursing care practices of the patient applied by the researcher. The coaching interview was held in the patient's room with the pain-oriented coaching strategy method for the experimental group.
	4. Step	**Post-operative (post op 1st, 2nd day)** Providing the care of the patient in the post-operative period with the nurse coaching strategy by the researcher. ▪ Conducting a coaching session for daily living activities with coaching strategy, (post op 1st day) ▪ Conducting a coaching session for self-care with coaching strategy, (post op 2nd day) Implementation of the VAS by the researcher.
	5. Step	**Discharge planning (Last 24-48 hours before discharge)** Providing discharge training with the nurse coaching strategy within the specified time interval (last 24-48 hours) to the patients whose discharge is planned by the researcher. ▪ Conducting a coaching session for anxiety with a coaching strategy, ▪ Conducting a coaching session for pain with a coaching strategy, ▪ Conducting a coaching session for daily living activities with a coaching strategy, ▪ Conducting coaching sessions for a self-care with coaching strategy, Application of measurement tools (VAS, State-Trait Anxiety Inventory, Self-care Agency Scale, Index for Activities of Daily Living, New Castle Satisfaction with Nursing Scale) by the researcher.
	6.Step	**First control to the outpatient clinic after discharge, examination time (Day 14-17)** Providing information, education and counseling of the patient during the discharge process with the nurse coaching strategy by the researcher. ▪ Conducting a coaching session for anxiety with a coaching strategy, ▪ Conducting a coaching session for pain with a coaching strategy, ▪ Conducting a coaching session for daily living activities with a coaching strategy, ▪ Conducting coaching sessions for a self-care with coaching strategy, Application of measurement tools (VAS, State-Trait Anxiety Inventory, Self-care Agency Scale, Index for Activities of Daily Living) by the researcher.
	7.Step	**Second control to the outpatient clinic after discharge, examination time (Day 45)** Continuing the patient's information, education, and counseling with the nurse coaching strategy by the researcher. ▪ Conducting a coaching session for anxiety with a coaching strategy, ▪ Conducting a coaching session for pain with a coaching strategy, ▪ Conducting a coaching session for daily living activities with a coaching strategy, ▪ Conducting coaching sessions for a self-care with coaching strategy, Application of measurement tools (VAS, State-Trait Anxiety Inventory, Self-care Agency Scale, Index for Activities of Daily Living) by the researcher.
	8. Step	**Third control to the outpatient clinic after discharge, examination time (Day 90)** Continuing the patient's information, education and counseling with the nurse coaching strategy by the researcher. ▪ Conducting a coaching session for anxiety with a coaching strategy, ▪ Conducting a coaching session for pain with a coaching strategy, ▪ Conducting a coaching session for daily living activities with a coaching strategy, ▪ Conducting coaching sessions a self-care with coaching strategy, Application of measurement tools (VAS, State-Trait Anxiety Inventory, Self-care Agency Scale, Index for Activities of Daily Living, New Castle Satisfaction with Nursing Scale) by the researcher.
3.Stage Reporting Stage		Statistical analysis of the data and writing the research report.

Table 2. Statistical methods used in the research

Statistics Areas		Statistical methods used
"According to the expected value levels in examining the relations of two qualitative variables with each other"		"Fisher-Exact," "Continuity Correction" or "Pearson-χ^2"
Parametric Methods	"In comparison with the measured values of two independent groups"	"Independent Sample t-test (t- table value) "
	"In comparison with measurement values of three or more dependent groups"	"Repeated Measures" test (F- table value)"
	"In the study of the relationships of two quantitative variables"	"Pearson Correlation Analysis"
Non-Parametric Methods	"In comparison with the measured values of two independent groups"	"Mann-Whitney U" test (Z- table value)"
	"In comparison with measurement values of three or more dependent groups"	"Friedman test" (χ^2-table value)"
	"For pairwise comparisons of variables with a significant difference for three or more groups"	"correction"
	"In the study of the relationships of two quantitative variables"	"Spearman Correlation Analysis"
Effect size analysis, MoITT ve ITT		

Ethical Dimension of Research

To collect the data, the ethics committee permission with the date of 10/07/2020 and the decision number 2020/5- E. 93804542-020 from Selcuk University Faculty of Nursing Non-Interventional Ethics Committee and institutional permission from the hospital where the research will be conducted were obtained before the research. This study was registered in the Clinical Trials database (NCT04683588). Informed consent was obtained from the patients, both verbally and in writing. Scale usage permissions were obtained from scale owners. All stages of this study were carried out in accordance with the Declaration of Helsinki. This research was prepared, applied, and reported according to the Reporting Criteria for Randomized Parallel Group Studies (CONSORT 2017) (20).

Discussion and Conclusions

This study aimed to determine the effects of continuing nursing education, counseling, and care, which started with the decision of the operation process and applied with a nurse coaching strategy until the third month after the operation, on patients with TKA, pain, anxiety, self-care agency, activities of daily living, nursing care satisfaction, hospital readmission rates, and analgesic drug use. As a result of this research, it was concluded that the patients in the experimental group showed a positive change in pain, analgesic use, anxiety, self-care agency, activities of daily living, and patient satisfaction compared to the patients in the control group, while the rates of readmission were similar.

In the literature, there are studies on coaching strategies applied to different surgical patient groups (16,19,21,22). In the randomized controlled study by Prvu Bettger et al. (23), the effectiveness of the internet-based coaching program after TKA was evaluated and the patients were followed for 12 weeks. At the end of the program, there was a significant decrease in the pain scores of the patients in the experimental group. In the multicentered randomized controlled study conducted by Kassymova et al. (22), patients who underwent hysterectomy (n=525) were followed for six weeks using the coaching method, and it was determined that the pain level of the patients in the experimental group was lower than the control group at the end of the program. In another randomized controlled study, patients who had knee arthroscopy surgery (n=102) were divided into experimental and control groups. The patients in the experimental group were coached for a week, in the evening before the surgery, at the 24th hour, 48th hour and 72nd hour after the surgery and at the end of the program. It was observed that the amount of analgesic medication consumed after the surgery was reduced in patients who received coaching (16). In another study in which the coaching strategy was applied, a coaching interview was applied to the patients with bone fractures about whether pain during the exercises to increase the elbow joint range is healthy and expected pain, about the need to continue the exercise despite the pain during the exercises to increase the elbow joint range, and about increasing and decreasing the elbow opening. The patients were asked to think/imagine goal-oriented in the coaching given during the exercise. It was observed that the mental processes of the patients were healthier in the exercises performed after the application (21). In the randomized controlled study conducted by Losina et al. (24), the patients in the intervention group of 202 adult patients who followed up with the diagnosis of osteoarthritis were applied physical exercises integrated with coaching for six months and coached by telephone. At the end of the program, the physical movements and self-care status of the patients were evaluated. It was determined that the quality of life of the children who performed the activity was significantly higher than the control group after a 6-month study in which the patients were given one-on-one physical activity by the coach.

When the literature is examined, it has been determined that the training, counseling, and care practices given with the coaching strategy have a positive effect on the recovery status of the patients. Also, in this study, it was thought that the training, counseling, and care related to the nurse coaching strategy given to the patients at certain periods before and after the surgery had a positive effect on the patients' pain, anxiety, analgesia use status, self-care agency, daily living activities and satisfaction rates in nursing. To our knowledge, this is the first study presented using the coaching strategy given to TKA patients by the nurse; it is implemented as a randomized controlled nursing intervention to increase the recovery status of patients after surgery; it sets an example and provides evidence for care studies in the literatıre. The results of this study showed that the training, counseling, and care practices given with the nurse coaching strategy in pre-and post-operative patients have significant

effects on the recovery status of the patients.

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References

1.Dahlen L, Zimmerman L, Barron C. Pain perception and its relation to functional status post total knee arthroplasty: a pilot study. Orthopaedic Nursing 2006; 25:264-70.

2.Savcı A, Bilik O. Integration of the model into the nursing care: continuous care structured according to the roy adaptation model in the patients with total knee replacement. E- Journal of Dokuz Eylul University Nursing Faculty 2015; 8:145-54.

3.Wainwright TW, Gill M, McDonald DA, Middleton RG, Reed, M.,... Sahota O.Consensus statement for perioperative care in total hip replacement and total knee replacement surgery:Enhanced Recovery After Surgery (ERAS®) Society recommendations, Acta Orthopaedica 2020; 9:3-19.

4.Altıntas F, Ulucay C, Kılıncoglu V. indications, contraindications and complications of total knee arthroplasty.Turkey Clinics Orthopaedics and Traumatology-Special Topics 2009;2:55-62.

5.Husted H. Fast-track hip and knee arthroplasty: clinical and organizational aspects. Acta Orthopaedica 2012; 83:1-39.

6.Lucas B, Cox C, Perry L, Bridges J. Pre-operative preparation of patients for total knee replacement: An action research study. International Journal of Orthopaedic and Trauma Nursing 2013;17:79-90.

7.Jones CA, Suarez-Almazor, ME. Patient expectations and total knee arthroplasty. Journal of Clinical Outcomes Management 2017; 24: 8-22.

8.Ay F. That is a new approach for provide competence in the nursing education: guide nurse (mentorship) System. Journal of Fırat Health Services 2007;4:52-65.

9.Tuluce D, Kutluturkan, S. An efficient approach to care cost effectiveness in patients diagnosed with stable COPD: patient coaching. Journal of Human Sciences 2016;13:2697-709.

10.Senyuva E, Tasocak G. Patient Education activites of nurses and patient education process. Florence Nightingale Journal of Nursing 2007;15:100-6.

11.Dilles A, Heymans V, Martin S, Droogne W, Denhaerynck K, De Geest S. Comparison of a computer assisted learning program to standard education tools in hospitalized heart failure patients. European Journal of Cardiovascular Nursing 2011;10:187-93.

12.Dossey, BM, Keegan L.Holistic Nursing Holistic nursing: A handbook for practice. 6rd ed. Burlington; MA: Jones & Bartlett Learning, 2013;189-99.

13.Campell L, Gilbert MA, Laustsen GR. Clinical coach for nursing excellence. 3rd ed.Philadelphia; FA. Davis, 2014; 117-86.

14.Kivela K, Elo S, Kyngas H, Kaariainen M. The effects of health coaching on adult patients with chronic diseases: a systematic review. Patient Education Couns 2014; 97:147-57.

15.Daly B, Tian CJL, Scragg RKR. Effect of nurse-led randomised control trials on cardiovascular risk factors and HbA1c in diabetes patients: a meta-analysis. Diabetes Research And Clinical Practice 2017;131:187-99.

16.Jones D, Duffy ME, Flanagan J. Randomized clinical trial testing efficacy of a nurse-coached intervention in arthroscopy patients. Nursing research 2011;60: 92-9.

17.Dwinger S, Dirmaier J, Herbarth L, Konig HH, Eckardt M, Kriston L, Bermejo I, Harter M. Telephone-based health coaching for chronically ill patients: study protocol for a randomized controlled trial. http://www.trialsjournal.com/content/14/1/337, 2013;14:1-7.

18.Xu H, Mou L, Cai Z. A nurse-coordinated model of care versus usual care for chronic kidney disease: meta-analysis. Journal of Clinical Nursing 2017;26:1639–49.

19.Bennell KL, Campbell PK, Egerton T, Metcalf B, Kasza J, Forbes A, Bills C, Gale J, Harris A, Kolt GS. Telephone coaching to enhance a home□ based physical activity program for knee osteoarthritis: a randomized clinical trial. Arthritis Care & Research 2017; 69: 84-94.

20.Schultz FK, Altman DG, Moher D, & Çevirenler: Sunay DŞ, Oral M, Aktürk Z. The consort statement: revised recommendations for improving the quality of reports of parallel group randomized trials. Euras J Fam Med 2013;2:1-10.

21.Teunis T, Thornton ER, Guitton TG, Vranceanu A-M, Ring D. Coaching of patients with an isolated minimally displaced fracture of the radial head immediately increases range of motion. Journal of Hand Therapy 2016;29:314-9.

22.Kassymova G, Sydsjö G, Wodlin NB, Nilsson L, Kjølhede P.Effect of nurse-led telephone follow-up on postoperative symptoms and analgesics consumption after benign hysterectomy: a randomized, single-blinded, four-arm, controlled multicenter trial. 2022;1:1-22.

23.Prvu Bettger J, Green CL, Holmes DN, Chokshi A, Mather RCI, Hoch BT, de Leon AJ, Aluisio F, Seyler TM, Del Gaizo DJ, Chiavetta J, Webb L, Miller V, Smith JM, Peterson ED. Effects of virtual exercise rehabilitation in-home therapy compared with traditional care after total knee arthroplasty: veritas, a randomized controlled Trial. The Journal of Bone and Joint Surgery. 2020;102:101-9.

24.Losina E, Collins JE, Deshpande BR, Smith SR, Michl GL, Usiskin IM, Klara KM, Winter AR, Yang HY, Selzer F. Financial incentives and health coaching to improve physical activity following total knee replacement: a randomized controlled trial. Arthritis care & research 2018;70:732-40.

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ORIGINAL ARTICLE

Vitamin D Deficiency in Children Admitted to a Tertiary Care Hospital

Üçüncü Basamak Bir Hastaneye Başvuran Çocuklarda D Vitamini Eksikliği

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ABSTRACT

Introduction: This study aims to determine the prevalence of vitamin D deficiency/insufficiency according to age, gender, and seasonal variables in children admitted to a tertiary hospital.
Methods: A cross-sectional study was conducted in the pediatric clinic of a tertiary care hospital in Ankara. Healthy children whose 25-hydroxyvitamin D levels were measured for any reason from January 2015 to January 2020 were included in the study. The vitamin D levels of the participants were analyzed according to age, gender, and measuring season. Children were divided into 4 subgroups according to their age: infancy (0-1 years), preschool (2-5 years), school (6-11 years), and adolescence (12-18 years). 25-hydroxyvitamin D less than 12ng/ml was defined as a deficiency, 12-19 ng/ml were insufficiency, 20-50 ng/ml sufficiency and more than 50ng/ml were defined as the risk of potential adverse effects
Results: A total of 16321 children were included in the study. The participants detected Vitamin D deficiency in 5243 (32.1%). The deficiency was mostly detected during adolescence (n:3313, 63.2%). This was followed by the school period (23.5%), preschool period (10.5%), and infancy (2.7%), respectively. The deficiency was mostly detected during the winter months. While vitamin D deficiency was more common in females over the age of six, no difference was found between the sexes under the age of six.
Conclusions: In this study, a high frequency of vitamin D deficiency/insufficiency was found in children. We believe that screening programs to be determined according to age groups can be beneficial to realize this deficiency without delay.

Keywords: Vitamin D deficiency, children, age, gender

ÖZ

Giriş: Bu çalışmanın amacı üçüncü basamak bir hastaneye başvuran çocuklarda yaş, cinsiyet ve mevsimsel değişkenlere göre D vitamini eksikliği/yetmezliği sıklıklarını belirlemektir.
Metot: Ocak 2015- Ocak 2020 yılları arasında üçüncü basamak bir hastanenin çocuk kliniğinde, herhangi bir nedenle 25-hidroksivitamin D düzeyi ölçülen sağlıklı çocukların D vitamini düzeylerinin yaş, cinsiyet ve mevsim özellikleri ile ilişkisinin analiz edildiği kesitsel bir çalışmadır. Çocuklar yaşlarına göre infant (0-1 yaş), okul öncesi (2-5 yaş), okul dönemi (6-11 yaş) ve adolesan (12-18 yaş) olmak üzere 4 alt gruba ayrılmıştır. 25-hidroksi vitamin D düzeyleri <12 ng/ml ise eksiklik, 12-19 ng/ml yetmezlik, 20-50 ng/ml normal, > 50ng/ml potansiyel yan etki açısından riskli düzey olarak kabul edilmiştir.
Bulgular: Çalışmaya toplam 16321 çocuk dahil edildi. Katılımcıların 5243(%32.1)'ünde D vitamini eksikliği tespit edildi. Eksiklik en sık ergenlik döneminde saptandı (n: 3313, %63.2). Bunu sırasıyla okul dönemi (%23.5), okul öncesi dönem (%10.5) ve infant dönemi (%2.7) izledi. Eksiklik çoğunlukla kış aylarında tespit edildi. D vitamini eksikliği altı yaş üstünde kızlarda sık görülürken, altı yaş altında cinsiyetler arasında fark yoktu.
Sonuç: Bu çalışmada çocuklarda D vitamini eksikliği/ yetmezliği yüksek sıklıkta saptanmıştır. Bu eksikliğin gecikmeden fark edilmesi için yaş gruplarına göre belirlenecek olan tarama programlarının faydalı olabileceğine inanıyoruz

Anahtar kelimeler: D vitamini eksikliği, çocuk, yaş, cinsiyet

Introduction

Vitamin D deficiency and insufficiency have impacts on the skeleton as well as non-skeletal organs While the effects of vitamin D deficiency on skeletal health have been known since the 17th century, its extraskeletal effects have been demonstrated in the last few decades (1). The extraskeletal effects of vitamin D have been increasingly understood since the 1980s, with the demonstration of vitamin D receptors (VDRs) and biological effects in various cells. At least 37 cell types are expressed to have VDR. Vitamin D shows its effect on target cells by binding to VDR. One of its effects on target cells is to regulate the transcription of about 2000 genes (2).

Approximately 90% of the vitamin D in the human body is synthesized from the skin after UVB exposure, while 10% enters the body through the diet (2). Therefore generally thought that populations in regions with plentiful sunshine during the year would have sufficient vitamin D status. However, the prevalence of vitamin D deficiency may be high even in areas with abundant sunlight. It is thought that genetic factors play an essential role

in this deficiency, apart from diet and environmental circumstances (2, 3). Recent studies show that genetic tendency plays an important role in sensitivity to vitamin D deficiency and that both vitamin D intake via diet and supplements and cutaneous generation after sun exposure are strongly linked to individual genetic variations (4).

Vitamin D deficiency has been associated with many diseases such as asthma (5), type 1 diabetes mellitus (6), and inflammatory bowel disease (7, 8). Although the importance of vitamin D on human health is understood more and more every day, vitamin D deficiency is widespread all over the world, regardless of climate and economy (1, 9).

In the present study, we primarily aimed to test the hypothesis that vitamin D deficiency and insufficiency are prevalent in children. Secondly, we aimed to determine the relationship between vitamin D deficiency/insufficiency with gender, age, and seasonal variations.

Methods

A retrospective, single-center, cross-sectional study was conducted on patients admitted to the pediatric outpatient clinic of a tertiary hospital over five years. The results of the children younger than 18 years whose vitamin D levels were measured during the visits were determined from the hospital database. Exclusion criteria were defined as chronic kidney or liver disease and the use of drugs that affect bone metabolism. Eventually, 16321 children were included study. Subjects were divided into four groups according to their ages; infancy (0-1years), preschool (2-5 years), school-age (6-11years), and adolescence (12-18 years). Participants' 25 (OH) D level, age, gender, and seasonal information were recorded. Vitamin D status was categorized by using the Institute of Medicine's definition of a serum 25(OH)D. 25-hydroxyvitamin D less than 12ng/ml was defined as a deficiency, 12-19 ng/ml insufficiency, 20-50 ng/ml sufficient, and more than 50ng/ml were defined as the risk of potential adverse effects (10)

25 (OH) D levels were measured by competitive electrochemiluminescence protein binding assay using Cobas e601 Immunoassay analyzer (Roche Diagnostics, Kaiseraugst, Switzerland).

This study was approved by the Ministry of Health Ankara Training and Research Hospital Clinical Research Ethics Committee in terms of compliance with the Declaration of Helsinki(no: 318/2020, 10 July 2020).

Statistical Analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and minimum-maximum where appropriate. The Chi-square test was used to compare categorical variables between the groups. To evaluate the correlations between measurements, Pearson Correlation Coefficient was used. All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package. The statistical level of significance for all tests was considered to be 0.05.

Results

A total of 16,321 children, 9174(56.2%) female, and 7147(43.8%) male were included in this research. The mean age of patients was 9.5 ± 5.3 years (median 10 years). Vitamin D deficiency was detected in 10777 (66%) of participants. The participants were separated into four age groups. The first group was 0-1 years (n= 1308), the second group was 2-5years (n=3312), the third group was 6-11 years (n=4983) and the fourth group was 12-18 years (n=6718). The frequency of vitamin D deficiency increased with increasing age and it was most common in adolescents (p<0.001) (Table 1, Figure 1). In other words, 25(OH)D levels of children decrease with increasing age(r=-0.413, p<0.001). Descriptive statistics for gender and season characteristics based on vitamin D levels for each age group are given in Table 2. While there was no significant difference between vitamin D levels according to gender in groups 1 and 2 (p=0.307 and p=0.997 respectively), it was shown that low vitamin D levels were more prevalent in females in groups 3 and 4 (both p<0.001). Besides, in all age groups, the concentration of vitamin D changed according to the seasons (p<0.001 for all) (Table 2). In each age group, vitamin D deficiency (≤20) was most prevalent in winter (33.1% in group 1, 42.7% in group 2, 44.7% in group 3, and 39.1% in group 4)(Figure 2)

Table 1. Vitamin D levels distribution for each age group

	Vitamin D Levels				
	Deficiency (n=5243)	Insufficiency (n=5534)	Sufficiency (n=5222)	Potential side effects (n=322)	p
Age Groups, n(%)					
0-1 years	144(11.0)	149(11.4)	848(64.8)	167(12.8)	<0.001
2-5 years	552(16.7)	1072(32.4)	1621(48.9)	67(2.0)	
6-11 years	1234(24.8)	2128(42.7)	1589(31.9)	32(0.6)	
12-18 years	3313(49.3)	2185(32.5)	1164(17.3)	56(0.8)	

Table 2. Gender and season characteristics based on vitamin D levels for each age group

		Vitamin D Levels				
Age Groups		**Deficiency (n=5243)**	**Insufficiency (n=5534)**	**Sufficiency (n=5222)**	**Potential side effects (n=322)**	**p**
	n	144	149	848	167	
	Gender					
	Female	67(46.5)	78(52.3)	382(45.0)	86(51.5)	0.224
	Male	77(53.5)	71(47.7)	466(55.0)	81(48.5)	
0-1 years	Season					
(Group 1)	Spring	42(29.2)^{a}	35(23.5)^{a,b}	156(18.3)^{b,c}	19(11.4)^{c}	
	Summer	21(14.6)^{a}	25(16.8)^{a,b}	243(28.7)^{c}	49(29.3) ^{b,c}	<0.001
	Autumn	32(22.2)^{a}	41(27.5)^{a}	232(27.4)^{a}	48(28.8)^{a}	
	Winter	49(34.0)^{a}	48(32.2)^{a}	217(25.6)^{a}	51(30.5)^{a}	
	n	552	1072	1621	67	
	Gender					
	Female	269(48.7)	495(46.2)	763(47.1)	31(46.3)	0.808
2-5 years	Male	283(51.3)	577(53.8)	858(52.9)	36(53.7)	
(Group 2)	Season					
	Spring	166(30.1)^{a}	252(23.5)^{b}	233(14.4)^{c}	9(13.4)^{b,c}	
	Summer	41(7.4)^{a}	176(16.4)^{b}	482(29.7)^{c}	16(23.9)^{b,c}	<0.001
	Autumn	57(10.3)^{a}	239(22.3)^{b}	485(29.9)^{c}	12(17.9)^{a,b,c}	
	Winter	288(52.2)^{a}	405(37.8)^{b}	421(26.0)^{c}	30(44.8)^{a,b}	
	n	1234	2128	1589	32	
	Gender					
	Female	727(58.9)	1118(52.5)	681(42.9)	13(40.6)	<0.001
6-11 years	Male	507(41.1)	1010(47.5)	908(57.1)	19(59.4)	
(Group 3)	Season					
	Spring	354(28.7)^{a}	374(17.6)^{b}	116(7.3)^{c}	3(9.4)^{a,b,c}	
	Summer	92(7.5)^{a}	448(21.0)^{b}	558(35.1)^{c}	9(28.1)^{b,c}	<0.001
	Autumn	141(11.4)^{a}	449(21.1)^{b}	567(35.7)^{c}	13(40.6)^{c}	
	Winter	647(52.4)^{a}	857(40.3)^{b}	348(21.9)^{c}	7(21.9)^{b,c}	
	n	3313	2185	1164	56	
	Gender					
	Female	2642(79.7)	1278(58.5)	509(43.7)	35(62.5)	<0.001
	Male	671(20.3)	907(41.5)	655(56.3)	21(37.5)	
12-18 years	Season					
(Group 4)	Spring	722(21.8)	302(13.8)	84(7.2)	4(7.1)	
	Summer	537(16.2)	621(28.5)	409(35.2)	21(37.5)	<0.001
	Autumn	574(17.3)	593(27.1)	417(35.8)	10(17.9)	
	Winter	1480(44.7)	669(30.6)	254(21.8)	21(37.5)	

Data were expressed as n(%).

Percentages with different subscript letters ($^{a, b, c}$) within columns are significantly different at the 0.05 level.

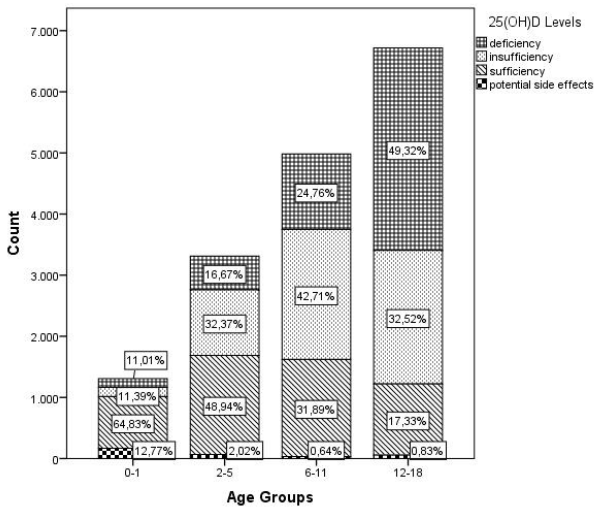

Fig 1. Vitamin D levels distribution according to age groups

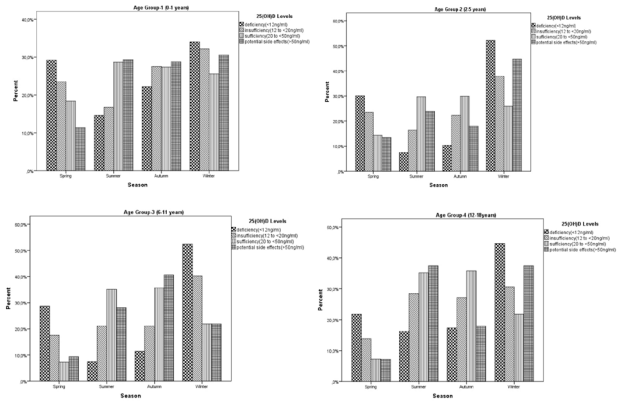

Fig 2. Vitamin D levels distribution according to seasons in four age groups

Discussion

The present study demonstrated that vitamin D deficiency is extremely prevalent (n= 10777, 66%) in children admitted to our pediatric clinics. Deficiency was detected most frequently in winter(n= 4443, 41.2%). While this deficiency is more common in females over the age of six, no gender difference was found under the age of six. Our data demonstrated that vitamin D deficiency increases with increasing age. So the prevalence was highest in adolescents and lowest in participants younger than one-year-old. We believe that the reason why there is less vitamin D deficiency under the age of one is the campaign carried out by the Ministry of Health since 2005. In this campaign, 400 IU/day of free vitamin D support is started for each newborn and continues until the age of one year. A study conducted in our country before this campaign found that the incidence of rickets due to vitamin D deficiency in children aged 0-3years was 6.09%, while the other study conducted in the second year of the campaign with the same team in the same region, this frequency was found to be 0.099% (11).

Vitamin D supplements are routinely used in children only to prevent rickets. However, childhood and adolescence are also critical periods for skeletal development. 90% of adult bone mineralization is completed by the end of adolescence, and 40% of this rate occurs during adolescence. Therefore, vitamin D supplementation is important for bone health during these periods. Although it has been reported that vitamin D supplementation may be beneficial for bone health in children and adolescents, there is still uncertainty about vitamin D supplementation after infancy in the guidelines (12). The Institute of Medicine recommends a daily allowance of at least 15 mcg of vitamin D for children older than one year (10). The American Academy of Pediatrics recommends 10 mcg/day (400 IU) for breastfed and partially breastfed infants until they are fed at least 1 L/day of vitamin D–fortified formula or whole milk. In addition, the APA recommends taking 400 IU/day of vitamin D supplements for adolescents who do not obtain 400 IU of vitamin D daily through vitamin D fortified foods (13). European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) reported that children younger than one year old should take 10 mcg/day of vitamin D. For children older than 1 year, they suggested that vitamin D supplementation should only be considered for the risk group (dark skin, lack of adequate sun exposure, use of sunscreen with high SPF, staying indoors for much of the day, wearing clothes covering most of the skin, living in northern latitudes during wintertime, and obesity) (14).

The reports demonstrated there is no need and no sufficient evidence to support universal screening for vitamin D status. Despite this, it is reported that the cost of vitamin D analysis is increasing rapidly in the National Health Systems of many countries. To reduce these unnecessary costs, it is recommended to use questionnaires for those outside the risk group who need supplements (sunlight exposure, daily supplement intake, etc.). Thus, it will be easier to identify patients with vitamin D deficiency. It is recommended that these be supplemented first and then a serum 25(OH)D test be ordered to confirm that proficiency has been achieved (9).

Different study results have been reported on the prevalence of vitamin D deficiency in children in different parts of the world. A study in Poland reported that 46.7% of children aged 3-18 had vitamin D deficiency (15). In a study conducted in Colombia, a tropical region, this rate was found to be 23.7% in children under the age of 18 (16). In southern China, a sunny region 22.6% of children aged 0 to 18 years had a vitamin D deficiency(17). In a study conducted between 11-16 years of age in Kuwait, another sunny region, vitamin D deficiency was found to be 81.2%(18). In a study examining vitamin D deficiency in Turkey, this frequency was found to be 63% in the general population, 86.6% in infants, and 39.8% in children(19). Although different results are expected due to reasons such as age group differences, different geographical features, genetic structure, and nutritional differences

between studies, a high rate of vitamin D deficiency was found in our study. We found that this deficiency increased with increasing age, so it was most common in adolescents, and it was detected least in infants. This result is in agreement with those of previously investigated studies that demonstrated an association between lower levels of vitamin D and increasing age(15, 17). We think that the sufficiency of vitamin D levels in the first years of life is due to the inclusion of these periods by the national support campaign. In addition, assuming that young children spend more time outside to play than older children, the decrease in their contact with sunlight over the years may be another reason for vitamin D deficiency, which increases with age. In addition, decreased consumption of dairy products may be another reason for low vitamin D, as parental control is reduced in the feeding of older children.

In our study, no gender difference was found in the first 6 years of life in terms of vitamin D deficiency. From 6 years of age, this deficiency was more common in females. Similar results have been reported in different studies(15-17, 20, 21).

In these studies, some ideas have been put forward to explain the tendency of vitamin D deficiency to be higher in females than in males. The first is that females have less physical activity than males. The other is that females spend less time outdoors and, according to the beliefs and cultures of some societies, wearing completely closed clothing reduces sun exposure and prevents the synthesis of vitamin D. However, we think that the lifestyles of males and females in very different cultures cannot be parallel enough to affect vitamin levels similarly. We assume that hormonal mechanisms may also be effective in the relative increase in vitamin D levels in males with increasing age. For example, we think that it will be useful to examine whether the androgen hormone has a positive effect on vitamin D synthesis, similar to its effect on erythropoietin and its contribution to erythrocyte production.

The present study evaluated the prevalence of vitamin D deficiency according to seasonal variability. In all age groups, vitamin D deficiency was detected most frequently in winter. Similar results have been reported in previous studies (15, 22, 23). We believe that the high prevalence of vitamin D deficiency during the winter is a result of insufficient sun exposure.

We have some limitations in this study. Our study is retrospective and single-center. Therefore, the results may not reflect the entire pediatric population in Ankara. In addition, since our study was retrospective, we could not obtain sufficient data to determine the prevalence of rickets in those with vitamin D deficiency. Although it is considered a limitation that we did not evaluate the factors that may be associated with vitamin D levels (sunlight exposure, vitamin supplementation, exercise, body mass index, etc.), our aim in this study was to determine the prevalence of the vitamin. D deficiency.

We have some limitations in this study. Our study is retrospective and single-center. Therefore, the results may not reflect the entire pediatric population in Ankara. In addition, since our study was retrospective, we could not obtain sufficient data to determine the prevalence of rickets in those with vitamin D deficiency. Although it is considered a limitation that we did not evaluate the factors associated with vitamin D level (sunlight exposure, vitamin supplementation, exercise, body mass index, etc.), we aimed to determine the prevalence of vitamin D deficiency.

In conclusion, vitamin D deficiency was common in our study. Vitamin D deficiency causes nonspecific complaints in children and does not always present symptoms on physical examination. The lack of routine screening programs to determine the vitamin D status of children in clinical practice suggests that many deficiencies may not be noticed. However, in childhood, when there is a high bone growth rate, bone mineralization deficiency that can be caused by vitamin D deficiency is very important. To prevent this, it is crucial to take anamnesis in terms of daily vitamin D intake in children. Children with insufficient daily intake should be supported. After that, it is essential to measure serum 25(OH)D levels for determining whether vitamin D levels reach optimal levels.

References

1.Sirajudeen S, Shah I, Al Menhali A. A narrative role of vitamin D and its receptor: with current evidence on the gastric tissues. International journal of molecular sciences. 2019;20(15):3832.

2.Alonso M, Mantecón L, Santos F. Vitamin D deficiency in children: a challenging diagnosis! Pediatric research. 2019;85(5):596-601.

3.Rahman A, Elmi A. Air pollutants are negatively associated with vitamin D-synthesizing UVB radiation intensity on the ground. Scientific Reports. 2021;11(1):1-10.

4.Hansen L, Tjønneland A, Køster B, Brot C, Andersen R, Cohen AS, et al. Vitamin D status and seasonal variation among Danish children and adults: a descriptive study. Nutrients. 2018;10(11):1801.

5.Wang Q, Ying Q, Zhu W, Chen J. Vitamin D and asthma occurrence in children: A systematic review and meta-analysis. Journal of Pediatric Nursing. 2021.

6.Gavrilov A. Relationship of the vitamin D deficiency and the prevalence of type 1 diabetes mellitus. 2020.

7.Fletcher J, Cooper SC, Ghosh S, Hewison M. The role of vitamin D in inflammatory bowel disease: mechanism to management. Nutrients. 2019;11(5):1019.

8.Gubatan J, Chou ND, Nielsen OH, Moss AC. Systematic review with meta□analysis: association of vitamin D status with clinical outcomes in adult patients with inflammatory bowel disease. Alimentary pharmacology & therapeutics. 2019;50(11-12):1146-58.

9.Minisola S, Colangelo L, Pepe J, Occhiuto M, Piazzolla V, Renella M, et al. Vitamin D screening. Journal of endocrinological investigation. 2020:1-5.

10.Board N, CRDRIVD C. Dietary reference intakes for calcium and vitamin D. Washington, DC: National Academy Press; 2010.

11.Ozkan B, Doneray H, Karacan M, Vançelik S, Yıldırım ZK, Ozkan A, et al. Prevalence of vitamin D deficiency rickets in the eastern part of Turkey. European journal of pediatrics. 2009;168(1):95-100.

12.Taylor SN. Vitamin D in toddlers, preschool children, and adolescents. Annals of Nutrition and Metabolism. 2020;76(2):30-41.

13.Wagner CL, Greer FR, Breastfeeding So, Nutrition Co. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008;122(5):1142-52.

14.Braegger C, Campoy C, Colomb V, Decsi T, Domellof M, Fewtrell M, et al. Vitamin D in the healthy European paediatric population. J Pediatr Gastroenterol Nutr. 2013;56(6):692-701.

15.Smyczyńska J, Smyczyńska U, Stawerska R, Domagalska-Nalewajek H, Lewiński A, Hilczer M. Seasonality of vitamin D concentrations and the incidence of vitamin D deficiency in children and adolescents from central Poland. Pediatric Endocrinology Diabetes and Metabolism. 2019;25(2):54-9.

16.Beer RJ, Herrán OF, Villamor E. Prevalence and correlates of vitamin D deficiency in a tropical setting: results from a nationally representative survey. The American Journal of Clinical Nutrition. 2020;112(4):1088-98.

17.Guo Y, Ke H-J, Liu Y, Fu M, Ning J, Yu L, et al. Prevalence of vitamin D insufficiency among children in southern china: A cross-sectional survey. Medicine. 2018;97(25).

18.Al-Taiar A, Rahman A, Al-Sabah R, Shaban L, Al-Harbi A. Vitamin D status among adolescents in Kuwait: a cross-sectional study. BMJ open. 2018;8(7):e021401.

19.Alpdemir M, Alpdemir MF. Meta Analysis Vitamin D deficiency status in Turkey: A meta-analysis. Int J Med Biochem. 2019;2(3):118-31.

20.Babaniamansour S, Hematyar M, Babaniamansour P, Babaniamansour A, Aliniagerdroudbari E. The prevalence of vitamin D deficiency among one to six year old children of Tehran, Iran. Journal of Kermanshah University of Medical Sciences. 2019;23(4).

21.Yang C, Mao M, Ping L, Yu D. Prevalence of vitamin D deficiency and insufficiency among 460,537 children in 825 hospitals from 18 provinces in mainland China. Medicine. 2020;99(44).

22.Ando E, Morisaki N, Asakura K, Sasaki S, Fujiwara T, Horikawa R. Serum 25-hydroxyvitamin D levels showed strong seasonality but lacked association with vitamin D intake in 3-year-old Japanese children. British Journal of Nutrition. 2018;120(9):1034-44.

23.Beyitler İ, Uncu M, Bahceciler N, Şanlıdağ B, Dalkan C, Kavukcu S. Impact of mediterranean climate and seasonal variation on vitamin D levels in children. Cyprus J Med Sci. 2018;1:15-8.

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ORIGINAL ARTICLE

Autologous pericardium may be an alternative carotid patch material in patient with undergoing simultaneous carotid endarterectomy and coronary artery bypass grafting

Eş zamanlı karotis endarterektomi ve koroner arter baypas greftleme operasyonu yapılan hastalarda otolog perikard alternatif bir karotis yama materyali olabilir.

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ABSTRACT

Backround: Dacron, polytetrafluoroethylene, great saphenous vein, and bovine pericardium are the commonly used as patch materials. However, there is no comparative study about autologous pericardial as a patch material in carotid endarterectomy surgery. We aimed to assess the results of the use of autologous pericardial patch in patients undergoing concomitant carotid endarterectomy and coronary artery by-pass graft surgery.
Materials and Methods: The study involved 30 patients who underwent concomitant carotid endarterectomy with patch angioplasty and coronary artery bypass grafting surgery from January 2016 to February 2020. Patchplasty is performed with autologous pericardium for 13 patients and dacron patch for 17 patients during carotid endarterectomy.
Results: No statistical difference was found between the groups in terms of reoperation, arterial occlusion, restenosis, operation time, and neurological events. In the postoperative follow-up, it was determined that the amount of drainage from the area on which the carotid surgery was applied was less in the those in whom autologous pericardium was used compared to those in whom Dacron patch was used. (p=0.001)
Conclusion: We concluded that the use of autologous pericardium as a carotid artery patch is a safe, feasible, and effective method in patients undergoing combined carotid artery and coronary bypass surgery.

Keywords: Pericardium, carotid stenosis, endarterectomy, dacron, coronary artery bypass grafting

ÖZ

Amaç: Dakron, politetrafloroetilen, büyük safen damarı ve sığır perikardı yaygın olarak yama malzemeleri olarak kullanılır. Ancak karotis endarterektomi cerrahisinde yama materyali olarak otolog perikardiyal ile ilgili karşılaştırılmalı bir çalışma bulunmamaktadır. Bu çalışmada, eş zamanlı karotis endarterektomi ve koroner arter baypas greft cerrahisi uygulanan hastalarda otolog perikardiyal yama kullanımının sonuçlarını değerlendirmeyi amaçladık.
Gereç ve Yöntem: Çalışmaya Ocak 2016 ile Şubat 2020 arasında yama anjiyoplasti ve koroner arter baypas greftleme cerrahisi ile birlikte karotis endarterektomi uygulanan 30 hasta dahil edildi. Karotis endarterektomi sırasında 13 hastada otolog perikard ve 17 hastada dakron yama ile patchplasti yapıldı.
Bulgular: Gruplar arasında reoperasyon, oklüzyon, restenoz, operasyon süresi ve nörolojik olaylar açısından istatistiksel fark bulunmadı. Postoperatif takipte otolog perikard kullanılanlarda karotis cerrahisi uygulanan bölgeden drenaj miktarının Dacron yama uygulananlara göre daha az olduğu belirlendi. (p=0,001)
Sonuç: Karotis arter yaması olarak otolog perikardın kullanımının karotid arter ve koroner bypass cerrahisi uygulanan hastalarda güvenli, uygulanabilir ve etkili bir yöntem olduğu sonucuna vardık.

Anahtar Kelimeler: Perikard, karotis darlığı, endarterektomi, dakron, koroner arter baypas greftleme

Introduction

Stroke is a dreaded complication after coronary artery bypass grafting (CABG) due to high risk of mortality, morbidity, long hospitalization, and impaired quality of life. Although many risk factors have been defined for CABG-related stroke, some authors have considered the presence of aortic atheroma, carotid stenosis, and peripheral vascular disease as more effective factors (19. The prevalence of significant carotid artery stenosis(CAS) (>70%) in patients who are candidate for CABG varies from 3.6% to 8.8% (2,3). Although there is consensus in the guidelines on treatment management in patients in whom coronary artery disease or CAS exists alone, there are many controversial issues in the surgical management of the patient group in which both exist at the same time. One of them, there is no consensus on the best patch material to use in such patients. Dacron, polytetrafluoroethylene, great saphenous vein, and bovine pericardium are the commonly used patch materials, and there are many studies in the literature about these patches (4). The use of autologous pericardium as an alternative carotid patch in concomitant carotid endarterectomy (CEA) and CABG surgery in four cases has been described previously (5). However, there is no comparative study between autologous pericardial patch and Dacron patch material. Therefore, in this comparative study, we

aimed to assess the results of the use of autologous pericardial patch in patients undergoing concomitant CEA and coronary artery by-pass graft surgery.

Materials and Methods

Patient population

This retrospective, cross□sectional comparative study involved 30 patients who underwent concomitant CEA with patch angioplasty and CABG surgery from January 2016 to February 2020. Patients who underwent CEA with primary suturing OR eversion technique and staged surgery (such as CEA after CABG) were excluded. The patients were divided into two groups according to the patch material. Thirteen patients underwent CEA and patchplasty with autologous pericardium (group 1) and 17 patients had CEA and patchplasty with Dacron (Group 2). Data such as demographics, procedures, doppler ultrasonography(DUS) results and outcomes were collected from the electronic database of the hospital and patient files. Postoperative bleeding, 30-day stroke, and mortality were the primary endpoint of the study. Carotid restenosis and thrombosis were the secondary endpoint of the study.

In patients undergoing CABG, carotid DUS was performed in symptomatic patients or asymptomatic patients with age ≥ 70 years, multivessel coronary artery disease, concomitant lower extremity arterial disease, or carotid bruit (6,7). Symptomatic patient was defined as having a recent (<6 months) history of stroke/TIA (6,7). Stenosis grade was determined based on the CT scan screening according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. Concomitant CEA surgery was planned according to guideline recommendation (6-8). Restenosis threshold of the carotid artery after endarterectomy was accepted as 70% (at the endarterectomy site), which was diagnosed with either conventional angiography or computed tomography (CT) angiography (7). Post-operative stroke was confirmed by an attending neurologist based on any major neurological deficit diagnosed either clinically or with a head CT scan.

The Institutional Review Board approved the study protocol (Date:09.02.2021 #2021/3/474). The study was conducted in accordance with the principles of the Declaration of Helsinki. A written informed consent was obtained from each patient for surgical procedure.

Surgical procedure

Near-infrared spectroscopy monitoring was used routinely to assess oxygen saturation of the brain in all surgical procedures. Carotid shunt was applied selectively according to carotid stump pressure.

Group 1 consisted of patients who underwent CEA and patchplasty with autologous pericardium. Following classical incision medial to the sternocleidomastoid muscle, the common carotid, external carotid, and internal carotid arteries were explored. After midline sternotomy, at least a 2×5 cm pericardium (pericardial size may change according to stenotic segment) were harvested. Adipose tissue over the pericardium was removed. Pericardium was attached on the plate with the rough surface facing upwards. The pericardium was soaked in 2% glutaraldehyde solution for 5 min for fixation. It was, then, rinsed with saline solution. Diaphragmatic side of the pericardium is thicker than the other side (9). Therefore, the diaphragmatic side of the pericardium was used for this procedure. After 5000 IU of heparin was administered, vascular clamps were applied. After the longitudinal arteriotomy was extended from the common carotid artery to the internal carotid artery, carotid shunt canula was inserted. The plaque inside the carotid artery was carefully separated and removed. After the removal of the plaque by de-airing maneuvers, surgical closure was performed with a pericardial patch using 6/0 polypropylene with the continuous-suturing technique. The smooth surface of the pericardium should be placed towards the lumen of the vessel. Then, the vascular clamps were removed in an appropriate order and the flow was restored. After the procedure was completed, standard on-pump CABG was performed in all patients.

Group 2 involving CEA and surgical closure with the Dacron patch was performed by the same technique as described above for Group 1. After the CEA procedure was completed, midline sternotomy was performed for on-pump CABG surgery.

Follow-up

Following the surgery, all patients were taken to the Cardiovascular Surgery Intensive Care Unit for follow-up. Postoperative bleeding volume was recorded on a daily basis from all surgical drains until the removal of these instruments. The patients were then transferred to the cardiovascular surgery clinic when their general condition and hemodynamics were good. Dual anti-platelet therapy, consisting of 100-mg acetylsalicylic acid and 75-mg clopidogrel was routinely administered in all patients. At follow-up, the patients were evaluated with physical examination and color DUS in the outpatient clinic.

Statistical Analysis

The data obtained in this study were analyzed using the Statistical Package for the Social Sciences version 11.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed in mean standard±deviation (SD) or median(min-max), while categorical variables were expressed in number and percentage. The Student's t-test was used to analyze significant differences between normally distributed data, and the Mann-Whitney U test was used to analyze nonnormally distributed data. The chi-square and Fisher exact tests were used to examine quantitative variables. A p value of <0.05 was considered statistically significant.

Results

A total of 30 patients who underwent concomitant CEA with patchplasty and CABG were included in this analysis. Of the patients included, 8 (26.7%) were females and 21 (73.3%) were males. The mean age of the patients was 67.8 ± 8.1 years (range, 52 to 82).

The mean body mass index (BMI) was 28.2 ± 4.9 kg/m2 (range, 16.7 to 42.7). Hypertension (70%) was the most common comorbidity. Eight patients(26.7%) were smokers. A comparison of the groups in terms of their demographic data are presented in Table 1. There was no significant difference between groups in terms of demographics and intraoperative variables (Table 1,2).

Transient neurologic deficit was seen in three patients(10%). In the group in which autologous pericardium was used, 2/5 muscle strength loss occurred in the left upper extremity in 1 (7.7%) patient. In the group in which Dacron patch was used, neurocognitive impairment was seen in two patients (11.6%). These symptoms resolved two weeks after the surgery. Permanent neurologic deficit was not seen in both groups. Postoperative cardiac complication was seen in five patients (29.1%) in group in which Dacron patch was used. There was no statistical difference between groups in terms of sternal drainage. However, the amount of postoperative drainage from the carotid region was significantly higher in the Dacron patch group than in the autologous pericardium group (75.9±50.3; 27.3±23.8, respectively, p=0.001). Postoperative re-exploration was performed for the carotid region in one patient due to neck hematoma in the Dacron patch group.

There were statistical differences between groups in terms of ICU and hospital stay among postoperative variables (p=0.01, both) (Table 3). There was no difference between the groups in terms of hospital and 30-day mortality due to CEA. Mean follow up was 27.4±14.3 months (range:7.1-55.9). Postoperative DUS controls of the patients revealed that there were no residual stenosis, thrombosis, or aneurysm formation in both groups.

Table 1. Preoperative charecteristics of the patients

	Perikardial Patch (n=13)	Dacron Patch (n=17)	P value
	Mean±SD	Mean±SD	
Age	66.6±8.7	68.7±7.8	0.95[a]
EF	53.1±12.2	55.9±10.6	0.56[b]
BMI	28±2.9	28.3±6.1	0.06[a]
	n (%)	n (%)	
Gender			0.24[c]
Male	5 (38.5%)	3 (17.6%)	
Female	8 (61.5%)	14(82.4%)	
HT	10 (76.9%)	11 (64.7%)	0.691[c]
DM	7 (53.8%)	7 (41.2%)	0.491[d]
COPD	4(30.8%)	7 (41.2%)	0.708[c]
Smoking	5 (38.5%)	3 (17.6%)	0.242[c]

EF: Ejection fraction ; BMI: Body mass index; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; DM: Diabetes Mellitus; SD: Standard deviation; a: Student T test; b: Mann–Whitney *U* test; c: Fischer's exact test; d: Chi-square test.

Table 2. Intraoperative variables of the patients

	Perikardial Patch (n=13)	Dacron Patch (n=17)	P value
	Mean±SD	Mean±SD	
Duration of Operation (min)	330.8±42.3	313.2±50.1	0.48[a]
Duration of XCL (min)	63.6±16.9	61.6±35.1	0.26[b]
Duration of CPB (min)	111.1±24.2	107.4±37	0.32[b]
	n (%)	n (%)	
Side of CEA			0.96[c]
Right	6 (46.2%)	8(47.1%)	
Left	7 (53.8%)	9 (52.9%)	
Carotid shunt usage	9 (69.2%)	9 (52.9%)	0.367[c]

XCL: Cross clamp; CPB: Cardiopulmonary bypass; CEA: Carotid endarterectomy
SD: Standard deviation; a: Student T test; b: Mann–Whitney *U* test; c: Chi-square test;

Table 3. Postoperative outcomes of the patients

	Perikardial Patch (n=13)	Dacron Patch (n=17)	P value
	Mean±SD	Mean±SD	
Intubation period (hours)	23.8±41.1	30.3±45.7	0.17[a]
Length of stay at intensive care unit (hours)	55.9±40.7	117.8±86.3	0.03[a]
Length of stay at the hospital (days)	7.2±2.2	13.8±10.3	0.01[a]
Drainage from the carotid region (ml)	27.3±23.8	75.9±50.3	0.001[a]
Drainage from the mediastinal region (ml)	546.2±335.1		0.86[b]
	n (%)	n (%)	
Cardiac complication	0 (0%)	5 (29.4%)	0.05[c]
Neurologic complication	1 (7.7%)	2 (11.8%)	1[c]
Re-explorasyon at the carotid region	0 (0 %)	1 (5.9%)	1[c]

SD: Standard deviation; a: Mann–Whitney *U* test ; b :Student T test; c: Fischer's exact test

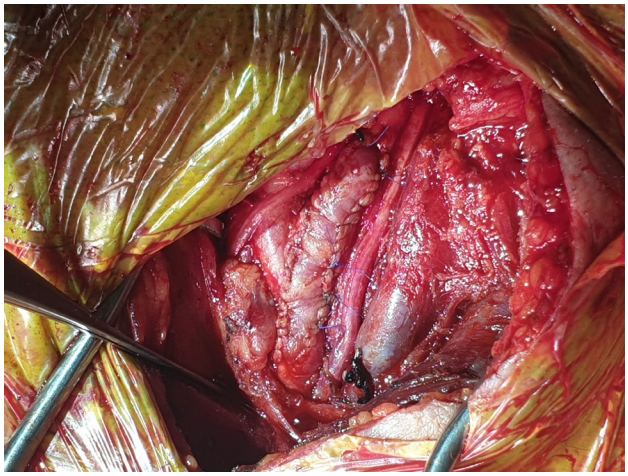

Figure 1. Intraoperative image of carotid endarterectomy and patchplasty with autologous pericardium

Discussion

Hemodynamically significant internal carotid artery stenosis, which was detected before cardiac surgery, simultaneous or staged CEA was performed. The timing and modality of the carotid revascularization is controversial, and it should be individualized based on the clinical situation, the level of emergency, and the severity of the carotid and coronary artery diseases (6,7). Staged CEA strategies cause a higher risk of periprocedural MI if the carotid artery is revascularized first, and a trend toward increased cerebral risk occurs if CABG is performed first. In a study examining different strategies that can be applied, it was found that 3-month stroke and mortality rates were higher in patients with unilateral CAS in CAE performed after CABG compared to prior CAE in concomitant CABG or staged surgery (10). It has been known that staged or simultaneous techniques have advantages and disadvantages compared to each other. In a recent meta-analysis, it was found that there was no significant difference in 1-year mortality, transient neurological deficit, or MI rates, despite longer hospital stay and less 30-day mortality and stroke in staged surgery (11). However, it should be kept in mind that when staged surgery is preferred, patients are likely to be exposed to an interstage cardiovascular event. Since our surgical center has a high patient circulation, simultaneous surgery is preferred because it requires shorter hospital stay. Therefore, simultaneous surgery was performed in all patients included in our study.

With the developments in technology, the number and variety of bio-prosthesis materials used in cardiovascular surgery are increasing. Compared to synthetic materials, pericardial patches are an inexpensive, readily available, infection-resistant, and biocompatible material (12). Autologous pericardium can be used fresh or treated with glutaraldehyde. However, autologous pericardium may be retracted when used fresh. For this reason, glutaraldehyde-fixed autologous pericardium has been used for many years in many congenital or reconstructive operations in cardiac surgery. When autologous pericardium is fixed with glutaraldehyde, it becomes tougher, stronger, more resistant to proteolytic degradation, and more convenient to surgical manipulation (13,14). However, the autologous pericardium does not have an optimal method and duration of glutaraldehyde fixation (14). However, residual unstable glutaraldehyde polymers remaining during fixation are known to cause inflammatory reaction, cytotoxicity, and calcification, in addition to inhibiting endothelialization (13). In a study, it was determined that five-minute fixation with 2% glutaraldehyde caused optimal tensile strength and elongation for the autologous pericardium (5). In our study, autologous pericardium was fixed with 2% glutaraldehyde for 5 minutes. In this way, surgical manipulation of the fixed pericardium was easy and the operation time was not prolonged. However, no inflammatory reaction, stroke, or mortality was observed associated with the use of autologous pericardium.

Many materials such as autologous, synthetic, or biological patches have been used as patch material in patients undergoing CEA (4). Although the great saphenous vein has some theoretical advantages such as being an autologous graft and resistant to infection, undesirable complications such as harvesting site complications, pseudoaneurysm, or rupture have been reported, albeit not with statistically significant results (4,16). Biologically, bovine pericardium is a material that has been used for a long time in cardiac surgery. It has been reported that CEA has similar results with other patch materials in terms of restenosis and stroke in the long term. In addition, it has been suggested that it has a comparable cost to other alternative patching techniques due to its low postoperative bleeding rate and very low risk of infection (17). Synthetic patches are materials that have been used for years in CEA operations (4). Dacron patch is a polyester fiber with high tensile strength. When Dacron patch and other synthetic materials were compared, the risk of early thrombosis and restenosis was higher in the Dacron patch group; therefore, it was thought that it may have caused an increase in perioperative stroke and transient ischemic attacks. However, these outcomes were not statistically significant (4). In a meta-analysis, no statistical difference was found between synthetic, autologous vein, or bovine pericardial patches in terms of early and long-term outcomes (18). Furthermore, other important long-term sequelae associated with synthetic patches are pseudoaneurysm formation and infection development. However, these are very rare and treatable complications (19). Dacron patch is mostly used in our clinic in patients undergoing isolated CEA. In our study, Dacron patch and pericardial patch were compared in patients who were operated concurrently with CABG. One of the reasons for this is the use of Dacron patch as a carotid patch in almost all patients whose data were available. Another reason was to compare the results of patients using autologous pericardial patches with a more homogeneous patient group. There was no difference between groups in the early and late postoperative periods, except for drainage from the carotid region. The amount of bleeding in the autologous pericardium group was significantly lower than the patient group in which Dacron patch was used. In one patient in the Dacron patch group, the patient was reoperated due to bleeding from the suture line.

There are some limitations of our study. Our main limitation is that it is retrospective and the number of patients is small. However, we think that the results of our study will contribute to the literature because combined carotid artery surgery and CABG are performed less than those performed in isolation. Another limitation is that the autologous pericardial patch has not been compared with other used patch materials in the literature. Since the patches used other than Dacron patches were very limited in this patient group, these patients were excluded from the study in order not to cause heterogeneity in the patient population.

In conclusion, we consider that the use of autologous pericardium as a carotid artery patch is a safe, feasible, and effective method in patients undergoing combined carotid artery and coronary bypass surgery since it is resistant to infection, has a low postoperative bleeding profile, and is sterile, not immune-reactive, biocompatible, and an easily available low-cost material. Large scale prospective, randomized studies are needed to confirm our study results.

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References

1.Drakopoulou M, Oikonomou G, Soulaidopoulos S, Toutouzas K, Tousoulis D. Management of patients with concomitant coronary and carotid artery disease. Expert Rev Cardiovasc Ther 2019; 17:575-583.

2.Kiernan TJ, Taqueti V, Crevensten G, Yan BP, Slovut DP, Jaff MR. Correlates of carotid stenosis in patients undergoing coronary artery bypass grafting- a case control study. Vasc Med 2009;14: 233-237.

3.Wanamaker KM, Moraca RJ, Nitzberg D, Magovern GJ Jr. Contemporary incidence and risk factors for carotid artery disease in patients referred for coronary artery bypass surgery. J Cardiothorac Surg 2012;7:78.

4.Orrapin S, Benyakorn T, Howard DP, Siribumrungwong B, Rerkasem K. Patches of different types for carotid patch angioplasty. Cochrane Database Syst Rev 2021;2:CD000071.

5.Başar V, Hançer H. Usage of Autologous Pericardıum as an Alternative Carotid Patch in Concomitant Carotid Endarterectomy and Coronary Artery By-Pass Graft Surgery. Bozok Med J 2019; 9:58-63.

6.Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U. 2018 ESC/EACTS Guidelines on myocardial revascularization [published correction appears in Eur Heart J 2019;40:87-165.

7.Naylor AR, Ricco JB, de Borst GJ, et al. Editor's Choice - Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018;55:3-81.

8.Akay T. Karotis arter darlıkları. In: Bozkurt AK, editor. Periferik Arter ve Ven Hastalıkları. Ulusal Tedavi Kılavuzu İstanbul: Bayçınar Tıbbi Yayıncılık. 2021:100-130.

9.Ozaki S, Kawase I, Yamashita H, et al. A total of 404 cases of aortic valve reconstruction with glutaraldehyde-treated autologous pericardium. J Thorac Cardiovasc Surg 2014;147:301-306.

10.Illuminati G, Ricco JB, Calio F, et al. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting. J Vasc Surg 2011;54:993-999.

11.Chan JSK, Shafi AMA, Grafton-Clarke C, Singh S, Harky A. Concomitant severe carotid and coronary artery diseases: a separate management or concomitant approach. J Card Surg 2019;34:803-813.

12.Filová E, Staňková L, Eckhardt A, et al. Modification of human pericardium by chemical crosslinking. Physiol Res. 2020;69:49-59.

13.Jayakrishnan A, Jameela SR. Glutaraldehyde as a fixative in bioprostheses and drug delivery matrices. Biomaterials 1996;17:471-484.

14.Lee C, Lim HG, Lee CH, Kim YJ. Effects of glutaraldehyde concentration and fixation time on material characteristics and calcification of bovine pericardium: implications for the optimal method of fixation of autologous pericardium used for cardiovascular surgery. Interact Cardiovasc Thorac Surg 2017;24:402-406.

15.Kapısız NS, Kapısız HF, Doğan OV, Dolgun A, Yücel E. Glutaraldehyde fixation of autologous pericardial patches. Trakya Univ Tip Fak Derg 2008;25:124-129.

16.Gaunt ME, Thompson M, White S, Naylor AR, Bell PR. Vein-patch rupture after carotid endarterectomy: an avoidable catastrophe. Br J Surg 1993;80:1490-1491.

17.Oldenburg WA, Almerey T, Selim M, Farres H, Hakaim AG. Durability of Carotid Endarterectomy with Bovine Pericardial Patch. Ann Vasc Surg 2018;50:218-224.

18.Texakalidis P, Giannopoulos S, Charisis N, et al. A meta-analysis of randomized trials comparing bovine pericardium and other patch materials for carotid endarterectomy. J Vasc Surg 2018;68:1241-1256.

19.Muto A, Nishibe T, Dardik H, Dardik A. Patches for carotid artery endarterectomy: current materials and prospects. J VascSurg 2009;50:206-213.

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ORIGINAL ARTICLE

The Relationship Between Vitamin D levels and Severity of Menopausal Symptoms

Vitamin D ve Menopozal Semptomların Şiddeti Arasındaki İlişki

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ABSTRACT

Aim: Our aim was to investigate the relationship between menopausal symptoms and serum vitamin D levels.
Material-Method: We analyzed 110 postmenopausal women aged between 42-65 years among menopause symptoms by using Menopause Rating Scale (MRS) questionnaire. Patients were divided into three groups according to their serum 25-OH vitamin D levels; sufficient (>20 ng/mL), insufficient (12-20 ng/mL), deficient (<12 ng/mL), then compared. Serum vitamin D cut-off level was determined for menopausal symptoms. The correlations between symptoms and vitamin D status were calculated.
Results: Vitamin D deficiency was detected in 38,1% (42/110) of the participants. The total MRS score was 22,97±2,71 in Vitamin D deficiency group and significantly higher than others (p<0,001). In deficiency group, somatic, psyhcological and urogenital subscale scores were higher than other groups (p<0,001, p=0,007 and p=0,036, respectively). Evaluation of the correlations among independent variables revealed a negative relationship between vitamin D level and MRS scores. The threshold value at which serum vitamin D causes severe MRS scores in those with sufficient levels was calculated as 25.31 ng/ml. The area under the ROC curve was 0,876 (95% CI, 0,702-1,00, p=0.003).
Conclusion: In the present study, a relationship between serum vitamin D levels and menopause-related symptoms in postmenopausal population was demonstrated. Low levels of vitamin D in menopausal period might aggravate menopause-related symptoms.
Keywords: Menopause-related symptoms, vitamin D, postmenopausal

ÖZ

Amaç: Amacımız menopoz semptomları ile serum D vitamini düzeyleri arasındaki ilişkiyi araştırmaktı.
Gereç-Yöntem: Menopoz semptomları, 42-65 yaş arası 110 postmenopozal kadında Menopoz Derecelendirme Ölçeği (MDÖ) anketi kullanılarak analiz edildi. Hastalar serum 25-OH D vitamini düzeylerine göre üç gruba ayrıldı; yeterli (>20 ng/mL), azalmış (12-20 ng/mL), eksik (<12 ng/mL), sonra karşılaştırıldı. Şiddetli menopoz semptomlarına yol açan serum D vitamini düzeyi için ROc eğirisi ile eşik değer belirlendi. Semptomlar ve vitamin D seviyesi arasındaki korelasyon hesaplandı.
Bulgular: Katılımcıların %38,1'inde (42/110) D vitamini eksikliği saptandı. D vitamini eksikliği grubunda toplam MDÖ puanı 22,97±2,71 olup diğerlerinden anlamlı olarak yüksekti (p<0,001). Eksiklik grubunda somatik, psikolojik ve ürogenital alt ölçek puanları diğer gruplara göre daha yüksekti (sırasıyla p<0,001, p=0,007 ve p=0,036). Bağımsız değişkenler arasındaki korelasyonlar değerlendirildiğinde, D vitamini düzeyi ile MDÖ puanları arasında negatif bir ilişki ortaya çıktı. Yeterli düzeyde olanlarda serum D vitamininin ciddi MDÖ skorlarına neden olduğu eşik değer 25.31 ng/ml olarak hesaplandı. ROC eğrisi altında kalan alan 0,876 (%95 CI, 0,702-1,00, p=0,003) idi.
Sonuç: Bu çalışmada postmenopozal popülasyonda serum D vitamini düzeyleri ile menopoza bağlı semptomlar arasında ilişki olduğu gösterilmiştir. Menopoz dönemindeki düşük D vitamini seviyeleri menopoza bağlı semptomları şiddetlendirebilir.

Anahtar Kelimeler: Menopozla ilişkili semptomlar, Postmenopozal, Vitamin D

Introduction

Natural menopause is defined as the absence of menstruation for one year in women without any other underlying causes. In the menopausal period, low estrogen and high follicle stimulating hormone (FSH) concentrations are observed due to the decrease or disappearance of ovarian follicles (1). This hormonal instability in menopausal period may cause a number of physical and psychological complaints such as vasomotor symptoms, genito-urinary symptoms, mood and sleep disturbance(2). These menopause-related symptoms can negatively affect the individual's quality of life, work life and personal relations (3).

Vitamin D is a fat-soluble vitamin that has important roles in calcium metabolism and musculoskeletal system. In addition to its role in calcium and bone homeostasis, vitamin D potentially regulates many other cellular functions. In this regard Vitamin D deficiency can cause many infectious, autoimmune and cardiovascular diseases(4). It was also shown that Vitamin D has a protective impact againsts cardiovascular risks in women (5). In addition, there are several data showing that there may be a relationship between vitamin d deficiency and hot flushes, irritability and genitourinary sypmtoms(6–8). Arvold et al showed a correlation of severe vitamin D deficiency with anxiety, depression and impaired functionning in their randomized control trial in men and women population(9).

Given this background, it could be understood that the symptoms seen in vitamin D deficiency coincide with the symptoms seen in women during menopause. Therefore, we aimed to investigate whether there is a relationship between vitamin D levels and menopause-

related symptoms in postmenopausal women.

Material and Methods

This cross-sectional study consisted of 110 postmenopausal women who applied for routine gynecological examination to a tertiary center gynecology clinic. After obtaining the local ethical approval and written informed consent of each patient, demographic characteristics, medical histories, physical and gnynecological examination findings including body mass index (BMI), time since menopause of subjects were recorded. Menopause was defined as not having menstruel bleeding more than a year. Patients' serum follicule stimulating hormone (FSH), estradiol (E2), calcium (Ca), 25-OH vitamin D levels were measured.

Menopausal symptoms of all patients were evaluated using Meopause Rating Scale (MRS) questionnaire validated for Turkish-speaking populations (10). The MRS includes 11 items assigning a score of 0-4 for the severity of the symptom (0, absent; 1, mild; 2, moderate; 3, severe; 4, very severe). This questionnaire is divided into three domains; somatic subscale including hot flushes, heart discomfort, sleep problems, muscle and joint discomfort (items 1-3,11); psychological subscale including depressive mood, irritability, anxiety, physical and mental exhaustion (items 4-7); urogenital subscale including sexual problems, bladder problems, vaginal dryness (items 8-10). Total MRS score is the sum of the scores obtained in each subscale. The values above 8 for somatic score, 6 for psychological score, 3 for urogenital score and 16 for total MRS score were defined as severe scores (11).

The study included postmenopausal women aged between 40-65 years. Patients using hormon replacement therapy (HRT), with systemic diseases and medical conditions associated with vitamin D deficiency, taking any supplemental medications, smoking, with surgical menopause were excluded from study.

The subjects were divided into three groups according to their serum 25-OH vitamin D levels; sufficient (>20 ng/mL), insufficient (12-20 ng/mL), deficient (<12 ng/mL) (12) and then compared among the parameters mentioned.

Data were analyzed by SPSS 21.0 for Windows (SPSS Inc, Chicago, IL, USA) statistics programme. The normality of distribution was assessed by Shapiro-Wilk test. Analysis of variance (ANOVA) and Kruskall-Wallis tests were used for analysis of continuous variables. Post-Hoc analysis was performed. Spearman rho coefficients were calculated for correlation analysis. The ROC curve was plotted for vitamin D level associated with severity of menopausal symptoms. P<0.05 was considered statistically significant.

Results

The mean age of the patients was 53,8 years (range, 42 to 65 years). Mean time since menopause for patients was 6,1 years (range, 1 to 20 years). Vitamin D deficiency was detected in 38,1% (42/110) of the participants. Serum 25-OH Vitamin D levels of 30 women were ≥20 ng/mL, sufficient. The Vitamin D levels of the remaining 38 patients were insufficient, between 12-19 ng/mL. There were no differences among age, BMI, time since menopause and laboratory characterictics between groups (Table 1).

The total MRS score was 22,97±2,71 in Vitamin D deficiency group and significantly higher than others (p=0,001) (Table 1). Besides that, in deficiency group, somatic, psyhcological and urogenital subscale scores were higher than other groups (p=0,012, p=0,007 and p=0,036, respectively)(Table 1). According to post-hoc analysis, psychological scores of the deficiency group (8,02±2,87 and 9,42±5,15) were significantly different from the other groups. Urogenital subcale and total scores of deficiency group (n=42) were similar to insufficiency group (n=38), significantly higher than sufficieny group (Table 1).

Anxiety, physical and mental exhaution, sexual problems and dryness of vagina scores of patients were similar between groups. Besides that, there were significantly differences among groups according to the remaining parameters of MRS questionnaire (Table 2).

Evaluation of the correlations among independent variables revealed a negative relationship between vitamin D level and MRS scores (Table 3).

The ROC curve for 25-OH vitamin D to detect the severe scores of MRS in women with sufficient vitamin D level in Figure 1. The area under the ROC curve was 0,876 (95% CI, 0,702-1,00, p=0.003) for vitamin D. The cut-off value of serum vitamin D level was 25,31 ng/ml, at which the sensitivity was 85,7% and specificity was 87%.

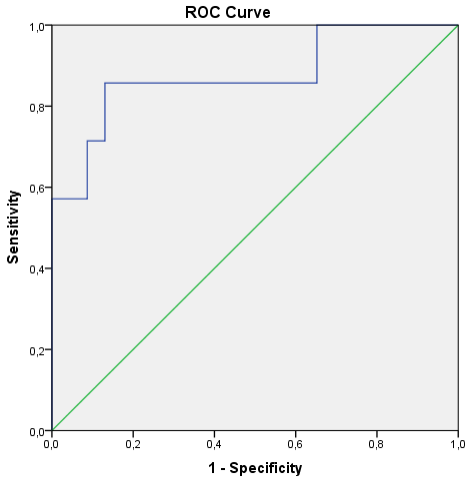

Figure 1. Receiver operating characteristic (ROC) curve for serum 25-OH Vitamin D level The estimate of the area under curve (AUC) and its 95% confidence interval is shown. Cut-off value of vitamin D was 25,31 (sensitivity 85,7 % and specificity 87%). AUC, area under curve. $p < 0.05$ was considered significant .

Table 1. Demographic, laboratory characteristics and rating scores of the subjects among groups.

	25-OH vitamin D levels			
	≥20 ng/mL n=30	12-19 ng/mL n=38	<12 ng/mL n=42	*p*
Age (y)	53,20±4,98	53,50±4,43	54,71±3,94	NS
BMI (kg/m^2)	30,00±5,00	30,04±4,27	30,66±4,84	NS
Time since menopause (y)	5,50±4,03	6,38±5,68	6,98±4,99	NS
Serum FSH (mIU/mL)	65,00±23,78	62,29±19,82	63,28±20,74	NS
Serum E_2 (pg/mL)	18,47±15,99	20,09±12,18	16,56±10,90	NS
Serum Ca (mg/dL)	9,76±0,35	9,63±0,42	9,62±0,40	NS
Somatic subscale score	4,33±2,42	6,39±2,94	8,02±2,87	<0,001
Psychological subscale score	6,46±3,10	7,07±3,73	9,42±5,15*	0,007
Urogenital subscale score	3,90±2,02	5,23±3,09	5,52±2,71**	0,036
Total MRS score	14,73±5,93	18,71±7,55	22,97±2,71**	<0,001

y: years, BMI: body mass index, kg: kilogram, m:meter, FSH: Follicule stimulating hormone, E2: estradiol, Ca: calcium, MRS: Menopause reting scale, NS: non-significant.

*Statistical difference arises from group 1 and 2.

** Statistical difference arises from group 1.

p <0.05 was considered significant.

Table 2. Results of Menopause Rating Scale parameters among serum 25-OH Vitamin D levels.

Parameters	25-OH vitamin D levels			
	≥20 ng/mL n=30	12-19 ng/mL n=38	<12 ng/mL n=42	*p*
Hot flushes	1,26±1,11	1,86±0,99	2,30±1,02	<0,001
Heart discomfort	0,40±0,56	1,00±0,95	1,50±1,01	<0,001
Sleep problems	1,20±1,09	1,34±1,23	1,83±1,05	0,043
Depressive mood	1,53±1,04	1,57±1,13	2,30±1,07	0,003
Irritability	1,53±1,07	1,76±1,19	2,38±1,16	0,006
Anxiety	1,36±1,03	1,81±1,13	2,83±4,88	NS
Physical and mental exhaustion	2,03±1,21	1,92±1,26	1,90±1,07	NS
Sexual problems	1,56±0,93	1,97±1,28	1,73±1,38	NS
Bladder problems	1,10±1,09	1,60±1,28	2,09±1,22	0,040
Dryness of vagina	1,23±1,04	1,65±1,32	1,69±1,17	NS
Joint and muscular discomfort	1,46±1,10	2,18±1,20	2,38±1,24	0,006

NS: non-significant *p* <0.05 was considered significant.

Table 3. Correlations among variables.

	r	p
Vitamin D- SSS	-0,469	<0,001
Vitamin D- PSS	-0,295	0,002
Vitamin D- USS	-0,251	0,008
Vitamin D- Total MRSS	-0,432	<0,001

SSS: Somatic subscale score, PSS:Psycholocigal subscale score, USS: Urogenital subscale score, MRSS: Menopause rating scale score, r: correlation coefficient. *p* <0.05 was considered significant.

Discussion

In the present study, we demonstrated a relationship between serum vitamin D levels and menopause-related symptoms in postmenopausal population. We were able to show a significant negative correlation between vitamin D levels and MRS total/subscale scores. Our results also represented that symptoms such as hot flushes, heart discomfort, depressive mood, irritability, bladder problems and joint and muscular discomfort in postmenopausal period were significantly severe in women with vitamin D deficiency. We also calculated a 25-OH vitamin D cut-off for women complaining from menopause-related symptoms despite having sufficient vitamin D levels.

In a study reported in 2014, LeBlanc et al. could not find an association between menopausal symptoms and serum vitamin D levels (13). In their study, they identified some menopausal symptoms, then participants rated these symptoms according to intensity of the symptom. A total score was defined as the total number of symptoms of any severity. So unlike ours, any validated questionnaire were not used in that study. Besides that, their subjects were older (66 years) and the mean time since menopause in the mentioned study was about ten years higher than our study. The reason they failed to report any association between vitamin D levels and menopausal symptoms could be explained by the high number of women with menopause duration of more than ten years.

Vitamin D taken in diet or synthesized in the skin is biologically inactive and requires enzymatic conversion to active metabolites. It was shown that estrogen plays a role in the increase of vitamin D activating enzyme (14). Therefore, it could be thought that the decrease of estrogen levels in postmenopausal period might worsen the symptoms of subclinical vitamin D deficiency such as neuropsychiatric symptoms. There are few data evaluating the neuroprotective role of vitamin D. An experimental study investigating the effect of menopause on behavioral status found that menopause could cause an impairment in memory (15). Siebert et al showed that vitamin D supplementation reverses the hippocampal cytoskeletal changes caused by ovariectomy, in vivo. In another animal

testing, increasing calcidiol levels by vitamin D supplementation in ovariectomized rats was reported to reduce the hippocampal inflammatory mediators such as nuclear factor-kappa B and interleukin-6(16). Besides the hippocampal effects, cholecalciferol was concluded as an anxiolytic agent in ovariectomized rats (17). It could be seen that these data support the psychological outcome in our study. Depressive mood and irritability scores of the subjects were significantly higher in the deficiency group. Furthermore, anxiety score was also higher in this group although it was not statistically significant. Evaluating the total psychiatric score, a significant difference had been already encountered in the deficiency group. Similarly, in a report with a high patient population discoursing vitamin D and symptoms in menopause, it was mentioned that 25-OH vitamin D levels were low and depression scores were high in the postmenopausal period (18).

Although psychological score differed significantly among patient groups, this score was severe, higher than six, in all groups. The severity of this score might be due to our patients' high BMIs. In a cross-sectional study from Turkey using MRS, Tan et al. reported that BMI higher than 30 kg/m2 was signifacntly associated with higher depressive mood score (19).

Another finding in our study was the high scores of urogenital subscale in the insufficiency and deficiency groups. In this subscale especially bladder problems section score was noticed as significantly high. Considering the literature, it was seen that low urinary tract symptoms could be associated with serum vitamin D levels. Because pelvic floor muscle strength might be affected by low vitamin d levels. In a study including both patients in pre and postmenopausal periods, pelvic floor muscle strength was calculated lower in postmenopausal patients with vitamin D levels lower than 20 ng/mL (20). In the same study, it was reported that urinary incontinence score was higher in women with vitamin D deficiency, but they could not find statistical difference (20). Unlike that study, our results about the vitamin D levels and urinary system symptoms were statistically significant. Similiarly, Foti et al concluded that prevelance of low urinary tract symptoms was significantly higher in women with low vitamin D levels comparison to those with normal levels (8). Moreover, the siginificant improvement of lower urinary symptoms in postmenopausal patients treated with high dose vitamin D for one year was documented in a randomized controlled trial published in 2017 (21).

Somatic symptoms like hot flashes could often be challenging for menopausal women. Regardless of vitamin D levels, most of the women complain about these symptoms (22). In our study, we found a negative correlation between somatic scores and vitamin D levels. Vitamin D was described to prevent seratonin depletion in rats (6). Seratonin was known as a neurotransmitter playing role in thermoregulation, a decline seratonin levels might cause hot flashes(7). In this context, high levels of vitamin D might protect against somatic symptoms, especially hot flashes, during menopause. In addition, in a recent study, it was mentioned that menopausal symptoms are less common in women with normal vitamin D levels than in women with vitamin D deficiency (23).

In this study, we hoped to clarify whether vitamin D deficiency caused spesific menopause-related symptoms. In this regard, we used a validated questionnaire-MRS, tried to minimized external factor that could affect scale rates by excluding patients with any other comorbidities. Our patient groups were similar among demographic and hormonal characteristics. Besides that, we presented a cut-off 25-OH vitamin D level for women suffering from menopause releated symptoms with sufficient levels of vitamin D. Unlike the literature, time since menopause in our patients was short. Apart from these strengths, the study had limitations. Our patient population consisted of one geographic area. We could not able to evaluate the parathormone levels of the patients and we could not distinguish whether menopause-related symptoms associated with vitamin D deficieny would change when treated with supplementation.

In conclusion, low levels of vitamin D in menopausal period might aggravate menopause-related symptoms. It could be considered that menopausal women with a high intensity of symptoms might benefit from vitamin D supplementation. Further prospective studies are needed to clearly enlighten this complex and multicomponent relationship.

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References

1.Roberts H, Hickey M. Managing the menopause: An update. Maturitas. 2016, 86: 53-58.

2.Proceedings from the NIH State-of-the-Science Conference on Management of Menopause-Related Symptoms, March 21-23, 2005, Bethesda, Maryland, USA. In: The American journal of medicine. 2005. 142.12_Part_1: 1003-1013

3.Conde DM, Pinto-Neto AM, Santos-Sá D, Costa-Paiva L, Martinez EZ. Factors associated with quality of life in a cohort of postmenopausal women. Gynecol Endocrinol. 2006; 22.8: 441-446.

4.Bouillon R, Carmeliet G, Verlinden L,et al. Vitamin D and human health: lessons from vitamin D receptor null mice. Endocr Rev. 2008 Oct;29(6):726-76.

5.Cyboran Katarzyna, Kuc Monika, Lis Jakub, Machaj Damian, Polak Jakub. The benefits of vitamin D3 supplementationfor menopausal women - literature review. Journal of Education, Health and Sport. 2021;11(6):47-51.

6.Cass WA, Smith MP, Peters LE. Calcitriol protects against the dopamine- and serotonin-depleting effects of neurotoxic doses of methamphetamine. In: Annals of the New York Academy of Sciences. 2006, 1074.1: 261-271.

7.Rossmanith WG, Ruebberdt W. What causes hot flushes? The neuroendocrine origin of vasomotor symptoms in the menopause. Gynecol Endocrinol Off J Int Soc Gynecol Endocrinol. 2009 May;25(5):303–14.

8.Foti D, Greco M, Cantiello F, et al. Hypovitaminosis D and Low Urinary Tract Symptoms in a Female Population. Eur J Inflamm [Internet]. 2014 May 1;12(2):365–72.

9.Arvold DS, Odean MJ, Dornfeld MP, et al. Corelation of symptoms with vitamin D deficiency and symptom response to cholecalciferol treatment: A randomized controlled trial. Endocr Pract. 2009; 15(3), 203-212.

10.Metintas S, Arikan I, Kalyoncu C, Ozalp S. Menopause Rating Scale as a screening tool in rural Turkey. Rural Remote Health. 2010 10(1), 27-37.

11.Potthoff P, Heinemann LAJ, Schneider HPG, Rosemeier HP, Hauser GA. Menopause-Rating-Skala (MRS II): Methodische standardisierung in der deutschen bevolkerung. Zentralbl Gynakol. 2000; 122: 280-6.

12.Giustina A, Adler RA, Binkley N, et al. Controversies in Vitamin D: Summary Statement from an International Conference. J Clin Endocrinol Metab. 2019, 104.2: 234-240.

13.LeBlanc ES, Desai M, Perrin N, et al. Vitamin D levels and menopause-related symptoms. Menopause. 2014; 21(11), 1197.

14.Buchanan JR, Santen R, Cauffman S, Cavaliere A, Greer RB. The effect of endogenous estrogen fluctuation on metabolism of 25-hydroxyvitamin D. Calcif Tissue Int. 1986; 39.3: 139-144.

15.Siebert C, Pierozan P, Kolling J, et al. Vitamin D(3) Reverses the Hippocampal Cytoskeleton Imbalance But Not Memory Deficits Caused by Ovariectomy in Adult Wistar Rats. Neuromolecular Med. 2017 Sep;19(2–3):345–56.

16.Siebert C, Bertó CG, Ferreira FS,et al. Vitamin D partially reverses the increase in p-NF-κB/p65 immunocontent and interleukin-6 levels, but not in acetylcholinesterase activity in hippocampus of adult female ovariectomized rats. Int J Dev Neurosci. 2018; 71: 122-129.

17.Fedotova JO. Vitamin D (3) treatment differentially affects anxiety-like behavior in the old ovariectomized female rats and old ovariectomized female rats treated with low dose of 17β-estradiol. BMC Med Genet. 2019 Apr;20(Suppl 1):49.

18.Bener A, Saleh N. Low vitamin D, and bone mineral density with depressive symptoms burden in menopausal and postmenopausal women. J Midlife Health. 2015; 6.3: 108.

19.Tan MN, Kartal M, Guldal D. The effect of physical activity and body mass index on menopausal symptoms in Turkish women: A cross-sectional study in primary care. BMC Womens Health. 2014; 14.1: 1-9.

20.Aydogmus H, Demirdal US. Vitamin D Deficiency and Lower Urinary Tract Symptoms in Women. Eur J Obstet Gynecol Reprod Biol. 2018; 228: 48-52.

21.Oberg J, Verelst M, Jorde R, Cashman K, Grimnes G. High dose vitamin D may improve lower urinary tract symptoms in postmenopausal women. J Steroid Biochem Mol Biol. 2017; 173: 28-32.

22.Simon JA, Reape KZ. Understanding the menopausal experiences of professional women. Menopause. 2009; 16.1: 73-76.

23.Askin M, Koc EM, Soyoz M, Aksun S, Aydogmus S, Sozmen K. Relationship between postmenopausal vitamin D level, menopausal symptoms and sexual functions. J Coll Physicians Surg Pak 2019; 29(9):823-7

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ORIGINAL ARTICLE

Factors Associated with Acetabular Degeneration and Protrusion in Bipolar Hip Hemiarthroplasty

Bipolar Kalça Hemiartroplastisinde Asetabuler Dejenerasyon ve Protrüzyon ile İlişkili Faktörler

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ABSTRACT

Purpose: This study aims to investigate the effect of some factors such as the diameter of bipolar prosthetic heads, body mass index (BMI), age, gender, bone mineral density (BMD) and leg length discrepancy (LLD) on the acetabular protrusion in elderly patients who had hip bipolar hemiarthroplasty (BHA) after femoral neck fractures.
Methods: The study included a total of 209 patients with a mean age of 77.4 ± 6.0 years who underwent BHA. The difference between the femoral head diameter of the patients and the diameter of the bipolar prosthetic head was divided into two groups, ranging from 0 to -2 mm (same and 1,2 mm small size) . Acetabular enlargement and cartilage degeneration were followed by standard AP pelvis radiographs and clinical outcomes were evaluated by the Harris Hip Score (HHS) after surgery and during 5 years of follow-up.
Results: During the 5-year follow-up, while HHS values decreased, acetabular diameter increased. Acetabular protrusion developed in 21 (10%) patients, acetabular revision surgery was performed for 36 (17%) patients, the difference between native femoral head diameter and prosthetic head diameter was significantly higher in these groups, as was mean LLD (p = 0.0001). Mean T scores obtained with BMD were lower in these groups (p = 0.0001).
Conclusion: It is safer and more reliable to use a bipolar prosthetic head the same size as the patient's native femoral head in BHA. When considering the acetabular protrusion and revision surgery rate in this study, small-size bipolar prosthetic head implantation is not recommended and may cause devastating complications.

Keywords: Bipolar hip hemiarthroplasty, Acetabular protrusion, Revision surgery, Femoral neck fracture

ÖZ

Amaç: Çalışmanın amacı, femur boyun kırığı sonrasında bipolar kalça hemiartroplastisi uygulanan yaşlı hastalarda bipolar protez başlarının çapı, vücut kitle indeksi, yaş, cinsiyet, kemik mineral yoğunluğu ve bacak uzunluk farkı gibi bazı faktörlerin asetabular protrüzyon üzerine etkisini araştırmaktır.
Gereç ve Yöntem: Çalışmaya bipolar kalça hemiartroplastisi uygulanan toplam 209 hasta dahil edildi. Hastaların ortalama yaşı 77.4 ± 6.0 yıldı. Hastaların femur başı çapı ile bipolar protez başı çapı arasındaki fark 0 ile -2 mm 2 gruba (aynı çap ve 1 veya 2 mm küçük çap) ayrıldı. Asetabular genişleme ve kıkırdak dejenerasyonunu standart AP pelvis radyografileri ile değerlendirildi. Takip süresince klinik sonuçlar Harris Hip Skor'u (HHS) ile değerlendirildi.
Bulgular: Beş yıllık izlemde HHS değerleri düşerken asetabulum çapı arttı. 21 (%10) hastada asetabuler protrüzyon gelişti, 36 (%17) hastaya asetabular revizyon cerrahisi yapıldı. Bu gruplarda doğal femur başı çapı ile protez baş çapı arasındaki fark ve bacak uzunluk farkı anlamlı olarak daha yüksekti. (p = 0.0001) . Kemik mineral yoğunluğu ile elde edilen ortalama T skorları bu gruplarda daha düşüktü (p = 0.0001).
Sonuç: Bipolar kalça artroplastisi'nde hastanın doğal femur başı ile aynı boyutta bipolar protez başı kullanmak daha güvenilirdir. Bu çalışmada asetabular protrüzyon ve revizyon cerrahi oranı göz önüne alındığında, küçük boyutlu bipolar protez baş implantasyonu önerilmemektedir ve yıkıcı komplikasyonlara neden olabilir.

Anahtar Kelimeler: bipolar kalça hemiarthroplastisi,, asetabular protrusyon, revizyon cerrahisi, femur boyun kırığı

Introduction

Bipolar hip hemiarthroplasty (BHA) is a common procedure in the treatment of hip fractures in elderly patients [1,2]. For several decades, bipolar prostheses replacement have been the most widely used implants with the less acetabular wear rate and lower dislocation rate compared to unipolar prostheses, which is out-of-date today [3]. Despite favorable outcomes in mid-term follow-up studies with BHA implants, acetabular protrusion of the bipolar cup as a result of excessive acetabular cartilage degeneration in the long-term decrease the success rates [4,5]. This is mostly attributed to excessive pressure due to the incongruence between the metallic bipolar head and the acetabulum. Besides, the bipolar head functions as a unipolar head after a few months, which may lead to higher acetabular degeneration and protrusion [6,7].

It is postulated that the cartilage damage is associated with the interaction between the acetabular cartilage and the artificial metal cup [4]. Therefore, the bipolar head size should be the same in diameter as the patient's native femoral head, but this may not be practically possible in some situations where the native head size is measured as odd numbers intraoperatively. Native femoral heads cannot be perfectly replaced with currently available implants as the native head

is not a spherical structure [8]. Prosthetic designs are spherical and produced in increments ranging from 1 to 2 mm. Therefore, in some cases, the size of the bipolar prosthetic head determined by intraoperative femoral head measurement may not be suitable for the acetabulum and a smaller prosthetic head may be preferred. Since some prostheses are produced at 2 mm intervals, the appropriate head diameter cannot be used and a smaller one may have to be used. On the other hand, in some cases, a smaller sized head is chosen to facilitate intraoperative reduction of the hip joint.

Regarding the arc of motion provided by the bipolar head, its size should be as close as possible to the extracted native head to avoid further cartilage degeneration in the acetabular cavity. Otherwise, the degenerative process can lead to linear and volumetric acetabular erosion, which may result in intrapelvic migration of the implants. Patient-related factors (age, gender, body mass index (BMI), bone mineral density (BMD) and surgical technique related factors may cause and accelerate acetabular protrusion.

Our aim in this study is to evaluate the effect of consistency between the bipolar prosthetic head diameter and the patient's femoral head diameter on acetabular wear. We also investigated the effects of leg discrepancy, osteoporosis, and gender on acetabular erosion.

Methods

After ethical approval, we retrospectively reviewed a series of 362 patients (362 hips) who underwent primary BHA for the treatment of femur neck fractures between January 2009 and March 2016. Patients aged between seventy and ninety-five years at the time of surgery, BMI < 35, and mobilized without support after surgery were included in the study. The exclusion criteria of the study were the patients who were not in the specified age range, those who were operated for pathological fractures, those who had osteoarthritic changes in the hip joint before surgery, those who had revision surgery for reasons other than acetabular erosion, and those with a follow-up period of less than 3 years. Thirteen patients with missing data and 140 patients who died before we conducted this study were excluded. Thus, a total of 209 patients (140 female, 69 male 209) were enrolled in the study. Preoperative height and weight of the patients were recorded, and BMI values were calculated as $kg/m^{2.}$

Surgical technique

The bipolar hip prosthesis used in this study were Biomet's Echo™ Hip System (UK). All surgeries were done by a single surgeon via a posterior approach with cemented technique. During the operation, after the femoral head of the patients was excised, the diameter of the bipolar prosthetic head was determined by measuring the diameter of the femoral head with a caliper at the head equator. The diameter of the bipolar prosthetic heads ranged between 42 and 58 mm. The implanted bipolar prosthetic heads were of the same diameters as the femoral heads in 127 hips, 1 mm smaller (the next smaller size) in 53 hips, 2 mm smaller in 29 hips. No bipolar prosthetic head larger than the measured femoral head diameter was used for any of the patients. The median duration of surgery was 38 minutes (range: 30-58 minutes).

Rehabilitation

Standard antibiotic prophylaxis (intravenous 1 gr cefazolin) and anticoagulants (subcutaneous enoxaparin sodium 4,000 IU (40 mg) were administered and compression stockings were used to prevent deep vein thrombosis. Weight-bearing was allowed as tolerated on the postoperative first day.

Radiographic evaluation

Radiographic assessment was performed on a standard anteroposterior (AP) view of the pelvis immediately after surgery by a computer program and annually. In these radiographs, three points were marked: the superior outer margin of the acetabulum, the inferior lower margin of the acetabulum, and the acetabular bony margin (Fig. 1) [9]. The distance between the superior outer margin and the inferior inner margin of the acetabulum was measured as the acetabulum diameter. Finally, the acetabular articular cartilage degeneration was calculated from the vertical distance between the acetabular bony margin and the acetabulum diameter [9]. Acetabular protrusion was defined as the crossing of the bipolar prosthetic head over Kohler's line. The kohler's line, also known as the ilioischial line, runs along the lateral border of the obturator foramen to the medial border of the iliac wing. The kohler's line passes through the acetabular teardrop in normal hip joints.

In the first postoperative year of follow-up, t scores measured by BMD were recorded for all patients. Dual-energy X-ray absorptiometry (DEXA) scanning was used to evaluate patients' BMD scores.

Clinical evaluation

Clinical evaluation included the Harris Hip Score (HHS) and complications. Functional assessment was performed via the HHS in the third month, the first year, the third year, and the fifth year after surgery.

The patients were divided into two groups as those with (n=21) and without (n=188) acetabular protrusion, those with (n=36) and without (n=173) revision surgery, those with the same size bipolar prosthetic head (n=127) and those with the small size (1 and 2 mm) bipolar prosthetic head (n=82) use. The indications of revision surgery were acetabular protrusion for 16 patients, acetabular degeneration and worsening of HHS for 20 patients. Five patients with protrusion have rejected revision surgery because of their bad general

medical conditions. Demographic characteristics of these patients, BMI and BMD values, leg length discrepancy (LLD) (measured from anterior superior iliac spine to medial malleolus clinically), and HHS scores at 5-year follow-up, acetabular diameter and acetabular degeneration measured annually for 5 years, the difference in diameter between the femoral head and the bipolar prosthetic head were evaluated.

Statistical analysis

Statistical analysis was performed using the SPSS statistical package (Version 25.0, IBM Corp., Armonk, NY, USA). If continuous variables were normal, they were described as mean ± standard deviation ($p > 0.05$ in Kolmogorov-Smirnov or Shapiro-Wilk tests ($n < 30$)), and if the continuous variables were not normal, they were described as medians. Comparisons between groups were applied using the Student t-test for normally distributed data and the Mann-Whitney U test for the data not normally distributed. Repeated measures data were analyzed with repeated-measures ANOVA. Categorical variables were analyzed between the groups by using the chi-square test or Fisher exact test. Correlations between variables were tested by Pearson's correlation coefficient. Values of $p < 0.05$ were considered statistically significant.

Results

The demographic data of all patients, postoperative LLD, BMD values, the patient's mean femoral head diameter, the head diameter of the bipolar prosthesis used, and the diameter difference between them are shown in Table 1. The mean age of the patients was 77.4 ± 6.0 years and the average LLD was 0.8 ± 1.2 cm. Since the patients were from the elderly population, mean T-score values as measured by BMD indicated that the patients were osteoporotic. Also, a mean difference of -0.6 ± 0.9 mm was detected between the patients' femoral head diameter and the head diameter of the prosthesis used.

Table 2 presents the change over time in the HHS values used in functional evaluation in the postoperative follow-up of the patients and acetabular diameter values measured radiographically. In patients with greater diameter difference between the femoral head and bipolar prosthetic head, the HHS scores decreased faster and the acetabular diameter increased more rapidly in the 5-year follow-up period (Fig. 2,3).

When the mean follow-up period of 5 years is taken into account, a statistically significant decrease in HHS values over time was detected in those who used small size compared to those who used the same size. (Table 3) The diameter of the acetabulum was measured annually radiographically during the first 5-year follow-up period, and a significant increase was seen in the small size used in all measurements except the first postoperative measurement compared to the same size measurements. (Table 3) The mean degeneration of the acetabular cartilage was 0.6 ± 0.03 mm/year in all patients, 2.94 ± 0.21 mm/year in patients with the acetabular protrusion, and 1.45 ± 0.09 mm/year in patients with smaller cups. Patients undergoing acetabular revision surgery were not included when calculating HHS, acetabulum diameter, and acetabular cartilage measurements.

Protrusion group: Comparison of the characteristics of the patients with and without acetabular protrusion during postoperative follow-up is shown in Table 4. The preoperative and postoperative LLD and the difference between femoral head diameter and bipolar prosthetic head diameter were significantly higher in the acetabular protrusion group ($p = 0.001$) (Table 4). Also, the mean T score measured by BMD was lower in the protrusion group than the other ($p = 0.001$). In addition, 20 of the 21 patients with acetabular protrusion were female ($p = 0.003$). (Fig. 4) On the other hand, there was no statistically significant difference between parameters such as age and BMI.

Revision group: In patients who underwent acetabular revision surgery, the difference between the preoperative and postoperative leg length and the difference between femoral head diameter and bipolar prosthetic head diameter was higher, as in patients with the acetabular protrusion, and this was statistically significant ($p = 0.001$) (Table 5). Likewise, it was noticed that the mean T score values measured by BMD were lower in the group undergoing revision surgery ($p = 0.001$). Again, in correlation with patients with the acetabular protrusion, more revision surgery was required in the female population ($p = 0.001$). No significant difference was found in terms of parameters such as age and BMI.

Table 1. Demographic characteristics of the patients, leg length change, BMD values, femoral head diameter of the patients, the diameter of the bipolar prosthetic head and the difference between them

	n	Mean ± SD	Median (Min-Max)
Age (year)	209	77,4 ± 6,0	76 (72-94)
BMI (kg/m^2)	209	26,4 ± 3,2	25,9 (19,3-34,6)
LLD (cm)	209	0,8 ± 1,2	1 ((-2)-3)
BMD (T score)	209	-2,0 ± 1,0	-2,1 ((-3,5)-1)
Patient's femoral head diameter (mm)	209	50,2 ± 3,7	49 (44-60)
Bipolar prosthetic head diameter (mm)	209	49,5 ± 3,8	48 (42-58)
Diameter difference (mm)	209	-0.6±0.9	0 ((0)-2)

n: Number of patients, SD: Standard deviation BMI: Body mass index, LLD: Leg length discrepancy, BMD: Bone mineral density

Table 2. The change of HHS scores and acetabular diameters of the patients by years during the 5-year follow-up period.

HHS		n	Mean ± SD	Median (Min-Max)	p
	3. Month	209	84,6 ± 3,5	84 (72,1-91,5)	0,003*
	1. Year	209	82,6 ± 4,6	82 (65,5-93,5)	0,0001*
	3. Year	205	81,8 ± 6,5	80 (54,9-90,5)	0,0001*
	5. Year	173	80,8 ± 3,8	82 (62-90)	0,030*
Acetabulum diameter (mm)					
	0. Year	209	51,5 ± 4,0	51 (45-62)	0,134
	1. Year	209	52,1 ± 3,8	52 (45-62)	0,013*
	2. Year	209	53,1 ± 3,9	52 (46-64)	0,0001*
	3. Year	205	53,9 ± 3,9	53 (47-65)	0,005*
	4. Year	196	54,9 ± 4,0	54 (48-69)	0,0001*
	5. Year	173	55,5 ± 4,0	55 (49-68)	0,0001*

HHS: Harris hip score, n: Number of patients, SD: Standard deviation, *: Statistically significant

Table 3 The change of acetabular diameters of the patients (same and smaller size) by years during the 5-year follow-up period.

Acetabular Diameters	Same Size(0) (n=127)	Smaller Size (-1,-2) (n=82)	p
0. Year	51,1±3,8	51,9±4,2	0,179
1. Year	51,6±3,6	52,9±4,0	**0,022***
2. Year	52,3±3,6	54,2±4,0	**0,0001***
3. Year	52,9±3,6	55,4±4,0	**0,0001***
4. Year	53,8±3,5	56,6±4,2	**0,0001***
5. Year	54,6±3,4	57,4±4,5	**0,0001***
HHS			
3. Month	85,0±3,5	83,9±3,2	**0,022***
1. Year	84,2±3,5	80,4±5,2	**0,0001***
3. Year	83,2±3,7	77,1±7,9	**0,0001***
5. Year	82,2±3,3	80,6±4,7	**0,010***

HHS: Harris hip score, n: Number of patients, *: Statistically significant

Table 4. Distribution of demographic and clinical characteristics of patients with and without acetabular protrusion.

	Non acetabular protruding (Mean ± SD)	Acetabular protruding (Mean ± SD)	p
n (number of patients)	188	21	
Age (year)	77.2 ± 5.9	79.5 ± 6.8	0,093
BMI (kg/m^2)	26.5 ± 3.1	26.3 ± 3.4	0,803
LLD (cm)	0.1 ± 1.7	2.3 ± 1.9	0,0001*
BMD (T score)	-1.1 ± 1.3	-2.9 ± 0.8	0,0001*
Diameter difference between femoral head and bipolar prosthetic head (mm)	0.1 ± 1.4	2.2 ± 2.1	0,0001*
Gender (n and %)			
Male	68 (36.2%)	1 (4,8%)	0,003*
Female	120 (63,8%)	20 (95,2%)	

SD: Standard deviation, n: Number of patients, BMI: Body mass index, LLD: Leg length discrepancy, BMD: Bone mineral density, *: Statistically significant

Table 5. Distribution of demographic and clinical characteristics of patients who had and did not undergo acetabular revision surgery.

	No revision surgery (Mean ± SD)	Revision surgery (Mean ± SD)	p
n (number of patients)	173	36	
Age (year)	77.4 ± 5.9	77.4 ± 6.3	0,959
BMI (kg/m^2)	26.4 ± 3.2	26.4 ± 2.9	0,976
LLD (cm)	0.3 ± 2.3	2.4 ± 1.4	0,0001*
BMD (T score)	-1.9 ± 1.5	-2.9 ± 0.9	0,0001*
Diameter difference between femoral head and bipolar prosthetic head (mm)	0.2 ± 0.9	1.7 ± 1.2	0,0001*
Gender (n and %)			
Male	66 (38,2%)	3 (8,3%)	0,0001*
Female	107 (61,8%)	33 (91,7%)	

SD: Standard deviation, n: Number of patients, BMI: Body mass index, LLD: Leg length discrepancy, BMD: Bone mineral density, *: Statistically significant

Revision survival analysis graph of patients who underwent hemiarthroplasty is shown in figure 5. Revision was applied to 63.9% (n=23) patients at 5 years, 25% (n=9) at 4 years, and 11.1% (n=4) at 3 years.

An 85-year-old patient had sciatic nerve palsy after surgery; however, it resolved spontaneously at the

postoperative sixth month. Prosthesis dislocation occurred in 8 patients within the first month after surgery due to a simple fall. All patients were treated with closed reduction under anesthesia and mobilization restrictions for 3 weeks. No recurrent dislocation was observed in any of them. There were no deep vein thromboses or heterotopic ossifications during follow-up. Infection developed in five patients during follow-up. While intravenous antibiotics (IV teicoplanin) were sufficient in the treatment of three patients, the treatment of two patients who developed an infection in the acute period were completed with wound debridement, irrigation, and intravenous antibiotics (IV teicoplanin and IV sulperazone).

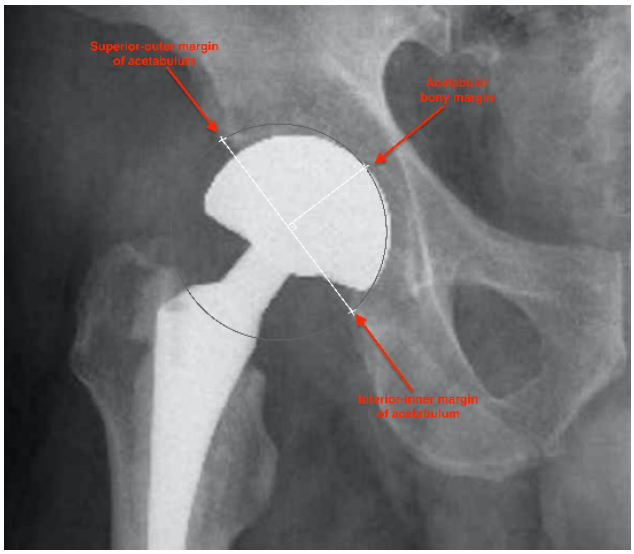

Figure 1. Measurement of acetabular articular cartilage degeneration on an AP pelvis radiograph. First, three points are marked: the superior outer margin of the acetabulum, the inferior inner margin of the acetabulum, and the acetabular bony margin. A circle is drawn through these three margins. The distance between the superior outer margin and the inferior inner margin of the acetabulum is measured as the acetabulum diameter. Finally, the estimated acetabular erosion is calculated by measuring the vertical distance of the acetabular bony margin to the acetabulum diameter

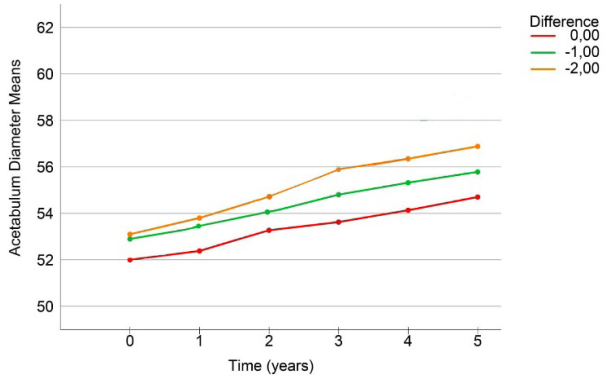

Figure 2. The mean acetabular diameter changes in the 5-year follow-up of the patients are shown in this graphic. As the diameter difference between the native femoral head and bipolar prosthetic head increases, acetabular erosion and enlargement progress faster

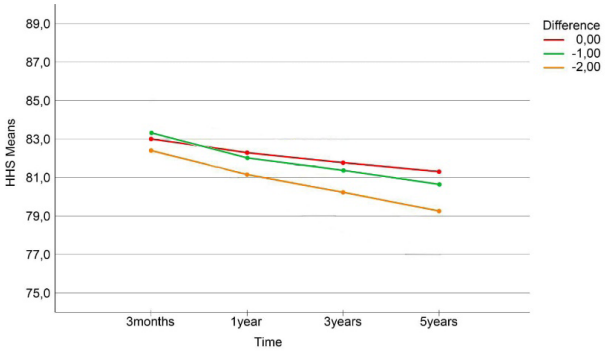

Figure 3. The mean HHS changes in the 5-year follow-up of the patients are shown in this graphic. As the diameter difference between the native femoral head and bipolar prosthetic head increases, the decrease in HHS values is greater

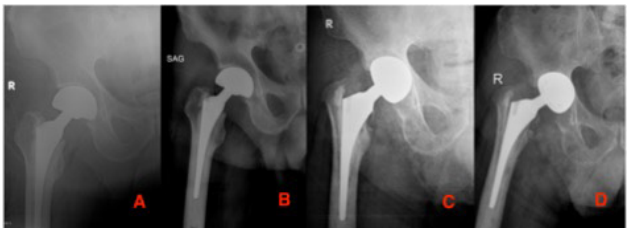

Figure 4. A 70-year-old male patient underwent bipolar hemiarthroplasty for right femoral neck fracture (A). It was seen that acetabular erosion started at the 6 month of follow-up (B). On the 20-month follow-up radiograph, advanced erosion was observed (C), and on the 26-month radiograph, protrusion had occurred (D)

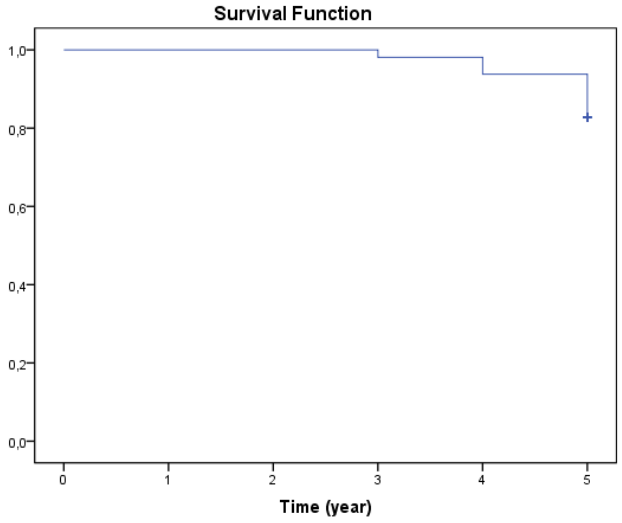

Figure 5. Revision survival analysis graph of patients who underwent bipolar hemiarthroplasty by years

Discussion

Acetabular erosion after BHA has been investigated in various studies because it has a great negative effect on health-related quality of life even in elderly patients [10]. Kurrat et al. [11] reported that the mean thickness of the acetabular cartilage was 1.0-3.3 mm.

In another study, Moon et al. [9] reported that mean linear and volumetric degeneration rates caused by BHA were 0.23 ± 0.107 mm/year and 114 ± 47.2 mm3/year, respectively. Considering that the patient's acetabular cartilage experiences millions of loading cycles during the period of implant use, subsequent acetabular cartilage wear due to the friction between the metal and cartilage increases, which leads to osteolysis and the protrusion of the metallic head, so it is believed that the acetabular cartilage thickness will have been fully lost at approximately 7-10 years after surgery and the risk of protrusion will increase [12,13]. In our study, acetabular diameters of the patients were measured regularly every year and it was found that the acetabulum diameter increased significantly. The presence of acetabular enlargement proves that the bipolar prosthetic head causes wear on the acetabular cartilage.

Many studies have concluded that the progression of acetabular cartilage degeneration is correlated directly with time after BHA surgery, and the acetabular protrusion is a known late complication following BHA. Rubio et al. [14] reported an acetabular erosion rate of 23.6% with uncemented BHA after a mean period of 10 years. Mazen et al. [15] had an erosion rate of 33% with bipolar prostheses during a follow-up period of 3 years. Animal studies about this process also showed abnormal stress delivered to the acetabular surface by the hard bipolar cup that causes the secretion of degenerative enzymes and cartilage erosion [16,17]. In this study, acetabular protrusion developed in 21 (10%) patients during the 5-year follow-up period, and when compared with the literature, we see that the rate of acetabular protrusion development was lower in our patients. Although we have obtained more positive results in this regard compared to the literature, acetabular protrusion remains a possible late complication in elderly patients who undergo BHA surgery due to cartilage degeneration.

One of the main aims of this study was to evaluate the effect of the difference between the patient's femoral head diameter and bipolar prosthetic head diameter on acetabular wear and protrusion. In a study conducted by Schiavi et al. [18], 209 patients who underwent BHA surgery were followed for at least 10 years, acetabular revision rates of bipolar heads smaller than 48 mm 3-fold higher than the revision rates of bigger bipolar heads. The authors stated that a small implant head was a risk factor for acetabular erosion and migration [18]. In this study, we found faster acetabular cartilage degeneration in patients who had smaller bipolar prosthetic cups according to the native femoral head. These findings support the idea that acetabulum degeneration is higher in patients with a prosthetic head smaller than the femoral head excised from the patient and acetabular protrusion occurs subsequently.

In studies investigating the accuracy of head measurement, Harris et al. [19] reported that 1/16-inch undersized femoral heads increased the pressure on the articular cartilage twofold. In two similar studies, Baker et al. [20] emphasized an acetabular erosion rate of 66% with 2-mm increments, while D'Arcy and Devas [21] reported acetabular erosion of 11% with sizing increments of 3.2 mm. None of these authors determined the relation between acetabular protrusion and prosthetic femoral head size. In our study, we found that the difference between the diameter of the patient's femoral head and the diameter of the bipolar prosthetic head used was significantly greater in patients who developed acetabular protrusion and who underwent acetabular revision surgery. Also, the acetabular enlargement increased faster as the diameter difference between the patient's femoral head and bipolar prosthetic head increased over 5 years of follow-up. This is the first study in the literature demonstrating acetabular cartilage loss in a short period due to the incongruency of articulation surfaces following BHA in an elderly population in terms of bipolar prosthetic head size. We think that measuring the femoral head removed from the patient with the correct technique by a caliper and choosing the appropriate bipolar prosthetic head is an important and protective factor in preventing the development of acetabular protrusion and possible revision surgery.

Another aim of our study was to measure the effect of preoperative and postoperative LLD on acetabular protrusion and thus revision surgery. In some cases, surgeons may wish to increase implant stability to prevent dislocation, so they may need to vary the leg length to increase abductor arm tension. Lengthening of the leg increases the tension in the hip joint, causing the bipolar prosthetic head to apply more compression force to the acetabular cartilage and resulting in an increase in acetabular erosion [22]. In our study, while the preoperative and postoperative leg lengths were almost equal in the groups that did not develop acetabular protrusion and did not undergo acetabular revision surgery, a mean increase of 2 cm in postoperative leg length was found in the groups that developed acetabular protrusion and underwent acetabular revision surgery.

The HHS is one of the most preferred scoring systems for evaluating the results after hip surgery and it provides important data in follow-up after BHA surgery [23]. In a report by Moon et al. [9], it was emphasized that higher HHS values are related to slower degeneration rates. In our study, it was seen that HHS values decreased significantly over the years. Furthermore, as the difference in diameter between the patient's femoral head and bipolar prosthetic head increased, we found faster decreases in HHS values over 5 years of follow-up. We think that there was a decrease in HHS values in our patients because the bipolar prosthetic head caused pain and wear in the acetabular cartilage.

Osteoporosis is a disease with loss of trabecular bone and impaired bone quality [24]. The risk of osteoporosis increases with age and postmenopausal estrogen decline in the female population [24]. In

our study, T scores measured by BMD were found to be significantly lower in patients who developed acetabular protrusion and underwent revision surgery compared to the other groups. Besides, it is significant that the female population is at higher risk in terms of acetabular protrusion and revision surgery due to the faster development of osteoporosis at postmenopausal ages. We concluded that the current bone quality of the patients directly affects acetabular protrusion and the results of the surgery.

There are some limitations in our study. First, we performed the measurements on coronal planes; however, the joint motion in bipolar hemiarthroplasty should be considered three-dimensionally. Secondly, the follow-up period was relatively short, and a more extensive follow-up period might influence the results.

Conclusion

In elderly patients undergoing BHA surgery, there is a risk of acetabular erosion in the long term due to the metallic prosthetic head abrading the acetabular cartilage. Patients with bipolar prosthetic heads smaller than the native femoral heads have a higher rate of acetabular cartilage degeneration after BHA. Besides, the LLD and low BMD as in the elderly female population accelerate this protrusion process. While performing BHA surgery, the estimated life expectancy of the patient should be considered in terms of possible complications and revision surgery.

Declarations

Funding: There is no funding source.

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Ethics approval: Ethics committee approval was obtained from our institution.

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References

1. Yang B, Lin X, Yin XM, Wen XZ. Bipolar versus unipolar hemiarthroplasty for displaced femoral neck fractures in the elder patient: a systematic review and meta-analysis of randomized trials. Eur J Orthop Surg Traumatol. 2015;25:425-33.

2. Guyen O. Hemiarthroplasty or total hip arthroplasty in recent femoral neck fractures? Orthop Traumatol Surg Res. 2019 Feb;105(1S):S95-S101.

3. Liu Y, Tao X, Wang P, Zhang Z, Zhang W, Qi Q. Meta-analysis of randomised controlled trials comparing unipolar with bipolar hemiarthroplasty for displaced femoral-neck fractures. Int Orthop. 2014;38:1691–6.

4. Kim YS, Kim YH, Hwang KT, Choi IY. The cartilage degeneration and joint motion of bipolar hemiarthroplasty. Int Orthop. 2012;36:2015-20.

5. Lim JB, Ang CL, Pang HN. Acetabular Prosthetic Protrusio after Bipolar Hemi-Arthroplasty of the Hip: Case Report and Review of the literature. J Orthop Case Rep. 2016;6:28-31.

6. Inngul C, Hedbeck CJ, Blomfeldt R, Lapidus G, Ponzer S, Enocson A. Unipolar hemiarthroplasty versus bipolar hemiarthroplasty in patients with displaced femoral neck fractures: a four-year follow-up of a randomised controlled trial. Int Orthop. 2013;37:2457-64.

7. Ong BC, Maurer SG, Aharonoff GB, Zuckerman JD, Koval KJ. Unipolar versus bipolar hemiarthroplasty: functional outcome after femoral neck fracture at a minimum of thirty-six months of follow-up. J Orthop Trauma. 2002;16:317-22.

8. Kosashvili Y, Backstein D, Safir O, Ran Y, Loebenberg MI, Ziv YB. Hemiarthroplasty of the hip for fracture-what is the appropriate sized femoral head? Injury. 2008;39:232-7.

9. Moon KH, Kang JS, Lee TJ, Lee SH, Choi SW, Won MH. Degeneration of Acetabular Articular Cartilage to Bipolar Hemiarthroplasty. Yonsei Med J. 2008;49:719-24.

10. Söderman P, Malchau H. Is the Harris hip score system useful to study the outcome of total hip replacement? Clin Orthop Relat Res. 2001;384:189-97.

11. Kurrat HJ, Oberländer W. The thickness of the cartilage in the hip joint. J Anat. 1978;126:145-55.

12. Drinker H, Murray WR. The universal proximal femoral endoprosthesis. A short-term comparison with conventional hemi- arthroplasty. J Bone Joint Surg Am. 1979;61:1167-74.

13. Bochner RM, Pellicci PM, Lyden JP. Bipolar hemiarthroplasty for fracture of the femoral neck. Clinical review with special emphasis on prosthetic motion. J Bone Joint Surg Am. 1988;70:1001–10.

14. Rubio I, Bellostas L, Garcia-Rey E. Radiological subsidence and acetabular erosion after tapered uncemented hemiarthroplasty in femoral neck fractures a 10- to 13- year follow-up study. Injury. 2020;51 Suppl 1:S37-41.

15. Mazen S, Julien G, Riad F. Retrospective evaluation of bipolar hip arthroplasty in fractures of the proximal femur. N Am J Med Sci. 2010;2:409–15.

16. Minihane KP, Turner TM, Urban RM, Williams JM, Thonar EJ, Sumner DR. Effect of hip hemiarthroplasty on articular cartilage and bone in a canine model. Clin Orthop Relat Res. 2005;437:157–63.

17. van der Meulen MCH, Beaupré GS, Smith RL, Giddings VL, Allen WA, Athanasiou KA, et al. Factors influencing changes in articular cartilage following hemiarthroplasty in sheep. J Orthop Res. 2002;204:669–75.

18. Schiavi P, Pogliacomi F, Colombo M, Amarossi A, Ceccarelli F, Vaienti E. Acetabular erosion following bipolar hemiarthroplasty: A role for the size of femoral head? Injury. 2018;50 Suppl 4:S21-5.

19. Rushfeldt PD, Mann RW, Harris WH. Improved techniques for measuring in vitro the geometry and pressure distribution in the human acetabulum. II Instrumented endoprosthesis measurement of articular surface pressure distribution. J Biomech. 1981;145:315-23.

20. Baker RP, Squires B, Gargan MF, Bannister GC. Total hip arthroplasty and hemiarthroplasty in mobile, independent patients with a displaced intracapsular fracture of the femoral neck. A randomized, controlled trial. J Bone Joint Surg Am. 2006;88:2583-9.

21. D'Arcy J, Devas M. Treatment of fractures of the femoral neck by replacement with the Thompson prosthesis. J Bone Joint Surg Br. 1976;58:279-86.

22. Athanasiou KA, Agarwal A, Dzida FJ. Comparative study of the intrinsic mechanical properties of the human acetabular and femoral head cartilage. J Orthop Res. 1994;12:340-9.

23. Nilsdotter A, Bremander A. Measures of hip function and symptoms: Harris Hip Score (HHS), Hip Disability and Osteoarthritis Outcome Score (HOOS), Oxford Hip Score (OHS), Lequesne Index of Severity for Osteoarthritis of the Hip (LISOH), and American Academy of Orthopedic Surgeons (AAOS) Hip and Knee Questionnaire. Arthritis Care Res (Hoboken). 2011;63 Suppl 1:S200-7.

24. Lane JM, Russell L, Khan SN. Osteoporosis. Clin Orthop Relat Res. 2000;372:139-50.

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ORIGINAL ARTICLE

Do Body Mass Index, Q Angle, and Pes Planus Affect Walking Age in Children with Down Syndrome and Their Typically Developing Peers?

Down Sendromlu Çocuklarda ve Tipik Gelişime Sahip Akranlarında Vücut Kitle İndeksi, Q Açısı ve Pes Planus Yürüme Yaşını Etkiler Mi?

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ABSTRACT

Objective: To investigate the effects of body mass index (BMI), quadriceps angle (Q0) and pes planus on walking age in children with Down syndrome (DS) and typically developing peers.
Methods: Bodyweight, height and Q0 were measured and footprints were obtained in 50 children with DS and 50 typically developing children (control), ages between 2-6 years. BMI and Staheli index (SI) were calculated.
Results: The mean walking age was 26±8 months in the DS group and 12±2 months in the control group (p<0.0001). While BMI was 85 percent in all age groups in girls in the DS group, it increased with age in boys this group. SI was 1.17±0.28 in the DS group and 0.93±0.04 in the control group (p<0.001). Although there was no significant relationship between walking age and BMI, Q0, pes planus, the difference in walking age between the two groups decreased statistically as Q0 increased (p<0.001).
Conclusion: In the DS group, regular monitoring of BMI, keeping it within healthy limits, and adding exercises related to Q0 and pes planus to physical therapy programs will reduce the delay in walking age.

Keywords: Body mass index, Down syndrome, Pes planus, Q angle, Walking age

ÖZ

Amaç: Down sendromlu (DS) olan çocuklar ve tipik gelişime sahip yaşıtlarında vücut kitle indeksi (VKİ), kuadriseps açısı (Q0) ve pes planusun yürüme yaşı üzerine etkilerini araştırmak.
Yöntem: Yaşları 2-6 arasında 50 DS'lu çocuk (DS grubu) ve 50 tipik gelişim gösteren çocukda (kontrol grubu) vücut ağırlığı, boy uzunluğu ve Q açısı ölçüldü ve ayak izleri elde edildi. VKİ ve Staheli indeksi (SI) hesaplandı.
Bulgular: DS grubunda ortalama yürüme yaşı 26±8 ay, kontrol grubunda 12±2 ay idi (p<0.0001). VKİ, DS grubundaki kız çocuklarında tüm yaş gruplarında %85 iken, bu gruptaki erkek çocuklarda yaşla birlikte artış gösterdi. SI, DS grubunda 1.17±0.28 ve kontrol grubunda 0.93±0.04 idi (p<0.001). Yürüme yaşı ile VKİ, Q0, pes planus arasında anlamlı bir ilişki olmamasına rağmen, Q0 arttıkça iki grup arasındaki yürüme yaşı farkı istatistiksel olarak anlamlı azaldı (p<0,001).
Sonuç: DS grubunda VKİ'nin düzenli izlenmesi, sağlıklı sınırlarda tutulması ve fizik tedavi programlarına Q0 ve pes planus ile ilgili egzersizlerin eklenmesi yürüme yaşındaki gecikmeyi azaltacaktır.

Anahtar Kelimeler: Down sendromu, Pes planus, Q açısı, Vücut kitle indeksi, Yürüme yaşı

Introduction

Down syndrome (DS) is a genetic anomaly that results from the extra presence of all or part of the 21st chromosome, with common features as well as remarkable differences according to each individual (1). It is characterized by structural, mental and organismal changes that cause mental retardation and delay in motor performance. Often these changes are accompanied by a range of medical problems, including cardiac and respiratory problems (2, 3). Although the incidence varies by ethnicity and geographic region, DS occurs in about 1 in 800 births worldwide (4).

From early childhood to adulthood, individuals with DS continue to show deficits in the motor areas of postural control and movement skills. These deficiencies may have a causal link with delays in reaching motor development milestones (independent walking, climbing stairs) in children (2, 5, 6). Although the neuropathological basis of motor dysfunction in DS is unknown, cerebellar dysfunction, delayed myelination, proprioceptive and vestibular deficits have been suggested as possible causes (2).

The available evidence indicates that overweight and obesity in individuals with DS begin in late infancy and remain evident over the years. It has also been reported that the degree of overweight and obesity in children and adolescents with DS varies according to the clinical characteristics specific to that individual (7-9).

In the literature, it has been stated that normally developing children sit without support at 7 months and begin walking independently at 12 months,

whereas children with DS sit at 15 months and walk at 30 months (10). It is also stated that joint laxity and hypotonia, which are common in DS children, increase the risks of some musculoskeletal disorders and are associated with delay in walking (11). Pes planus, which is considered one of these disorders, is observed at a higher rate (60-88%) in children with DS than in children with normal development. There are studies investigating the effect of pes planus on gait pattern in children with DS (2, 11, 12).

Quadriceps (Q) angle is a measurement index used to evaluate the functions of the knee joint and patellofemoral joint and the etiology of patellofemoral pain (13-16). Q angle is defined as the angle between two axes drawn in the frontal plane, from anterior superior iliac spine to the mid-point of patella, and from the mid-point of patella to tibial tuberosity (17). It is considered normal that the Q angle value is between 8°-15° in healthy adult males and between 12°-19° in females. The rate of deviation of this angle from normal increases the risk of skeletal-muscle problems in the lower extremities of the people (15,18). Recently, studies investigating the relationship between Q angle and patella femoral instability, genu varum-valgum and cerebral palsy especially in children and adolescents have attracted attention (19, 20). However, a study on the measurement and evaluation of the Q angle in children with DS could not be found.

The aim of this study is to investigate the effects of some parameters (body mass index [BMI], pes planus and Q angle), each of which has been the subject of different studies, on the age of walking in children with DS and typically developing peers.

Materials and Methods

The study was carried out in accordance with the principles of the Declaration of Helsinki, with the approval of the Research Ethics Committee (approvel number, 2018/1582) and necessary permissions from the relevant institutions. A total of one hundred children aged 2-6 years, 50 with DS (who applied to four special education centers) and 50 with normal development (kindergarten children), were taken as the study sample. There was no developmental anomaly in the lower extremities of the children included in both groups. The parents of the children were informed and their written consent was obtained. Age and independent walking age were learned from parents. Measurements, data recordings and evaluations were made by the same physiotherapist. Measurements were repeated at least twice and the averages were recorded.

Initally, the children's height (cm) and weight (kg) were measured in light clothes and without shoes. Then, in the supine position, the Q angle was measured using a standard goniometer. Anterior superior iliac spine, midpoint of the patella and tibial tuberosity were marked for this measurement. The Q angle was determined and recorded in degrees by aligning the midpoint of the goniometer to the midpoint of the patella, one arm to the anterior superior iliac spine point, and the other arm to the tibial tuberosity point (20).

Pes planus was evaluated in the standing position. For this evaluation, a footprint was first obtained using a foot imprinter. The foot imprinter consists of a rigid platform and a plastic-coated mat on both sides. The front surface of the mat on which the foot will be stepped on is supported by rubber from the bottom. The back surface, impregnated with stamp ink, is the side facing the platform where the footprinted paper will be placed. For obtaining the footprint, a sheet of paper was placed on the rigid platform and the ink-impregnated surface was covered over the paper. With the aid of a physiotherapist, the child was stepped the foot to be studied on the rubber layer, with contralateral foot out of the platform. The process was also repeated for the other foot. During the procedure, the researcher controlled the foot position on the platform to prevent the foot from slipping (21).

Later, BMI and Staheli index (SI) were calculated. Using growth curves created for children (22), corresponding percentiles were determined for body weight, height, and BMI data. Body mass index (BMI) was calculated by dividing body weight by the square of the body height (kg/cm2). In the footprint, the length of the narrowest part of the midfoot (A) and the length of the widest part of the heel (B) were measured in mm. Staheli index was obtained by dividing the A value by the B value (SI:A/B). If the SI>1, it was considered pes planus (21,23).

Analysis of Data

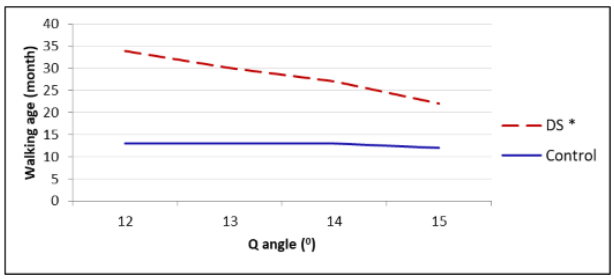
The obtained data for this study were evaluated by SPSS 21.0 (Statistical Package for Social Sciences). The subjects' age, weight, lenght, BMI, Q angle and SI were as the mean and standart deviation. Statistically analysis were using the Mixed model according to sex and age. Twelve-month groups were formed between the ages of 2 and 6 years to detect age-related changes (24-35 months, 36-47 months, 48-59 months, 60-72 months). Means and differences between means were determined by t test and Chi-Square test. The relationship between the parameters was investigated with the Pearson Coorrelation test. In all tests, $p<0.05$ was considered statistically significant.

Results

The study included 50 children with DS (26 boys, 24 girls) and 50 typically developing children (control) (24 boys, 26 girls) aged 2-6 years. Thirty-six (72%) children with DS were able to walk independently, and the mean walking age was 26±8 months (boys 28±1 months; girls 25±1 months). All of the children in control group could walk independently and the mean walking age was 12±2 months (boys 13±2 months; girls 12±1 months). It was determined that the walking age of children with

DS was statistically significantly (p<0.0001) delayed compared to the children in the control group. In addition, it was observed that this delay was statistically significant (p<0.05) more in boys with DS than in girls. While the mean height of children with DS was shorter than the children in control group in all age groups, it was observed that mean body weight was lower at 24-35 months, similar at 36-59 months, and higher at 60-72 months (Table 1). The distribution and percentile values of BMI by age group and gender are shown in Table 2. BMI in girls with DS was found to be at the upper limit of normal weight (85%) in all age groups. In boys with DS, an increase in BMI was observed with age. Although BMI was generally higher in girls with DS, the difference was not statistically significant (p>0.05). There was no significant relationship between BMI and walking age (p>0.05; r, -0.036).

In all age groups, independent of DS, Q angle values were higher in girls, but the difference was not statistically significant (p>0.05). Even though there was no difference between the right and left side Q angle values, there was a strong correlation between the two sides' angles (p<0.0001; r, 0.98)(Table 3). In addition, no significant relationship was found between Q angle and walking age (p>0.05; r, -0.32). However, as the Q angle value increased, the difference in walking age between the two groups decreased statistically (p<0.001) (Figure 1).



* p<0.001

Figure 1. The effect of the Q angle (0) on the difference between the walking onset age of children with Down syndrome (DS) and children in the control group

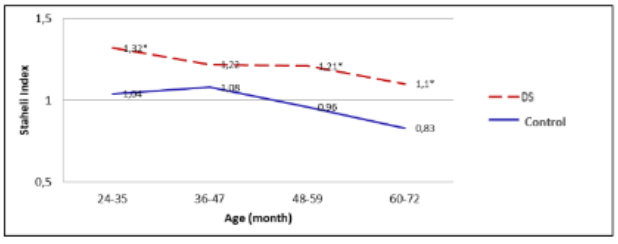


Figure 2. Comparison of Staheli index by age and Down syndyome (DS)

The SI calculated from the footprints of the children was found to be statistically significantly higher in the right foot (DS group, 1.17±0.28; control group, 0.94±0.04) and left foot (DS group, 1.11±0.27; control group, 0.93±0.06) of the children with DS, regardless of age and gender (p<0.001). According to age groups, SI>1 was observed in both groups at 24-47 months, while SI values were higher in children with DS and SI>1 continued until the 72nd month in children with DS. There was no difference between the SI values of the right and left sides, as well as a strong relationship was detected between the two sides (p<0.0001; r, 0.72) (Table 4)(Figure 2). SI>1 before the age of 4 was considered physiological. However, SI>1 persisting until 6 years of age in children with DS was accepted as pes planus. No statistically significant correlation was observed between the SI preferred to evaluate the presence and degree of pes planus and the walking age (p>0.05; r, 0.11).

Table 1. Comparison of Bodyweight, Height and Percentile (%) Values According to Age in Children with DS and Control Group

Age	Weight (kg)				Height (cm)			
(Month)	DS		Control		DS		Control	
24-35	10.2±2.2*	3%	12.5±1.9	25%	80.8±6.1*	3%	91±5.2	50%
36-47	14.8±2.5	25%	14.2±2.9	25%	93.7±4.7*	10%	96.4±5.4	25%
48-59	16.3±2.4	25%	16.2±2.5	25%	98.5±3.1*	3%	102.6±6.6	25%
60-72	22.5±4.1*	75%	19.3±1	50%	107±3.1*	10%	109±1.5	25%

*, p<0.05

Table 2. Distribution of BMI (kg/m2) of Children with DS and Control Group by Age and Gender (mean±standard deviation)

Age		DS			Control		
(Month)	Gender	n	BMI	PV	n	BMI	PV
24-35	Boy	4	14.82±2.07	15%	6	15.95±2.67	50%
	Girl	7	17.30±2.75	85%	5	18.90±2.80	95%
36-47	Boy	8	16.73±1.93	75%	6	16.78±0.98	75%
	Girl	4	17.55±1.68	85%	8	15.93±2.74	50%
48-59	Boy	4	16.95±0.51	75%	5	15.21±1.46	25%
	Girl	3	17.11±2.24	85%	5	15.46±1.18	50%
60-72	Boy	10	20.38±1.40	95% +	7	15.88±0.96	50%
	Girl	10	17.89±2.34	85%	8	15.69±1.42	50%

n: number of cases, PV: percentile value

Table 3. Comparison of Q Angle (0) Values by Age, Gender and Side (mean±standard deviation; n, number of cases)

Age (Month)	Gender	Q° DS n	DS Right	DS Left	Control n	Control Right	Control Left
24-35	Boy	4	13.05±1.17	13.13±1.09[a,b]	6	12.98±1.46	12.90±1.37[a,b]
	Girl	7	14.86±0.87	14.96±0.77[a,b]	5	14.66±1.11	14.66±1.11[a,b]
36-47	Boy	8	12.43±0.86	12.40±0.67[a,b]	6	12.60±0.37	12.77±0.26[a,b]
	Girl	4	13.93±0.83	13.93±0.83[a,b]	8	14.31±1.24	14.40±1.24[a,b]
48-59	Boy	4	13.18±0.78	13.25±0.74[a,b]	5	13.06±1.14	13.06±1.14[a,b]
	Girl	3	14.93±1.10	15.10±1.51[a,b]	5	14.42±0.54	14.32±0.66[a,b]
60-72	Boy	10	12.54±0.78	12.59±0.80[a,b]	7	13.01±0.63	13.16±0.54[a,b]
	Girl	10	14.48±0.95	14.48±0.95[a,b]	8	14.83±0.82	14.76±0.98[a,b]

a: p<0.0001, b: r=0.90-0.98

Table 4. Comparison of Staheli Index by age, gender and side (mean±standard deviation; n, number of cases)

Age (Month)	Staheli Index DS Gender	DS n	DS Right	DS Left	Control Gender	Control n	Control Right	Control Left
24-35	Boy	4	1.30±0.17*	1.29±0.10*[a,b]	Boy	6	1.05±0.17	1.03±0.06[a,b]
	Girl	7	1.36±0.17*	1.38±0.20*[a,b]	Girl	5	1.05±0.22	1.03±0.24[a,b]
36-47	Boy	8	1.28±0.31*	1.29±0.16[a,b]	Boy	6	1.19±0.11	1.17±0.15[a,b]
	Girl	4	1.30±0.25*	1.33±0.27*[a,b]	Girl	8	1.11±0.39	1.01±0.25[a,b]
48-59	Boy	4	1.18±0.31*	1.19±0.23*[a,b]	Boy	5	0.98±0.13	1.04±0.09[a,b]
	Girl	3	1.27±0.24*	1.24±0.17*[a,b]	Girl	5	0.93±0.29	0.90±0.25[a,b]
60-72	Boy	10	1.08±0.28*	1.05±0.29*[a,b]	Boy	7	0.82±0.22	0.77±0.23[a,b]
	Girl	10	1.14±0.31*	1.01±0.26*[a,b]	Girl	8	0.86±0.21	0.89±0.17[a,b]

DS: Down Syndrome, *: p<0.001, a: p<0.0001, b: r=0.72

Discussion

Growth, heart, thyroid, vision and hearing screenings required for monitoring the health status of children with DS are clearly defined in medical guidelines. Regarding the evaluation and management of the musculoskeletal system in these children, there are inconsistent and variable recommendations due to the lack of data, and the focus is usually cervical spine problems (11). The neuropsychological profile defined for children with DS is closely related to motor development. Studies supporting this knowledge have also shown that motor development is strongly associated with both cognitive and language development (24,25). One of the indicators of motor development is the ability to walk independently. In this study, the possible effects of BMI, Q angle and the presence of pes planus on the reported delay in walking age in children with DS were investigated.

It has been reported that the walking age in children with DS is later than those of normally developing children (average 26-30 months), and the male gender affects the delay in walking age more (10,11,25,26). Similar to the literature, in our study, it was determined that the age of walking was statistically delayed (p<0.0001) in children with DS (DS group, 26±8 months; control group, 12±2 months). This delay was more statistically significant (p<0.0001) in boys (boys 28±1 months; girls 25±1 months). No relationship was observed between gender and walking age in children the control group.

Body weight, height and BMI are basic elements in assessing growth, which is an excellent indicator of health status. Using the data of these parameters, the researchers have obtained growth curves that are very helpful in the routine monitoring of growth in children. Growth curves were created not only for healthy children but also for children with DS (7,22,27-29). Short height is the characteristic feature of DS, showing distinct individual differences depending on comorbidities and hereditary factors (7,28,29). Body weight begins to increase in late infancy in DS children and evolves into overweight and obesity over time (8,9). Body weight, height and BMI values obtained in this study were compared with percentile values defined for healthy children (22). It was found that height in DS children was lower in the percentile (3-10%) than healthy children in all age groups, and body weight increased with age (3%-25%-75%, respectively). The increase in body weight with increasing age and the persistence of short height in children with DS caused increased BMI. The mean BMI was found to be 75-85 percentile in children with DS and 50 percentile in children the control group. Short height in children with DS was independent of age and gender. There was no significant relationship between BMI and walking age.

The Q angle, first described by Brattström (30), can be measured in the supine position (traditional) and standing, as well as calculated on images (plain

radiographs, magnetic resonance images, computed tomography)(13). The results of the studies in which the Q angle was measured in healthy individuals, students, athletes and patients with gonarthrosis are accessed from databases (14-18, 31,32). However, a study in which the Q angle, which is known to be associated with patellofemoral pain and instability, was measured in children with DS has not been found in the literature. In this study, besides other parameters, the effect of Q angle on the age of walking in DS children was investigated. Since it is not possible for all children to stand up and it would be unethical for them to receive radiation for the study, our Q angle measurements were made with the traditional method in the supine position.

In some studies, it has been reported that the Q angle is higher in female than in male, and higher on the right side than on the left side in the young and adult population (14,17,18,31). Q angle over 150or male and over 200for female is considered pathological. Rauh et al. (18), on the other hand, found that runners with a Q angle of more than 20° were 1.7 times more likely to be injured, and if the difference between the right and left Q angles were greater than 4°, the risk of injury was 1.8 times higher. While Mandigo and Livingston (32) said that Q angle was affected by dominance, Jaiyesimi and Jedede (14) found that higher right Q angle was independent of leg dominance. Cankaya et al. (16) reported that in healthy children aged 2–8, the Q angle decreases with age (mean 140 to 120), and the angular value is not dependent on factors such as gender, pes planus, and measurement position. In this study, independent of DS, Q angle values were higher in girls in all age groups, but the difference was not statistically significant ($p>0.05$). There was also no significant difference between the right and left Q angles. Contrary to the results of Cankaya et al. (16), no significant decrease in Q angle was observed with increasing age in children with DS and control group. There was no statistically significant relationship between Q angle and DS, pes planus and walking age ($p>0.05$). Whereas, as the Q angle value increased, the difference between the walking age of children with DS and control group decreased ($p<0.05$).

Pes planus (flat feet), defined by the loss of the medial longitudinal arch where the foot touches or nearly touches the ground, is common among young children and is usually asymptomatic. This congenital condition typically improves with age as the foot muscles become stronger or may persist in older children and adults (33-36). The medial longitudinal arches of boys mature 1 year later than girls (36). The relationship between overweight and obesity in children and flat feet is known (36,37). Children with asymptomatic flat-footed are followed with the recommendation to maintain a healthy weight, treatment up to surgical intervention may be required for resistant symptomatic pediatric pes planus (painful and/or stiff) (33). Pes planus can be identified by footprints, heel-to-arch ratio, subjective evaluation, and radiographic measurements (12,21,23,38). Despite all these known facts, there is no generally accepted classification system or definition of pediatric flatfoot (38).

In a study of kindergarten children aged 3 to 6 years, it is mentioned that there is an average of 44% pes planus in all children, and the prevalence decreases from 54 to 24 from 3 to 6 years of age (36). It has been reported that the prevalence of pes planus in DS is 60-88%, even almost universal (91%) (11,12,39). In the accessible literature, there is no study investigating the relationship between the presence of pes planus and walking age in children with DS. In our study, in which the aforementioned relationship was investigated, a low-cost, radiation-free and simple measurement method was preferred for the detection of pes planus. Footprints could not be taken in 2% of the children with DS who participated in the study because they could not stand. The SI was >1 in 74% of children with DS and 60% of children the control group. While SI decreased after 4 years of age in children the control group, values above 1 continued in children with DS. There was no significant difference in SI values according to gender ($p>0.05$). In this study, in which only the presence of pes planus was evaluated without distinguishing its degree and etiology, no significant relationship was found between pes planus and walking age in children with DS. There was no significant relationship between pes planus and BMI in children with DS and the control group ($p>0.05$).

Conclusion

Parents of children with DS are concerned about how delayed their child's walking age will be. According to the results of this study, the following recommendations can be made to parents and physiotherapists of children with DS who do not have serious additional health problems to reduce the delay in walking age and to prevent the ignored physiological pes planus from becoming rigid:

- To regulate the nutrition programs of children with DS, who are expected to be shorter than the general population, and to keep the BMI within healthy limits by controlling their weight gain.

- Regular exercise of the quadriceps muscle in an assisted and controlled manner, in addition to other physical therapy procedures.

- To carefully evaluate the presence of pes planus in all children with DS, to provide the right shoe selection and to give detailed information about the importance of foot health.

Sources of Support: None.

Conflict of Interest: There is no conflict of interest.

Ethical Approval: The ethical approval of the study was gathered from the Ethical Committee for Non-

Pharmaceutical and Non-Medical Device Researches of the Necmettin Erbakan University (Approval Date: 16.11.2018, Approval Number: 2018/1582).

Informed Consent: Since this study was conducted in children, consent was obtained from the parents.

Author Contributions:

Concept-GE, IIU; Design-GE, IIU; Supervision-GE, IIU; Resources and Financial Support-GE, IIU; Materials-GE; Data Collection and/ or Processing-GE, IIU, MSI; Analysis and/or Interpretation-MSI, IIU; Literature Research-GE, IIU; Writing Manuscript-IIU, GE; Critical Review-GE, IIU, MSI.

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References

1. Wang HY, Long IM, Liu MF. Relationships between task-oriented postural control and motor ability in children and adolescents with Down syndrome. Research in Developmental Disabilities. 2012;33(6):1792-8.

2. Galli M, Rigoldi C, Brunner R, Virji-Babul N, Giorgio A. Joint stiffness and gait pattern evaluation in children with Down syndrome. Gait Posture. 2008;28(3):502-6.

3. Boontan N, Rojnueangnit K. Growth patterns of Thai children with Down Syndrome from birth to 5 years. J Pediatr Genet. 2021;10(1):16-22.

4. Bull MJ. Down Syndrome. N Engl J Med. 2020;382(24):2344-52.

5. Rigoldi C, Galli M, Albertini G. Gait development during lifespan in subjects with Down syndrome. Res Dev Disabil. 2011;32(1):158-63.

6. Carmeli E, Ariav C, Bar-Yossef T, Levy R, Imam B. Movement skills of younger versus older adults with and without Down syndrome. Res Dev Disabil. 2012;33(1):165-71.

7. Tüysüz B, Topal Göknar N, Oztürk B. Growth charts of Turkish children with Down syndrome. Am J Med Genet A. 2012;158A(11):2656-64.

8. Bertapelli F, Pitetti K, Agiovlasitis S, Guerra-Junior G. Overweight and obesity in children and adolescents with Down syndrome-prevalence, determinants, consequences, and interventions: a literature review. Res Dev Disabil. 2016;57:181-92.

9. Bindayel IA. Relationship between Down syndrome (DS) and obesity in children and adolescents and its relation to dietary and lifestyle factors. Progress in Nutrition. 2021;23(4): e2021180.

10. Tudella E, Pereira K, Basso RP, Savelsbergh GJP. Description of the motor development of 3–12 month old infants with Down syndrome: the influence of the postural body position. Res Dev Disabil 2011;32:1514–20.

11. Foley C, Killeen OG. Musculoskeletal anomalies in children with Down syndrome: an observational study. Arch Dis Child. 2019;104(5):482-7.

12. Kanai Y, Mutsuzaki H, Watanabe M, et al. Use of malleoli as an indicator for flatfoot in patients with Down syndrome: development of a simple and non-invasive evaluation method through medial longitudinal arch. J Phys Ther Sci. 2020;32(5):315-8.

13. Smith TO, Hunt NJ, Donell ST. The reliability and validity of the Q-angle: a systematic review. Knee Surg Sports Traumatol Arthrosc. 2008;16(12):1068-79.

14. Jaiyesimi AO, Jegede OO. Influence of gender and leg dominance on Q-angle among Adult Nigerians. Afr J Phys and Reh Sci. 2009;1:18−23.

15. Park SK, Stefanyshyn DJ. Greater Q angle may not be a risk factor of patellofemoral pain syndrome. Clin Biomech. 2011;26(4):392-6.

16. Cankaya T, Dursun Ö, Davazlı B, et al. Assessment of quadriceps angle in children aged between 2 and 8 years. Turk Pediatri Ars. 2020;55(2):124-30.

17. Havaslı F, Demir M, Ciçek M, Yoldas A. Association between Q angle and predisposition to gonarthrosis*. Anatomy 2017;11(1):21–25.

18. Rauh MJ, Koepsell TD, Rivara FP, Rıce SG, Margherita AJ. Quadriceps angle and risk of injury among high school cross-country runners. J Orthop Sports Phys Ther. 2007;37(12):725-33.

19. Antinolfi P, Bartoli M, Placella G, et al. Acute patellofemoral instability in children and adolescents. Joints. 2016;4(1):47–51.

20. Jimshad TU, Mainali S, Swethankh KS, John AT. Does Q angle change in spastic diplegia children? Indian J Pediatr 2016; 2: 85−9.

21. Hernandez AJ, Kimura LK, Laraya MHF, Favaro E. Calculation of staheli's plantar arch index and prevalence of flat feet: a study with 100 children aged 5-9 years. Acta Ortopédica Bras. 2007;2:68-71.

22. Neyzi O, Bundak R, Gokcay G, et al. Reference Values for Weight, Height, Head Circumference, and Body Mass Index in Turkish Children. J Clin Res Pediatr Endocrinol. 2015;7(4):280-93.

23. Staheli LT, Chew DE, Corbett M. The longitudinal arch. A survey of eight hundred and eighty-two feet in normal children and adults. J Bone Joint Surg Am. 1987;69(3):426-8.

24. Vicari S. Motor development and neuropsychological patterns in persons with Down syndrome. Behavior Genetics. 2006;36(3):355-64.

25. Yamauchi Y, Aoki S, Koike J, Hanzawa N, Hashimoto K. Motor and cognitive development of children with Down syndrome: The effect of acquisition of walking skills on their cognitive and language abilities. Brain Dev. 2019;41(4):320-6.

26. Corrado B, Sommella N, Ciardi G, et al. Can early physical therapy positively affect the onset of independent walking in infants with Down syndrome? A retrospective cohort study. Minerva Pediatr. 2022;74(1):31-9.

27. Cronk C, Crocker AC, Pueschel SM, et al. Growth charts for children with Down syndrome: 1 month to 18 years. Pediatrics. 1988;81:102-10.

28. Myrelid A, Gustafsson J, Ollars B, Anneren G. Growth charts for Down's syndrome from birth to 18 years of age. Arch Dis Child. 2002;87:97-103.

29. Meguid NA, El-Kotoury AI, Abdel-Salam GM, El-Ruby MO, Afif HH. Growth charts of Egyptian children with Down syndrome (0–36 months). East Mediterr Health J. 2004;10:106–15.

30. Brattström H. Shape of the intercondylar groove normally and in recurrent dislocation of the patella. Acta Orthop Scand 1964;68:1-44.

31. Woodland LH, Francis RS. Parameters and comparisons of the quadriceps angle of collage-aged men and women in the supine and standing positions. Am J Sports Med. 1992; 20(2):208-211.

32. Mandigo JL, Livingston LA. Bilateral Q angle symetry and anterior knee pain syndrome. Clinical Biomechanics. 1999;14(1):7-13.

33. Ford SE, Scannell BP. Pediatric flatfoot: pearls and pitfalls. Foot Ankle Clin. 2017; 22(3):643–56.

34. Michaudet C, Edenfield KM, Nicolette GW, Carek PJ. Foot and ankle conditions: pes planus. FP Essent. 2018;465:18-23.

35. Carr 2nd CB, Yang S, Lather LA. Pediatric pes planus: A state of the art review. Pediatrics. 2016;137(3):e20151230.

36. Pfeiffer M, Kotz R, Ledl T, Hauser G, Sluga M. Prevalence of flat foot in preschool-aged children. Pediatrics. 2006;118:634-9.

37. Bordin D, De Giorgi G, Rigon F. Flat and cavus foot, indexes of obesity and overweight in a population of primary-school children. Minerva Pediatr. 2001;53(1):7-13.

38. Pereira K, Basso RP, Lindquist AR, da Silva LGP, Tudella E. Infants with Down syndrome: percentage and age for acquisition of gross motor skills. Res Dev Disabil. 2013;34(3):894-901.

39. Concolino D, Pasquzzi A, Capalbo G, Sinopoli S, Strisciuglio P. Early detection of podiatric anomalies in children with Down syndrome. Acta Paediatr. 2006;95(1):17-20.

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ORIGINAL ARTICLE

Halp Score: A Simple and Easily Accessible Index for Predicting Prognosis in Colorectal Cancer Patients

Kolorektal Kanser Hastalarında Prognozu Tahmin Edebilen Basit ve Kolay Erişilebilir Bir İndeks

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ABSTRACT

Objective: Colorectal cancer is the fourth most common malignant tumor in the world, and survival times are seen to increase together with the increase in the options for targeted therapies, local ablative applications, and supportive care. The Hemoglobin, Albumin, Lymphocyte and Platelet (HALP) score is used as a prognostic factor in different types of cancers. The aim of this study was to analyze the prognostic value of the HALP score in patients diagnosed with de novo metastatic colorectal cancer (mCRC).
Methods: De novo mCRC patients who were followed-up in the period from January 2017 to December 2021, were retrospectively evaluated. The optimal cut-off point for the HALP score was calculated with the Receiver Operating Characteristic (ROC) curve analysis. Predictive factors for overall survival (OS) were assessed with univariate analysis. Survival times were assessed with the Kaplan-Meier analysis.
Results: A total of 213 patients were included in the study. Univariate analysis showed that patients with low Body Mass Index (BMI), high Eastern Cooperative Oncology Group (ECOG) Performance Status score, and tumors located in the right colon, and RAS mutant patients, and those with a low HALP score were associated with worse survival rates. Namely, the overall survival time of patients with a HALP score >16.74 was found as 91 months, while the overall survival time of patients with a HALP score ≤16.74 was found as 16 months (p<0.001).
Conclusion: Our study showed the HALP score to be a simple, cost-effective, and useful marker that can predict OS in mCRC patients.

Keywords: hemoglobin-albumin-lymphocyte-platelet (HALP) score, metastatic, colorectal cancer, prognostic

ÖZ

Amaç: Kolorektal kanser (KRK), dünyada en sık karşılaşılan malign tümörlerden dördüncüsü olup, artan hedefleyici tedavi seçenekleri, lokal ablatif uygulamalar ve destek bakımdaki artış ile sağkalım sürelerinin de uzadığı görülmektedir. Hemoglobin, albümin, lenfosit ve trombosit (HALP) skoru, farklı kanserler türlerinde prognostik bir faktör olarak kullanılmaktadır. Bu çalışmanın amacı, de novo metastatik kolorektal kanser (KRK) tanılı hastalarda HALP skorunun prognostik değerini analiz etmektir.
Yöntemler: Ocak 2017-Aralık 2021 tarihleri arasında de novo metastatik KRK tanısıyla takip edilen hastalar retrospektif olarak değerlendirildi. HALP skoru için optimal kesme noktası, ROC (receiver operating characteristic) eğrisi analizi ile belirlendi. Genel sağkalım için öngördürücü faktörler, tek değişkenli analiz ile değerlendirildi. Sağkalımı değerlendirmek için Kaplan-Meier analizi yapıldı.
Bulgular: Toplam 213 hasta çalışmaya dahil edildi. Tek değişkenli analiz, düşük Vücut Kitle İndeksi'nin (VKİ), yüksek Eastern Cooperative Oncology Group (ECOG) Performans Statüsü skorunun, sağ kolon yerleşimli tümörlerin, RAS mutant hastaların ve düşük HALP skorunun daha kötü sağkalım oranları ile ilişkili olduğunu gösterdi. Özellikle HALP skoru >16.74 olan hastaların genel sağkalım süresi 91 ayken, HALP skoru ≤16.74 olan hastaların genel sağkalım süresi 16 ay bulundu. (p<0.001)
Sonuç: Sonuç olarak HALP skoru metastatik KRK hastalarında sağkalımı predikte eden basit, maliyeti düşük ve kullanışlı bir belirteçlerdir.

Anahtar Kelimeler: hemoglobin-albümin-lenfosit-trombosit (HALP) skoru, metastatik, kolorektal kanser, prognostik

Introduction

Colorectal cancer (CRC) is the third leading cause of death from cancer worldwide, with about 1.9 million new cases identified in 2020. (1,2) About 20% of the patients present with metastasis at the time of initial diagnosis, and 30 to 40% additionally develop metachronous metastasis after primary tumor resection. A 5-year survival time can be achieved at a rate of 40% with multimodal systemic treatment combinations. (3)

In recent years, there has been an increasing focus on identifying the molecular changes that are critical to the oncogenic phenotype of colorectal cancer and on therapies that target these molecular changes. Still, however, a great majority of the patients are treated with cytotoxic chemotherapy due to their molecular/pathological characteristics or the lack of access to treatment. Availability of prognostic and predictive indexes that allow physicians to make the most suitable treatment decision in these patients are of vital importance.

Current studies show that the systemic inflammatory response is associated with tumor characteristics such as proliferation, invasion, metastasis, and that inflammation has an important role in tumor formation

and growth. (4,5) Blood cells affect tumor cells through adaptive immune response by secreting different cytokines that help various inflammatory processes. (6) The neutrophil-to-lymphocyte ratio (NLR), the platelet-lymphocyte ratio (PLR), the lymphocyte-monocyte ratio (LMR), and inflammatory indexes such as the prognostic nutritional index have been used to predict prognosis in different cancer types. (7,8)

It is known that a combination of these parameters can predict the patient's prognosis better than a single index. To that end, the HALP score—an index which is calculated based on hemoglobin, albumin, lymphocyte, and platelet levels—has been recently defined. The HALP score assesses both the immune system and the nutritional status of the patient. The score has been reported to be a good prognostic marker in various types of cancers, including gastrointestinal, lung, and genitourinary cancers. (9,10,11) These parameters can be calculated simply based on the laboratory parameters of patients used in everyday practice. In this study, we aimed to determine the relationship between the HALP score examined before treatment and prognosis in metastatic colorectal cancer (mCRC) patients.

Material and Methods

Data Collection and Follow-Up

The institutional and national research committees' ethical standards, as well as the 1964 Declaration of Helsinki and its later revisions or comparable ethical standards were followed in the study. The method and procedure for the study were approved by the Ethics Committee of the University. The study included 213 patients diagnosed with de novo mCRC and treated and/or followed-up by our medical oncology clinic from January 2017 to December 2021. Patients who had severe comorbidities, were receiving anti-inflammatory treatment, had active infection or inadequate organ function were excluded, as these might affect inflammatory parameters. Patients' age, weight, height, body mass index (BMI), comorbidities, Eastern Cooperative Oncology Group (ECOG) status, and demographic data were recorded. Lymphocyte and platelet counts, and serum albumin levels were recorded from the laboratory parameters examined one week before the first course of chemotherapy.

HALP scores were calculated using the laboratory data obtained. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score was calculated according to the following formula: hemoglobin (g/L)×albumin (g/L)×lymphocytes (/L)/platelets (/L).

Statistical Analyses

The Statistical Package for Social Sciences for Windows 20.0 (BM SPSS, IBM Corp., Armonk, NY, USA) was used for analysis. OS was defined as the time from diagnosis to death or the last visit. Descriptive statistics summarized frequencies and percentages for categorical, mean, and standard deviation for continuous variables. Categorical variables were compared with the Independent Samples T-test and categorical parameters with the $\chi 2$ test. The power of the HALP score was analyzed using the ROC curve analysis. A significant cut-off point was observed, and sensitivity, specificity, and positive and negative predictive values were detected. Survival analyses of prognostic indexes, and clinical and pathological features were calculated using the Kaplan-Meier method (log-rank test). Parameters that appeared significant in univariate analysis for survival and did not show multicollinearity were included in the Cox multivariate regression analysis. The 95% confidence interval (CI) was used to indicate the relationship between survival time and each independent factor. Statistical significance level was $p<0.05$.

Results

Of the 213 patients included in the study, 182 patients were <75 years and 31 were ≥75 years of age with a mean of 61±12.91 years. 58.7% (125) of the patients were male. The most common histopathological type was adenocarcinoma with a rate of 90.6% (193 patients), followed by mucinous adenocarcinoma 8% (17 patients). 61% of the tumors were moderately differentiated. While all patients were de novo metastatic, the most common site of metastasis was the liver (52.6%). The mean follow-up time of the patients was 31 (2-126) months. 77% (164 patients) had died by the end of the follow-up period. The main characteristics of the patients are shown in Table 1.

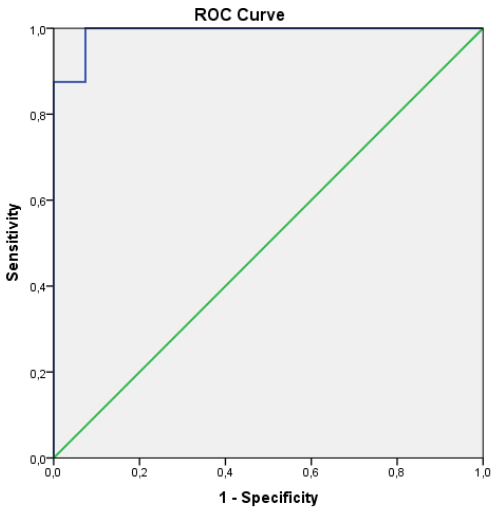

Figure 1. ROC curve for HALP score

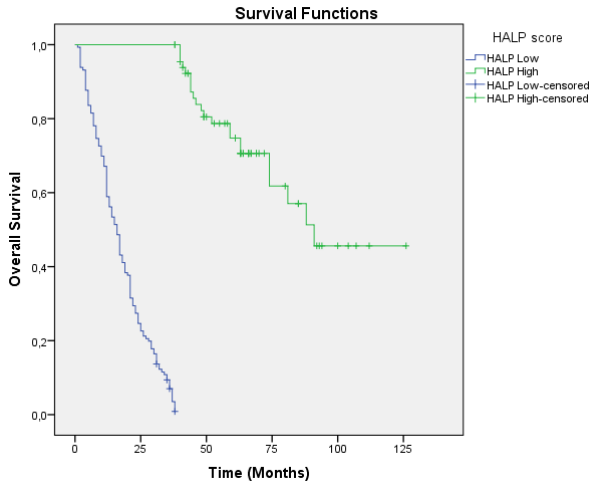

Figure 2. Kaplan-Meier curves for OS in patients with mCRC according to HALP score

Table 1. Clinical and pathological features of patients

Parameters	Number of patients (%)
Age	
<75	182 (85.4%)
≥75	31 (14.6%)
Gender	
Female	88 (41.3%)
Male	125 (58.7%)
Histology	
Adenocarcinoma	193 (90.6%)
Mucinous adenocarcinoma	17 (8%)
Neuroendocrine carcinoma	3 (1.4%)
Differentiation	
Well differentiated	78 (36.6%)
Moderately differentiated	130 (61%)
Poorly differentiated	5 (2.3%)
BMI (kg/m2)	
BMI <24	86 (40.4%)
BMI ≥24	127 (59.6%)
ECOG	
ECOG 0-1	168 (78.9%)
ECOG 2-3	45 (21.1%)
Localization	
Left colon	90 (42.3%)
Right colon	123 (57.7%)
RAS Type	
Wild	110 (51.6%)
Mutant	103 (48.4%)
Localization of Metastasis	
Liver	112 (52.6%)
Lung	47 (22.1%)
Peritoneum	29 (13.6%)
Bone	1 (0.5%)
Other	24 (11.2%)

BMI: Body Mass Index, ECOG: Eastern Cooperative Oncology Group, RAS: Rat Sarcoma Gene

The median HALP score of the patients was 17.49 (Range: 1.98-47.3). ROC analysis was done to determine the most appropriate cut-off point for the HALP score. The ROC curve showed the optimal cut-off point to be 16.74 (AUC=0.991; 95% CI 0.97-1.0, p<0.001) (Figure 1). Based on this cut-off point, patients were grouped as those with a low HALP score and those with a high HALP score.

Table 2. The relationship between basic clinicopathological characteristics and HALP scores

Parameters	HALP score		
	High (n)	Low (n)	*p*
Age			
<75	60	122	
≥75	7	24	0.174
Gender			
Female	34	54	
Male	33	92	0.41
Histology			
Adenocarcinoma			
Mucinous	62	131	
adenocarcinoma	5	12	
Neuroendocrine	0	3	0.484
carcinoma			
Differentiation			
Well differentiated	28	50	
Moderately	38	92	
differentiated	1	4	0.518
Poorly differentiated			
BMI (kg/m2)			
BMI <24	17	69	
BMI ≥24	50	77	**0.002**
ECOG			
ECOG 0-1	59	109	
ECOG 2-3	8	37	**0.018**
Localization			
Left colon	63	27	
Right colon	4	119	**<0.001**
RAS Type			
Wild	42	67	
Mutant	24	77	**0.015**
Localization of Metastasis			
Liver	30	82	
Lung	22	25	
Peritoneum	10	19	
Bone	0	1	
Other	5	19	0.283

BMI: Body Mass Index, ECOG: Eastern Cooperative Oncology Group, RAS: Rat Sarcoma Gene

Univariate analysis showed that low BMI, high ECOG score, tumors located in the right colon, RAS mutant patients, and low HALP score were associated with

worse survival rates (Table 3). Particularly, the overall survival time of patients with a HALP score >16.74 was found as 91 months, while the overall survival time of patients with a HALP score ≤16.74 was found as 16 months (p<0.001) (Figure 2).

Table 3. Univariate analysis of prognostic factors for OS

Parameters	Univariate Analysis of OS		
	Number of patients (%)	Median OS in Months (95% CI)	p
Age			
<75	182 (85.4%)	25 (19.82-30.17)	0.110
≥75	31 (14.6%)	16 (8.75-23.24)	
Gender			
Female	88 (41.3%)	25 (14.91-35.08)	0.187
Male	125 (58.7%)	23 (19.08-26.91)	
BMI (kg/m2)			
BMI <24	86 (40.4%)	17 (13.50-20.49)	**<0.001**
BMI ≥24	127 (59.6%)	32 (21.97-42.02)	
ECOG			
ECOG 0-1	168 (78.9%)	28 (21.32-34.67)	**<0.001**
ECOG 2-3	45 (21.1%)	19 (11.37-26.62)	
Localization			
Left colon	90 (42.3%)	74 (47.30-100.69)	**<0.001**
Right colon	123 (57.7%)	14 (12.02-15.97)	
RAS Type			
Wild	110 (51.6%)	31 (22.99-39.00)	**0.002**
Mutant	103 (48.4%)	18 (14.89-21.10)	
HALP score			
High	67 (31.5%)	91 (15.56-19.03)	**<0.001**
Low	146 (68.5%)	16 (13.50-18.49)	

BMI: Body Mass Index, ECOG: Eastern Cooperative Oncology Group, RAS: Rat Sarcoma Gene

When the relationship between the HALP scores and the clinicopathological characteristics of patients were evaluated, ECOG performance score, BMI, localization of the tumor (right/left colon), and RAS mutation status were found to be associated with the HALP score (p<0.005) (Table 2).

Discussion

This study investigated the relationship between the HALP score examined before the first cycle of chemotherapy and overall survival in patients with de novo mCRC. We assessed simple prognostic markers such as complete blood count parameters and serum albumin levels that are obtained from basic laboratory measurements done as part of the routine evaluation process for every patient. Review of the literature showed our study to be the first to demonstrate that low HALP scores (≤16.74), similar to important prognostic factors such as RAS mutation and tumor location, could be used as a biomarker predicting survival in mCRC patients.

While in the recent past, until about ten or fifteen years ago, survival times of about one year could be achieved in mCRC patients, today this period can exceed three years thanks to the availability of targeted therapies and the effective local therapies. (12,13) However, when the studies were examined in detail, despite all the favorable factors, some mCRC patients were seen to have lower survival times, and research on the prognostic factors and markers that affect overall survival continued.

It is widely accepted that inflammatory response and nutritional status are associated with prognosis in cancer patients. Serum albumin is one of the most commonly used indicators showing the nutritional status of patients and has been used to assess progression and prognosis in different types of cancers. Low albumin levels are associated with poorer survival in cancer patients. (14,15) Lymphocytes are critical in the host's anticancer defense. Lymphocytes, which can release cytokines such as interferon-γ and tumor necrosis factor-alpha (TNF-α), can improve the prognosis by causing apoptosis, suppressing cancer cell proliferation, invasion, and migration. (16,17) As a result, lymphocytopenia can contribute to tumor growth. Anemia is a commonly observed result in various cancers, including CRC. (18) That hemoglobin levels are directly related to survival and tumor development in cancer patients have been shown in several studies. (19,20,21) Platelet stimulation is linked to metastasis, and platelets can also protect cancer cells from immune attack. (22)

The HALP score is the integration of four hematological parameters—hemoglobin, lymphocytes, platelets, and albumin levels—and basing on the data obtained in our study, we can say that the HALP score is a comprehensive index that measures the nutritional status and immune health of patients. It has been shown to have prognostic effect in gastric cancer (23), squamous cell carcinoma of the esophagus (24), colorectal cancer (25), renal cell carcinoma (26), bladder cancer (10) and small cell lung cancer. (27) However, the prognostic significance of the HALP score in mCRC patients has not been previously studied in the literature. Our results confirmed that the HALP score is an independent prognostic factor in de novo mCRC patients, and that improvements in the HALP score could, in turn, significantly improve overall survival in CRC patients.

Various prognostic models based on different hematological parameters have been proposed for CRC patients. (28) There are studies that include preoperative carcinoembryonic antigen (CEA) levels and examine (29) the Glasgow prognostic score in high-risk stage II or stage III CRC patients to predict prognosis after resection of pulmonary metastases in CRC patients. (30) However, as stated earlier, the HALP score is both simple and cost-effective marker as it is calculated using the complete blood count parameters and albumin levels that are used in the assessment of every patient.

Based on the retrospective data of studies on colon cancer, the localization of a primary tumor has been shown to be factor affecting survival and chemotherapy response. In a recently published meta-analysis, survival was found to be significantly shorter in metastatic colon cancer patients when the tumor was localized on the right side rather than on the left side. (Overall survival [HRright=2.03 (95% CI: 1.69-2.42) and HRleft=1.38 (95% CI: 1.17-1.63)], respectively). (31) In our study, primary tumors in the right colon were found to be associated with worse prognosis.

The Rat Sarcoma (K-RAS) gene, CRC, functions as a proto-oncogene in the tumor suppressor pathway, which is one of the genetic pathways in its development. It is also a membrane protein capable of binding GTP, which is involved in the transmission of extracellular mitogenic signals. (32) RAS gene mutations are found at different incidences in different cancer types. This mutation is encountered mostly in pancreatic cancers (90%), followed by colon cancers (50%), lung adenocarcinomas (30%) and thyroid tumors (50%), and in myeloid leukemia (30%). (33) The prognostic significance of the mutation status has been demonstrated, alongside the changes in treatment targets according to the RAS mutation in CRC. (34,35,36) Similar to the literature, in our study, we observed that patients with wild-type RAS had better prognosis.

Whilst being the first to demonstrate the HALP score as an independent predictive factor for overall survival in de novo mCRC patients, our study has some major limitations. This is a retrospective study conducted in a single center. The BRAF mutation statuses of the patients have not been included in the analysis. A prospective multi-center study is needed to more clearly assess how these scores should be used in the follow-up and for the survival benefit of patients.

To conclude, the HALP score is a reliable, simple, easily accessible, and inexpensive biomarker that can be used to predict the prognosis of advanced colorectal cancer patients. Our results suggest that prognostic models based on the HALP score are a useful tool that can be used to predict survival in mCRC patients.

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Consent for publication: Patients signed informed consent regarding publishing their data.

References

1.Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87-108.

2.Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249.

3.Jones RP, Kokudo N, Folprecht G, et al. Colorectal Liver Metastases: A Critical Review of State of the Art. Liver Cancer. 2016;6(1):66-71.

4.McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. Curr Opin Clin Nutr Metab Care. 2009;12(3):223-226.

5.Colotta F, Allavena P, Sica A, Garlanda C, Mantovani A. Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis. 2009;30(7):1073-1081.

6.Varga G, Foell D. Anti-inflammatory monocytes-interplay of innate and adaptive immunity. Mol Cell Pediatr. 2018;5(1):5.

7.Hong YF, Chen ZH, Wei L, et al. Identification of the prognostic value of lymphocyte-to-monocyte ratio in patients with HBV-associated advanced hepatocellular carcinoma. Oncol Lett 2017;14:2089-96.

8.Magdy M, Hussein T, Ezzat A, Gaballah A. Pre-treatment Peripheral Neutrophil-Lymphocyte Ratio as a Prognostic Marker in Gastric Cancer. J Gastrointest Cancer. 2019;50(4):763-768.

9.Jiang H, Li H, Li A, et al. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer. Oncotarget. 2016;7(44):72076-72083.

10.Peng D, Zhang CJ, Gong YQ, et al. Prognostic significance of HALP (hemoglobin, albumin, lymphocyte and platelet) in patients with bladder cancer after radical cystectomy. Sci Rep. 2018;8(1):794.

11.Güç ZG, Alacacıoğlu A, Kalender ME, et al. HALP score and GNRI: Simple and easily accessible indexes for predicting prognosis in advanced stage NSCLC patients. The Izmir oncology group (IZOG) study. Front Nutr. 2022;9:905292.

12.Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005 [published correction appears in CA Cancer J Clin. 2005 Jul-Aug;55(4):259]. CA Cancer J Clin. 2005;55(1):10-30.

13.Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin. 2016; 66(4): 271-89.

14.Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J. 2010;9:69.

15.Oñate-Ocaña LF, Aiello-Crocifoglio V, Gallardo-Rincón D, et al. Serum albumin as a significant prognostic factor for patients with gastric carcinoma. Ann Surg Oncol. 2007;14(2):381-389.

16.Lim JA, Oh CS, Yoon TG, et al. The effect of propofol and sevoflurane on cancer cell, natural killer cell, and cytotoxic T lymphocyte function in patients undergoing breast cancer surgery: an in vitro analysis. BMC Cancer. 2018;18(1):159.

17.Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature. 2008;454(7203):436-444.

18.Keeler BD, Mishra A, Stavrou CL, Beeby S, Simpson JA, Acheson AG. A cohort investigation of anaemia, treatment and the use of allogeneic blood transfusion in colorectal cancer surgery. Ann Med Surg (Lond). 2015;6:6-11.

19.Belcher DA, Ju JA, Baek JH, et al. The quaternary state of polymerized human hemoglobin regulates oxygenation of breast cancer solid tumors: A theoretical and experimental study. PLoS One. 2018;13(2):e0191275.

20.Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent

prognostic factor for survival in patients with cancer: a systemic, quantitative review. Cancer. 2001;91(12):2214-2221.

21.Xia L, Hu G, Guzzo TJ. Prognostic Significance of Preoperative Anemia in Patients Undergoing Surgery for Renal Cell Carcinoma: A Meta-analysis. Anticancer Res. 2017;37(6):3175-3181.

22.Zhang GM, Zhu Y, Luo L, et al. Preoperative lymphocyte-monocyte and platelet-lymphocyte ratios as predictors of overall survival in patients with bladder cancer undergoing radical cystectomy. Tumour Biol 2015;36:8537-43.

23.Chen XL, Xue L, Wang W, et al. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget. 2015;6(38):41370-41382.

24.Cong L, Hu L. The value of the combination of hemoglobin, albumin, lymphocyte and platelet in predicting platinum-based chemoradiotherapy response in male patients with esophageal squamous cell carcinoma. Int Immunopharmacol. 2017;46:75-79.

25.Jiang H, Li H, Li A, et al. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer. Oncotarget. 2016;7(44):72076-72083.

26.Peng D, Zhang CJ, Tang Q, et al. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy. BMC Urol. 2018;18(1):20.

27.Shen XB, Zhang YX, Wang W, Pan YY. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score in Patients with Small Cell Lung Cancer Before First-Line Treatment with Etoposide and Progression-Free Survival. Med Sci Monit. 2019;25:5630-5639.

28.Kawai K, Sunami E, Yamaguchi H, et al. Nomograms for colorectal cancer: A systematic review. World J Gastroenterol. 2015;21(41):11877-11886.

29.Kanemitsu Y, Kato T, Hirai T, Yasui K. Preoperative probability model for predicting overall survival after resection of pulmonary metastases from colorectal cancer. Br J Surg. 2004;91(1):112-120.

30.Toiyama Y, Miki C, Inoue Y, Tanaka K, Mohri Y, Kusunoki M. Evaluation of an inflammation-based prognostic score for the identification of patients requiring postoperative adjuvant chemotherapy for stage II colorectal cancer. Exp Ther Med. 2011; 2:95-101.

31.Arnold D, Lueza B, Douillard JY, et al. Prognostic and predictive value of primary tumour side in patients with RAS wild-type metastatic colorectal cancer treated with chemotherapy and EGFR directed antibodies in six randomized trials. Ann Oncol. 2017;28(8):1713-1729.

32.Zeng M, Kikuchi H, Pino MS, Chung DC. Hypoxia activates the K-ras proto-oncogene to stimulate angiogenesis and inhibit apoptosis in colon cancer cells. PLoS One. 2010;5(6):e10966. Published 2010 Jun 4.

33.Jiang Y, Mackley H, Cheng H, Ajani JA. Use of K-Ras as a predictive biomarker for selecting anti-EGF receptor/pathway treatment. Biomark Med. 2010;4(4):535-541.

34.Ribeiro KB, Ribeiro KB, Feres O, et al. Clinical-Pathological Correlation of KRAS Mutation Status in Metastatic Colorectal Adenocarcinoma. World J Oncol. 2013;4(4-5):179-187.

35.Morris VK, Lucas FAS, Overman MJ, et al. Clinicopathologic characteristics and gene expression analyses of non-KRAS 12/13, RAS-mutated metastatic colorectal cancer. Ann Oncol. 2014;25(10):2008-2014.

36.Kawazoe A, Shitara K, Fukuoka S, et al. A retrospective observational study of clinicopathological features of KRAS, NRAS, BRAF and PIK3CA mutations in Japanese patients with metastatic colorectal cancer. BMC Cancer. 2015;15:258.

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ORIGINAL ARTICLE

The Views of Urology Doctors in Turkey Towards Regional Anaesthesia

Türkiye'deki Ürologların Rejyonel Anesteziye Bakışı

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ABSTRACT

Despite regional anaesthesia (RA) being the most appropriate anaesthesia method in several surgeries, primarily urology surgery, it is not widely practised by anaesthetists. We aimed to research the knowledge, opinions and attitudes of urologists towards regional anaesthesia(RA) A questionnaire consisting of 29 questions to be answered with Likert type answers was applied face to face to urology specialists and assistants in hospitals in the center of Ankara. By stating the preferred anaesthesia method it was aimed to evaluate the knowledge and opinions of urologists to RA. A total of 152 urology assistants or specialists were included in the study. The source of the knowledge related to RA was determined as from experience during specialist training in 38%, from observation and learning from anaesthetists when working together in 25% and from medical faculty education in 25%. The most common reasons for selecting RA were determined as a better state of consciousness in the patient compared to general anaesthesia (92.8%), that it is a safe anaesthesia method (86.2%), lower rates of postoperative nausea and vomiting (73.7%) and greater patient satisfaction (73%). Reasons for not selecting RA were determined as the risk of complications developing associated with unwanted movements of the patient (45.4%) and that the patient can follow their own endovision monitor and hear the doctors talking amongst themselves, as they are conscious during surgery (40.8%). The results of this study showed that the majority of urologists knew the advantages of RA and supported the use of RA in appropriate operations. The disadvantages of the RA can be eliminated with anaesthesia applications such as sedation or nerve blockage additional to RA. Periodic training sessions between clinics and meetings may be useful both in terms of updating information and in reducing negative opinions of RA. Inter-clinical meetings and periodic training can be beneficial both in terms of updating information and reducing negative opinions about RA.

Keywords: Regional anaesthesia, Urologist, General anaesthesia

ÖZ

Rejyonel anestezi (RA) başta ürolojik cerrahiler olmak üzere birçok ameliyatta en uygun anestezi yöntemi olmasına rağmen anestezistler tarafından yaygın olarak uygulanamamaktadır. Bu çalışmada Ürologların rejyonel anestezi(RA) konusundaki bilgi, görüş ve tutumlarını araştırmayı amaçladık. Ankara merkezindeki hastanelerde üroloji uzman ve asistanlarına, Likert tipi yanıtlarla yanıtlanmak üzere 29 sorudan oluşan bir anket yüz yüze uygulandı. Ürologların tercih ettikleri anestezi yöntemi belirlenerek RA konusundaki bilgi ve görüşlerinin değerlendirilmesi amaçlanmıştır. Toplam 152 üroloji asistanı veya uzmanı çalışmaya dahil edildi. RA ile ilgili bilgilerin kaynağı olarak; %38'i uzmanlık eğitimi sırasındaki deneyimlerden, %25'i birlikte çalışırken anestezistlerden gözlem ve öğrenmeden, %25'i tıp fakültesi eğitiminden olduğu saptandı. RA'yı seçme nedenleri; hastaların genel anesteziye göre bilinç durumunun daha iyi olması (%92,8), güvenli bir anestezi yöntemi olması (%86,2), ameliyat sonrası bulantı kusma oranlarının daha düşük olması (%73,7) ve daha fazla hasta memnuniyeti (%73) olarak değerlendirildi. RA'yı seçmeme nedenleri; hastanın istenmeyen hareketlerine bağlı komplikasyon gelişme riski (%45.4) ve hastanın ameliyat sırasında bilinci açık olduğu için kendi endovizyon monitörünü takip edebilmesi ve doktorların kendi aralarında konuşmalarını duyabilmesi (40.8) olarak belirlendi. Bu çalışmanın sonuçları, ürologların çoğunluğunun RA'nın avantajlarını bildiğini ve uygun operasyonlarda RA kullanımını desteklediğini göstermiştir. RA'ya ek olarak sedasyon veya sinir blokajı gibi anestezi uygulamaları ile RA'nin dezavantajları ortadan kaldırılabilir. Klinikler arası toplantılar ve periyodik eğitimler, hem bilgilerin güncellenmesi açısından hem de RA hakkındaki olumsuz görüşlerin azaltılması açısından faydalı olabilir.

Anahtar Kelimeler: Rejyonel anestezi, Ürolog, Genel anestezi

Introduction

Despite regional anaesthesia (RA) being the most appropriate anaesthesia method in several surgeries, primarily urology surgery, it is not widely practised by anaesthetists (1, 2). The main reasons for this lack of use are that there should be conformity among surgeons, patients and the anaesthesia team. Because patients spend more time with the surgeon preoperatively, the recommendations and suggestions of the surgeon are as influential on the anaesthetist as the choice of a certain anaesthesia method.

Therefore, when the anaesthetist is not involved in the preoperative evaluation, and the surgeon has insufficient or incorrect knowledge of RA, a patient can easily be directed to the application of general anaesthesia, even when the case is suitable for RA. There have been many studies to date related to the expectations and preferences of patients. However, there have been very few studies researching the anaesthesia preferences and knowledge of RA of surgeons, which would shed further light on the subject. Studies of this subject in the literature have generally been conducted with orthopaedists and have been limited in number (3). To the best of our knowledge, there are no previous

studies in literature related to the subject of this current research, in which the knowledge, opinions and attitudes of urologists towards RA are examined.

Material and Methods

The study was conducted between July 2013 and October 2013 after approval from the Ethics Committee of Ankara Numune Training and Research Hospital (meeting no: 30/2013; date: 26.06.2013).

Urology specialists and urology assistants working in state hospitals in the centre of Ankara were interviewed face to face. The questionnaire, which is attached in Appendix 1, was administered to the volunteer participants of the study.

The questionnaire consisted of 29 questions: 4 in section 1, 10 in section 2 and 15 in section 3. In the first section, the age, information about the institution where the respondent worked and educational status of the participant was asked. In the second section, the anaesthesia method (regional anaesthesia, general anaesthesia, regional + general anaesthesia) that the urologist would select for a patient undergoing ureterorenoscopy, transurethral bladder tumour resection, transurethral prostate resection, open transvesical prostatectomy and genital surgery was asked, as well as which of the same three methods the urologist would prefer if they were undergoing the same operations. In the third section of the questionnaire, questions were asked with responses using a 5-point Likert scale to ascertain the urologist's opinions of the advantages and disadvantages of regional anaesthesia.

Statistical analysis

The data were analysed using the SPSS (Statistical Package for the Social Sciences Inc., Chicago, IL, USA) software program, version 16.0 for Windows. The chi-square test and Fisher's exact test as non-parametric methods were used in the comparison of two non-continuous variables. To evaluate missing data in the chi-square analysis, the Monte Carlo simulation method was used. A value of $p<0.05$ was accepted as statistically significant.

Results

The study included a total of 152 urologists working in state hospitals in the centre of Ankara. The data, including the age, gender and urology experience of the participants, are shown in Table 1.

The participants were questioned regarding the source of their knowledge related to RA, and they could select one or more responses to this question. Of the total of 152 participants, 94 (61.8%) indicated that it was experience during their specialist training, 62 (40.8%) said it was collaboration with anaesthesia department colleagues, 62 (40.8%) said it was medical faculty training, 23 (15.1%) said it was articles and books related to RA, 4 (2.6%) said it was seminars, and 2 (1.3%) reported other sources. Both of these participants who reported other sources had worked as anaesthesia assistants for approximately 1 year before urology specialist training.

The sources from which urology specialists obtained information related to RA are shown in Figure 1.

Reliability analysis was applied to the questionnaire, which asked the preferred anaesthesia methods of the urologists both for patients and themselves in different urological operations. No item on the questionnaire was found to have a Cronbach's alpha (α) coefficient less than 0.20. Because these 10 items had high reliability values, no item was removed from the questionnaire. Then, the reliability coefficients of the questionnaire were examined. In the calculation of reliability coefficients, differences are shown according to the type of variable and the source and number of applications. Differences in methods of calculation change the interpretation of the reliability coefficient. The reliability coefficient provides information regarding the extent of removing random errors and the amount of error confused with measurement results. Although values are considered to range between 0 and +1, reliability requires values close to +1. The desired result is a reliability coefficient greater than 0.70. The calculated Cronbach's α reliability coefficient for the 10 items on the questionnaire used in the research was 0.875. Because this coefficient was greater than 0.70, the questionnaire could be said to have strong reliability (Table 2).

Table 1: Demographic characteristics.

		n (%)
Sex		
	Male	152 (100)
	Female	0 (0)
Age (yrs)		
	≤30	56 (36.8)
	31-40	57 (37.6)
	41-50	26 (17.1)
	51-60	11 (7.2)
	≥61	2 (1.3)
Urology experience (yrs)		
	≤5	63 (41.4)
	6-10	34 (22.4)
	11-15	33 (21.7)
	16-20	13 (8.6)
	21-25	6 (3.9)
	≥26	3 (2.0)

Table 2: Reliability coefficients of the questionnaires applied in the study

	Number of items	Reliability coefficient (Cronbach's alpha)
1st questionnaire	10	0.875
2nd questionnaire	15	0.732

Table 3: Anaesthesia preferences of the urologists for patients and for themselves.

		Regional Anaesthesia - n (%)	General Anaesthesia - n (%)	RA + GA n (%)	P value
Ureterorenoscopy operation for stones in the lower third of the ureter	D	42 (27.6)	104 (68.4)	6 (3.9)	0.001*
	P	33 (21.7)	113 (74.3)	6 (3.9)	
TUR-M operation for bladder tumour	D	68 (44.7)	78 (51.3)	6 (3.9)	0.001*
	P	70 (46.1)	73 (48)	9 (5.9)	
TUR-P operation for BPH	D	105 (69.1)	40 (26.3)	7 (4.6)	0.001*
	P	110 (72.4)	31 (20.4)	11 (7.2)	
Open prostatectomy for BPH	D	49 (32.2)	92 (60.5)	11 (7.2)	0.001*
	P	47 (30.9)	91 (59.9)	14 (9.2)	
Surgery in the genital region	D	98 (64.5)	46 (30.3)	8 (5.3)	0.002*
	P	93 (61.2)	49 (32.2)	10 (6.6)	

D: the preference of the doctor for him- or herself; H: the preference of the doctor for the patient; RA+GA: Reginal anaesthesia + general anaesthesia. *p<0.05; for comparisons between the D and P groups, the Mann Whitney U test and the t-test were used.

Reliability analysis was applied to the 15 Likert-type items on the questionnaire, which examined the reasons for selecting or not selecting regional anaesthesia. No item was found to have a Cronbach's alpha (a) coefficient less than 0.20. Because these 15 items had high reliability values, no item was removed from the questionnaire. Then, the reliability coefficients of the questionnaire were examined. The Cronbach's a reliability of the Likert scale from 1 to 5 for each item indicated reliability in the sense of internal reliability. The Cronbach's a reliability coefficient calculated for the 15 items on the questionnaire used in the research was 0.732. Because this coefficient was greater than 0.70, the questionnaire could be said to have strong reliability (Table 2).

The preferences of anaesthesia methods of the urologists participating in the study for patients and themselves for different urology operations are shown in Table 3.

The reasons of the urology doctors for the selection of RA are shown in Figure 2. According to these findings, the reasons for selection were a good postoperative state of consciousness of the patient and that RA is a safe anaesthesia method.

The reasons of urology doctors for not selecting RA are shown in Table 3. According to these findings, the reasons for not selecting RA were the perceived possibility of complications developing associated with movements of the abdomen or lower extremities and that the patient can hear the surgical team talking amongst themselves and can see the endovision monitor.

Discussion

In this study, which was applied to research the knowledge, opinions and attitudes of urologists towards RA, it was determined that the source of knowledge about RA for urology doctors was most often experience during specialist training (38%), followed by observation and collaboration with anaesthetist colleagues (25%). In addition, a small proportion of the study participants reported the sources of their knowledge as medical articles and books (9%) and seminars (2%), which are actually the most current and accurate sources. In a study by Akçaboy et al.(1), in which a questionnaire was administered to orthopaedists, articles, books and seminars to determine the source of knowledge related to RA, the same low rates were reported as by the urologists in the current study. These results suggested that, in Turkey in general, doctors in different surgical specialities do not have a sufficient level of current and accurate knowledge of RA. Periodic training sessions and collaboration between clinics oriented towards eradicating this deficiency would also increase understanding between surgeons and anaesthetists.

In the current study, the preference of anaesthesia methods of urologists for patients and themselves in different urology operations was researched. Generally, RA was not selected by the urologists in the study for ureteroscopy in the treatment of stones in the lower third of the ureter for either patients or themselves. In addition, it was determined that GA was preferred at a statistically significantly higher rate for patients than for the urologists themselves. However, in several studies, it has been reported that there was no increase in complications in ureterorenoscopy operations performed under RA and that it was well tolerated by patients (4, 5). The underlying reasons for the lower preference by urologists of RA as the anaesthesia method in ureteroscopy operations could be that, during these operations, there is sometimes the need to advance the ureteroscope as far as the upper third of the ureter; there can be concerns such as not being able to prevent renal pain at the level of the regional block applied, and unwanted ureter trauma can develop associated particularly with not being able to keep respiratory activity under complete control.

As in ureteroscopy operations, it was determined that, in open prostatectomy surgery, the urologists generally preferred GA. The choice of RA+GA was selected at a much higher rate for open prostatectomy surgery

than for other types of operations, and the rate of the preference for RA+GA was greater for patients than for themselves. The underlying reason for not selecting RA alone for open prostatectomy might be that, because the patient is awake during RA, it is thought that there might be difficulties working in the surgical field because of abdominopelvic muscle contractions, which cannot be curarised, and there will therefore be a narrower field of vision.

However, in patients undergoing open prostatectomy with RA, there are known to be advantages, such as less urethral tenesmus, pain and pain-related hypertension in the early stage, less need for blood transfusion and less need for re-operation in the early postoperative period (6). To benefit from these postoperative early period advantages provided by RA in open prostatectomy operations, combining GA with RA by the anaesthetist will become a more preferred method than RA for urologists performing open prostatectomy.

In the application of TUR-M surgery for bladder tumours, it was noted that, while urologists selected GA for themselves, their preference for patients was RA or RA+GA. This finding suggested that the urologists had concerns about the risk of complications associated with movement when the patient was conscious and that the endovision monitor could be observed; therefore, they preferred GA for themselves. In TUR-P operations applied for BPH and surgery in the genital region, RA was the preferred anaesthesia method both for themselves and for patients, although in these operations, the anaesthesia method preferred for patients was sometimes not the one preferred for themselves. More detailed studies are required to shed light on the underlying reasons for this difference.

The primary reasons for the urologists participating in the current study not selecting RA were the possibility of complications, such as perforation, occurring in areas such as the ureter, bladder or prostate capsule due to unexpected movements of the patient. These types of complications in particular can be due to adduction movements in the leg associated with stimulation of the obturator nerve during resection of the prostate lateral lobes or tumours located in the lateral bladder walls. In addition to a set of precautions that can be undertaken by surgeons to prevent complications that might develop in this way, applications by anaesthetists, such as obturator nerve blockage in addition to RA, can be effective.

In a study by Tatlisen et al. (7) of obturator nerve blockage applied in 61 patients with tumours located in the lateral bladder wall, it was reported that there was no adduction movement in 59 patients. In another study by Jo et al., pubic or inguinal route obturator nerve blockage was applied following spinal anaesthesia for TUR-M surgery, and it was reported that injections could be administered more easily from the inguinal region and that reduction in the adductor reflex was more successful (8). Among the reasons for not selecting RA were primarily the provision of a more comfortable working environment for the urologists during surgery, with the application of sedation aimed at preventing complications that could occur due to hand and arm movements, as well as the patient talking during surgery.

Another reason for the urologists not preferring RA was that, if sedation were applied to conscious patients using RA alone, the patient would be able to hear the surgical team talking amongst themselves and be able to observe the endovision monitor. One of the reasons given by the urologists for not selecting RA was that, in lengthy operations, there might be the need to convert from RA to GA. The application of an epidural catheter so that anaesthesia can be continued by that route if there is a need for an additional dose can be beneficial, if applied prior to surgeries with the potential of being lengthy and if the patient is informed by the surgeon.

In a study by Oldman et al. (9), the primary reasons for orthopaedists not preferring RA were that RA takes a long time and thus slowed down operating theatre turnover time. Similarly, Akçaboy et al. (1) revealed comparable results in a study conducted with orthopaedists. Although the reason for the slower operating theatre turnover was not at the forefront of the reasons for not preferring RA in the current study, it was seen as a disadvantage by the urologists. Oldman et al. (9) reported that a solution for this issue was the application of RA in a separate room, which would require the creation of a separate RA team. However, in another study, it was shown that a separate RA team and room did not expedite the operating theatre turnover time, and it increased the anaesthesia-related costs (10). There are several factors that slow down operating theatre turnover. These factors are not only anaesthesia-related, but they can be associated with the surgeon, nurses or other assistant personnel. Training activities, including all of the operating theatre personnel, could accelerate the operating theatre turnover time. In the application of RA by anaesthetists, undertaking some steps, such as the use of local anaesthetic agents with rapid onset of effects, can provide the possibility of a more rapid start to surgery. Apart from these suggestions, it is obvious that deficiencies in the knowledge and experience of anaesthetists will extend the operating theatre turnover time.

In studies related to the problems of anaesthesia training, it has been reported that the doctors in training could not perform sufficient RA applications during training, and they therefore lacked experience in this subject (11, 12). Although previous studies have suggested that a separate block room and a separate RA team are not very effective in shortening operating theatre turnover time, we are of the opinion that, particularly for assistant doctors, RA training in a separate block room led by a separate RA team would at least reduce the experience and knowledge deficiencies to a minimum.

The factors with the most significant effects on the preferences of urologists for RA were, respectively, a better postoperative state of consciousness (less sedation and confusion), greater safety compared to GA, less nausea and vomiting, greater patient satisfaction, less postoperative pain compared to GA and lower rates of thromboembolism. It was determined that the urologists had general knowledge about several advantages of RA, which have been proved in various studies. In addition, there have been several studies supporting that there is better bleeding control in patients under RA, particularly in orthopaedic surgery, in which there can be more problems with bleeding (13, 14).

However, it cannot be definitively said that, in urology surgery, there is less blood loss in patients under RA than in those under GA. There has not yet been consensus in studies on this topic. It has been suggested that the advantage of bleeding control with RA compared to GA is valid in open prostate surgery in particular (radical prostatectomy or open prostatectomy) (5, 6, 7). In urological endoscopy surgery, there is a more dominant view that RA offers no advantages over GA in terms of bleeding control (8, 9). In the current study, it was determined that the urologists did not believe that there was any advantage to RA in urology surgery in terms of bleeding control. This finding might have been due to the young ages of the urologists participating in this study: 74.4% of the participants were younger than 40 years old, and because open surgery is not currently performed as much as endoscopic surgery in urology, the respondents might have been thinking of endoscopic surgery.

In conclusion, it was determined from this research that the majority of urologists were aware of the advantages of RA and supported the use of RA in appropriate operations. The most significant obstacle to RA for urologists was the possibility of complications developing due to movements of the patient during the operation and that the conscious patient would be able to hear the surgical team talking and be able to observe the endovision monitor. These disadvantages could be eliminated with anaesthesia applications such as sedation and nerve blockage, in addition to RA. Although previous studies have reported the most important disadvantage of RA to be the slowing of operating theatre turnover time, it was not seen as a significant disadvantage by the urologists in the current study.

Although there are several known advantages of regional anaesthesia, even in appropriate operations, it cannot be applied as often as desired, sometimes for patient-related reasons and sometimes because of the surgeon's prejudice against RA. Periodic training and meetings between clinics would be useful in terms of both updating knowledge and reducing the negative opinions of surgeons towards RA.

References

1.Akçaboy EY, Akçaboy ZN, Ekren D, Göğüş N. Bir Eğitim ve Araştırma Devlet Hastanesinde Ortopedistlerin Rejyonal Anestezi ile İlgili Tutum ve Bilgilerinin Değerlendirilmesi. Turkiye Klinikleri J Anest Reanim 2009;7(3): 143-7

2.Ngan Kee WD, Hung VY, Roach VJ, Lau TK.A survey of factors influencing patients' choice of anaesthesia for caesarean section. Aust N Z J Obstet Gynaecol 1997;37(3):300-3.

3.Masursky D, Dexter F, McCartney CJ, Isaacson SA, Nussme-ier NA. Predicting orthopedic surgeons' preferences for peripheral nerve blocks for their patients. Anesth Analg. 2008 Feb;106(2):561-7.

4.Park HK, Paick SH, Oh SJ, Kim HH. Ureteroscopic lithotripsy under local anaesthesia: analysis of the effectiveness and patient tolerability. Eur Urol. 2004 May;45(5):670-3.

5.Shaikh AH, Khalid SE, Zaidi SZ. Ureteroscopy under spinal versus general anaesthesia: morbidity and stone clearance. J Coll Physicians Surg Pak. 2008 Mar;18(3):168-71.

6.Fasciolo A, Baldini C. Transvesical prostatic adenomectomy: general or local anaesthesia. Urologia. 2008;75(4):221-227.

7.Tatlisen A, Sofikerim M. Obturator nerve block and transurethral surgery for bladder cancer.Minerva Urol Nefrol. 2007;59(2):137-41.

8.Jo YY, Choi E, Kil HK. Comparison of the success rate of inguinal approach with classical pubic approach for obturator nerve block in patients undergoing TURB. Korean J Anesthesiol. 2011;61(2):143-7.

9.Oldman M, McCartney CJ, Leung A, Rawson R, Perlas A, Gadsden J, et al. A survey of orthopedic surgeons' attitudes and knowledge regarding regional anaesthesia. Anesth Analg 2004;98(5):1486-90

10.Eappen S, Flanagan H, Lithman R, Bhattacharya N. The addition of a regional blockteam to the orthopedic rooms does not improve anaesthesia controlled times and turnover time in the setting of long turnover times. J Clin Anesth 2006;19(2):85-91.

11.Smith MP, Sprung J, Zura A. A survey of exposure to regional anaesthesia in American anaesthesia residency training programs. Reg Anesth Pain Med 1999;24(2):11-6.

12.Kopacz DJ, Neal JM, Pollock JE. The regional anaesthesia "Learning Curve": what is the minimum number of epidural and spinal blocks to reach consistency? Reg Anesth 1996;21(3):182-90.

13.Juelsgaard P, Larsen UT, Sørensen JV, Madsen F, Søballe K. Hypotensive epidural anaesthesia in total knee replacement without tourniquet: reduced blood loss and transfusion. Reg Anesth Pain Med. 2001;26(2):105-10.

14.Niemi TT, Pitkänen M, Syrjälä M, Rosenberg PH. Comparison of hypotensive epidural anaesthesia and spinal anaesthesia on blood loss and coagulation during and after total hip arthroplasty. Acta Anaesthesiol Scand. 2000;44(4):457-64.

APPENDIX 1

Dear urology colleague,

We are conducting a questionnaire study to evaluate the knowledge and attitudes of urologists working in state hospitals in the centre of Ankara towards the application of regional anaesthesia in surgical approaches to the urinary system.

The responses provided to the 27-question questionnaire and your personal information will remain confidential. Participation in the study is on a completely voluntary basis. If you wish to participate in the study, please provided your name and signature in the relevant section below.

We thank you for your time and assistance.

Participant Name – Surname Signature

Institution where you work						
Age						
How many years have you been working as a urologist?	<5 yrs	5-10 yrs	10-15 yrs	15-20 yrs	20-25 yrs	>25 yrs
What is the source of your knowledge of RA?	Experience during specialist training	Colleagues in the anaesthesia dept.	Medical faculty training	Articles and books related to RA	Seminars	Other

	Regional Anaesthesia	General Anaesthesia	RA + GA
1 - If you were undergoing ureterorenoscopy surgery for stones in the ureter lower third, which anaesthesia method would you select for yourself?			
2 - If you were undergoing TUR-M surgery for bladder tumour, which anaesthesia method would you select for yourself?			
3 - If you were undergoing TUR-P for BPH, which anaesthesia method would you select for yourself?			
4 - If you were undergoing open prostatectomy for BPH, which anaesthesia method would you select for yourself?			
5 - If you were undergoing genital surgery, which anaesthesia method would you select for yourself?			
6 - For a patient undergoing ureterorenoscopy surgery for stones in the ureter lower third, which anaesthesia method would you select?			
7- For a patient undergoing TUR-M surgery for a bladder tumour, which anaesthesia method would you select?			
8 - For a patient undergoing TUR-P surgery for BPH, which anaesthesia method would you select?			
9 - For a patient undergoing open prostatectomy for BPH, which anaesthesia method would you select?			
10 - For a patient undergoing genital surgery, which anaesthesia method would you select?			

NB: The application of regional anaesthesia and general anaesthesia was decided with the intention of reducing postoperative pain.

	Definitely agree	Agree	Neither agree nor disagree	Disagree	Definitely disagree
1 - I prefer RA because lower rates of thromboembolism complications are seen in patients receiving surgery under RA.					
2 - I prefer RA because bleeding control is better in patients receiving surgery under RA.					
3 - I prefer RA because lower rates of postoperative nausea and vomiting are seen in patients receiving surgery under RA.					
4 - I prefer RA because lower rates of postoperative pain are seen in patients receiving surgery under RA.					
5 - I prefer RA because it is a reliable method of anaesthesia in surgical interventions in the lower urinary system.					
6 - I prefer RA because the postoperative consciousness status is better in patients receiving surgery under RA.					
7 - I prefer RA because patient satisfaction is greater in patients receiving surgery under RA.					
8 - I prefer RA because perioperative surgical complications, such as bladder or prostate capsule perforation, can be diagnosed more easily in patients receiving surgery under RA.					
9 - I do not prefer RA because the application is time-consuming and it slows down the operating theatre turnover time.					
10 - I do not prefer RA because there is a high possibility of failure and having to transfer to GA.					
11 - I do not prefer RA as preoperative and postoperative anxiety has been seen to be greater in patients undergoing surgery with RA.					
12 - I do not prefer RA because, during application, total spinal block can develop, and there will then be a need for general anaesthesia.					
13 - I do not prefer RA because conscious patients can hear the surgical team talking among themselves and can observe the endovision monitor.					
14 - I do not prefer RA because there is a risk of complications, such as perforations, occurring due to abdominal or lower extremity movements.					
15 - I do not prefer RA because, when the operating time is extended, the regional anaesthetic effect will not be sufficient, and it will be necessary to transfer to general anaesthesia.					

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ORIGINAL ARTICLE

Morphometric Analysis of Orbit in Turkish Population: a MDCT Study

Türk Popülasyonunda Orbita'nın Morfometrik Analizi: MDBT Çalışması

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ABSTRACT

Objective: The orbit is an important cavity containing vision-related formations and important neurovascular structures, and adjacent to various regions. This study aimed to evaluation, by multidedector computed tomography (MDCT) images, the morphometry of orbit by examining its changes according to gender and body side, and developments according to age, in Turkish population.
Materials and Methods: A total of 200 individuals's (94 females,106 males;400 sides) MDCT images were evaluated. Images were examined according to the gender, body side, and the anatomical structures development.
Results: The height, width and depth of the orbit were determined as 36.04±2.97 mm, 32.33±2.59 mm, 38.35±3.32 mm on the right side, 35.79±3.18 mm, 32.29±2.67 mm, 38.13±3.21 mm on the left side, respectively, in healthy subjects. The height and width of the orbit were found to be statistically significantly larger on both sides in men than in women ($p<0.05$).
Conclusion: Comprehensive information about the orbit and associated apertures is quite important for clinicians working in this area, damage to these structures can cause serious complications. In addition, determining the morphometry of the orbit can be used as an important parameter for determining gender, age and race in forensic medicine.

Keywords: Anatomy, morphometry, multislice computed tomography, orbit

ÖZ

Amaç: Orbita bağlantı sağladıkları boşluklar, komşu olduğu bölgeler ve içerdiği yapılar sebebiyle oldukça önemli bir bölgedir. Çalışmamızda Türk popülasyonunun orbita morfometrisini, çok kesitli bilgisayarlı tomografi (ÇKBT) görüntülerinde cinsiyete, vücut tarafına göre farklılıklarını, yaşa bağlı gelişimini değerlendirmeyi amaçladık.
Gereç ve Yöntem: 94'ü erkek, 106'sı kadın olmak üzere toplam 200 bireyin (400 taraf) ÇKBT görüntüleri üzerinde ölçümler yapıldı. Görüntüler cinsiyet, vücut tarafı ve anatomik yapıların gelişimlerine göre değerlendirildi.
Bulgular: Sağlıklı bireylerde orbita yüksekliği, genişliği ve derinliği sırasıyla sağ tarafta ortalama 36,04±2,97 mm, 32,33±2,59 mm, 38,35±3,32 mm iken sol tarafta 35,79±3,18 mm, 32,29±2,67 mm, 38,13±3,21 mm olarak belirlendi. Orbita'nın yüksekliği ve genişliği her iki tarafta da erkeklerde kadınlardan istatistiksel olarak anlamlı derecede büyük olduğu tespit edildi ($p<0,05$).
Sonuç: Orbita ve ilişkili açıklıklar hakkında kapsamlı bilgi, ilgili bölgede çalışan klinisyenler açısından oldukça önemlidir, bu yapıların zarar görmesi ciddi komplikasyonlara neden olabilir. Bununla birlikte, orbita'nın morfometrisi adli tıpta cinsiyet, yaş ve ırk tespiti için önemli bir parametre olarak kullanılabilir.

Anahtar Kelimeler: Anatomi, morfometri, çok kesitli bilgisayarlı tomografi, orbita

Introduction

The orbit is an important anatomical region containing the eye and related formations and extensions of the central nervous system, with connections to the nasal and paranasal sinuses (1). Intraorbital structures, thanks to the four walls of the orbit, are separated from the formations associated with the brain and face. These walls have their own characteristics and are connected to neighboring structures by openings that allow the passage of important structures such as nerves and blood vessels (2). Therefore, even single lesions of the orbit can cause multiple complication (3).

Various diseases and event, including trauma, infection, and tumors, can affect the orbit. Orbit plays an important role in surgical procedures, in particular orbital decompression, enucleation, exenteration, optic nerve decompression and vascular ligation (4). Therefore, the orbit is an important anatomical region where tissues and organs belonging to different specialties such as ophthalmology, otolaryngology and neurosurgery are located. The surgical approach to the structures located in the orbit is difficult due to the fact that this region has a relatively small volume and the richness of neurovascular structures located in the region (5). Comprehensive anatomical information about the orbit is important for regional surgery (2). In addition, determining the morphometry of the orbit can be used as an important parameter for determining gender, age and race in forensic medicine. Accurate measurements of the orbital anthropometry are valuable for the purpose of designing protective equipment for the eye (6). Thus, we believe that the results of our study will contribute to the existing literature knowledge, the prevention of possible complications in surgical interventions, and shed light on possible new designs.

Materials and Methods

Images were performed with a 256-slice MDCT scanner (Siemens Somatom Flash, Erlangen, Germany). Imaging

parameters were as follows: kV = 120; mA = 160; rotation time = 0.5 s; collimation = 64 × 0.625; FOV = 220 mm. According to power analysis using the GPower 3.1.9.4. program, the sample size was detected in 200 cases (the effect size was 0.75, the reliability was 0.95, and the power was 0.95).

The images of 355 patients who underwent orbital or paranasal CT imaging for different complaints between 2013 - 2021 were evaluated. A total of 155 cases were not included (orbital fractures, pathology in orbital structures, tumors, patients who underwent orbital surgery, foreign body in the relevant region, and poor image quality). Images of a total of 200 individuals (400 sides, 94 male and 106 female), were evaluated. In these cases, prepubertal age was accepted as below 15 years old, postpubertal age was accepted as above 15 years old, and geriatric age limit was accepted as 60 years old (7,8). Taking into account these limits, the cases were evaluated in eight different groups as 0–9 years old, 10–14 years old, 15–19 years old, 20–29 years old, 30–39 years old, 40–49 years old, 50–59 years old, and over 60 years old. In axial and coronal images, height, width, depth, and lengths of the medial and lateral walls of the orbit were measured. Area of orbital apertura was calculated. Measurements were taken three times by the same person for both parties and averaged.

Height and width of the orbit

The height of the orbit was measured as the longest vertical distance between the midpoints of the supraorbital and infraorbital margins at the superficial level of the infraorbital foramen, in coronal section images (9,10) (Figure 1). In the same images, width of the orbit was measured as the longest horizontal distance between medial and lateral margins at the superficial level of the frontozygomatic suture (1, 9) (Figure 1).

Depth of the orbit

In order to determine the orbital depth, firstly, the level at which the optic nerve is monitored continuously was determined, in axial section images. In the section at this level, the line has been drawn from anterior corner of lateral wall of the orbit to anterior lacrimal crest. And from this line to midpoint of the optic canal descending perpendicularly another line was determined as depth of the orbit (1) (Figure 2).

Lengths of the medial and lateral walls of the orbit

The medial and lateral wall lengths of the orbit were evaluated on axial section images at the level where the optic nerve was monitored continuously and the superior orbital fissure was observed. The medial wall length was measured as distance between the anterior lacrimal crest and the anteromedial point of the optic canal (1, 4, 10, 11) (Figure 3A). The lateral wall length was measured as distance between the anterior corner this wall and the anterolateral margin of the superior orbital fissure (10-12) (Figure 3B).

Area of orbital apertura

The area of orbital apertura was calculated by using the software for both sides by following certain anatomical points on the edges of the orbit on coronal section images. This anatomic landmarkers are supraorbital foramen, the anterior edge of flor of lacrimal fossa, frontozygomatic suture, lateral and infraorbital edges throughout ceiling of maxillary sinus, infraorbital foramen, junction point with this edge and medial margin. The area of the closed bone line drawn, provided that the medial edge passes through the bone line, is calculated automatically with the help of software (13, 14) (Figure 4).

Statistical Analyses

The SPSS for Windows version 24.0 program was used in the analysis, and the p-value less than 0.05 was considered statistically significant. The data conformity to the normal distribution was tested with the Shapiro Wilk test. Student's t-test (for normally distributed variables) and Mann–Whitney u test (for non-normally distributed variables) were used in the comparison of numerical variables in two groups. The Kruskal Wallis test and Dunn's multiple comparison test (for non-normally distributed variables) were used to compare numerical variables in more than two groups.

Results

In our study, data from 400 orbit of a total of 200 individuals, 94 male (47%) and 106 female (53%), were evaluated. Individuals aged between 3 months old and 90 years old were examined in eigth different age groups. The distribution of age groups by gender was similar (p=0.344). Morphometric measurements were made on the images and the reference values of these structures according to gender, side and age were determined in healthy individuals.

Height, width and depth of the orbit

The height and width of the orbit were found to be statistically significantly larger on both sides in males than in females ($p<0.05$). Depth of the orbit was found to be statistically significantly greater in males than in females on the left side ($p<0.05$), but its was not statistically significant right side ($p>0.05$).

The height, width and depth of the orbit were found to be greater in the right side than in the left side, but this difference was not statistically significant ($p>0.05$) (Table 1).

The height, width and depth of the orbit were compared according to age groups and a statistically significant difference was observed between the sides ($p<0.05$). The largest hight of orbit was 40-49 age group, while the widest orbit was observed in the 50-59 age group, for both sides. The largest depth of the orbit

Table 1. Orbital parameters according to body side and gender

	Height of the orbit (mm)		Width of the orbit (mm)		Depth of the orbit (mm)		Length of the medial wall (mm)		Length of the lateral wall (mm)		Area of orbital apertura (mm²)	
	Mean±SD		Mean±SD		Mean±SD		Mean±SD		Mean±SD		Mean±SD	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Male (n=94)	36.96±2.19	36.64±2.52	32.97±2.34	32.87±2.32	38.71±2.66	38.85±2.68	38.5±2.65	38.68±2.47	42.72±3.27	42.7±3.22	1055.26±117.82	1048.57±104.01
Female (n=106)	35.22±3.33	35.03±3.51	31.76±2.68	31.77±2.85	38.03 ±3.8	37.48±3.5	37.58±3.2	37.72±3.26	40.94±3.58	41.31±3.05	994.74±144.17	991.14±143.99
p	0.001*	0.001*	0.001*	0.007*	0.281	0.014*	0.070	0.070	0.001*	0.001*	0.005*	0.004*
Total (n=200)	36.04±2.97	35.79±3.18	32.33±2.59	32.29±2.67	38.35±3.32	38.13±3.21	38.01±2.98	38.17±2.95	41.78±3.54	41.96±3.2	1023.18±135.54	1018.13±129.7
p	0.187		0.418		0.129		0.147		0.386		0.144	

*Show statistical signifcance p<0.05, SD: Standard Deviation

Table 2 Orbital parameters according to age groups and body side

Age groups	Height of the orbit (mm)		Width of the orbit (mm)		Depth of the orbit (mm)		Length of the medial wall (mm)		Length of the lateral wall (mm)		Area of orbital apertura (mm²)	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
0-9 (n=33)	32.68±3.5	32.44±3.46	29.05±2.72	29.48±3.08	36.22±3.74	35.79±3.68	36.01±3.39	36.3±3.76	38.22±4.54	38.92±3.8	839.53±129.57	845.87±128.39
10-14 (n=15)	34.17±2.64	34.35±2.12	30.82±1.92	30.45±2.18	37.46±3.17	37.63±3.09	38.23±2.42	37.93±2.93	41.17±3.44	40.98±2.43	932.86±97.66	950.67±92.79
15-19 (n=13)	36.54±2.2	36.06±3.44	32.94±3.2	32.61±2.48	38.39±4.47	38.13±4.23	38.73±3.5	39.59±3.84	42.21±2.76	42.76±2.84	1038.19±143.15	1020.59±136.05
20-29 (n=22)	36.03±1.61	35.6±1.82	32.48±1.84	32.49±1.88	37.9±2.18	38.13±1.76	38.55±3	38.35±2.5	42.87±2.99	42.78±2.83	1029.36±68.46	1014.36±65.04
30-39 (n=28)	36.49±2.11	36.04±2.26	33.25±1.84	33.18±2.1	39.37±2.28	39.03±2.65	38.58±2.98	38.45±2.51	42.62±2.94	42.74±3.19	1055.93±84.68	1071.01±89.95
40-49 (n=30)	37.81±2.54	37.63±3.19	33.02±1.49	32.85±1.92	39±3.68	38.57±2.96	37.85±2.71	38.25±2.44	42.45±2.96	42.59±2.85	1105.51±103.04	1081.28±117.92
50-59 (n=30)	37.37±2.17	37.05±2.9	33.66±1.82	33.76±2.33	39.22±2.77	38.74±1.84	37.96±2.09	38.26±1.91	43.15±2.27	42.59±2.15	1108.35±92.27	1094.76±85.53
60 years and over (n=29)	36.99±1.94	36.9±1.84	33.49±1.64	33.14±1.71	39.01±3.07	39.08±3.83	39.1±2.76	39.2±2.83	42.21±2.73	42.9±2.5	1062.57±74.96	1055.15±57.62
p	0.001*	0.001*	0.001*	0.001*	0.006*	0.005*	0.015*	0.041*	0.001*	0.001*	0.001*	0.001*

*Show statistical signifcance p<0.05, SD: Standard Deviation, Kruskal Wallis Test

Table 3 Multiple comparison table of orbital parameters according to age groups

		0–9	10-14	15-19	20-29	30-39	40-49	50-59
Height of the orbit on right	**0–9**							
	10-14	0.350						
	15-19	0.001*	0.019*					
	20-29	0.001*	0.046*	0.524				
	30-39	0.001*	0.012*	0.785	0.644			
	40-49	0.001*	0.001*	0.240	0.029*	0.067		
	50-59	0.001*	0.001*	0.495	0.109	0.226	0.526	
	60 years and over	0.001*	0.001*	0.590	0.154	0.305	0.419	0.858
Height of the orbit on left	**0–9**							
	10-14	0.169						
	15-19	0.001*	0.103					
	20-29	0.001*	0.126	0.762				
	30-39	0.001*	0.052	0.993	0.702			
	40-49	0.001*	0.001*	0.063	0.010*	0.019*		
	50-59	0.001*	0.006*	0.450	0.204	0.345	0.156	
	60 years and over	0.001*	0.002*	0.246	0.081	0.147	0.377	0.601
Width of the orbit on right	**0–9**							
	10-14	0.147						
	15-19	0.001*	0.009*					
	20-29	0.001*	0.034*	0.419				
	30-39	0.001*	0.001*	0.895	0.251			
	40-49	0.001*	0.003*	0.864	0.421	0.700		
	50-59	0.001*	0.001*	0.527	0.079	0.529	0.302	
	60 years and over	0.001*	0.001*	0.670	0.133	0.712	0.444	0.795
Width of the orbit on left	**0–9**							
	10-14	0.465						
	15-19	0.001*	0.014*					
	20-29	0.001*	0.011*	0.825				
	30-39	0.001*	0.001*	0.540	0.321			
	40-49	0.001*	0.002*	0.920	0.693	0.512		
	50-59	0.001*	0.001*	0.271	0.115	0.543	0.198	
	60 yaş ve üzeri	0.001*	0.001*	0.540	0.319	0.996	0.511	0.537
Depth of the orbit on right	**0–9**							
	10-14	0.295						
	15-19	0.129	0.653					
	20-29	0.175	0.888	0.724				
	30-39	0.001*	0.065	0.211	0.056			
	40-49	0.003*	0.189	0.460	0.189	0.506		
	50-59	0.001*	0.119	0.332	0.112	0.709	0.766	
	60 years and over	0.002*	0.151	0.391	0.147	0.613	0.875	0.890
Depth of the orbit on left	**0–9**							
	10-14	0.060						
	15-19	0.044*	0.850					
	20-29	0.028*	0.957	0.879				
	30-39	0.001*	0.187	0.296	0.156			
	40-49	0.003*	0.594	0.770	0.592	0.335		
	50-59	0.001*	0.436	0.598	0.416	0.504	0.763	
	60 years and over	0.001*	0.390	0.545	0.367	0.575	0.688	0.918

Length of the medial wall on right	0–9							
	10-14	0.04*						
	15-19	0.006*	0.48					
	20-29	0.005*	0.68	0.71				
	30-39	0.002*	0.58	0.78	0.89			
	40-49	0.03*	0.77	0.28	0.41	0.31		
	50-59	0.03*	0.74	0.28	0.39	0.29	0.96	
	60 years and over	0.001*	0.43	0.95	0.69	0.77	0.19	0.17
Length of the medial wall on left	0–9							
	10-14	0.16						
	15-19	0.003*	0.15					
	20-29	0.04*	0.73	0.22				
	30-39	0.01*	0.59	0.27	0.84			
	40-49	0.09	0.98	0.1	0.66	0.5		
	50-59	0.06	0.9	0.13	0.78	0.6	0.87	
	60 years and over	0.001*	0.21	0.66	0.32	0.4	0.12	0.17
Length of the lateral wall on right	0–9							
	10-14	0.050						
	15-19	0.005*	0.410					
	20-29	0.001*	0.182	0.700				
	30-39	0.001*	0.152	0.664	0.969			
	40-49	0.001*	0.317	0.990	0.642	0.590		
	50-59	0.001*	0.052	0.361	0.549	0.549	0.247	
	60 years and over	0.001*	0.467	0.808	0.445	0.391	0.743	0.140
Length of the lateral wall on left	0–9							
	10-14	0.126						
	15-19	0.001*	0.091					
	20-29	0.001*	0.057	0.992				
	30-39	0.001*	0.055	0.938	0.936			
	40-49	0.001*	0.061	0.887	0.877	0.937		
	50-59	0.001*	0.096	0.732	0.695	0.740	0.797	
	60 years and over	0.001*	0.034*	0.914	0.889	0.815	0.750	0.566

Table 4 A comparison of height and width of orbit among various studies (mm) (Mean±SD).

Height of the orbit								Width of the orbit							
Metod		**Male**		**Female**		**Total**		**Male**		**Female**		**Total**			
Right		**Left**	**Right**	**Left**	**Right**	**Left**	**Right**		**Left**	**Right**		**Left**	**Right**	**Left**	
Bones	Sangvichien et al. (2007) (20) (n=101) (age range: 18–86 year)	33.44±2.33		32.89±2.28				40.1±1.89			38.09±2.25				
	Nitek et al. (1) (2009) (n=100) (No age information)	3.36±0.27 cm	3.36±0.26 cm	3.36±0.29 cm	3.46±0.29 cm	3.35±0.28 cm	3.46±0.27 cm	42.6		42.4	40.3	41.6			
	Rajangam et al. (2012) (9) (n=72) (No age information)	35±0.27	33.7±0.26	32±0.28	30.8±0.21			41.7±0.21		40.8±0.19	37.2±0.16	36.9±0.16			
	Kumar and Gnanagurudasan (2015) (n=50) (No age information)	31.56±2.36	31.28±2.34	32.86±2.66	30.16±2.06			41.44±2.08		40.56±2.24	41.23±2.04	40.04±2.10			
Direct graphy	Ghorai et al. (2017) (16) (n=101) (age range: 20–50 year)	28.54±1.95	28.51±1.91	33.23±1.74	28.69±2.16			32.79±1.4		32.36±1.54	31.65±1.26	30.81±1.44			
Co-ne-Beam CT	Sinanoglu et al. (2016) (18) (n=182) (age mean: 32.6 year)	40.3± 4.0	40.3± 4.2	33.5± 2.5	34.3± 2.7			37.3±3.1		38.3±3.0	30.2±2.2	29.7±2.2			
CT	Weaver et al. (2010) (6) (n=39) (age mean: 45.1 year)	32.44±1.89		31.75±2.51				32.44±1.89			31.75±2.51				
	Kaya et al. (2014) (17) (n=112) (age range: 13–86 year)	33.9± 2.27	34.5 ±2.20	32.6 ±2.40	33.16± 2.19	33.3 ±0.22	33.8 ±0.21	37.04± 1.79		36.86 ±1.57	35.78 ±1.50	35.39 ±1.58	36.45 ±0.16	36.18 ±0.16	
	Ozer et al. (2016) (24) (n=198) (age range: 5–74 year)	37.7	37.77	36.55	36.97			33.99		34.17	33.07	33.27			
MDCT	Attia et al. (2018) (13) (n=92) (128 section) (age range: 18–65 year)	37.3 ± 3.2	36.9 ± 2.9	35.9 ± 2.8	35.9 ± 2.8			37.2±4.7		36.7±4.1	37.1±3.7	37± 3.6			
	Acar et al. (2019) (14) (n=100) (128 section) (age range: 18–90 year)	36.2±1.8		35.0 ± 1.3		35.9±1.7		39.4±2.1			38.5±1.6		39.2±2		
	El-Farouny et al. (2021) (19) (n=89) (128 section) (age range: 20–70 year)	34.92 ± 5.01	35.18 ± 1.73	35.08 ± 3.26	34.77 ± 3.25			36.79± 1.34		37.03±1.37	37.39± 1.77	36.11 ±1.34			
	Present study (n=200) (256 section) (age range: 3 month–90 year)	36.96±2.19	36.64±2.52	35.22±3.33	35.03±3.51			32.97±2.34		32.87±2.32	31.76±2.68	31.77±2.85			

CT: Computerized tomography, MDCT: Multidetector computerized tomography

Table 5 A comparison of lengths of the medial and lateral walls of orbit among various studies (mm) (Mean±SD).

		Length of the medial wall						Length of the lateral wall					
Metod		**Male**		**Female**		**Total**		**Male**		**Female**		**Total**	
Right		**Left**	**Right**	**Left**		**Right**	**Left**	**Right**	**Left**				
	Karakas et al. (2002) (12) (age range: 30–50 year)					41.7±3.1						37.7±3.6	
	Thanasil Huanmanop et al. (2007) (4)	42.3±3.1	41.8±2.5	42.2±2.1	42.4±1.5	**Right**	**Left**						
					42.3± 2.6	42.1± 2.1							
	Nitek et al. (2009) (1)	42.1	42.6	39.9	40								
Bones	Kumar and Gnanagurudasan (2015) (10) (No age information)	42.40±2.60	41.84±2.10	42.08±2.33	41.64±2.18			36.60±2.42	35.44±2.79	37.00±2.22		35.72±1.97	
CT	Oester Jr et al. (2012) (11) (Aldult individual)	43.9±3.0				Healthy individual	Individuals with vision loss					Healthy individual	Individuals with vision loss
				46.9±3.3						41.6±5.6	45.7±4.0		
	Nitek et al. (2015) (23) (Age mean: 56 year)	40.40±2.76		38.39±1.85									
MDCT	*Present study* (age range: 3 month–90 year)	38.5±2.65	38.68±2.47	37.58±3.2	37.72±3.26			42.72±3.27	42.7±3.22	40.94±3.58	41.31±3.05		

CT: Computerized tomography, MDCT: Multidetector computerized tomography

Table 6 A comparison of area of orbital apertura among various studies (Mean±SD).

		Area of orbital apertura				
Method		**Female**		**Male**		**Total**
	Right	**Left**	**Right**	**Left**		
Bones	Nitek et al. (2009) (1)	10.83 cm²	11.19 cm²	11.39 cm²	11.46 cm²	
MDCT	Attia et al. (2018) (13) (128 section)	97.8±10.2 cm²	97.7±10.8 cm²	103.8 ± 14.5 cm²	104.7±11.1 cm²	
	Acar et al. (2019) (14) (128 section)	1205 ± 66 mm²		1258± 67 mm²		1246± 70 mm²
	El-Farouny et al. (2021) (19) (128 section)	100.40±7.23 cm²	99.57± 6.14 cm²	111.964± 11.44 cm²	109.67±11.47 cm²	
	Present study (256 section)	994.74 ± 144.17 mm²	991.14 ± 143.99 mm²	1055.26 ± 117.82 mm²	1048.57 ± 104.01 mm²	

MDCT: Multidetector computerized tomography

was 30-39 age group in right side, 60 age and over in left side. The narrowest height, width and depth of the orbit were observed in the 0 – 9 age group (Table 2).

When the height and width of the orbit were evaluated according to age groups for both sides, it was observed that there was a statistically significant difference between the mean values between the 0-9 age range and the 10-14 age range and all other age groups ($p<0.05$). This result showed that the development of these structures continued until the age of 15-19 years on both sides, and reached the adult size from the age of 15-19 years (Table 3).

The difference between the mean values 0-9 age range years, except to 10-14, 15-19, 20–29 age range, all other age groups was found to be statistically significant. ($p<0.05$). In left side, depth of the orbit were evaluated according to age groups for both sides, it was observed that there was a statistically significant difference between the mean values between the 0-9 age range and the 10-14 age range and all other age groups ($p<0.05$) (Table 3). This result showed that the development of depth of the orbit continued until the age of 30-39 years, and reached the adult size from the age range, in right side. In contrast to in left, development of depth of the orbit continued until the age of 15-19 years, and reached the adult size from this age range (Table 3).

Medial and Lateral Wall Lengths of Orbit

There was no statistically significant difference in the length of the medial wall of the orbit by gender for both sides ($p>0.05$). On the other hand, the length of the lateral wall was found to be statistically significantly larger on both sides in male than in female ($p<0.05$) (Table 1).

The medial and lateral wall lengths were found to be greater in left side than in right side, but this difference was not statistically significant ($p>0.05$). The medial and lateral wall mean lengths are given in Table 1 separately for each groups.

The medial and lateral wall mean lengths were compared according to age groups and a statistically significant difference was observed ($p<0.05$). The longest medial wall of the orbit were found to be 60 years old and over on the right side, 15-19 year group on the left side, and the longest lateral wall was observed to be 50-59 year group on the right side and 60 years old and over on the left side. The shortest lengths for these parameters were observed in the 0 – 9 age group for both sides (Table 3).

When the lateral wall was evaluated according to age groups for both sides, it was observed that there was a statistically significant difference between the mean values between the 0-9 age range and the 10-14 age range and all other age groups ($p<0.05$). This result showed that the development of these structure continued until the age of 15-19 years on both sides, and reached the adult size from the age of 15-19 years (Table 3).

Area of orbital apertura

The area of the orbital aperture was found to be statistically significantly larger in males than in females, on both sides ($p<0.05$) (Table 1).

The means area of the orbital aperture were larger in right sides than in left sides, but this difference was not statistically significant ($p>0.05$). The means areas of the orbital aperture are given in Table 1 separately for each groups.

When the areas of the orbital aperture was compared according to age groups, a significant difference was

found for both sides (p<0.05). On both sides, the age group with the largest area was 50-59 years, while the smallest area was 0-9 years (Table 3).

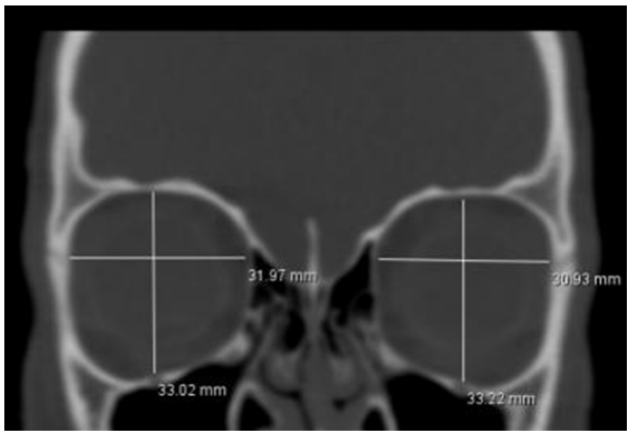

Figure 1 Measurement of height and width of the orbit

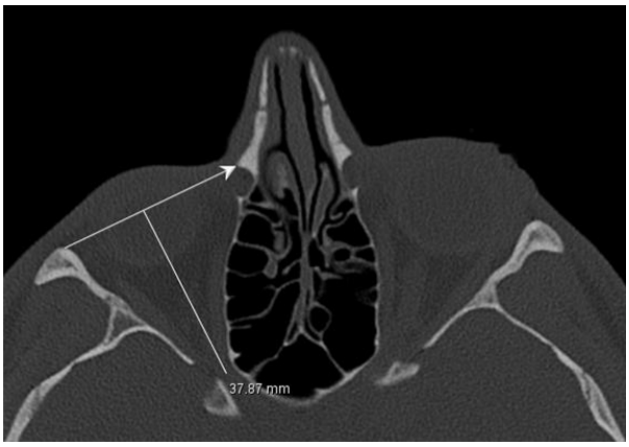

Figure 2 Measurement of depth of the orbit

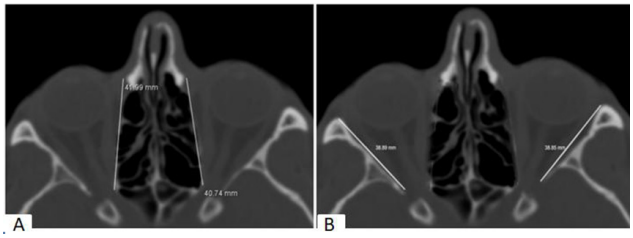

Figure 3 Measurement of medial (A) and lateral (B) wall lengths of orbit

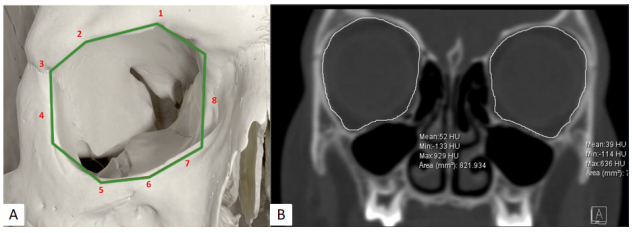

Figure 4 Measurement of area of orbital apertura (A:The supraorbital foramen (notch) on the supraorbital margin bone line (1), the anterior edge of the lacrimal fossa flor (2), the frontozygomatic suture (3), lateral margin of orbit (4), the infraorbital margin (5), the level of infraorbital foramen (6), the point of junction of the infraorbital margin and the medial magrin (7) and the medial margin bone line (8), B: Coronal section)

Discussion

The detailed anatomy of the orbit is important because it concerns many pathologies and surgical approaches, including orbital trauma, thyroid orbitopathy, and chronic orbital hyperesthesia (15).

Orbital nerves and their accompanying structures have a high risk of injury during orbital surgery. For this reason, the anatomy of the region has been the subject of study for many years. In most of the studies, dry bones have been examined, and the study data obtained with the MDCT method, which is a newly developed technology, is quite limited. In addition, researchers have generally focused on examining the differences in gender and in right-left sides, and studies evaluating the changes according to age in detail are very limited in the available literature. In our study, the MDCT method was used to examine the morphometry of orbit, its differences according to gender and body side, and its changes and developments according to age.

The skeleton plays an important role in determining gender from the point of view of forensic medicine. Morphological features of various structures of the skull have been the subject of studies due to the fact that it has the potential to identify the individual (1). The orbit is a valuable structure for determining gender, as it has a structure that is relatively resistant to trauma (16).

The studies in which the height of the orbit is evaluated are summarized in Table 4. It has been reported from these studies that the height of the orbit is generally not affected by gender. As in the study of Kaya et al. (2014) (17), Sinanoglu et al. (2016) (18) and Acar et al. (2019) (14), it was observed that the orbital height was statistically higher in males than in females in our study (p<0.05). This similarity suggests that the height of the orbit is influenced by race (These studies were conducted in the Turkish population.). In Nitek et al (2009)'s study (1), it was noted that this parameter varies depending on the body side and is significantly larger on the left side (p<0.05). Similarly to previous studies (9, 10, 13, 16, 19), it was found in our study that the height of the orbit was not affected by the body side. In our study, while the orbital height was similar to CT studies (13, 14, 17, 19), it was found that it was larger than the results of dry bone and direct graphy studies. The difference in the results of the study may be different methods, race and age groups. In dry bone studies, the age range of Sangvichien et al. (2007) (20) was reported as 18-86 years, while other studies do not have age information. In the study conducted with direct radiography, the age range was reported as 20-50 years. Although the Turkish population was examined in the study of Sinanoglu et al. (2016) (18), the results of this study are larger than our results. The reason for this situation may be the evaluation of only

adult individuals (average age: 32.6) in the relevant study. Because according to our study results, the orbital height reaches adult dimensions between the ages of 15 and 19.

The studies in which the width of the orbit is evaluated with various methods are summarized in Table 4. As in some studies (10, 14, 16, 17, 18, 19), it was found in our study that man have a statistically significantly wider orbit than female ($p<0.05$). Consistent with the dry bone (1, 9) and MDCT (13, 19) studies evaluating the orbital width according to the side, it was also found in our study that the width did not show a significant difference between the sides ($p>0.05$). In our study, it was observed that the orbital width was generally smaller than the other studies in the table, which is because it was thought that the method used may be due to the age and race differences of the individuals. In addition, in the studies that provided age information from the studies in the table, it was seen that only adults were included in the study. In our study, individuals between the ages of 3 months and 90 were evaluated, and it was determined that the 0-9 age group had the narrowest orbit and the 50-59 age group had the widest orbit. In addition, the fact that the orbital width reaches adult sizes in the 15 - 19 age group according to our study explains and supports this situation.

Orbital depth was found to be unaffected by the body side in Nitek et al's (2009) (1) (n=100, male; right: 50.3 mm, left: 50 mm; female; right: 46.8 mm, left: 47 mm) research and in our study ($p>0.05$). In the study of Acar et al. (2019) (14) (n=100), it was reported that this value is more in male (46.5±2 mm) than in female (45.5±2.4 mm). In our study, it was also found that the it was larger in male in left side ($p<0.05$), while the right side was not affected by gender ($p>0.05$).

The orbit is an important region due to its close relationship with the paranasal sinuses and the neurovascular formations passing through the openings in its structure (21). The anatomy of the medial orbital wall is important for the successful results of some orbital procedures such as ethmoidal vessel ligation, medial wall fractures, orbital decompression, ethmoid sinus exenteration, and transethmoidal sphenoidotomy. Damage to this structure may result in herniation of the orbital fat tissue into the ethmoidal sinus with careless dissection, complicating vision during surgery and resulting in enophthalmos after surgery (22). An important anatomical point on this wall is the anterior lacrimal crest (12). The studies in which the distance between the anterior lacrimal crest and the anteromedial of the optic canal is evaluated are summarized in Table 5. In accordance with the study of Thanasil Huanmanop et al. (2007) (4), it was also observed in our study that this distance was not affected in terms of gender and side ($p>0.05$). In the study of Kumar and Gnanagurudasan (2015) (10), it was reported that this distance was not affected by the body side difference, but it was longer in male than in female. Similarly, in the study of Nitek et al. (2009) (1), the medial wall was found to be longer in male than in female, while in the study of Nitek et al. (2015) (23) it was stated that this distance was longer on the right than on the left ($p<0.05$). In the study of Oester Jr et al (2012) (11), it was evaluated in healthy individuals and individuals with vision loss, and it was reported that there was no significant difference between the two groups ($p>0.05$).

The lateral wall of the orbit is an important site for lateral orbitotomy and excision of the lacrimal gland. The reference point in this area is the superior orbital fissure, through which important neurovascular structures pass (12). Anterolateral edge of the superior orbital fissure and front corner of this wall with the distance between has been investigated in some studies and these studies are also summarized in Table 5. In the study of Kumar and Gnanagurudasan (2015) (10), it was reported that this distance is significantly longer on the right side than on the left. In our study, no difference was found in terms of the body side where it was located ($p>0.05$). In addition, in our study, it was found that the lateral wall is longer in male than in female, on both sides ($p<0.05$). In the study of Oester Jr et al (2012) (11), healthy and visually impaired individuals were evaluated and it was reported that there was no significant difference ($p>0.05$).

The studies in which the area of orbital apertura is evaluated with various methods are summarized in Table 6. As in some studies (13, 14, 19), it was found in our study that male have a statistically significantly larger area of orbital apertura than female ($p<0.05$). In the study of Nitek et al. (2009) (1), it was reported that the area of orbital apertura mainly depends on the body side and is statistically significantly larger on the left side. In contrast to this result, in the study of Acar et al. (2019) (14), it was found that the area of orbital apertura was not affected in terms of the body side. Similarly, the area averages in our study are not affected by the side where they are located ($p>0.05$).

Conclusion

The orbit is an important cavity containing vision-related formations and important neurovascular structures, and adjacent to various regions. Due to the varying sizes of this complex region among individuals, it has been studied by anatomists and clinicians for many years. Our study shows that the orbit is a dynamic structure, its dimensions continues to change with growth and development during youth and with the effect of aging throughout adulthood. In the available literature, studies have usually been conducted with adult individuals, and very few studies have evaluated only the young population. In our study, both pediatric and adult individuals were examined in 8 different age groups by accepting that prepubertal age limit is before 15, postpubertal age limit is after 15 and geriatric age limit is 60 (7, 8). The development of height, width and lateral wall of the orbit continued until the age of 15-19 years, and reached the adult size from this age range. This result shows that the development of the

orbit is influenced by the pubertal period. In addition, the effect of gender and the side where it is located on the orbital dimensions was investigated. The height, width, area, lateral wall of the orbit were found to be statistically significantly larger in male than in female ($p<0.05$). In all the orbital parameters evaluated, it was found that the structure was not affected by the side in which it was located ($p>0.05$).

In this study presents reference ranges for the morphometry of orbits that maintain structural integrity and are intact in Turkish population, and evaluates them separately according to gender, body side and developmental age. Due to the neurovascular structures contained in this structure, there is a restriction for surgical procedures, as well as the fact that their size changes during growth increases the importance of this region. In addition, our study provides data that proves the evaluability of the orbit for gender determination, so we think that it will contribute to the existing literature for forensic medicine.

Ethical approval: All procedures performed in this study 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. Ethical approval (approval number 2020/01) was given by the Local Ethics Committee of the Medical Faculty. This single-center retrospective study was approved by the local institutional review board with a waiver of the requirement for written, informed consent. This study was conducted at Selcuk University Faculty of Medicine.

Declaration of Interests: The authors declare that they do not have any conflict of interest.

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References

1.Nitek S, Wysocki J, Reymond J, Piasecki K. Correlations between selected parameters of the human skull and orbit. Med Sci Monit. 2009; 15 (12): 370-7.

2.Cheng AC, Lucas PW, Yuen HK, Lam DS, So K-F. Surgical anatomy of the Chinese orbit. Ophthalmic Plastic Reconstr Surg. 2008; 24 (2): 136-41.

3.Servat JJ, Black EH, Nesi FA, Gladstone GJ, Calvano CJ. Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery, Springer International Publishing; 2020. p. 3-65.

4.Thanasil Huanmanop M, Sithiporn Agthong M, Vilai Chentanez M. Surgical anatomy of fissures and foramina in the orbits of Thai adults. J Med Assoc Thai. 2007; 90 (11): 2383-91.

5.Hayek G, Mercier P, Fournier H. Anatomy of the orbit and its surgical approach. Adv Tech Stand Neurosurg. 2006; 35-71.

6.Weaver AA, Loftis KL, Tan JC, Duma SM, Stitzel JD. CT based three-dimensional measurement of orbit and eye anthropometry. Invest Ophthalmol Vis Sci. 2010; 51 (10): 4892-7.

7.Alkofide EA. The shape and size of the sella turcica in skeletal Class I, Class II, and Class III Saudi subjects. Eur J Orthod. 2007; 29 (5): 457-63.

8.Chauhan P, Kalra S, Mongia SM, Ali S, Anurag A. Morphometric analysis of sella turcica in North Indian population: a radiological study. Int J Res Med Sci. 2014; 2 (2): 521-6.

9.Rajangam S, Kulkarni R, Quadrilos L, Sreenivasulu S. Orbital dimensions. Indian J Anat. 2012; 1: 5-9.

10.Kumar SS, Gnanagurudasan E. Morphometry of bony orbit related to gender in dry adult skulls of South Indian population. Int J Health Sci Res. 2015; 5: 207-14.

11.Oester Jr AE, Sahu P, Fowler B, Fleming JC. Radiographic predictors of visual outcome in orbital compartment syndrome. Ophthalmic Plast Reconstr Surg. 2012; 28 (1): 7-10.

12.Karakas P, Bozkir M, Oguz O. Morphometric measurements from various reference points in the orbit of male Caucasians. Surg Radiol Anat. 2002; 24 (6): 358-62.

13.Attia AM, Ghoneim M, Elkhamary SM. Sex discrimination from orbital aperture dimensions using computed tomography: Sample of Egyptian population. Journal of Forensic Radiology and Imaging. 2018; 14: 32-8.

14.Acar G, Buyukmumcu M, Guler I. Computed tomography based analysis of the lamina papyracea variations and morphology of the orbit concerning endoscopic surgical approaches. Braz J Otorhinolaryngol. 2019; 85 (5): 551-9.

15.Leong SC, Karkos PD, MacEwen CJ, White PS. A systematic review of outcomes following surgical decompression for dysthyroid orbitopathy. The Laryngoscope. 2009; 119 (6): 1106-15.

16.Ghorai L, Asha M, Lekshmy J, Rajarathnam BN, Kumar HM. Orbital aperture morphometry in Indian population: A digital radiographic study. Journal of Forensic Dental Sciences. 2017; 9 (2): 61.

17.Kaya A, Uygun S, Eraslan C, Akar GC, Kocak A, Aktas E, Govsa F. Sex estimation: 3D CTA-scan based on orbital measurements in Turkish population. Rom J Leg Med. 2014; 22 (4): 257-62.

18.Sinanoglu A, Orhan K, Kursun S, Inceoglu B, Oztas B. Evaluation of optic canal and surrounding structures using cone beam computed tomography: considerations for maxillofacial surgery. J Craniofac Surg. 2016; 27 (5): 1327-30.

19.El-Farouny RH, Hassanien SA, Azab RM. Morphometric Evaluation Of Piriform And Orbital Aperture In Sex Discrimination By Using Computed Tomography In Egyptian Population. Egypt J Forensic Sci Appli Toxicol. 2021; 21 (1): 1-12.

20.Sangvichien S, Boonkaew K, Chuncharunee A, Komoltri C, Piyawinitwong S, Wongsawut A, Namwongsa S. Sex determination in Thai skulls by using craniometry: multiple logistic regression analysis. Siriraj Med J. 2007; 59 (5): 216-21.

21.Aziz SR, Marchena JM, Puran A. Anatomic characteristics of the infraorbital foramen: a cadaver study. J Oral Maxillofac Surg. 2000; 58 (9): 992-6.

22.Akdemir G, Tekdemir I, Altin L. Transethmoidal approach to the optic canal: surgical and radiological microanatomy. Surg Neurol. 2004; 62 (3): 268-74.

23.Nitek S, Bakoń L, Sharifi M, Rysz M, Chmielik LP, Sadowska-Krawczenko I. Morphometry of the orbit in East-European population based on three-dimensional CT reconstruction. Advances in Anatomy. 2015; 1-10.

24.Ozer MO, Oz II, Serifoglu I, Buyukuysal MC, Barut C. Evaluation of Eyeball and Orbit in Relation to Gender and Age. J Craniofac Surg. 2016; 27 (8): e793-e800.

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ORIGINAL ARTICLE

Association of Celiac Disease and Plasminogen Activator Inhibitor-1 Polymorphism

Çölyak Hastalığı ve Plazminojen Aktivatör İnhibitör-1 Polimorfizminin İlişkisi

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ABSTRACT

Objective: Celiac disease (CD) is an autoimmune disease. Although susceptibility to thrombosis in celiac patients has been reported in case studies, the cause is not yet known. PAI-1 inhibits fibrinolysis. In this study, the association between celiac disease and PAI-1 4G/5G polymorphism was investigated among celiac patients whose disease were confirmed by intestinal biopsy and healthy controls.
Methods: Biopsy-diagnosed celiac patients (n=56) and healthy controls (n=52) were included in the study. PCR-RFLP method was used for PAI-1 genotyping and the results were compared according to statistical significance.
Results: The PAI-1 4G allele associated with thrombotic risk and inflammation was found to be higher than the 5G allele in cases (0.63 and 0.36, respectively, p=0.054). When the age at diagnosis was compared according to the PAI-1 variants, no significant difference was found (p=0.3). Although the genotype frequencies were similar in 4G/4G patients and controls, the 5G/5G genotype, known as the protective genotype, was found to be higher in controls (35% and 18%).
Conclusion: In our study, the 4G allele of PAI-1, which plays a role in the susceptibility to thrombosis, was observed more frequently in celiac patients compared to the control group. Studying genetic markers of thrombosis in celiac patients is important for individual prophylaxis.

Keywords: Celiac disease; Plasminogen Activator Inhibitor 1; Polymorphism; Thrombosis

ÖZ

Amaç: Çölyak hastalığı (ÇH) otoimmün bir hastalıktır. Çölyak hastalarında tromboza yatkınlık vaka çalışmalarında bildirilmiş olmasına rağmen nedeni henüz bilinmemektedir. Plazminojen aktivatör inhibitörü-1 (PAI-1), fibrinolizi inhibe eder. Bu çalışmada biyopsi ile çölyak tanısı konulmuş kişiler ve sağlıklı kontrollerde çölyak hastalığı ile PAI-1 4G/5G polimorfizmi arasındaki ilişki araştırılmıştır.
Yöntemler: Çalışma için 56 biyopsi ile tanı konulmuş çölyak hastası ve 52 sağlıklı kontrol seçilmiştir. PAI-1 genotiplendirmesi PZR-RFLP metodu ile yapılmış, sonuçlar istatistiksel anlamlılığa göre karşılaştırılmıştır.
Bulgular: Trombotik risk ve enflamasyonla ilişkilendirilen PAI-1 4G aleli vakalarda 5G aleline oranla yüksek bulundu (sırasıyla 0.63 ve 0.36, p=0.054). PAI-1 varyantlarına göre tanı yaşları kıyaslandığında anlamlı bir fark bulunmadı (p=0.3). Genotip olarak 4G/4G hastalar ve kontrollerde benzer olsa da koruyucu genotip olarak bilinen 5G/5G genotipi kontrollerde hastalara kıyasla yüksek bulunmuştur (35% ve 18%).
Sonuç: Çalışmamızda çölyak hastalarında kontrol guruba göre PAI-1'in tromboza yatkınlıkta rol oynayan 4G aleli daha sık gözlenmiştir. Çölyak hastalarında tromboz genetik belirteçlerinin çalışılması bireysel proflaksi açısından önem taşımaktadır.

Anahtar Kelimeler: Çölyak hastalığı; Plazminojen aktivatör inhibitörü 1; Polimorfizm; Tromboz

Introduction

Celiac Disease is a multifactorial disease in which both environmental (gluten) and genetic (HLA and non-HLA genes) factors play a role. An abnormal immune response to gluten, causes inflammation and injury to the small intestine mucosa (1). The world prevalence of celiac disease is 0.5-1.0% (2). People with autoimmune diseases and diabetes, and relatives of Celiac patients are at high risk for the disease. Gastrointestinal complaints such as diarrhea, steatorrhea, and weight loss due to malabsorption is common. Anemia, osteoporosis, dermatitis, herpetiformis, neurological problems and dental enamel hypoplasia may accompany as atypical symptoms. Celiac disease is diagnosed by biopsy and by the presence of a genetic factor predisposing to positive anti-tissue transglutaminase and/or antiendomysial antibodies (HLA) DQ2/8 antigen (3). Although a predisposition to thrombosis in celiac patients has been reported in case studies, the cause is not yet known (4). To date, hyperhomocysteinemia, B12 deficiency, endothelial or platelet dysfunction have been investigated for predisposition to thrombosis (5). The diversity of hypercoagulation-related diseases associated with celiac disease indicates that the etiology of hypercoagulability in celiac disease is multifactorial, and that thromboembolism prophylaxis should be regulated according to the variety of predisposing factors. Plasminogen activator inhibitor-1 (PAI-1) is found in the alpha granules of platelets and in plasma. It inhibits fibrinolysis by inhibiting the conversion of plasminogen to plasmin. At the same time, as a serine protease, it has an important role in many cellular

activities such as wound healing, organ fibrosis, aging, autophagy, digestion, immune system and tumor metastasis (6-9).

Although many variants have been reported in the *PAI-1* gene, the 1bp ins/del 4G/5G polymorphism in the transcription start region affects PAI-1 levels. Although both alleles bind to the transcriptional activator, 5G also binds to the transcriptional repressor. Thus, the 4G allele increases the transcription of PAI-1, especially in the homozygous form (10). The aim of the study is to compare *PAI-1* 4G/5G polymorphism genotypes and allele frequency in individuals diagnosed with celiac and healthy controls.

Materials and Methods

Study group:

The study included 56 patients who applied to the gastroenterology outpatient clinic of Ümraniye State Hospital between July 2017 and December 2018 and were diagnosed with celiac disease as a result of small bowel biopsy, and 52 healthy controls without any gastrointestinal complaints. The study was performed according to the Helsinki declaration and was approved by the Institutional Review Board with the decision number 2017-3/36. Written informed consent was obtained from all participants. Exclusion criteria from the study were defined as people who read the consent form and refused to participate in the study, people with an autoimmune disease before the diagnosis of celiac disease, cancer patients, celiac patients with infectious diseases (eg. hepatitis B). Subjects were asked to fill out a questionnaire about their demographic information, dietary habits, physical activity, family history in terms of celiac and cardiovascular diseases.

Peripheral blood collection and DNA isolation:

All genetic analysis were done in Acibadem Mehmet Ali Aydınlar University Research Laboratory. Two cc of blood from the peripheral vein (Median cubital vein) from the patients and controls was taken into EDTA tubes and stored at 4°C. Commercial kit were used for DNA isolation according to the protocol described by manufacturers (NucleoSpin® Tissue XS- Macherey Nagel, Düren, Germany). After DNA isolation, DNA purity was measured with Varioskan Flash® Thermo Scientific (Waltham, MA, USA). DNA isolation was considered successful, if A260/280 absorbance ratio was 1.7-2.0 for all samples. DNA amounts were calculated as 40-60 ng/µl.

PCR (Polymerase Chain Reaction) and RFLP (Restriction Fragment Length Polymorphism) experiments

DNA was amplified by PCR with appropriate primers. Genetic variants were analyzed using the RFLP method. Primers required to amplify the region with the *PAI-1* 4G/5G polymorphism (rs1799889) was

F: 5'- CACAGAGAGAGTCTGGCCACGT-3',

R: 5'-CCAACAGAGGACTCTTGGTCT-3' (11). MyTaq™ Mix (Meridan Bioscience, Memphis, TN, USA) was used for the PCR Reaction. Samples were amplified on the BIO-RAD T100 Thermal Cycler (BIO-RAD Laboratories, CA, USA). PCR cycles were determined as (94°C, 3', (94°C, 30'', 53°C 30'', 68°C 20'')x 35 cycles, 68°C 2', 4°C ∞). PCR products were analyzed by 2% agarose (Low EEO) gel electrophoresis and visualized on the ChemiDoc MP Imaging System (BIO-RAD, CA, USA).

The restriction enzyme *BslI* (New England Biolabs®, *Inc. MA,* USA) was used to identify the *PAI-1* variants in the amplified region. RFLP is based on the principle that variations in the DNA sequence can alter restriction enzyme cleavage patterns. Since there was no enzyme cut in the region of 4G/4G genotype, the product was seen as a single band of 100 bp, the enzyme cuts in 5G/5G genotype, and it was observed as 2 bands of 77 bp and 23 bp. In heterozygous 4G/5G genotype, 3 bands (100,77,23) were observed for both cleaved and uncleaved fragments (Figure 1)

Statistical analysis

The SPSS program (version 20.0 for Windows, SPSS Inc. Chicago, IL) was used to evaluate the statistical data. One Sample Kolmogorov-Smirnov test was used to analyze the normality of the data. Parametric tests were used for normally distributed data and otherwise non-parametric tests were used. Continuous variables with normal distribution were expressed as mean ± standard deviation, and variables in non-parametric distribution were expressed as median and interquartile range (IQR). Categorical variables were expressed in percentiles (%). Values with $p< 0.05$ were considered statistically significant.

Results

The study included 56 cases and 52 controls. Gender distribution was different between the cases and controls. Of the case group (n=56), 11% were male, 89% were female; 39% of the control group (n=52) were male and 61% were female ($p<0.001$). The mean ages of the case and control groups were 38±11 and 22±3 ($p=0.001$), respectively. There was no statistically significant difference in body mass index (BMI) between cases and controls (24.5±4.7, 23±4.5 ($p=0.3$)). The mean age at which the patients were diagnosed was 32.8 years. In the survey, 11.5% of the patients stated that they started a diet after the diagnosis of Celiac disease.

There was no statistically significant differences in the family history of cases and controls. Cardiovascular disease was present in 7.6% of patients and 12.5% of controls ($p=0.375$). Patients exercised less than the controls. The questionnaire results displayed that walking 2 km at least 3 times a week as exercise was present in 12% of patients and 69% of controls ($p<0.001$). Genotype frequencies of cases and controls were as

shown in Table 1. Allele frequencies for 4G and 5G were as shown in Table.2.

Allele frequencies were compatible with Hardy Weinberg equilibrium (X2 =1.5, p=0.2) When the allele frequencies were compared between the cases and controls, the 4G allele was more frequently observed in cases versus controls (0.63 and 0.37, respectively; p=0.054). The 5G/5G genotype, known as the protective genotype, was found to be more frequent in controls than the cases (35% and 18%). No statistically significant difference was found in the age at diagnosis between the genotype groups in celiac patients.

Table 1. Genotype frequencies according to PAI-1 variants in cases and controls

PAI-1 4G/5G	4G/4G	4G/5G	5G/5G
Cases n(%)	24(43)	22(39)	10(18)
Controls n(%)	23(44)	11(21)	18(35)

Table 2. Frequency of 4G and 5G alleles in patients and controls

	4G	5G
Cases	0.63	0.37
Controls	0.55	0.45

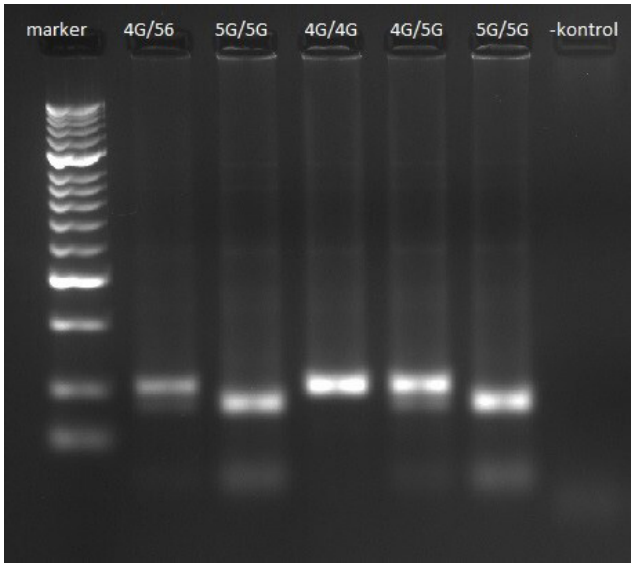

Figure 1. The detection of *PAI-1* variants by *BslI* enzyme restriction of PCR amplified DNA on 2% agarose gel (4G/4G=100bp, 4G/5G=100bp,77bp,23 bp, 5G/5G= 77bp,23 bp)

Discussion

Celiac disease is a complex phenotype with vascular effects. Thromboembolic events in celiac patients are included in the literature. The pathophysiology in Celiac disease involves thrombosis, and inflammation (12). Plasminogen activator inhibitor 1 (PAI-1) is a serpin inhibitor of the plasminogen activators urokinase-type plasminogen activator (uPA) and tissue plasminogen activator. PAI-1 plays a role in thrombosis and inflammation, and its relationship with celiac disease is the subject of experimental and clinical research. PAI-1 is involved in a wide range of biological and pathological processes such as wound healing and angiogenesis, extracellular matrix remodeling.

In the literature, PAI-1 blood levels have also been found to have an effect on autonomic nervous system disorder seen in Celiac patients (15), and PAI-1 levels have been associated with inflammatory changes in the colonic mucosa (16). Inflammatory changes seen in celiac disease question the role of PAI-1 in this disease.

The *PAI-1* 4G/5G polymorphism results from a single nucleotide deletion/insertion (4G/5G). Depending on the increase in PAI-1 concentration in the 4G/4G genotype, fibrinolytic activity is impaired and susceptibility to thrombotic events increases. Studies report that 4G allele of the polymorphism increases the tendency to inflammation and clotting in coronary patients.

Celiac disease is in the class of complex diseases in which genetic and environmental factors play a role. The aim of our study is to evaluate the effects of *PAI-1* 4G/5G polymorphism, which affects PAI-1 levels, on the pathogenesis of Celiac.

According to our results, the *PAI-1* 4G/4G variant was not associated with age at diagnosis in 56 celiac patients. All cases were diagnosed with biopsy and 52 healthy controls were included for comparison. The study findings indicate that 4G allele frequency is higher in Celiac cases compared to the controls. The study findings can explain the increased thrombotic events in Celiac cases. There are limited studies in the literature on this subject. The limitation of the study is that it was studied with a small number of cases and controls. It is important to expand studies in larger cohorts to include other thrombotic factors. In addition, polymorphism studies alone are not sufficient to understand the complex diseases. In addition to polymorphism studies, studies examining gene expression at the transcription level are required to assess the functional effects.

The expressions of cells affected by different diseases can be compared with the gene expressions of healthy cells and used in disease diagnosis and target drug design. Investigation of genetic susceptibility to thrombosis is recommended for thromboembolic prophylaxis in adult celiac patients (17). For this reason, the importance of thrombosis genetic markers in celiac patients is a current research topic.

References

1.Farrell RJ, Kelly CP. Celiac sprue. N Engl J Med 2002;346(03):180–88.

2.Gujral N, Freeman HJ, Thomson ABR. Celiac disease: Prevalence, diagnosis, pathogenesis and treatment World J Gastroenterol. 2012;18(42):6036–59.

3.ESPGN Group: Revised criteria for diagnosis of coeliac disease. Report of Working Group of European Society of Paediatric Gastroenterology and Nutrition. Arch Dis Child 1990;65:909-11

4.Ghannouchi Jaafoura N, Atig A, Bouker A, Alaoua O, Ben Jazia E, Khalifa M, Bahri F. Intracardiac thrombosis during celiac disease. J Mal Vasc. 2014;39(3):203-6.

5.Lerner A, Blank M. Hypercoagulability in celiac disease--an update. Autoimmun Rev. 2014;13(11):1138-41.

6.Agirbasli M. Pivotal role of plasminogen-activator inhibitor 1 in vascular disease. Int J Clin Pract 2005;59(1):102-6.

7.Flevaris P, Vaughan D.The Role of Plasminogen Activator Inhibitor Type-1 in Fibrosis. Semin Thromb Hemost. 2017;43(2):169-77.

8.Wang ZH, Ren WY, Zhu L, Hu LJ. Plasminogen activator inhibitor-1 regulates LPS induced inflammation in rat macrophages through autophagy activation. Sci World J. 2014;2014:189168.

9.Pham BT, van Haaften WT, Oosterhuis D, Nieken J, de Graaf IA, Olinga P. Precision-cut rat, mouse, and human intestinal slices as novel models for the early-onset of intestinal fibrosis. Physiol Rep. 2015;3(4). pii: e12323

10.Eriksson P, Kallin B, van 't Hooft F M, Båvenholm P, and Hamsten A. Allele-specific increase in basal transcription of the plasminogen-activator inhibitor 1 gene is associated with myocardial infarction. Proc Natl Acad Sci U S A. 1995;92(6):1851–55.

11.Rossaak JI, Van Rij AM, Jones GT, Harris EL. Association of the 4G/5G polymorphism in the promoter region of the plasminogen activator inhibitor-1 with abdominal aortic aneurysms. J Vasc Surg 2000;31:1026–32.

12.Ludvigsson JF, Welander A, Lassila R, Ekbom A, Montgomery SM. Risk of thromboembolism in 14,000 individuals with coeliac disease. Br J Haematol 2007;139(01):121–7.

13.Ciacci C, Tortora R, Scudiero O, Di Fiore R, Salvatore F, Castaldo G. Early pregnancy loss in celiac women: The role of genetic markers of thrombophilia. Dig Liver Dis. 2009;41(10):717-20.

14.Picchi A1, Pasqualini P, D'Aiello I, Cortese B, Micheli A, Limbruno U. Acute ST-elevation myocardial infarction in a 15-year-old boy with celiac disease and multifactorial thrombotic risk. Thromb Haemost. 2008 Jun;99(6):1116-8.

15.Zimmerman M, Rolandsson E, Skärstrand H, Pourhamidi K, Gottsäter A, Wollmer P, Rolandsson O, Westergren-Thorsson G, Dahlin LB. Temporal trend of autonomic nerve function and HSP27, MIF and PAI-1 in type 1 diabetes. J Clin Transl Endocrinol. 2017;8:15-21.

16.Grabarczyk E1, Szaflarska-Popławska A, Góralczyk K, Rość D. Tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1) in children with ulcerative colitis. Pol Merkur Lekarski. 2006;20(117):326-8.

17.Berthoux E, Fabien N, Chayvialle JA, Ninet J, Durieu I. Adult celiac disease with thrombosis: a case series of seven patients. Role of thrombophilic factors. Rev Med Interne 2011;32(10):600–604.

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ORIGINAL ARTICLE

Evaluation of Hematologic Parameters in Children with Down Syndrome

Down Sendromlu Çocuklarda Hematolojik Parametrelerin Değerlendirilmesi

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ABSTRACT

Objective: Congenital hematological disorders are frequently observed in patients with Down syndrome (DS). In this study, we aimed to investigate peripheral blood-derived inflammation biomarkers such as neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and eosinophil-monocyte ratio in patients with Down syndrome.
Material and Methods: Ninety-eight patients with karyotypically ascertained DS and 103 healthy controls were included. All subjects were divided into three age groups: 0-2 years (34 patients, 34 controls), 2-6 years (32 patients, 33 controls), and >6 years (32 patients, 36 controls). Demographic, clinical, and laboratory data of patients with DS who were admitted between June 2010 and December 2021 were reviewed from the file records from the pediatric allergy and immunology department.
Results: Lymphocyte, eosinophil, and eosinophil-monocyte ratio were found to be significantly lower in children with DS compared to controls in group 2 (2-6 years) and group 3 (>6 years). Platelet-lymphocyte ratio was found to be higher in children with DS in group 2 and group 3. There was no statistically significant difference between DS and controls in group 1 (<2 years) in terms of all parameters.
In group 2 (2-6 years) and group 3 (>6 years), there was a statistically significant difference between DS and controls in terms of lymphocyte, eosinophil, platelet-lymphocyte ratio, and eosinophil-monocyte ratio variables (P>0.05).
Conclusion: We found significant differences among lymphocyte, eosinophil, platelet-lymphocyte ratio, and eosinophil-monocyte ratio in patients with DS. As a result, these parameters should be evaluated carefully for clinical outcomes.

Keywords: Down syndrome, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, eosinophil-monocyte ratio, monocyte-lymphocyte ratio

ÖZ

Amaç: Konjenital hematolojik bozukluklar Down sendromunda (DS) sıklıkla gözlenmektedir. Bu çalışmada Down sendromlu hastalarda nötrofil-lenfosit oranı, trombosit-lenfosit oranı ve eozinofil-monosit oranı gibi periferik kan kaynaklı inflamasyon biyobelirteçlerini araştırmayı amaçladık.
Gereç ve yöntem: Çalışmaya karyotipik olarak tanısı konulan DS'li 98 hasta ve 103 sağlıklı kontrol dahil edildi. Hasta ve kontroller üç yaş grubuna ayrıldı: 0-2 yaş (34 hasta, 34 kontrol), 2-6 yaş (32 hasta, 33 kontrol) ve 6-18 yaş (32 hasta, 36 kontrol). Haziran 2010 ile Aralık 2021tarihleri arasındaki demografik, klinik ve laboratuvar verileri, Çocuk Alerji ve İmmünoloji bölümündeki dosya kayıtlarından yazıldı.
Bulgular: Lenfosit, eozinofil ve eozinofil-monosit oranı, DS'li çocuklarda grup 2 (2-6 yaş) ve grup 3'te (>6 yaş) kontrollere göre anlamlı derecede düşük bulundu. Grup 2 ve grup 3'te DS'li çocuklarda trombosit-lenfosit oranı daha yüksek bulundu. Grup 1'de (<2 yaş) DS ve kontroller arasında tüm parametreler açısından istatistiksel olarak anlamlı fark yoktu.
Sonuç: DS'li hastalarda lenfosit, eozinofil, trombosit-lenfosit oranı ve eozinofil-monosit oranı arasında anlamlı farklılıklar bulduk. Sonuç olarak, bu parametreler klinik sonuçlar için dikkatli bir şekilde değerlendirilmelidir.

Anahtar Kelimeler: Down sendromu, nötrofil-lenfosit oranı, trombosit-lenfosit oranı, eozinofil-monosit oranı, monosit-lenfosit oranı

Introduction

Down syndrome (DS) is a syndromic disorder that occurs once in 600-700 live births, characterized by the presence of an extra copy of chromosome 21. DS is characterized by various dysmorphic features, congenital malformations (congenital heart disease and gastrointestinal disease, etc.), and increased respiratory morbidity. DS is also associated with various immunological disorders (1). Hematological malignancies and autoimmune diseases (hypothyroidism, celiac disease, diabetes mellitus, etc.) are more common in children with DS. Recurrent respiratory tract infections are important causes of morbidity and mortality (2). 10% of newborns with DS present with anemia, thrombocytopenia, increased white blood cell count, and a picture that goes with the blast and cannot be distinguished from congenital leukemia because of clonal anomalies (3). Cocchi et al followed 30 DS children from birth to 5 years of age and found that the absolute number of white blood cells (WBC) in DS children gradually decreased from the third to the twelfth month of age and then remained fairly constant over the years. They also showed that absolute lymphocyte counts were lower in children with DS compared to healthy children (1).

Children with DS develop more infections, an increased death rate from sepsis, and an increased incidence of chronic inflammatory conditions (4). The relationship between complete blood count and neutrophil-lymphocyte (NLR), platelet-lymphocyte (PLR), and eosinophil-monocyte (EMR) ratios with inflammation in different diseases have been demonstrated (5-7). Manuel et al. (8) compared the preoperative neutrophil-lymphocyte ratios in children with 30 tetralogies of Fallot (TOF) and 30 ventricular septal defects (VSD) and found a higher neutrophil-lymphocyte ratio in children with TOF compared to children with VSD. The relationship between congenital heart diseases and comorbidities such as hypothyroidism and hypogammaglobulinemia in patients with Down syndrome is unknown.

In this study, we aimed to investigate peripheral blood-derived inflammation biomarkers such as neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and eosinophil/monocyte ratio in patients with DS. In the literature, there are no studies on this subject that reveal the relationship of these parameters with age and clinical findings in children with DS. In this study, the relationship between inflammatory parameters in peripheral blood and clinical findings in different age groups will be evaluated in children with DS.

Material and Methods

Study Population

The study included 98 patients with karyotypically ascertained DS and 103 healthy children. Patients and healthy controls ages ranged from 2 months to 16 years. All subjects were divided into three age groups: 0-2 years (34 patients, 34 controls), 2-6 years (32 patients, 33 controls), and >6 years (32 patients, 36 controls). Demographic, clinical, and laboratory data of the patients who were admitted between June 2010 and December 2021 were evaluated from the file records from the pediatric allergy and immunology department. The patient group who had clinical signs of infection and positive C-reactive protein was excluded from this study. The control group was selected among healthy children who did not suffer from allergic disease, active infection, or immune deficiency. The medical records of all the patients were checked for the presence of a cardiac defect, cardiac operation, adenoidectomy, and hypothyroidism. The study was approved by the University Ethical Board (2021/336).

Table 1: Demographic and clinical features of **patients with** Down syndrome (DS) and controls

	<2 years (group 1)		2–6 years (group 2)		>6 years (group3)	
	DS	Control	DS	Control	DS	Control
	n=34	n=34	n=32	n=33	n=32	n=36
Age, (years)	0 (0-1)	1 (0-1)	4 (2-4.8)	3 (2-4)	8.5 (7-11)	10 (7-13)
***P*-value[1]**	0.09		0.295		0.249	
Gender, n (%)						
Male	20 (51.3)	19 (48.7)	17 (54.8)	14 (45.2)	15 (48.4)	16 (51.6)
Female	14 (48.3)	15 (51.7)	15 (44.1)	19 (55.9)	17 (45.9)	20 (54.1)
***P*-value[2]**	1.000		0.538		1.000	
Congenital heart disease, n (%): Total: 66 (67.4%)						
yes	27 (79.4)	–	21 (65.6)	–	18 (56.3)	–
no	7 (20.6)	–	11 (34.4)	–	14 (43.7)	–
***P*-value[2]**			0.130			
Heart surgery, n (%): Total: 38 (38.8%)						
yes	14 (41.2)	–	13 (40.6)	–	11 (34.4)	–
no	20 (58.2)	–	19 (59.4)	–	21 (65.6)	–
***P*-value[2]**			0.823			
Adenoidectomy, n (%): Total: 17 (17.3%)						
yes	3 (8.8)	–	6 (18.8)	–	8 (2.05)	–
no	31 (91.2)	–	26 (81.3)	–	24 (75.0)	–
***P*-value[2]**			0.215			
Hypothyroidism, n (%): Total: 46 (46.9%)						
yes	16 (47.1)	–	13 (40.6)	–	17 (53.1)	–
no	18 (52.9)	–	19 (59.4)	–	15 (46.9)	–
***P*-value[2]**			0.605			

DS: Down syndrome, Data are median (interquartile range (IQR): 1st quartile-3rd quartile) or numbers (n) and percentages (%), 1: Mann-Whitney *U* test, 2: Chi-square test, $P < 0.05$ was considered a statistically significant

Table 2: Laboratory findings of **patients with** Down syndrome (DS) and controls

Laboratory findings	<2 years (group 1)		*P*-value	2–6 years (group 2)		*P*-value	>6 years (group 3)		*P*-value
	DS n=34	Control n=34		DS n=32	Control n=33		DS n=32	Control n=36	
WBC count (K/uL)	7.62±2.24	8.06±1.99	0.392[1]	6.94±2.37	8.05±1.39	**0.025**[1]	6.22 (5.10-7.75)	6.85 (5.77-7.73)	0.203[2]
Hemoglobin (g/dL)	12.3±1.57	11.6±1.21	0.052[1]	12.8±1.25	12.2±0.83	**0.016**[1]	13.8±1.15	13.3±1.14	0.075[1]
Platelet count (K/uL)	361.9±99.3	332.5±83.5	0.190[1]	331.1±79.4	339.4±86.5	0.690[1]	311.0 (266.0-338.8)	298.5 (246.3-352.0)	0.645[2]
Neutrophil count (K/uL)	2.74±1.22	2.67±1.28	0.818[1]	3.30±1.40	3.48±0.86	0.539[1]	3.39 (2.02-3.78)	3.37 (2.31-3.93)	0.663[2]
Lymphocyte count (K/uL)	3.89±1.51	4.30±1.47	0.261[1]	2.89±1.07	3.67±1.01	**0.003**[1]	2.46±0.82	2.89±0.89	**0.044**[1]
Monocyte count (K/uL)	0.63 (0.52-0.86)	0.73 (0.55-0.93)	0.290[2]	0.53 (0.40-0.75)	0.60 (0.51-0.70)	0.237[2]	0.50 (0.39-0.64)	0.51 (0.44-0.60)	0.417[2]
Eosinophil count (K/uL)	0.16 (0.10-0.28)	0.28 (0.10-0.46)	0.091[2]	0.09 (0.06-0.13)	0.20 (0.14-0.26)	**0.001**[2]	0.08 (0.02-0.12)	0.10 (0.08-0.19)	**0.005**[2]
NLR	0.68 (0.44-1.18)	0.55 (0.38-1.09)	0.411[2]	1.07 (0.84-1.54)	0.95 (0.74-1.18)	0.126[2]	1.49±0.76	1.26±0.56	0.147[1]
PLR	109.8 (69.6-127.3)	82.3 (61.6-98.1)	0.480[2]	119.8 (94.3-149.5)	92.4 (77.0-114.2)	**0.002**[2]	131.9 (107.7-155.9)	103.8 (84.3-138.9)	**0.017**[2]
EMR	0.23 (0.18-0.32)	0.36 (0.16-0.59)	0.164[2]	0.18 (0.12-0.27)	0.34 (0.22-0.47)	**0.001**[2]	0.13 (0.06-0.22)	0.20 (0.15-0.33)	**0.015**[2]
MLR	0.21±0.10	0.21±0.11	0.902[1]	0.19 (0.14-0.25)	0.16 (0.13-0.22)	0.164[2]	0.19 (0.17-0.27)	0.17 (0.14-0.24)	0.188[2]
SIRI	0.51 (0.25-0.88)	0.41 (0.31-0.80)	0.854[2]	0.68±0.38	0.65±0.34	0.749[1]	0.61 (0.45-0.94)	0.51 (0.39-0.96)	0.503[2]
SII	231.8 (167.8-420.9)	197.0 (121.2-302.9)	0.206[2]	383.2±140.2	333.2±121.8	0.129[1]	456.7±224.0	379.5±179.7	0.120[1]

DS: Down syndrome, WBC: white blood cell, NLR: neutrophil-lymphocyte ratio, PLR: platelet- lymphocyte ratio, EMR: eosinophil-monocyte ratio, MLR: monocyte-lymphocyte ratio, SIRI: systemic inflammation response index, SII: systemic immune inflammation index

Values are presented as mean ± standard deviation or median (interquartile range (IQR): 1st quartile-3rd quartile), 1 Independent sample t-test, 2 Mann–Whitney U test

P < 0.05 was considered a statistically significant

Laboratory measurements

Laboratory results including WBC, hemoglobin, platelet, neutrophil, lymphocyte, monocyte, and eosinophil were collected from the electronic medical record network. NLR, PLR, and MLR were calculated using the ratio of neutrophil, platelet, and monocyte counts to lymphocyte counts, respectively. EMR was calculated using the ratio of eosinophil to monocyte. SIRI (systemic inflammation response index) and SII (systemic immune inflammation index) were calculated as follows (SIRI = neutrophil count x monocyte count/lymphocyte count; SII = platelet count x neutrophil count/lymphocyte count).

Statistical Analysis

All analyses were performed using a statistical software package (SPSS for Windows, version 21.0, IBM Corporation, Armonk, NY, USA). Numerical data were expressed as mean ± standard deviation (SD) or median (interquartile range) and categorical variables were described as count (n) and percentages (%). Moreover, we also calculated the numbers (n) and percentages (%) of the patients with DS for some of the important comorbidities (such as hypothyroidism, and cardiac defect). The normality test after Kolmogorov–Smirnov was performed to verify the normal distribution of the continuous variables.

The Chi-square test was used the compare comorbidity distribution and gender between the study groups. Clinical characteristics between groups were evaluated using Student's t-test or the Mann–Whitney U test, as appropriate. Correlations were analyzed with the Pearson test. *P* < 0.05 was considered statistically significant.

Results

Characteristics of the Study Population

The demographical characteristics and clinical features of DS were summarized in Table 1. DS and controls were divided into three groups: group 1 (<2 years) was composed of 34 DS with a median age of 0 ages (IQR: 0-1 years), and 34 controls with a median age of 1 year (IQR: 0-1 years), the group 2 (2-6 years) by 32 DS with a median age of 4 years (IQR: 2-4.8 years), and 33 controls with a median age of 3 years (IQR: 2-4 years) and the group 3 (>6 years) by 32 DS with a median age of 8.5 years (IQR: 7-11 years), and 36 controls with a median age of 10 years (IQR: 7-13 years). No statistically significant difference was found between all three age groups between the DS and control group (group 1: P=0.09, group 2: P=0.295, and group 3: P=0.249).

The gender distribution of the three groups was similar. Group 1 (14 males and 15 females), group 2 (15 males and 19 females), and group 3 (17 males and 20 females). According to their clinical history, 67.4% (66/98) of the DS children had congenital heart disease. The frequency of heart surgery was 38.8% (38/98). Seventeen of the 98 (17.3%) children with DS had a history of adenoidectomy.46.9% (46/98) of the DS children had hypothyroidism. No statistically significant difference between all three age groups of DS for the clinical features (Table 1).

Laboratory findings

We compared simple hemogram parameters and NLR, PLR, EMR, MLR, SIRI, and SII values of three age groups in DS and controls. These results were given in Table 2. There was no statistically significant difference between DS and controls in group 1 (<2 years) in terms of all parameters. In group 2 (2-6 years) and group 3 (>6 years), there was a statistically significant difference between DS and controls in terms of lymphocyte, eosinophil, PLR, and EMR variables (P>0.05). The mean value of lymphocyte count was lower (group 2: P=0.003 and group 3: P=0.044) in both DS groups compared with controls. While the median value of PLR was higher in both of the DS groups (group 2: P=0.002 and group 3: P=0.017), eosinophil count (group 2: P=0.001 and group 3: P=0.005) and EMR (group 2: P=0.001 and group 3: P=0.015) was lower. In group 2 patients with DS had lower WBC level (P=0.025), but hemoglobin concentration was higher (P=0.016).Also, there was a positive correlation between cardiac defect and WBC levels (r = 0.257, P =0.011). NLR and SII variables were positively correlated with a history of cardiac operation (r = 0.221, P = 0.029 and r = 0.250, P = 0.013, respectively). Monocyte and WBC levels were negatively correlated with adenoidectomy history (r = -0.230, P = 0.023 and r = -0.227, P = 0.024, respectively), which was statistically significant.

Discussion

This study identified the changes in the hematological parameters of patients with DS who ranged in age from 2 months to 16 years. To our knowledge, this is the first study in which all NLR, PLR, EMR, MLR, SIRI, and SII were evaluated simultaneously in patients with DS. In the present study, we observed that PLR variables increased and EMR variables decreased in children with DS who were older than two years of age. Also, lymphocyte count was found to be low in patients >2 years old.

Total WBC count and its subtypes count and their ratios (NLR, PLR, EMR, MLR, SIRI, and SII) have recently been used as an indicator of chronic inflammation and can be easily calculated from peripheral blood analysis (9-14). The proportion of circulating leukocytes changes during the inflammatory processes. Neutrophilia is accompanied by relative lymphopenia. In the literature, it has been suggested that NLR and PLR have prognostic importance in cardiovascular diseases and diabetes mellitus, hypertension, hepatic cirrhosis, familial Mediterranean fever, and malignancies (15). It has been reported that high NLR and PLR are associated with the severity of inflammation (16). In our study, although we excluded patients with an active infection, there was a significant increase in PLR values in patients DS >2 years old. These results may be related to low lymphocyte count.

Several groups have proposed that lymphocytes are significantly lower in children with DS at all ages (17-19). In the present report, all the patients >2 years old included in the study had lower lymphocyte counts compared with controls. Reduced ranges of the different lymphocyte subsets were found to be of most significance in childhood, with subsequent improvement over age. Comorbidities and recurrent infections in patients with DS affect peripheral blood distribution in age groups. The patient group under two years of age that had very-severe morbidity and mortality was excluded from the study. Therefore, we think that the lymphocyte count was not found to be low in patients under 2 years of age in our study.

The majority of the studies on children with DS in the literature consisted 0-18 age group and these children were not divided into age groups. In one of these studies that did not divide DS children by age groups, no differences were observed in NLR and lymphocyte count (20). Another study found that WBC count, neutrophil count, total lymphocyte count, monocyte count, and platelet count were lower in patients with DS (19). In this study, we thought that it would be more accurate to divide the patient groups according to age groups. İkincioğullari et al (21) found that immune system cells differ according to age groups in healthy children. In our other study, we also divided patients into three groups and age-related changes were found in memory B cell subsets and CD19 complex (22).

Joshi et al (23) and Mitwalli et al (19) found that the WBC count was lower in children with DS compared to controls. While there was no difference in platelet count in the study of Joshi et al (23), Mitwalli et al (19) reported a significant decrease compared to controls. In our study, WBC count was found to be lower in DS

patients in group 2 compared to the control group, but there was no significant difference in platelet count.

In our study, we found that eosinophil count and EMR were lower than controls in patients with DS >2 years old. The literature concludes that allergen sensitization is not a major contributor to respiratory illnesses in children with DS (24). Verstegen et al. (25) found six of 44 DS patients with elevated IgE, and none of the 28 DS individuals tested had an allergen identified as a trigger for allergy symptoms.

Age-related changes and the relationships between some clinical co-morbidities including cardiac defects and cardiac operation were detected in peripheral blood parameters of children with DS. While cardiac defect was related to WBC count; NLR and SII values were found to be related to a history of cardiac operation. In addition, monocyte counts and WBC were negatively correlated with adenoidectomy. In our control groups, there are no co-morbidities including cardiac manifestation. So, we could not evaluate the association between the cardiac findings and peripheral blood parameters in this study. The relationships in these parameters may be related to the pathogenetic changes in DS. As a result, these parameters should be evaluated carefully for clinical outcomes.

References

1. Cocchi G, Mastrocola M, Capelli M, Bastelli A, Vitali F, Corvaglia L. Immunological patterns in young children with Down syndrome: is there a temporal trend? Acta Paediatr 2007; 96: 1479-1482.

2. Lockitch G, Singh VK, Puterman ML, Godolphin WJ, Sheps S, Tringle A, et al. Age-related changes in humoral and cell-mediated immunity in Down syndrome children living at home. Pediatr Res 1987; 22: 536–40.

3. Kuşkonmaz B, Çetin M. Down Sendromunda AML. Katkı Pediatri Dergisi 2004; 26:397.

4. Huggard D, Kelly L, Ryan E, McGrane F, Lagan N, Roche E, et al. Increased systemic inflammation in children with Down syndrome. Cytokine. 2020; 127: 154938.

5. Guthrie GJ, Charles KA, Roxburgh CS, Horgan PG, McMillan DC, Clarke SJ. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. Crit Rev Oncol Hematol. 2013; 88(1): 218-30.

6. Mertoglu C, Gunay M. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as useful predictive markers of prediabetes and diabetes mellitus. Diabetes Metab Syndr. 2017; Suppl 1: S127-S131.

7. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, et al. The relation between atherosclerosis and the neutrophil-lymphocyte ratio. Clin Appl Thromb Hemost. 2016; 22(5): 405-11.

8. Manuel V, Miana LO, Solla DJF, Fernandes N, Carrillo G, Jatene MC. Preoperative level of neutrophil□lymphocyte ratio: Comparison between cyanotic and acyanotic congenital heart disease. J Card Surg. 2021; 36(4): 1376-1380.

9. Kim HS, Jung J, Dong SH, Kim SH, Jung SY, Yeo SG. Association between high neutrophil to lymphocyte ratio and delayed recovery from Bell's palsy. Clin Exp Otorhinolaryngol. 2019; 12(3): 261-266.

10. Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A. Neutrophil lymphocyte ratio and cardiovascular disease risk: A systematic review and meta-analysis. Biomed Res Int. 2018; 2703518.

11. Mochimaru T, Ueda S, Suzuki Y, Asano K, Fukunaga K. Neutrophil to lymphocyte ratio is a novel independent predictor of severe exacerbation in asthma patients. Ann Allergy Asthma Immunol. 2019; 122(3): 337-339.e1.

12. Renaud S, Seitlinger J, St-Pierre D, Garfinkle R, Al Lawati Y, Guerrera F, et al. Prognostic value of neutrophil to lymphocyte ratio in lung metastasectomy for colorectal cancer. Eur J Cardiothorac Surg. 2019; 55(5): 948-955.

13. Hasselbalch IC, Søndergaard HB, Koch-Henriksen N, Olsson A, Ullum H, Sellebjerg F, et al. The neutrophil-to-lymphocyte ratio is associated with multiple sclerosis. Mult Scler J Exp Transl Clin. 2018; 4(4): 2055217318813183.

14. Cho Y, Kim JW, Yoon HI, Lee CG, Keum KC, Lee IJ. The prognostic significance of neutrophil-to-lymphocyte ratio in head and neck cancer patients treated with radiotherapy. J Clin Med. 2018; 7(12): 512.

15. Kara A, Guven M, Yilmaz MS, Demir D, Elden H. Are neutrophil, platelet, and eosinophil-to-lymphocyte ratio and red blood cell distribution width can be used for nasal polyposis? Eur Arch Otorhinolaryngol. 2018; 275(2): 409-413.

16. Elbistanli MS, Koçak HE, Acipayam H, Yiğider AP, Keskin M, Kayhan FT. The predictive value of neutrophil-lymphocyte and platelet-lymphocyte ratio for the effusion viscosity in otitis media with chronic effusion. J Craniofac Surg. 2017; 28(3) :e244-e247.

17. Bloemers BLP, van Bleek GM, Kimpen JLL, Bont L. Distinct abnormalities in the innate immune system of children with Down syndrome. J Pediatr 2010; 156: 804-809.

18. Kusters MAA, Verstegen RHJ, Gemen EFA, de Vries E. Intrinsic defect of the immune system in children with Down syndrome: a review. Clin Exp Immunol. 2009; 156: 189–193.

19. Mitwalli M, Wahba Y, Shaltout A, Gouida M. Lymphocyte subgroups and recurrent infections in children with Down syndrome – a prospective case control study. Cent Eur J Immunol 2018; 43: 248-254.

20. Yazar A, Yorulmaz A, Ture E, Akin F, Sert A. A relationship between subclinical hypothyroidism and hematologic parameters in patients with Down Syndrome. Fam Pract Palliat Care 2018; 3(2): 92-97.

21. İkincioğullari A, Kendirli T, Doğu F, Eğin Y, Reisli İ, Cin S, et al. Peripheral blood lymphocyte subsets in healthy Turkish children. Turk J Pediatr 2004; 46(2): 125-130.

22. Seckin AN, Ozdemir H, Ceylan A, Artac H. Age-related alternations of the CD19 complex and memory B cells in children with Down syndrome. Clin Exp Med 2018; 18: 125-131.

23. Joshi AY, Abraham RS, Snyder MR, Boyce TG. Immune evaluation and vaccine responses in Down syndrome: Evidence of immunodeficiency? Vaccine 2011; 29: 5040-5046.

24. Ram G, Chinen J. Infections and immunodeficiency in Down syndrome. Clin Exp Immunol 2011; 164(1): 9-16.

25. Verstegen RH, Kusters MA, Gemen EF, deVries E. Down syndrome B-lymphocyte populations, intrinsic defect or decreased T lymphocyte help. Pediatr Res 2010; 67: 563–6.

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ORIGINAL ARTICLE

Determination of Depression, Anxiety, Stress and Coronavirus Anxiety Levels of Parents Waiting for PCR Test Results

PCR Test Sonucu Bekleyen Ebeveynlerin Depresyon, Anksiyete, Stres ve Koronavirüs Kaygı Düzeylerinin Belirlenmesi

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ABSTRACT

Aim: This study aimed to determine the depression, anxiety, stress and coronavirus anxiety levels of parents waiting for PCR test results.
Methods: The cross-sectional study was conducted between April-October 2021. The sample of the study consisted of 372 parents determined by power analysis. Data were collected from parents awaiting their children's PCR test results in the pediatric COVID service of the Training and Research Hospital in a province in the Eastern Anatolia Region. Data were collected using a personal information form, Depression, Anxiety, Stress Scales (DASS-21) and Coronavirus Anxiety Scale (CAS). The results were evaluated at $p<0.05$ significance level.
Results: According to the study, it was determined that parents with had ≥3 children, who were ≥36 years old, married for ≥11 years, educated at high school and below had higher levels of depression, anxiety, stress and coronavirus anxiety. It was determined that the level of anxiety experienced by the parents was 2.16±4.39 in women and 1.26±3.39 in men, and the difference between the parents' mean total score on the Coronavirus Anxiety Scale was statistically significant ($p<0.05$). On the other hand, it was determined that the difference between depression, anxiety and stress between men and women was not statistically significant ($p>0.05$).
Conclusion: It was determined that PCR testing from their children due to the suspicion of COVID-19 caused depression, anxiety, stress and anxiety in parents, and the anxiety level of women was higher than men. Accordingly, parents should be given the opportunity to determine their anxiety and stress and take initiatives for it, and appropriate counseling services should be provided to reduce anxiety and stress during the pandemic process.

Keywords: COVID-19, parents, child, depression, anxiety, stress

ÖZ

Amaç: Bu araştırma, PCR test sonucu bekleyen ebeveynlerin depresyon, anksiyete, stres ve koronavirüs kaygı düzeylerini belirlemek amacıyla yapıldı.
Yöntem: Kesitsel tipte tasarlanan çalışma, Nisan-Ekim 2021 tarihleri arasında yürütüldü. Araştırmanın örneklemini güç analizi ile belirlenen 372 ebeveyn oluşturdu. Veriler, Doğu Anadolu Bölgesinde bir ilde yer alan Eğitim ve Araştırma hastanesinin çocuk COVID servisinde, çocuklarının PCR test sonucunu bekleyen ebeveynlerden toplandı. Veriler kişisel bilgi formu, Depresyon Anksiyete Stres Ölçeği (DASÖ) ve Koronavirüs Kaygı Ölçeği (KKÖ) kullanılarak toplandı. Sonuçlar $p<0.05$ anlamlılık düzeyinde değerlendirildi.
Bulgular: Çalışma bulgusuna göre ≥36 yaş olan, ≥11 yıl evli olan, lise ve altı düzeyinde eğitim gören, ≥3 çocuk olan ebeveynlerin depresyon, anksiyete, stres yaşama durumları ile koronavirüs kaygı düzeylerinin daha fazla olduğu belirlendi. Ebeveynlerin yaşadığı kaygı düzeyinin kadınlarda 2.16±4.39; erkeklerde 1.26±3.39 olduğu ve ebeveynlerin Koronavirüs Kaygı Ölçeği toplam puan ortalamaları arasındaki farkın istatistiksel olarak anlamlı olduğu belirlendi ($p<0.05$). Bununla birlikte kadın ve erkek arasında depresyon, anksiyete ve stres yaşama durumları arasındaki farkın istatistiksel olarak anlamlı olmadığı belirlendi ($p>0.05$).
Sonuç: Çocuklarından COVID-19 şüphesi nedeniyle PCR testi alınması ebeveynlerde depresyon, anksiyete stres ve kaygıya neden olduğu, kadınların kaygı düzeyinin erkeklerden daha fazla olduğu belirlendi. Buna göre ebeveynlerin kaygı ve stresinin belirlenmesine yönelik girişimlerin yapılabilmesine fırsat tanınmalı, pandemi sürecinde kaygı ve stresin azaltılması için uygun danışmanlık hizmetleri sağlanmalıdır.

Anahtar Kelimeler: COVID-19, ebeveyn, çocuk, depresyon, anksiyete, stres

Introduction

COVID-19 has been defined as an epidemic/pandemic by the World Health Organization (WHO), as it has caused a disease on a global scale in all societies across the world (1). The infection was first detected in Wuhan city of the People's Republic of China, and the first child cases were also reported by the People's Republic of China. In some reports from all over the world, it was stated that the virus caused permanent damage to the lungs in children, and that some of these damages resulted in death (2). Although it has been reported in studies that the COVID-19 epidemic has fewer negative effects on children compared to the adult population, reporting of disease and death rates in children can lead to anxiety and stress in families (3).

The most important responsibility in the development of societies and ensuring its permanence belongs to the family. Societies need powerful and strong family values in creating their culture and maintain its continuity. A powerful and strong family consists of parents who provide the physiological and social needs of the child, particularly the psychological needs, in a holistic

manner. Parents assuming common responsibility in meeting the child's needs is an undeniable fact for the development of the child and the family (4). Parents who assume common responsibility protect the child while providing care, ensure that they grow up as individuals in harmony with the society, and thus constitute a role model for future generations. In the pandemic process, the families of the children who test positive in the PCR test have difficulty in providing care for their children due to the anxiety and stress they experience, and find it difficult to be a role model for their children. Children, on the other hand, cannot fulfill their developmental responsibilities, and this situation exacerbates the families' depression, stress, and anxiety levels (5, 6).

Anxiety is the total response of a human being to threat or danger. Each experience of anxiety involves a perception of danger, thoughts about harm, and a process of physiological alarm and activation. Diagnostic criteria are include excessive anxiety and worry for at least six months, difficulty controlling the worrying (7). The accompanying behaviors display an emergency effort toward "fight or flight". The short-term perceived threat experienced by the individual leads to temporary and short-term anxiety, which is defined as state anxiety, and when the perceived threat experienced by the individual is long-term or permanent, this situation is called trait anxiety (8).

The society in which individuals live and the family environment in which they are raised affect their reaction to anxiety. The perception and duration of anxiety have individual, social, and biological roots. The ongoing pandemic process and children being infected can increase families' anxiety levels. The child being hospitalized with a potential diagnosis of coronavirus disease negatively affects the parents' mental health and can lead to affective disorders. Uncertainties related to the disease and the process we are currently in can lead to obscurities in parents, decrease their trust in future, and may trigger thoughts that the continuation of their generation is under threat (2, 4). In the previous literature review, no study has yet been found on a similar sample group. Therefore, in the present study, it was aimed to determine parents' approach to the diseases of their children, and to reveal the depression, anxiety, and stress levels of parents and children, and the attitudes that the parents whose children were tested with PCR displayed towards this situation were measured.

Materials and Methods

The present study with a cross-sectional design was conducted in the Child COVID-19 clinic of a Training and Research Hospital located in a province in the east of Turkey between April-October 2021. The sample size was calculated by using Open Source Epidemiologic Statistics for Public Health (OpenEpi) version 3.01 (9). The sample size was calculated to be 372 parents with 5% margin of error, 95% confidence interval at bilateral significance level, and 80% power.

The inclusion criteria for parents are:

- Not experiencing problems in establishing communication,
- Being literate,
- Having a child in the age range of 0-18 years from whom swab sample was taken for PCR test.

The exclusion criteria for parents are:

- Having a mental and cognitive health problem history (both in the parents and the child-based on verbal statements of parents),
- Being illiterate,
- Having a diagnosed chronic disease (both in the parents and the child)
- Having a diagnosed psychological disorder (both in the parents and the child-based on verbal statements of parents),
- Being separated/divorced from the spouse

Data Collection

Parents who met the inclusion criteria and volunteered to participate in the study were informed about the purpose and content of the study, and their written consents were taken. Data collection tools were administered face-to-face by the researcher to the parents from whose children swab sample was taken for PCR test in the patient rooms of the Child COVID-19 clinic at Malatya Training and Research Hospital. The administration of the data collection tools took about 10 minutes in one session.

Data Collection Tools

The study data were collected through Personal Information Form, Depression, Anxiety, Stress Scales (DASS-21) and Coronavirus Anxiety Scale (CAS).

Personal Information Form

Personal Information Form was developed by the researchers in two sections. In the first section of the form, there are questions identifying some descriptive characteristics of the parents (age, education level, employment status, income level, family type, etc.). The second part consists of questions inquiring about the opinions of the parents about COVID-19 (level of knowledge about COVID-19, thinking whether the COVID-19 pandemic affected the child's health). The participating parents were asked to respond to the questions on a scale of 10 (0 = I have no knowledge, 10 = I know very well; 0 = Not affected at all, 10 = Affected a lot) (10, 5, 11).

Depression, Anxiety, Stress Scales (DASS-21)

The scale is the short form of DASS-42 developed by Lovibond and Lovibond (1995) in order to evaluate individuals' depression, anxiety, and stress levels (12). Turkish adaptation and factor analyses were

performed by Saricam (2018). The scale has three subscales, which are depression, anxiety, and stress. The scale consists of 21 items, with 7 items in each subscale. The items of the 4-point Likert type scale are scored between 0 (Never) and 3 (Always). The Cronbach's alpha reliability coefficients of the subscales were found a=0.87 for the depression subscale, a=0.85 for the anxiety subscale, and a=0.81 for the stress subscale (13). In the present study, the Cronbach's alpha reliability coefficients were found as 0.863 for the depression subscale, 0.896 for the anxiety subscale, and 0.893 for the stress subscale.

Coronavirus Anxiety Scale (CAS)

The scale was developed by Lee (2020) in order to determine the anxiety cases in individuals created by the pandemic and identify the severity of anxiety symptoms (14). The Turkish adaptation and factor analyses were performed by Akkuzu et al. (2020). The 5-point Likert type scale consists of 5 items. The items of the scale are scored between 0 and 4, and there are no reversely scored items. In the single-factor scale, high scores indicate high level of anxiety (15). The scale's Cronbach's alpha reliability coefficient was found as a=0.81. The Cronbach's alpha reliability coefficient of the scale was found to be 0.915 in the present study.

Statistical Analysis

The data were analyzed by using SPSS 25.0 for Windows software (SPSS, Chicago, IL, USA). Descriptive statistics were presented as numbers, percentages, means, and standard deviations, the intergroup comparison of categorical variables was made through Chi-square test. In the intergroup comparisons for variables that meet the parametric test conditions, t-test in independent groups was performed. The results were evaluated at $p<0.05$ significance level.

Ethical Considerations

Before starting the study, ethical approval was obtained from Inonu University Non-Interventional Clinical Research and Publications Ethics Committee (Decision No: 2021/1911), and written permission was taken from the Provincial Health Directorate (Decision No: E-72527474-771). In addition, permission for COVID-19 scientific research was taken from the Turkish Republic Ministry of Health (Form code: 2021-04-26T14_32_49). In addition, this study was conducted in accordance with the Good clinical Practice (GCP) and Declaration of Helsinki. Information about the research was given to the participating parents on the first page of the survey form, and their informed consents were taken.

Results

It was determined that 56.5% of the participating parents were 36 years old and above, 56.21% had an educational status of high school and below, 74.5% had middle income status, 56.7% were unemployed, 61.0% had at least one and two children, and 57.5% had been married for more than 11 years. Among the parents waiting for PCR test results, 54.6% were waiting for the PCR results for their sons (Table 1).

Table 1. The distribution of parents according to some characteristics

Characteristics	Woman (n =203)		Man (n=169)		Total (n=372)	
	n	%	n	%	n	%
Age						
20-35 years	104	51.2	58	34.3	162	43.5
≥36 years	99	48.8	111	65.7	210	56.5
Education status						
≤ High school	125	61.6	106	62.7	231	62.1
≥ University	78	38.4	63	37.3	141	37.9
Income status						
Low	21	10.3	15	8.9	36	9.7
Medium	148	72.9	129	76.3	277	74.5
High	34	16.8	25	14.8	59	15.8
Employment status						
Employed	69	34.0	142	84.0	211	56.7
Unemployed	134	66.0	27	16.0	161	43.3
Number of living children						
≤2 children	121	59.6	106	62.7	227	61.0
≥3 children	82	40.4	63	37.3	145	39.0
Gender of the child						
Girl	98	48.3	71	42.0	169	45.4
Boy	105	51.7	98	58	203	54.6
Marriage years						
1-10 years	82	40.4	76	45.0	158	42.5
≥11 years	121	59.6	93	55.0	214	57.5

The comparison of the parents by gender in terms of depression, anxiety, and stress subscale scores and CAS mean score is presented in Table 2. Accordingly, it was determined that the difference between the parents in terms of experiencing depression, anxiety, and stress was not statistically significant ($p>0.05$). However, according to the results of the t-test in independent groups, it was found that females' anxiety levels were higher compared to the anxiety levels of males, and that the difference between the parents' CAS total mean scores was statistically significant ($p<0.05$) (Table 2).

Table 3. The distribution of the parents' scores obtained from CAS according to some characteristics (n=372).

Characteristics	Depression			Anxiety			Stress		
	Yes (n, (n, %)	**No** (n, %)	**Test* and *p* value**	**Yes** (n, %)	**No** (n, %)	**Test* and *p* value**	**Yes** (n, %)	**No** (n, %)	**Test* and *p* value**
Age									
20-35 years	74,38.5	88,48.9	χ^2=4.046	76,34.4	86,57.0	χ^2=18.579	54,34.8	108,49.8	χ^2=8.199
≥36 years	118,61.5	92,51.1	***p*=0.044**	145,65.6	65,43.0	***p*=0.000**	101,65.2	109,50.2	***p*=0.004**
Education status									
≤ High school	113,58.9	118,65.6	χ^2=1.773	127,57.5	104,68.9	χ^2=4.960	98,63.2	133,61.3	χ^2=0.144
≥ University	79,41.1	62,34.4	*p*=0.183	94,42.5	47,31.1	***p*=0.026**	57,36.8	84,38.7	*p*=0.704
Income status									
Low	19,9.9	17,9.4	χ^2=3.370	21,9.5	15,9.9	χ^2=0.126	15,9.7	21,9.7	χ^2=3.666
Medium	149,77.6	128,71.1	*p*=0.185	166,75.1	111,73.5	*p*=0.939	122,78.7	155,71.4	*p*=0.160
High	24,12.5	35,19.4		34,15.4	25,16.6		18,11.6	41,18.9	
Employment status									
Employed	108,56.3	103,57.2	χ^2=0.036	130,58.8	81,53.6	χ^2=0.981	83,53.5	128,59.0	χ^2=1.089
Unemployed	84,43.8	77,42.8	*p*=0.850	91,41.2	70,46.4	*p*=0.322	72,46.5	89,41.0	*p*=0.297
Number of living children									
≤2 children	110,57.3	117,65.0	χ^2=2.321	128,57.9	99,65.6	χ^2=2.204	96,61.9	131,60.4	χ^2=0.093
≥3 children	82,42.7	63,35.0	*p*=0.128	93,42.1	52,34.4	*p*=0.138	59,38.1	89,39.6	*p*=0.760
Gender of the child									
Girl	93,48.4	76,42.2	χ^2=1.448	99,44.8	70,46.4	χ^2=0.088	75,48.4	94,43.3	χ^2=0.937
Boy	99,51.6	104,57.8	*p*=0.229	122,55.2	81,53.6	*p*=0.766	80,51.6	123,56.7	*p*=0.333
Marriage years									
1-10 years	72,37.5	86,47.8	χ^2=4.016	76,34.4	82,54.3	χ^2=14.562	55,35.5	103,47.5	χ^2=5.312
≥11 years	120,62.5	94,52.2	***p*=0.045**	145,65.6	69,45.7	***p*=0.000**	100,64.5	114,52.5	***p*=0.021**

*****Pearson Chi-Square test, DASS-21: Depression, Anxiety, Stress Scales

Table 2. Comparison of the distribution of the parents according to the mean scores of DASS-21 and CAS (n=372)

		Woman (n =203)		Man (n=169)		Total (n=372)		
	Scales	**n**	**%**	**n**	**%**	**n**	**%**	**Test* and *p* value**
DASS-21	**Depression**							
	Yes (5-21 score)	108	53.2	84	49.7	192	51.6	X^2=0.452
	No (0-4 score)	95	46.8	85	50.3	180	48.4	*p*=0.501
	Anxiety							
	Yes (4-21 score)	129	63.5	92	54.4	221	59.4	X^2=3.173
	No (0-3 score)	74	36.5	77	45.6	151	40.6	*p* =0.075
	Stress							
	Yes (8-21 score)	93	45.8	62	36.7	155	41.7	X^2=3.160
	No (0-7 score)	110	54.2	107	63.3	217	58.3	*p* =0.075
		Mean±SD		**Mean±SD**		**Mean±SD**		**Test** and *p* value**
	CAS	2.16±4.39		1.26±3.39		1.78±3.99		*t*=2.228 **p=0.026**

*****Pearson Chi-Square test, ** Independent samples *t*-test, DASS-21: Depression, Anxiety, Stress Scales, CAS: Coronavirus Anxiety Scale

The distribution of the parents' status of experiencing depression, anxiety and stress according to certain characteristics is presented in Table 3. According to the table, the difference between the parents' status of experiencing depression, anxiety, and stress in terms of the parents' educational level, income status, employment status, the number of living children, and the gender of the child waiting for the PCR test result was determined to be statistically insignificant (p>0.05). However, while there was a statistically significant difference between the status of experiencing anxiety according to the educational status, the difference between the distribution of the status of experiencing depression, anxiety, and stress according to age and duration of marriage was determined to be statistically significant (p<0.05) (Table 3).

The comparison of the parents' scores obtained from CAS according to certain characteristics is presented in Table 4. Accordingly, it was determined the difference between the parents' status of experiencing coronavirus anxiety mean scores did not change according to their education and income status and the gender of the child waiting for the result of the PCR test, and that the difference between the groups was not statistically significant (p>0.05). On the other hand, it was found that those who were 36 years old and above, unemployed, had three children and more, and married for more than 10 years experienced higher coronavirus anxiety, and that the difference between CAS total mean scores was statistically significant (p<0.05) (Table 4).

Table 4. The comparison of the parents' scores obtained from CAS according to some characteristics (n=372)

Characteristics			**CAS**	
Age	**n**	**%**	**Mean±SD**	**Test* and *p* value**
20-35 years	162	43.5	0.92**±2.99**	*t*=-3.585, **p=0.000**
≥36 years	210	56.5	2.40**±4.52**	
Education status				
≤ High school	231	62.1	1.64**±4.06**	*t*=-0.725, *p*=0.469
≥ University	141	37.9	1.95**±3.88**	
Income status				
Low	36	9.7	2.44**±5.21**	F**=0.782, *p*=0.458
Medium	277	74.5	1.74**±3.74**	
High	59	15.8	1.38**±4.31**	
Employment status				
Employed	211	56.7	1.38**±3.61**	*t*=-2.051, **p=0.041**
Unemployed	161	43.3	2.24**±4.40**	
Number of living children				
≤2 children	227	61.0	1.30**±3.41**	*t*=-2.768, **p=0.006**
≥3 children	145	39.0	2.46**±4.68**	
Gender of the child				
Girl	169	45.4	1.43**±3.56**	*t*=-1.439, *p*=0.151
Boy	203	54.6	2.02**±4.31**	
Marriage years				
1-10 years	158	42.5	1.00**±3.10**	*t*=-3.183, **p=0.001**
≥11 years	214	57.5	2.31**±4.46**	

* Independent samples *t*-test, ** One-way ANOVA test, CAS: Coronavirus Anxiety Scale

The comparison of the parents' opinions about COVID-19 is presented in Table 5. It was determined that the parents' knowledge levels of COVID-19 were similar, and that the difference between the groups was not statistically significant (p>0.05). On the other hand, it was found that it was the females who mostly thought that the COVID-19 pandemic affected their children's health, and that the difference between the groups was statistically significant (p<0.05) (Table 5).

Table 5. The comparison of the parents' opinions about COVID-19

Opinions	**Mean ± SD**		**Test¥ and *p* value**
	Woman	**Man**	
Describe your level of knowledge about COVID-19*	6.78±2.61	7.06±2.43	*t*=-1.068, *p*=0.286
Do you think the COVID-19 pandemic is affecting your child's health?**	7.29±2.96	6.55±3.25	*t*=2.273, **p=0.024**

*¥Independent samples t-test, * 0: I have no knowledge-10 I know very well, **0: Not affected at all-10 Affected a lot*

Discussion

In the present study conducted in order to determine the status of experiencing depression, anxiety, and stress of the parents who were waiting for the PCR test results of their children and their anxiety levels, it was determined that the rate of experiencing depression, anxiety, and stress was higher in females, but that the difference between the groups was not statistically significant. Considering Coronavirus Anxiety Scale mean scores, similarly it was found that females (2.16±4.39) experienced more anxiety compared to males (1.26±3.39), and that the difference between the groups was statistically significant (Table 2). The reason for females experiencing more depression, anxiety, and stress compared to males can be explained through several causes. The caregiver culturally being the mother, the care of the sick child belonging to the mother, and the father assuming an assisting role are some of these causes (16). However, the fact that home caregivers are usually mothers in infectious diseases also increases the level of anxiety and anxiety in women. As a matter of fact, in a systematic review conducted to evaluate the risk factors of Ebola or Marburg virus, it was stated that home caregivers are at higher risk and it was stated that caregivers may have high anxiety (17). In addition, it can be said that the fact that women have less decision-making powers than men during the epidemic also contributes to this situation. In a study investigating the effect of gender in the management of the Ebola virus, it was stated that women are less likely than men to have the authority to make decisions about the epidemic, and the needs of women are not met to a large extent (19). In another study conducted, parents' care responsibilities were evaluated, and it was found that the mean score of females were higher in terms of their burden of providing care compared to the mean score of males (19). In yet another study conducted in order to determine the factors related with depression, anxiety, and stress in parents in the COVID-19 pandemic process, it was determined that being a female positively predicted anxiety (20).

According to the findings obtained in the present study, it was found that the parents at more advanced age ((≥36 years) were more likely to experience depression, anxiety, stress, and coronavirus related anxiety, and that the status of experiencing coronavirus related anxiety increased in parallel with the increasing number of children (≥3 children) and being unemployed (Table 3, Table 4). In a study in which the stress levels of families with disabled children were examined, it was determined that families with high school education experienced more stress (21). In another study conducted on parents' depression, anxiety, and stress levels in the COVID-19 quarantine process, it was revealed that having a low level of education positively predicted anxiety (20). Similarly, in another study which examined parents' stress levels and related factors, it was found that as the level of education decreased, stress scores increased (11). In yet another study which evaluated the stress levels of parents, it was reported that as the number of children increased, the parents' stress levels also increased (11). According to the findings of a study in which the depression levels of parents who had children with chronic diseases were examined, it was determined that parents with advanced age had higher depression scores (10). Finally, in a study in which emotional states of parents in relation to the coronavirus epidemic were analyzed, it was found that the negative emotional states of parents increased along with increasing age (22).

According to the results of the present study, it was determined that parents with longer duration of marriage (≥11 years) experienced more depression, anxiety, stress and coronavirus related anxiety. It can be thought that this situation may have resulted from the decrease in marital harmony and the increasing number of children along with the increasing duration of marriage. As a matter of fact, there are studies in the literature which found that as the number of children in the family increased, the stress and anxiety levels of parents also increased (10, 11), in addition to studies that evaluated the relationship between duration of marriage and anxiety level. In a study in which the relationship between anxiety level and marital harmony was investigated, it was determined that as the duration of marriage and the number of children increased, spouse harmony decreased, and the anxiety levels of spouses whose spouse harmony decreased increased (23). These results support the findings of the present study.

According to another finding obtained as a result of the study, it was determined that those who thought that the health of their children affected the health of their children in the COVID-19 pandemic were mostly women ($p<0.05$) (Table 5). It can be said that one of the reasons for this situation is that more women are the caregiver parents at home, and therefore the care power of women during the pandemic process increases. As a matter of fact, according to OECD Policy Responses to Coronavirus (COVID-19), it has been stated that women spend more time (35 minutes) caring for their children, and this rate is twice as high as men (15 minutes) (24). Therefore, it is thought that women experience more anxiety than men.

Conclusion and Recommendations

As a result of the study, it was determined that swab sample being taken for PCR test from their children due to disease symptoms caused depression, anxiety, stress, and coronavirus related anxiety in parents, and that the anxiety levels of females were higher than those of males. There is a need for more comprehensive studies that will determine the anxiety and stress levels of parents during PCR test and will enable interventions in this regard. In order to reduce the anxiety that parents experience during their children's PCR test, parents should be informed in detail about the COVID-19 disease and the purpose of PCR test, and they should be allowed to express their

concerns. Along with direct intervention, permanent support rather than spontaneous support should be provided to parents in reducing their depression, anxiety, and stress symptoms. Healthcare professionals should be provided with periodical training on coping with depression, anxiety, and stress, and thus they should be enabled to effectively consult the parents by establishing empathy with them.

Limitations of the Study

This study has some limitations. One of them is that generalization cannot be made because the parents participating in the study were reached in a single center. Another limitation is that the anxiety and anxiety states of the parents could not be evaluated in the long term.

Declaration of Conflicting Interests

The authors declare that there were no potential conflicts of interest with regard to the research, authorship and/or publication of this article.

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References

1.World Health Organization Coronavirus disease (COVID-19) [Accessed 12.10.2021]. Accessed adress: hptts://www.who.int/emergencies/diseases/novel-coronavirus-2019.

2.Zhang S, Tuo J, Huang X, et all. Epidemiology characteristics of human coronaviruses in patients with respiratory infection symptoms and phylogenetic analysis of HCoV-OC43 during 2010-2015 in Guangzhou. Plos one 2018; 13(1): e0191789.

3.Ovalı F. COVID-19 Infections in Newborns. Anatolian Clinical 2020; 25(1): 23-35.

4.Duyan V. Crisis management in the family. Family Life Cycle Ankara: Hedef Publishing, 2020 (In Turkish).

5.Sağlam M. Family communication İn: Aral N, editor Children and communication. Ankara: Vize Publıshıng, 2017; p.308-324 (In Turkish).

6.Yenilmez Ç. Family relationships İn: Yenilmez Ç, editor Family structure and relationship Eskişehir: Açıköğretim Publishing, 2012; p. 20-41 (In Turkish).

7.Munir S, Gondal Z, Takov V. Generalized anxiety disorder (GAD) [İnternet]. [Accessed 25.10.2021]. Access adress: https://www.ncbi.nlm.nih.gov/books/NBK441870/

8.Alavi N, Omrani M. What is depression? What is anxiety?. In Online cognitive behavioral therapy Springer, Cham. 2019; p. 17-31.

9.Dean A.G. OpenEpi: open source epidemiologic statistics for public health, version 2.3. 1. [İnternet]. [Accessed 25.10.2021]. Accessed adress: http://www. openepi. com.

10.Evgin D, Erdem E, (2018). The ways of coping stress na levels of depression of the parents of children with chronic renal failure. Bozok Tıp Dergisi 2018; 8(2), 33-41 (In Turkish).

11.Söğüt R, Çekiç, A. Comparison of stress level and perceptions of competence related to parenting of parents with gifted and non-gifted children. Journal of Development and Psychology (JODAP) 2020; 1(1); 1-15.

12.Lovibond P.F, Lovibond S.H. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behaviour research and therapy 1995; 33(3): 335-343.

13.Sarıçam, H. The psychometric properties of Turkish version of Depression Anxiety Stress Scale-21 (DASS-21) in health control and clinical samples JCBPR 2018; 7(1): 19−30.

14.Lee, S. A. Coronavirus Anxiety Scale: A brief mental health screener for COVID-19 related anxiety. Death studies 2020; 44(7): 393-401.

15.Akkuzu H, Yumuşak F. N, Karaman G. Ladikli N, Zeynep T, Bahadir E. The reliability and validity of Turkish version of coronavirus anxiety scale. Cyprus Turkish Journal of Psychiatry and Psychology 2020; 63-67.

16.Özdemir Ü, Taşçı S. Psychosocıal problems and care of chronıc dıseases. Journal of Erciyes University Faculty of Health Sciences 2013; 1: 57-72.

17.Brainard J, Hooper L, Pond K, Edmunds K, Hunter P. R. Risk factors for transmission of Ebola or Marburg virus disease: a systematic review and meta-analysis. International journal of epidemiology 2016; 45(1): 102-116.

18.Harman S. Ebola, gender and conspicuously invisible women in global health governance. Third World Quarterly 2016; 37(3): 524-541.

19.Ağkaya A.N, Aylaz R, Yetiş G. The Burden of Care in The Parents of The Children With Chronic Disease. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2015; 4: 1-5.

20.Arıkan G, Acar B. COVID-19 Factors Associated with Parents Depression, Anxiety and Stress During COVID-19 Quarantine Process. Turk J Child Adolesc Ment Health 2022; 29: 22-28.

21.Kaytez N, Durualp E, Kadan G. Evaluation of requirements and stress levels of the families having disabled child. Journal of Research in Education and Teaching 2015; 4(1): 197-214.

22.Yalçın H, Hilal D, Erkoç E. Parents' emotıonal states at vırus outbreak and theır effects on chıldren. Eurasian Journal of Researches in Social and Economics (EJRSE) 2020; 7: 128-142.

23.Sarı E. Examination of family functionality, marital satisfaction and family resilience in mothers whose children were diagnosed with cancer.nMaster's thesis, Maltepe Unıversıty, Graduate School of Education; 2022.

24.OECD Time Use Database, OECD Family Database, [İnternet]. Accessed adress: 25.10.2021. http://www.oecd.org/els/family/database.htm.

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ORIGINAL ARTICLE

Laparoscopic Ventral Mesh Rectopexy in Patients with Full Thickness Rectal Prolapse: Our Experience

Tam Kat Rektal Prolapsus'lu Hastalarda Laparoskopik Ventral Mesh Rektopeksi Deneyimlerimiz

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ABSTRACT

Objective: The gold standard method for the treatment of rectal prolapse is still unclear. This study aims to share the results of patients who underwent laparoscopic ventral mesh rectopexy surgery for rectal prolapse.
Design: Only cases who underwent laparoscopic procedure were included in the study.
Subjects/Patients: A total of 22 patients who were operated for rectal prolapse were analyzed.
Methods: The patient's data were evaluated including preoperative data, postoperative course and recurrence.
Results: Complications were observed in 6 patients in the early postoperative period (p=0.077). Complications observed in two patients, which resolved spontaneously during follow-up with minimal bleeding and postoperative ileus. Mean follow-up time was 16 months. There was no recurrence or mortality during this period.
Conclusion: Laparoscopic ventral mesh rectopexy still maintains its importance as one of the most effective options in the treatment of rectal prolapse, due to its high success rates, rapid and permanent resolution of clinical symptoms, and the positive effects of laparoscopy on quality of life.

Keywords: Rectal prolapse, laparoscopic surgery, mesh, recurrence

ÖZ

Amaç: Rektal prolapsus için optimal cerrahi yöntem halen netleşmemiştir. Bu çalışma, tam kat rektal prolapsus nedeniyle laparoskopik ventral meş rektopeksi cerrahisi uygulanan hastaların sonuçlarını paylaşmayı amaçlamaktadır.
Yöntem: Rektal prolapsus nedeniyle opera edilen 22 hasta incelendi. Hastalar, preoperatif veriler, postoperatif iyileşme dönemi ve nüks açısından değerlendirildi.
Bulgular: Tüm operasyonlar laparoskopik olarak yapıldı. Hastaların 6'sında erken postoperatif dönemde komplikasyon gelişti. (p=0.077). Erken postoperatif ileusu ve minimal kanaması olan 2 hastada takipte ek girişime ihtiyaç olmaksızın düzeldi. Ortalama takip süresi 16 ay idi. Bu dönemde nüks veya mortalite olmadı.
Sonuç: Laparoskopik ventral meş rektopeksi, klinik semptomların hızlı ve kalıcı çözümü ve laparoskopinin yaşam kalitesi üzerindeki olumlu etkileri nedeniyle rektal prolapsus tedavisinde en etkili seçeneklerden biridir.

Anahtar Kelimeler: Rektal prolapsus, laparoskopik cerrahi, meş, rekürrens

Introduction

Rectal prolapse is identified as full thickness protrude of the rectum out of the anal canal. Although the etiology of rectal prolapse has not been fully clarified, redundant sigmoid colon, levatory ani diastasis, anal sphincter pathologies and weakness of recto-sacral ligaments are considered as the most likely causes in the pathogenesis (1).

The incidence of rectal prolapse in female to male ratio is 6/1. In females, it reaches its peak towards the 7th decade (2,3). Depending on the degree and type of prolapse in patients was seen some complaints including rectal bloating, tenesmus, anal incontinence, constipation, mucous discharge, and bleeding can be seen. Fecal incontinence is seen in approximately 50-75% of patients and constipation is observed in 25-50% of them (4,5).

The aim of rectal prolapse treatment is to treat anatomical and functional abnormalities that cause incontinence and constipation. This can be ensured by 1) hanging of the rectum and/or 2) resection of the prolapsed section. The procedure can be performed by the transanal/perineal or transabdominal route (6). Transabdominal repairs are the gold standard treatment options due to low recurrence rates. Recently, abdominal approaches are performed laparoscopically because of their known advantages. There are several procedures described for laparoscopic mesh rectopexy (6-8). In comparative studies and Cochrane meta-analyses, laparoscopic ventral mesh rectopexy (LVMR) was seen to be a more effective procedure than others (1,4). However, the cost-effective results of these procedures are still unclear. This study aims to share the results of patients who underwent LVMR surgery for rectal prolapse.

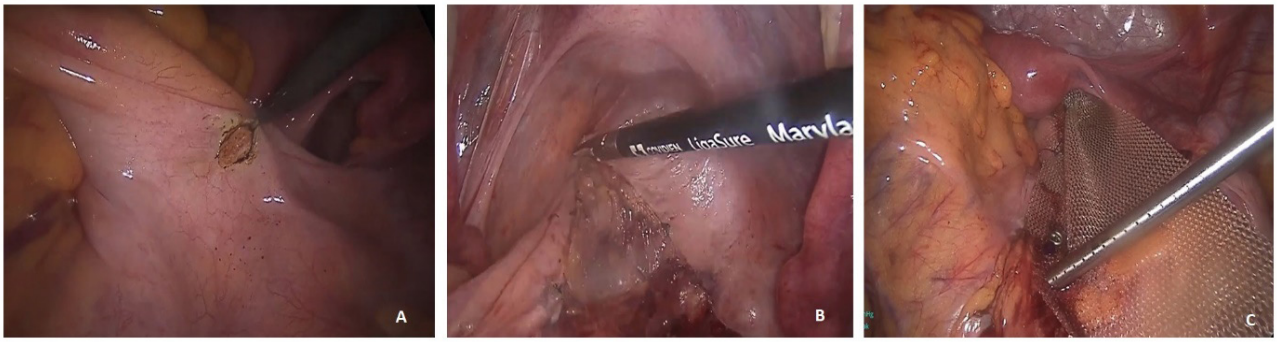

Fig 1. 'J' shaped peritoneal incision extending from the promontorium to the anterior peritoneal reflection (A), Accessing the rectovesical and rectovajinal/prostatic space by preserving the right ureter and hypogastric nerves without posterior dissection (B), Fixing the prolene mesh with prolene sutures first to the anterior rectum wall, and then to the promontorium using a tacker (C).

Material and Methods

Study Plan

A total of 22 patients who were rectal prolapse surgery between December 2019 and January 2022 were included in this retrospective study. Patient data were obtained from the hospital automation system and patient archive records. Two patients who underwent resection rectopexy, one patient whose perineal rectal prolapse was primary repaired due to serious comorbidities, 4 patients with solitary rectal ulcer syndrome with internal prolapse and 2 patients with rectal prolapse accompanied by rectocele were excluded from the study. Data of 13 patients were evaluated.

Preoperative Evaluation

Detailed medical histories of all patients were taken. The complaints, duration and toilet habits of the patients were recorded. In addition to detailed anal examinations, general physical examinations of all patients were performed. All patients underwent colonoscopy to exclude redundant colon and other colorectal pathologies. Manometry, defecography and measurement of colonic emptying time could not be applied to all patients due to technical difficulties.

Surgical Procedure

All operations were performed in the modified Lloyd Davies position. Four ports were used in the operations. One 10 mm port for optics above the umbilicus; 10 mm and 5 mm ports in the right lower quadrant and 5 mm port in the left lower quadrant were placed. If necessary, another 5 mm port was placed in the suprapubic region. After entering the abdomen, a 'J' shaped peritoneal incision was made from the right side of the promontory extending to the anterior reflection of the peritoneum. Right ureter and hypogastric nerves were preserved. Then, a 15x3 cm prolene mesh was fixed to the anterior surface of the rectum with a 3/0 prolene suture, and then to the promontory with a tacker proximally. After hemostasis, the previously opened peritoneum was then reapproximated to completely cover the mesh, and the operation was terminated (Figures 1A, 1B and 1C).

Statistical Analysis

Data were obtained using the SPSS 15.0 packet program. Chi-square test was used to compare categorical variables. Student t test was used to compare the means of two independent groups.

Results

In this retrospective analysis, 8 out of 13 patients were male, with a mean age of 54 (range, 19-73). Demographic data of the patients are given in Table 1. The most common symptom in the patients was constipation (10 patients, 76.9%) and the number of patients with multiple symptoms was 4 ($p<0.001$).

Data about the surgical procedure of the patients and information about the complications observed in the postoperative period are given in Table 2. The median operative time was 153 minutes. There was no conversion to open surgery related to any per-operative complication in any of the patients. Complications occurred in 6 patients in the early perioperative period ($p=0.077$). Primary repair was performed in one patient who had an intraoperative bladder injury, one patient with wound infection recovered after broad-spectrum antibiotic therapy, Urinary retention in 2 patients, early postoperative paralytic ileus and minimal bleeding in 2 patients resolved spontaneously after follow-up. The mean long-term follow-up period was 16 months and there was no recurrence or mortality in this period. Late complications occurred in 2 patients ($p=0.277$), Laparoscopic bridectomy was performed in one patient with late ileus due to adhesion. Constipation was recurred in 1 patient.

Table 1. General demographic data

Data		n/%	p
Gender (n/%)			<0.001
	Male	8 (61.5%)	
	Female	5 (38.5%)	
Age (years) (median)		54 (19-73)	
BMI (median)		22 (18-30)	
Symptoms (n/%)			<0.001
	Constipation	10 (76.9%)	
	Incontinence	3 (23.1%)	
	Bleeding	1 (7.7%)	
	Mucous rectal discharge	2 (15.4%)	
	Multiple	4 (30.8%)	

Table 2. Operative process and postoperative complications

Features		n/%	p
Operative process			
	Mean operating time (min.)	153 (70-220)	
	Mean hospital stay (days)	1.3 (1-4)	
	Conversion to open surgery (n/%)	0	
Mean follow-up time (months)		16 (8-25)	
Early Complications (n/%)			0.077
	Urinary retention	2 (15.4%)	
	Wound infection	1 (7.7%)	
	Early paralytic ileus	1 (7.7%)	
	Bleeding	1 (7.7%)	
	Close organ injury	1 (7.7%)	
Late Complications (n/%)			0.277
	Recurrence	0	
	Delayed ileus	1 (7.7%)	
	De-novo constipation	1 (7.7%)	
	Mortality	0	

Discussion

In this study, data of 13 patients who underwent LVMR surgery for full-thickness rectal prolapse were presented and it was concluded that LVMR is a highly effective treatment option in rectal prolapse.

The definite etiology of rectal prolapse is yet unclear. Etiologic factors may be congenital or acquired, and involve poor bowel habits, neurological disorders, female gender, and previous anorectal surgery. Anatomical pathology that causing of rectal prolapse include prolapsed sigmoid colon, levator ani diastasis, anal sphincter pathologies and weakness of the rectosacral ligaments (9,10).

Rectal prolapse is seen in women especially and its incidence increase with age. It reaches peak levels in the seventh decade (2,3). This protrusion can be reduced spontaneously or by manual intervention. Fecal incontinence is seen in approximately 50-75% of patients and constipation is observed in 25-50% (4,5). Less frequent presenting symptoms include tenesmus, mucus discharge, hemorrhage, and pain (11). Chandra et al. (12) in their retrospective study involving 15 patients, found that the female gender was higher, and the mean age was 50. In addition, they found that the rates of incontinence and constipation in the patients were close to each other, while they found that the majority of the patients had redundant colon. In the series of 75 cases by Hammond et al. (11) which has almost the highest volume of patients in the literature, the number of women with rectal prolapse was found to be 10 times more than men. In addition, in this study, the mean age was 60.8 years and the most common symptom was a protruding rectal mass, and the rate of fecal incontinence was found to be 39%. In our study, median age of patients is 54. Contrary to the literature data, male gender was higher (8 vs 5 patients) ($p<0.001$). The most common symptoms in patients are constipation (76.9%) and fecal incontinence (%23.1).

Nowadays, many surgeries are performed laparoscopically in line with increasing technological developments and innovations. The duration of hospital stay and return to work of patients are shortened. Likewise, transabdominal repairs required for rectal prolapse are often performed laparoscopically. In the study by Hammand et al. (11) which included both abdominal and perineal repairs, the mean hospital stay was 3±2.5 days and the hospital stay was shorter in perineal repairs. In the LVMR series by Chandra et al. (12) they found the mean operative time to be 200 min (180-310 min) and the mean hospital stay to be 4 days (3-21 days). Similarly, Naeem et al. (2) found the mean operative time to be 150 min and the mean hospital stay to be 3 days (2-11 days). In addition, in the same study, they found the rate of conversion from laparoscopy to open surgery as 6.4%. In our study, mean operation time was 153 minutes (70-220) and the mean hospital stay was 1.3 days (1-4 days). The operative time was similar to the data in the literature, and the hospital stay was shorter than the data in the literature. This may be attributed to the recent emphasis on recommendations in studies on early discharge.

In rectal prolapse surgeries, complications are possible due to colorectal region anatomy (narrow

pelvis, redundant colon, etc.) and physiology (clean-contaminated, contaminated area, etc.) and close organ neighborhoods (such as major vascular structures, ureter and bladder). In a study of 15 cases by Chandra et al. (12) iatrogenic injury was observed in 1 patient, urinary retention in 1 patient, and surgical site infection in 2 patients. Complications of similar type and frequency were also seen in the study of Naeem et al. (2). No data on mesh-related complications were found in any study. Urinary retention in 2 patients, wound infection in 1 patient, early paralytic ileus in 1 patient, minor bleeding in 1 patient, and iatrogenic injury in 1 patient were observed in our study, consistent with literature data.

In the literature, it is seen that patients are followed up for a long time in order to fully reveal conditions such as recurrence and de-novo constipation, which indicate the success or failure of the surgery. Chandra et al. (12) followed-up the patients who underwent LVMR for an average of 22 months, and they did not detect any recurrence, de-novo constipation and incontinence in any patient during this period. Naeem et al. (2) detected recurrence in 1 patient (3.2%) and prolonged ileus in 2 patients (6.4%) at the end of an average follow-up period of 6-18 months, but they did not see de-novo constipation. In our study, delayed ileus was observed in 1 patient and de-novo constipation was observed in 1 patient during the mean follow-up period of 16 months. However, no recurrence was observed.

Studies involving fecal incontinence data have reported that LVMR is associated with greater improvement in constipation and faster resolution of symptoms compared to procedures involving lateral and posterior rectal dissection. Functional results of the patients in our study were consistent with these studies in the literature, pre-existing constipation resolved in most patients, and de-novo constipation did not develop in any patient (13-15).

In conclusion, LVMR maintains its importance as one of the most effective options in the treatment of rectal prolapse due to its high success rates, rapid and permanent resolution of clinical symptoms, and positive effects of laparoscopy on quality of life. Before treating the prolapse, a thorough evaluation is essential to distinguish whether the prolapse is due to constipation or other pelvic floor diseases. Thus, the appropriate surgical option and multidisciplinary treatment support can be adjusted as needed. In addition, patients should be informed and counseled that not all damaged functions can be restored by surgery. Currently, it seems reasonable to recommend laparoscopic procedures to eligible patients.

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Conflicting of Interest

All authors declare no conflict of interest and financial relationships. This article, either in full or in part, has not been previously published or is not being assessed for publication in either printed form or as digital media.

References

1.Brodén B, Snellman B. Procidentia of the rectum studied with cineradiography. A contribution to the discussion of causative mechanism. Dis Colon Rectum 1968; 11: 330-47.

2.Naeem M, Anwer M, Qureshi MS. Short term outcome of laparoscopic ventral rectopexy for rectal prolapse. Pak J Med Sci 2016; 32: 875-879.

3.Hrabe J, Gurland B. Optimizing Treatment for Rectal Prolapse. Clin Colon Rectal Surg 2016; 29: 271-276.

4.Kim DS, Tsang CB, Wong WD, Lowry AC, Goldberg SM, Madoff RD. Complete rectal prolapse: evolution of management and results. Dis Colon Rectum 1999; 42: 460-466.

5.Madoff RD, Mellgren A. One hundred years of rectal prolapse surgery. Dis Colon Rectum 1999; 42: 441-450.

6.Tou S, Brown SR, Nelson RL. Surgery for complete (full-thickness) rectal prolapse in adults. Cochrane Database Syst Rev 2015; 11: CD001758

7.Fang SH, Cromwell JW, Wilkins KB, Eisenstat TE, Notaro JR, Alva S, et al. Is the abdominal repair of rectal prolapse safer than perineal repair in the highest risk patients? An NSQIP analysis. Dis Colon Rectum 2012; 55: 1167-1172.

8.Baker R, Senagore AJ, Luchtefeld MA. Laparoscopic-assisted vs. open resection. Rectopexy offers excellent results. Dis Colon Rectum 1995; 38: 199-201.

9.Nigro ND. An evaluation of the cause and mechanism of complete rectal prolapse. Dis Colon Rectum 1966; 9: 391-398.

10.Madiba TE, Baig MK, Wexner SD. Surgical management of rectal prolapse. Arch Surg 2005; 140: 63-73.

11.Hammond K, Beck DE, Margolin DA, Whitlow CB, Timmcke AE, Hicks TC. Rectal prolapse: a 10-year experience. Ochsner J 2007; 7: 24-32.

12.Chandra A, Kumar S, Maurya AP, Gupta V, Gupta V, Rahul. Laparoscopic ventral mesh rectopexy for complete rectal prolapse: A retrospective study evaluating outcomes in North Indian population. World J Gastrointest Surg 2016; 8: 321-325.

13.D'Hoore A, Cadoni R, Penninckx F. Long-term outcome of laparoscopic ventral rectopexy for total rectal prolapse. Br J Surg 2004; 91: 1500-1505.

14.Selvaggi F, Scotto di Carlo E, Silvestri A, festa L, Peigari V. Surgical treatment of rectal prolapse: a randomised study. Br J Surg 1993; 80 Suppl: S89 (Abstract).

15.Speakman CT, Madden MV, Nicholls RJ, Kamm MA. Lateral ligament division during rectopexy causes constipation but prevents recurrence: results of a prospective randomized study. Br J Surg 1991; 78: 1431-1433.

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CASE REPORT

Malnutrition Despite Adequate Nutrient Intake: A Clue For Diencephalic Syndrome

Yeterli Besin Alımına Karşı Yetersiz Büyüme: Diencefalik Sendrom için İpucu Olabilir

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ABSTRACT

Diencephalic syndrome is characterized by excessive weight loss and subcutaneous fatty tissue loss, hyperactivity, euphoria, and hypervigilance observed in early childhood. It usually accompanies space-occupying neoplastic lesions of the hypothalamic–optochiasmatic region. There is an inverse relationship between mass size and weight gain. In this case report, a patient aged 1 year and 2 months with hypothalamic–optochiasmatic glioma was presented. We aimed to draw attention to diencephalic syndrome, which is a rare cause of weight gain and vomiting.

Keywords: Diencephalic Syndrome, Severe Malnutrition, Tuberosclerosis type 1

ÖZ

Diensefalik sendrom, erken çocukluk döneminde gözlenen aşırı kilo kaybı ve deri altı yağ dokusu kaybı, hiperaktivite, öfori ve hipervijilans ile karakterizedir. Genellikle hipotalamik optokiazmatik bölgenin yer kaplayan neoplastik lezyonlarına eşlik eder. Kitle büyüklüğü ile kilo alımı arasında ters oran vardır. Bu olgu sunumunda hipotalamik-optokiazmatik gliomalı 1 yıl 2 aylık bir hasta sunuldu. Kilo alma ve kusmanın nadir bir nedeni olan diensefalik sendroma dikkat çekmeyi amaçladık.

Anahtar Kelimeler: Diensefalik Sendrom, Ağır Yetersiz Beslenme, Tüberoskleroz tip 1

Introduction

Diencephalic syndrome (DS) is a condition that often develops in infancy and early childhood. DS is associated with space-occupying lesions in the supratentorial midline region of the anterior hypothalamus (1, 2). It is often accompanied by recurrent persistent vomiting and nystagmus. DS is characterized by signs and symptoms caused by hypothalamic insufficiency secondary to space-occupying lesions of the hypothalamic-optic chiasmatic region. Growth hormone (GH) hypersecretion has often been described in patients with DS (2, 3). Despite adequate caloric intake, weight loss and cachexia with hypervigilance and hyperactivity are typical findings for DS (3). We aimed to present a 14-month-old case diagnosed with DS secondary to optic glioma (OG) of neurofibromatosis type 1 (NF type 1) with respect to the rarity of the condition in clinical practice.

Case

A 14-month-old girl with NF type 1 presented with complaints of restlessness, insomnia, swelling in both eyes, vomiting and inability to gain weight. In her family history, the patient's father and uncle were also NF type 1. In the patient's history, she had restlessness, unexplained crying spells, vomiting and weight loss since she was five months old. The daily nutritional requirement was supported as 120 kcal per kilogram of infant enteral product. Her weight, height and head circumference were 5500 gr (0,03 percentile, SD: −5.44), 74 cm (0.03 percentile, SD: −3.4) and 44 cm (0.33 percentile, SD: −2.72), respectively. On physical examination, there were bilateral horizontal nystagmus and proptosis in the eyes (Figure 1). In addition, ophthalmological examination revealed pallor of the optic disk in the fundus and a 1.5 x 1.5 cm nodule due to neurofibroma in the left frontal region. The patient also had a significant decrease in subcutaneous adipose tissue, flattening of the nasal

Table 1: Anthropometric measurements of the patient

Age (month)	Weight (gram)	Weight (percentile)	Weight (SDS)	Height (cm)	Height (percentile)	Height (SDS)	WFA (%)	HFA (%)	HFW (%)
22	5700	<0,02	-5,44	74	0,03	-3,4	45	86	64
28	5600	<0,02	-6,47	74	<0,02	-4,48	43	82	62
32	5500	<0,02	-6,58	76	<0,02	-4,37	40	83	57
37	5,850	<0,02	-6,58	76	<0,02	-4,94	41	79	59
39	6300	<0,02	-6,66	78	<0,02	-4,72	42	78	63
42	6200	<0,02	-7,47	79	<0,02	-4,8	41	80	56
44	7400	<0,02	-6,1	81	<0,02	-4,51	49	79	68
51	8750	<0,02	-5,14	81	<0,02	-5,24	51	76	83

Abbreviation: WFA, weight for age; HFA, height for age; HFW, height for weight

root and multiple café-au-lait spots on the whole body's skin (Figure 2). Upon neurological examination, no object tracking was observed, and the patient was found to be hyperactive. After the exclusion of other reasons explaining the weight loss of the patient with a neurofibromatosis type 1 diagnosis, cranial magnetic resonance imaging (MRI) showed bilateral optic glioma and a mass lesion with intense contrast. In the glucagon stimulation test, the growth hormone peak was insufficient (GH peak: 2.73 µg/L). The lesions filled the suprasellar cistern and caused compression at the base of the third ventricle (Figures 3, 4); therefore, gross total mass excision was performed with a left frontotemporal craniotomy. Histopathological examination of the surgically resected mass revealed neurofibroma. The patient was diagnosed with DS due to the presence of a mass in the hypothalamic region and severe malnutrition. During the patient's follow-up, a third ventriculostomy was performed due to the development of hydrocephalus in the fifth month after the first operation.

Since there was excessive weight loss despite having an adequate nutritional intake via the oral route, she underwent enteral feeding via a percutaneous endoscopic gastrostomy (PEG) tube. The patient was followed up with anthropometric measurements (Table I) and cranial MRI examinations.

Figure 1: A decreased amount of subcutaneous adipose tissue, cachectic appearance, and proptosis in the left eye

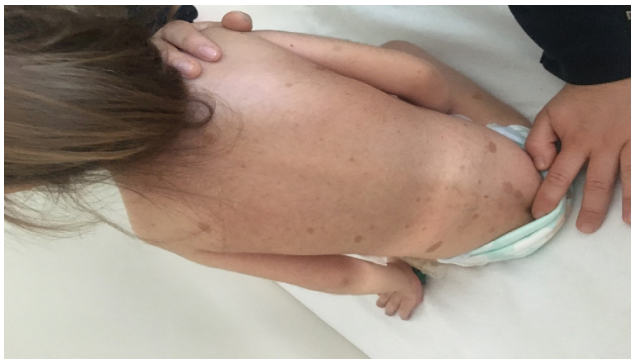

Figure 2: > 6 café-au-lait spots on the entire back

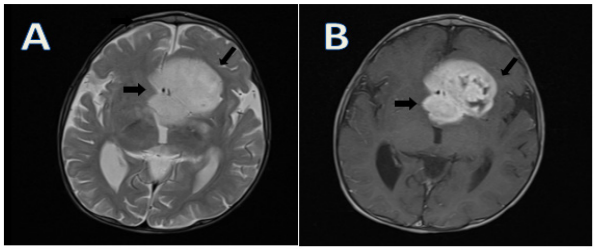

Figure 3: Cranial magnetic resonance imaging (MRI) showing a mass filling the suprasellar cistern and causing compression at the base of the third ventricle (A), and a mass lesion with intense contrast enhancement (B)

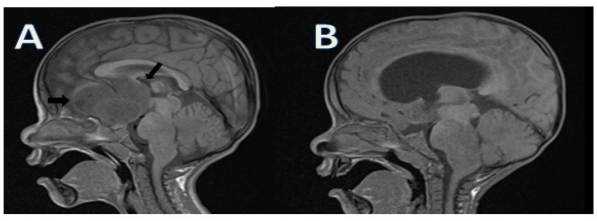

Figure 4: Cranial MR images of the patient before (A) and after treatment (B)

Discussion

NF type 1 is an autosomal dominant genetic disorder that causes a predisposition to OCG (4). NF type 1 affects nearly every organ system in the body with

broad clinical ramifications, such that children and adults with this condition may exhibit pigmentary abnormalities (café-au-lait macules, skinfold freckling, Lisch nodules), tumors of the peripheral and central nervous system (neurofibromas and gliomas), learning and attention problems, bone abnormalities (long bone dysplasias, scoliosis), seizures, sleep disturbances, vasculopathies and non-nervous system cancers (breast cancer, pheochromocytoma). In our patient, the presence of more than six café-au-lait spots on the skin and optic nerve tumor, together with her family history, confirmed the diagnosis of NF type 1 (5). DS has rarely been reported in children with NF type 1 and OCG. The development of hypothalamic-optochiasmatic-space occupying lesions in early childhood can lead to DS with extreme weight loss and restlessness (6). The most important symptom of the syndrome is excessive weight loss, despite having an adequate nutritional intake; this symptom is observed in almost all cases (3). Our case presented with complaints of weight loss and extreme restlessness despite having adequate nutritional intake. Tumors located in the third ventricle most frequently cause DS, followed by tumors in the optic nerves and chiasm, fourth ventricle and hypothalamus region, in that order (6). Our case had a neurofibroma in the hypothalamus and bilateral OCG.

It has been reported that the mean age of DS development in patients with NF type 1 is older. Only one patient younger than 12 months has been reported in the literature (6). Our case was one year and two months old at the time of admission. Although patients usually present with severe vomiting, severe weight loss, hydrocephalus and nystagmus, they may sometimes present with only growth percentile loss (7). Our case presented with severe vomiting and severe weight loss. The cause of weight loss in these patients remains unknown. However, increased GH levels and related pathways due to GH resistance are blamed in endocrinological examinations (8, 9). Fleishman et al. (10) showed that baseline GH levels were high in 9 of their 11-case series; there was insufficient suppression of the response to the GH in all cases that underwent an oral glucose tolerance test, and IGF-1 levels were within the normal limit. However, an insufficient response to the glucagon stimulation test performed during the endocrinological follow-up was observed in our case (peak GH: 2.72 µg/L). In these patients, a careful ophthalmologic examination is required to detect nystagmus, strabismus and optic atrophy, among others. Additionally, a neuroradiological examination should be performed based on the results of the ophthalmological examination. A careful ophthalmologic examination is crucial to detect symptoms such as nystagmus, strabismus and optic atrophy with the support of neuroradiological investigation. Neuroradiology, especially MRI, can describe the location, extension and association of hydrocephalus or other orbital pathologies.

Since these tumors in the optic chiasma of children under three years of age are usually very aggressive, neurosurgical intervention is necessary in children with symptomatic increases in intracranial pressure caused by the mass effect and in whom chemotherapy has failed. The cause of the symptomatic increase in intracranial pressure in these cases is often obstructive hydrocephalus. Although excising the giant neurofibroma mass in our case was sufficient to prevent hydrocephalus in the first step, hydrocephalus that developed in the fifth postoperative month also had to be performed because the tumor had an aggressive course.

Consequently, the appearance of DS syndrome symptoms should prompt the clinician to perform cranial MRI to rule out OCG with hypothalamic involvement. For this reason, intracranial pathologies should be considered in children with normal appetites who show decreased weight gain and growth-percentage losses.

References

1.Chheda E, Vora S, Prasad M. Nutritional management of diencephalic syndrome: a case series. Neurol India. 2021;69(2):524-5.

2.Işık U, Kuter Yılancıoğlu Ş, Eryılmaz S, Canpolat C. Aşırı Kilo Kaybının Nadir Bir Nedeni: Diensefalik Sendromlu Üç Olgu. 2017. ACU Sağlık Bil Derg. 2017(1):53-57

3.Salmon MA. Russell's diencephalic syndrome of early childhood. J Neurol Neurosurg Psychiatry. 1972;35(2):196-201.

4.Ly KI, Blakeley JO. The diagnosis and management of neurofibromatosis type 1. Medical Clinics. 2019;103(6):1035-54.

5.Campen CJ, Gutmann DH. Optic pathway gliomas in neurofibromatosis type 1. Journal of Child Neurology. 2018;33(1):73-81.

6.Cavicchiolo ME, Opocher E, Daverio M, Bendini M, Viscardi E, Bisogno G, et al. Diencephalic syndrome as sign of tumor progression in a child with neurofibromatosis type 1 and optic pathway glioma: a case report. Childs Nerv Syst. 2013;29(10):1941-5.

7.Kim A, Moon JS, Yang HR, Chang JY, Ko JS, Seo JK. Diencephalic syndrome: a frequently neglected cause of failure to thrive in infants. Korean J Pediatr. 2015;58(1):28-32.

8.Gianotti L, Pincelli AI, Scacchi M, Rolla M, Bellitti D, Arvat E, et al. Effects of recombinant human insulin-like growth factor I administration on spontaneous and growth hormone (GH)-releasing hormone-stimulated GH secretion in anorexia nervosa. The Journal of Clinical Endocrinology & Metabolism. 2000;85(8):2805-9.

9.Pimstone BL, Sobel J, Meyer E, Eale D. Secretion of growth hormone in the diencephalic syndrome of childhood. J Pediatr. 1970;76(6):886-9.

10.Fleischman A, Brue C, Poussaint TY, Kieran M, Pomeroy SL, Goumnerova L, et al. Diencephalic syndrome: a cause of failure to thrive and a model of partial growth hormone resistance. Pediatrics. 2005;115(6):e742-8.

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CASE REPORT

Concomitant Heart Surgery with Pulmonary Hamartoma Resection: A Case Report

Eş Zamanlı Kalp Cerrahisi ve Pulmoner Hamartom Rezeksiyonu: Olgu Sunumu

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ABSTRACT

Concomitant lesions of the heart and lung are rare, but when present, they pose a therapeutic challenge to surgeons. A combined procedure clears the need for a second major procedure, improving outcomes and providing economic benefits. However, cardiopulmonary bypass may adversely affect the natural history of pulmonary masses when malignancy is suspected. To avoid these suspects, off-pump techniques may be preferred in suitable patients.
This article presents a case of simultaneous off-pump coronary artery bypass grafting and pulmonary hamartoma resection in a 53-year-old man who detected a lung mass during preoperative preparation.

Keywords: coronary artery bypass grafting, hamartoma, off-pump

ÖZ

Kalp ve akciğerin eşlik eden lezyonları nadirdir, ancak mevcut olduklarında cerrahlar için terapötik bir zorluk oluştururlar. Kombine bir prosedür, sonuçları iyileştirerek ve ekonomik faydalar sağlayarak ikinci bir ana prosedüre olan ihtiyacı ortadan kaldırır. Ancak kardiyopulmoner baypas, maligniteden şüphelenildiğinde pulmoner kitlelerin doğal seyrini olumsuz etkileyebilir. Bu şüphelerin önüne geçmek için uygun hastalarda off-pump teknikler tercih edilebilir.
Bu makalede preoperatif hazırlık sırasında akciğerde kitle tespit edilen 53 yaşındaki erkekte eş zamanlı off-pump koroner arter baypas greftleme ve pulmoner hamartom rezeksiyonu yaptığımız bir olguyu sunuyoruz.

Anahtar Kelimeler: hamartom, koroner baypas, off-pump

Introduction

Patients who require both open heart surgery and lung resection because of a suspected lung mass and heart disease are a matter of debate among surgeons (1). However, most surgeons prefer simultaneous intervention due to acceptable results and low-cost (2). Among the factors forcing them to attempt a simultaneous intervention is a belief that the surgeons cannot afford two separate procedures due to the patient's advanced age and frailty (1, 2). Another factor is the concern that an open-heart operation to be performed at the first stage in a staged procedure will cause the spread of possible lung malignancy (2). Nevertheless, simultaneous cardiac revascularization and lung resections have been performed safely for five decades (3, 4).

Before planned cardiac surgery, pulmonary masses are rarely recognized and pose a therapeutic challenge for surgeons (1, 5). Pulmonary chondromatous hamartomas are the most common benign lung tumors. These hamartomas account for 8% of all pulmonary neoplasms (6). These neoplasms are developmental malformations arising from the peribronchial mesenchyme (1, 2, 7, 8).

Heart surgeries can be performed with (on-pump) or without (off-pump) cardiopulmonary bypass (CPB). The on-pump technique is a standard technique. The off-pump technique is well-known and widely used in coronary revascularization, especially in patients with low ejection fraction and severe left ventricular dysfunction (1, 2, 9). In patients requiring both lung resection and coronary revascularization, surgeons are concerned that CPB may cause mass metastasis. Therefore, the off-pump technique is preferred when suitable in such cases (1, 2).

This report aims to present our experience with concomitant off-pump coronary revascularization and pulmonary chondromatous hamartoma resection and discuss its benefit and safety.

Case Report

A 53-year-old man, diabetic and hypertensive for eight years, was admitted with unstable angina to the hospital. He had a 35-pack-year smoking history, had a history of an acute cerebrovascular accident a year ago, and his brother had died of myocardial infarction. On physical examination, the cardiovascular system examination was normal; however, there were signs and symptoms of chronic obstructive pulmonary disease.

Electrocardiography revealed subacute posteroinferior myocardial infarction. The x-ray revealed a well-circumscribed lesion in the left lung. A computerized chest tomography confirmed this finding (Figure 1). Coronary angiography showed three-vessel disease with severe left ventricular dysfunction.

We preferred off-pump coronary artery revascularization and simultaneous left lung mass resection technique because the patient had three-vessel disease with low left ventricle ejection fraction, lung mass, decreased respiratory function, and a history of cerebrovascular accident. In operation, firstly, the left internal mammary artery was harvested after median sternotomy. Secondly, a well-circumscribed mass of 3x3x2 cm was completely resected before systemic heparinization (Figure 2a). Finally, off-pump three-vessel coronary revascularization was performed. No postoperative complications were observed, and the patient was discharged on the sixth postoperative day.

The histopathology was pulmonary chondromatous hamartoma. Microscopically, the tumor tissue contained crypts of mature cartilage and clefts surrounded by respiratory epithelium. There was no sign of malignancy (Figure 2b).

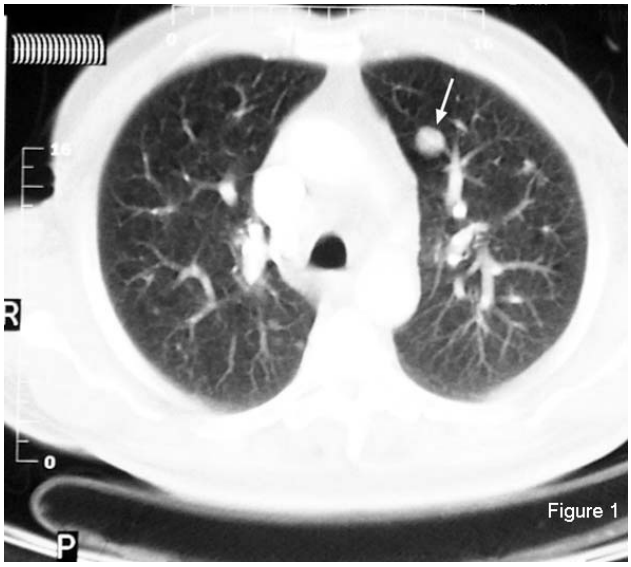

Figure 1: Computerized chest tomography showing a well-circumscribed mass at the superior segment of the lingula (white arrow).

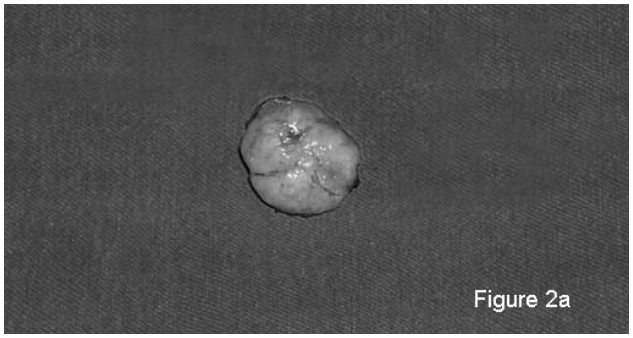

Figure 2a: Macroscopic view of the resected mass.

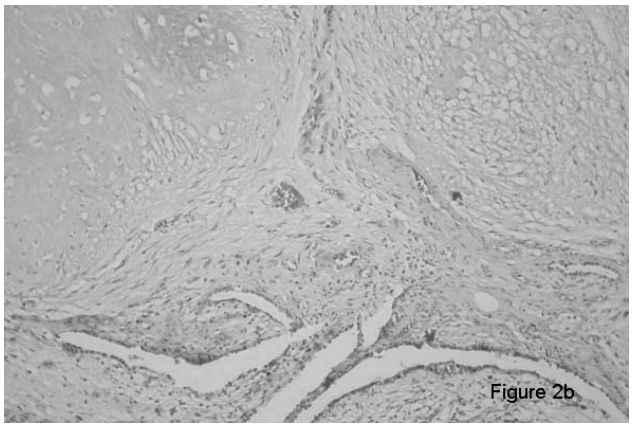

Figure 2b: Histopathological view showing mature cartilage islands and clefts surrounded by normal respiratory epithelium. These findings were regarded as the diagnosis of hamartoma under the light microscope (x10, hematoxylin-eosine-staining).

Discussion

Co-morbidities of the heart and lungs that require surgery are rare. However, most of these patients demonstrate cardiac complaints. Lung lesions are detected incidentally during preoperative examinations, as in our case (1, 2). While some surgeons prefer stepwise procedures in these patients, others prefer concomitant surgical intervention (1, 2). In coronary revascularization, surgeons use both on-pump and off-pump techniques. Considering the results, such as postoperative morbidity, mortality, and long-term survival, it is evident that the treatment option should be specific to the patient and the disease. Both techniques have advantages and disadvantages.

In on-pump coronary revascularization, patients are at risk of bleeding, which is an important cause of postoperative morbidity. In addition, the on-pump technique has disadvantages such as the potential to affect immunity, the concern of spreading the tumor, and shortening long-term survival. Most surgeons believe performing tumor resection before CPB will yield better results (1, 2, 10, 11). For these reasons, off-pump revascularization is preferred in appropriate cases. We chose this technique in our case because of its convenience. In addition, because off-pump revascularization is a technique that significantly

reduces the postoperative bleeding and needs for transfusion, it also protects the patient from the side effects of CPB, such as pulmonary dysfunction (1, 9).

Median sternotomy is the preferred approach in simultaneous heart and lung surgery. The exception to this technique is the left lower pulmonary lobectomy. Median sternotomy causes fewer complications than other techniques, and pulmonary functions are better tolerated in the postoperative period (1, 2, 10, 11).

We resected the left lung mass before systemic heparin was administered. We believe removing the lung mass and controlling bleeding before heparinization will reduce complications. Most surgeons prefer systemic heparinization after mass resection (2, 12).

Some surgeons argue against concomitant surgery. Instead, they advocate the step-by-step procedure (1, 2). The reason for their preference is the patient's age and general condition, size and location of the tumor, cardiac surgery strategy, and malignant or benign nature of the tumor (1, 2, 8). Therefore, this debate among surgeons continues. Unfortunately, there are few studies on both concomitant and step-by-step surgery. Furthermore, due to the lack of controlled randomized studies, there is no consensus yet on which method should be preferred (13, 14).

In our case, histopathological findings showed benign pulmonary chondromatous hamartoma. Pulmonary hamartomas are well-circumscribed and benign masses in the lung parenchyma. Most of these tumors are of parenchymal origin (15).

They are often detected incidentally by computerized chest tomography performed in patients presenting with cardiac complaints. We believe that simultaneous surgical intervention can generally be preferred in these patients due to the difficulty of performing a preoperative biopsy in patients requiring open heart surgery. In addition, surgical resection remains the gold standard in diagnosis and treatment, as a needle-aspiration biopsy of a patient with suspected pulmonary hamartoma rarely yields diagnostic findings (2, 7).

Conclusion

Based on our experience in our case and the limited number of studies in the literature, we think that the concomitant surgical approach in treating patients with coronary revascularization and suspected lung mass is safe and carries a low risk of morbidity and mortality. However, the chosen treatment method should still be patient-specific due to the lack of controlled randomized studies.

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Conflict of Interest

The authors have no conflict of interest.

References

1.Zhang R, Wiegmann B, Fischer S, et al. Simultaneous cardiac and lung surgery for incidental solitary pulmonary nodule: learning from the past. The Thoracic and cardiovascular surgeon 2012;60(02):150-5.

2.Šantavý P, Szkorupa M, Bohanes T, Lonský V. Simultaneous cardiac surgery with pulmonary resection. Cor et Vasa 2015;57(2):e82-e5.

3.Dalton Jr ML, Parker TM, Mistrot JJ, Bricker DL. Concomitant coronary artery bypass and major noncardiac surgery. The Journal of Thoracic and Cardiovascular Surgery 1978;75(4):621-4.

4.Girardet R, Masri Z, Lansing A. Pulmonary lesions in patients undergoing open heart surgery: approach and management. The Journal of the Kentucky Medical Association 1981;79(10):645-8.

5.Johnson JA, Landreneau RJ, Boley TM, et al. Should pulmonary lesions be resected at the time of open heart surgery? The American surgeon 1996;62(4):300-3.

6.Haberal MA, Dikis OS, Erkan A. Pulmonary hamartoma: Retrospective analysis of 24 cases. Dicle Tıp Dergisi 2019;46(1):27-32.

7.Bini A, Grazia M, Petrella F, Chittolini M. Multiple chondromatous hamartomas of the lung. Interactive Cardiovascular and Thoracic Surgery 2002;1(2):78-80.

8.Alqahtani YA, Fallatah RZ, Alnaimi M. Incidental Benign Giant Pulmonary Chondroid Hamartoma. Journal of Oncology Research Reviews & Reports SRC/JONRR-150 DOI: https://doi org/1047363/JONRR/2021 (2) 2021;146:2-3.

9.Ueki C, Miyata H, Motomura N, et al. Off-pump versus on-pump coronary artery bypass grafting in patients with left ventricular dysfunction. The Journal of thoracic and cardiovascular surgery 2016;151(4):1092-8.

10.Knaepen P, Van Swieten H, Vanderschueren R, Ernst J, Van den Bosch J. Concomitant open heart surgery and pulmonary resection for lung cancer. European journal of cardio-thoracic surgery: official journal of the European Association for Cardio-thoracic Surgery 1995;9(6):310-3; discussion 3.

11.Rao V, Todd TR, Weisel RD, et al. Results of combined pulmonary resection and cardiac operation. The Annals of thoracic surgery 1996;62(2):342-7.

12.Atılgan K, Demirdaş E, Metin B, Er ZC, Çiçekçioğlu F. A simultaneous coronary artery bypass grafting on beating heart and right upper lobectomy in a patient with a lung adenocarcinoma. Turkish Journal of Thoracic and Cardiovascular Surgery 2018;26(4):646.

13.Tourmousoglou CE, Apostolakis E, Dougenis D. Simultaneous occurrence of coronary artery disease and lung cancer: what is the best surgical treatment strategy? Interactive cardiovascular and thoracic surgery 2014;19(4):673-81.

14.Habal P, Simek J, Lonsky V, Novotny J. Possibilities of combined surgical treatment of lung tumours and heart diseases. ACTA MEDICA-HRADEC KRALOVE- 2006;49(3):175.

15.Minami Y, Iijima T, Yamamoto T, et al. Diffuse pulmonary hamartoma: a case report. Pathology-Research and Practice 2005;200(11-12):813-6.