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Research Article/Özgün Araştırma

The effect of *Thymus vulgaris* essential oil on the formation of *Candida albicans* biofilm on denture base materials: An *in vitro* study

Thymus vulgaris esansiyel yağının protez kaide materyalleri üzerinde *Candida albicans* biyofilm oluşumuna etkisi: *İn vitro* bir çalışma

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Abstract

Aim: This study aims to evaluate the antifungal properties of *Thymus vulgaris* (thyme) essential oil (TVEO) on *Candida albicans*-infested polymethyl methacrylate (PMMA) denture base materials and identify the volatile components of *T. vulgaris* essential oil.

Materials and Methods: The investigation involved establishing *C. albicans*'s presence on resin surfaces manufactured in 1x1x0.1 cm size. The resin surfaces on which the *C. albicans* biofilm had formed were then soaked in a 2% and 5% solution of TVEO and the effect on the amount of *C. albicans* colonisation were evaluated. The volatile components of TVEO were determined using the GC-MS method.

Results: Solutions prepared from 2% and 5% TVEO showed better antifungal activity than Corega. The major components detected by GC-MS in the TVEO were carvone 61.36%, linalool 8.32%.

Conclusion: TVEO, showed significant antifungal effects on PMMA resin surfaces. This oil can, therefore, be recommended as an inexpensive, uncomplicated and efficient natural cleaning agent for those wearing dentures.

Keywords: Antifungal activity; *C. albicans*; Denture cleansers; *Thymus vulgaris*.

Öz

Amaç: Bu çalışmanın amacı *Candida albicans* tutulumu sağlanmış polimetil metakrilat (PMMA) protez kaide materyallerine *Thymus vulgaris* (kekik) esansiyel yağının (TVEO) antifungal etkisini değerlendirmek ve TVEO'nun uçucu bileşenlerini belirlemektir.

Gereç ve Yöntem: Çalışmada ilk olarak 1x1x0,1 cm boyutunda hazırlanan rezin yüzeylerine *C. albicans* tutulumu sağlandı. Daha sonra rezin yüzeyleri, TVEO'dan hazırlanan %2 ve %5 oranındaki solüsyonunda bekletilerek *C. albicans* kolonizasyonundaki değişiklik değerlendirildi. TVEO'nun uçucu bileşenleri GC-MS yöntemi ile belirlendi.

Bulgular: TVEO'dan %2 ve %5 oranında hazırlanan solüsyonlar Corega'ya göre daha iyi antifungal aktivite gösterdi. TVEO'da GC-MS ile tespit edilen majör bileşenler carvone %61,36, linalol %8,32.

Sonuç: TVEO, PMMA rezin yüzeylerinde etkili antifungal aktivite gösterdi. Protez kullanıcıları için alternatif, ucuz, basit ve etkili bir doğal temizleyici olarak önerilebilir.

Anahtar Kelimeler: Antifungal aktivite; *C. Albicans*; Protez temizleyiciler, *Thymus vulgaris*.

Introduction

Denture stomatitis is a condition that results from oral candidiasis in denture wearers. Denture stomatitis is frequently caused by *Candida albicans*, which attach to the denture base and form a biofilm.[1] To avoid denture stomatitis, meticulous denture washing is essential, and the accumulation of biofilm on the denture surface must be prevented.[2-4] Denture cleaning is performed using mechanical and/or chemical methods.[5] Mechanical brushing, while often used for denture hygiene, can cause wear on the denture base and relining materials and increase surface roughness due to its abrasive nature.[2] Increased roughness promotes infestation with *C. albicans*. In addition, the use of chemical cleaning agents may be more effective and easier than mechanical cleaning in elderly patients due to their weakened manual dexterity.[6] Chemical cleansers often include alkaline peroxides, alkaline hypochlorite, acids, disinfectants, and enzymes.[7]

Polymethyl methacrylate (PMMA) is a versatile, long-lasting, safe, visually pleasing, and practical material that is easy to work with. Furthermore, it has limited permeability and solubility to oral fluids. Because of its physical qualities, it is simple to manufacture and fix.[8,9]

The study investigated *Thymus vulgaris*, a member of the Lamiaceae family, commonly known as thyme. *Thymus* species have strong antibacterial and antifungal properties. *Thymus* essential oil is extracted from the aerial parts of the plant by the water-steam distillation method.[10] *Thymus* essential oils exhibit strong antifungal properties against *C. albicans*. Essential oils consist of volatile compounds such terpenoids, phenylpropanoids, and fatty acids.[11]

In this study, the antifungal effect of the essential oil of *T. vulgaris* on the colonisation of *C. albicans* in heat-polymerised dental restorative material (PMMA) was investigated. This study aims to evaluate the antibacterial efficacy of a denture cleanser formulated with *Thymus* essential oil in comparison to the commercially available Corega denture cleanser.

Materials and Methods

Plant materials

The essential oils of Thyme (Thymus Vulgaris Flower/Leaf Oil) were sourced from Elantra Pharmaceuticals Health Cosmetics Ltd. Sti. Phytoil Aromatherapy brand (Turkey).

Preparation of the denture base material

PMMA resin samples, sized 1x1x0.1 cm, were utilised in the investigation. The samples were polished appropriately and kept in distilled water at 37°C for 48 hours. Roughness values of the samples were measured with a profilometer (Surtronic 25; Taylor Hobson, Leicester, United Kingdom) (0.845±0.2). In this study, the measurement length was set as 2.5 mm and the cut-off value was set as 0.25 mm. The surface roughness value of each sample was calculated by averaging repeated measurements in 3 different areas on the surfaces of the sample. The surface roughness values of the samples were standardized. The samples' average surface roughness values (Ra) were assessed using a prolithometer.[12]

Adhesion of *Candida albicans* to denture base materials

The prepared resins were sterilized by autoclaving before the study. 24-hour-old fresh *C. albicans* (ATCC 10231) strain was used to ensure colonization of resin surfaces with *C. albicans*. Standard suspension of 1-2 x 10^8 CFU (~0.5 McFarland) was prepared in Sabouraud Dextrose Broth (SDB) medium from young cultures of *C. albicans*. Then, the identical resin pieces were kept in this suspension at low shaking speed (120 rpm) for 1 hour to ensure the retention of *C. albicans*. Previous studies and the negative control in our study have shown that 1 hour is sufficient for *C. albicans* to adhere to resin surfaces. At the end of the period, the pieces removed from the suspension were gently washed with sterile isotonic solution (0.9% NaCl) in accordance with aseptic rules.[13-15]

Treatment of resin surfaces with essential oils

Resin surfaces contaminated with *C. albicans* were exposed to *T. vulgaris* essential oil (Elantra Pharmaceuticals, Turkey)

solutions of 2% and 5% diluted in 10% dimethyl sulphoxide (DMSO) for 1 hour in a shaken environment. It was then gently washed once with sterile isotonic solution to remove the essential oil from the resin surfaces. The resins were incubated in 5 mL SDB in a shaking oven for about 18 hours before being transferred to Sabouraud Dextrose Agar. Then, 100 μm of these samples were taken and plated on SDA medium and incubated at 35˚C for 24 hours. The results were analyzed not only by counting the colonies on a solid medium, but also by measuring the absorbance values at 600 nm. Resins treated with Corega (GlaxoSmithKline, Ireland) alone served as a positive control group, while resins that retained *C. albicans* but were not treated with essential oil served as a negative control. Corega cleansing tablet was prepared by placing 1 tablet in 200 mL of water. All treatments and controls were carried out under identical conditions.[13,14]

Gas chromatography-mass spectrometry (GC-MS) and GC-Flame Ionization Detector (GC-FID) analyses

An Agilent system at the Eastern Anatolia High Technology Application and Research Centre (DAYTAM) was used to evaluate the oil by GC-FID and GC-MS. GC-MS analysis was performed using a Shimadzu QP2010 Ultra GC-MS system equipped with an HP-5 MS column; 30 m length x 0.25 mm ID diameter, 0.25 μm film thickness. The GC analysis included an AOC-20i autoinjector, a mass spectrometry detector and an AOC-20s sampler. The carrier gas utilised in the experiment was helium with a flow rate of 1.02 mL/min. The chromatographic analysis was performed with a flow rate of 1.02 mL/min and an injection volume of 1 μL in split mode (20:1). The temperature of the GC oven was kept constant at 60 ºC for 10 minutes, after which it was raised by 4 ºC and kept at a fixed temperature of 220 ºC for a further 10 minutes. The incubation process was carried out at a temperature of 246 ºC for a duration of 1.0 minutes, gradually increasing the temperature by 1.0 ºC per minute. The injector and detector temperatures were set at 250 and 300 ºC, respectively. The MS detector parameters were set as follows: transfer line temperature of 300 °C, solvent delay of 3 minutes, electron energy of 70 eV, and the MS was operated in electron impact mode with selected ion monitoring for quantitative analysis.

Identification of components

The essential oils' components were identified by comparing their mass spectra with the W9N11, FFNSC library and validated by comparing the retention durations with authentic samples.

Statistics

The statistical analyses were conducted using the SPSS version 25.0 software. The variables' normal distribution appropriateness was assessed by histogram graphs and the Kolmogorov-Smirnov test. The presentation of the descriptive analysis included the mean, standard deviation, median, and min-max values. An independent T-test was conducted to analyze the absorption values of essential oils produced at 2% and 5%. Instances with a *p* value less than 0.05 were considered statistically significant.

Results

The absorbance value of 2% concentration of TVEO (0.084 ± 0.002) was lower than the absorbance value of 5% concentration (0.095 ± 0.003). Using the absorbance values of all experimental groups, the percentage of viability [(Absorbance experiment/ Absorbance control)*100] was calculated. Antibiofilm properties at 2% and 5% concentration values prepared for TVEO were compared with control and Corega® and are shown in Figure 1 and Table 1. The viability value of 2% Essential oil concentration was found to be 14.55%, the viability value of 5% Essential oil concentration was 16.46%, and Corega was found to be 18.54%. The viability value of the control group was accepted as 100%. The comparison of the % vitality values between TVEO concentration of 2% and 5% was made and the difference between them was found to be significant (*p*<0.05). Considering the anticandidal activity values, it was determined that TVEO was extremely effective, showing better effectiveness than Corega (*p*<0.05). (Figure 1, Table 1)
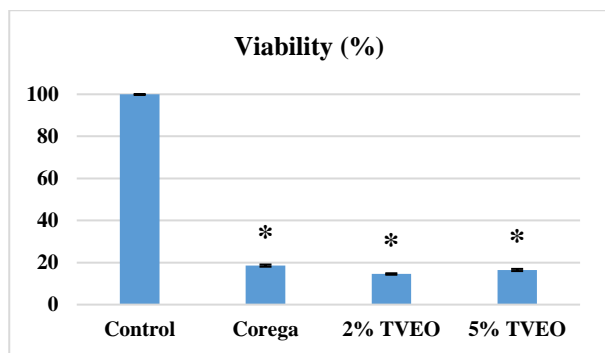
Figure.1. Evaluation of the effect of TVEO (2% and 5%) and Corega on *C. albicans* biofilm in the context of viability% *There is a statistically significant difference with the control group ($p<0.05$)

There was no colony growth on solid medium after treatment with 2% and 5% of *T. vulgaris* essential oil. An absorbance value of 0.107 ($<10^2$ CFU/mL) was measured in the resin treated with Corega, which was tested as a positive control in the study. The absorbance value of 0.577 ($>10^5$ CFU/mL) was measured in the resin tested as a negative control.

Table 1. Absorbance values of Corega and 2% and 5% TVEO

Samples	Absorbances	
	Mean±SD	Medyan (Min-Max)
2% TVEO	0.084±0.002	0.084 (0.082-0.086)
5% TVEO	0.095±0.003	0.095 (0.092-0.098)
Corega	0.107±0.003	0.107 (0.104-0.110)
Control	0.577±0.002	0.577 (0.575-0.579)

TVEO= *T. vulgaris* essential oil, sd=standard deviation
p^1=0.001 Corega vs 2% TVEO
p^2=0.018 Corega vs 5% TVEO
p^3=0.006 2% TVEO vs 5% TVEO

The GC-MS analysis of *T. vulgaris* essential oil revealed the following primary volatile components: carvone 61.36%, linalool 8.32%, thymol 5.44%, and p-cymene 5.18%, a comprehensive content analysis of which is presented in Table 2.

Table 2. Chemical composition (%) of the essential oil of *T. vulgaris*, confirmed by GC-MS

Peak	Name	Retation Time	Area%
1.	Butanoic acid, 2-methyl-, methyl ester	3.42	0.03
2.	α-Pinene	6.72	0.48
3.	β-fenchene	7.23	0.20
4.	1-Octen-3-ol	8.083	0.27
5.	Octan-3-one	8.351	0.02
6.	Myrcene	8.53	1.04
7.	Ethyl-hexanol	8.64	0.03
8.	α-Phellandrene	9.03	0.17
9.	δ-3-Carene	9.25	0.08
10.	α-Terpinene	9.47	0.89
11.	**p-Cymene**	9.76	**5.18**
12.	Sylvestrene	9.92	0.52
13.	Eucalyptol	10.02	0.29
14.	α-Pinene	10.22	0.04
15.	β-Ocimene	10.62	0.06
16.	γ-Terpinene	11.07	1.63
17.	Trans-sabinene hydrate	11.39	0.02
18.	Cis-Linalool oxide	11.60	0.06
19.	Terpinolene	12.26	0.30
20.	**Linalool**	12.73	**8.32**
21.	Trans-γ-Caryophyllene	12.87	0.07
22.	β-Thujone	12.99	0.03
23.	Trans-Pinocarveol	14.38	0.05
24.	(+)-2-Bornanone	14.61	0.10
25.	Borneol	15.53	1.54
26.	L-4-terpineol	16.03	1.59
27.	Cuminic alcohol	16.33	0.11
28.	α-Terpineol	16.60	0.49
29.	Thymol methyl ether	18.90	0.22
30.	Nerol	19.60	0.09
31.	Carvenone	20.12	0.05
32.	**Thymol**	21.04	**5.44**
33.	**Carvone**	21.75	**61.36**
34.	Octadecanoic acid, 9,10-dihydroxy-, methyl ester, bis(trifluoroacetate)	21.97	0.25
35.	1,3-Dioxolane, 2,2-dimethyl-4,5-di-1-propenyl-	22.27	0.04
36.	2-Ethyl-5-n-propylphenol	22.34	0.06

37.	Eugenol	23.81	0.03
38.	cis-Geranyl acetate	24.11	0.09
39.	Carvacryl acetate	24.45	0.29
40.	Copaene	24.65	0.05
41.	trans-Geranyl acetate	24.91	0.18
42.	β-Bourbonene	25.04	0.04
43.	Isoeugenol methyl ether	25.78	0.17
44.	Caryophyllene	26.49	1.55
45.	*α-Cis*-Bergamotene	27.11	0.09
46.	Aromadendrene	27.28	0.27
47.	*α*-Humulene	27.87	0.17
48.	γ-Cadinene	28.80	0.04
49.	Ledene	29.56	0.19
50.	β-Bisabolene	30.08	3.16
51.	γ-Cadinene	30.31	0.20
52.	δ-Cadinene	30.66	0.22
53.	trans-α-Bisabolene	31.40	0.06
54.	Spatulenol	32.77	0.21
55.	Caryophyllene oxide	32.99	0.37
56.	Epicubenol	34.20	0.03
57.	δ-Cadinene	35.15	0.36
58.	Cycloheptane, 4-methylene-1-methyl-2-(2-methyl-1-propen-1-yl)-1-vinyl-	35.36	0.04
59.	3-methyl-5-(2,6,6-trimethyl-1-cyclohexen-1-yl)-1-pentyn-3-ol	35.78	0.04
60.	Viridiflorol	36.26	0.03
61.	*α*-Bisabolol	36.70	0.05
62.	6-Isopropenyl-4,8a-dimethyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-2-ol	36.81	0.06
63.	Hexahydrofarnesyl acetone	42.29	0.06
64.	3-Benzylsulfonyl-2,6,6-trimethylbicyclo(3.1.1)heptane	45.14	0.42
65.	13-epi-Manoyl oxide	47.16	0.08
66.	5-Isopropyl-2-methylphenyl 3-methylbutanoate	47.97	0.12
67.	5-Androstene, 4,4-dimethyl-	50.41	0.04
68.	2-(7-Hydroxymethyl-3,11-dimethyl-dodeca-2,6,10-trienyl)-[1,4]benzoquinone	50.70	0.05
69.	4-p-Hydroxyphenyl-2,2,4-trimethylchroman	50.96	0.03
70.	Verticiol	51.51	0.08

Discussion

In this study, volatile components were determined by GC-MS analysis of TVEO. It was then investigated whether this essential oil could be used to prevent candida retention in the denture material and as a natural alternative to chemical cleaners used for general cleaning purposes.

Essential oils provide antispasmodic, anti-irritating, antiseptic, antifungal, antiviral, and antibacterial effects. Essential oils have antibacterial and antiseptic qualities that may effectively combat bacteria, molds, and yeasts. The most antiseptic oils include cinnamon, thyme, clove, lavender, and eucalyptus oil. Terpenes being the primary components of essential oils have prompted investigations into the biological characteristics of chemicals within this category. Thymol and carvacrol, which are contained in thyme oil, are 20 times more antiseptic than phenol, for example, and are also utilized in toothpastes. These chemicals possess antioxidant and antibacterial effects.[16] TVEO used in the current study showed antifungal activity by acting on *C. albicans* fungus.

C. albicans is a prevalent pathogen responsible for oral and/or systemic candidiasis. *Candida* species are recognized for their ability to create biofilms on medical surfaces.[17] Fungal infections, however less frequent than bacterial infections, may result in more severe complications. Fungi biofilm structure is resistant to antifungal medications, causing standard antifungal therapy to fail. Hence, there is a need to investigate alternative therapies and develop more effective anticandidal drugs with fewer side effects or

toxicity from various sources, including medicinal plants.[18] Medicinal herbs with essential oils have strong antifungal properties against fungi.[19] *Thymus* species are plants that belong to the Lamiaceae family and are known for their fragrant essential oils and beneficial antifungal and antibacterial properties, which have been widely used since time immemorial.[10] Several *Thymus* species, including *T. kotschyanus*[20], *T. vulgaris, T. zygis, T. satureioides, T. mastichina*[21], *T. capitatus*[22], *T. villous*[23], *T. ciliates*[24], are claimed to have an anticandidal effect. According to the results of the current study, it can be said that *T. vulgaris* essential oil can be used as an alternative anticandidal product.

Aslan et al.[25] conducted a study on the antibacterial and antifungal properties of essential oils. They found that geranium, lemongrass, rosemary, thyme, tea tree, and peppermint oils had inhibitory zones exceeding 5 cm for *C. albicans*. The study found that thyme oil was the most beneficial among the essential oils examined.

Karpinski et al.[26] discovered that peppermint oil (*Mentha piperita*), rosemary oil (*Rosmarinus officinalis*), and thyme oil (*Thymus vulgaris*) showed similar effectiveness against *Candida* species. The study's findings indicate that the essential oils of *T. vulgaris* had the most potent anti-biofilm action, eliminating almost 90% of the biofilm. The oil extracted from *Rosmarinus officinalis* (rosemary) had a diminished efficacy, eliminating around 75.85% of the biofilm. The *in silico* toxicity analysis in this study indicated that the primary chemicals found in the essential oils of plants from the Lamiaceae family are not expected to have carcinogenic, mutagenic, or cytotoxic effects. Nevertheless, it was shown that these oils can cause skin sensitization.[26] In the current study, TVEO showed a strong effect by destroying 83.54% of biofilm at a concentration of 2%.

In the study by Abers et al.[27], *C. albicans*, one of the fungal species, proved to be the most susceptible species to the volatile substances of thyme and rosemary.[27] Fani and Kohanteb[28] conducted a study to assess the antibacterial effects of the essential oil of *T. vulgaris* on certain oral pathogens such as *S. pyogenes*, *S.*

mutans, *C. albicans*, *P. gingivalis*, and *A. actinomycetemcomitans*. The study found that *T. vulgaris* oil, at doses ranging from 16 to 256 µg/mL, exhibited a potent inhibitory effect on all clinical isolates using the agar disc diffusion method.

Kavianirad et al.[29] conducted a study to examine the impact of *T. vulgaris* essential oil on *C. albicans* found in removable orthodontic apparatus, utilizing the disc diffusion method. The study found that the essential oil of *T. vulgaris* was substantially more efficient than chlorhexidine ($p<0.05$) in removing *C. albicans* from the surface of orthodontic apparatus. The study revealed that the essential oil of *T. vulgaris* has superior antifungal properties compared to Corega.

Thyme essential oil demonstrates more effective antifungal activity than black cumin oil and CD Clean®, according to the findings of a study conducted to evaluate and compare the efficacy of thyme essential oil, *Nigella sativa* oil and two commercially available denture cleansers (CD Clean® and Fittydent®) against *C. albicans* adhering to soft denture material.[30]

In a study conducted by Corticchiato et al.[31], it was reported that the essential oil extracted from the plant *Thymus herba-barona* has a concentration of 6.7% carvacrol, 74.6% carvone and 9.5% limonene in its composition. In another study, p-cymene (8.41%), γ-terpinene (30.90%) and thymol (47.59%) were named as the main constituents of the essential oil of *T. vulgaris*.[32] In our study, the essential oil of *T. vulgaris* was found to consist mainly of 61.36% carvone, 8.32% linalool, 5.44% thymol and 5.18% p-cymene (Table 1). When the studies are examined, there are differences in the composition of essential oils, which may be due to harvest location-date, soil and light conditions.[33,34]

Carvone, the first major ingredient in TVEO, is a monoterpene compound that exhibits antibacterial, antifungal, antioxidant, antiepileptic and anticancer effects. Essential oils rich in carvone possess fungicidal and bactericidal effects against a wide variety of pathogenic fungi (e.g. *C. albicans*) and bacteria. According to the findings of several

scientific investigations, essential oils that are abundant in carvone not only inhibit the growth of the *Candida fungus* but also prevent it from converting into its pathogenic form.[35] In a study investigating the fungicidal effect against various *Candida* species (*C. albicans*, *C. krusei, C. parapsilosis*, *C. tropicalis*), carvone was reported to have an antifungal effect.[36]

Linalool is a phenolic volatile compound and is the second major substance in TVEO. Hsu et al.[37] conducted a study demonstrating the antifungal properties of linalool against *C. albicans* (ATCC 14053) and its effects on the development of biofilms. It was also observed to inhibit the development of germ tubes and biofilms in this strain.

Thymol is one of the most important phenolic components found in *Thymus* species. It is also seen as the third major component in TVEO. A study by Braga et al.[38] reports that thymol not only inhibits the formation of *Candida* biofilms on *C. albicans* strains ATCC 3153A and ATCC MYA 2876, but also inhibits the initial stages of biofilm production.

It has also been reported in the literature that carvone, linalool and thymol major components in the *Thymus* essential oil used in our study have a significant anticandidal effect.[36-38] When used together, the volatile components have a synergistic effect that is more effective than when they are used separately.[39] In the study conducted, it is thought that the components in TVEO have a synergistic effect.

Effervescent tablet cleansers produce multiple oxygen bubbles on the denture surface, which stay longer and give a mechanical impact to remove debris and destroy biofilm. This provides a benefit compared to liquid cleansers.[40] The free radicals generated when using this cleaning agent can have mechanical effects on material surfaces. Microorganisms can therefore penetrate prosthetic restorations more easily due to wear. In a study the effect of tea tree oil on the surface roughness of PMMA, the surface roughness value of essential oil was found to be less. This suggests that *T. vulgaris* essential oil may make the surface of denture

base materials less rough.[41]

Conclusion

In this study, where the antifungal activity of TVEO was evaluated against the retention of *C. albicans* on the surface of PMMA resin material compared to Corega, TVEO showed better antifungal activity than Corega. The GC-MS analysis of the essential oil revealed the presence of volatile components including carvone, linalool, thymol, and p-cymene in significant amounts, suggesting that the antifungal activity may be attributed to these chemicals. Today, as the search for alternatives to chemical detergents continues unabated, the antimicrobial activities of various combinations of essential oils against multi-resistant microorganisms provide valuable information to the existing literature.

Ethics Committee Approval

There was no data obtained from animal or human experiments for this article.

Informed Consent

The consents were obtained from all of the authors for this article.

Author Contributions

All of the authors contributed at every stage of the study.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Research Article/Özgün Araştırma

Effect of tarhana soup on serum lipid profile in BALB/c male mice fed a high-fat-diet

Tarhana çorbasının yüksek yağlı diyetle beslenen BALB/c erkek farelerde serum lipit profili üzerine etkisi

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Abstract
Aim: With industrialization, there has been an increase in chronic diseases due to continuous change of nutrition. Tarhana is a traditional grain-based product fermented by lactic acid bacteria in Turkish cuisine. This study aims to evaluate possible effects of tarhana on the impaired lipid profile parameters and serum glucose values in male BALB/c mice fed a high-fat diet.
Materials and Methods: Male BALB/c mice were grouped into three different strain male mice groups: control group (n=10), high fat diet (HFD) (n=10) and high fat diet supplemented with tarhana (n=10). Standard pellet feed was given to the control group, high-fat feed with 60% fat content in the HFD group, high-fat feed and 0.3 mL (8-10mL/kg) of tarhana were given to the other group.
Results: A significant difference was detected in epididymal fat weights, lipid profiles and serum glucose values between the groups ($p<0.05$).
Conclusion: It may have beneficial effects in many metabolic diseases, especially coronary heart disease and diabetes with its positive effects on lipid profile, epididymal adipose tissue and glucose level.
Keywords: Fermented food; High fat diet; Lipid profile; Hyperlipidemia; Tarhana.

Öz
Amaç: Sanayileşme ile beslenme alışkanlıklarının değişmesine bağlı olarak kronik hastalıklarda artış meydana gelmiştir. Tarhana, Türk yemeklerinde laktik asit bakterileri tarafından fermente edilen geleneksel tahıl bazlı bir üründür. Fermente gıdalar probiyotikler, prebiyotikler ve organik bileşikler açısından oldukça zengindir. Bu araştırma, tarhananın yüksek yağlı diyetle beslenen erkek BALB/c farelerde bozulmuş lipit profili parametreleri ve serum glukoz değeri üzerindeki olası etkilerini değerlendirmeyi amaçlamaktadır.
Gereç ve Yöntem: BALB/c cinsi erkek fareler üç farklı gruba ayrılmıştır: kontrol grubu (n=10), yüksek yağlı diyet (YYD) (n=10) ve tarhana ilave edilmiş YYD (n=10). Kontrol grubuna standart pelet yem, YYD grubuna %60 yağ içeriğine sahip yüksek yağlı yem diğer gruba yüksek yağlı yem+0,3 mL (8-10mL/kg) tarhana verildi.
Bulgular: Gruplar arasında epididimal yağ ağırlıkları, lipid profilleri ve serum glukoz değerleri arasında anlamlı bir ilişki tespit edilmiştir ($p<0.05$).
Sonuç: Tarhananın lipid profili, epididimal yağ dokusu ve glukoz düzeyi üzerine olumlu etkisi ile başta koroner kalp hastalığı ve diyabet olmak üzere birçok metabolik hastalıkta faydalı etkileri olabileceği düşünülmektedir.
Anahtar Kelimeler: Fermente gıda; Yüksek yağlı diyet; Lipit profili; Hiperlipidemi; Tarhana.

Introduction

The diets of people living before industrial expansion and agricultural production included a wide variety of unprocessed wild herbs, eggs, fish, meat and various raw seeds. At the beginning of the 20th century, the refining, storage and processing of foods accelerated with industrialization.[1] Economic growth and prosperity have led to major changes in the eating habits of societies, such as an overall increase in total saturated and trans fats and an increase in intake of foods containing animal products. Economic development has also led people to turn to ready-made high-fat refined foods and high-sugar drinks. While these foods are low in vitamins, minerals, fiber, amino acids, α-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and antioxidants, they are rich in saturated fat, simple sugar and salt. Diets in which such foods are commonly consumed are called the "Western diet".[2] A diet rich in fats, particularly those with high saturated fat content, is linked to a higher risk of several diseases, including obesity, hyperlipidemia, hypertension, increased adipose tissue, insulin resistance, type 2 diabetes mellitus (T2DM), and heart diseases.[3] The 2017 Global Burden of Disease study reported that dietary risk factors were associated with 11 million deaths, primarily due to cardiovascular heart disease and T2DM. Globally, there is a suboptimal consumption of healthy foods/nutrients with overconsumption of unhealthy foods that, combined with insufficient physical activity, causes metabolic overload.[4] Around 650 million people worldwide are currently classified as obese, according to data from the World Health Organization. Obesity can have many possibilities, including cardiometabolic rates of T2DM, non-alcoholic fatty liver disease, and cancer.[4] The non-pharmacological and most effective method of preventing and treating metabolic syndrome includes changes in eating habits and lifestyle.[5] Tarhana is a traditional grain-based fermented food unique to Turkey, fermented by lactic acid bacteria. Tarhana has both probiotic and prebiotic nutritional properties characterized by rich biological value and easy digestibility.[6] The

positive effects of probiotic, prebiotic and symbiotic foods or supplements on lipid metabolism disorder and related diseases have been proven by many studies[7-9]. It has been observed that probiotics and prebiotics improve the lipid profile of the host, decrease in adipose tissue, decrease in weight gain, increase in intestinal hormones such as Glucagon-like peptid 1 (GLP-1) and Peptide YY(PYY), decrease in proinflammatory markers and improve insulin resistance.[10] Probiotics, prebiotics and symbiotics play an important role in reducing cholesterol levels.[9]

This investigation explores the influence of tarhana on altered lipid profiles cholesterol derivatives, (LDL, HDL and total cholesterol) triglycerides (TG) and serum glucose measurements in BALB/c male mice on a high-fat diet. This research enriches the literature by emphasizing the advantages of traditional natural foods in preventing and treating various diseases, including obesity, metabolic syndrome, coronary artery disease, and diabetes mellitus (DM), supported by scientifically validated data.

Material and Methods

The experimental study received authorization from the Gaziantep University Experimental Animal Local Ethics Committee with approval granted during the meeting on 18.02.2020 under decision number 2020/10. The study was conducted at in the Gaziantep University Medical Biochemistry Department. In addition, the study was supported by Gaziantep University Scientific Research Projects Management Unit no: TF.YLT.20.18.

Animals and treatments

Experimental animals and diets

In this study, 30 BALB/c male mice weighing 20±0.5 grams were used. The experimental animals were acquired from the Gaziantep University Center for Experimental Animal Research. Male BALB/c mice (20±5 g) were acclimated for 10 days in a 12 hours light/dark cycle at 23±2°C ambient temperature, 50-60% relative moisture and ventilation system. They were fed ad libitum with a standard diet and water. At the start of the study, the animals were weighed and

grouped into units of 10 per cage, then housed in standard plastic cages.

High fat diet (HFD)

A high-fat diet consisting of 60-70%[11] of the energy of saturated fats was prepared by melting and adding 100g /40g[12] of butter to the standard feed supplied in powder form from a private commercial feed producer by the Gaziantep University Experimental Animals Research Center. The carbohydrate, fat, protein, moisture, ash and caloric value analysis of the obtained high-fat feed was carried out at the Gaziantep University Food Engineering Department. Initial results showed the following values: carbohydrate 21.9 g/100, protein 9.3 g/100, fat 52.04 g/100, energy 589.37 kcal/100 g, moisture 11.2 g/100 and ash content 6.4 g/100. High-fat feeds given to experimental animals were prepared weekly and stored at -20°C.

Tarhana

Tarhana prepared for use in the study the stages of a traditional method[13] including the following ingredients: 3 kg of yogurt, 4 kg of whole wheat flour, 2 kg of onions, 2 cups of cooked chickpeas, 3 kg of strained yogurt, 1 kg of red peppers, 1 kg of jalapeno peppers, 1 bunch of parsley, 1 bunch of dill, salt and flour using mint fame. After mixing the ingredients, it was kneaded into the dough and left to fermentation process by covering it at room temperature for 7 days. After the fermentation process was completed, the dough was spread thinly and allowed to dry. After drying, it was powdered and stored. Tarhana reviewed content includes 17% protein, 15% fat, 68% carbohydrates and 547.3 grams of fiber (Carbs 74.4 g/100g, Protein 18.1 g/100 g, Fat 7.4 g/100g, 12.6 g/100g fiber). The pH of tarhana was 4.92.The total bacteria, mold-yeasts and lactic acid bacteria content of the obtained tarhana were made at Gaziantep University, Department of Food Engineering. Total bacteria were evaluated using the TS 7703/ISO 4833 test method and $1x10^2$ cfu/g result was found. The total mold-yeast was evaluated using the TS 6580 test method and was found to be $2.25x10^3$ cfu/g. The total lactic acid was evaluated using the TS 7725/ ISO 4831 test method and the result was found to be $3.5x10^2$

cfu/g. 10 grams of powdered tarhana were thoroughly mixed with 100 ml of boiled water, homogenized and passed through a fine wire strainer. Tarhana prepared daily by homogenizing with water was given to the experimental animals by oral gavage in an amount of 0.3 mL/kg.

Experimental groups

Thirty male mice of the BALB/c strain were allocated divided three groups of ten and followed specific dietary protocols over the course of 8 weeks (56 days)[14,15].

Control group (n=10): Mice in good health were provided with standard pellet feed and unrestricted water. They also received 0.3mL[16] (8-10mL/kg) of water through oral gavage, identical to the volume administered to the tarhana group.

High-fat diet group (HFD) (n=10): Mice were provided with a prepared high-fat diet and water ad libitum. Additionally, they received 0.3 mL (8-10mL/kg) of water via oral gavage, the same volume given to the tarhana group.

Tarhana + High-fat diet (n=10): Mice fed with HFD ad libutum were given 8-10mL/kg of tarhana prepared daily by oral gavage.

Weight tracking

Experimental animals were weighed with precision scales in the same group order between 09.00 and 10.00 every Monday for 8 weeks from the beginning of the study.

Collecting blood samples and obtaining serum samples

At the conclusion of the 8-week experimental period, BALB/c male mice received an intraperitoneal injection of 60 mg/kg Ketamine and 10 mg/kg Xylazine for anesthesia. Subsequently, intracardiac blood samples were collected into gel serum separation tubes.

After a 30-minute waiting period, blood samples were centrifuged at 4000 rpm for 10 minutes and the serum samples obtained were transferred into numbered Eppendorf tubes. Serum samples were stored at -80°C until analysis of biochemical parameters.

Removal of epididymal fat tissue

Post-euthanasia, epididymal visceral fat tissues were removed from the anterior, lateral and dorsolateral regions of the prostate in male BALB/c mice and precisely measured on a sensitive scale.

Measurement of biochemical parameters in blood samples

On the day the study was conducted, serums stored at -80°C were removed and mixed with a vortex after they were allowed to thaw at room temperature. Measurements of cholesterol derivatives (total cholesterol, HDL and LDL cholesterol), TG and serum glucose values in serum samples were conducted on a Beckman Coulter A45800 biochemistry autoanalyzer using commercial kits.

Statistical analysis

Statistical evaluation of the data was conducted using IBM SPSS version 22.00. The Kolmogorov-Smirnov test was utilized to assess whether the gathered data conformed to a normal distribution. Given that the data followed a normal distribution and involved more than two groups, a one-way analysis of variance (ANOVA) test was conducted. Subsequently, a post-hoc test for multiple comparisons was employed to assess the differences among the groups. One-way ANOVA and post-hoc (Tukey) tests were used to statistically evaluate the weight changes between the groups. A value of $p<0.05$ was used to determine statistical significance.

Ethics committee approval

The study received authorization from the Gaziantep University Experimental Animal Local Ethics Committee, with approval granted during the meeting on 18.02.2020 under decision number 2020/10.

Results

Body weight increase findings

The average weight changes of the groups during the 8-week experiment are shown in Table 1. At the start of the experiment, the weight changes among the groups did not show any statistically significant differences ($p>0.05$). Significant differences were observed between the groups during the 6th and 7th weeks ($p<0.05$). At these weeks, the weight gain of the control group was found to be significantly lower compared to the tarhana+HFD and HFD groups (p<0.05). There was no significant difference between the tarhana+HFD and HFD groups (p>0.05).

Table 1. Average body weight values of groups by day

Days	Control weight(g) (n=10)	HFD weight(g) (n=10)	Tarhana+ HFD weight (g) (n=10)	*p* value
	Mean±SD	Mean±SD	Mean±SD	
Beginning (week 1)	22.7±2.8	24.2±1.4	23.8±1.9	0,29
7th days (week 2)	24.1±3.2	23.7±1.7	24.4±2.2	0,82
14th days(week 3)	23.7±2.8	24.5±1.8	24.6±1.5	0,60
28th days(week 4)	25±3.2	25.4±1.5	24.9±1.2	0,86
35th days(week 5)	25.3±2.6	27.1±1.6	27.2±2.5	0,14
42th days(week 6)	24.5±2.3 c	26.8±1.8a	25.9±0.7	0,02
49th days(week 7)	25.1±2.07b	27±1.5	28.4±2.9ab	0,01
56th days(week 8)	25.8±2.3	26.7±1.5	28.3±3.09	0,08

ANOVA* $p<0.05$ (post-hoc multiple comparison test)
a: statistically significant compared to the control group ($p<0.05$). b: it is statistically significant according to the tarhana+HFD group ($p<0.05$).
c: statistically significant compared to the HFD group ($p<0.05$). HFD: high fat diet. SD: standart deviation

Epididymal fat weights

At the end of the 8-week period, the average epididymal fat weights obtained from the groups are shown in Table 2. There was a statistically notable difference in the average weights of epididymal fat among the experimental groups ($p<0.05$) (Figure 1).

Evaluation of biochemical parameters

A statistical analysis of the results obtained from the biochemical analysis of blood samples collected from experimental groups at the end of 8 weeks is shown in Table 3. Significant statistical differences were observed in the average serum glucose levels between the groups ($p<0.05$) as shown in Figure 2.

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Table 2. Average epididymal fat weights of the groups

Weight (g)	Control (n=10)	HFD (n=10)	Tarhana+HFD (n=10)
	Mean±SD	Mean±SD	Mean±SD
epididymal fat	0.54±0.34 [b c]	1.28±0.08 [a b]	1.02±0.04 [ac]

ANOVA* *p*<0.05 (post-hoc multiple comparison test)
a: statistically significant compared to the control group (*p*<0.05). b: it is statistically significant according to the tarhana+HFD group (*p*<0.05).
c: statistically significant compared to the HFD group (*p*<0.05). HFD: high fat diet. SD: standart deviation

Table 3. Average serum glucose and lipid profile values of the groups

Biochemical findings	Control	HFD	Tarhana+HFD
	Mean±SD	Mean±SD	Mean±SD
Glucose (mg/dL)	290.66±210.716 [c]	465.66±51.73 [ab]	325.8±65,28 [c]
Total cholesterol (mg/dL)	97.33±19.65 [b c]	227.0±30.61 [a b]	188.2±25.78 [ac]
HDL cholesterol (mg/dL)	69.6±16.8 [b c]	166.3±16.1 [a]	171.4±13.9 [a]
LDL cholesterol(mg/dL)	26.6±11.59 [b c]	74.3±15.9 [a b]	57.8±12.63 [ac]
Triglyceride (TG) (mg/dL)	131.3±20 [c]	169.3±32.59 [a b]	131.6±26.28 [c]

ANOVA * *p*<0.05
post-hoc multiple comparison test
a: statistically significant compared to the control group (*p*<0.05). b: it is statistically significant according to the tarhana+HFD group (*p*<0.05).
c: statistically significant compared to the HFD group (*p*<0.05).
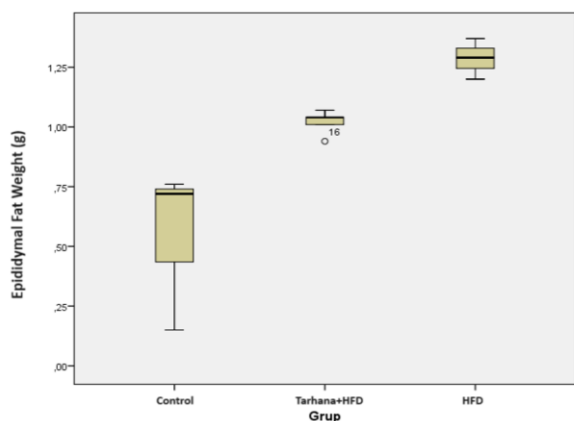
Figure 1. Comparison of epididymal fat weights across different groups
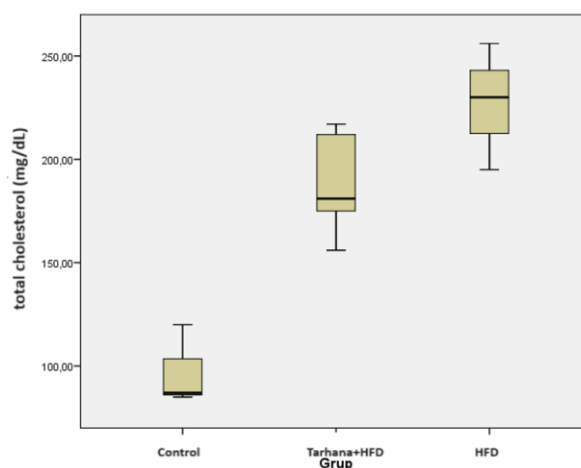
Figure 3. Comparision of the total cholesterol (mg/dL) between groups
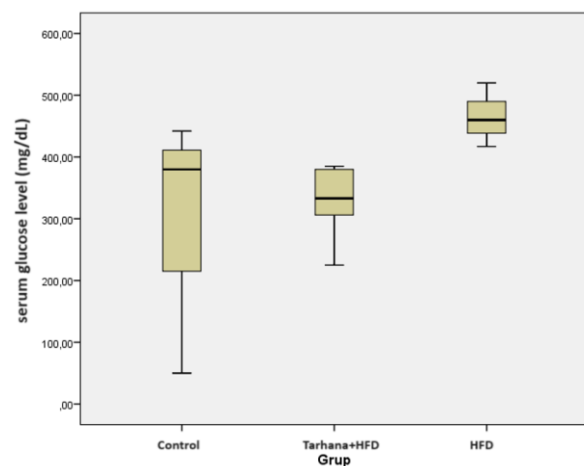
Figure 2. Comparision of the serum glucose (mg/dL)between groups
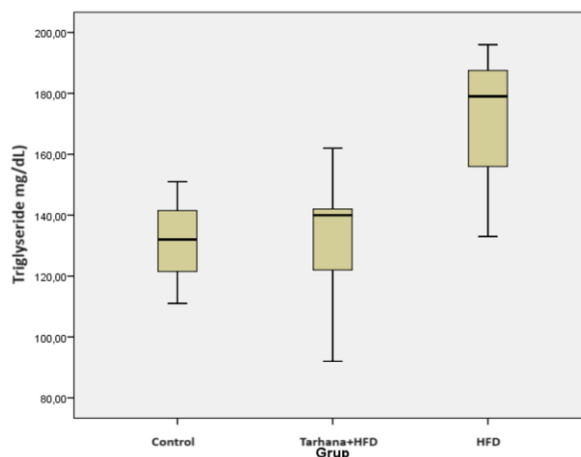
There was a statistically significant difference in the average total cholesterol levels among the groups (*p*<0.001) (Figure 3). There was a statistically significant difference in the average TG levels across the groups (*p*<0.001) (Figure 4).

Figure 4. Comparision of the triglyseride (mg/dL) between groups

Discussion

The World Health Organization reports that cardiovascular diseases top the list of global causes of death, accounting for around 32% of all deaths.[17] In Turkey, this rate is 38.4%

according to the 2018 data of TUIK (Turkish Statistical Institute).[18] Among the most important causes of cardiovascular diseases are obesity, metabolic syndrome and its components, hyperlipidemia, an increase in white adipose tissue, high blood pressure and insulin resistance.[5] According to the Turkey Nutrition and Health Research 2017, the incidence of obesity in Turkey is 30.3%. The regional data of the respective research indicate that, the obesity rate in the Southeastern Anatolia region is 22.9%. In Gaziantep province, which is located in the Southeastern Anatolia region where this study was conducted, the incidence of obesity was found to be 36.8% higher than the average in Turkey.[19] Hyperlipidemia is a primary contributor to mortality in coronary heart diseases.[20] Modifiable risk factors include eating habits, physical activity, lifestyle, etc. The most practical and effective method to enhance lipid profiles and lower the risk of cardiovascular diseases involves making lifestyle adjustments, such as adopting a healthy diet and interested in regular physical exercise.[21] Education is essential at all stages of intervention to achieve these behavioral changes in the management of obesity[22].

The study evaluated the effect of adding a strong symbiotic tarhana rich in probiotics and prebiotics, a traditional grain-based fermented Turkish food. We believe the results of this study point to the possibility that tarhana might be used as an alternative supplement to enhance lipid profiles, which would help to prevent metabolic disorders that are common throughout the world.

Fat-rich diets not only trigger obesity and associated disorders in humans, but they also trigger the same disorders in animals. Studies in both rats and mice have shown a positive relationship between the amount of fat in the diet and the increase in body weight and adipose tissue.[23]

In this study, serum glucose levels in the tarhana- supplemented group were significantly decreased compared to those in the HFD only group. Recent research has concentrated on exploring the connection between gut microbiota and the regulation of glucose levels. In a review conducted by Somayyeh Firouzi et al.[17] the main emphasis was on evaluating how probiotics influence glucose homeostasis. Parameters like lipid profiles, body weight, and energy consumption were also examined, but with secondary importance. In total 17 animal based and 4 human based studies were examined. Of these studies, 16 involving animals and three involving humans demonstrated improvements in at least one parameter related to glucose homeostasis.[24] The antidiabetic effect of a fermented food supplement consisting of rice bran and soy fermented by Bacillus sp. for 10 weeks on rats with type 2 diabetes was investigated by Seong Lim and Boo-Yong.[18] As a result of the study, diabetic rats receiving fermented food supplements showed decreased HbA1c, glucose and serum triglyceride levels.[25] In a Ray et al.[19] study conducted including HFD-Fed male mice fermented by Bifidobacterium sp during 8 weeks rice-based fermented beverage of fermented foods by supplementation in the control of obesity, lipid metabolism, effects on glucose homeostasis were investigated. As a result of the study, similar to this study, lower epididymal adipose weights were observed in the Bifidobacterium supplemented and HFD+fermented food supplemented groups compared to the groups fed only HFD. The anti-obesity effect of Bifidobacterium sp. fermented foods is thought to be due to the content of bioactive organisms and many compounds such as phenolic compounds, prebiotics, dietary fibers, vitamins, minerals, peptides, antioxidants. As a result of this experimental study, it was found that the development of grain-based fermented foods could be an alternative method for the cure of obesity and associated disorders.[26] In this study, epididymal fat content was significantly higher in the HFD-fed group compared to the other two groups. Nevertheless, the amount of epididymal fat in the tarhana supplemented fed group was found to be significantly lower than in the HFD-Fed group. In a research project carried out by Shouman Lasker et al.[20] yogurt supplementation was given to rats fed an HFD for 8 weeks. The study found that rats fed a diet of yogurt plus a high-fat diet exhibited significantly lower weights of epididymal fat and serum glucose levels compared to those

fed only an HFD. As a result of this study, it was found that yogurt supplementation used in the diet may provide an alternative option in the treatment of metabolic syndrome.[27] In the study, the total cholesterol level of the tarhana supplemented group was remarkably lower than the cholesterol level of the group fed only an HFD. It is believed that probiotics exert their effect on cholesterol metabolism through various mechanisms.[28] A study conducted by Rehab F.M. Ali examined the effect of different amounts of Kishk administration on pain, lipid parameters and biochemical parameters in rats fed a hypercholesterolemic diet[29]. Kishk is a traditional fermented grain food whose main ingredients are yogurt and whole wheat. The groups supplemented with Kishk experienced a notable reduction in body weight gain, which was attributed to the increased intake of fiber-rich foods, especially grains, as components of a nutritious diet. It was observed that the lipid profile of the Kishk-supplemented groups also improved significantly.[30] There is a significant inverse association between the level of HDL cholesterol in the plasma and the risk of cardiovascular diseases induced by atherosclerosis.[31] In animal based studies, it has been observed that the cholesterol and fat type of the diet can change the structure and function of HDL cholesterol. In particular, long-term HFD has been shown to impair the antioxidant and anti-inflammatory functions of HDL cholesterol in mice, and this effect was related to elevated HDL lipid hydroperoxide content.[32] In some studies, low HDL cholesterol levels were observed in obese mouse models, while in other studies, an increase in HDL cholesterol was observed.[33] Inulin is a functional plant derived polysaccharide consisting of a fructan blend of oligosaccharides and polysaccharides (also known as oligofructose). Onion, wheat, barley, garlic, artichoke, banana and chicory are the most important sources of inulin.[34]. It is known that inulin has an improving effect on lipid profile and glucose metabolism.[35] The tarhana used in the study was made at home by following traditional methods. Onion and whole wheat flour are important sources of inulin. Cooked onions contain 3g/100 inulin[36] and 2 kg of onions (60g inulin) are used in the

recipe. Whole wheat flour contains 2.4g/100[36] inulin and 4 kg of whole wheat flour (96 g inulin) is used in the recipe. In this study, the results obtained showed an important decrease in the blood glucose and lipid levels of the tarhana + HFD group compared to the HFD. In a rapidly developing and changing world, people's eating habits have also changed greatly. The demand for more easily accessible and ready-made foods has increased instead of home-prepared foods. As these diets become more common, a range of disorders is becoming more prevalent, including Type 2 diabetes, liver diseases, obesity, metabolic syndrome, and notably cardiovascular diseases. These diseases are also a great burden on countries from an economic point of view. The importance of nutrition in the treatment and prevention of diseases is increasing day by day. Protective foods with rich nutritional content, which are not in the form of drugs, capsules or powders, but are a part of our daily diet are called functional foods. Fermented foods belong to the class of functional foods. Almost 60-70% of the products called functional foods are probiotics.[37] It is pointed out that tarhana is a symbiotic and functional food due to its high nutritional value, probiotic bacteria strains and prebiotics[38]. Lactic acid bacteria are recognized as potential mediators of beneficial effects on hypercholesterolemia. Lactobacilli possess enzymes that participate in the deconjugation of bile salts to form bile acids, thus inhibiting micelle formation, intestinal cholesterol absorption and enterohepatic circulation of cholesterol[39]. Prebiotics may reduce cardiovascular diseases risk by reducing inflammatory markers[40]. The main mechanism of action of prebiotics on lipid metabolism is based on their ability to reduce lipid levels in the bloodstream by the presence of short-chain fatty acids (SCFA) produced upon selective fermentation of the prebiotic substrate by the gut microbiota[41].

A healthy diet should consist of a balanced pattern based on nutritional diversity. We can benefit from the protective effects by adding fermented foods to our daily diet in a way that does not disrupt the pattern. The production of traditional fermented foods is mostly done at home in a way that is sufficient for households.

By popularizing the consumption of these foods, it can be achieved to replace ready-made foods, and they are also easily accessibility also. Tarhana, a functional food used in study, significantly reduced the risk of developing many diseases with its positive effects on lipid profile, epididymal fat weight and glucose level.

Conclusion

As a result of our study, epididymal adipose tissue, blood glucose levels, total cholesterol and triglyceride levels decreased significantly. These effects indicate that the protective effect of tarhana on maintaining a healthy weight and preventing chronic diseases is important. Further similar studies contributing to the literature are needed to further investigate and analyze the different parameters of the effects of tarhana on maintaining healthy diet and well-being.

Ethics Committee Approval

The study received authorization from the Gaziantep University Experimental Animal Local Ethics Committee, with approval granted during the meeting on 18.02.2020 under decision number 2020/10.

Author Contributions

All of the authors contributed at every stage of the study.

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Declaration of Interest

There is no disagreement between the authors.

Financial Disclosure

Statements

This study was presented as a poster paper.

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Research Article/Özgün Araştırma

Does vertical pattern affect lip strain in open-bite patients?: A cephalometric study

Açık kapanış hastalarında dik yön gelişimi dudak gerilimini etkiler mi?

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Abstract
Aim: To examine effect of skeletal pattern on lip strain in open-bite, in individuals with normal and increased vertical pattern.
Materials and Methods: 56 open bite patients with Normovergent (NG) and Hyperdivergent (HG) vertical patterns (Mean age: 16.57 years) underwent cephalometric analysis. Soft tissue labial, hard tissue, and dental inclinations were measured. Statistical analyses were performed using Kolmogorov Smirnov, Mann Whitney-U, and independent sample t-tests; Pearson and Spearman correlation analyses; and Linear regression analysis.
Results: In HG, each degree of SN-UOP increase caused 0.371 mm increase in lower lip strain. While in NG, upper lip strain was associated with IMPA and SNB (each degree caused 0.14 mm increase and 0.207 mm decrease respectively).
Conclusion: IMPA, SN-UOP and SNB were found to be the determinants of lip strain. Dental, vertical, and sagittal variables showed association with lower face.
Keywords: Open bite; Cephalometry; Vertical dimension.

Öz
Amaç: Bu çalışmada açık kapanışlı bireylerde dik yön paterninin dudak gerginliği üzerine etkisinin, normal ve artmış dik yön paternine sahip bireylerle karşılaştırmalı olarak incelenmesi amaçlanmıştır.
Gereç ve Yöntem: Normoverjan (NG) ve Hiperdiverjan (HG) dik yön paternlerine sahip (Ortalama yaş: 16,57 yıl) 56 açık kapanış hastasının lateral sefalometrik röntgenleri analiz edilmiş, hastaların yumuşak doku, sert doku ve dental eğimleri ölçülmüştür. İstatistiksel analizler Kolmogorov-Smirnov, Mann Whitney-U ve bağımsız örneklem t-testleri; Pearson ve Spearman korelasyon analizleri; ve doğrusal regresyon analizi kullanılarak gerçekleştirilmiştir.
Bulgular: HG'de her derece SN-UOP artışı alt dudak geriliminde 0,371 mm artışa neden olmuştur. NG'de ise üst dudak gerilimi IMPA ve SNB ile ilişkili bulunmuştur (Her bir derece artış, sırasıyla 0,14 mm artış ve 0,207 mm azalmaya neden olmuştur).
Sonuç: IMPA, SN-UOP ve SNB'nin dudak geriliminin belirleyicileri olduğu düşünülmektedir. Dental, vertikal ve sagital parametreler alt yüz ile ilişkili bulunmuştur.
Anahtar Kelimeler: Açık kapanış; Sefalometri; Dikey boyut.

Introduction

Anterior open bite (AOB) malocclusion is commonly known for its need for the most complicated diagnostic steps and treatment process. High relapse tendency necessitates prolonged retention precautions. The multifactorial etiology and conflict amongst classifications frequently result in misdiagnosis.[1]

The etiology of increased vertical pattern by steepening of mandibular plane (MP) angle is disproportional growth in favor of vertical dimension. If antagonist dentition cannot compensate for the increasing interocclusal distance, a symmetrical AOB with posterior occlusal contacts is seen. Studies also report that trauma, inflammatory and autoimmune diseases, degenerative joint disease, functional factors, inheritance, and deleterious effects of bad habits may cause AOB.[2-4] Amongst functional factors, tongue posture or endogenous tongue thrust are the key etiologic factors in formation of functional AOB. However, confliction regarding lingual behavior, whether the tongue position is a contributor or a consequence, remains.[2, 5]

The contribution of MP angle as a causative component to AOB malocclusion was first suggested by Sassouni; who classified AOB as *dentoalveolar* or *skeletal*.[6] Today in clinical practice, MP is a strong indicative of vertical pattern.[7-9] However its relevance with AOB malocclusion is a matter of debate in literature.[10-12] Some authors claim that two conditions don't necessarily have to be seen together, while another group claims that skeletal origin of AOB can be distinguished from hyperdivergent cephalometric tracing results.[1, 13, 14]

Proclined anterior teeth and a normal vertical pattern usually indicate dental AOB.[14] Arat et al. classified AOB as *morphogenetic* or *functional* according to lower facial height and lip competency as diagnostic parameters.[1]

The chief concern of AOB individuals is often esthetic or functional problems such as inability to bite and speech problems.[3, 15, 16] However, the scale has another pan that is only visible to the clinician's eye. Evaluation of lip competence, incisal exposure, and inclination of occlusal plane (OP) are also crucial components of the clinical examination.[14] For example, lip incompetence is a pathological condition characterized by difficulty or inability to seal the lips and is commonly accompanied by AOB malocclusion. Etiologic factors are either skeletal, dental, or labial originated. If treatment is delayed, unappealing facial esthetics, speech problems and periodontal tissue reactions caused by mouth breathing are inevitable.[17]

Previous studies investigated the behavior of perioral soft tissues in different malocclusions, or mouth breathing as an etiologic factor of AOB.[18, 19] To best of our knowledge, none studied how vertical divergence affected the lip competence in AOB. Whether the soft tissue conditions are the response or cause is an issue that should be further investigated. The current study hypothesized that the increase in MP angle is an indisputable fact in AOB malocclusion, resulting in soft tissue response. So, primary aim of this study was to investigate the soft tissue response of labial structures to increased vertical dimension in a sample that has AOB malocclusion. The secondary aim was to analyze other contributory skeletal and dental factors of soft tissue response in AOB in normovergent and hyperdivergent patients.

Materials and Methods

Signed informed consent forms were obtained from all subjects at the beginning of their treatment.

The sample consisted of 56 AOB patients who received extraction treatment. The demographic data are presented in Table 1. The initial lateral cephalograms underwent cephalometric analysis following linear calibration, head orientation according to Frankfort horizontal by the same examiner (EB) using NemoStudio NX-Pro v.10.4.2 (Nemotec, Madrid, Spain). According to the tracing results, the sample was classified into two as (1) Normovergent Group ("NG"; n:28, $26° < GoMe-SN < 39°$, Mean: $35.53° \pm 3.57$) and (2) Hyperdivergent Group ("HG"; n:28, $GoMe-SN > 40°$, Mean: $45.28° \pm 3.7$).

Table 1. Demographic data of the sample

Variables		Hyperdivergent Group			Normovergent Group		
	Sex	**n**	**%**		**n**	**%**	
Demographic	**Female**	17	60.7		16	57.1	
data	**Male**	11	39.3		12	42.9	
	Total	28	100		28	100	
		Mean	**Median**	**SD**	**Mean**	**Median**	**SD**
Pretreatment Age (y)		17.06	16.53	3.04	16.08	16.18	2.76

The inclusion criteria were as follows:

- ANB between -2 and 4 degrees,
- Lateral cephalograms with high quality,
- No previous orthodontic treatment history,
- No syndromic disorders,
- Complete anterior dentition,
- Sealed lip postures were included in the sample.

The soft and hard tissue parameters that were used in cephalometric analysis and their descriptions are presented in Figure 1 and Table 2.

Type of the study

The study is retrospective.

The sample size of the study

A post-hoc power analysis was conducted using G*Power (Version 3.1.9.6, Heinrich-Heine-Universität, Düsseldorf, Germany) software. The calculation revealed that 28 participants for each group allowed preserving 94.7% power and an alpha of 0.05 to obtain an effect size of 0.99 with reference to SNA values of groups.
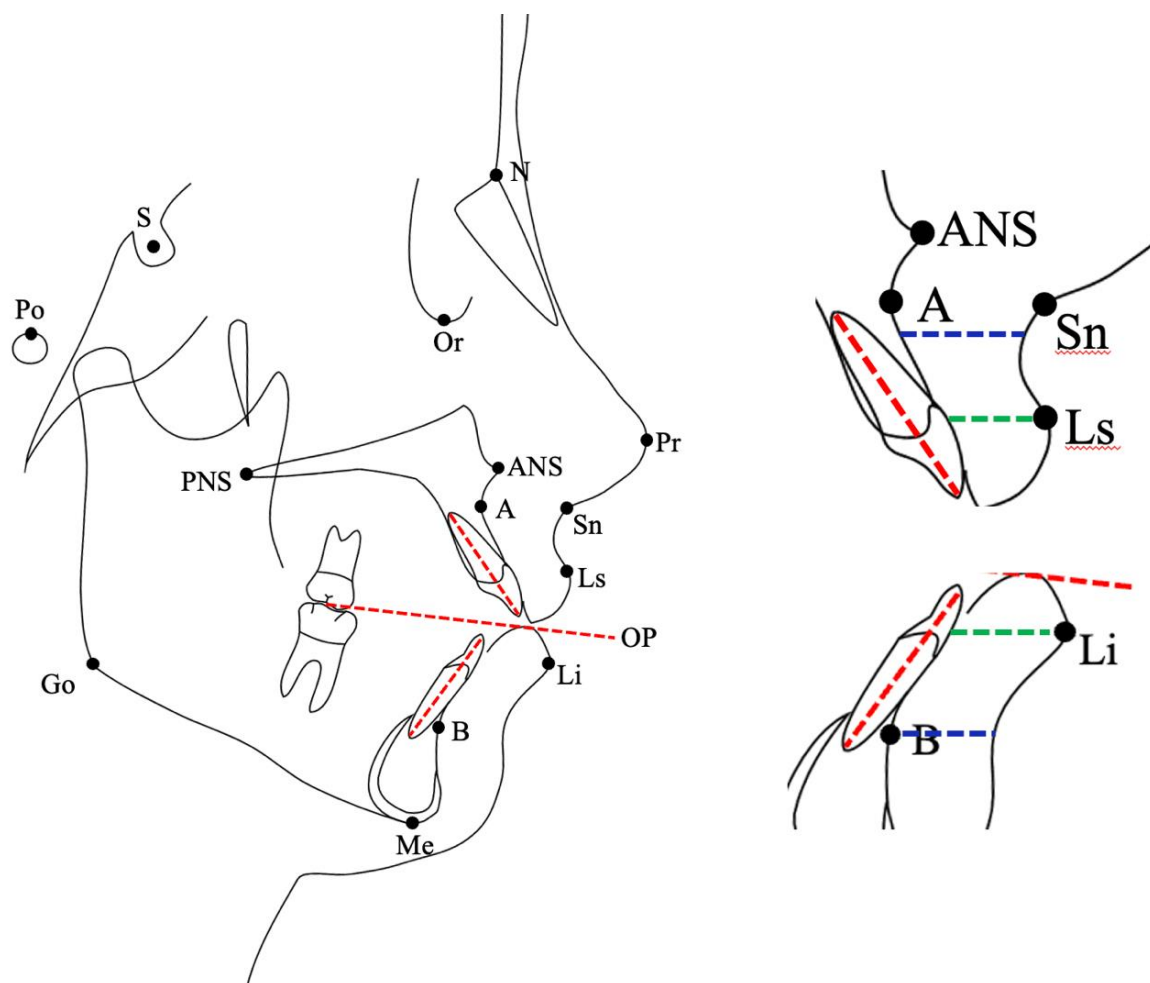
Figure 1. Cephalometric landmarks and lip strain. Lip strain is calculated by taking the arithmetic difference of lip thickness and basal lip thickness. Green dashed lines indicate lip thickness, blue dashed lines indicate basal lip thickness

Table 2. The cephalometric parameters that is used in the study, and their descriptions

Cephalometric Variables		Descriptions
Skeletal, Sagittal	**SNA (°)**	Angle formed between S, N and A point
	SNB (°)	Angle formed between S, N and B point
	ANB (°)	Arithmetic difference of SNA angle and SNB angle
	N⊥A (mm)	A true vertical line dropped from N and horizontal distance parallel to this true vertical line is measured from A point
Skeletal, Vertical	**SN-GoMe (°)**	Angle formed between S-N line and Go-Me line
	FMA (°)	Angle formed between Po-Or line and Go-Me line
	ANSMe/NMe	The ratio of lower facial height divided by total facial height (x100)
	Jarabak ratio	The ratio of posterior facial height divided by anterior facial height (x100)
	SN-PP (°)	Angle formed between S-N line and palatal plane
	SN-UOP (°)	Angle formed between S-N line and maxillary occlusal plane
Dental	**UI-SN (°)**	Angle formed between S-N line and and upper centrals axis
	UI-PP (°)	Angle formed between palatal plane and upper centrals axis
	IMPA (°)	Angle formed between lower centrals axis line and Go-Me line
	UI-OP (°)	Angle formed between upper centrals axis line and functional occlusal plane
	LI-OP (°)	Angle formed between lower centrals axis line and functional occlusal plane
	Ī-Ī (°)	Angle formed between upper and lower centrals axis lines
	Overjet (mm)	Distance between the incisal edges of maxillary and mandibular incisors, parallel to the functional occlusal plane
	Overbite (mm)	Distance between the incisal edges of maxillary and mandibular incisors, perpendicular to the functional occlusal plane
Soft Tissue	**Nasolabial Angle (°)**	The angle formed by a line tangent to the base of the nose and a line tangent to the upper lip
	UL Thickness (mm)	Horizontal thickness of upper lip overlying the incisors at the level of vermilion border
	Basal UL Thickness (mm)	Lip thickness near the base of alveolar process, about 3 mm below A point
	UL Strain (mm)	Arithmetic difference between upper lip thickness and basal upper lip thickness. Values >1 mm show lip redundancy, negative values or 0 mm show lip strain.
	UL Length (mm)	Distance between subnasale (Sn) and stomion superius (Sts)
	LL Thickness (mm)	Horizontal thickness of lower lip overlying the incisors at the level of vermilion border
	Basal LL Thickness (mm)	Lip thickness near the base of alveolar process, at about B point
	LL Strain (mm)	Arithmetic difference between lower lip thickness and basal lower lip thickness. Values >1 mm show lip redundancy, negative values or 0 mm show lip strain.
	LL Length (mm)	Distance between stomion inferius (Sti) and menton (Me)

Data collection tools

Subjects were collected retrospectively from the archive of Orthodontics Department in Marmara University, Faculty of Dentistry. Data was collected using a cephalometric tracing software (NemoStudio NX-Pro v.10.4.2, Nemotec, Madrid, Spain).

Data analysis

Statistical analyses were performed using SPSS software (Version 25.0, IBM Corp, Armonk, NY, USA). The conformity of the variables to the normal distribution was assessed using Kolmogorov-Smirnov test. Intergroup differences of variables were analyzed with Mann Whitney-U and independent sample t-tests. Significantly different hard tissue variables in HG and NG were analyzed using Pearson and Spearman correlation analyses. Then linear regression analysis was performed on the significantly correlated pairs to interpret and formulize the relationship between soft and hard tissue variables. Statistical significance was set at $p=0.05$.

Ethics committee approval

Ethics committee approval was obtained from Medical School Ethical Committee of Clinical Studies of the Marmara University (Protocol no 09.2023.1253; 08/02/2024). The study conformed to the principles of Helsinki Declaration.

Results

All variables were measured twice at one-month intervals by a second researcher (YBA).

Intraclass coefficient ranging between 0.893 to 1.000 revealed that measurements had high reliability. The intergroup differences are presented in Table 3. Regarding dentoskeletal structures, FMA, GoMe-SN, Jarabak, SNA, SNB, NperA, SN-UOP, IMPA showed significant differences between HG and NG. The significant variables were then subjected to correlation analyses with soft tissue parameters. There were no significant intergroup differences between the soft tissue values in HG and NG.

Table 3. Evaluation of intergroup differences

Variables		Hyperdivergent Group			Normovergent Group			
		Mean	Median	SD	Mean	Median	SD	*p*
Skeletal, Sagittal	**SNA (°)**	76.75	77	2.99	80.07	80	3.63	0.000*a
	SNB (°)	74.57	74.50	3.12	78.32	78.50	3.74	0.000*a
	ANB (°)	2.18	2.50	0.14	1.75	2	0.11	0.278b
	N⊥A (mm)	-4.05	-4.90	3.82	-1.97	-1.15	3.63	0.042*a
Skeletal, Vertical	**GoMe-SN (°)**	45.28	44.5	3.70	35.53	36.50	3.57	0.000*a
	FMA (°)	36.25	37	4.03	27.14	28	3.96	0.000*a
	ANSMe/NMe	56.70	56.80	1.94	55.76	56.35	4.65	0.533b
	Jarabak ratio	61.86	61.55	3.31	66.60	66.45	3.37	0.000*a
	SN-PP (°)	10.03	9.50	3.75	8.32	8	3.50	0.082a
	SN-UOP (°)	18.61	19	4.68	14.96	15	3.57	0.002*a
Dental	**UI-SN (°)**	113.15	112	6.95	115.03	115.5	6.34	0.293a
	UI-PP (°)	114.93	115	8.79	116.14	116.5	6.71	0.564a
	IMPA (°)	87	88	5.82	93.25	91.50	6.53	0.0003*a
	UI-OP (°)	55.03	56	4.86	57.61	57.61	5.49	0.069a
	LI-OP (°)	68.39	68.5	5.65	66.78	67.50	5.70	0.294a
	I̱-Ī (°)	121.71	123.5	9.74	123.21	122.5	8.78	0.548a
	Overjet (mm)	3.44	3.10	2.06	2.96	2.40	2.35	0.418a
	Overbite (mm)	-1.24	-0.80	1.58	-0.63	-0.50	1.56	0.081b
Soft tissue	**Nasolabial Angle (°)**	108.07	110	11.93	107.10	107	10.36	0.748a
	UL Thickness (mm)	12.40	12.33	2.24	12.53	12.51	1.97	0.814a
	Basal UL Thickness (mm)	16.06	16.45	2.41	15.33	15.27	2.28	0.247a
	UL Strain (mm)	-3,67	-3.69	2.20	-2,80	-2.15	2.13	0.140a
	UL Length (mm)	21.34	21.28	2.68	22.05	21.95	3.23	0.376a
	LL Thickness (mm)	14.83	14.44	2.62	16.23	14.31	9.06	0.954b
	Basal LL Thickness (mm)	13.29	13.69	2.00	13.04	13.04	1.51	0.594a
	LL Strain (mm)	1.53	1.36	2.47	4.27	1.80	10.33	0.583b
	LL Length (mm)	49.01	55.30	4.49	49.41	52.96	4.43	0.733a

a: Independent sample t-test, b: Mann Whitney-U test; UL: Upper lip, LL: Lower lip; *$p<0.05$*

In upper lip region, upper lip thickness and upper lip length had no association in NG, however, they had a moderate positive correlation with SNA (*r=0.474* and *r=0.449* respectively) in HG. Upper lip strain had also moderate positive correlation with SNA and SNB of HG (*r=0.521* and *r=0.502* respectively), and moderate negative with GoMe-SN (*r=-0.482*) in HG, while dental variables had no significant relation. In NG; IMPA had moderate negative (*r=-0.485*), and SNB had positive moderate correlations (*r=0.430),* and vertical dimension of the jaws had no significant effect on upper lip strain. Moreover, nasolabial angle of HG had moderate and strong positive correlations with SNA (*r=-0.547*) and SNB (*r=-0.664*) respectively. In NG, nasolabial angle had moderate negative with SNA (*r=-0.491*), moderate positive with SNB (*r=0.451*) and NperA (*r=0.414*), moderate negative with SN-OP (*r=-0.571*) and strong negative with SN-UOP (*r=-0.630*). (Table 4)

Regarding lower lip region; lower lip thickness of HG was found to have weak positive correlation with IMPA (*r=0.382*) and moderate negative correlation with SN-UOP (*r=-0.458*). NG, on the other hand, had moderate negative correlation with SN-OP (*r=-0.583*). Lower lip length of HG was seen to be affected with moderate positive correlation by SNA (*r=0.429*) and weak negative correlation by SN-UOP (*r=-0.376*). However, in NG, the length interacted with

SNB and NperA with weak negative correlations (r=-0.390, r=-0.378, respectively). In terms of lower lip strain, moderate negative correlations were found with SN-UOP (r=-0.583 in HG, r=-0.420 in NG) and SN-OP in both groups. (r=-0.488 in HG, r=-0.554 in NG). (Table 4)

Table 4. Correlation between soft and hard tissue variables in Hyperdivergent and Normovergent Groups

Variables			Upper lip thickness		Upper lip length		Upper lip strain		Nasolabial angle		Lower lip thickness		Lower lip length		Lower lip strain	
			HG	NG	HG	NG	HG	NG	HG	NG	HG	NG	HG	NG	HG	NG
Vertical	FMA (°)	r	-0.099	-0.135	0.058	-0.005	-0.172	-0.021	-0.064	0.163	0.143	0.286	0.081	-0.269	-0.072	0.196
		p	0.616a	0.493a	0.768a	0.980a	0.380a	0.914a	0.745a	0.408a	0.467b	0.139b	0.683a	0.166a	0.715b	0.319b
	GoMe-SN (°)	r	-0.099	-0.168	0.067	-0.064	-0.482	-0.064	0.221	0.020	0.016	0.031	0.031	0.320	-0.253	-0.121
		p	0.616a	0.393a	0.737a	0.745a	0.009*a	0.747a	0.258a	0.918a	0.937b	0.876b	0.875a	0.097a	0.195b	0.539b
	Jarabak ratio	r	-0.099	-0.035	0.103	-0.165	0.037	-0.233	0.013	0.150	0.032	0.229	-0.029	0.136	0.209	0.127
		p	0.616a	0.861a	0.603a	0.401a	0.851a	0.233a	0.950a	0.445a	0.873b	0.242b	0.884a	0.490a	0.285b	0.518b
	SN-UOP (°)	r	-0.233	-0.141	-0.140	-0.008	-0.162	-0.362	0.349	-0.630	-0.458	-0.346	-0.376	0.014	-0.583	-0.420
		p	0.233a	0.474a	0.476a	0.967a	0.412a	0.059a	0.069a	<0.001*a	0.014*b	0.072b	0.049*a	0.944a	0.001*b	0.026*b
Dental	IMPA (°)	r	0.357	-0.083	0.290	0.109	0.080	-0.485	0.186	0.127	0.382	0.117	0.326	-0.192	0.056	0.127
		p	0.063a	0.676a	0.135a	0.580a	0.684a	0.009*a	0.343a	0.521a	0.045*b	0.553b	0.090a	0.327a	0.776b	0.518b
Sagittal	SNA (°)	r	0.474	-0.082	0.449	-0.077	0.521	0.292	-0.547	-0.491	0.347	-0.201	0.429	-0.246	0.209	-0.170
		p	0.011*a	0.677a	0.017*a	0.699a	0.004*a	0.132a	0.003*a	0.008*a	0.071b	0.305b	0.023*a	0.207a	0.285b	0.387b
	SNB (°)	r	0.310	-0.220	0.172	0.073	0.502	0.430	-0.664	0.451	0.056	0.019	0.167	-0.390	0.213	0.163
		p	0.108a	0.260a	0.381a	0.710a	0.006*a	0.023*a	<0.001*a	0.016*a	0.778b	0.922b	0.395a	0.040*a	0.277b	0.407b
	NPerA (mm)	r	0.187	-0.195	0.278	0.085	0.231	0.200	-0.276	0.414	0.013	0.114	0.183	-0.378	-0.138	0.291
		p	0.341a	0.321a	0.152a	0.666a	0.237a	0.308a	0.155a	0.028*a	0.948b	0.563b	0.351a	0.048*a	0.484b	0.133b

a: Pearson correlation analysis, b: Spearman correlation analysis; HG: Hyperdivergent group, NG: Normovergent group; *$p<0.05$

In the last step of statistical analyses, significantly correlated pairs were investigated by linear regression analysis. (Table 5) When evaluating the components of upper lip region, it was found that one unit increase in SNA leads 0.355 unit increase in upper lip thickness (p=0.011, R^2=0.224) and 0.403 unit increase in upper lip length (p=0.017, R^2=0.201) in HG. However, in NG, there was no further significance. When upper lip strain of HG was investigated, there was no statistical significance. In NG; in case of one unit increase (1) in IMPA: strain increases 0.140 unit, (2) in SNB: strain decreases 0.207 unit (p=0.004, Adjusted R^2=0.312). For nasolabial angle of HG, each unit increase in SNB was found to cause 2.954-unit decrease in the angle (p=0.001, Adjusted R^2=0.400), while in pairwise comparisons of NG no statistical significance was found (p=0.015, Adjusted R^2=0.328).

In the lower lip region of HG; the increase in each unit of IMPA caused 0.208 unit of lower lip thickness increase, while SN-UOP caused 0.286 decrease (p=0.0002, Adjusted R^2=0.449). In NG, there was no significant relationship (p=0.086). Even if the regression model of lower lip length in HG is significant, no significant equation was obtained in either group. As the variable of the groups; lower lip strain of HG increased 0.371 unit, as a result of a unit increase of SN-UOP (p=0.002, Adjusted R^2=0.350), however in NG, there was no hard tissue interaction that could be related with lip strain.

Table 5. Linear regression analyses of hard and soft tissues

Dependent variables	Independent variables	Hyperdivergent group							
		β_0	%95 Confidence Interval		Std. Error	t	p	R^2	Adjusted R^2
			Lower bound	Upper bound					
UL Thickness	(Constant)	-14.853	-35.295	5.589	9.945	-1.493	0.147	0.224	0.195
	SNA	0.355	0.089	0.621	0.129	2.742	0.011*		
UL Length	(Constant)	-9.589	-34.439	15.261	12.089	-0.793	0.435	0.201	0.171
	SNA	0.403	0.079	0.726	0.157	2.560	0.016*		
ULStrain	(Constant)	-13.829	-44.401	16.743	14.813	-0.933	0.360	0.361	0.282
	GoMe-SN	-0.221	-0.483	0.041	0.127	-1.737	0.095		
	SNA	0.377	-0.146	0.902	0.254	1.486	0.150		
	SNB	-0.118	-0.692	0.455	0.278	-0.425	0.674		
Nasolabial angle	(Constant)	290.042	195.275	384.809	46.013	6.303	0.000001	0.445	0.400
	SNA	0.499	-1.982	2.979	1.204	0.414	0.682		
	SNB	-2.954	-5.33	-0.577	1.154	-2.559	0.017*		
LL Thickness	(Constant)	2.085	-9.950	14.120	5.844	0.357	0.724	0.490	0.449
	IMPA	0.208	0.075	0.340	0.064	3.229	0.003*		
	SN-UOP	-0.286	-0.451	-0.121	0.080	-3.583	0.001*		
LL Length	(Constant)	3.068	-71.996	78.134	36.447	0.084	0.933	0.231	0.170
	SNA	0.756	-0.154	1.666	0.442	1.711	0.099		
	SN-UOP	-0.348	-0.929	0.233	0.282	-1.234	0.228		
LL Strain	(Constant)	7.389	3.487	11.291	1.894	3.900	0.001	0.398	0.350
	SN-UOP	-0.371	-0.683	-0.058	0.152	-2.443	0.022*		
Dependent variables	Independent variables	Normovergent group							
		β_0	%95 Confidence Interval		Std. Error	t	p	R^2	Adjusted R^2
			Lower bound	Upper bound					
UL Thickness					NS				
UL Length					NS				
ULStrain	(Constant)	-5.955	-25.242	13.332	9.365	-0.636	0.531	0.363	0.312
	IMPA	-0.140	-0.249	-0.031	0.053	-2.649	0.014*		
	SNB	0.207	0.017	0,397	0.092	2.245	0.034*		
Nasolabial angle	(Constant)	216.623	81.621	351.625	65.096	3.328	0.003	0.452	0.328
	SNA	-1.107	-3.760	1.545	1.279	-0.865	0.396		
	SNB	-0.335	-2.836	2.165	1.206	-0.278	0.783		
	NPerA	-0.265	-1.613	1.084	0.650	-0.407	0.688		
	SN-UOP	1.290	-1.180	3.760	1.191	1.083	0.290		
LL Thickness	(Constant)				NS				
	SNB								

LL Length	(Constant) SN-UOP	NS
LL Strain	(Constant) SNA SNB	NS

Linear regression analysis; UL: Upper lip, LL: Lower lip; *p<0.05

Discussion

Soft tissue profile started to take more place in contemporary orthodontic diagnosis and treatment planning. Many studies have examined AOB malocclusion and its relationship with soft tissues.[1, 5, 20] However none focused on the effects of vertical dimension over labial structures in an AOB sample. Thus, the current study aimed to investigate the interaction between dental, skeletal, and soft tissue variables.

The vertical pattern of the sample comprised normovergent and hyperdivergent individuals since the etiologic nature of AOB malocclusion usually manifests in vertical direction.[1] The severity of AOB malocclusion in the present sample can be considered moderate. Cephalograms were preferred in this study since the technique provides the evaluation of both soft and hard structures, as well as its ease and availability in clinical routine.[21] Sealed lip posture was preferred to be able to evaluate lip strain which is the prominent goal of the current study.

During sample selection, GoMe-SN was used as the primary criterion to describe the vertical relationship. ANB angle was standardized to achieve similar anteroposterior relationship of the jaws relative to each other. Moreover, upper incisor inclination which is a robust determinant of both upper and lower lip support, was similar between two groups. Thus, these interfering factors were eliminated so that expression of soft tissue parameters due to vertical differences could be understood better. The significantly differing variables such as sagittal (HG<NG) and vertical (NG<HG) skeletal parameters, OP (NG<HG) and lower incisor inclinations (HG<NG) could undergo rather unbiased evaluation.

However, in contrast to the expected outcome, soft tissue characteristics of both groups were found to be similar, and the study hypothesis was rejected. Although there was a numerical difference in lip strain parameters between the two samples, they were statistically insignificant.

During interpretation of the statistical analysis results, the similarities and differences between structural natures of groups were examined (Table 3) to explain this outcome. The two groups were found to be similar in terms of some vertical parameters such as ANSMe/NMe, SN-PP, and negative overbite. This can be the reason for insignificant soft tissue differences between groups, preventing significant soft tissue expression of vertical variation. These findings conformed to a previous study, defining the characteristics of skeletal AOB.[22] Previous studies compared open and normal bite individuals in two groups and found no difference in SN-UOP value.[5, 23] Several studies also found similar results to the present study, suggesting that NG has increased IMPA and GoMe-SN values in comparison with normal bite individuals.[5, 24] In the same studies, upper incisor inclination of AOB group was higher than normal bite group. However, in our study, both NG and HG had no significant difference in terms of upper incisors.[5]

Another notable point is the significant difference in sagittal positions of the jaws (SNA, SNB; HG<NG). This raises the question whether the vertical excess restricts the sagittal growth. This may be a question to be further investigated. In comparison of normal bite and AOB patients with both normovergent patterns, Shenoy and colleagues found similar SNA and SNB values in both groups, while Hassan et al. suggested that the individuals who show lip incompetence have shorter anterior cranial

base, thus exhibiting more retrognathism.[25] This latter complies with the present results.

Even though the increasing vertical dimension was hypothesized to affect the soft tissue conditions in the first place, a few vertical parameters could reach out significance until linear regression analysis. Only upper lip strain had significant relationship with FMA and GoMe-SN. For other parameters, SNA, SNB, IMPA, and SN-UOP parameters were concluded as the fundamental determinants of lip structures.

Regarding upper lip length, each degree of increase in SNA of HG was found to cause 0.403 mm of upper lip length increase. Forward position of maxillary bone may be deemed to force the upper lip to extend to reach lip closure.

All negative strain values were interpreted as "increased lip strain" since values >1 mm show lip redundancy, and negative values or 0 mm show lip strain. (Table 2) E.g., in NG, the negative regression equation between IMPA and upper lip strain was reported as each degree of increase in IMPA, caused a 0.140 mm increase in upper lip strain. Vice versa, a degree of increase in SNB caused 0.207 mm lip redundancy. However, the noteworthy emphasis is significantly higher mean values of IMPA and SNB in NG may reinforce their regression significance on upper lip strain; unlike HG, which has a significant regression model, however, has no interaction with independent variables. Dixit and Shetty studied a sample consisting of children with tongue thrust.[20] They concluded half of the thrusters had also AOB, and none without thrust had AOB, while many of the thrusters also showed lip incompetency. Even so, whether tongue or lips are responsible for the imbalance remained unknown. Moreover, Hassan et al. reported that interincisal angle is the most prominent dental determinant, and MP angle is the vertical determinant of lip incompetence.[25] Our findings offered no significant intergroup difference of interincisal angle, however, the results about MP are concurrent with those, suggesting moderate negative correlation.

Nasolabial angle of HG is the second highest (40%) explained regression model of the study. In this model, each degree of SNB decreases nasolabial angle by 2.954 degrees. This interaction may be thought of as the mandible moves forward; the reducing tonus of perioral muscles will decrease nasolabial angle. In NG, skeletal values were in an acceptable range, so, even if significant correlations were observed, no significance was found in regression model.

Lower lip thickness of HG had the highest percentage of explanation by its regression model (44.9%) in current study. IMPA showed a synergetic relation such that each degree of this variable will cause 0.208 mm of lower lip thickness increase. The same interaction was also observed in upper lip thickness, increasing 0.355 unit for each unit of SNA. In normal conditions, increasing hard tissue support ends up with toned perioral musculature to be able to seal the lips. This contrary result can be explained by interindividual anatomic variability.

Increase in the SN-UOP caused 0.286 unit of lower lip thickness decrease in HG, which is an expected consequence. Increased tension of lip closure is anticipated when OP rotates clockwise. This result approves the regression model of lower lip strain which involves SN-UOP interaction as well, and each unit increase of the angle was found to lead to 0.371 units of strain in lower lip. Strain in the lower lip - which is also the primary study objective- was the third most explainable parameter (35%) by its regression model in HG. On the other hand, in NG, OP inclination was significantly lower than HG. This may be the reason that lower lip strain is not significantly interfering with a flatter OP of NG.

Regarding lower lip length, no interactions were observed both in NG and HG even if the regression model of HG had significance.

Limitations

The shortcomings of the study are, although cephalograms are practical in daily routine, the functional examination of soft tissues may be overlooked. On the present closed lip cephalograms, the lip length and thickness parameters were found similar in two groups.

However, we cannot compare and comment on soft tissue characteristics of the patients with lips in repose. Unfortunately, this comparison could not be done in the retrospective nature of the study. Therefore, the parameters related to soft tissue function and phenotype could not be discussed.

Conclusion

The inevitability of involvement of several etiologic factors puts AOB malocclusion in the hot spot. Lip strain may usually be deemed as a result of dentoalveolar protrusion, related to IMPA parameter by our findings as well. Before preferring an extraction treatment plan, the clinician should pay attention to the whole, considering whether a short upper lip, an increased lower facial height, or severe sagittal discrepancies might be the cause.[26] If the main goal is to achieve a neutral lip closure, the parameters that need to be taken into consideration and relevant treatment mechanics should be well planned for more stable treatment outcomes. Recommendations for future studies can be listed as examining similar correlations in individuals with more severe open bite malocclusions that may necessitate surgical correction and investigating the disagreements between diagnostic and treatment approaches.

Ethics Committee Approval

Marmara University Faculty of Medicine, Ethics Committee approved this study. (Protocol number: 09.2023.1253; dated 08/02/2024) This study conformed to the principles of Helsinki Declaration.

Informed Consent

Informed consent was obtained from the individuals participating in the study.

Author Contributions

Conceptualization: EB, YBA; Design: EB, YBA; Auditing: EB; Resources: EB, YBA, BE; Data collection: EB, BE; Data analysis and interpretation: EB, YBA; Literature review: EB; Writers: EB, YBA, BE; The final version of this article was read and approved by all authors.

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Conflict of Interest

The authors declare that there is no conflict of interest for this article.

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Statements

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Research Article/Özgün Araştırma

Calcaneal and dorsal spur morphological and morphometric measurements; 'A radiological study'

Kalkaneal ve dorsal spur ile ayağın diğer morfolojik özelliklerinin ilişkisinin radyolojik olarak araştırılması

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Abstract
Aim: The foot is one of the most neglected parts of our body. One of the causes of foot pain is the plantar calcaneal spur (PCS), which is the bone protrusion formed under the calcaneal bone, and the dorsal spur (DS), which is seen dorsal to the calcaneus. Our study aimed to examine PCS and DS morphologically.
Materials and Methods: 235 patients with PCS were included in this retrospective study. Plantar calcaneal spur length (PCSL), plantar calcaneal spur thickness (PCST), Fowler-Philip angle (FPA), and plantar calcaneal fat tissue thickness (PCFT) with radiology in patients with the calcaneal spur, and also to classify plantar calcaneal spur (PCS) and dorsal spur (DS).
Results: Bilateral PCS was found in 57.4% of the patients. DS was found in 43.5% of the patients with right PCS and 40.3% of the patients with left PCS. Large DS types were found at a higher level in males than females. Right PCFT was found to be significantly higher in patients with PCS compared to the control group (p=0.034).
Conclusion: It was concluded that the majority of PCS patients had bilateral PCS, DS could be seen and there was a strong correlation between PCSL and PCST.
Keywords: Adipose tissue; Calcaneus; Heel spur; Radiography.

Öz
Amaç: Ayak, vücudumuzun en çok ihmal edilen kısımlarından biridir. Ayak ağrısının nedenlerinden biri, kalkaneal kemiğin altında oluşan kemik çıkıntısı olan plantar kalkaneal mahmuz (PCS) ve kalkaneusun dorsalinde görülen dorsal mahmuzdur (DS). Çalışmamızın amacı PCS ve DS'yi morfolojik olarak incelemektir
Gereç ve Yöntem: PCS'li 235 hasta dahil edildi. Plantar kalkaneal mahmuz uzunluğu (PCSL), plantar kalkaneal mahmuz kalınlığı (PCST), Fowler-Philip açısı (FPA) ve plantar kalkaneal yağ dokusu kalınlığı (PCFT) bakıldı ve kalkaneal mahmuzlu hastalarda plantar kalkaneal mahmuzu (PCS) ve dorsal mahmuzu (DS) sınıflandırmaları yapıldı.
Bulgular: Hastaların %57,4'ünde bilateral PCS bulundu. Sağ PCS'li hastaların %43,5'inde ve sol PCS'li hastaların %40,3'ünde DS bulundu. Büyük DS tipleri erkeklerde kadınlardan daha yüksek düzeyde bulundu. Sağ PCFT'nin PCS'li hastalarda kontrol grubuna göre anlamlı olarak daha yüksek olduğu bulundu (p=0,034).
Sonuç: PKS hastalarının çoğunluğunun iki taraflı PKS'ye sahip olduğu, DS'nin görülebildiği ve PKSU ile PKSK arasında güçlü bir korelasyon olduğu sonucuna varıldı.
Anahtar Kelimeler: Yağ dokusu; Kalkaneus; Topuk dikeni; Radyografi.

Introduction

Bone spurs, also called enthesophytes, are found at the attachment sites of muscle to bone. These are bone growths that extend from the skeleton to the soft tissue. The most common bone spurs are the dorsal spur (DS) of the Achilles tendon in the calcaneus and the plantar calcaneal spur (PCS) of the plantar fascia.[1] PCS is defined as bone growth anteriorly from the medial calcaneal tuberosity. Its incidence in different populations varies between 11-21%.[1,2] Obesity, pes planus, microtrauma, aging, and some specific sports activities such as running, jumping and ballet are risk factors that may contribute to the development of PC.[3-5] The main symptom, usually in people over the age of 40, is increased pain along the inside of the heel. In some cases, mild swelling and erythema may be seen. The duration of symptoms can vary from a few weeks to many years.[6]

In the literature, there are studies in which the length of the plantar calcaneal spur (PCSL) was measured by computer-assisted linear measurement method on lateral calcaneal X-ray images. In these studies, PCSL was found to be associated with age and body mass index.[7,8] It was observed that the plantar calcaneal spur thickness (PCST) was not evaluated in these studies, and the relationship on this issue was not known. In addition to these, it has been reported that ossifications observed in the Achilles tendon attachment area at the posterior edge of the calcaneus may accompany patients with PCS.[9] These DSs can cause deformity in the calcaneus (Haglund's deformity) and be symptomatic. In the evaluation of this, the measurement of the Fowler-Philip angle (FPA) can be made.[10] However, no radiological study examining the morphological relationship between ossifications detected in the posterior calcaneus and PCS has been observed. Although the shock-reducing and protective effects of plantar calcaneal adipose tissue on the plantar fascia and calcaneus are known, the relationship between plantar calcaneal fat tissue thickness (PCFT) and PKS is not clear.[11-13] Different classifications of PCS have been made according to various morphological features. Among these, shape features such as vertical, horizontal, hook, and length measurement methods have been used.[15] PCS has also been evaluated with the visual evaluation method in the form of small, medium, and large.[16.]

This study aimed to radiologically investigate the relationship between PCSL, PCST, FPA, and PCFT. In addition, classification of PCS and DS was aimed.

Materials and Methods

Study population

This retrospective study included 235 patients (370 ankles) who were followed up in the Hatay Mustafa Kemal University Hospital Physical Therapy and Rehabilitation Outpatient Clinic between July 2016 and 2021. Patients were identified through the hospital electronic database using the International Classification of Diseases (ICD)-10 code M77.3 for PCS. Lateral ankle X-ray images were scanned retrospectively. Patients with no PCS, no X-ray images of the right and left feet, unclear measurement sites, previous fracture or surgery in the ankle and foot, and rheumatological disease were excluded from the study. The lateral ankle radiographs of 88 patients (135 ankles) without PCS and DS were included in the study in order to compare the FPA and PCFT values (Figure 1, Figure 2, Figure 3).
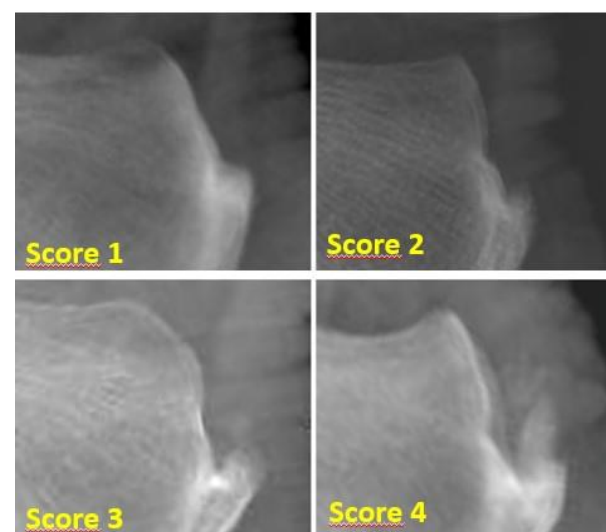
Figure 1. Classification of dorsal spur

Figure 2. Classification of calcaneal plantar spur

Figure 3. Morphometric measurements. (A: The plantar calcaneal spur thickness, B: Fowler-Philip angle, C: Plantar calcaneal fat tissue thickness)

Data collection

Age (at the time when foot radiograph was taken) and sex data of the patients were collected.

Measurements were made on lateral foot-ankle X-ray images. In the lateral X-ray images, PCST was measured from the junction of the PCS with the calcaneal tuberosity. PCSL was measured by drawing it between the midpoint of the line for the measurement of PCST and the most distal point of the spur.[7] The angle between the posterosuperior edge of the calcaneus and the calcaneus tuberosity-inferior cuboid joint line was used for FPA measurement. In the FPA measurement, between 44° and 69° was considered normal, and 75° and above was considered in favor of Haglund's deformity.[14] The shortest distance between the skin and the tip of the base of the calcaneus was measured on the lateral X-ray images for PCFT.[11] In accordance with the Duran et al.[16] classification, PCS scores were recorded between 1-3 and DS scores between 1-4. All images were taken from foot radiographs from the PASC system by a person with at least 10 years of radiological experience. Morphometric measurements were examined by two different researchers, and in cases where a consensus could not be reached, the images were re-examined with a third researcher and an agreement was reached (Figure 2).

Statistical analysis

To estimate the sample size, the type 1 error (α) was set to 0.05 in the power analysis G Power (version 3.1.9.4) program. The test was performed at 95% power and 95% confidence intervals, and it was calculated that the hypothesis was suitable for testing. The sample confidence interval was determined as %95. It was calculated that 40 cases should be taken. Analyzes were performed using SPSS 21.0 (IBM, New York, USA) for Windows. Kolmogorov-Smirnov, Skewness, and Kurtosis were used for the normal distribution of the data[17]. Data determined by measurement were expressed as mean (Mean) and standard deviation (SD), while categorical variables were expressed as percentage (%). Chi-Square Test was used to calculate descriptive statistics of variation types according to lateralization The Student's t-test was used to compare normally distributed variables between sexes, and Mann-Whitney U-test was used for non-normally distributed numerical variables.

Pearson correlation analysis was performed to evaluate the relationship between the data *p*-value less than 0.05 was considered to be statistically significant.

Ethics committee approval

Hatay Mustafa Kemal University Faculty of Medicine Clinical Research Ethics Committee with the ethics committee decision numbered 11/29 and dated 04.10.2021. This study conformed to the Helsinki Declaration This study conformed tothe Helsinki Declaration.

Results

A total of 235 patients (168 (72%) female, 67 (28%) male) were included in the study. The mean age of the patients taking part in the study was 50.54±10.59 (25-79). 184 patients had right PCS and 186 patients had left PCS. Bilateral PCS was detected in 135 patients (57.4%). DS was detected in 80 (43.5%) patients with right PCS and 75 (40.3%) patients with left PCS. Bilateral PKS was detected at a rate of 52.2% in men and 59.5% in women (Table 1).

Table 1. Distribution of PCS and DS by sex

		Total		Male		Female			
		N	%	N	%	N	%	p	x^2
PCS	B	135	57.4	35	52.2	100	59.5		
	R	49	20.9	14	20.9	35	20.8	0,516	1,322
	L	51	21.7	18	26.9	33	19.6		
PCS	R	184	100	49	100.0	135	100.0	0.008	7.020
	L	186	100	53	100.0	133	100.0	0.023	5,137
RDS	+	80	43.5	25	51.0	55	40.7	0,905	0.014
	-	104	56.5	24	49.0	80	59.3		
LDS	-	75	40.3	22	41.5	53	39.8	0,411	0,676
	-	111	59.7	31	58.5	80	60.2		

(+: yes, -: No, N: Number of individuals, PCS: plantar calcaneal spur, DS: Dorsal spur, B: bilateral, R: right, L: left)

PCS classification scores were determined as right (1; 32.6%, 2; 42.9%, 3; 24.5%) and left (1; 30.1%, 2; 43.5%, 3: 26.3%). Left PCS score 1 was detected 39.6% in men and 26.3% in women. Left PCS score 2 was detected 47.4% in women and 34.0% in men. Right PCS score 1 was found to be 32.7% in men and 32.6% in women. Right PCS score 2 was found to be 42.9% in men and 43.0% in women (Table 2). 67.5% of patients with right DS and 62.7% of patients with left DS were in score 1 and 2 groups (Table 1, Figure 1). While DS was detected at a rate of 51.0% on the right and 41.5% on the left in men, this rate was determined as 40.7% on the right and 39.8% on the left in women. Percentage distributions of advanced scores were found to be higher in DS types in males compared to those in females. Right DS scores 3 and 4 were 48.0% in men, 25.4% in women, while left DS scores 3 and 4 were 45.5% in men and 34.0% in women (Table 2).

Table 2. Distribution of PKS and DS scores by sex

	Score	Total		Male		Female	
		N	%	N	%	N	%
RPCS (N=184)	1	60	32.6	16	32.7	44	32.6
	2	79	42.9	21	42.9	58	43.0
	3	45	24.5	12	24.5	33	24.4
LPCS (N=186)	1	56	30.1	21	39.6	35	26.3
	2	81	43.5	18	34.0	63	47.4
	3	49	26.3	14	26.4	35	26.3
RDS (N=80)	1	34	42.5	6	24.0	28	50.9
	2	20	25.0	7	28.0	13	23.6
	3	18	22.5	10	40.0	8	14.5
	4	8	10.0	2	8.0	6	10.9
LDS (N=75)	1	24	32.0	5	22.7	19	35.8
	2	23	30.7	7	31.8	16	30.2
	3	16	21.3	6	27.3	10	18.9
	4	12	16.0	4	18.2	8	15.1

(N: Number of individuals, PCS: Plantar calcaneal spur, DS: Dorsal spur, R: Right, L: Left)

PCSL was found to be 4.92±2.05 mm on the right and 5.03±2.12 mm on the left. PCST was determined as 6.56±2.19 mm on the right and 6.54±2.15 mm on the left. There was no significant difference between the patient group with PCS and the control group in the

right and left FPA measurements *(p>0.05)*. While right PCFT was found to be significantly higher than the control group in patients with PCS (*p*=0.034), although it was found to be higher on the left, it was not significant *(p>0.05)* (Table 3).

Table 3. Comparison of PCS characteristics, FPA and adipose tissue between patient and control groups

	Patient (with PCS)				Control (no PCS)				*p*
	N	Min.	Max.	Mean±SD	N	Min.	Max.	Mean±SD	
Age	235	25.00	79.00	50.54±10.59	88	18.00	79.00	40.89±13.82	**0.001***
RPCSL	184	1.03	13.18	4.92±2.05					
LPCSL	186	1.19	12.43	5.03±2.12					
RPCST	184	1.99	14.61	6.56±2.19					
LPCST	186	2.19	15.13	6.54±2.15					
RFPA	184	48.00	75.18	63.03±5.39	73	46.37	77.47	62.15±5.99	0.275
LFPA	186	37.06	78.73	63.04±5.89	62	50.92	81.88	62.26±6.09	0.383
RPCFT	184	9.85	32.45	20.25±3.75	73	9.45	29.80	19.12±3.87	**0.034***
LPCFT	186	11.67	32.24	20.17±3.73	62	10.79	26.00	19.12±3.72	0.580

(N: Number of individuals, PCSL: Plantar calcaneal spur length (mm), PCST: Plantar calcaneal spur thickness (mm),FPA: Fowler-Philip angle (°), PCFT: Plantar calcaneal fat tissue thickness (mm), *p<0.05 significant, R: Right, L: Left)

There was no significant difference between the sexes on the right and left in PCSL and PCST values *(p>0.05)*. There was no significant difference between the sexes in the FPA values of patients with PCS, both in the control group and in the patient group

(p>0.05). There was no significant difference between sexes in PCFT values in patients with PCS, both in the control group and in the patient group (*p*>0.05) (Table 4, Table 5, Figure 3).

Table 4. Comparison of patient groups by sex

	Patient (with PCS)								
	Male				Female				*p*
	N	Min.	Max.	Mean±SD	N	Min.	Max.	Mean±SD	
Age (year)	67	25	76	51.22±11.38	168	29	79	50.26±10.28	0.549
RPCSL	49	1.03	9.56	4.95±2.28	135	1.34	13.18	4.91±1.97	0.921
LPCSL	53	1.45	12.43	4.63±2.02	133	1.19	12.00	5.18±2.15	0.101
RPCST	49	1.99	14.36	7.05±2.54	135	2.47	14.61	6.38±2.03	0.098
LPCST	53	3.08	13.05	6.79±2.28	133	2.19	15.13	6.44±2.09	0.339
RFPA	49	48.87	72.80	62.38±5.35	135	48.00	75.18	63.27±5.41	0.324
LFPA	53	37.06	78.73	62.11±7.07	133	46.17	75.67	63.41±5.34	0.234
RPCFT	49	13.72	26.64	21.05±3.47	135	9.85	32.45	19.96±3.81	0.070
LPCFT	53	13.43	32.24	20.97±3.53	133	11.67	30.99	19.85±3.77	0.600

(PCSL: Plantar calcaneal spur length (mm), PCST: Plantar calcaneal spur thickness (mm), FPA: Fowler-Philip angle (°), PCFT: Plantar calcaneal fat tissue thickness(mm), R: Right, L: Left)

Table 5. Comparison of control groups by sex

	Control (no PCS)								
	Male				Female				*p*
	N	Min.	Max.	Mean±SD	N	Min.	Max.	Mean±SD	
Age (year)	37	18	64	39.24±12.96	51	18	79	42.08±14.43	0.337
RFPA	30	46.37	74.33	60.8±6.85	43	55.48	77.47	63.08±5.18	0.129
LFPA	29	50.92	81.88	62.54±7.05	33	52.46	74.32	62.02±5.2	0.746
R PCFT	30	13.02	29.80	19.22±3.57	43	9.45	25.90	19.04±4.1	0.840
LPCFT	29	11.76	26.00	20.04±3.31	33	10.79	24.86	18.31±3.92	0.066

(PCSL: Plantar calcaneal spur length (mm), PCST: Plantar calcaneal spur thickness (mm), FPA: Fowler-Philip angle (°), PCFT: Plantar calcaneal fat tissue thickness (mm), R: Right, L: Left)

In the comparison of the right and left sides, a strong positive correlation was detected between the values of PCSL, PCST, FPA, and PCFT *(*r=0.473; 0.567; 0.683; 0.922, respectively). There was a weak negative

correlation between the right PCST and the right FPA (r=-0.145). There was a strong positive correlation between PCSL and PCST on the right and left sides (r=0.666; 0.635, respectively) (Table 6).

Table 6. Correlation values of patients with PCS

		Right PCSL	Right PCST	Right FPA	Right PCFT	Left PCSL	Left PCST	Left FPA	Left PCFT
Left	r	-0.120	-0.077	0.087	0.922**	0.103	0.057	0.082	1
PCFT	p	0.166	0.373	0.316	0.000	0.160	0.439	0.265	
Left	r	-0.084	-0.045	0.683**	0.175*	0.048	0.091	1	
FPA	p	0.331	0.602	0.000	0.042	0.516	0.218		
Left	r	0.384**	0.567**	-0.006	0.071	0.635**	1		
PCST	p	0.000	0.000	0.942	0.412	0.000			
Left	r	0.473**	0.371**	-0.133	0.101	1			
PCSL	p	0.000	0.000	0.124	0.246				
Right	r	-0.049	0.008	0.045	1				
PCFT	p	0.508	0.912	0.543					
Right	r	-0.142	-0.145*	1					
FPA	p	0.055	0.049						
Right	r	0.666**	1						
PCST	p	0.000							
Right	r	1							
PCSL	p								

(PCS: Plantar calcaneal spur, PCSL: Plantar calcaneal spur length, PCST: Plantar calcaneal spur thickness, FPA: Fowler-Philip angle, PCFT: Plantar calcaneal fat tissue thickness. **Correlation is significant at the 0.01 level, *Correlation is significant at the 0.05 level)

Discussion

In this study, the relationship between spur measurements of PCS patients and other morphometric features of the foot was investigated. Bilateral PCS was observed in 57.4% of the patients in the study. DS was detected in nearly half (40.3%-43.5%) of the patients with PCS. The incidence and characteristics of PCS on the right and left were similar between the sexes. While right PCFT was found to be significantly higher than the control group in patients with PCS, although it was found to be higher on the left, it was not significant. PCST was determined as 6.56±2.19 mm on the right and 6.54±2.15 mm on the left. PCSL was found to be 4.92±2.05 mm on the right and 5.03±2.12 mm on the left. A strong positive correlation was detected between PCSL and PCST on the right and left sides.

PCS is an important cause of heel pain. It can cause pain and functional limitation as well as being asymptomatic. Kuyucu et al.[7] detected bilateral PCS in 20% of 84 patients with a diagnosis of plantar fasciitis. In this study, the rate was 57.4%, which differs from the literature. It is thought that the higher rate in this study may be related to the inclusion of patients with radiological PCS in the study.

Baytemur et al.[9] evaluated 1335 lateral ankle radiographs associated with trauma. In their study, they found PCS in 32.2%, DS in

13.1%, and both PCS and DS in 9.8% of all patients. They found that the presence of PCS and DS did not differ in terms of sex and side. In this study examining patients with PCS, the coexistence of PCS and DS ranged from 40.3% to 43.5%. This value is higher than that in the previous study. This may be related to the fact that the mean age of the patients in this study was high. In addition, patients with non-traumatic foot pain were included in this study. In this study, the incidence of spur was found to be similar to the literature in terms of sexes and sides.

In the study of Hayta et al.[19], the PCSL value was found to be 5.7±1.0 mm in 80 PCS patients. Ercan et al.[18] found the PCSL value of the patients as 4.5 (0.1-11.3) mm in their study with 54 PCS patients. In the study of Ermutlu et al.[20], PCSL was found to be 5.44 (2.20–9.81) mm in 70 patients. In this study, PCSL was found to be 4.92 (1.03-13.18) mm on the right and 5.03 (1.19-1243) mm on the left, which was similar to the literature.

Different typing methods have been used for PCS. Zhou et al.[21] examined PCS in two groups, as inside the plantar fascia and superior to the plantar fascia. Ahmad et al.[15] used four groups (absent, horizontal, vertical and hooked) for PCS classification in their study involving 109 patients. They were found to be absent (23.8%), horizontal (60.6%), vertical (3.7%) and hooked (11.9%). In another study, PCS (1; small, 2; moderate, 3 severe) and DS

(1; small, 2,3,4; large) classifications of gout patients were made. While 44.7% of the patients had a PCS of 2 or more, a DS of 2 or more was found in 44.7%.[16] In this study, spur values of 2 and above were found to be higher for both PCS and DS. This difference may be due to the fact that the study of Duran et al.[16] included gout patients and that the study group also included patients without PCS. This study included patients with PCS. In this study, values of 2 and above for PCS were determined as 67.4-69.9%, and values of 2 and above for DS were determined as 57.5-68%.

PCS may occur as a result of damage to the plantar fascia by repetitive microtraumas. The shock absorbing effect of plantar adipose tissue reduces the damage of microtraumas. Belhan et al.[12] examined PCFT in 50 patients with plantar fasciitis using ultrasonography. In their study, they determined the adipose tissue thickness as 19.45 mm. In the same study, the other non-symptomatic feet of patients with plantar fasciitis were evaluated as the control group. In addition they determined that the PCFT value of the side with plantar fasciitis was significantly lower. In another study, PCFT was evaluated by weight bearing with ultrasonography. PCFT was found to be significantly higher in patients with heel pain than that in healthy individuals.[13] Turgut et al.[11] found similar PCFT values between the groups in their study with 120 healthy people (240 feet) and 73 patients with heel pain (103 feet). In this study, PCFT was evaluated radiologically, and the mean value of PCFT was found to be 20.25 mm on the right and 20.17 mm on the left. PCFT was found to be 19.12 mm in the control group, and no significant difference was found between the patient groups. Although the results of this study are similar to those of the study of Turgut et al.[11] there was no significant difference between the patient and control groups, unlike the literature. It may be due to the difference in the measurement method and the mean age of the patient group.

PCS can also be seen in psoriatic arthritis, which is in the spondyloarthritis disease group. Gladman et al.[22] compared PCSL and PCST values of 101 psoriatic arthritis patients with the control group in their study. Both PCSL and PCST were higher in the psoriatic arthritis group than those in the control group.Başdelioğlu [23] stated in his study that obesity is one of the important causes of PCS. The incidence of PCS is significantly increased in people with a BMI > 30, and the incidence of PCS in women is significantly higher than in men. Changes in the CIA change the mechanical forces acting on the foot, causing PCS. However, no study examining the relationship between PCSL and PCST has been found in the literature. In this study, a strong positive correlation was found between PCSL and PCST values on the right and left sides.

Riepert et al.[24] reported that the rates of PCS in the right and left feet were similar. A similar result was found in our study.

FPA is an angle in which the posterosuperior part of the calcaneus is evaluated, and a high angle is in favor of Haglund's deformity.[14] Bulstra et al.[10] found this angle as 60.91±6.81 in patients with Haglund's deformity in their study. Gutierrez et al.[25] found the FPA values on the right and left as 61.2±5.1 and 62.9±5.9, respectively, in their study. The FPA values of the patients in this study are similar to the values in both studies.

Limitations

There are some weaknesses of the study. Among these, it can be said that the study was done retrospectively through hospital records, the number of people in the control group was low and the average age was low. There is also a need for studies investigating the relationship between PCS parameters and clinical findings.

Conclusion

Our study may offer a new perspective on PCS with unclear pathophysiology. In this study, it was concluded that bilateral PCS can be observed in the majority of patients, DS may accompany those with PCS, and there is a strong correlation between PCSL and PCST values. The relationship of these data with patient clinical findings, weight, occupational and environmental exposure is also an area open to research.

Ethics Committee Approval

Hatay Mustafa Kemal University Faculty of Medicine Clinical Research Ethics Committee with the ethics committee decision numbered 11/29 and dated 04.10.2021. This study conformed to the Helsinki Declaration This study conformed tothe Helsinki Declaration.

Author Contributions

Study concept/design, data collecting: HÖ., BT., DAS., data analysis and interpretation BT, NA, DAS., literature review, writers: HÖ., DAS., MTY., The final version of this article was read and approved by all authors.

Conflict of Interest

There is no conflict of interest to declare.

Financial Disclosure

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Peer-review

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Research Article/Özgün Araştırma

The effect of tumor laterality on prognosis in metastatic renal cell carcinoma

Metastatik renal hücreli karsinomda tümör lateralitesinin prognoza etkisi

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Abstract

Aim: In metastatic renal cell carcinoma (RCC), prognosis relies on various factors. Tumor lateralization's role is still debated. Our study examined how tumor localization affects survival in metastatic RCC patients.

Materials and Methods: The study retrospectively analyzed 80 patients with metastatic renal cell carcinoma, diagnosed between January 1999 and December 2021.

Results: Eighty patients were evaluated. The median age at diagnosis was 60 (range 37-86). Tumors were in the right kidney for 39 patients (48.8%) and in the left kidney for 41 patients (51.2%). Of these patients, 58 (72.5%) had de novo metastatic disease, while 22 (27.5%) had recurrences during follow-up. Tumor localization showed no significant association with age ($p=0.684$), gender ($p=0.761$), ECOG performance status ($p=0.326$), primary tumor surgery ($p=0.697$), or lung metastasis ($p=0.495$). However, a significant association was found with liver metastasis (p=0.032). There was no significant difference in median survival between right and left-sided tumors ($p=0.266$).

Conclusion: In our study, survival showed no correlation with tumor lateralization in metastatic RCC.

Keywords: Renal cell carcinoma; Lateralization; Metastazis; Kidney.

Öz

Amaç: Metastatik renal hücreli kanserlerde (RCC) prognoz prognostik faktörlere bağlıdır. Tümör lateralizasyonun bu faktörlerden biri olup olmadığı halen tartışmalıdır. Çalışmamızda metastatik RCC ile takip edilen hastalarda tümörün yerleşiminin sağkalım üzerine etkisini araştırdık.

Gereç ve Yöntem: Çalışmada Ocak 1999 ve Aralık 2021 arasında metastatik renal hücreli kanser tanısı alan 80 hasta retrospektif olarak incelendi.

Bulgular: 80 hasta değerlendirildi. Median tanı yaşı 60 (37-86) idi. 39 (%48,8) hastada tümör sağ böbrekte, 41(%51,2) hastada sol böbrekte idi. Hastaların 58'i (%72,5) denova metastatik iken 22 (%27,5) hastada takipte nüks gelişmişti. Tümör lokalizasyonu ile yaş ($p=0.684$), cinsiyet ($p=0.761$), ECOG ps ($p=0.326$), tümör primerine cerrahi yapılması ($p=0.697$) ve akciğer metastazı ($p=0.495$) arasında anlamlı ilişki yokken, karaciğer metastazı arasında anlamlı ilişki saptandı ($p=0.032$). Sağ ve sol lokalizasyonlu tümör arasında median sağkalım açısından anlamlı fark yoktu ($p=0.266$).

Sonuç: Çalışmamızda, metastatik RCC'de sağkalım ile tümör lateralizasyonu arasınd ilişki bulunamadı.

Anahtar Kelimeler: Renal hücreli karsinom; Lateralizasyon; Metastaz; Böbrek.

Introduction

Renal cancer is the 13th most common cancer with a gradually increasing incidence.[1] Aproximately 90% of kidney cancers are renal cell cancers.[2] Renal cell cancer, seen 2 times more in men than in women, is responsible for 5% of the malignities seen in men and 3% in women. [1,3] Most of the patients are diagnosed at the age of 60-70 years.[4]

Due to the increased use of ultrasonography and computed tomography in recent years, its incidence has been increasing, so most patients are diagnosed at an early stage.[5,6] Surgery is the main treatment method in these patients. While approximately 30% of the patients are metastatic at the time of diagnosis, recurrence develops in 30-40% of the patients during follow-up after curative surgery.[7-10] Approximately 75% of the metastases involve lung, 36% lymph nodes, 20% bone, 18% liver, and less than 10% brain and skin.[10] The prognosis in metastatic disease is generally poor depending on the prognostic factors at the time of diagnosis, and the median survival is less than 12 months. Various studies have been carried out for predicting prognosis, and some prognostic models have been developed.[11-16] Accordingly, age, Karnofsky performance status (KPS), histological grade and tumor subtype, tumor size, lymph node involvement and stage, some laboratory values (hemoglobin, albumin, calcium, etc.) were defined as prognostic, and started to be used in these models.[13-15,17]

Although the kidneys ar.e known as a pair of identical organs, there are some anatomical and physiological differences between each other. How these differences affect tumor prognosis is the subject of research. The effect of tumor localization either in the right or left kidney on the prognosis has not been clarified. Studies have shown that the right or left kidney localization rate of renal cancers was almost equal or close to equal.[18,19] Nevertheless, in a few studies, several results were found on the relationship between the location of the tumor in the right or left kidney and survival.[17,18,20] Therefore, tumor localization has not been accepted as prognostic yet.

In this study, we aimed to determine the effect of tumor location, either on right or left kidney, on survival in patients followed-up due to metastatic renal cell cancer.

Materials and Methods

We retrospectively screened a cohort of 100 patients diagnosed with metastatic renal cell cancer between January 1999 and December 2021. Patients classified as intermediate or high risk based on IMDC risk scoring were included in our study. Those with incomplete medical records were excluded. Ultimately, 80 patients met our inclusion criteria. Patient information was sourced from both written medical files and computerized records. Demographic and clinicopathological data were collected for analysis.

Statistical Analysis

Windows Statistical Package for the Social Sciences (SPSS) version 20.0 was used. (Chigo, Illinois, USA). The Kolmogrow-Smirnov test was used to examine whether continuous variables had a normal distribution. Depending on the aim, continuous variables were given as mean + SD or median (minimum-maximum). The fisher exact test or the chi-square test were used to evaluate categorical variables. Using the Kaplan-Meier long rank test, the impact of tumor localization on survival was examined.

Ethics committee approval

The study was conducted according to the principles of the Helsinki Declaration and was approved by the Ankara Etlik City Hospital Ethics Committee on April 5, 2023, with approval number 2023-043.

Results

52 (65%) of the 80 patients were men. The median age of diagnosis was 60 (37-86) years. 49 (61.2%) of the patients were under the age of 65. There were 20 (25%) patients with 0 points performance score (PS), 24 (30%) patients with 1 points, 27 (33.8%) patients with 2 points, and 9 (11.2%) patients with 3 or 4 points. The tumor was located in the right kidney in 39 (48.8%) patients, and in the left kidney in 41 (51.2%) patients. While 58 (72.5%) of the patients were de novo

metastatic, 22 (27.5%) patients developed recurrence during follow-up. In 23% of patients with de novo metastatic disease, the tumor was located in the right kidney, while in 22% it was in the left kidney, and this difference was not statistically significant in terms of survival. Primary tumor surgery was performed on 57 patients (71.3%). Liver metastases were present in 21 (26.6%) patients and lung metastases were present in 38 (47.5%) patients (Table 1).

Table 1. Demographic characteristics of patients

Gender	
Female	28(%35)
Male	52(65)
Age	
<65 years	49(61.2)
≥65 years	31(38.8)
Tumor location	
Right	39(48.8)
Left	41(51.2)

Surgical excision of primary tumor	
Yes	57(71.3)
No	23(28.8)
ECOG PS	
0,1, or 2	71(88.8)
3 or 4	9(11.2)
Liver metastasis	
Yes	22(27.5)
No	58(72.5)
Lung metastasis	
Yes	38(47.5)
No	42(52.5)

ECOG PS: Eastern Cooperative Oncology Group performance score

Tumor localization did not significantly correlate with age (*p*=0.684), gender (*p*=0.761), ECOG PS (*p*=0.326), primary tumor surgery (*p*=0.697), or lung metastasis (*p*=0.495), but it did significantly correlate with the emergence of liver metastases (*p*=0.032). Liver metastasis was more common in right sided RCC (Table 2).

Table 2. The relationship between clinicopathological characteristics of patients and tumor localization

	Right sided	Left sided	Significance (*p*)
Age			
<65 years	23(59)	26(63.4)	0.684
≥65 years	16(41)	15(36.6)	
Gender			
Female	13(33.3)	15(36.6)	0.761
Male	26(66.7)	26(63.4)	
ECOG PS			
0,1, or 2	36(92.3)	35(85.4)	0.326
3 or 4	3(7.7)	6(14.6)	
Primary tumor surgery			
No	12(30.8)	11(26.8)	0.697
Yes	27(69.2)	30(73.2)	
Liver metastasis			
No	24(61.5)	34(82.9)	**0.032**
Yes	15(38.5)	7(17.1)	
Lung metastasis			
No	22(56.4)	20(48.8)	0.495
Yes	17(43.6)	21(51.2)	
Denovo metastasis			
No	16 (41)	19 (46.3)	0.632
Yes	23 (59)	22 (53.7)	

ECOG PS: Eastern Cooperative Oncology Group performance score

The median survival of all patients was 13 months. Patients with a right-localized tumor had a median survival of 16 months, whereas those with a left-localized tumor had a median survival of 11 months. No significant difference was found between right and left localized tumors (*p*=0.266; Figure 1).Three-year survival was 21% in patients with right-localized tumors, while it was 14% in left-localized tumors.

The median survival was 11 months in right kidney tumors with liver metastases, it was 28 months in those without liver metastases. There was no statistically significant difference between the patients with and without liver metastasis in right-sided tumors (*p*=0.299). Median survival was 3 months in patients with liver metastases in left kidney tumors, and 15 months in patients without liver metastases. No statistically significant difference was detected, despite a

quantitatively significant difference in median survival between individuals with a left-sided malignancy and those without liver metastases. (*p*=0.512).
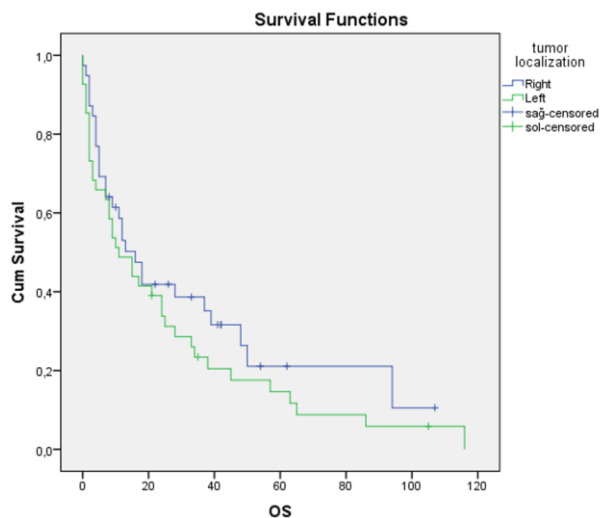
Figure 1. Kaplan Meier curve of the effect of tumor localization on survival

Discussion

Various prognostic models are used to determine the prognosis during the course of renal cell cancer.[12,13] In these models, age, Karnofsky performance status (KPS), histological grade, tumor histological subtype, tumor size, lymph node involvement and stage, some laboratory tests (hemoglobin, albumin, calcium, etc.) are used. Another issue that has been researched in recent years is whether the location of tumor, either on right or left kidney, makes a difference in prognosis. The reason for this is some anatomical and physiological differences between right and left kidneys.

The organs, that right and left kidneys are adjacent in the abdomen, differ. The right kidney is positioned anatomically in the lower abdomen, compared to the left, due to its adjacency to the liver.[21] Because the left kidney is positioned more cranially and is more difficult to visualize on ultrasonography, there may be a time difference between the two kidneys in terms of tumor diagnosis. Besides, there is a difference between arterial venous circulation and lymphatic drainages due to different embryonic sources.[22] Because of this situation, right and left kidney metastases may progress differently from each other. Due to these factors, it is thought that tumor

lateralization may make a difference in survival.

Right-sided tumors had a better prognosis than left-sided tumors, with a 5-year survival rate for right-sided RCC of 47.6% and 39.6% for left-sided RCC (*p*=0.34), according to a study by Deluhan et al[18]. In the same study it was stated that right-sided tumors were more localized, and the rate of radical surgery was higher Strauss et al.[23] also found in their study that the survival for left-sided tumor was lower than right-sided. Similarly, Guo et al.[17], found that right-sided tumor had a better prognosis, was more associated with less frequent lymph node involvement and metastasis, stage 1-2 and low grade-tumor were more common, and had higher rate of partial nephrectomy. Nini et al.[24], also showed that left-sided RCC was associated with more frequent lymph node involvement than right-sided RCC. In terms of right and left localization and tumor incidence, Roychoudhuri et al. observed no statistically significant difference between the two groups.[25] Similar findings were made by Russo et al.[26] who discovered no difference between right-sided and left-sided RCC in terms of 5-year progression-free survival and overall survival.

We investigated whether the prognosis of patients diagnosed with metastatic RCC in our center differed according to tumor laterality. In our study, similar to the literature, the number of male patients was approximately twice that of female patients, and the median age at diagnosis was 60 years. Nevertheless, similar to the literature, the ratio of right and left localized tumor was almost equal (right RCC 48.8%, left RCC 51.2%). Most of our patients were metastatic at the time of diagnosis. The reason for this may be that the primary treatment of early-stage tumor is surgery, following up of patients by urology department during post-surgical period, or applying of patients to oncology unit during metastatic stage. There was no significant relationship between tumor localization and age, gender, ECOG PS, primary tumor surgery, and lung metastasis. There was a significant relationship between tumor localization and development of liver metastasis. Liver metastases were present in 38.5% of our patients with right

RCC and 17.1% of our patients with left RCC (p=0.032). The rate of liver metastasis was higher in patients with right-sided tumor due to its adjacency to liver. Although there was a quantitatively significant difference in median survival between patients having left sided RCC with and without liver metastases, this difference was not statistically significant (p=0.512). The median survival of all patients was 13 months, while it was 16 months in patients with right sided tumor and 11 months in those with left sided. The 3-year survival rate was 21% in patients with right-localized tumors, while it was 14% for those with left-sided tumors. Similar to previous studies, no significant difference was found in 3-year survival between right and left localized tumors.[18,26]

Our study has some limitations such as being single-centered and having retrospective design with a small sample size.

Conclusion

This study did not detect a median overall survival difference between right and left-sided metastatic RCCs. The relationship between disease course and laterality remains uncertain due to differing data in many studies. Perhaps future research investigating the molecular and genetic basis of RCC may yield definitive results.

Ethics Committee Approval

The study was conducted according to the principles of the Helsinki Declaration and was approved by the Ankara Etlik City Hospital Ethics Committee on April 5, 2023, with approval number 2023-043.

Informed Consent

All authors have approved the manuscript and consent for publication.

Author Contributions

O.D. took part in the planning, data collection, ethics committee application and writing of the manuscript. H.S. contributed to the statistical analysis and writing of the data. Y.D. contributed to the planning and data collection of the manuscript. P.P. and E.Z. contributed to data collection.

Conflict of Interest

The authors declare that there is no conflict of interest for this article.

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Research Article/Özgün Araştırma

Assessment of micronutrients in pediatric vertigo

Pediatrik baş dönmesinde mikronutrisyon değerlerinin değerlendirilmesi

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Abstract

Aim: This study aimed to evaluate the clinical characteristics of patients admitted to the pediatric neurology outpatient clinic with the complaint of vertigo and to investigate the role of micronutrients in the etiology of vertigo

Materials and Methods: This study retrospectively evaluated the patients aged four to 18 years who were admitted to the pediatric neurology outpatient clinic with the complaint of vertigo to evaluate the clinical characteristics and the role of micronutrients in the etiology of vertigo. Patients, for whom the Z00.1 code, the routine child health examination code, was entered in the pediatric outpatient clinic in the same period when the patients presented with the complaint of vertigo were included as the healthy control group. Hemogram and hormone profiles [25(OH)D, FT4, TSH, vitamin B12, folic acid and ferritin] of the groups were compared.

Results: There was no statistically significant difference between the study group and healthy controls in terms of age and gender. Hematocrit ($p<0.001$), platelet ($p<0.001$), vitamin B12 ($p=0.015$), vitamin D ($p=0.043$) and TSH ($p=0.013$) levels were found to be significantly lower in the vertigo group compared to the control group.

Conclusion: The importance of micronutritional deficiencies cannot be denied in patients presenting with vertigo symptoms. Main point that makes our study valuable is that there are limited number of studies in the literature comparing laboratory parameters of pediatric patients with vertigo symptoms and healthy controls. There is a need for prospective studies, involving more cases and awareness on this issue.

Keywords: Children; Deficiency; Micronutrient; Vertigo; Vitamin.

Öz

Amaç: Bu çalışmada çocuk nörolojisi polikliniğine baş dönmesi şikâyeti ile başvuran hastaların klinik özelliklerinin değerlendirilmesi ve mikro besinlerin baş dönmesi etiyolojisindeki rolünün araştırılması amaçlandı.

Gereç ve Yöntem: Bu çalışma, çocuk nörolojisi polikliniğine vertigo şikayeti ile başvuran 4-18 yaş arası hastaların klinik özelliklerini ve vertigo etiyolojisinde mikro besinlerin rolünü değerlendirmek amacıyla retrospektif olarak değerlendirildi. Çocuk polikliniğine rutin çocuk sağlığı muayene kodu olan Z00.1 kodu girilen olgular sağlıklı kontrol grubu, vertigo şikâyeti ile başvuran hastalar çalışma grubu olarak kabul edildi. Grupların hemogram ve hormon profilleri [25(OH)D, FT4, TSH, B12 vitamini, folik asit ve ferritin] karşılaştırıldı.

Bulgular: Çalışma grubu ile sağlıklı kontroller arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı bir fark yoktu. Hematokrit ($p<0,001$), trombosit ($p<0,001$), B12 vitamini ($p=0,015$), D vitamini ($p=0,043$) ve TSH ($p=0,013$) düzeylerinin vertigo grubunda kontrol grubuna göre anlamlı derecede düşük olduğu görüldü.

Sonuç: Vertigo semptomlarıyla başvuran hastalarda mikronütrisyonel eksikliklerin önemi inkâr edilemez. Çalışmamızı değerli kılan en önemli nokta ise literatürde vertigo semptomlu çocuk hastalar ile sağlıklı kontrollerin laboratuvar parametrelerini karşılaştıran çalışmaların sınırlı sayıda olmasıdır. Bu konuda daha fazla olgu içeren ve farkındalığın arttığı prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Vertigo; Vitamin; Mikrobesin; Çocuklar; Eksiklik.

Introduction

Vertigo is the perception of rotational movement of the self or surrounding objects. Complaints such as dizziness, feeling sick, drunkenness, or feeling that the ground is slipping under feet can be defined as non-vertiginous dizziness.[1] There is limited information on pediatric vertigo in the literature. Its prevalence ranges from 8% to 15%.[2] The approach to vertigo in children is challenging due to the difficulty of obtaining a clear and reliable history. Pediatric vertigo was first described by Harrison in 1962.[3] Diagnosis and necessary treatment management is clearly established after a detailed history is obtained and clinical examination and neurological evaluation are performed.[4] There are many factors causing dizziness in children, such as trauma, infection, migraine, central nervous system disorders, benign paroxysmal vertigo (BPV), vestibular neuritis caused by viral infections, and psychosomatic disorders.[5]

Relevant studies in the literature have generally been conducted among adults.[3] The number of studies on vertigo in the pediatric age group is limited. There are controversial data in the literature regarding the diagnostic criteria and management of vertigo in this age group.[6] Micronutrients (vitamins and minerals) are essential components of the diet and required for normal cellular and molecular functions.[7] Micronutrient deficiencies may occur in the presence of vitamin B12, folic acid, vitamin A, vitamin D, thiamine, zinc, selenium, and iron deficiencies. Micronutrient deficiencies are the underlying cause of diseases that affect the quality of life, as well as morbidity and mortality of populations, and threaten health globally.[8]

This study aimed to evaluate the clinical characteristics of patients admitted to the pediatric neurology outpatient clinic with the complaint of vertigo and to investigate the role of micronutrients in the etiology of vertigo.

Materials and Methods

This study evaluated the patients aged four to 18 years who were admitted to the pediatric neurology outpatient clinic of Adiyaman University Hospital with the complaint of vertigo to evaluate the clinical characteristics and the role of micronutrients in the etiology of vertigo.

The attack frequency, duration of attacks and accompanying complaints (tinnitus, hearing loss, gait disturbance, migraine and attack history) were questioned in patients who presented with the complaint of vertigo. Hemogram, biochemical parameters (glucose, liver function tests, kidney function tests, and electrolytes), and hormone profile (25-hydroxy vitamin D [25(OH)D], vitamin B12, folic acid, ferritin, free T4, and thyroid-stimulating hormone [TSH]), and if requested, electroencephalography (EEG) and brain imaging findings were recorded from the patient files. Patients with missing data were excluded from the study. Participants were divided into three groups: preschool age (up to 6 years old), primary school age (7–12 years old) and adolescents (13–18 years old). Blood pressure was measured in all patients during the initial examination performed at the time of admission. When the file was scanned, the existing consultations [ear nose throat (ENT), pediatric cardiology and ophthalmology outpatient clinic] were evaluated.

Patients, for whom the Z00.1 code, the routine child health examination code, was entered in the pediatric outpatient clinic in the same period when the patients presented with the complaint of vertigo (Group 1), were included as the healthy control group (Group 2).

Hemogram and hormone profiles [25(OH)D, FT4, TSH, vitamin B12, folic acid and ferritin] of the groups were compared.

Serum vitamin B12 levels below 300 pg/mL were accepted as vitamin B12 deficiency.[9,10] Hemoglobin and serum ferritin levels were utilized for the diagnosis of iron deficiency anemia. World Health Organization defined hemoglobin threshold values to classify anaemia according to the age of the child.[11] Serum 25(OH)D measurement reflects the vitamin D stores in the body. Vitamin D level should be 30–50 ng/mL to maximize calcium absorption and maintain normal ranges of parathyroid hormone (PTH). Accordingly,

values below 25(OH)D 30 ng/mL were considered as vitamin D deficiency.[12]

Type of the study

The study was planned as a descriptive retrospective study

The sample size of the study

The records of 94 patients were examined between 01.08.2017 and 01.08.2019.

Data collection tools

The patients aged four to 18 years who were admitted to the pediatric neurology outpatient clinic of Adiyaman University Hospital with the complaint of vertigo to evaluate the clinical characteristics and the role of micronutrients in the etiology of vertigo.

Data analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) Version 23.0 software and descriptive and comparative analyzes were performed. Independent Samples t-test was used for

normally distributed parameters and Mann-Whitney U test was used for the non-normally distributed parameters. Chi-square test was used to evaluate categorical variables. A *p* value of <0.05 was considered statistically significant.

Ethics committee approval

This study was approved by the local ethics committee (Approval no.: 2021/02-30). The principles of the Declaration of Helsinki conducted the research.

Results

The study included a total of 94 patients presenting with the complaint of vertigo. Of the cases, 62 (66%) were female and 32 (34%) were male. The mean age of the patients was 12.09 ± 3.90 (3–17) years. Nine (9.6%) cases were in the 4–6 age group, 34 (36.2%) in the 7–12 age group, and 51 (54.3%) in the 13–18 age group. A total of 118 cases, 65 (55.1%) female and 53 (44.9%) male were included in the control group. The mean age of the control group was 11.64 ± 3.40 (4–17) years (Table 1).

Table 1. Clinical characteristics of patients with vertigo complaints

Average age at time of application (years)	12.09±3.90 (3-17) years	
	n	**(%)**
Total number of patients	94	100
Male	62	66
Female	32	34
Age range (year)		
4-6	9	9.6
7-12	34	36.2
13-18	51	54.3
Vertigo Duration		
Instant/A few seconds	74	78.7
Less than a minute	10	11
A few minute	4	4.2
5-15 minutes	3	3.1
15-30 minutes	1	1
30-60 minutes	1	1
> 60 minutes	1	1
Vertigo Frequency		
Daily/Rare	77	82
A large number of daily	7	7.4
Several times a week	3	3.1
Once a week	3	3.1
Several times a month	4	4.4
Time period of vertigo		
0-1 month	39	41.5
2-6 months	31	33
7-12 months	7	7.4
13-24 months	9	9.6
>24 months	8	8.5

While an episode lasted a few seconds in majority of cases (n=74, 78.7%), it was observed to last 15–30 minutes in one (1%) case, 30–60 minutes in one (1%) case and >60 minutes in one (1%) case. The vertigo frequency was once a day in most of the cases (n=74, 82%) whereas it occurred once or several times a week in only three patients (3.1%). The duration of vertigo symptoms was found to last zero to one month in 39 cases (41.5%), two to six months in 31 (33%), and seven to 12 months in seven (7.4%). Symptoms accompanying vertigo were headache in 54 cases (57.4%), blackout/presyncope/syncope in 51 (54.3%), tinnitus in 10 (10.6%), nausea and vomiting in 21 (22.3%), photophobia or phonophobia in 12 (12.8%) (Table 1). A total of 51 cases underwent EEG and slowing of the background rhythm for age was observed only in one case.

In the etiology of vertigo, upper respiratory tract infection (URTI) was observed in five (5.3%) cases, psychogenic vertigo in five (5.3%), migraine in eight (8.4%) cases, BPV in 13 (14%), gastrointestinal bleeding in one (1%), cerebral pathologies in three (3.2%), and orthostatic hypotension in 12 (12.8%). The remaining 47 patients had iron deficiency anemia, vitamin D deficiency and vitamin B12 deficiency [iron deficiency anemia in 3 (3.2%), vitamin B12 deficiency in 4 (4.3%), vitamin D deficiency 11 (11.7%), vitamin D deficiency and iron-deficiency anemia in 11 (11.7%), and vitamin D and vitamin B12 deficiency in 14 (14.8%), vitamin B12 deficiency and iron-deficiency anemia in 4 (4.3%)]. The frequency and number of vertigo attacks of varying degrees regressed/decreased during pediatric neurology follow-up of these cases following the administration of vitamin B12, vitamin D and iron therapy (Table 2).

Table 2. Etiological profile of vertigo in children

Etiology	n	(%)	4-6 years n (%)	7-12 years n (%)	13-18 years n (%)
Orthostatic hypotension	12	12.8	0	7 (7.47)	5 (5.33)
Sinusitis/mastoiditis/labyrinthitis/otitis media	5	5.3	1 (1.06)	3 (3.18)	1 (1.06)
Benign paroxysmal vertigo	13	14	1 (1.08)	6 (6.46)	6 (6.46)
Migraine	8	8.4	0	3 (3.15)	5 (5.25)
Psychogenic Vertigo	5	5.3	0	2 (2.12)	3 (3.18)
Cerebral pathology (Intracranial mass, Central nervous system infections)	3	3.2	0	2 (2.13)	1 (1.07)
Gastrointestinal bleeding	1	1	0	1 (1)	0
Iron deficiency anemia	3	3.2	1 (1.07)	1 (1.07)	1 (1.07)
Vitamin D deficiency	11	11.7	3 (3.2)	4 (4.3)	3 (3.2)
Vitamin B12 deficiency	4	4.3	1 (1.1)	2 (2.1)	1 (1.1)
Vitamin D deficiency + iron deficiency anemia	11	11.7	3 (3.2)	3 (3.2)	4 (4.3)
Vitamin D deficiency + Vitamin B12 deficiency	14	14.8	4 (4.23)	4 (4.23)	6 (6.34)
Vitamin B12 deficiency + iron deficiency anemia	4	4.3	1 (1.1)	1 (1.1)	2 (2.1)

There was no statistically significant difference between the study group and healthy controls in terms of age and gender. Hematocrit ($p<0.001$), platelet ($p<0.001$), vitamin B12 ($p=0.015$), vitamin D ($p=0.043$) and TSH ($p=0.013$) levels were found to be significantly lower in the vertigo group compared to the control group (Table 3).

Discussion

Due to the small number of studies both in clinical practice and literature, this study aimed to highlight the clinical characteristics of patients presenting with vertigo and the micronutrient deficiencies that take part in the etiology of pediatric vertigo.

Vitamin D is a hormone with an important function in maintaining calcium-phosphorus balance and bone health. The prevalence of vitamin D deficiency among the general population is reported to be 25–50%.[13] It is particularly common in children and associated with many diseases. Symptoms such as rickets, fatigue, muscle pain, numbness in the extremities, and convulsions may be observed in the presence of vitamin D deficiency.[14] In a study by Zhang et al. involving 268 cases, dizziness was reported in

29 cases with vitamin D deficiency and regression was observed in the complaints of 28 patients with vitamin D treatment.[14] Symptoms of nutritional vitamin B12 deficiency include weakness, fatigue, dizziness, pale skin, pain, weight loss, diarrhea, constipation, and muscle weakness, as well as paresthesia in the extremities, gait ataxia, dizziness, loss of sensation, personality change, convulsion, orthostatic tachycardia and developmental retardation.[15] Serin et al. detected dizziness in four of 38 patients with vitamin B12 deficiency.[16] Similarly, Arican et al. reported dizziness in 9% of patients with various neurological symptoms associated with vitamin B12 deficiency.[17] The authors further reported borderline vitamin B12 deficiency in the majority of patients with dizziness and stated that clinicians should be aware of this issue.[17] Iron deficiency anemia is a common health problem in the world. It is estimated that 30-50% of the world's population has iron-deficiency anemia.[18] Nonspecific symptoms, including headache, paleness, palpitation, tinnitus, vertigo, tachycardia, syncope, and heart failure, may accompany iron deficiency anemia.[19] In a study by Erdogan et al. involving 30 cases with vertigo, iron deficiency anemia was reported in two cases and vitamin B12 deficiency in two cases.[20]

Table 3. Comparison of laboratory parameters of cases with vertigo symptoms and healthy controls

	Group 1 (Vertigo Group) n:94 Mean±SD (Min.-Max.)	Group 2 (Control Group) n:118 Mean ±SD (Min.-Max.)	*p*
Age (years)	12.09±3.90 (3-17)	11.64±3.40 (4-17)	0.2
WBC (/mm3)	7.64±1.90 (4.07-13.55)	7.65±2.04 (4.33-13.39)	0.463
Hemoglobin (gr/dl)	13.35±1.72 (3.97-16.64)	13.52±1.28 (9.41-16.33)	0.267
Hct (%)	40.29±5.21 (11.11-57.10)	41.06±4.14 (29.76-48.85)	**< 0.001**
MCV (fL)	81.52±6.18 (58.97-93.05)	73.36±5.32 (55.11-96.97)	0.128
Platelet (10^3/µL)	262.30±66 (29.11-501.20)	310.46±139.35 (117.9-865)	**< 0.001**
Vitamin B12 (pg/ml)	198.61±83.83 (75-575)	235.99±103.12 (63-619)	**0.015**
Ferritin (ng/ml)	23.67±18.68 (1.80-113.7)	29.58±14.36 (3.5-81.7)	0.316
Folate (ng/ml)	9.09±3.52 (4.31-21.86)	8.72±4.56 (2.06-35.50)	0.316
Vitamin D (ng/ml)	18.03±8.20 (4.6-48.67)	23.05±17.76 (4.61-171)	**0.043**
FT4 (ng/dL)	0.94±0.47 (0.61-5.02)	0.88±0.18 (0.51-1.54)	0.264
TSH (mIU/L)	2.31±1.08 (0.54-5.49)	2.62±1.42 (0.16-7.74)	**0.013**

MCV: mean corpusculer volume; WBC: white blood cell

Yildirim et al. reported that only one of 132 patients with the complaint of dizziness had iron deficiency anemia.[21] In a series of 183 cases, Korkmaz et al. found vitamin B12 deficiency in nine cases and iron deficiency anemia in three cases.[22] The incidence of iron-deficiency anemia, vitamin B12 and vitamin D deficiency in the present study was found to be higher than in the literature. In the pediatric neurology outpatient clinic controls performed every three months after the administration of vitamin B12, vitamin D and iron treatment, the frequency and number of vertigo attacks were observed to decrease/regress in all patients.

The literature review has shown that there is a limited number of studies comparing the hemogram, vitamin B12 and folic acid levels of adult patients, who were admitted to the hospital with the complaint of vertigo, with those of healthy controls. In a study, vitamin B12 and folic acid levels of patients admitted to the adult emergency department with the complaint of dizziness were compared with those of healthy controls and as a result of the study, vitamin B12 levels were found to be statistically significant (*p*=0.000) whereas there was no significance in terms of folic acid levels (*p*=0.83).[23] In another study comparing 160 adult patients suffering from vertigo and 120 healthy individuals, vitamin B12 level (*p*<0.001), hemoglobin (*p*<0.01), ferritin (*p*=0.004) and mean MCV values (*p*=0.001) were found to be statistically significant in the vertigo group while there was no significant difference in terms of folic acid levels.[24]

Pediatric vertigo is a rare condition with an estimated incidence of <1%.[25] In a study, the prevalence of vertigo was reported to be higher in the 12–17 age group.[26] In the present study, the age group with the highest number of cases

with vertigo was the 13- to 17-year-old age group.

The differential diagnosis of pediatric vertigo is different from that seen in adults as many etiologies are specific to pediatric age and pathologies are quite different in children and adults.[4] Compared to adults, response to the vertigo treatment is better and recovery is faster among children. Pediatricians, clinicians, otolaryngologists and neurologists often have difficulty in establishing the appropriate diagnosis in these cases. The inability of affected children to explain the characteristics of their symptoms may prevent diagnosis, particularly in very young children.[27]

Vertigo is observed to be more common in female gender.[28] The female to male ratio was reported to be 1.57 by Swain et al., 1.17 by Batu et al., 1.94 by Erbek et al., and 1.81 by Korkmaz and Ekici.[6,22,28,29] Compatible with the literature, female to male ratio was 1.93 in the present study.

Headache and nausea are the most common symptoms accompanying vertigo. In the literature, headache is reported in 35–60% of children presenting with vertigo.[30] In the study by Bhandari and Goswami, symptoms accompanying vertigo were reported to be headache (66.6%), nausea (42.2%), hearing loss (31.1%), tinnitus (13.3%) and loss of consciousness (10%).[31] Swain et al. reported the accompanying symptoms as follows: nausea and vomiting (78.70%), headache (37.96%), hearing loss (13.88%), tinnitus (6.48%), aural fullness (6.48%), visual impairment (2.77%), altered state of consciousness (1.85%) and diaphoresis (3.70%).[6] Erbek et al. stated that headache (66%), nausea-vomiting (26%), hearing loss-tinnitus (22%), visual impairment (20%), loss of consciousness (10%) and diaphoresis (4%) were the symptoms accompanying vertigo in their study.[28] Korkmaz and Ekici reported that headache (41%), syncope (27%) and nausea-vomiting (10%) were the most common findings accompanying vertigo.[22] In the present study, the most common symptoms accompanying vertigo were headache (57.4%), blackout (41.5%) and nausea-vomiting

(22.3%). Bhandari and Goswami reported that vertigo symptoms lasted most commonly for zero to one month, two to six months and 13-24 months, respectively.[31] Compatible with the literature, the duration of symptoms was observed to last for zero to one month most frequently (n=39, 41.5%), followed by two to six months (n=31, 33%) and seven to 12 months (n=7, 7.4%) in the present study. Swain et al. reported that the duration of vertigo lasted minutes in the majority of the cases (41.66%), whereas the attack lasted seconds (26.85%) and more than a day (6.48%) in others.[6] In a study by Batu et al., the duration of vertigo was reported to last less than one minute in 36% of the cases and one to five minutes in 34% while Erbek et al. reported the duration of vertigo as seconds in 52%, minutes in 28%, hours in 14% and >24 hours in 6% of the cases.[28,29] In the present study, the duration of vertigo was observed to last seconds in 78.7% of the cases.

The medical history of a patient with vertigo is the most important part of the evaluation. Parents should carefully observe these episodes as young children are unable to describe the symptoms. History and a detailed physical examination, including otological and neurological examination, may be utilized to establish diagnosis in most pediatric patients.[32] Benign paroxysmal vertigo and migraine-associated vertigo are the most common causes of dizziness in childhood.[33] Migraine-associated vertigo is much more common in pediatric patients compared to the adult population. The prevalence of migraine-associated vertigo is reported to be 35% among pediatric patients with vertigo whereas only 6% of adults suffering from vertigo are diagnosed with migraine.[34] Orthostatic hypotension may cause vertigo in 3–9% of symptomatic children.[35] In the pediatric age group, BPV is a common cause of vertigo, with a prevalence of 2.6%.[36] In the study by Gruber et al., the most common etiology of vertigo was reported to be migraine (32%), acute labyrinthitis/neuritis (22%) and psychogenic dizziness (22%).[4] Batu et al. reported the most common etiological causes as BPV (39%), psychogenic vertigo (21%), epileptic vertigo (15%) and migraine-associated vertigo

(11%).[29] In a study by Swain et al., the authors observed the most common etiologies of pediatric vertigo as vestibular migraine, BPV, and vestibular neuritis.[6] In a study by Davitt et al. involving 2,726 cases, the most common etiology of vertigo among children aged two months to 19 years was vestibular migraine (23.8%) followed by BPV (13.7%), idiopathic/unspecified causes (11.7%), and labyrinthitis/vestibular neurinitis (8.47%).[37] Korkmaz and Ekici reported that the most common causes that may accompany vertigo were BPV (23%), orthostatic hypotension (22%), migraine-associated vertigo (8%), psychogenic vertigo (7%) and vitamin B12 deficiency (5%), respectively.[22] Karatoprak et al reported the most common diagnoses were migraine associated vertigo (21.7%) and orthostatic hypotension (20%) in children with dizziness.[38] In the present study, the most common reason accompanying vertigo symptoms was found to be nutritional reasons. Among other etiologies, BPV was the most common one, followed by orthostatic hypotension and migraine.

The literature review has shown that studies on vitamin B12, vitamin D and anemia in the etiology of pediatric/adult vertigo are limited. Unlike other studies, the rate of micronutrient deficiencies was high in the etiology of vertigo (iron-deficiency anemia, vitamin B12 and vitamin D deficiency) in the present study.

Limitations of the study

The limitations of our study were that it was conducted in a single center, the number of patients was limited, and retrospective study.

Conclusion

The importance of micronutritional deficiencies cannot be denied in patients presenting with vertigo symptoms. Main point that makes our study valuable is that there are limited number of studies in the literature comparing laboratory parameters of pediatric patients with vertigo symptoms and healthy controls. There is a need for prospective studies, involving more cases and awareness on this issue.

Ethics Committee Approval

Ethics committee approval was obtained with the decision of the Ethics Committee for Non-Interventional Procedures of Adiyaman University, numbered no.:2021/02-30. The principles of the Declaration of Helsinki conducted the research.

Informed Consent

The ethical committee consented to the study being conducted without patients' consent because of its retrospective nature.

Authors' Contributions

All authors gave approval to the final version of the manuscript to be submitted and all authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final version of the manuscript

Conflict Interests

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

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Research Article/Özgün Araştırma

Is there a relationship between vascular flow parameters of carotid arterial system and trigeminal neuralgia?

Karotis arteryel sistem vasküler akım parametreleri ile trigeminal nevralji arasında ilişki var mıdır?

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Abstract
Aim: To investigate the flow velocity values and resistance parameters determined by carotid artery doppler ultrasonography (DUS) examination in patients with trigeminal neuralgia (TN).
Materials and Methods: 79 patients diagnosed with TN and who underwent carotid DUS were included in the study. Spectral examination results were recorded for the TN side and the healthy side.
Results: Peak systolic velocity (PSV) internal carotid artery (ICA), resistive index (RI) (ICA) and PSV (ICA)/PSV external carotid (ECA) values in patients were relatively higher in arterial structures on the TN clinical side compared to the healthy side. RI (ICA)/RI common carotid artery (CCA) value was also high in arterial structures on the TN diagnosed side.
Conclusion: It was shown that especially ICA flow velocity and vascular resistance parameters increased in the carotid arterial system on the TN side. These findings indicate that flow parameters in the carotid artery system may also be effective in TN pathophysiology.
Keywords: Trigeminal neuralgia; Carotid artery; Doppler ultrasound imaging.

Öz
Amaç: Trigeminal nevralji (TN) hastalarında karotis arter doppler ultrasonografi (DUS) incelemesi ile saptanan akım hızı değerleri ve direnç parametrelerini araştırmak.
Gereç ve Yöntem: TN tanısı almış 79 hastaya karotis DUS yapıldı. Spektral inceleme sonuçları TN'li bölge ve sağlam bölge için kaydedildi.
Bulgular: Hastalarda peak sistolik hız (PSV) internal karotis arter (ICA), rezitif indeks (RI) (ICA) ve PSV (ICA)/PSV eksternal karotis (ECA) değerleri TN kliniği olan taraftaki arteriyel yapılarda sağlıklı tarafa göre nispeten yüksekti. RI (ICA)/RI common carotis arter (CCA) değeri de TN tanısı olan taraftaki arteriyel yapılarda yüksekti.
Sonuç: Özellikle ICA akım hızı ve vasküler direnç parametrelerinin TN tarafında karotis arteriyel sistemde arttığı gösterildi. Bu bulgular karotid arter sistemindeki akış parametrelerinin TN patofizyolojisinde etkili olabileceğini göstermektedir.
Anahtar Kelimeler: Trigeminal nevralji; Karotis arteri; Doppler ultrason görüntüleme.

Introduction

Trigeminal neuralgia (TN) is a unilateral facial pain originating from one or more divisions of the trigeminal nerve (fifth cranial nerve-CN V).[1] The pain is unilateral, severe, brief, paroxysmal, typically described as electrical or sharp, and is "triggered" by touching the face, talking, eating, and drinking.[2] Trigeminal neuralgia affects 4-13/100000 people every year.

Women are more affected than men; presenting a 3:2 ratio of female-to-male. TN is commonly diagnosed in the elderly population, mostly occurring after age 50.[1]

The International Headache Society divides TN into three subtypes in the third edition of the International Classification of Headache Disorders; classical, secondary, and idiopathic.[3] The diagnosis of TN is made clinically according to the diagnostic criteria, but imaging is required to identify its subtypes.[4] Classical trigeminal neuralgia is proceed from neurovascular compression that causes morphological changes in the trigeminal nerve root demonstrated by imaging or surgery. Secondary trigeminal neuralgia is associated with demyelination of the trigeminal nerve root. Idiopathic trigeminal neuralgia is defined as TN with neither electrophysiological tests nor magnetic resonance imaging (MRI) showing significant abnormalities.[3] Its pathologies think about from neuronal voltage-gated ion channel gain-of-function mutations and non-specific brainstem lesions.[5]

TN is a unilateral facial pain, bilateral cases are rare.[6] The case series show that right side pain is more frequent.[7] Pain is described according to the three branches of the trigeminal nerve: the ophthalmic (V1), maxillary (V2), and mandibular (V3) nerves[2]. V2 and V3 are the most commonly affected together, V1 branch affected solely is rarest.[6] Treatment alternatives include some medications, surgery, and complementary therapies.[2]

The most common diagnostic tool used in the evaluation of patients with trigeminal neuralgia is MRI.[7,8] MRI is particularly useful in the detection of TN secondary to neurological pathologies such as multiple sclerosis. In addition, imaging of the nerve root level detects neurovascular pathologies at this level and findings such as compression of the nerve root by vascular structures. In this way, long-term results can be obtained with simple neurovascular compression surgery.[9] MRI imaging provides information not only in the detection of etiological problems but also about morphological changes in the trigeminal nerve root. It helps in the detection of features such as increased signal in T2A series in the nerve root, hypertrophy in the nerve root/atrophy findings in long-term cases.[9] It can also provide information about the success of treatment in these patients. It has been stated in various publications that the success rate is low in patients with atrophic and deformed nerve structures.[10,11]

The carotid arterial system consists of the main vascular structures that provide vascularization of the central nervous system. Pathologies that may develop in these vascular structures, such as possible stenosis, aneurysm or steal phenomenon, cause pathologies in a spectrum ranging from simple headache and dizziness symptoms to ischemic cerebrovascular events. Carotid ultrasonographic imaging is a non-invasive, cheap and easily applicable examination used to examine atherosclerotic changes in the carotid arteries and to evaluate the flow velocity patterns of these vascular structures. The data obtained are quantitative and the results are mostly consistent with the examination findings of the patients.[12,13] The presence of findings such as gliotic changes in the brain caused by changes in the flow patterns in the carotid artery system and associated symptoms such as headache and dizziness have revealed the necessity of investigating whether the flow parameters in the carotid arterial system play a role in the pathophysiology of TN originating from the cranial nerve roots. Considering that TN can develop secondary to possible vascular compression in the vicinity of the nerve root, it is thought that it may be affected by arterial flow and pressure changes in the carotid arterial system. The aim of this study is to investigate the flow velocity values and

resistance parameters detected by carotid arterial doppler ultrasonography (DUS) examination in patients with trigeminal neuralgia (TN).

Materials and Methods

Type of the study

This is a cross-sectional study.

The sample size of the study

The study was conducted using the anamnesis and imaging results of 79 patients diagnosed with TN registered in our hospital's database who applied to our radiology outpatient clinic affiliated with a tertiary center between 2019-2022. Ethics committee approval for this study was obtained from the regional hospital ethics committee Medicine Non-invasive Clinical Research Ethics Committee (Date: 16/02/2022, Decision No: 2022/2-4). All procedures were utilized in accordance with the Declaration of Helsinki.

Informed consent form was obtained from all patients.

In patients diagnosed with TN, carotid DUS and brain MRI are routinely requested by neurology during the diagnosis phase to rule out possible vascular causes and space-occupying lesions or vascular compression in the brain. Carotid vertebral doppler ultrasonographic examination was performed with using a Samsung RS85 Prestige ultrasonography device (Figure 1). Among these patients in our system, patients with vascular compression findings in MRI and patients with atherosclerotic changes leading to stenosis in carotid DUS imaging findings, plaque formations, and hypoplasia in the vertebral arteries (vertebral artery diameter < 2 mm) were excluded from the study. In the patient diagnosed with trigeminal neuralgia, measurements were made separately for the right and left carotid arterial systems and noted.
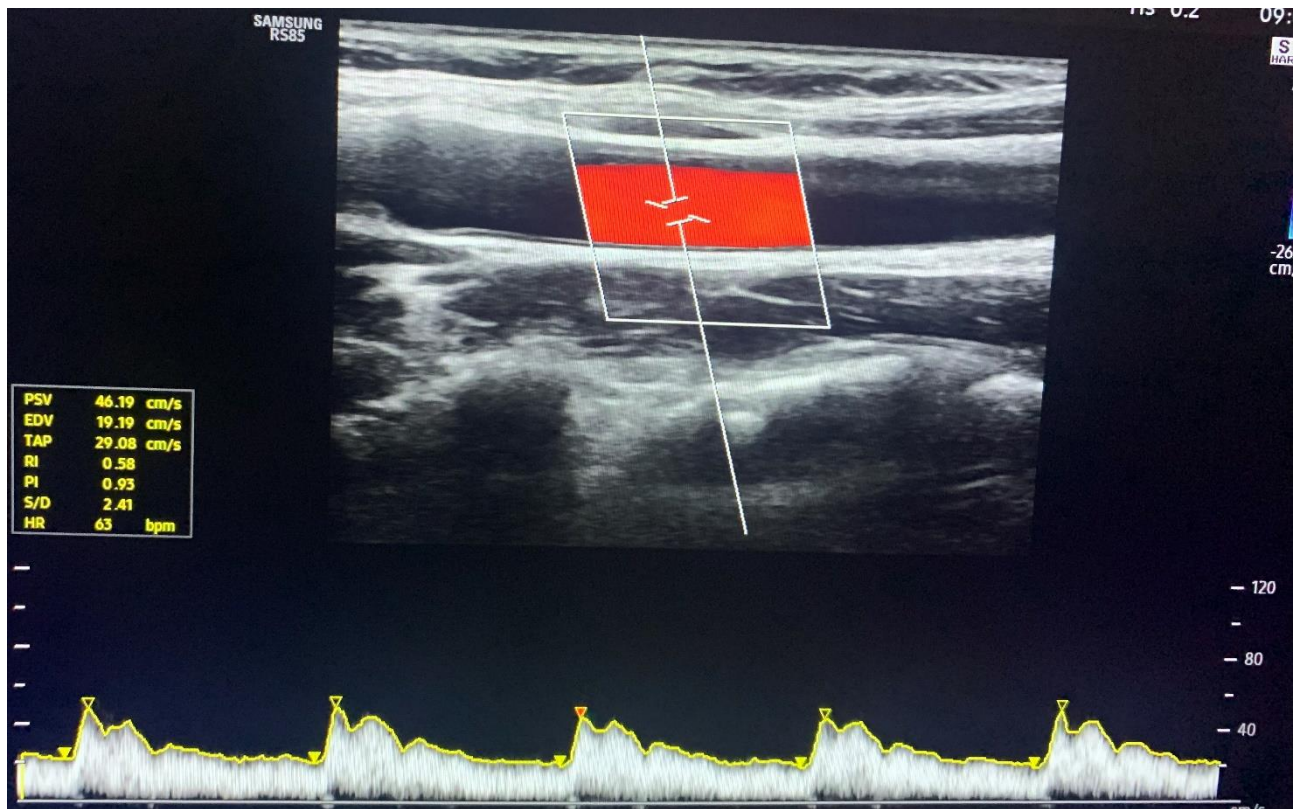
Figure 1. Internal carotid artery power doppler ultrasonography examination and spectral imaging

Carotid DUS was performed as standard with a 12 MHz probe using B-mode grayscale imaging, color flow doppler in transverse and longitudinal planes, and spectral doppler to evaluate flow parameters. First, the intimal level and possible plaque presence were

excluded by evaluating from the visible segment of the common carotid artery (CCA) to the level of the internal carotid artery (ICA) and external carotid artery (ECA) bifurcation and to the furthest point that could be examined. Flow directions were examined

with color doppler. Flow patterns were evaluated with spectral examination by placing the spectrum at an angle of 30-60 degrees. When the images were completely filled with color, Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Resitive Index (RI), Pulsatility Index (PI) values were measured by the automatic software of the device and noted for both sides. PSV (ICA)/PSV (CCA) value was obtained by dividing the ICA PSV value to the CCA PSV value for both sides. Again, ICA RI value was dividing the CCA RI value to obtain ICA (RI)/CCA (RI) values. These values were included in the patient group for the side with trigeminal neuralgia and in the control group for the healthy side without trigeminal neuralgia.

Data collection tools

The demographic data of all patients were recorded in the hospital database. The patient's age, clinical and anamnesis information, and imaging features of the ultrasonography reports were noted from this database.

Data analysis

Statistical analysis was performed using the SPSS 2.2 (IBM, Armonk, NY, USA) program. The Mann-Whitney U test was used for independent binary groups that did not fit the normal distribution. Categorical variables presented as ratio, continuous variables were presented as median (min-max) value and standart deviation (SD). A $p<0.05$ value was considered significant.

Ethics committee approval

Ethics committee approval for this study was obtained from the regional hospital ethics committee Medicine Non-invasive Clinical Research Ethics Committee (Date: 16/02/2022, Decision No: 2022/2-4). All procedures were utilized in accordance with the Declaration of Helsinki.

Results

The mean age of the patients was 48.05±10.43 (min: 21 max: 73). Fifty one (64.6%) of the patients had right-sided pathology, 28 (35.4%) had left-sided pathology. While 25 (31.7%) of the patients were within the first year of the disease, 34 (43%) had been diagnosed for periods ranging from 1 to 3 years. 20 (25.3%) patients had been suffering from the disease for more than 3 years (Table 1).

Table 1. Demographic characteristics of trigeminal neuralgia patients

	n/%
Age	48.05±10.43
	(Min: 27- Max: 63)
Gender (W/M)	45/34 (%57/%43)
Half of the face with TN findings (R/L)	51/28 (%64.6/%35.4)
Disease history	
<1 year	25 (%31.7)
1-3 year	34 (%43)
>3 year	20 (%25.3)

n: number min: minimum, max: maximum

PSV (ICA), RI (ICA) and PSV (ICA)/PSV (ECA) values in the patients were relatively higher in the arterial structures on the side with TN clinic compared to the healthy side. In addition, RI (ICA)/RI (CCA) value was also high in the arterial structures on the side with TN diagnosis. There is no significant difference between the RI (CCA) and PSV (CCA) values. (Table 2).

Table 2. Parameters of carotid doppler ultrasonography imaging of the patient and healthy side in patients with trigeminal neuralgia

	Trigeminal Neuralgia (+)	Trigeminal Neuralgia (-)	*p* value
PSV (ICA)	61.49±14.2	53.39±21.62	**0.004**
PSV(CCA)	54.26±17.05	51.07±23.41	**0.41**
PSV (ICA/CCA)	1.23±0.07	1.02±0.03	**0.001**
RI(ICA)	0.51±0.07	0.44±0.02	**0.049**
RI(CCA)	0.62±0.13	0.63±0.17	**0.81**
RI(ICA/CCA)	0.81±0.09	0.76±0.11	**0.031**

Peak Sistolik Velocity (PSV), End Diastolic Velocity (EDV), Resitive Index (RI)

Discussion

According to the results of this study examining the changes in carotid DUS examination parameters on the diseased side in patients with TN, a significant increase was observed in the resistance parameters and flow velocities of the CCA and ICA, the main vascular structures of the carotid artery system.

In previous studies, vascular structures are evaluated with T2-weighted sequences using MRI-specific imaging methods in the detection of findings secondary to compression in neurovascular structures. Possible aberrant vascular structures in the trigeminal nerve tract, compressions secondary to aneurysms or ectasia in vascular structures can be easily visualized with three-dimensional angiography images created.[14-16] At these levels, T2-weighted signal increase due to nerve edema secondary to compression in the trigeminal nerve root and nerve root diameter increase can be evaluated. Moreover, changes secondary to atrophy in nerve roots secondary to long-term compression symptoms at this level can also be evaluated. It has been stated in some studies that microdamage can be visualized with new methods such as diffusion tensor imaging (DTI).[14,17]. However, MRI is an expensive and difficult to access imaging method and DTI imaging is not performed in most centers. In addition, there are many patients diagnosed with TN who have normal MRI imaging findings. In such patients, the pathophysiology of TN cannot be understood and the patient tries to benefit from symptomatic treatments. The carotid arterial system is a vascular structure located in the proximal and it is known that the flow patterns at this level change before intracranial pathologies develop and cause gliotic changes in microdamages in the brain.

The vascular structures examined in MRI are ICA segments and branches from the main carotid arterial system. It has been stated that the presence of ectasias, aneurysms or rotations in the traces of these vascular structures may lead to TN. It is known that stenoses at the CCA and ICA levels cause significant differences in flow and pressure values, and the risk of ischemic stroke increases in patients with increased intimal media thickness and stenotic findings in the carotid artery.[18,19] This was the reason why patients with stenosis in the carotid artery system were excluded from the study in our study. Although plaque formations and stenosis develop in the carotid artery system and the plaque diameter and vascular diameter are measured and evaluated, the most important point determining the degree of stenosis is the changes in flow velocity parameters. The increase in flow velocity causes an increase in vascular pressure, turbulent flow at this level and changes in blood fluidity. It first causes changes in the microvascular level and then in the macrovascular structures, causing brain ischemia. At this point, we thought that carotid DUS results could be effective in determining whether the increase and/or decrease in carotid flow parameters would have an effect at the microvascular level, even though there was no vascular compression finding in TN patients.

Parameters obtained with carotid artery DUS such as maximum systolic velocity (Vmax), minimum diastolic velocity (Vmin), mean velocity and pulsatility index (PI) are used to measure hemodynamic parameters.[20] No previous study has investigated the values of carotid artery doppler parameters in TN patients. The aim of this study is to determine whether carotid doppler hemodynamic parameters will differ on the TN side compared to the healthy side. In our study, the significant increase in the flow velocity values and RI values in arterial structures on the TN clinical side may suggest that the increase in the flow pattern may be effective in the etiology of TN.

Limitations

This study has some limitations. First and foremost, ultrasonographic examination can be affected by factors such as the experience of the radiologist and the imaging features of the device. Therefore, there may be bias in the study results. Secondly, in this study, data were obtained with the results recorded in the system in a limited number of patients and no control examination was performed on the patients. Finally, diabetes mellitus, coronary artery changes in flow parameters in patients with diseases such as may have affected the study results. Patients with stenosis findings on carotid artery DUS were excluded from the study to prevent this situation.

Conclusion

TN etiology and treatment methods are still being investigated and are an important pathology affecting the quality of life of patients. Although there are studies

investigating the effects of vascular compression on trigeminal neuralgia, there is no study in the literature investigating its relationship with vascular nutrition. The fact that the change in carotid DUS flow parameters was significant in TN patients suggests that vascular nutrition may also play a role in the pathophysiology of this disease. In this study, it was shown that especially the ICA flow velocity and vascular resistance parameters increased in the carotid arterial system on the TN side. These findings indicate that the flow parameters in the carotid arterial system may also be effective in pathophysiology of TN. Evaluation of carotid arterial system flow patterns in patients suffering from TN may be a new method for measures to be taken against possible pressure and flow rate increases in patients, in attack treatments or in reducing the frequency of attacks. However, comprehensive studies are required in larger patient populations.

Ethics Committee Approval

Ethics committee approval for this study was obtained from the regional hospital ethics committee Medicine Non-invasive Clinical Research Ethics Committee (Date: 16/02/2022, Decision No: 2022/2-4). All procedures were utilized in accordance with the Declaration of Helsinki.

Informed Consent

Informed consent form was obtained from all patients.

Author Contributions

E.K: Data collection and processing, analysis, materials, writing and literature review. M.K. Design, data collection, literature review and writing.

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Conflict of Interest

There is no conflict of interest to declare.

Financial Disclosure

Peer-review

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Research Article/Özgün Araştırma

Change of ectropion surgery on astigmatic vector and ocular biometry

Ektropion cerrahisinin astigmatik vektör ve oküler biyometrideki etkisi

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Abstract

Aim: To evaluate corneal astigmatism change and intraocular lens (IOL) power values following ectropion surgery.

Materials and Methods: This comparative prospective research included patients with involutional ectropion who were divided using the snap-back test. The severity of ectropion increased progressively to reach the highest levels in Group 4. Patients underwent lateral tarsal strip procedures, and preoperative and 3-month postoperative biometry measurements were performed.

Results: While the mean flattest keratometry (K1), steepest keratometry (K2), and mean keratometry (Km) values exhibited nonsignificant increases at 3 months after surgery in Groups 1 and 2 ($p>0.05$ for all), the mean values of K1, K2, and Km were increased with statistical significance in Groups 3 and 4 at 3 months postoperatively ($p<0.05$ for all).

Conclusion: According to the snap-back test, ectropion in advanced stages will affect topographic values and IOL power calculations. If surgeons are going to perform cataract or refractive surgery after ectropion repair, they may consider changing the lens power selection accordingly.

Keywords: Ectropion; Keratometry; Intraocular lens measurement.

Öz

Amaç: Ektropiyon cerrahisi sonrası korneal astigmatizma değişimi ve göz içi lens (GİL) güç değerlerini değerlendirmek.

Gereç ve Yöntem: Bu karşılaştırmalı prospektif çalışmada involüsyonel ektropiyon hastaları snap-back testi kullanılarak şiddetlerine göre derecelendirildi. Ektropion şiddeti Grup 1'de en hafif Grup 4'te en ağır seviyedeydi. Hastalara lateral tarsal şerit işlemleri uygulandı ve ameliyat öncesi ve ameliyat sonrası 3. ayda biyometri ölçümleri yapıldı.

Bulgular: Ortalama en düz keratometri (K1), en dik keratometri (K2) ve ortalama keratometri (Km)) değerleri Grup 1 ve 2'de ameliyattan sonraki 3 ayda anlamlı olmayan artışlar gösterirken (hepsi için $p>0,05$), K1, K2 ve Km ortalama değerleri ameliyat sonrası 3. ayda Grup 3 ve 4'te istatistiksel anlamlı artış gösterdi (hepsi için $p<0,05$).

Sonuç: Snap-back testine göre ileri evredeki ektropiyonda topografik değerleri ve GİL gücü hesaplamalarını etkileyecektir. Cerrahlar ektropiyon onarımı sonrası katarakt veya refraktif cerrahi ameliyatı yapacaklarsa lens gücü seçimini buna göre değiştirmeyi düşünebilirler.

Anahtar Kelimeler: Ektropion; Keratometri; İntraoküler lens ölçümü.

Introduction

Ectropion is the outward turning of the ciliated edge of the eyelid. The most common form, involutional ectropion, is an age-related eyelid malposition that primarily affects the elderly population.[1] The underlying cause is either increased lateral laxity or horizontal laxity.[2] A number of different procedures have been devised to correct this valve laxity, including the lateral tarsal strip (LTS) surgical technique. In some of these cases, the scope of the surgical procedure can be expanded. A well-known procedure used in the treatment of horizontal eyelid laxity, which significantly influences the occurrence of involutional ectropion, is tarsus fixation to the lateral orbital edge's periosteum.[3]

According to clinical studies, the effects of LTS surgery may include more benefits than merely the provision of a more cosmetically pleasing appearance of the eyelid. In addition, changes in corneal topography, the evaluation of corneal aberrations, and increases in intraocular pressure (IOP) after LTS surgery have been presented in the literature.[4-6] Attention is increasingly being devoted to the possible impact that LTS surgery may have on both the functional and structural properties of the eye. The present study was undertaken with the aim of exploring the effects of LTS surgery on astigmatism vector analysis and ocular biometry in patients with lower eyelid ectropion of varying severity.

Materials and Methods

This research had a prospective comparative design and was conducted in the setting of a tertiary hospital. The research protocol was granted approval by the Local Research Ethics Committee (2021-3-6). The patients provided informed consent prior to their examinations and all procedures were carefully undertaken in accordance with the ethical standards presented in the Declaration of Helsinki.

A total of 44 Caucasian patients (44 eyelids) who underwent LTS procedures for lower eyelid ectropion and satisfied the specified inclusion criteria were enrolled as participants. The inclusion criteria were as follows: 1) lower eyelid involution ectropion; 2) IOP of ≤21 mmHg; 3) third- or fourth-degree anterior chamber angle based on the Van Herick technique; 4) spherical equivalent of apparent refraction within ±3 D; and 5) normal anterior segment (except mild nuclear sclerotic cataract) and fundus examination results.

Patients meeting any of the following criteria were excluded from enrollment: 1) a history of any ocular surgery; 2) eyebrow ptosis or sagging adipose tissues; 3) a history of contact lens use; 4) media opacity; 5) any chronic ocular disease or a history of relevant drug use; and 6) histories of any conditions that could have an effect on wound healing.

The patients' systemic and ocular diseases were evaluated. All patients were subjected to basic ophthalmologic evaluations comprising best corrected visual acuity with a Snellen chart, IOP measurement by Goldmann applanation tonometry, slit lamp biomicroscopy, and posterior segment evaluation with a 90 D lens.

The patients included in the study had horizontal lower lid laxity without medial tendon laxity, involutional lower lid ectropion, and no scars on the lower lid. All patients had positive snap-back test results and pinch tests and negative medial canthal tendon laxity test results.[7]

According to the results of the snap-back test, representing different severity levels of ectropion, the patients were categorized within 4 groups. Among the patients of Group 1, the lid position improved in a short time after the snap-back test. In Group 2, the lid position was restored within 4–5 s without blinking; in Group 3, blinking was required to fulfill the lid position; and in Group 4, the lid position could not be achieved with a blink of the eye.[8] The patients were evaluated by 2 ophthalmologists and divided into groups. (EA, GAA)

The patients' initial central corneal thickness (CCT), flattest keratometry value (K1), steepest keratometry value (K2), mean keratometry value (Km), anterior chamber depth (ACD), axial length (AL), corneal astigmatism (CA), and intraocular ocular biometric variables such as intraocular lens (IOL) power (obtained with a constant value of 118.7 mm using an Acrysof IQ device (Alcon

Laboratories, Inc., Fort Worth, TX, USA), aiming for the emmetropia and using the Holladay 2, Haigis, Hoffer Q, SRK/T, and Barrett equations) were obtained via optic biometric methods (LenStar LS 900, Haag Streit Diagnostics, Köniz, Switzerland). These ophthalmological evaluations and measurements were conducted again 3 months after the patients' LTS surgeries. Comparisons of these postsurgical corneal topography indices with the initial measurements were conducted and any changes were recorded. Relevant changes in astigmatism were diagnosed upon identification of a change in the axis of greater than 10° and a change in power of greater than 0.2 D, because smaller changes in the axis and the power may not have significant impacts on visual acuity. Breaks were analyzed in the negative cylinder form for the sake of consistency. With-the-rule (WTR) astigmatism was accepted as a steep axis determined within a range of 90° ± 30°, while against-the-rule (ATR) astigmatism was diagnosed in the event of a steep axis determined within a range of 0° ± 30°. Any axis determined to be beyond these ranges was taken as oblique astigmatism.

All of the LTS surgeries were performed by one experienced surgeon (E.A.) under local anesthesia. A solution comprising povidone and iodine was used to sterilize the surgical site. A sterile surgical pen was used to mark the surgical incision line on the lateral canthal region while patients were in upright positions. For infiltration anesthesia, 4 mL of 2% lidocaine and 1:100,000 epinephrine were administered simultaneously by subcutaneous route. A lateral canthotomy incision was made following the drawn line and then the anterior lamella and posterior lamella were separated in the eyelid. The tarsal plate were released from the retractors and conjunctiva along the posterior surface and inferior border, and the marginal epithelium was cut in a strip. Hand cautery was used in cases when hemostasis was deemed necessary. The free tarsal strip was sutured to the lateral orbital margin's periosteum with 5.0 polypropylene sutures. The lateral canthal angle was corrected and the skin was sutured with a 6.0 Vicryl suture. Ophthalmic Terramycin (Pfizer Inc., New York, NY, USA), a topical oxytetracycline ointment, was prescribed for patients as postoperative care. One week after the surgeries, the sutures were removed in follow-up appointments.[9,10]

Statistical analysis

IBM SPSS Statistics 22.0 for Windows (IBM Corp., Armonk, NY, USA) was utilized in the analysis of the study data. For descriptive statistics, the calculated values were given as mean ± standard deviation (SD) and minimum to maximum (max–min) ranges. The Kolmogorov–Smirnov test was applied in determinations of whether variables reflected normal distribution, while the Mann–Whitney U test was utilized for comparing variables that were independent and the Wilcoxon test for those that were dependent. The threshold of statistical significance was taken to be $p<0.05$.

Ethics committee approval

Permission was received from Adiyaman University Clinical Research Ethics Committee to conduct the research (decision no: 2021-3-6 and decision date: 11 February 2021). The study was in compliance with the Helsinki Declaration.

Results

The mean ages and gender of patients in Groups 1–4 did not differ with statistical significance ($p=0.362$ and $p=0.489$, respectively). Thirteen patients were included in Group 1, 11 patients in Group 2, 12 patients in Group 3, and 8 patients in Group 4. The mean ages of the patients in Groups 1–4 were respectively 63.62±8.76 (51–75), 61.79±8.16 (50–75), 67.54±7.29 (58–77), and 64.87±6.61 (54–74) years. The male-to-female ratios in Groups 1–4 were respectively 6/7, 7/4, 5/7, and 3/5.

The IOL measurement parameters of the patients (keratometry, ACD, and AL) and the IOL power values according to different calculations are provided in Table 1. Similar mean values of CCT and IOP were determined preoperatively in Groups 1–4 and at 3 months postoperatively, without statistical significance (for all, $p>0.05$). For K1, K2, and Km, it was similarly found that the mean

values had increased without statistical significance at 3 months after the surgeries in Groups 1 and 2 (for all, $p>0.05$), while the mean values obtained for K1 ($p=0.006$), K2 ($p=0.005$), and Km ($p=0.006$) in Group 3 and for K1 ($p=0.025$), K2 ($p<0.001$), and Km ($p<0.001$) in Group 4 were seen to have increased significantly at 3 months postoperatively. The mean CA size was also increased in Group 1 ($p=0.810$), Group 2 ($p=0.186$), Group 3 ($p=0.268$), and Group 4 ($p=0.013$) at 3 months postoperatively.

Table 1. Clinical characteristics of groups of patients with ectropion ranging from least severe (Group 1) to most severe (Group 4)

	Group 1			Group 2			Group 3			Group 4			*p*-value†
	Preoperative	Postoperative	*p*-value*	Preoperative	Postoperative	*p*-value*	Preoperative	Postoperative	P-value*	Preoperative	Postoperative	*p*-value*	
IOP (mmHg)	15.78 ± 1.72	16.02 ± 2.13	0.785	15.33 ± 2.10	16.00 ± 2.86	0.246	17.72 ± 2.83	17.36 ± 3.26	0.341	16.15 ± 3.05	15.69 ± 3.32	0.323	0.864
CCT (µm)	542.87 ± 35.94	543.25 ± 36.10	0.197	542.91 ± 36.10	543.16 ± 36.02	0.186	539.63 ± 22.83	539.54 ± 22.85	0.341	540.38 ± 34.67	540.15 ± 34.72	0.190	0.975
K_1 (D)	43.96 ± 0.90	43.99 ± 0.90	0.147	44.18 ± 0.56	44.20 ± 0.58	0.276	43.83 ± 0.62	44.00 ± 0.61	**0.006**	43.74 ± 0.29	43.86 ± 0.19	**0.025**	0.671
K_2 (D)	44.87 ± 0.81	44.88 ± 0.81	0.535	45.19 ± 0.42	45.27 ± 0.44	0.073	44.72 ± 0.66	44.92 ± 0.66	**0.005**	44.43 ± 0.50	44.74 ± 0.56	**<0.001**	0.611
K_m (D)	44.41 ± 0.82	44.43 ± 0.82	0.198	44.68 ± 0.44	44.70 ± 0.41	0.245	44.28 ± 0.63	44.46 ± 0.63	**0.006**	44.08 ± 0.33	44.29 ± 0.31	**<0.001**	0.596
CA (D)	0.90 ± 0.49	0.88 ± 0.49	0.810	0.93 ± 0.37	0.86 ± 0.48	0.186	0.89 ± 0.23	0.91 ± 0.21	0.268	0.69 ± 0.49	0.88 ± 0.53	**0.013**	0.968
ACD (mm)	3.27 ± 0.48	3.28 ± 0.45	0.527	3.07 ± 0.28	3.10 ± 0.24	0.407	3.50 ± 0.36	3.51 ± 0.35	0.160	3.36 ± 0.36	3.36 ± 0.33	0.497	0.380
AL (mm)	23.24 ± 0.52	23.31 ± 0.55	0.252	22.93 ± 0.59	22.94 ± 0.61	0.097	22.78 ± 0.61	22.78 ± 0.63	1	23.04 ± 0.77	23.04 ± 0.78	0.421	0.749
IOL power (SRK/T) (D)	21.25 ± 1.10	21.18 ± 1.03	0.104	22.12 ± 1.46	22.16 ± 1.41	1	22.54 ± 1.90	22.22 ± 1.91	**0.011**	23.11 ± 1.83	22.80 ± 1.98	**0.040**	0.191
IOL power (Haigis) (D)	21.12 ± 1.02	20.87 ± 1.12	0.164	21.87 ± 1.50	21.91 ± 1.48	0.186	22.63 ± 1.93	22.18 ± 1.94	**0.010**	23.30 ± 2.05	22.88 ± 2.11	**0.009**	0.085
IOL power (Holladay 2) (D)	20.75 ± 1.10	20.93 ± 1.08	0.164	21.41 ± 1.54	21.50 ± 1.53	0.166	22.13 ± 1.81	21.72 ± 1.91	**0.020**	22.76 ± 1.95	22.30 ± 2.02	**0.011**	0.136
IOL power (Hoffer Q) (D)	20.62 ± 1.12	20.68 ± 1.03	0.351	21.18 ± 1.50	21.20 ± 1.47	0.329	22.09 ± 1.84	21.68 ± 1.94	**0.020**	22.80 ± 2.05	22.38 ± 2.11	**0.009**	0.097
IOL power (Barrett Universal II) (D)	21.18 ± 1.13	21.06 ± 1.01	0.351	21.63 ± 1.41	21.61 ± 1.36	0.665	22.45 ± 1.82	22.04 ± 1.94	**0.005**	23.26 ± 2.02	22.84 ± 2.08	**0.009**	0.095

IOP: Intraocular pressure; CCT: central corneal thickness; K_1: flattest keratometry; K_2: steepest keratometry; K_m: mean keratometry; CA: corneal astigmatism; ACD: anterior chamber depth; AL: axial length; IOL: intraocular lens. Bold font indicates statistical significance. *: Comparisons of preoperative and postoperative values. †: Comparisons of preoperative values

Preoperatively, 4 patients (50%) were found to have WTR astigmatism, with a steep meridian at 90° ± 30°, while oblique astigmatism was present in 2 patients (25%) and ATR astigmatism in 2 patients (25%). At 3 months postoperatively, 6 (87.5%) of 8 patients had WTR astigmatism, which included the same 4 patients diagnosed with

this astigmatism before surgery and 2 additional patients previously diagnosed with oblique astigmatism. The 2 patients (25%) with preoperative ATR astigmatism retained that type of astigmatism in the postoperative period. Table 2 provides K and axis values of the 8 patients in Group 4, the group with the most severe ectropion.

Table 2. Keratometry values of Group 4, comprising patients with the most severe ectropion

Patient	Preop K1	Preop K2	Preop Axis	Postop K1	Postop K2	Postop Axis
1	42.90	43.85	**24**	42.95	43.90	12
2	45.01	45.74	35	45.10	45.80	10
3	43.02	43.89	**165**	43.10	43.92	176
4	44.90	45.95	**173**	44.94	45.96	182
5	43.75	44.15	**20**	43.70	44.10	9
6	44.02	45.13	133	44.00	45.10	152
7	44.98	45.25	80	44.99	45.24	102
8	43.14	45.02	110	43.16	45.03	97

K1: Flat meridian, K2: steep meridian

At 3 months after the surgeries, the mean values obtained for ACD and AL were found to be statistically similar to the preoperative values obtained for all groups of patients ($p>0.05$ for all).

Mean IOL powers were evaluated with the application of 5 different equations, and they were found to be similar in Groups 1 and 2 when the preoperative and postoperative values were compared (for all, $p>0.05$). In Groups 3 and 4, however, these comparisons revealed significant postoperative decreases (for all, $p<0.05$). For each of the equations used in calculating the power values, the mean decreases in Groups 3 and 4 were approximately 0.40 D. The mean changes in Group 4 following LTS surgery were obtained as 0.30 D ± 0.48 with the SRK/T equation, 0.42 D ± 0.49 with the Hoffer Q equation, 0.42 D ± 0.49 with the Haigis equation, 0.42 D ± 0.49 with the Barrett Universal II equation, and 0.46 D ± 0.55 with the Holladay 2 equation.

Discussion

Involutional ectropion may cause some refractive errors and astigmatism by irregularizing the corneal surface.[11,12] In adult patients diagnosed with age-related involutional ectropion, we see poor distribution of tears on the ocular surface because of the outward turning of the eyelids. Blurred vision and watery eyes are expected to exert a negative impact on the quality of life for these patients. In patients experiencing

eyelid ectropion, the cornea possesses the normal curvature but symmetry is lost between the eyes.[12] In addition, the calculation of the IOL power in patients with cataract is important because of the keratometric changes that may occur due to ectropion. No studies could be found in the literature investigating the effects of surgery for the treatment of involutional ectropion on IOL power, making the current research important because it is the first to explore that relationship.

In the literature, different results were reported for corneal keratometry parameters in different series of eyelid surgeries such as those for ptosis and blepharoplasty.[13,14] Detorakis et al. evaluated 18 eyelids of 18 patients newly diagnosed with ectropion following LTS surgery and they reported significantly increased residual astigmatism using corneal topography at 6 months postoperatively.[7] In another relevant study, Eshraghi et al. evaluated 19 eyes (10 with ectropion; 9 with entropion) of 15 patients.[4] They performed LTS surgery and evaluated the patients at 3 months postoperatively. At that point, they were unable to detect any changes of statistical significance in postoperative keratometry values (i.e., mean keratometry and vertical and flat meridian values).

In the current study, the final keratometry and CA values of Group 4 were found to be significantly decreased compared to baseline.

Additionally, a significant decrease was observed for all of the calculated IOL measurements. While keratometry and astigmatism values were similarly examined in some studies, there is not yet consensus in the literature regarding these outcomes. The reasons for these variable results include the small sizes of sample populations, evaluations being conducted for one eye or both eyes, differences in surgical methods, the failure of some studies to appraise the degree of ectropion in patients, and different durations of follow-up times. In comparison to the previous works available in this body of literature, the present research has a relatively adequate number of patients and those patients were grouped according to their degrees of ectropion. These characteristics of our research can be listed as strengths of the study.

Our hypothesis was that corneal deformation may differ depending on the degree of ectropion. The differences observed in the keratometry values and CA sizes between Group 1 and Group 4 pre- and postoperatively supported this hypothesis.

According to our findings, decreases in RA associated with ectropion levels occurred in patients with involutional ectropion. After ectropion surgery, the corneal shape has been affected and astigmatism may change. Although the axis of astigmatism does not change systematically in these cases, it is more common for the operated eyes to experience a change of the axis towards WTR depending on the level of ectropion. In ectropion surgery, corneal keratometry and astigmatism changes may be seen in consequence of the eyelid's contact with the anterior surface of the cornea as a result of the tightening of loose eyelids. The horizontally tightened lower eyelid exerts pressure on the lower limbus and eyeball, causing local flattening in the lower limbus running parallel to the horizontal meridian. The steep meridian becomes steeper and WTR astigmatism is further increased by the merging effect.

In Group 4, which included patients with the most severe ectropion, the extent of astigmatism increased with surgical correction. More than 10° of astigmatism axis change was observed in 7 patients (87.5%).

Even if these changes do not affect vision, it is important to consider them in procedures such as planning for astigmatic correction in the course of cataract surgeries, refractive surgeries, or toric IOL implantation.

Eshraghi et al. conducted a study that included 19 eyes of 15 patients (10 with ectropion; 9 with entropion) and found relevant changes of more than 0.2 D in astigmatism strength in 14 of those eyes (73.6%).[4] Among these patients, 6 of the 10 patients diagnosed with ectropion and 4 of the 9 patients diagnosed with entropion were found to have experienced axis changes of more than 10°. The value obtained for surgically induced astigmatism was 0.47 ± 1.34 D. These authors concluded that the applied treatment had induced WTR astigmatism, with axis values of 91 ± 23.[4] Detorakis et al. included 18 patients in their research and found that the 6-month postoperative RA values were increased significantly compared to preoperative values. When the pre- and postoperative astigmatic axis distributions were evaluated, they found that the percentage of eyes with WTR had increased after surgery, although this finding did not reach a level of statistical significance.[7]

These changes in the curvature of the cornea can be either increases or decreases depending on the size and axis of the astigmatism before surgery and the vertical pressure vector applied during surgery. However, further testing of our hypothesis should be done by conducting other studies that investigate alterations of the values of astigmatic vectors with longer follow-up periods to clearly assess the implications for patients. Although the decrease in the IOL power following LTS surgery was limited to patients with severe ectropion, the mean reduction was calculated with 5 different equations and found to be about 0.40 D. It was observed that as the severity of ectropion increased, the decrease in IOL power could be affected by as much as 1 D. It is surprising that, under these circumstances, the difference in severity was not significant from a clinical perspective. Clinicians need to consider these points so that they can prevent refractive deviation from developing after cataract surgery. These astigmatic errors can become

problematic if special lens implantation (toric-multifocal) is planned. It may be more ideal to perform the LTS procedure in advance and follow the outcome for a while prior to cataract surgery. If the severity of ectropion is mild, cataract surgery is recommended at any time since the IOL measurement will not change.

The AL and ACD values used in the IOL calculations did not change after surgery. In order to interpret the changes in keratometry more accurately, the IOL was calculated with 5 different equations. To apply the Haigis equation, the value of anterior chamber depth (ACD) is required.[15] Variations between the different IOL equations should be considered here. LenStar OLCR measurements do not convey the full emmetropia data since the IOL is obtained in 0.50 D steps. This process returns the closest possible IOL value. In this study, the predicted target emmetropization value was used in calculations of IOL power. Only patients who had been diagnosed with involutional ectropion were accepted as participants in this study. Those who had undergone previous surgical procedures applied in cases of recurrent ectropion were not included in the study because those procedures impact the corneal topography and aberrations.[5] In future studies, it would be beneficial to evaluate the impacts exerted by recurrence on IOL calculations.

Limitations

The homogeneity of the patient group (including only involutional ectropion patients), the evaluation of a single surgical method (only LTS was applied), and the grading of ectropion levels are the strengths of this study. Not including cicatricial ectropion patients and not evaluating different surgical methods (not including wedge resection or medial spindle) are limitations. The small number of patients included in the study is another limitation.

The amount of outward rotation of the eyelid and the amount to be corrected according to the patient's eyelid anatomy are evaluated intraoperatively by surgeons. A second surgery may be required because of the over- or undercorrection that may occur as a result of these evaluations. Another strength of the present work was that patients requiring such revisions were not included in the analysis.

Conclusion

This research has explored postoperative corneal topographic changes and their effects on IOL in patients with involutional ectropion. Increases of statistical significance were observed in the corneal keratometry values of patients with severe ectropion, and a particularly significant increase of 0.20 D in CA was observed in Group 4. The resulting reduction in IOL power was found to be approximately 0.40 D. Surgeons should be aware of the corneal topographic changes of patients who will undergo treatment by LTS. This should also be taken into account when planning cataract or refractive surgeries.

Ethics Committee Approval

Informed Consent

Verbal permission and written informed consent forms were obtained from volunteers to participate in the study.

Author Contributions

Study concept/design: EA., GAA. Data collecting: EA., GAA., MK. Data analysis and interpretation: MK Literature review, writers: EA., GAA. The final version of this article was read and approved by all authors.

Acknowledgments

Conflict of Interest

There is no conflict of interest regarding the research.

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Research Article/Özgün Araştırma

Investigation of situation for development of infection, nutritional and length of hospital stay in elderly hospitalized in a palliative clinic

Palyatif klinikte yatan yaşlılarda enfeksiyon gelişimi, beslenme durumu ve hastanede kalış süresinin araştırılması

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Abstract

Aim: In our study, we aimed to evaluate patients' nutritional status, compare frequently used nutritional scales with each other and with the duration of hospitalization, and measure the effect of nutritional status on infection and mortality who are in the elderly.

Materials and Methods: Nutritional Risk Screening-2002, Mini Nutritional Assessment, and Geriatric Nutritional Risk Index were used. Patients were monitored for infection and mortality throughout the hospitalization period.

Results: The prevalence of malnutrition was found 98.6% with Mini Nutritional Assessment, 97.3% with Nutritional Risk Screening-2002, and 87.1% with Geriatric Nutritional Risk Index. A high correlation was found between the Geriatric Nutritional Risk Index and albumin, body mass index, arm, and calf circumference.

Conclusion: The malnutrition rate is quite high in patients who need palliative care. The Geriatric Nutritional Risk Index, compared to Nutritional Risk Screening-2002 and Mini Nutritional Assessment, is an effective and user-friendly scale that contains objective variables in bed-dependent patients for nutrition.

Keywords: Infection; Malnutrition; Elderly; Palliative care.

Öz

Amaç: Çalışmamızda, palyatif bakım ünitesinde takip edilen yaşlı hastaların beslenme durumlarını değerlendirmeyi, sık kullanılan nutrisyon ölçeklerini birbirleriyle ve hastanede yatış süresiyle karşılaştırmayı, nutrisyonel durumun enfeksiyon ve mortalite üzerindeki etkisini ölçmeyi amaçladık.

Gereç ve Yöntem: Nutrisyonel Risk Taraması-2002, Mini Nutrisyonel Değerlendirme ve Geriatrik Nutrisyonel Risk İndeksi kullanıldı. Yatış süresi boyunca hastalar enfeksiyon ve mortalite açısından takip edildi.

Bulgular: Malnutrisyon sıklığı Mini Nutrisyonel Değerlendirme ile %98,6, Nutrisyonel Risk Taraması-2002 ile %97,3 ve Geriatrik Nutrisyonel Risk İndeksi ile %87,1 olarak bulundu. Geriatrik Nutrisyonel Risk İndeksi ile albumin, vücut kitle indeksi, kol çevresi ve baldır çevresi arasında yüksek düzeyde korelasyon mevcuttu.

Sonuç: Palyatif bakıma ihtiyaç duyan hastalarda malnütrisyon oranı oldukça yüksektir. Geriatrik Beslenme Risk İndeksi, Beslenme Risk Taraması-2002 ve Mini Nutrisyonel Değerlendirme ölçeği ile karşılaştırıldığında, yatağa bağımlı yaşlı hastalarda beslenme açısından objektif değişkenler içeren etkili ve kullanıcı dostu bir ölçektir.

Anahtar Kelimeler: Enfeksiyon; Malnutrisyon; Yaşlılık; Palyatif bakım.

Introduction

Palliative care is a discipline that aims to improve the quality of life of end-stage patients with limited treatment options, including cancer, and their relatives. By providing support for physical, social, psychological, and spiritual aspects.[1] In the palliative care unit, besides infections, pressure sores, organ failures, neurological diseases, and malignancies, malnutrition is one of the important problems.[2] Malnutrition is a nutritional status in which systemic, metabolic, and mental functional disorders are seen as a result of taking macronutrients and micronutrients either more or less than needed. Although the term malnutrition includes the concepts of over-nutrition (obesity) and undernutrition, it is used synonymously with undernutrition.[3] Malnutrition starts to develop as a result of the intake of nutrients as low as it cannot continue the body functions (anorexia, malabsorption, etc.) or failure of food intake to satisfy the increasing need due to illness, trauma, and infection. It is also seen as a combination of these two mechanisms.[4] In a study conducted in Turkey, patients evaluated in hospitalization period, with a Subjective Global Assessment (SGA) of 30%, with a Nutrition Risk Index (NRI) of 36% of malnutrition identified. Prevalence of malnutrition varies between 20-50%. according to the place and shape of the application.[5]

There is no single examination finding, laboratory test and scale for the diagnosis of malnutrition. In the evaluation of the patient comprehensive research is required involving; anamnesis, physical examination, anthropometric and functional measurements, hematological and biochemical markers, and imaging methods.[6] Versatile scales have been developed to screen and evaluate malnutrition. Among the most commonly used are Mini Nutritional Assessment (MNA) for the geriatric population, Nutritional Risk Screening (NRS-2002) for hospitalized patients, and Geriatric Nutritional Risk Index (GNRI) for nutritionally-related risk calculation over 65 years of age.[7,8] Albumin, prealbumin, transferrin, retinol-binding protein, and lymphocytes are frequently used in laboratory assessment of nutritional assessment.[9,10]

Nutrition methods are divided into two subgroups; enteral and parenteral. Enteral feeding can be done orally or by utilizing a tube. Oral nutrition, if possible, is the method of first choice. If the daily energy requirement cannot be met orally, enteral nutrition should be provided either by nasogastric and nasoduodenal catheterization, gastrostomy, or jejunostomy. Parenteral nutrition can be done as peripheral and central. It is not a permanent method except in special cases, It is preferred until enteral feeding is provided or to support enteral feeding.[11,12]

In our study it was aimed to evaluate the patients who are in the palliative care unit for malnutrition, to compare used nutritional scales, ways of feeding, infections, hospitalization time, and mortality.

Materials and Methods

This study was designed as a sectional. It included 70 patients aged 65 years and over having at least one chronic disease (diabetes mellitus, hypertension, etc.) and those who had been followed up in the palliative care unit for at least three days between April - September 2018. Patients with amputation and musculoskeletal deformity in the extremities were excluded from the study.

The sociodemographic and clinical data forms created by the researchers were filled. Sociodemographic data included gender, age, educational status, occupation, marital status, and income level. Clinical data from included medical history, nutrition type, infection, culture results, NRS-2002, GNRI, MNA, height, body weight, body mass index (BMI), knee height (KH), arm circumference (AC), calf circumference (CC), hemoglobin, thrombocyte, neutrophil, lymphocyte, leukocyte, high-density lipoprotein (HDL), monocyte, ferritin, albumin, c-reactive protein (CRP), hospitalization time and outcome. The nutrition type was recorded as oral or percutaneous endoscopic gastrostomy (PEG). The predominant nutrition type in the last month was taken as the basis.

In a supine position, while the femur and knee flexed 90 degrees, KH and CC were measured with non-elastic tape. While the patient is sitting and the front arm is at supination, AC was measured with non-elastic tape from the midpoint of acromion and olecranon. Body weight, height, BMI were calculated by the following formulas:

- Height:
  - Man: (KHx2.08)+59.01
  - Woman: (KHx1.91)-(Ax0.17)+75
- Body weight:
  - Man: (KHx1.10)+(ACx3.07)-75.81
  - Woman: (KHx1.09)+(ACx2.68)-65,51
- Body mass index (kg/m^2):
  - Body weight (kg)/height (m)xheight(m)
- KH: Knee Height A: Age AC: Arm Circumference

The NRS-2002 and MNA scales were applied by the researchers. The GNRI score was calculated by the following formula:

- GNRI = [1.489x Albumin (g/L)]+[41.7x(patient body weight/ideal body weight)]
- Body weight calculated using the formulas above
- Ideal Weight: Body Mass Index was calculated in a way to be 22
- If the body weight is greater than the ideal body weight patient's body weight/ideal body weight ratio was taken 1

The patient was followed up for infections during the period of hospitalization. The duration of hospitalization was calculated in days. Mortality was accepted as death within the period of hospitalization in the palliative care unit.

Statistics

Data were analyzed with the SPSS 25 computer statistics program. Data were presented in number, percentage, mean and standard deviation (SD), median, and 95% confidence interval (CI). Normality distribution of numerical data by Kolmogorov-Smirnov test reviewed. Chi-square test was used to analyze categorical data. The Kruskal-Wallis test followed by Dunn's post hoc test was used (with Bonferroni correction). The statistical significance level was taken as $p<0.05$.

Ethics committee approval

The present study was performed in line with the principles of the Declaration of Helsinki. Ethics committee approval for our study was received from Kutahya Dumlupinar University Faculty of Medicine Non-invasive Clinical Research Ethics Committee (dated 28.03.2018, decision No. 2018/5-4)

Results

A total of 70 patients with a mean age of 80.29±6.98 (65-96) years were included in the study. 57.1% (n=40) of the patients were female, 47.1% (n=33) were primary school graduates, 30% (n=21) were illiterate, 57.1% (n=40) of the patients were housewives and 42.9% (n=30) were retired.

51.4% (n=36) of the patients were married and 95.7% (n=67) were in the low-income class. 68.6% percent (n=48) of the patients were fed orally and 31.4% (n=22) of them were fed via PEG. According to their medical history, it was found that the three most common diseases were cerebrovascular disease (28.6%), Alzheimer's Disease (AH) (25.7%), and coronary artery disease (20%). In patients, it was revealed that urinary tract infection (UTI) was 37.1% (n=26), wound infection was 34.3% (n=24), and lower respiratory tract infection (LRTI) was 28.6% (n=20). The mean and normal values of the patient's laboratory tests are given in Table 1.

The mean BMI of the patients was found 21.40±6.50 kg/m2, the mean of AC was 24.24±5.13 cm and the mean of CC was 27.75±5.03 cm. The mean NRS-2002 score of the patients was 4.06±0.89, the GNRI score was 79.88±15.48, and the MNA score was 8.55±5.48. According to the NRS-2002 grouping, 97.1% (n=68) of the patients had high and 2.9% (n=2) had low nutritional risk. According to the MNA grouping, 90% of the patients had malnutrition (n=63), 8.6% (n=6) of them had malnutrition risk and 1.4% (n=1) normal nutritional status was detected.

According to the GNRI grouping, 55.7% (n=39) of the patients had high nutritional risk, 22.6% (n=16) of them had moderate, and 8.6% (n=6), and 12.9% of them had no risk was found.

Table 1. Mean and normal values of patient's laboratory tests

Laboratory Test	Mean Value (±SD)	Normal Value
Hemoglobin (g/dL)	11,60±1,91	11,5-16,5
Thrombocyte (10^3cells/mm^3)	275,14±111,58	130-400
Leukocyte (10^3cells/mm^3)	10,90±5,15	5,2-12,4
Neutrophil (10^3cells/mm^3)	8,54±4.96	0,9-6
Lymphocyte (10^3cells/mm^3)	1,54±0,86	0,9-5,2
Monocyte (10^3cells/mm^3)	0,58±0,33	0,3-0,9
Ferritin (ng/dl)	276,92±280,50	11-306,8
Albumin (g/dL)	2,74±0,51	3,5-5,2
CRP (mg/L)	54,10±47,29	<5

SD: Standart Deviation, CRP: C-Reactif Protein

There was a high correlation between GNRI and BMI, and arm and calf circumference. A moderate correlation was found between BMI and arm circumference and a weak correlation was detected with calf circumference according to NRS-2002. A moderate correlation was detected between MNA and anthropometric measurements (Table 2).

Table 2. Correlation between nutritional scales and anthropometric measurements of palliative care unit patients

	NRS	GNRI	MNA	BMI	AC	CC
NRS	Mean:4.06 SD:0.89	r=-0.355** p=0.003	r=-0.534** p=0.000	r=-0.454** p=0.000	r=-0.464** p=0.000	r=-0.293* p=0.015
GNRI	r=-0.355** p=0.003	Mean:79.88 SD:15.48	r=0.468** p=0.000	**r=0.813** p=0.000**	**r=0.801** p=0.000**	**r=0.676** p=0.000**
MNA	r=-0.534** p=0.000	r=0.468** p=0.000	Mean:8.55 SD:5.48	r=0.550** p=0.000	r=0.554** p=0.000	r=0.501** p=0.000
BMI	r=-0.454** p=0.000	r=0.813** p=0.000	r=0.550** p=0.000	Mean:21.40 SD:5.13	r=0.972** p=0.000	r=0.811** p=0.000
AC	r=-0.464** p=0.000	r=0.801** p=0.000	r=0.554** p=0.000	r=0.972** p=0.000	Mean:24.24 SD:5.13	r=0.825** p=0.000
CC	r=-0.293* p=0.015	r=0.676** p=0.000	r=0.501** p=0.000	r=0.811** p=0.000	r=0.825** p=0.000	Mean:27.75 SD:5.03

NRS: Nutritional Risk Screening-2002, GNRI: Geriatric Nutritional Risk Index, MNA: Mini Nutritional Assessment, BMI: Body Mass Index, AC: Arm Circumference, CC: Calf Circumference, Mean: Mean, SD: Standard Deviation
Pearson Correlation Test, Spearman Correlation Test, $p < 0.05$ *, $p < 0.01$ **

A high correlation was detected between albumin and GNRI and a weak correlation with the MNA score. A correlation was found between HDL/monocyte and GNRI, MNA, BMI, AC, and CC (Table 3).

Table 3. Correlation of biochemical markers of patients hospitalized in palliative care unit with nutritional scales and anthropometric measurements

	NRS	GNRI	MNA	BMI	AC	CC
Lymphocyte	**r=-0.254*** **p=0.034**	r=0.090 p=0,457	r=0.197 p=0,102	r=0.170 p=0.159	r=0.204 p=0.090	r=0.077 p=0,528
Albumin	**r=-0.318*** **p=0.007**	**r=0.671** p=0.000**	**r=0.359** p=0.002**	**r=0.342** p=0.004**	**r=0.348** p=0.003**	**r=0.298* p=0.013**
CRP	r=0.177 p=0.142	r=-0.194 p=0.108	r=-0.071 p=0.559	r=-0.062 p=0.610	r=-0.062 p=0.610	r=-0.023 p=0.854
Ferritin	**r=0.285*** **p=0.022**	r=-0.186 p=0.141	**r=0.324** p=0.009**	**r=-0.262* p=0.037**	r=-0.226 p=0.073	**r=-0.328** p=0.009**
HDL/ monocytes	r=0.159 p=0.188	**r=-0.308** p=0.010**	**r=-0.266* p=0.026**	**r=-0.347** p=0.003**	**r=-0.422** p=0.000**	**r=-0.362** p=0.002**

The mean length of hospitalization was 13.69±9.13 days. The final status of the patients was as; 72.9% (n=51) was discharged, 15.7% (n=11) had ICU (Intensive Care Unit) transfer, and 11.4% mortality (n=8).

There was no statistically significant difference between NRS-2002, GNRI, and MNA groups according to the nutrition type. There was no statistically significant difference between the duration of hospitalization in NRS-2002, GNRI, and MNA groups. There was no statistically significant difference in NRS-2002, GNRI, and MNA groups in terms of mortality. The median duration of hospitalization was 10 days in oral feeding patients while it was 13.5 days in PEG-fed patients. The difference between the duration of feeding and length of stay was not found statistically significant.

Discussion

Nutritional problems are among the most important problems in the community, elderly care institutions, and hospitals in various services, especially in palliative care units. Nutritional disorders may cause problems such as increased infection, prolonged recovery, increased morbidity and mortality, and prolonged hospitalization. Although there is no consensus on how to diagnose, there is consensus on performing a comprehensive nutritional assessment of each patient, especially those at risk with screening, to make necessary interventions if the risk of malnutrition/malnutrition is detected and to follow up on the results.[12-15] Nutritional risk was found to be 32.6% in a study conducted on 5051 patients in 26 different departments in 12 countries in Europe and the Middle East. In the study, the highest risk rate although ranged from 93-100%, was found in ICUs.[16] In a study by Cereda et al. conducted on 177 patients who applied to long-term care centers, the frequency of nutritional risk was found 51.5% with GNRI and 55.8% with NRI.[17] In a multicenter study conducted by Korfalı, organized by the Clinical Enteral Parenteral Nutritional Association (KEPAN), 29139 patients from 34 hospitals in 19 cities were screened for nutritional risk at admission with the NRS-2002 scale. While nutritional risk prevalence was 15%, the highest rate was 52% in ICU patients; it was found the lowest in ear-nose-throat patients with a rate of 3.9%. In the same study, the prevalence of nutritional risk under 60 years was found to be 9.3%, while it increased to 25% above 60 years of age.[18] The frequency of malnutrition in our study was found to be quite high compared to many other studies in which prevalence was evaluated. We think that this difference originates from the chosen population. Most of the studies have an adult population as well as the elderly population. Only patients aged 65 years or older were included in our study. The frequency of malnutrition (93%-100%) found by Sorensen in ICUs is similar to the frequency of malnutrition we find.

In a study conducted by Portero, 170 elderly inpatients were examined and a positive correlation was found between AC, CC, and BMI values. Its use was recommended for nutritional status follow-up.[19] In a study Bonnefoy conducted on 911 elderly patients hospitalized in the geriatric unit, the use of CC in nutritional status assessment. The correlation of the CC with BMI and AC was found to be significant.[20] In the study of Vellas et al., the correlation between MNA score and AC and CC was found to be significant.[21] The results we found are consistent with the study of Portero and Bonnefoy. In palliative care patients, a significant proportion is bed-dependent, in most cases, height and body weight cannot be measured. As such AC and CC be used instead of BMI and body weight for nutritional assessment.

Cereda et al. in a study GNRI and NRI were compared, and a significant correlation was found between albumin and lymphocyte count.[17] In our study, a moderate correlation was found between albumin and GNRI. There was a weak correlation between albumin and NRS-2002, MNA, BMI, AC, and CC. Lymphocyte count correlated poorly with NRS-2002. No correlation was detected between lymphocyte count and GNRI, MNA, BMI, and CC. In the study of Alert, MNA and GNRI were moderately correlated with albumin; but no correlation was found with CRP and ferritin.[22] In our study, there was a correlation between albumin and GNRI, while there was no correlation between albumin and MNA (NRS-2002: 4.06, GNRI:79.88, MNA:8.55). In a study by Sungurtekin, SGA and NRI correlated with albumin, lymphocyte count, and total cholesterol.[5]

In our study, between HDL/monocyte ratios, GNRI, MNA, BMI, CC negative, weak; between the AC a moderate correlation was found in a negative direction.

In the study of Sorensen, the mean length of hospital stay in patients with a high risk of malnutrition was 9 days, while the mean length of hospitalization in patients with a low risk was 6 days.[16] In the study of Kyle et al., 995 patients were evaluated with SGA, NRS-2002, Malnutrition Universal Screening Tool (MUST), and NRI. The NRI scores of the patients who were hospitalized for eleven days or more were found to be higher.[23] The duration of hospitalization was longer in patients with malnutrition.[5,24,25] In the study of Correia et al., the mean length of hospital stay was 16.7 days for patients with malnutrition detected with SGA, and the mean length of hospitalization for those who had no malnutrition was found to be 10.1 days.[14] It has been shown that malnutrition is an independent risk factor for longer hospitalization. Patients with malnutrition with SGA had an average hospitalization of 6.9 days, while those without malnutrition had an average hospitalization of 4.6 days.[13] In a study on 173 patients by Chima et al., the mean length of hospital stay was 6 days in patients with malnutrition risk and four days in patients without malnutrition.[26] Two separate studies conducted by Sorensen and Kyle found similar results of an average length of hospitalization to those found in patients with a risk of malnutrition. Compared to the results found by Correia lower hospitalization time was found in our study.

In a multicentral study conducted by Sorenson with 5051 patients in Europe and the Middle East, the mortality rate was 12% in patients with a risk of malnutrition and 1% in non-risk patients.[16] In a study by Correia, evaluating 709 inpatients with SGA, one-year mortality in patients with malnutrition was found to be 12.4% and in patients without malnutrition was found to be 4.7%.[14] In Singapore, in a fourth-step hospital, patients were evaluated with SGA. In the non-malnutrition group, the mortality rate during hospitalization was 0.3%. The mortality rate was 4.3% in the patients with malnutrition. The difference in mortality between properly nourished and malnourished patients was statistically significant.[13] The mortality rate was 11.4% in our study. Similar results were found in our study regarding mortality in the studies of Sorensen and Correia. According to Lim, the mortality rate in our study was found to be high.

In our study, there is no relationship between nutrition method and length of hospital stay. There are different results in studies in the literature.[5,6,11,13,14]

Limitations

There are some limitations to the study. First, the sample of the present study consisted of the elderly. Our study is cross-sectional and single-centered. The main limitation of our article is the smaller population than other studies in the literature. Finally, the number of patients can be increased. Similar multicenter studies are needed.

Conclusion

The risk of malnutrition or malnutrition was found to be high with the three scales applied. Nutritional status should certainly be evaluated in patients who need palliative care. When nutritional scales are compared among themselves, they appear to be compatible with their results. Although NRS-2002 and MNA are used more frequently than GNRI, it may be difficult to obtain information about nutrition and background information during bedtime from bed-dependent patients, who have limited orientation and cooperation. We think that the use of GNRI in a patient in these circumstances is a more effective way. Height and body weight measurement and BMI calculation are important problems in bed-dependent patients. Therefore it could often be neglected. We think that AC and CC are important anthropometric measurements that can be used instead of height, body weight, and BMI. The three scales used in our study appear to be consistent with each other as well as with some of the anthropometric measurements and biochemical markers. Among these scales, we recommend the use of GNRI because it is easy to apply, especially effective in bed-dependent elderly patients, and contains objective variables.

Ethics Committee Approval

The present study was performed in line with the principles of the Declaration of Helsinki. Ethics committee approval for our study was received from Kutahya Dumlupinar University Faculty of Medicine Non-invasive Clinical Research Ethics Committee (dated 28.03.2018, decision No. 2018/5-4)

Informed Consent

Data concerning the study were collected with the permission of the Kütahya Health Sciences University Medical Faculty Evliya Çelebi Training and Research Hospital.

Author Contribution

All of the authors contributed at every stage of the study

Conflict of Interests

There is no conflict of interest to declare.

Financial Disclosure

No person/organization is supporting this study financially.

Statements

These research results have yet to be presented anywhere previously. Data related to the study is available on request.

Peer-review

Externally peer-reviewed.

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Research Article/Özgün Araştırma

The relationship of stigma level and healthy lifestyle behaviors in individuals with type 2 diabetes

Tip 2 diyabetli bireylerde stigma düzeyi ile sağlıklı yaşam tarzı davranışları arasındaki ilişkinin incelenmesi

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Abstract

Aim: This study is a descriptive research aiming to examine the relationship between the level of stigma and healthy lifestyle behaviors in patients with Type 2 diabetes.

Materials and Methods: This study was conducted with 142 patients who were admitted to a university hospital between October 1 and December 15, 2022. Data were obtained with the sociodemographic form, Stigma Assessment Scale (SAS) and Healthy Lifestyle Behaviors Scales (HLBS).

Results: The mean SAS score of the patients participating in the study was 43.66±12.09, and the mean HLBS score was 125.83±21.48. The highest scores were in physical activity and interpersonal relationships, HLBS was generally at a moderate level, and a statistically significant negative correlation was found between SAS and HLBS scores ($p<0.05$).

Conclusion: It was observed that the SAS and HLBS scores were at a moderate level in type 2 diabetes patients, education affected the level of stigma, gender and marital status affected the HLBS score, and healthy lifestyle scores significantly decreased as the level of stigma increased.

Keywords: Diabetes; Stigma; Lifestyle; Nursing.

Öz

Amaç: Bu çalışma, Tip 2 diyabet hastalarında damgalanma düzeyi ile sağlıklı yaşam tarzı davranışları arasındaki ilişkiyi incelemeyi amaçlayan tanımlayıcı bir araştırmadır.

Gereç ve Yöntem: Bu çalışma, 1 Ekim-15 Aralık 2022 tarihleri arasında bir üniversite hastanesine başvuran, 142 hasta ile gerçekleştirildi. Veriler, sosyodemografik form, Damgalanma Değerlendirme Ölçeği (DDÖ) ve Sağlıklı Yaşam Tarzı Davranışları Ölçekleri (SYTDÖ) ile elde edildi.

Bulgular: Araştırmaya katılan hastaların DDÖ puan ortalaması 43,66±12,09, SYTDÖ puan ortalaması 125,83±21,48'dir. En yüksek puanlar fiziksel aktivite ve kişilerarası ilişkilerdeydi, SYTDÖ genel olarak orta düzeyde ayrıca, DDÖ ile SYTDÖ puanları arasında istatistiksel olarak anlamlı bir negatif ilişki tespit edildi ($p<0.05$).

Sonuç: Tip 2 diyabet hastalarında DDÖ ve SYTDÖ puanlarının orta düzeyde olduğu, eğitimin damgalanma düzeyini etkilediği, cinsiyet ve medeni durumun SYTDÖ puanını etkilediği, ayrıca damgalanma düzeyi arttıkça sağlıklı yaşam tarzı puanlarının anlamlı düzeyde azaldığı görüldü.

Anahtar Kelimeler: Diyabet; Damgalanma; Yaşam Tarzı; Hemşirelik.

Stigma and healthy lifestyle in patients with type 2 diabetes.

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Introduction

Diabetes Mellitus (DM) is a chronic, broad-spectrum endocrine and metabolic disorder. The body cannot adequately utilize carbohydrates, fats, and proteins due to insulin deficiency or impairments in insulin action. It requires frequent medical follow-up and can lead to microvascular and macrovascular complications. The prevalence of diabetes mellitus is progressively increasing globally, emerging as a significant health concern. Additionally, diabetes mellitus leads to a range of mental, emotional, social, and psychological problems and conflicts. The presence of social and emotional issues related to diabetes is attributed to observable behaviors such as food choices, insulin injections or oral tablet use, and blood sugar measurements being part of daily life activities. During the struggle with diabetes mellitus, individuals tend to isolate themselves from social life while trying to cope with many complications related to the disease. Patients often feel irritable, angry, overwhelmed, or disheartened in the face of complex, difficult, and confusing care instructions. Social withdrawal and self-stigmatization, both the cause and the result of the problems patients experience, are frequently encountered situations. An increase in stigmatization and discrimination faced by diabetic individuals due to their conditions has been reported. In one study, it was reported that one out of every five people with diabetes experiences discrimination. Diabetes mellitus-related stigma has numerous negative effects. Stigma associated with diabetes also affects mental health and healthy lifestyle behaviors. Healthy lifestyle behaviors are defined as actions that serve to maintain and enhance individuals' well-being levels. These behaviors encompass adequate and balanced nutrition, stress management, regular physical activity, effective spiritual development, positive interpersonal relations, and taking responsibility for preserving and improving one's health. Particularly in preventable and controllable diseases like diabetes mellitus, which require lifestyle changes, healthy lifestyle behaviors play a crucial role in disease prognosis and effective cost management related to the disease. There are individual,

societal, and environmental differences in the adoption and integration of healthy lifestyle behaviors into daily life activities among individuals with chronic illnesses. Patients diagnosed with diabetes may disrupt healthy lifestyle behaviors due to stigma, causing difficulties in maintaining and protecting health, which may lead to hospitalizations. Consequently, this may lead to an increase in health care costs and an increase in the workload of nurses. In this context, the objective of the study is to explore the relationship between stigma level and healthy lifestyle behaviors in individuals diagnosed with diabetes mellitus, which is becoming increasingly prevalent worldwide.

Materials and Methods

The sample size of the study

The study was carried out as a descriptive cross-sectional study. The study population comprised patients who sought medical attention at the Internal Medicine department, Endocrinology, and Metabolic Diseases outpatient clinics of the hospital where the research was conducted with a diagnosis of type 2 diabetes between October 1 and December 15, 2022. The research did not involve any sample selection, and all patients who met the inclusion criteria during the specified dates were included in the sample. The sample of the research was composed of 140 patients through power analysis with 0.05 error, 0.95 confidence interval and 0.95 representative power of the universe. A total of 142 patients who had been followed for at least one year with a type 2 diabetes diagnosis, could communicate verbally, had no neurological, mental, or sensory issues, and were willing to participate in the research constituted the study sample. The research data were obtained by having type 2 diabetes patients who agreed to participate in the study fill out data collection tools through face-to-face interviews conducted by the researcher.

Data collection tools

The research data were collected using a patient information form, Stigma Assessment Scale for Type 2 Diabetes, and a Healthy Lifestyle Behaviors Scale.

Sociodemographic Questionnaire: This is a form consisting of 7 questions covering participants' socio-demographic characteristics and disease-related features.

Type 2 Diabetes Stigma Assessment Scale (SDAS): The Turkish adaptation of the scale, which was developed by Browne et al.[8], was conducted by İnkaya and Karadağ. The scale consists of three sub-dimensions: Differential Treatment, Blaming and Judging and Self-stigma and 19 items in total. The lowest possible score is 19, and the highest score is 95, with an increase in the score indicating a higher level of stigmatization. The cronbach alpha value for the entire scale is expressed as 0.92.[9] In this study, the Cronbach alpha value of the scale was found to be 0.84.

Healthy Lifestyle Behaviors Scale (HLBS): Developed by Walker et al. (1987) and revised in 1996, the Turkish adaptation, validity, and reliability study of the Healthy Lifestyle Behaviors Scale-II was conducted by Bahar et al. 2008. The scale measures health-promoting behaviors associated with an individual's healthy lifestyle. The scale is a 4-point Likert-type scale consisting of 52 items and 6 sub-dimensions. The sub-dimensions of the scale are health responsibility, physical activity, nutrition, spiritual growth, interpersonal relations and stress management. There are no negative items in the scale. The lowest score obtainable from the entire scale is 52, and the highest is 208. An increase in the scale score indicates better healthy lifestyle behaviors of individuals. The cronbach alpha value for the entire scale is expressed as 0.94.[6] In this study, the Cronbach alpha value of the scale was found to be 0.72.

Data analysis

The analyses were performed using SPSS 25.0 software. In the statistical analysis of the data, the Shapiro-Wilk normality test was used to assess the normal distribution of the data and the Levene test was used to evaluate the homogeneity of variances. In the analysis of the data, descriptive statistics such as percentage, mean, and standard deviation were used, along with Kruskal Wallis, Mann Whitney U and Pearson correlation analysis was used. Cronbach's alpha coefficient was calculated for the reliability of the scales. The significance level was accepted as $p<0.05$ with a 95% confidence interval.

Ethics committee approval

Prior to commencing the research, written permission was obtained from the clinical research ethics committee (Date: 28.09.2022/Decision no: 2022/327), the relevant institution, and both written and verbal consent from the participants. The research was conducted in compliance with the Helsinki Declaration.

Results

The mean age of the type 2 individuals with diabetes participating in the study was determined as 62.92±14.06 years. It was found that 52.1% of the patients were female, 82.4% were married, 41.5% were illiterate, 31.0% had primary education, 45.1% had diabetes for 11 years or more, 40.8% received insulin therapy, 37.3% received oral anti-diabetic (OAD) and insulin therapy, and 56.3% had an additional chronic disease (Table 1).

It was determined that there was a significant difference between the DSAS mean scores, self-stigma and different behavior scores according to the educational status of the patients. ($p<0.05$) (Table 2).

It was determined that there was a significant difference between the average scores of the stress management subscale of HLBS according to the patients' gender and marital status. ($p<0.05$) (Table 3).

When the mean scores of the DSAS and its sub-dimensions were examined for the Type 2 diabetic individuals participating in the study, the different treatment sub-dimension was 13.90±5.01, the blame-judgment sub-dimension was 17.22±7.31, the self-stigma sub-dimension was 13.23±5.50, and the overall DSAS total mean score was 43.66±12.09. When examining the mean scores of HLBS and its sub-dimensions, the health responsibility sub-dimension was 21.98±7.28, the physical activity sub-dimension was 17.19±6.83, the nutrition sub-dimension was 24.27±7.79, the spiritual growth sub-dimension was 23.07±7.71, the interpersonal relations sub-dimension was

24.20±7.00, the stress management sub-dimension was 17.40±3.89, and the overall HLBS total mean score was 125.83±21.48. It was found that patients' highest scores were in

the physical activity and interpersonal relations sub-dimensions and that their healthy lifestyle behaviors were at a moderate level (Table 4).

Table 1. Distribution of socio-demographic characteristics of patients (n=142)

		n	%
(Mean Age 62.92±14.06)			
Gender	Women	74	52.1
	Men	68	47.9
Marital Status	Married	117	82.4
	Unmarried	25	17.6
Education Status	Illiterate	59	41.5
	Primary education	44	31.0
	Secondary education	24	16.9
	High School	15	10.6
Working status	Yes	31	21.8
	No	111	78.2
Diabetes duration	1-5 years	36	25.4
	6-10 years	42	29.6
	11 year and over	64	45.1
Diabetes treatment	OAD	31	21.8
	İnsulin	58	40.8
	İnsulin+OAD	53	37.3
Do you have a chronic disease	Yes	80	56.3
	No	62	43.7
Total		142	100.0

Table 2. Comparison of the total and subscale score averages of DSAS according to the socio-demographic characteristics of individuals with Type 2 diabetes

		Different Behavior	Blaming and Judging	Self-stigma	DSAS Total
Gender	Women	13.90±5.82	17.66±9.27	13.01±6.28	43.22±12.53
	Men	13.91±3.98	16.75±4.26	13.48±4.54	44.14±11.67
	Z/p	-0.629/0.529	-0.090 / 0.928	-1.231 / 0.218	-0.731 / 0.465
Marital Status	Married	14.04±5.28	17.31±7.69	13.30±5.66	43.81 ±12.20
	Unmarried	13.28±3.48	16.80±5.23	12.92±4.76	43.00±11.77
	Z/p	-0.468 / 0.640	-0.290 / 0.772	-0.148 / 0.883	-0.284 / 0.776
Education Status	Illiterate	14.72±6.03	18.32±10.01	14.55±6.42	45.91±12.00
	Primary education	13.02±3.92	16.79±4.14	12.09.±4.55	41.90±11.47
	secondary education	15.12±4.54	17.04±5.17	14.20±4.49	46.37±13.29
	High School	11.33±2.41	14.46±3.50	9.86±3.46	35.66 ±8.31
	KW/p	**8.657 / 0.013**	3.028/0.220	**8.845 / 0.012**	**8.016 / 0.018**
Working status	Yes	13.12±4.10	16.48±4.98	12.58±5.08	42.19±12.64
	No	14.12±5.23	17.43±7.84	13.42±5.62	44.08±11.96
	Z/p	-0.910 / 0.363	-0.225 / 0.822	-0.805 / 0.421	-0.632 / 0.527
Diabetes duration	1-5 years	13.75±3.51	17.00±4.59	13.22±4.94	43.97±11.65
	6-10 years	14.61±7.23	19.21±11.62	14.38±7.58	45.83±14.90
	11 year and over	13.53±3.85	16.04±3.98	12.50±3.91	43.66±12.09
	KW/p	0.326 / 0.849	4.137 / 0.126	0.771 / 0.680	1.332 / 0.514
Diabetes treatment	OAD	13.87 ±3.88	17.32±4.40	14.74±4.97	45.93±11.74
	Insulin	13.34±3.37	16.43±3.94	12.77±4.17	42.55±10.15
	Insulin+OAD	14.54±6.79	18.03±10.73	12.86±6.86	43.66±12.09
	KW/p	0.234 / 0.890	0.382 / 0.826	3.986 / 0.136	1.377 / 0.502
Do you have a chronic disease	Yes	14.05±5.85	18.17±9.02	13.86±6.37	44.83±13.46
	No	13.72±3.69	16.00±3.92	12.43±4.03	42.16±9.96
	Z/p	-0.382 / 0.703	-1.861 / 0.063	-1.083 / 0.279	-0.934 / 0.350

*KW= Kruskal Wallis Test, **Z= Mann-Whitney U Test, p<.05. DSAS= Diabetes Stigma Assessment Scale

Table 3. Comparison of HLBS total and subscale score averages according to socio-demographic characteristics of individuals with Type 2 diabetes

		Health responsibility	Physical	Nutrition	Spiritual	İnterpersonal	Stress management	HLBS Total
Gender	Women	22.09±9.15	17.33±8.38	25.28±10.16	23.09±9.38	24.28±8.19	16.89±4.09	124.12±23.89
	Men	21.86±4.52	17.02±4.67	23.17±3.59	23.05±5.40	24.11±5.48	17.97±3.60	127.70±18.50
	Z/p	-0.659/0.510	-0.819/0.413	-0.803/0.422	-0.209/0.835	-0.289/0.773	**-2.090/0.037**	-0.958/0.338
Marital Status	Married	22.24±7.65	17.55±7.24	24.11±11.22	23.27±8.30	24.55±7.33	17.76±3.96	126.58±21.59
	Unmarried	20.76±5.18	15.48±4.17	25.00±4.76	22.16±3.90	22.56±5.00	15.76±3.09	122.32±21.03
	Z/p	-0.614/0.539	-1.500/0.133	-0.930/0.352	-0.349/0.727	-1.467/0.142	**-2.389/0.017**	-1.283/0.199
Educational status	Illiterate	20.86±5.66	16.32±6.45	24.96±7.09	22.50±4.51	23.88±5.05	17.72±4.15	126.59±21.44
	Primary education	21.79±7.53	16.56±4.29	23.43.±7.83	22.38±6.16	22.88±4.51	17.06±3.68	123.50±19.76
	Secondary education	24.83±10.85	19.62±11.21	25.00±10.81	25.33±14.67	26.83±13.25	17.62±3.62	125.12±25.15
	High School	22.40±3.79	18.53±4.30	22.86±3.97	23.73±5.66	25.13±4.35	16.80±4.07	130.86±21.36
	KW/p	2.129/0.345	2.403/0.301	0.495/0.781	1.663/0.435	3.990/0.136	0.951/0.621	2.129/0.345
Working status	Yes	22.54±8.28	17.09±4.51	23.96±8.52	23.16±6.81	23.51±4.9	17.16±3.41	125.96±19.37
	No	21.82±7.01	17.21±7.37	24.36±7.62	23.05±7.97	24.39±7.50	17.47±4.02	125.80±22.11
	Z/p	-0.045/0.964	-0.606/0.544	**-1**.237/0.216	-0.324/0.746	**-**0.354/0.723	-0.067/0.947	**-**0.138/0.890
Diabetes duration	1-5 years	22.97±8.09	17.55±4.74	24.52±9.50	23.02±6.70	23.00±4.67	17.27±4.24	128.13±23.12
	6-10 years	22.83±9.15	17.71±8.98	24.76±10.24	21.21±11.60	24.54±9.93	18.07±4.27	123.11±23.56
	11 years and over	20.87±5.05	16.64±6.24	23.81±4.15	22.35±4.37	24.65±5.69	17.04±3.41	126.32±19.14
	KW/p	0.228/0.633	0.687/0.407	0.049/0.825	0.049/0.825	0.004/0.948	0.561/0.454	0.228/0.633
Diabetes treatment	OAD	22.25 ±5.25	16.64±5.01	23.74±4.94	23.12±7.19	23.32±5.15	17.67±4.07	127.19±23.75
	İnsulin	21.46±8.27	17.53±9.05	25.17±10.04	23.96±10.05	24.89±9.15	17.43±3.41	124.82±21.61
	İnsulin+OAD	22.39±7.24	17.13±4.69	23.60±6.20	22.07±4.34	23.96±4.98	17.22±4.32	126.15±20.28
	KW/p	2.628/0.269	0.946/0.623	0.375/0.829	0.647/0.724	0.311/0.856	0.646/0.655	2.628/0.269
Do you have chronic disease	Yes	21.42 ±7.70	16.66±7.31	25.53±9.61	23.07±8.87	24.36±7.75	17.25±4.24	124.32±22.07
	No	22.70±6.70	17.87±6.16	22.64±3.99	23.08±5.96	24.00±5.96	17.61±3.41	127.79±20.70
	Z/p	-1.617/0.106	-1.727/0.084	-1.540/0.124	-0.200/0.841	-0.035/0.972	-1.207/0.227	-0.870/0.384

*KW= Kruskal Wallis Test, **Z= Mann-Whitney U Test, p<.05. HLBS= Healthy Lifestyle Behaviors Scale

Table 4. Score average distribution of DSAS and HLBS total scale and subscales

	X±SS	Minimum	Maximum
DSAS Total	**43.66±12.09**	**19.00**	**89.00**
Different Behaviors	13.90±5.01	6.00	51.00
Blame and Judgment	17.22±7.31	7.00	87.00
Self-Stigma	13.23±5.50	6.00	51.00
HLBS Total	**125.83±21.48**	**61**	**176**
Health Responsibility	21.98±7.28	11.00	71.00
Physical Activity	17.19±6.83	8.00	67.00
Nutrition	24.27±7.79	12.00	72.00
Spiritual Development	23.07±7.71	12.00	92.00

		24.20±7.00	13.00	80.00
Interpersonal Relations		24.20±7.00	13.00	80.00
Stress Management		17.40±3.89	10.00	34.00

DSAS= Diabetes Stigma Assessment Scale, HLBS: Healthy Lifestyle Behavior Scale

In the study, a medium-level positive relationship was found between the healthy lifestyle scale and the sub-dimensions of health responsibility, physical activity, nutrition, spiritual development and interpersonal relations and a low-level positive relationship was found between stress management. It was found that there was a low-level negative relationship between the stigma scale and the sub-dimensions of the healthy lifestyle scale, namely health responsibility, physical activity, nutrition, spiritual development and interpersonal relations and it was not statistically significant. It was determined that there was a positive, moderately significant relationship between the stigma scale and spiritual development and stress management ($p<0.05$). A moderately positive, statistically significant relationship was found between the stigma scale and stress management, which is the sub-dimension of the healthy lifestyle scale. A statistically significant relationship was found between the mean scores of the stigma level and the Healthy Lifestyle Behaviors Scale score averages of the type 2 diabetic patients participating in the study (*p<0.05*). (Table 5).

Discussion

While the majority of studies conducted with individuals diagnosed with diabetes focus on medical methods and physical complications, there has been an increase in research on the psychosocial aspects of diabetes in recent years.[4] The psychosocial problems experienced by individuals diagnosed with diabetes affect the prognosis of the disease and their adherence to treatment approaches.[10] In this study, the relationship between stigma, which is among the psychosocial problems of diabetic individuals, and healthy lifestyle behaviors, an important concept for effective management of the disease process, was examined.

Table 5. The relationship between stigma levels and healthy lifestyle behaviors in individuals with Type 2 diabetes

		1	2	3	4	5	6	7	8
Health Responsibility (1)	r								
	p								
Physical Activity (2)	r	.653							
	p	.000							
Nutrition (3)	r	.427	.422						
	p	.000	.000						
Spiritual Development (4)	r	.553	.640	.479					
	p	.000	.000	.000					
Interpersonal Relations (5)	r	.606	.533	.604	.662				
	p	.000	.000	.000	.000				
Stress Management (6)	r	.211	.248	.276	.166	.188			
	p	.012	.003	.001	.049	.025			
HLBS Total (7)	r	.315	.347	.359	.214	.309	.481		
	p	.000	.000	.000	.011	.000	.000		
DSAS Total (8)	r	.006	-.104	.102	-.187	-.051	.514	-.039	
	p	.948	.216	.227	.025	.544	.000	.642	

r=correlation test, p<.05, HLBS: Healthy Lifestyle Behaviors Scale, DSAS: Diabetes Stigma Assessment Scale

Type 2 diabetes is reported to expose individuals to negative stigma due to the lifestyle changes it brings along.[11] Among the significant findings of this study are the level of diabetes-related stigma in individuals with type 2 diabetes in Turkish society and the variables that affect the stigma level. In this study, the stigma status in individuals with type 2 diabetes was found to be at a moderate level. There is a significant difference between the patients' stigma levels according to their educational level. This difference may be thought to be due to university graduate patients. In a study conducted by Zhang and colleagues with young and middle-aged individuals with diabetes in a Chinese sample, it was found that the participants' perceived stigma was moderate and the stigma levels of individuals with higher education levels were lower.[12] In another study conducted in a Swiss sample, it is reported that a large portion of individuals with diabetes experience type 2 related stigma.[13] In a study conducted in the Latin American sample, it was found that 16.4% of the participants experienced high levels of stigma, and the experienced stigma level was related to low socio-economic status.[14] In a study conducted with individuals diagnosed with type 1 diabetes in Iran, participants stated that "a person with type 1 diabetes is stigmatized as a miserable person, constantly sick, helpless, a reminder of death, and an unbearable burden, deprived of a normal life, captive to 'obligation', and devoid of pleasures and rejected".[14] In the literature, there are studies conducted with different ethnic groups in different geographical regions regarding diabetic individuals and perceived stigma level. This study was conducted in the Southeast region of Turkey, and it was found that the perceived stigma level of individuals diagnosed with type 2 diabetes living in this region is similar to the studies in the literature, and the level of education variable affects the stigma level. In addition, in this study, it was determined that male and married participants also had a higher perceived stigma level.

Adopting healthy lifestyle behaviors is crucial for achieving successful results in diabetes management. Healthy lifestyle behaviors are actions that contribute to the maintenance and improvement of individuals' well-being. These behaviors encompass maintaining a balanced and adequate nutrition, managing stress, engaging in regular physical activity, fostering effective spiritual development, nurturing positive interpersonal relationships, and taking responsibility for safeguarding and enhancing one's health.[6] In this study, the healthy lifestyle behaviors for individuals with type 2 diabetes were determined to be at an average level. It was determined that gender, marital status, and duration of illness did not make a difference in healthy lifestyle behaviors. However, it was determined that there was a statistically significant relationship between the gender status of the patients and their higher average stress score, which is the HLBS sub-dimension (*p*<0.05) and the stigma level of men was found to be higher than women. Zhang et al. In his study with individuals with diabetes, the stigmatization level of men was found to be high.[12] Men's working life outside, not being able to eat all meals at home in accordance with their diet, and having difficulty accessing foods suitable for their diet due to their working life may increase their stress situations. In Gezer and Ulusan's study, healthy lifestyle behaviors of individuals with diabetes were not found to be at a sufficient level.[15] Taşkın Yılmaz and colleagues' study reported that healthy lifestyle behaviors of individuals diagnosed with diabetes were at a low level.[6] The average score of middle-level healthy lifestyle behaviors obtained in this study is similar to the literature.

It is essential for individuals with type 2 diabetes to maintain high motivation levels during the disease process to sustain healthy lifestyle behaviors.[16] In this study, it was determined that healthy lifestyle behaviors increased as the level of perceived stigma decreased in individuals with type 2 diabetes. In a study, it was reported that the level of stigma in individuals diagnosed with diabetes acted as a barrier to self-care and treatment adherence skills.[17] In Cho and colleagues' study, it was found that an increase in the perceived stigma level of diabetic individuals was associated with a decrease in self-care behaviors.[18] In individuals with type 2

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diabetes, it is stated that an increase in stigma level is related to a decrease in self-efficacy and self-esteem.[10] In Lin and colleagues' study, it was reported that self-stigmatization in diabetic individuals negatively affected glycemic control. No research was found in the literature on the relationship between stigma and healthy lifestyle behaviors in individuals with type 2 diabetes. In this study, it was found that as the stigma level increased in individuals with type 2 diabetes, healthy lifestyle behaviors decreased. It can be said that this situation negatively affects healthy lifestyle behaviors by disrupting compliance with nutrition and medication use, which are important elements in disease management, due to the concern of stigmatization.

Conclusion

The study found that individuals with type 2 diabetes perceived a moderate level of stigma and had insufficient healthy lifestyle behaviors. As the perceived stigma level of individuals with type 2 diabetes increased, their average healthy lifestyle behavior scores decreased. In this regard, it is suggested to investigate the stigma-related barriers to healthy lifestyle behaviors in the treatment and care processes of individuals with type 2 diabetes, to inform family members living with the individual about the disease and lifestyle behaviors, and to expand public awareness campaigns by health authorities through mass communication elements.

Ethics Committee Approval

Prior to commencing the research, written permission was obtained from the clinical research ethics committee (Date: 28.09.2022/Decision no: 2022/327), the relevant institution, and both written and verbal consent from the participants. The research was conducted in compliance with the Helsinki Declaration.

Author Contributions

Study concept/design, data collecting: EB., SMİ., data analysis and interpretation SMİ., NA., EB., literature review, writers: EB., AN., NA., SMİ., The final version of this article was read and approved by all authors.

Conflict of Interest

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

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Research Article/Özgün Araştırma

Refugee adolescents' future hopes, stigmatisation and mental health problems

Mülteci ergenlerin gelecek umutları, damgalanmaları ve ruhsal sorunları

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Abstract
Aim: In this study, it is aimed that refugee adolescents' hopes for the future, their stigmatisation status and mental health problems.
Materials and Methods: The research was conducted as descriptive, relational and instrumental. Research sample of the study was refugee adolescents between the ages of 11-18. It was used the Adolescent Information Form, Brief Symptom Inventory, Internalised Stigma Scale for Children and Adolescents and Children's Hope Scale to collect the data. In total, it was excluded 78 refugee adolescents and conducted with 484 refugee adolescents.
Results: It was found that refugee adolescents' mental symptoms (anxiety, depression, hostility, somatisation and negative self) explained 54.6% of the stigmatisation they experienced. In addition, It was determined refugee adolescents' mental problems explained 42.7% of their hope for the future.
Conclusion: It can be said that adolescents' hopes for the future play a mediating role in the relationship between their psychological symptoms and stigma.
Keywords: Stigma; Refugee adolescent; Mental symptoms; Hope.

Öz
Amaç: Bu araştırmada, mülteci ergenlerin geleceğe dair umutları, damgalanma durumları ve ruhsal sağlık sorunlarını belirlemek amaçlanmıştır.
Gereç ve Yöntem: Araştırmanın modeli; tanımlayıcı, ilişkisel ve aracı modeldir. Araştırmanın örneklemini 11-18 yaşları arasında mülteci ergenler oluşturmaktadır. Verilerin toplanmasında Ergen Bilgi Formu, Kısa Semptom Envanteri, Çocuklar ve Ergenler için İçselleştirilmiş Damgalanma Ölçeği ve Çocukların Umut Ölçeğini kullanılmıştır. Toplamda 78 mülteci ergen kapsam dışı bırakılmış ve 484 mülteci ergen ile yürütülmüştür.
Bulgular: Mülteci ergenlerin ruhsal belirtilerinin (anksiyete, depresyon, hostilite, somatizasyon ve olumsuz benlik) yaşadıkları damgalanmalarının %54.6'sını açıkladığı tespit edilmiştir. Ayrıca, mülteci ergenlerin ruhsal sorunlarının geleceğe dair umut düşüncelerinin %42.7'sini açıkladığı belirlenmiştir.
Sonuç: Ergenlerin geleceğe dair umutlarının, yaşadıkları ruhsal semptomlar ile damgalanma arasındaki ilişkide aracı rol oynadığı söylenebilir.
Anahtar Kelimeler: Damgalanma; Mülteci ergen; Ruhsal semptomlar; Umut.

Introduction

Refugee status is defined as "a well-founded fear of being persecuted in the country of nationality for reasons of race, religion, nationality, membership of a particular social group or political opinion".[1] The negative social and psychological effects of migration are more evident for migrant women and children. Child migrants are among the most vulnerable, even after arriving at their destination.[1,2] Because of their dependency, children need support from adults not only for physical resilience but also for psychological and social well-being.[3]

According to UNICEF's September 2016 report, there are approximately 50 million "uprooted children in the world" and 28 million of these children have been forced to leave their homes to seek a safer and better life because of internal or interstate conflict.[4] According to the United Nations report published in 2022, 3.1 million children have fled the violent civil war in Syria and today 6.1 million children are in need of water, food, sanitation, hygiene, health, education and psychological support.[5] Turkey is the country with the largest refugee population in the world, especially since April 2011, hosting an intensive wave of migrants displaced by the war in Syria.[6] Although there are requests for international protection in Turkey from Afghanistan, Iraq, Iran and other countries, the number of individuals under temporary protection is much higher than these applications. According to the report published by the Ministry of Internal Affairs Directorate of Migration Management in 2022, the number of Syrian migrant children between the ages of 0 and 18 is 1,747.67.[7]

Much research in the literature on refugee adolescents mental health has focused on post-trauma stress, anxiety and depression symptoms.[8–10] In a study conducted by Ünver et al. (2021) with 156 refugee adolescents in Turkey between the ages of 7 and 18 years old, it was found that 26.9% of the children complained of attention deficit and hyperactivity disorder, 26.9% complained of post-traumatic stress disorder, 25% complained of major depressive disorder, 23.1% complained of anxiety disorders and

8.3% complained of sexual abuse.[11] In a study of children aged 4-10 years, parents reported that these children showed anxiety and withdrawal (49%), emotional problems (45%), behavioural problems (38%) and symptoms of hyperactivity (20%).[12] However, alienation, marginalisation and isolation of refugees, especially by the society in the countries where they migrate, lead to the concept of stigma. Internalised stigma or self-stigma means that the individual becomes aware of the negative stereotypes in the society and internalizes and accepts them with his/her personal value system and self-perception. As a result of negative consequences such as decreased self-esteem and shame, the individual withdraws from the society.[13] However, high hope levels of individuals protect their mental and physical health, well-being, life satisfaction, motivation and quality of life. On the other hand, low hope levels of individuals decrease their resilience in risky conditions.[14] There should be a shift to a strength-based approach that focuses on resilience. In order for refugee adolescents to overcome internalised stigma, mental health promotion programs should be promoted through communication between clinicians and the community.[2,15]

Refugee experience has a strong psychological impact on adolescents. This study will be the first study in the literature to investigate the relationship between mental symptoms, internalised stigma and hope levels in refugee adolescents. The aim of this study is to examine the mental health problems, stigmatisation and hope for the future of refugee adolescents living in Turkish region and to reveal the mediating role of hope in the relationship between mental health problems and stigmatisation.

Research Questions

Question-1. Is there a mediating effect of hope for the future in the relationship between mental health problems experienced by adolescents and their stigmatization status?

Materials and Methods

Design of the research

It was conducted the research as descriptive, relational and mediator model.

This study was designed as a quantitative study using structural equation modelling to determine the mental health symptoms, stigma and hope levels of refugee adolescents and the relationship between these concepts.[16]

The population of the research and the sample

The study was conducted in the outpatient clinics and clinics of the Department of Paediatrics of Harran University. It was conducted the study with refugee adolescents who were followed up for diagnosis and control purposes in the outpatient clinics of the Department of Pediatrics and who were hospitalised in paediatric clinics for treatment. It was preferred the quota sampling method, which is a non-probability sampling method.[17]

Here, it was conducted the research with refugee adolescents who met the inclusion criteria. The research was conducted between 1 November 2023 and 31 March 2024.

It was reached 562 refugee adolescents in the study. Nine adolescents with Type I diabetes mellitus, fifteen adolescents with heart diseases, seventeen adolescents with epilepsy, fourteen adolescents with cerebral palsy, twelve adolescents were excluded due to lack of parental consent and eleven adolescents dropped out of the study. In total, it was excluded 78 refugee adolescents and conducted with 484 refugee adolescents.

Inclusion criteria

- Being between the ages of 11 and 18,
- Having no communication problems,
- Not having any diagnosed mental and neurological health diseases (Down Syndrome, CP),
- Those without chronic illness
- Agreeing to participate in the study,
- They migrated after the outbreak of the war in Syria in 2011,
- They have lived in Turkey for at least six years.
- Refugee children who can read and write in Turkish
- Refugee children with legal permission from their parents

Exclusion criteria

- Adolescents under 11 years of age,
- Adolescents over 18 years of age,
- Diagnosed with diabetes,
- Diagnosed with Down's syndrome,
- Diagnosed with epilepsy,
- Diagnosed with Cerebral Palsy
- Diagnosed with any heart disease,
- Adolescents who dropped out halfway through the study were excluded.

Data collection tools

Data were collected by using Adolescent Information Form, Brief Symptom Inventory, Internalised Stigma Scale for Children and Adolescents and Children's Hope Scale.

Adolescent information form

The form was created by the researchers by reviewing literature.[11,13] The Refugee Child Monitoring Form consists of questions such as the child's age, gender, educational status, experiencing losses during war and migration, number of losses, separation from family, etc.

Brief symptom inventory – BSE

The original scale was developed by Derogatis (1992).[18] The scale has been adapted to the Turkish population by Şahin et al. (1994).[19] The inventory assesses general psychopathology. The Cronbach alpha of the scale was reported to be between 0.70-0.88. The Brief Symptom Inventory (BSI)SE consists of 53 items. It has five subscales. The scale is made up of five sub-dimensions, including anxiety, depression, negative self, somatisation and hostility.[19] In this research, the Cronbach's alpha coefficient of the scale was found to be 0.94. Permissions were obtained from the people who developed the scale and conducted the validity study.

Internalised stigma scale for children and adolescents (ISSCA)

It is a self-report scale developed to assess the phenomenon of internalised stigma in children and adolescents. Its validity and reliability study was conducted by Çağlayan (2019). The scale consists of 32 items. The items of ISSCA are answered in two different subscales as the thoughts of others (people sub-

dimension) and my own thoughts (me sub-dimension). Each item is evaluated on a Likert-type scale ranging from 1 to 5 (1: I do not believe at all that this thought is true, 5: I strongly believe that this thought is true). Higher values of this scale indicate higher levels of internalised stigma.[20] The Cronbach alpha of the scale was 0.90.The scale had a Cronbach alpha coefficient of 0.91 in this research. Permissions were obtained from the people who developed the scale and conducted the validity study.

Children's hope scale

The Children's Hope Scale (CHS) was developed by Snyder et al. (1997).[21] Turkish validity and reliability study of the scale was conducted by Atik and Kemer. In terms of internal consistency, the Cronbach alpha coefficient was .74 for the overall scale.The scale consists of 6 items and two sub-dimensions: "pathways" and "agency". The scale is scored as "Never=1, Rarely=2, Sometimes=3, Often=4, Most of the time=5 and Always=6" according to Likert-type rating. The scale can range from 6 to 36. [22] The Cronbach alpha coefficient of the scale was found to be 0.74 in this research. Permissions were obtained from the people who developed the scale and conducted the validity study.

Data collection

The research data was collected using face-to-face interviewing in the hospital waiting room. The interviews were conducted by the researcher with refugee adolescents and their families in the appropriate waiting rooms of the outpatient clinic by using face-to-face interview techniques. The data collected from the adolescents hospitalized in the clinic for treatment were obtained by face-to-face interview technique in the periods when adolescents were available in their rooms. Data collection took an average of 30-60 minutes. The researcher was present in the paediatric outpatient clinics five days a week and in the clinic during working hours seven days a week to collect data.

Data analysis

The data were analysed with IBM AMOS V23. Descriptive statistics (number, percentage, standard deviation, minimum and maximum) were used to show socio-demographic data. Compliance with the normal distribution was analysed with the assumption of multiple normality. Relational survey model was used in the design of the study. The reason for using a correlational survey model is to examine the interactions between two or more sets of variables in multiple directions (direct and indirect effects). For this purpose, structural equation modeling is preferred. Therefore, structural equation modeling was used in this research. The maximum likelihood method was used to test the model. In order to test whether the Hope Scale had a mediating role in the relationship between mental health problems and internalised stigma, an analysis based on the bootstrap method was conducted. The mediator model was run with 5000 samples and a confidence level of 95%. Model 4 was used in the analysis and the significance was considered to be $p<0.050$. In structural equation modeling, which shows whether the model established with the factors obtained as a result of the research is verified or not with more than one fit index, all indices are evaluated together instead of a single fit index. The fit indices of the mediator model were acceptable (CMIN/df=3.907; CFI=0.996; GFI=0.979; AGFI= 0.958; NFI=0.994; TLI=0.993; RMSEA= 0.059; SRMR=0.009). Figure 1 about modeling is given below.

Ethical considerations

Ethical approval (23.06.2023-237165) was obtained from Harran University Human and Human Science Ethics Committee. Written informed consent and verbal consent were obtained from the parents of each child. Informed consent and verbal consent were obtained from refugee children. Institutional approval was obtained from the university's department of paediatrics. The research was conducted according to the Declaration of Helsinki principles.

Results

In the study, it was found that 51% (247) of the refugee adolescents were girls, 52% (252) were separated from their families after the war and 56% (271) of them experienced the loss of

one of their family members. It was found that the average age of the adolescents was eleven years and they had an average of eight siblings. We found that each adolescent was separated

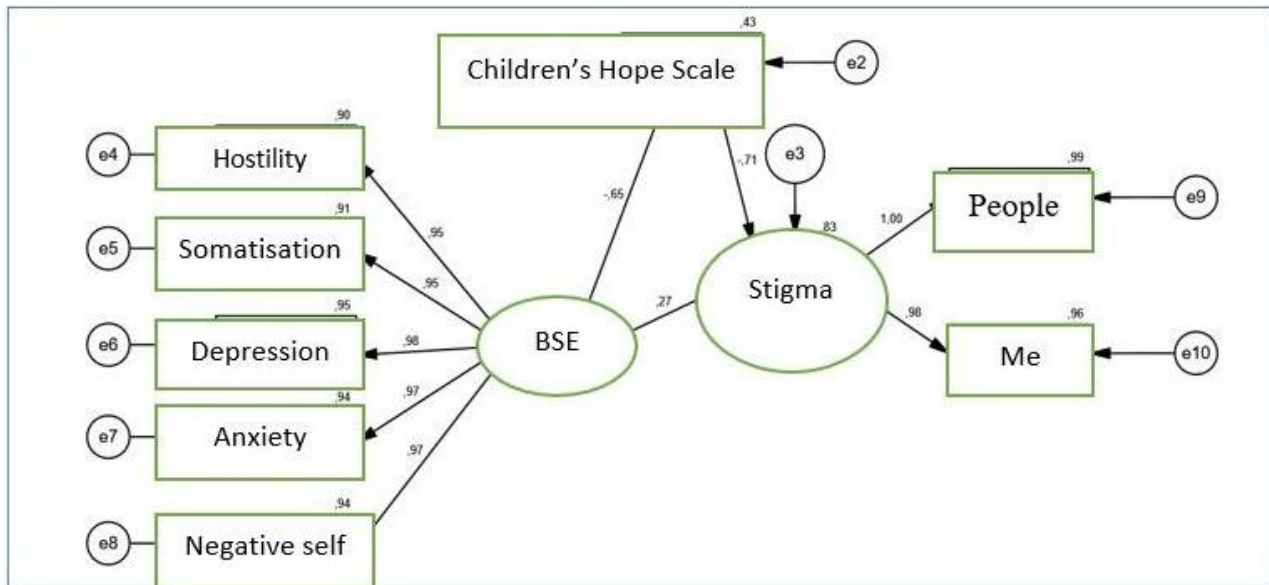from his/her family for an average of eight months and had average monthly earnings of $226 (Table 1).

Figure 1. Standardized path coefficients

Table 1. Mean and distribution of demographic characteristics of refugee adolescents

Mean of demographic characteristics	Mean ± SD	
Age	11.24 ± 2.67	
Number of siblings	8.65 ± 2.36	
Time separated from the family(Month)	0.80 ± 0.78	
Number of losses	0.50 ± 1.06	
Average monthly income of the family(Dollars)	226.10 ± 0.091	
Distribution of demographic characteristics	**n**	**%**
Gender		
Female	247	51
Male	237	49
The status of being separated from the family		
No	232	48
Yes	252	52
The status of having losses		
No	213	44
Yes	271	56

A one-unit increase in refugee adolescents' mental health problems causes a 1.011-unit decrease in their hope levels($p<0.001$) and a 0.840-unit increase in their internalised stigma($p<0.001$), A one-unit decrease in refugee adolescents hope levels leads to a 1.444-unit increase in their internalised stigma($p<0.001$). Health problems causes a one-unit increase in somatisation symptoms of refugee adolescents leads to 0.025-unit increase in mental health problems($p<0.001$). A one-unit increase in depression symptoms leads to 0.027-unit increase in mental health problems ($p<0.001$). A one-unit increase in anxiety symptoms leads to 0.031-unit increase

in mental health problems($p<0.001$). A one-unit increase in refugee adolescents' negative self-perception leads to a 0.027-unit increase in their mental health symptoms ($p<0.001$). A one-unit increase in the people sub-dimension of refugee adolescents leads to a 0.995-unit increase in their internalised stigmatisation ($p<0.001$) (Table 2).

In Table 3, the relationship between refugee adolescents' mental health states and internalised stigma and the mediating role of hope between their mental health states and internalised stigma states were examined. According to the results of the analysis, it was found that refugee adolescents mental health

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problems predicted their internalised stigma (β= 0.739; $p<0.001$) and explained 54.6% of their internalised stigma (R^2) (Table 3).

Table 2. Results of the PATH model for refugee adolescents. (n=484)

			β^1	β^2	S. error	Test statistics	*p*
Hope	<---	Mental problems	-0.654	-1.011	0.043	-23.682	**<0.001**
Stigma	<---	Hope	-0.714	-1.444	0.039	-36.886	**<0.001**
Stigma	<---	Mental problems	0.269	0.840	0.062	13.641	**<0.001**
Hostility	<---	Mental problems	0.947	1.000			
Somatization	<---	Mental problems	0.952	1.550	0.025	61.013	**<0.001**
Depression	<---	Mental problems	0.976	1.918	0.027	70.178	**<0.001**
Anxiety	<---	Mental problems	0.968	2.051	0.031	66.538	**<0.001**
Negative self	<---	Mental problems	0.971	1.836	0.027	67.944	**<0.001**
People	<---	Stigma	0.996	1.000			
Me	<---	Stigma	0.979	0.995	0.009	116.344	**<0.001**

β^1: Standardized coefficients, β^2: Unstandardized coefficients

Table 3. The mediating role of hope scale in the effect of mental problems on stigma

	Dependent variables			
Predictor variables	**Hope**		**Stigma**	
	β (95 CI%)*	SE	β (95% CI)*	SE
Mental problems (total effect)			0,739 (0,696; 0,774)	0,020
R^2			0,546	
Mental problems	-0,654 (-0,700; -0,599)[1]	0,026		
R^2	0,427			
Mental problems (indirect effect)			0,269 (0,231; 0,307)[1]	0,019
Hope			-0,714 (-0,747; -0,679)[1]	0,017
R^2			0,832	
Indirect effect			0,467 (0,428; 0,502)	

[1]<0,001; SE Standard Error; β: Standardized coefficients; R^2: Determination coefficient; *Bootstrap effect (95% CI)

In structural equation modelling was constructed in which refugee adolescents hope status was considered as a mediating variable. According to the results of the mediated structural model analysis, refugee adolescents mental health problems predicted their hope status (β=-0,654; $p<0.001$) and explained 42.7% of their hope status (R^2). It was concluded that the increase in adolescents' mental health problems caused a decrease in their hope status (Table 3).

In the mediator model for refugee adolescents, the effect of hope on the dependent variable internalised stigma was found significant (β=-0.714; $p<0.001$). It was observed that the path coefficient between mental health problems and internalised stigma became important when the mediating variable hope was included in the model (β=0.269; $p<0.001$). Mental problems and hope status of refugee adolescents together explain 83.2% of the change (R^2) in internalised stigma. Bootstrap analysis revealed that the indirect effect of refugee adolescents mental health problems on internalised stigma through their

hope status was statistically significant (β=0.467; 95% CI [0.428-0.502]) (Table 3).

Discussion

It has been reported that many families and their adolescents have been forced to leave their homes due to the wars and conflicts that have emerged in recent years and are still continuing to do so. Although long years have passed since the forced migration and war, adolescents have continued to experience the effects.

In this study, it was found that hope levels of refugee adolescents were a mediating factor in the relationship between their mental health problems and internalised stigma. It was also found that internalised stigma and mental health problems of adolescents are related to each other and positive expectation for the future is an important trigger in this relationship.

Refugee adolescents and adolescents have to cope with numerous challenges of conflict, displacement, exposure to uncertain life situations and resettlement at the most

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important stages of their physical, emotional, social and cognitive development.[10,23] These situations put refugee children and adolescents at high risk for mental health problems.[24,25] As a result of analysis examining the relationship between refugee adolescents mental problems and stigma, it was found that refugee adolescents mental health problems predicted their internalised stigma. Similarly, internalised stigma levels were found to be high among individuals with mental problems in literature [26,27] and it was stated that stigma is associated with psychological phenomena. A meta-analysis and two systematic reviews conducted in this field, which included 127 studies, showed that approximately one quarter of people with mental illness experience internalised stigma.[27,28] Similarly, it has been stated in studies that an increase in the severity of mental health symptoms, including positive, negative and depressive symptoms, is associated with high levels of internalised stigma.[29–31] It can be seen that internalised stigma has been reported to be associated with low self-esteem, low quality of life and low recovery rate, which are the risks faced by refugee children and adolescents.[32,33] It is thought that the ongoing exclusion of refugee adolescents by the society they live in even though many years have passed since the war they have been through causes them to experience mental problems such as anxiety, depression, hostility, negative self-perception and somatisation. It can be seen that the feelings of stigmatisation that adolescents experience by people and themselves are also an effective trigger for mental health problems.

Another important finding of this study is that refugee adolescents' mental health problems predicted their hope status. Factors such as depression, anxiety, somatisation, negative self and hostility experienced after the war were found to be important triggers of adolescents hope status (Table-3). Similarly negative relationship was reported between hope and psychological symptoms.[15,34] Studies examining the relationship between hope and psychological functioning have shown that hope fosters meaning and purpose in life[35], while hopelessness is the main component of depression.[36] It has also been reported to be a determinant for hopelessness, dysfunctional coping, general maladjustment and suicidal ideation.[37] In another study, it was stated that high hope level is a protective factor that increases resilience in terms of psychological symptoms, and being hopeful as a psychological resource or hopelessness when this resource is exhausted is effective on the psychological functioning of individuals.[38,39]

Hope is defined as an important emotion for adolescents in coping, overcoming negativities, and continuing to live under uncertain and stressful life experiences.[40,41] A review of the literature has also found that a sense of hope among adolescents exposed to violence and armed conflict has an important protective and developmental effect on mental health.[42,43] Adolescents who report higher levels of hope have been found to have increased internalising behavioural problems and decreased life satisfaction when faced with negative life events[44] and that the feeling of hope can contribute to the well-being of children in all these negativities.[45,46] Therefore, it can be said that hope is a resilience factor for children and adolescents in the face of psychological problems. While adults may never be able to protect children and teenagers from all the negative events in their lives, these results highlight the importance of providing parents and health professionals with programmes that promote cognitive and motivational skills, like hopeful thinking, to help them cope better with stress.

In this study, the indirect effect of mental problems of refugee adolescents on internalised stigma through hope states was found to be statistically significant (Table 3). When the literature was examined, no studies were found addressing the mediating role of hope status in refugee adolescents with the same or different dimensions. However, research examining the impact of internalised stigma on people with mental illness shows that the experience of internalised stigma leads to a decline in self-concept, hope, self-esteem, social interactions, academic and vocational success, life chances and quality of life.[47] In a qualitative study conducted by Goodman, it was found that one of the factors that sustained Sudanese refugee children living in the United

States without their families after traumatic experiences and difficult processes related to the war was hope.[48] It was also found that the mean hope scale scores of people with high internalised stigma were lower than the mean scores of individuals with low internalised stigma. Also results similar research findings were found between internalised stigma and hope.[49] In a research study of patients with mental health problems, resistance to stigma was found to be associated with higher self-esteem, better quality of life and less depression, which is thought to be associated with hope.[49,50] It can be seen that the increase in the level of hope for the future in adolescents who have experienced war is an important factor in reducing the internalised stigma and mental health problems created in children by the society. In social studies, it is thought that the sense of hope will play a protective role against internalisation and externalisation problems in risky groups such as refugee adolescents. This shows the importance of the feeling of hope especially in adolescents who are victims of war and who have been exposed to numerous traumatic experiences.

Limitations

This study has several limitations. First, the study was cross-sectional and single centered. Second, the findings of the study were obtained from the scales. Third there is no control group in the study to help clarify the role of refugee adolescents' hopes for the future in general between stigmatization and mental symptoms.

Conclusion

As a conclusion, refugee adolescents were found to be at high risk for negative mental health outcomes. In line with the data of this study, four important results were obtained. It was determined that there is a strong relationship between adolescents' mental problems (anxiety, depression, negative self, somatisation and hostility) and stigma and that these affect each other. Also, refugee adolescents' mental problems were effective on stigma through their future hope levels. The most important result is that hope has a mediating role between adolescents' mental health problems and internalised stigma.

Interventions that reduce self-stigmatisation and promote empowerment by the health team working with risky groups can be an important point of focus in ensuring mental well-being.[10] From this point of view, it can be concluded that both intervention programs to change the stigma of the society and intervention plans that address stigma as a part of treatment are needed.

In particular, research on individual and contextual factors that can protect adolescents from negative outcomes and promote psychosocial well-being is of critical importance. Identifying protective and promotive factors in these studies can provide information for interventions that aim to promote positive aspects of mental health and prevent mental health problems.

On the other hand, although hope is included in the literature as a protector and provider of resilience in adolescents exposed to traumatic experiences related to war and migration, it can be seen that many dimensions of hope have not been studied with this group of children and adolescents to the best of our knowledge. In particular, it is essential to protect and develop psychological resilience in refugee adolescents as a growing and uncertain population. On the other hand, in the face of this ongoing uncertainty, especially for Syrian refugee adolescents, it is important and necessary to identify the characteristics, conditions and factors that protect and enhance resilience and to develop protective and preventive interventions.

Ethics Committee Approval

Ethics committee approval number (2023/06-23) of this research was obtained from Harran University. The research was conducted according to the Declaration of Helsinki principles.

Informed Consent

Informed Consent and Parental Consent Forms were obtained from the refugee adolescents participating in the study.

Author Contributions

All authors involved in the study contributed to the article.

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