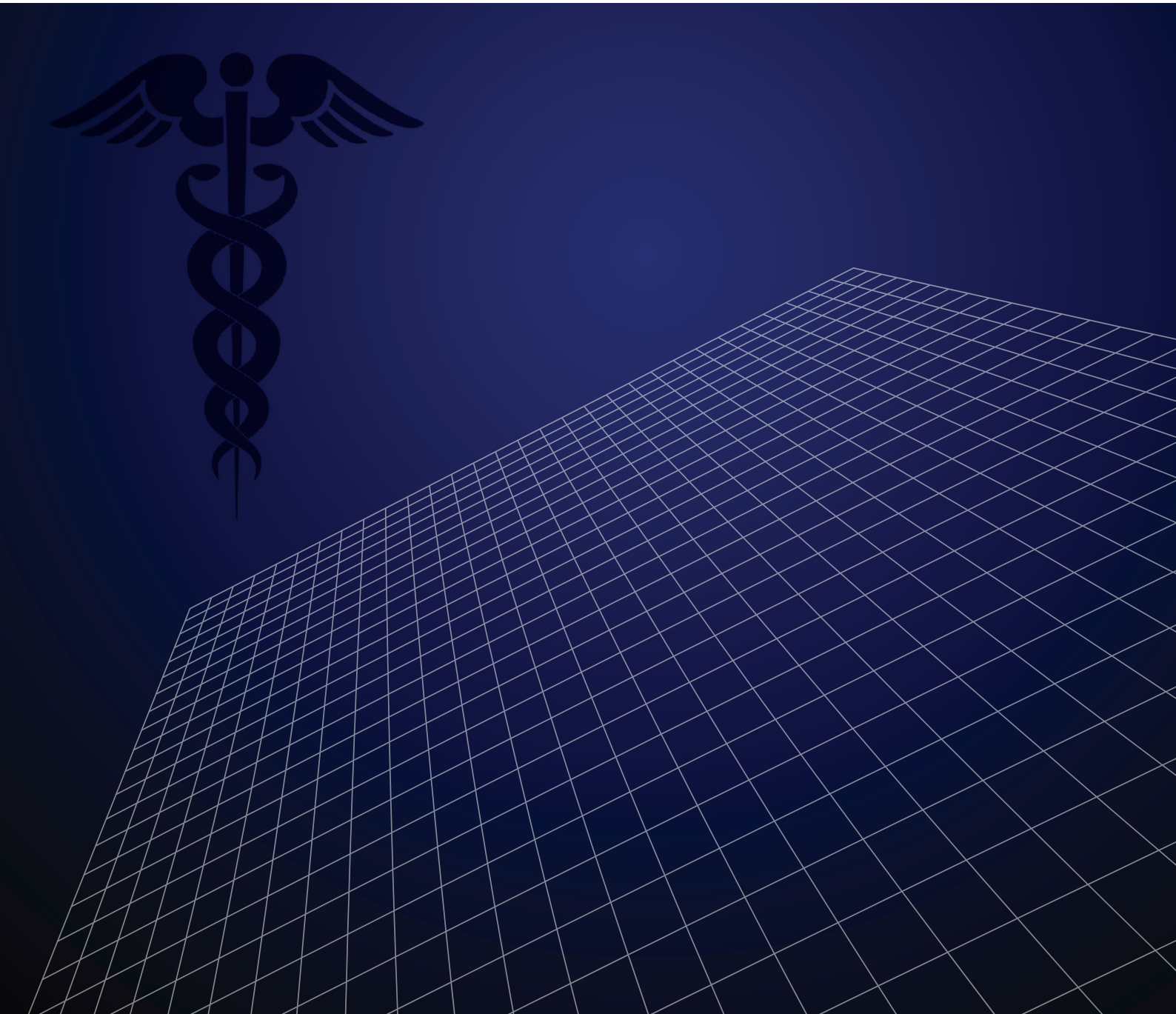
e-ISSN:2149-8296

Turkish Journal of Clinics and Laboratory

Türk Klinik ve Laboratuvar Dergisi

Aralık 2023, Cilt:14 Sayı:4



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To cite this article: Aydin n, Tufek M, Capraz M, Nalcacioglu. Are the optic nerve head parameters and retinal nerve fiber layer thickness affected in patients who had a mild Covid- 19 infection?. Turk J Clin Lab 2023; 4: 658-664

Research Article

Are the optic nerve head parameters and retinal nerve fiber layer thickness affected in patients who had a mild Covid- 19 infection?

Hafif Covid-19 enfeksiyonu geçiren hastalarda optik sinir başı parametreleri ve retina sinir lifi tabakası kalınlığı etkilenir mi?

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ABSTRACT

Aim: The aim of this study was to evaluate the peripapillary retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) parameters by using a spectral domain optical coherence tomography (SD-OCT) device in patients who had a history of a mild-COVID-19 infection.

Material and Methods: This prospective cross-sectional study included 70 patients who had a history of a mild COVID-19 infection and 65 healthy individuals. After detailed ophthalmological examination, the peripapillary RNFL thickness and ONH parameters were measured with the SD-OCT device in all patients.

Results: No significant difference was present between the groups in terms of age and gender (p=0.907, p=0.979, respectively). The mean, superior, inferior, nasal, and temporal peripapillary RNFL thicknesses were not statistically significantly different between the groups (p=0.797, p=0.488, p=0.079, p=0.820, p=0.820, respectively). Regarding the ONH parameters, no significant difference was found between the groups in terms of disc area, cup area, rim area, cup/disc ratio, horizontal and vertical cup/disc ratio and cup and rim volume (p=0.239, p=0.995, p=0.522, p=0.959, p=0.716, p= 0.873, p=0.476, p=0.701, respectively).

Coclusion: No significant difference was found between the patients who had a mild COVID-19 infection and the control group in terms of the peripapillary RNFL thickness and ONH parameters. However, the results may vary according to the severity of the infection and the acute and long-term data.

Key words: COVID-19, peripapillary retinal nerve fiber layer thickness, optic nerve head parameters, optic coherence tomography,

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Doi: 10.18663/tjcl.1268946
Recevied: 21.03.2023 accepted: 09.11.2023

TJCL Volume 14 Number 4 p: 658-664

ÖZ

Amaç: Bu çalışmanın amacı hafif COVID-19 enfeksiyonu geçiren hastalarda peripapiller retina sinir lifi tabakası (RSLT) kalınlığı ve optik sinir başı (OSB) parametrelerini, spektral domain optik koherens tomografi (SD-OKT) cihazı kullanarak değerlendirmektir.

Gereç ve Yöntemler: Bu prospektif cross-sectional çalışmaya hafif COVID -19 enfeksiyonu geçirmiş 70 hasta ile 65 sağlıklı birey dahil edildi. Ayrıntılı oftalmolojik muayene sonrası tüm hastalara SD-OKT cihazı ile peripapiller RSLT kalınlığı ve OSB parametrelerinin ölçümleri yapıldı.

Bulgular: Gruplar arasında yaş ve cinsiyet açısından anlamlı farklılık yoktu (p=0.907, p=0.979, sırasıyla). Ortalama, superior, inferior, nazal ve temporal peripapiller RSLT kalınlığı, gruplar arasında istatistiksel açıdan anlamlı değildi (p=0.797, p=0.488, p=0.079, p=0.820, p=0.820, sırasıyla). OSB parametrelerine bakıldığında disc alanı, cup alanı, rim alanı, cup/disc oranı, horizontal ve vertical cup/disc oranı, cup ve rim volume açısından gruplar arasında anlamlı farklılık tespit edilmedi (p=0.239, p= 0.995, p=0.522, p=0.959, p=0.716, p= 0.873, p=0.476, p=0.701, sırasıyla).

Sonuçlar: Hafif COVID-19 enfeksiyonu geçiren hastalarla kontrol grubu arasında peripapiller RSLT kalınlığı ve OSB parametreleri açısından anlamlı farklılık tespit edilmedi. Ancak bulduğumuz bu sonuçlar enfeksiyonun şiddeti ile enfeksiyonun akut ve uzun dönem verilerine göre değişkenlik gösterebilir.

Anahtar Kelimeler: COVID-19, peripapiller retina sinir lifi tabakası kalınlığı, optik sinir başı parametreleri, optik koherens tomografi

Introduction

Coronavirus disease 2019 (COVID-19) infection, caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus, which emerged in the city Wuhan in China and spread globally was later declared a pandemic by the World Health Organization (WHO). The SARS-CoV-2 virus is an enveloped, single-stranded RNA virus [1, 2]. Although COVID-19 infection mostly progresses with respiratory system findings such as fever, cough, and dyspnea, many neurological and ophthalmological symptoms are also encountered [3, 4]. The angiotensin-converting enzyme (ACE)-2 receptor is the main entry receptor of SARS-CoV-2 into the body, and neurons and glial cells are targeted by the virus because they express ACE-2 [5]. ACE-2 receptor activation has also been detected in the aqueous humor, retina, ciliary body, vitreous, and inner nuclear layer, and the photoreceptors, and Müllerian and ganglion cells [6]. Conjunctivitis, keratoconjunctivitis, episcleritis, uveitis, retinitis, retinal vascular occlusion as well as optic neuritis, viral encephalitis, cerebrovascular disease, acute transverse myelitis, leukoencephalopathy, toxic encephalopathy, acute disseminated encephalomyelitis have been reported in COVID-19 patients [4, 7]. Another target tissue of the SARS-CoV-2 virus is the vascular endothelium. The endothelium is responsible for immunological response regulation, the inflammatory balance, hemodynamic stability, and hemostasis through thrombotic and fibrinolytic pathways in healthy individuals [8]. Ischemic lesions such as cotton wool spots and microhemorrhages have been observed in the retina after thrombosis and inflammation caused by direct invasion of the endothelial cells [9, 10]. Besides, hyperreflective lesions have been detected in the inner plexiform layer (IPL) and ganglion cell layer (GCL), more prominently in the papillomacular bundle, during imaging performed with spectral domain optical coherence tomography (SD-OCT) [10].

The retinal nerve fiber layer (RNFL) consists of neuronal axon bundles. Structural changes due to loss of ganglion cell axons occur in the RNFL in ocular diseases such as glaucoma and in conditions such as aging. The SD-OCT device is a non-invasive method used to measure RNFL thickness and evaluate the structural features of the optic nerve [11]. Our aim in this study was to detect the changes in the optic nerve head (ONH) parameters and peripapillary RNFL thickness in patients with a history of a mild COVID-19 infection with the SD-OCT device and compare them with a healthy control group since SARS-Cov-2 has been reported to be a neurotropic virus [5] with retinal and optic nerve involvement in previous studies [10, 12]. Material and Methods This prospective cross-sectional study was conducted at the Sabuncuoğlu Şerefeddin Training and Research Hospital between March 2022 and September 2022. The study was approved by the Ethics Committee of Amasya University. All research procedures were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects.

The 70 eyes of 70 patients who had a history of a mild COVID-19

infection and the 65 eyes of 65 age- and gender-matched healthy individuals were included in the study. The patients were divided into 2 groups. Group 1 consisted of patients who had received a diagnosis of COVID-19 infection at the Sabuncuoğlu Şerefeddin Training and Research Hospital's Infectious Disease Outpatient Department and had then been referred to the Ophthalmology Outpatients Department after their treatment was completed, while Group 2 included healthy individuals with a negative rRT-PCR test and without any symptoms. Mild COVID-19 infection was defined as symptoms such as fever, cough, sore throat, malaise, muscle pain, headache, and the loss of taste and smell; no dyspnea or lung involvement findings on imaging; no need for hospitalization; a blood oxygen saturation value in room air (SpO2) of >93%; and no need for oxygen support or systemic steroid treatment. A detailed history of ocular and systemic disease was obtained from all patients.The diagnosis of COVID-19 infection was made by detecting the viral genome in a nasopharyngeal swab sample with the rRT-PCR test. Ophthalmological examination and SD-OCT were performed within 2 weeks to 3 months after rRT-PCR test positivity. All patients had negative PCR tests and were asymptomatic during the ophthalmologic examination. The demographic characteristics of all participants and the clinical course of their disease were recorded.

Exclusion criteria were a history of COVID-19 infection with hospitalization or systemic steroid therapy; diabetes, systemic hypertension, or neurodegenerative disease; previous intraocular surgery; a history of ocular trauma, glaucoma, optic neuritis, congenital optic disc anomaly, or retinal and choroidal disease; age < 18 years; pregnancy; a refractive error > ± 2 diopters (D); corneal or lens opacities that prevented SD-OCT imaging; and a history of smoking.

All participants underwent a detailed ophthalmologic examination including best-corrected visual acuity (BCVA) with the Snellen chart, anterior segment and dilated fundus examination with the slit-lamp, central corneal thickness (CCT) measurement with the Nidek UP-1000 (Nidek Co., Ltd., Aichi, Japan), and intraocular pressure (IOP) measurement with the Goldmann applanation tonometer. The right eye of all participants was included in the study. The SD-OCT device (3D OCT-2000, Topcon, Japan) was used for the measurement of peripapillary RNFL thickness and ONH parameters. OCT scans were performed by an experienced technician after pupil dilation and images were evaluated at different time intervals by two experienced physicians (NA, MT), with the groups masked. Sections with a signal strength index < 6/10 were excluded. Optic disc scanning was performed within a 6X6 mm2 area during the analysis of ONH parameters. Thanks to the software, the end of the retinal pigment epithelium, choriocapillaris and photoreceptors was considered the beginning of the ONH with the disc borders being determined automatically. Peripapillary RNFL thickness was measured with an automatic computer algorithm after the user placed a 3.4 mm diameter circle around the disc at an equal distance to all quadrants, and the average of three consecutive circular scans was taken (Figure 1). ONH parameters including the mean, superior, inferior, nasal and temporal peripapillary RNFL thicknesses in addition to the disc area, rim area, cup area, cup/disc ratio, vertical and horizontal cup/disc ratio, and cup and rim volume values of all patients were recorded.

Statistical analysis

Statistical analysis was performed using the SPSS software for Windows, version 22 (SPSS Inc., Chicago, IL, USA). The continuous variables were reported as mean±standard deviation while the categorical variables were summarized with the use of frequencies. The normality of all data samples was checked with the Kolmogorov–Smirnov test. Only the right eye values were used for statistical purposes. The chi-square test was used in the analysis of categorical variables. The independent t-test for paired data was used to compare the parameters between the two groups when the normality criteria were met. The Mann-Whitney U test was performed if the data distribution was not normal. A p value <0.05 was accepted as statistically significant.

Results

The 135 eyes of 135 patients were included in this study. Group 1 consisted of 70 patients (40 females, 30 males) and Group 2 of 65 patients (37 females, 28 males). The mean age was 45.4±12.6 years in Group 1 and 45.2±9.8 years in Group 2. No significant difference was present between the groups in terms of age or gender (p=0.907, p=0.979, respectively). Besides, no significant difference was observed in terms of IOP, BCVA, refractive error, and CCT (p=0.814, p=0.335, p=0.865, p=0.750, respectively). The demographic and clinical characteristics of the patients are summarized in Table-1.

Comparison of the groups in terms of peripapillary RNFL thickness revealed that the mean, superior, inferior, nasal, and temporal RNFL thickness values were lower in Group 1 than Group 2 but without statistical significance (p=0.797, p=0.488, p=0.079, p=0.820, p=0,820, respectively). Besides, no

significant difference was found between the groups in terms of ONH parameters including disc area, cup area, rim area, cup/disc ratio, horizontal and vertical cup/disc ratio, and cup and rim volume (p=0.239, p=0.995, p=0.522, p=0.959, p=0.716, p= 0.873, p=0.476, p=0.701, respectively). Data regarding peripapillary RNFL thickness and ONH parameters have been summarized in Table-2 and Table-3.

Table 1. The demographic and clinical characteristics of the subjects

Parameters mean±SD	COVID-19 group (n=70)	Control group (n=65)	p value
Age, years	45.4±12.6		
Sex (%) Female	40 (57.1%)		
Male	30 (42.9%)	45.2±9.8	0.907*
IOP (mmHg)	15.1±2.8	37 (56.9%)	0.979**
Refractive Error (D)	-0.08±0.7	28 (43.1%)	
CCT (µm)	532.1±25.4	-0.08±0.6	0.814***
Visual acuity	1.0 (1.0)	533.5±24.8	0.750*
Duration after COVID 19 (days)	43.9±20.7	1.0 (1.0)	0.335***

IOP: Intraocular pressure, D: Diopter, CCT: Central corneal thickness, *:Independent t-test, **: Chi square test, ***: Mann-Whitney U test

Table 2. Comparison of the peripapillary retinal nerve fiber layer thickness between the groups

Parameters mean±SD	COVID-19 group (n=70)	Control group (n=65)	p value
Mean RNFL (µm)	111.5±10	112.6±11.5	0.797*
Superior RNFL (µm)	135.3±17.2	137.3±15.8	0.488**
Inferior RNFL (µm)	135.7±16.2	140.6±16.3	0.079**
Nasal RNFL (µm)	86.7±15.4	87.2±12.9	0.820**
Temporal RNFL (µm)	80±12.9	80.5±11.5	0.820**

RNFL: retinal nerve fiber layer, *: Mann-Whitney U test, **: Independent t-test

Table 3. Comparison of the optic nerve head parameters between the groups

Parameters mean±SD	COVID-19 group (n=70)	Control group (n=65)	p value
Disc area	2.6±0.5	2.6±0.3	0.239*
Cup area	0.7±0.4	1.9±0.3	0.995**
Rim area	1.9±0.4	0.3±0.1	0.522*
C/D ratio	0.3±0.1	0.5±0.1	0.959**
Horizontal C/D ratio	0.5±0.1	0.5±0.1	0.716*
Vertical C/D ratio	0.5±0.1	0.5±0.1	0.873**
Cup volume	0.15±0.1	0.14±0.1	0.476*
Rim volume	0.6±0.2	0.6±0.2	0.701**

C/D: cup/disc ratio, *: Mann-Whitney U test , **: Independent t-test

Discussion

The SARS-CoV-2 virus is a neurotropic virus and has been observed to involve the optic nerve in humans and animal models [5, 12, 13]. Our aim in this study was to investigate whether SARS-Cov-2 affects the peripapillary RNFL thickness and ONH parameters in patients with mild-COVID-19 infection by using the SD-OCT device, which allows non-invasive evaluation of the optic nerve. Mean peripapillary RNFL and sectoral thickness values were lower in the group with a history of SARS-CoV-2 infection in our study, but this difference was not statistically significant. No significant difference was observed between the groups in terms of ONH parameters either.

The SARS-CoV-2 virus often causes respiratory system findings, and at least one neurological symptom has been reported in more than 90% of the patients. These neurological symptoms may begin before the typical respiratory symptoms or may be the only symptom of SARS-CoV-2 infection in asymptomatic carriers [3]. While the most common of these COVID-19 infection symptoms are headache, confusion, and dizziness, serious life-threatening diseases such as stroke, encephalitis, Miller Fisher Syndrome, Guillain-Barr'e syndrome, acute myelitis, and sinus vein thrombosis can also be encountered [3, 12]. The spread of the virus to the central nervous system (CNS) occurs either through the blood circulation or directly through the nerve endings, and detection of the RNA of SARS-CoV-2 in the cerebrospinal fluid of symptomatic patients indicates the invasion of the virus into the CNS [14, 15]. The SARS-CoV-2 virus has also been shown to cause ocular involvement [4, 10]. As in the CNS, the RNA of the SARS-CoV-2 virus has been found in the retina of patients who have died because of COVID-19 [6].

COVID-19 infection-related optic neuritis cases have also been reported [12, 16]. Direct invasion of the SARS-CoV-2 virus into the optic nerve is mediated by the ACE-2 receptor. This receptor is a highly expressed cell surface receptor in the heart, kidney, and lung, where SARS-CoV-2 enters the host cell; it is also found in retinal vascular endothelial cells, Müller cells, ganglion cells, photoreceptors, and the choroid and ciliary body [6, 17]. Fundus examination of patients with COVID-19 infection has revealed peripapillary flame-shaped hemorrhages and cotton wool spots, peripheral retinal hemorrhages, hard exudates, and retinal sectoral pallor, while OCT imaging has shown hyperreflective lesions in the GCL and IPL [10, 18].

The RNFL consists of the unmyelinated retinal ganglion cell axons that form the optic nerve. The radial peripapillary

capillary (RPC) plexus is parallel to the axons of the RNFL and is responsible for supplying the ganglion cell axons. A positive correlation has been reported between RPC plexus density and RNFL thickness in the human retina [19, 20]. Uğurlu et al. have reported significantly lower RPC plexus values in symptomatic COVID-19 patients than in asymptomatic patients and the control group, and significantly lower thickness values of the RNFL and ganglion cell complex (GCC) layers in the COVID-19 patient group with neurological symptoms compared to the control group [21]. Cennamo et al. have found lower RPC and RNFL values in the group with patients who had COVID-19 infection than the control group [22]. These studies indicate that one of the mechanisms of how COVID-19 infection affects the optic nerve is through the vascular structures since the binding of SARS-CoV-2 to endothelial cells triggers systemic inflammation, thrombosis, and microvascular dysfunction [9]. The microangiopathic changes that develop as a result affect the RNFL thickness and the optic nerve.

SARS-CoV-2 infection causes various degrees of inflammatory response and alveolar damage, and leads to hypoxemia that predisposes to multiple organ and especially CNS dysfunction [23]. The neural retina has high metabolic needs and is highly susceptible to hypoxia. Neuronal nitric oxide synthase (nNOS) and inducible nitric oxide synthase (iNOS) are expressed in CNS neuronal injuries, and excessive NO production via nNOS and iNOS in the retina during hypoxia has been shown to cause neuronal damage in rats [24]. CNS injuries also cause changes in the microglial cells, which are immunocompetent cells located in the retina that are known to be activated in response to hypoxia [24]. An increase in the number of microglia mediated by interferon γ (INF-γ) also occurs in the outer retinal layers and subretinal space in systemic viral infections and triggers neurodegenerative diseases [25]. All these indicate that changes in RNFL thickness and ONH parameters may occur secondary to the hypoxemia and immunological response caused by COVID-19 infection.

There are various studies on the effect of COVID-19 infection on RNFL and ONH parameters. Various other studies have found no significant difference between the group of patients with a history of COVID-19 infection and healthy individuals in terms of mean peripapillary RNFL, similar to our results [26, 27]. Ozmen et al. have found no significant difference between the groups in terms of RNFL and ganglion cell- inner plexiform layer (GC-IPL) thickness in all quadrants in their study on patients with a history of severe COVID-19 infection [28]. However, Burgos-Blasco et al. have reported an increase in the thickness of the peripapillary RNFL and macular GCL in patients with neurological symptoms such as anosmia and ageusia compared to asymptomatic patients and the control group in their study on early stage COVID-19 patients [29]. Another study found the peripapillary RNFL thickness to be thicker in all quadrants after COVID-19 infection compared to the control group; however, this change was not statistically significant and no such difference was reported between the groups in terms of ONH parameters either [30]. We believe that these differences in the results may be related to the severity of the COVID-19 infection, the presence of neurological symptoms, and the stage of the infection. Besides, the difference in the time elapsed between the diagnosis of COVID-19 infection and the ophthalmological examination and thus the corresponding difference in the level of inflammatory cytokines may also explain the different results.

Our study had various limitations. The first of these was that it was conducted with a small sample group. Another limitation was the lack of acute and chronic COVID-19 infection data of our patients, and that we could not compare them with these data. Besides, only patients with mild-COVID-19 infection were included in our study, and moderate and severe COVID-19 patients who required hospitalization or needed intensive care were excluded. Therefore, we cannot generalize our results to all patients with COVID-19 infection.

Conclusion

Although peripapillary RNFL thickness was lower in the group with patients who had a history of COVID-19 infection in our study, this difference was not statistically significant. There was no significant difference between the groups in terms of ONH parameters either. The fact that our patient group had a history of mild-COVID-19 infection and that we evaluated the post-infection quarterly data may have influenced our results. Therefore, it is necessary to support these results with future studies on larger sample groups and subjects in the acute and late stages of infections of various severity levels.

Funding

No funding was obtained in this study

Disclosure statement

The authors declare that they have no conflict of interest

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Turkish Journal of Clinics and Laboratory

To cite this article: Kayikcioglu E. Colon cancer awareness among male relatives of cancer patients. Turk J Clin Lab 2023; 4: 665-670

Research Article

Colon cancer awareness among male relatives of cancer patients

Kanser hastalarının erkek yakınları arasında kolon kanseri farkındalığı

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Abstract

Aim: Colorectal cancer (CRC) is a major global health concern, and awareness of risk factors, symptoms, and screening methods is crucial for early detection and prevention. This study aimed to assess the level of CRC awareness among male relatives of cancer patients attending a medical oncology outpatient clinic.

Material and Methods: A survey was conducted among 192 male relatives of cancer patients collecting demographic information and assessing their knowledge of CRC risk factors, symptoms, and screening methods. Statistical analyses were performed using IBM SPSS version 26.

Results: The study included 192 male relatives of patients with colon cancer. The mean age of the participants was 43.8±13.2 years (18-78). Of the participants, 149 (77.6%) were married, 41 (21.4%) were single. The study revealed significant knowledge gaps among participants. While most were aware that age is a risk factor for CRC, there was limited awareness of other important risk factors, such as family history, obesity, smoking, and unhealthy diet. Similarly, participants demonstrated awareness of some CRC symptoms, such as occult blood in the stool and abdominal pain, but lacked knowledge of other symptoms like black stools, anemia, and nausea/vomiting. There was a statistically significant difference between education and awareness of overweight, alcohol consumption, red meat consumption, black stools and anemia among cancer symptoms ($p<0.05$). No statistically significant difference was found between unhealthy diet and seeing blood in stool among risk factors ($p>0.05$). Moderate levels of awareness regarding CRC screening were observed, but there was insufficient knowledge about recommended screening methods and the appropriate age for screening.

Conclusion: The findings emphasize the need for targeted educational interventions to improve CRC awareness among male relatives. Efforts should focus on addressing the knowledge gaps related to risk factors, symptoms, and screening methods. Educational initiatives should employ community-based programs, mass media campaigns, and healthcare provider involvement to promote understanding and encourage proactive engagement in CRC screening.

Keywords: Colorectal cancer, Awareness, Risk factors, Screening methods

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Recevied: 07.06.2023 accepted: 20.10.2023
*This original article is presented at 'INTERNATIONAL GEVHER NESIBE HEALTH SCIENCES CONFERENCE-X' between February 3-5, 2023 / Ankara, Türkiye.

Öz

Amaç: Kolorektal kanser (KRK), önemli bir küresel sağlık sorunudur ve risk faktörleri, belirtiler ve tarama yöntemleri hakkında farkındalık, erken teşhis ve önleme için önemlidir. Bu çalışmanın amacı, bir tıbbi onkoloji polikliniğine gelen kanser hastalarının erkek yakınlarının KRK farkındalık düzeyini değerlendirmektir.

Gereç ve Yöntemler: Çalışmada kolon kanseri hastası yakını 192 erkek üzerinde bir anket yapıldı ve katılımcıların demografik bilgileri toplandı, KRK risk faktörleri, belirtiler ve tarama yöntemleri hakkındaki bilgileri değerlendirildi. İstatistiksel analizler IBM SPSS 26 versiyonu kullanılarak gerçekleştirildi.

Bulgular: Çalışmaya 192 kolon kanseri hastası yakını erkek dahil edildi. Katılımcıların yaş ortalaması 43.8±13.2 yıl (18-78) idi. Katılımcıların 149'u (%77.6) evliydi, 41'i (%21.4) bekar. Çalışma, katılımcılar arasında önemli bilgi eksikliklerini ortaya koydu. Katılımcıların çoğu yaşın KRK için bir risk faktörü olduğunu bilmekle birlikte, aile öyküsü, obezite, sigara içme ve sağlıksız beslenme gibi diğer önemli risk faktörleri konusunda sınırlı farkındalığa sahipti. Benzer şekilde, katılımcılar dışkıda gizli kan ve karın ağrısı gibi bazı KRK belirtilerinin farkındaydı, ancak siyah dışkı, anemi ve bulantı/kusma gibi diğer belirtiler hakkında bilgi eksikliği vardı. Eğitim seviyesi ile kilo fazlalığı, alkol tüketimi, kırmızı et tüketimi, siyah dışkı ve kanser belirtileri arasındaki fark istatistiksel olarak anlamlıydı ($p<0.05$). Risk faktörleri arasında sağlıksız beslenme ile dışkıda kan görme arasında ise istatistiksel olarak anlamlı bir fark bulunamadı ($p>0.05$). KRK taraması ile ilgili orta düzeyde bir farkındalık gözlendi, ancak önerilen tarama yöntemleri ve uygun yaş konusunda yetersiz bilgi mevcuttu.

Sonuç: Bulgular, kolon kanseri hastalarının erkek yakınları arasında KRK farkındalığını artırmak için hedefe yönelik eğitim müdahalelerinin gerekliliğini vurgulamaktadır. Çalışmalar risk faktörleri, belirtiler ve tarama yöntemleri ile ilgili bilgi eksikliklerini ele almalıdır. Eğitim girişimleri, toplum tabanlı programlar, kitle iletişim araçları kampanyaları ve sağlık hizmeti sağlayıcılarının katılımını içermelidir. Bu şekilde, KRK anlayışının artırılması ve KRK taramalarına aktif katılımın teşvik edilmesi sağlanabilir.

Anahtar kelimeler: Kolorektal kanser, Farkındalık, Risk faktörleri, Tarama yöntemleri

Introduction

Colorectal cancer (CRC) is the 3rd most common cancer in the world and the 3rd most common cause of cancer-related death. According to 2020 data, 21.191 new cases were seen in Turkey and 10,798 people died due to CRC (1). American College of Gastroenterology (ACG) 2021 guidelines recommend CRC screening in average-risk individuals of age 50 to 75 years, and suggest screening in average-risk individuals of age 45 to 49 years (2). The ACG recommends colonoscopy and fecal immunochemical test (FIT) as the primary modalities for CRC screening (3, 4). In Turkey routine screening program is not applied except for fecal occult blood evaluation. In a study investigating CRC awareness among first-degree relatives of patients diagnosed with CRC in Iran, 35% of the participants had never heard of colonoscopy; only 22% of respondents correctly stated the age of screening (5). In a study on CRC awareness in Poland, 55.3% of participants had never even heard of CRC (6). In a study investigating CRC knowledge and awareness in Kuwait, 75% of participants had heard of CRC. When asked about the symptoms of CRC, the most common answers were weight loss, abdominal pain and change in bowel habits (7).

The incidence of CRC in men is 56.6%, higher than in women (1). The aim of this study was to determine the awareness of male relatives of patients applying to medical oncology outpatient clinic about CRC risk factors, symptoms and screening methods and their approaches to screening methods.

Material and Methods

Male relatives of patients who applied to Süleyman Demirel University medical oncology outpatient clinic were asked to answer survey questions that would determine their demographic characteristics and evaluate their knowledge about CRC risk factors, symptoms and screening methods. Informed consent was obtained before participating in the survey.

Statistical analysis

The data were transferred to IBM SPSS.26 (IBM Inc, Chicago, IL, USA) and analyzed statistically. Before statistical analyses, it was checked whether the parameters were within the expected range to avoid data entry errors. Mean and standard deviation were used for descriptive statistics of continuous variables and number of people (n) and percentage (%) were used for categorical variables.

Results

The study included 192 relatives of patients with colon cancer. The mean age of the participants was 43.8±13.2 years (18-78). Of the participants, 149 (77.6%) were married, 41 (21.4%) were single. Demographic data of the participants are summarized in Table 1.

Table 1. Demographic characteristics

	n	%
Marital Status		
Single	41	21.4
Married	149	77.6
Other	2	1.0
Education		
Primary School	72	37.5
High School	62	32.3
University	58	30.2
Relatedness		
1.degree	144	75
2. degree	48	25
Child		
Yes	145	75.5
No	47	24.5
Chronic disease		
Yes	56	29.2
No	136	70.8
Smoking		
Yes	86	44.8
No	106	55.2
Relatedness		
Spouse	32	16.7
Child	119	62
Parent	25	13
Other	16	8.3

When the participants were asked about CRC risk factors, the majority of them stated that it was true that the risk of CRC increases with age. The majority of the participants stated that they had no idea that having a family history of cancer, being overweight, excessive and processed red meat consumption increased the risk of CRC and that smoking, alcohol consumption and unhealthy diet increased the risk of CRC. The answers about CRC risk factors are summarized in Table 2.

When asked about the symptoms of CRC, participants said that occult blood in the stool, change in frequency of defecation and abdominal pain were symptoms of CRC. They stated that they had no idea that black stools, anemia and nausea and vomiting would be symptoms of CRC. Participants' answers to questions about CRC symptoms are summarized in Table 3.

There was a statistically significant difference between education and awareness of overweight, alcohol consumption, red meat consumption, black stools and anemia among cancer symptoms ($p<0.05$). No statistically significant difference was found between unhealthy diet and seeing blood in stool among risk factors ($p>0.05$). Participants' answers to questions about CRC screening are summarized in Table 4.

Table 2. CRC risk factors

	n	%
Age		
Correct	96	50.0
False	9	4.7
No idea	87	45.3
Family history		
Correct	84	43.8
False	19	9.9
No idea	89	46.4
Obesity		
Correct	57	29.7
False	16	8.3
No idea	119	62.0
Smoking		
Correct	90	46.9
False	14	7.3
No idea	88	45.8
Alcohol		
Correct	103	53.6
False	13	6.8
No idea	76	39.6
Excessive and processed red meat consumption		
Correct	80	41.7
False	16	8.3
No idea	96	50.0
Unhealthy Diet		
Correct	149	77.6
False	12	6.3
No idea	31	16.1

Discussion

The present study aimed to assess the level of awareness among male relatives of patients visiting the medical oncology outpatient clinic regarding CRC risk factors, symptoms, and screening methods. The findings reveal significant gaps in knowledge and awareness, indicating the need for improved education and awareness campaigns targeting this particular population.

In terms of CRC risk factors, the majority of participants were aware that age is a risk factor for CRC. However, there was a notable lack of awareness regarding other important risk factors such as family history of cancer, being overweight,

excessive and processed red meat consumption, smoking, alcohol consumption, and unhealthy diet. In a study on awareness of CRC risk factors among health sciences students, the majority of health sciences students correctly knew smoking and alcohol use, family history and obesity (8). In a study investigating pre-diagnostic awareness of CRC risk factors and screening methods in patients with advanced CRC, 65.1% of the patients had no related knowledge of the CRC risk factors, and 84.9% were unaware of the CRC screening-related information (9). Studies conducted in different countries have also found very low awareness of CRC risk factors in the population (10-13). These findings suggest a lack of comprehensive knowledge about the various factors that contribute to CRC development. Efforts should be made to educate male relatives about the significance of these risk factors and their potential impact on CRC risk.

Table 3. Symptoms of CRC

	n	%
Fecal blood		
Correct	137	71.4
False	3	1.6
No idea	52	27.1
Black stool		
Correct	74	38.5
False	2	1.0
No idea	116	60.4
Anemia		
Correct	88	45.8
False	11	5.7
No idea	93	48.4
Frequency of defecation		
Correct	116	60.4
False	2	1,0
No idea	74	38.5
Abdominal pain		
Correct	125	65.1
False	9	4.7
No idea	58	30.2
Nausea and vomiting		
Correct	83	43.2
False	11	5.7
No idea	98	51.0

Similarly, the study findings highlight insufficient awareness regarding CRC symptoms. In a study investigating awareness of CRC symptoms in a colorectal surgical unit outpatient clinic, the majority of respondents considered bleeding per rectum as a possible symptom of CRC. However, a significant proportion incorrectly selected less ominous symptoms as relevant, while only fifty percent correctly cited weight loss (14). In a study conducted in Palestine on awareness of the signs and symptoms of CRC, the most frequently identified sign/symptom of CRC was 'abdominal distension' and the least frequently identified was 'back pain' (15). In the present study while participants demonstrated awareness of some common symptoms such as occult blood in the stool, change in frequency of defecation, and abdominal pain, they displayed limited knowledge about other symptoms such as black stools, anemia, and nausea/vomiting. This knowledge gap could hinder early detection and timely medical intervention. Public health initiatives should emphasize the importance of recognizing and reporting a wide range of CRC symptoms to improve early diagnosis rates.

Table 4. Knowledge about Screening in CRC

	n	%
Awareness of screening		
Correct	109	56.8
False	14	7.3
No idea	69	35.9
Screening method		
Colonoscopy	111	57.8
Fecal occult blood test (FOBT)	25	13.0
Computed tomography (CT)	34	17.7
CT and FOBT	6	3.1
Colonoscopy and CT	2	1.0
Colonoscopy, FOBT and CT	12	6.3
No idea	2	1. 0
Age of screening		
<50	93	48.4
≥50	8	4.2
No idea	91	47.4
Acceptance of Self-screening		
Yes	97	50,5
No	67	34.9
No idea	28	14.6
Method of screening		
Colonoscopy	60	31.3
FOBT	51	26.6
CT	56	29.2
Colonoscopy+FOBT	8	4.2
FOBT+CT	5	2.6
Colonoscopy+FOBT+CT	3	1.6

Regarding CRC screening, the study revealed moderate levels of awareness among male relatives. However, a considerable proportion of participants lacked knowledge about the recommended screening methods and the appropriate age for screening. The most commonly known screening method was colonoscopy, while the knowledge of other methods such as fecal occult blood tests (FOBT) and computed tomography (CT) was relatively lower. In a study conducted in Saudi Arabia, almost (49.7%) knew that it is possible to detect CRC before symptoms appear. About 64% of respondents mentioned colonoscopy as a screening method for CRC. More than half of the participants (58.1%) indicated that they would like to be screened for CRC, while only 2.8% reported having been screened before (16). In a study on CRC screening awareness in women in Italy overall, only 20.3% of respondents knew about the three cancer screening tests available to women, and this knowledge was limited (17). In this study additionally, the majority of participants were unaware of the optimal age for initiating screening. These findings underscore the need for targeted educational campaigns to improve understanding of the available CRC screening modalities, their respective benefits, and the recommended age range for screening initiation.

Interestingly, education level demonstrated a significant association with awareness of certain risk factors and symptoms. Participants with higher education levels exhibited greater knowledge regarding overweight, alcohol consumption, red meat consumption, black stools, and anemia as risk factors and symptoms of CRC. This suggests that educational interventions could be particularly effective in bridging knowledge gaps and promoting awareness among this population.

To address these knowledge gaps and enhance CRC screening awareness among male relatives of cancer patients, tailored educational initiatives are crucial. These initiatives should employ various strategies such as community-based educational programs, mass media campaigns, and targeted messaging through healthcare providers. By improving knowledge and awareness, we can empower male relatives to take proactive steps in reducing their own CRC risk and encourage them to engage in timely screening, leading to earlier detection and improved outcomes.

This study has certain limitations that should be considered. Firstly, the sample size was relatively small, limiting the generalizability of the findings. Secondly, the study focused on male relatives attending a specific medical oncology outpatient clinic, which may introduce selection bias and limit the representation of the wider population. Future research with larger and more diverse samples is necessary to validate these findings and gain a more comprehensive understanding of CRC awareness among male relatives.

Conclusion

This study highlights significant gaps in knowledge and awareness of CRC risk factors, symptoms, and screening methods among male relatives of cancer patients. It is imperative to develop targeted educational interventions to improve awareness and promote proactive engagement in CRC screening. By enhancing knowledge and awareness, we can potentially reduce the burden of CRC through early detection and appropriate preventive measures. Further research and collaborative efforts are needed to develop effective strategies that can address the specific needs of this population and achieve better CRC outcomes.

Conflict of Interest/ Funding

The study received no financial support from any individual or organization, and the authors declare no conflict of interest.

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Turkish Journal of Clinics and Laboratory

To cite this article: Benli S, Tazeoglu D, Ziblak A, Colak T. Correlation of two different bowel dysfunction questioneria on the Psychological State of the rectal cancer patients. Turk J Clin Lab 2023; 4: 671-677

Research Article

Correlation of two different bowel dysfunction questioneria on the Psychological State of the rectal cancer patients

İki farklı bağırsak disfonksiyonu anketinin rektal kanser hastalarının psikolojik durumu üzerindeki korelasyonu

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Abstract

Aim: Most patients have impaired bowel function after sphincter-sparing surgery (SPS) combined with total mesorectal excision (TME). This study evaluated bowel dysfunction's effect on a patient's psychological state using the LARS Questionnaire (LARS-Q) and the Memorial Sloan Kettering Bowel Function Instrument (MSK-BFI).

Material and Methods: Between June 2019 and June 2022, 127 patients operated on for rectal cancer with TME and SPS were examined regarding bowel dysfunction in the sixth postoperative month. The LARS score and MSK-BFI assessed bowel function. Beck anxiety inventory (BAI), Beck depression inventory (BDI), and Beck hopelessness inventory (BHI) were also applied to the patients. The correlation of LARS-Q and MSK-BFI questionnaire scores was examined with each other and the other three questionnaire scores.

Results: Major LARS was seen in 29.9% of the patients. MSK-BFI scores were found to be 60. The median MSK-BFI scores for no LARS, minor LARS, and major LARS were 77, 68, and 52, respectively. Strong correlations were found between MSK-BFI and LARS-Q (rs -0.63). When the correlation between LARS-Q and BAI, BDI, and BHI was evaluated, rs 0.38, rs 0.49, and rs 0.56 were found, respectively. When the correlation between MSK-BFI and BAI, BDI, and BHI was evaluated, rs -0.67, -0.71, and -0.74 were found, respectively.

Conclusion: Bowel dysfunction is a prevalent condition after sphincter-sparing rectal cancer surgery. Impaired sphincter functions significantly affect patients' social and emotional aspects and negatively affect their quality of life.

Keywords: Anorectal function, MSK-BFI, LARS-Q, bowel dysfunction, low anterior resection syndrome.

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Recevied: 22.06.2023 accepted: 07.11.2023

Öz

Amaç: Sfinkter koruyucu cerrahi ile birlikte total mezorektaleksizyon (TME) sonrasında hastaların çoğunda barsak fonksiyonları bozulur. Bu çalışma, LARS Anketi (LARS-Q) ve MemorialSloanKettering Bağırsak Fonksiyonu Ölçeği (MSK-BFI) kullanılarak bağırsak disfonksiyonunun hastanın psikolojik durumu üzerindeki etkisini değerlendirmeyi amaçladı.

Gereç ve Yöntemler: Haziran 2019-Haziran 2022 tarihleri arasında rektum kanseri nedeniyle TME ve SPS ile opere edilen 127 hasta postoperatif 6. ayda barsak disfonksiyonu açısından incelendi. LARS skoru ve MSK-BFI bağırsak fonksiyonunu değerlendirdi. Hastalara Beckanksiyete envanteri (BAI), Beck depresyon envanteri (BDI) ve Beckumutsuzluk envanteri (BHI) de uygulandı. LARS-Q ve MSK-BFI anket puanlarının birbirleriyle ve diğer üç anket puanları ile korelasyonu incelenmiştir.

Bulgular: Majör LARS hastaların %29.9'unda görüldü. MSK-BFI skorları 60 bulundu. LARS olmayan, minör LARS ve majör LARS için ortanca MSK-BFI skorları sırasıyla 77, 68 ve 52 idi. MSK-BFI ve LARS-Q arasında güçlü korelasyonlar bulundu (rs -0.63). LARS-Q ile BAI, BDI ve BHI arasındaki korelasyon değerlendirildiğinde sırasıyla rs 0.38, rs 0.49 ve rs 0.56 bulundu. MSK-BFI ile BAI, BDI ve BHI arasındaki korelasyon değerlendirildiğinde sırasıyla rs -0,67, -0,71 ve -0,74 bulundu.

Sonuç: Sfinkter koruyucu rektal kanser cerrahisi sonrası barsak disfonksiyonu sık görülen bir durumdur. Bozulmuş sfinkter fonksiyonları hastaların sosyal ve emosyonel yönlerini önemli ölçüde etkilemekte ve yaşam kalitelerini olumsuz etkilemektedir.

Anahtar Kelimeler: Anorektal fonksiyon, MSK-BFI, LARS-Q, bağırsak fonksiyon bozukluğu, lowanterior rezeksiyon sendromu.

Introduction

Although there are various treatment modalities in the treatment of rectal cancer, surgery is the backbone of the treatment. In the treatment of rectal cancer, low anterior resection (LAR) combined with total mesorectal excision (TME) is a standard and common approach [1]. In this technique, the patients' quality of life is increased by preserving the sphincter. In some patients, intestinal, sexual, and urinary complications are seen, which seriously affect the long-term quality of life [2]. However, the relationship between health-related quality of life and bowel functions after rectal cancer surgery is complex [3]. All findings, such as fecal incontinence, increased bowel frequency, urgency, clustering, difficulty in discriminating between gas and stool, and nocturnal defecation, are seen in a wide range of symptoms after rectal resection, are called Low anterior resection syndrome (LARS) [4]. These symptoms can be seen immediately after resection and after ileostomy reversal. Over time, some patients return to normal bowel functions or decrease the severity of symptoms; in some patients, these symptoms continue permanently [5]. Unfortunately, patients often see this as an inevitable part of rectal cancer treatment and tend to hide their symptoms, in which case patients should be questioned proactively as a clinician [6]. The questionnaire used to evaluate bowel functions after rectal resection has been examined in many studies primarily focused on incontinence, and no questionnaire evaluates bowel dysfunction completely [7, 8]. The LARS Questionnaire [9] and the Memorial Sloan Kettering Cancer Center Bowel Function Instrument (MSK-BFI) [10] are the two most commonly validated questionnaires used in the evaluation of bowel dysfunctions. Although both Questionnaires were developed to assess bowel dysfunction, they differ significantly in their clinical applicability and scope. Although the applicability of the LARS Questionnaire is faster and easier, MSK-BFI provides more comprehensive information in evaluating LARS [11]. The present study aims to evaluate the effect of two different Questionnaires on quality of life to evaluate bowel dysfunction after rectal resection.

Material and Methods

Patient Selection and Data collection

Between June 2019 and June 2022, patients who underwent sphincter-sparing mesorectal excision with the diagnosis of rectum cancer in a tertiary health center were examined with the Nested Case-Control design. Patients diagnosed with rectal cancer during the study underwent low anterior resection, came to the follow-up examination, agreed to participate when they came for the follow-up, and whose data were not missing were included in the study. Patients with a diagnosis of rectosigmoid, colon, or anal canal tumor, who underwent end-colostomy without anastomosis after LAR, who did not attend the follow-up examination, whose data were missing, and who refused to participate in the study were excluded from the study. Ethics committee approval of the study was obtained from a tertiary university hospital, and the Declaration of Helsinki designed the study.

Demographic data of the patients (age, gender), comorbid disease, ASA score, tumor location and distance to anal canal (cm), presence of synchronous tumor, neoadjuvant chemoradiotherapy, cancer stage (AJJC), adjuvant chemotherapy or radiotherapy data were recorded. As surgical information, the timing of the operation (emergency, elective), type of operation (open, laparoscopy), surgical technique (LAR, data LAR), anastomosis technique (manual, stapler), and ileostomy data were recorded.

Study Design

The patients were called for routine control examination at six months postoperatively. The LARS-Q and MSK-BFI were used to evaluate bowel dysfunction after LAR. In addition, the Beck Anxiety Inventory (BAI), Beck depression inventory (BDI), and Beck Hopelessness Inventory (BHI) were used to evaluate the mood of the patients. The data from the questionnaires were recorded.

The patients were grouped as non-LARS, minor, and major LARS according to their LARS score and compared. In addition, the correlation of LARS-Q and MSK-BFI questionnaire scores and the other three questionnaire scores (BAI, BDI, BHI) were also examined.

LARS-questionnaire

The LARS-Q is a questionnaire evaluating bowel function after sphincter-sparing surgery for rectal cancer [12]. According to the questionnaire results, it can be divided into severity categories (0-20 = non-LARS, 21-29 = minor-LARS, and 30-42 = major-LARS). The LARS-Q questionnaire does not use incremental scoring with equal weights. Higher scores indicate worse bowel function.

Memorial Sloan Kettering Bowel Function Instrument (MSK-BFI)

The core strength of MSK-BFI is the detailed and comprehensive evaluation of LARS. Urgency, diet, and frequency subscales allow the interpretation of different dimensions of LARS. There are 18 items in total. MSK-BFI uses four weeks of recall and an equally weighted scoring system. Higher scores indicate better bowel function [13].

Statistical Analysis

The conformity of the data to the distribution with the norm was examined using visual (histogram and probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Mean and standard deviation were used for continuous data statistics. Median, minimum, and maximum values were used for ordinal variables. Frequency and percentage values were used to define categorical variables. One Way ANOVA test statistic was used to compare the means of more than two independent groups. Tukey was used as a Post Hoc test in case of difference detected by ANOVA. Chi-square test statistics were used to evaluate the relationship between categorical variables. The correlation coefficients and statistical significance of the LARS-Q and MSK-BFI questionnaires with each other and with the other questionnaires were calculated using the Spearman correlation test. The statistical significance level of the data was taken as $p<0.05$. The software www.e-picos.com (New York) and the MedCalc statistical package program were used to evaluate the data.

Results

During the study, our clinic applied LAR to 164 patients diagnosed with rectal cancer. Fifteen patients with rectosigmoid colon tumors, four patients underwent end-colostomy after LAR, seven did not attend the follow-up examination, nine did not want to participate in the study, and two with missing data were excluded from the study. One hundred twenty-seven patients who met the inclusion criteria were included in the study.

The mean age of the patients was 57.87+17.11 years. 49 (38.6%) of the patients were female, and 78 (61.4%) were male. Comorbidity was present in 76 (59.8%) patients. The mean anal verge distance of the tumor was 8.26+6.03 cm. Tumor localization was in the upper rectum in 49 (38.6%), middle in 44 (34.6%), and lower in 34 (26.8%) patients. The synchronous tumor was present in 15 (12.6%) patients. Neoadjuvant CRT was administered to 72 (56.7%) patients (Table 1).

The median values of the patients on the questionnaire were LARS-Q 15 (0-42), MSK-BFI 60 (42-86), BAI 27 (12-54), BDI 20 (4-47), and BHI 6 (0-20). When the patients were evaluated according to the LARS score, 73 (57.5%) patients were found in the non-LARS group, 16 (12.6%) patients in the minor LARS group, and 38 (29.9%) patients in the major LARS group. There was a statistically significant difference between the mean age groups ($p=0.016$). The mean age of the major and minor LARS groups was similar. The mean age of the non-LARS group was statistically lower than the other groups.

There was no statistical difference between the groups in terms of gender distribution, comorbid disease, mean distance from the anal verge of the tumor, and presence of synchronous tumor ($p>0.05$). There was a statistically significant difference between the groups regarding ASA score ($p=0.012$). Major and minor LARS group results were similar. The ASA score of the minor and major LARS groups was higher in stages III and IV than in the non-LARS group. There was a statistically significant difference between the tumor localization groups ($p=0.003$). This difference was because the non-LARS group was primarily in the upper rectum. There was a significant difference between the groups regarding neoadjuvant CRT ($p=0.014$). This difference was due to the use of neoadjuvant CRT in the major-LARS group (Table 1).

In the postoperative evaluation, there was a significant difference between the groups regarding all questionnaires ($p<0.001$). The median value of the MSK-BFI score was significantly higher than the other two in the major-LARS group and significantly higher than the non-LARS in the minor LARS group (Figure 1 and Figure 2). In all other questionnaires, the median value of the questionnaire score was significantly higher than the other two in the major-LARS group and significantly higher than the non-LARS in the minor-LARS group (Table 2).

Table1. Preoperativeclinicopathologicalfeaturesofthepatients

	All patient (n=127)	Non-LARS (n=73)	MinorLARS (n=16)	MajorLARS (n=38)	p value
	x±SD	x±SD	x±SD	x±SD	
Age (years)	57.87±17.11	54.22±13.53	60.73±14.49	61.54±13.21	0.016
Anal verge distance (cm)	8.26±6.03	8.59±4.95	8.71±5.05	6.59±5.88	0.143
	n (%)	n (%)	n (%)	n (%)	
Gender					
Male	78 (61.4)	39 (53.4)	11 (68.7)	28 (73.7)	0.093
Female	49 (38.6)	34 (46.6)	5 (31.3)	10 (26.3)	
Comorbid disease					
Yes	76 (59.8)	39 (53.4)	10 (62.5)	27 (71.1)	0.193
No	51 (40.2)	34 (46.6)	6 (37.5)	11 (28.9)	
ASAscore					
ASAI	32 (25.2)	24 (32.9)	1 (6.3)	7 (18.4)	0.012
ASAII	56 (44.1)	36 (49.3)	8 (50)	12 (31.6)	
ASAIII	30 (23.6)	10 (13.6)	5 (31.2)	15 (39.5)	
ASAIV	9 (7.1)	3 (4.2)	2 (12.5)	4 (10.5)	
Tumor location					
Upper	49 (38.6)	37 (50.7)	6 (37.4)	6 (15.8)	0.003
Middle	44 (34.6)	24 (32.9)	5 (31.3)	15 (39.5)	
Lower	34 (26.8)	12 (16.4)	5 (31.3)	17 (44.7)	
Synchronoussurgery					
Yes	15 (12.6)	5 (6.8)	4 (25)	6 (15.8)	0.084
No	112 (87.4)	68 (95.2)	12 (75)	32 (84.2)	
Neoadjuvant CRT					
Yes	72 (56.7)	35 (47.9)	8 (50)	29 (76.3)	0.014
No	55 (43.3)	38 (52.1)	8 (50)	9 (23.7)	

ASA: American Society of Anesthesiologists, CRT: neoadjuvant chemoradiotherapy, LARS: Low Anterior Resection Syndrome

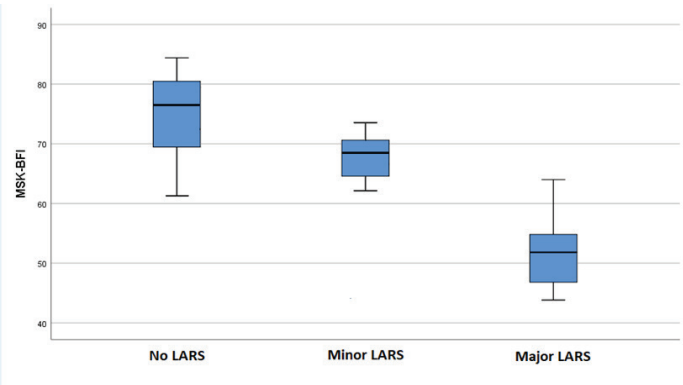

Figure 1. Box-and-whiskers plot of the MSK-BFI total score when patients were divided into 3 groups, defined as no LARS (57.5%,), minor LARS (12.6%), and major LARS (29.9%).

There was a significant difference between the groups in terms of operation time and operation type (p=0.022 and p=0.007, respectively). This difference was due to the greater use of emergency surgery and VLAR in the major-LARS group. There was no difference between the groups in terms of surgical technique, anastomosis technique, ileostomy opening, tumor stage, chemotherapy, or radiotherapy (p>0.05) (Table 2).

A good correlation was found between LARS-Q and MSK-BFI (rs=-0.63). The correlation was found between LARS-Q and BAI, BDI, and BHI (rs=0.38, rs=0.49, rs=0.56, respectively). A good correlation was found between MSK-BFI and BAI, BDI, and BHI (rs=-0.67, rs=-0.71, rs=-0.74, respectively) (Table 3).

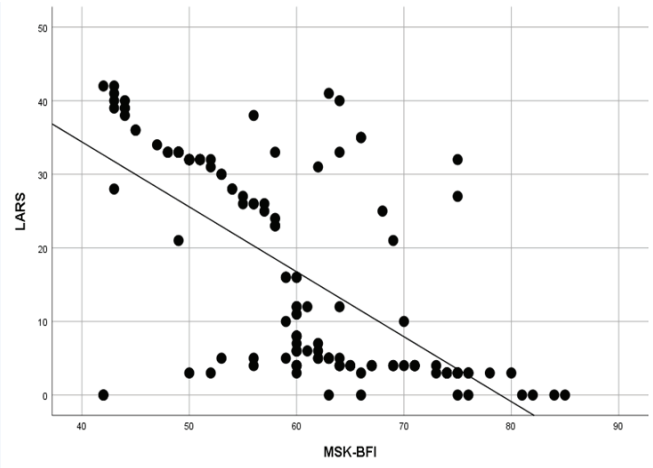

Figure 2. MSK-BFI and LARS-Q score scatter plot. A strong negative correlation was observed between the two questionnaires (rs –0.63).

Table2.Postoperativeclinicopathologicalfeaturesofthepatientsandtheirdifferencebetweengroupswith LARS.

	All patient n=127	Non-LARS n=73	MinorLARS n=16	MajorLARS n=38	pvalue
	Mean (min-max)	Mean (min-max)	Mean (min-max	Mean (min-max)	
LARS-Q	15 (0-42)	4 (0-16)	26 (21-28)	33 (30-42)	<0.001
MSK-BFI	60 (42-86)	77 (54-86)	68 (58-74)	52 (42-66)	<0.001
BAI	27 (12-54)	23 (12-31)	36 (26-49)	41 (29-54)	<0.001
BDI	20 (4-47)	11 (4-20)	24 (13-32)	36 (25-47)	<0.001
BHI	9 (0-20)	2 (0-13)	9 (2-15)	15 (6-20)	<0.001
	n (%)	n (%)	n (%)	n (%)	
Operation timing					
Urgent	11 (8.7)	2 (2.7)	2 (12.5)	7 (18.4)	0.022
Elective	116 (91.3)	71 (97.3)	14 (87.5)	31 (81.6)	
Type of operation					
VLAR	15 (11.8)	3 (4.1)	3 (18.8)	9 (23.7)	0.007
LAR	112 (88.2)	70 (95.9)	13 (81.2)	29 (76.3)	
Surgical Technique					
Open	78 (61.4)	42 (57.5)	9 (56.3)	28 (73.7)	0.224
Laparoscopy	49 (38.6)	31 (42.5)	7 (43.7)	10 (26.3)	
Anastomosis technique					
Handsewn	12 (9.4)	5 (6.8)	2 (12.5)	5 (13.2)	0.512
Stapler	115 (90.6)	68 (93.2)	14 (87.5)	33 (86.8)	
Ileostomy					
Yes	99 (77.9)	53 (72.6)	12 (75)	34 (89.5)	0.119
No stoma	28 (22.1)	20 (27.4)	4 (25)	4 (10.5)	
AJCC stage					
Stage 1	18 (14.2)	11 (15.1)	2 (12.5)	5 (13.2)	0.091
Stage 2	56 (44.1)	35 (47.9)	7 (43.8)	14 (36.8)	
Stage 3	42 (33.1)	25 (34.2)	6 (37.5)	11 (28.9)	
Stage 4	11 (8.6)	2 (2.7)	1 (6.2)	8 (21.1)	
Chemotherapy					
Yes	95 (78.8)	57 (78.1)	12 (75)	26 (68.4)	0.539
No	32 (21.2)	16 (21.9)	4 (25)	12 (31.6)	
Radiotherapy					
Yes	71 (55.9)	38 (52.1)	10 (62.5)	23 (60.5)	0.591
No	56 (44.1)	35 (47.9)	6 (37.5)	15 (39.5)	

AJCC: American Joint Committee on Cancer, BAI: Beck anxiety inventory, BDI: Beck depression inventory, BHI: Beck hopelessness inventory, LAR: Low Anterior Resection, LARS: Low Anterior Resection Syndrome, LARS-Q: Low anterior resection syndrome-questionnaire, VLAR: Very Low Anterior Resection, MSK-BFI: Memorial Sloan Kettering Bowel Function Instrument

Discussion

In line with the data we have shown in this study, most patients who underwent sphincter-preserving surgery (SPS) for rectal cancer had various degrees of bowel dysfunction. Among the most critical factors about bowel dysfunction after SPS are tumor localization, type of operation, and chemoradiotherapy status. To our knowledge, this study is critical because it is among the only studies created using two different bowel dysfunction questionnaires. These questions evaluate the general psychological state of patients related to anxiety, depression, and hopelessness.

This study indicated that 29.9% of patients have major LARS. In a meta-analysis conducted in 2018, the prevalence of major LARS after oncologic rectal cancer surgery was 41% [14]. However, since most studies on LARS do not include an evaluation of the bowel functions of the patients before the operation, it needs to be evaluated whether the dysfunction occurs after treatment. Therefore, it is not appropriate to reach a definite conclusion about the prevalence of LARS without evaluating the sphincter functions of the patients before treatment [15].

Tablo 3. Correlation of LARS and MSK-BFI with Beck inventory of anxiety, depression and hopelessness

	LARS-Q	MSK-BFI
LARS-Q	-	0.63
MSK-BFI	0.63	-
BAI	0.38	0.67
BDI	0.49	0.71
BHI	0.56	0.74

LARS-Q: Low anterior resection syndrome-questionnaire, MSK-BFI: Memorial Sloan Kettering Bowel Function Instrument, BAI: Beck anxiety inventory, BDI: Beck depression inventory, BHI: Beck hopelessness inventory.

In this study, it was shown that there is a strong correlation between MSK-BFI and LARS-Q in terms of assessing bowel function. It was observed that most patients in the major LARS group had a lower score in MSK-BFI score. Similar to our study, in a study evaluating these two questiniores, it was found that LARS scores were high and MSK-BFI scores were found to be low in distal tumors according to tumor localization, and there was a positive correlation in the evaluation of bowel functions [16].

According to the bowel dysfunction symptoms demonstrated in our study, the localization of the tumor and the distance of the anastomosis line from the anal canal are among the most critical factors affecting bowel dysfunction, secondary to the operation performed accordingly, similarly according to both MSK-BFI and LARS-Q. The most significant disadvantage of the distal anastomosis level is decreased neorectal compliance and capacitance [17]. In the literature, similar to our study, it has been shown by various studies that low anastomosis level is directly related to bowel dysfunction [18, 19].

Sphincter problems that occur after rectal cancer surgery directly affect patients' quality of life (QoL) [20, 21]. Psychiatric symptoms such as anxiety, depression, and hopelessness are common in patients whose quality of life is affected. In line with the data we had shown in our study when patients with low MSK-BFI and high LARS-Q were evaluated in terms of anxiety, depression, and hopelessness, higher BAI, BDI, and BHI scores were observed in these patients. These results suggest that bowel dysfunction may not significantly affect all aspects of health-related QoL and that the most affected areas are associated with social and emotional function [22].

Detecting LARS risk factors in the preoperative period provides essential information about how seriously patients will be affected by this condition in the postoperative period [23]. The education given by a multidisciplinary team consisting of a colorectal surgeon, pelvic physiotherapist, psychologist, and nurses specialized in anal incontinence to the patient group at high risk for the development of LARS detected in the preoperative period is of great importance in helping patients combat LARS in case LARS develops in the postoperative period.

Our study had several limitations. First, the MSK-BFI bowel function instrument and LARS-Q have yet to be validated in a Turkish patient. Another limitation is the small number of patients included in the study. Another significant limitation is that the baseline sphincter functions of the patients were not evaluated before treatment. In a study, LARS score ≥ 30 (major LARS) was found to be high in the non-operated population, especially between the ages of 50 and 79 [24]. Another limitation is the nonrandomized design of the study due to sample size inadequacy and the heterogeneity of the groups.

In conclusion, LARS-Q and MSK-BFI show similar properties in demonstrating bowel dysfunction after sphincter-sparing TME. Similarly, patients with low MSK-BFI and high LARS-Q scores have higher BAI, BDI, and BHI scores. Therefore, detecting this situation and providing the necessary psychological support to the patients are very effective in their adherence to treatment and quality of life.

Conflict of Interest statement

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

Funding statement

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

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To cite this article: Artykov MS, Özaslan GN. İntrakraniyal kitle cerrahisinde preoperatif dönemdeki ısıtmanın hipotermiyi önlemedeki etkisi. Turk J Clin Lab 2023; 4: 678-684

Araştırma Makalesi

İntrakraniyal kitle cerrahisinde preoperatif dönemdeki ısıtmanın hipotermiyi önlemedeki etkisi

The efficacy of preoperative warming at prevention of involuntary hypothermia in patients undergoing surgery for intracranial mass lesions

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Öz

Amaç: Perioperatif hipotermi anestezi uygulaması sırasında sık karşılaşılan bir sorundur. Amacımız intrakraniyal kitle cerrahisinde hipoterminin hasta üzerindeki olumsuz etkilerini önlemek için preoperatif dönemden başlayarak ısıtmanın etkilerini araştırmaktır.

Gereç ve Yöntemler: Prospektif, randomize olarak intrakraniyal kitle cerrahisi geçiren hastalar iki gruba ayrıldı. Çalışma grubu aktif ısıtma cihazıyla operasyon öncesi ısıtıldı. Kontrol grubuna ise yalnızca pike örtüldü. Her iki grup da intraoperatif dönemde ısıtıldı. 15 dakikada bir vital bulgular (standart monitörizasyona ek olarak invaziv arteriyel kan basıncı),30 dakikada bir vücut sıcaklığı, saatlik olarak arter kan gazından laktat bakıldı. Titreme skorları, toplam anestezi ve operasyon süresi, tüketilen ilaç miktarları, iv mayi ve kanama miktarı not edildi.

Bulgular: Her grupta 36'şar olmak üzere toplam 72 hasta değerlendirildi. Gruplar arasında demografik ve klinik özellikler açısından anlamlı fark yoktu. Gruplar arasında cerrahinin 15-255. dakikaları arasında ölçülen ısı değerleri arasında anlamlı fark bulundu ($p<0,05$). Ön ısıtma yapılmayan hastaların tümünde en az bir defa hipotermik vücut sıcaklık değeri vardı. Önceden ısıtılan grupta ise yalnızca %11,1 hastada hipotermi saptandı.

Sonuç: İntrakraniyal kitle cerrahisi geçirecek hastalarda aktif eksternal ısıtıcı sistemler ile intraoperatif ve postoperatif dönemde hipoterminin önlenebileceği tespit edilmiştir.

Anahtar Kelimeler: Hipotermi, preoperatif ısıtma, sıcak hava üflemeli ısıtma sistemleri, intrakraniyal kitle cerrahisi

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Geliş Tarihi: 28.06.2023 Kabul Tarihi: 11.09.2023

TJCL Volume 14 Number 4 p: 678-684

Abstract

Aim: Perioperative hypothermia is a common problem during anesthesia procedure. In this study we aimed to determine if preoperative warming was effective at preventing involuntary hypothermia in patients undergoing neurosurgery for intracranial mass.

Material and Methods: Patients undergoing surgery for intracranial mass lesions were prospectively and randomly assigned into two groups. The study group was warmed up before the operation with an active warming device. In the control group, only the blanket was covered. Both groups were warmed intraoperatively. Vital signs (invasive arterial blood pressure in addition to standard monitoring), body temperature every 30 minutes, and lactate from arterial blood gas hourly were measured every 15 minutes. Shivering scores, total anesthesia and operation time, amount of drug consumed, amount of iv fluid and bleeding were noted.

Results: A total of 72 patients were included and divided into two groups of 36 patients each. There was no significant difference in terms of demographics and clinical characteristics between the groups. There was a statistically significant difference between the groups in terms of the temperature values during the period between 15–255 minutes of surgery. There was statistically significant difference between the groups in terms of inadvertent hypothermia incidence ($p<0.05$). At least one hypothermic measurement was spotted in all of control patients. Only %11.1 of patients in pre-warmed group had hypothermic temperature incidence.

Conclusion: Active pre-warming with body surface warming systems is effective at preventing of inadvertent hypothermia in patients undergoing intracranial surgery for mass lesions.

Keywords: hypothermia, preoperative warming, active body surface warming systems, brain neoplasms

Giriş

Perioperatif dönemde vücut kor sıcaklığının 36°C'nin altında olması perioperatif hipotermi olarak tanımlanır. Perioperatif hipotermi insidansı oldukça yüksek olup (%50-70) anestezi uygulaması sırasında sık karşılaşılan bir sorundur, cerrahi sonuç ve postoperatif seyir üzerinde birçok olumsuz etkisi (metabolizmanın yavaşlaması, metabolik asidoz, kas gevşeticilerin etkilerinin uzaması, pıhtılaşma fonksiyonlarının değişmesi, enfeksiyon artışı, miyokardiyal iskemi vb.) vardır [1].

Genel anestezi sırasında ısı kaybı hasta veya çevreye ait faktörlerden kaynaklanabilir. Hastayla ilgili olanlar, hastalığın ciddiyetini ve planlanan müdahaleyi (örneğin, açık vücut boşlukları) içerir. Çevre ile ilgili faktörler, vücut kor sıcaklığının altındaki sıcaklıklarda sıvılara ve yüzeylere maruz kalmayı ve ortamdaki soğuk havanın sürekli sirkülasyonunu içerir [2].

Hipoterminin mortalite, nörolojik hasar riskini azaltma, intrakraniyal kanama-iskemi, konjestif kalp yetmezliği ve miyokardiyal iskemi üzerine etkisi bulunamamıştır. Aksine postoperatif dönemdeki hipoterminin ise enfeksiyon riskini artırabileceği düşünülmektedir [3].

ERAS (cerrahi sonrası hızlandırılmış iyileşme) protokolleri gereği elektif kraniyotomilerde perioperatif normotermi, sıvıların ısıtılması, hastanın sıcak hava üflemeli sistemlerle ısıtılması ve sıcaklığın monitörizasyonu önerilmektedir [4].

Bu çalışma hastaların normotermik tutulmasının gerekliliği hipotezi ile planlanmıştır. İntrakraniyal kitle nedeniyle opere olan hastaların preoperatif dönemde ısıtılmasının hipotermiyi önlemedeki etkisi araştırılmıştır.

Gereç ve Yöntemler

Prospektif, randomize olarak yapılması planlanan çalışma için kurumumuzdan etik kurul onayı alındı (E1-20-1298) ve Helsinki İlkeler Deklerasyonuna uygun olarak gerçekleştirildi. Amerikan Anestezistler Derneği (ASA) skoru I-II, 18-65 yaş arasında olan 72 hasta çalışmaya dahil edildi. Preoperatif hazırlık odasına alınan olgular operasyon için başvuru sırasına göre 36'şar kişilik iki gruba ayrıldı. Hastalar cerrahi kliniklere başvuru yaptıktan sonra preoperatif rutin hazırlık yapılarak, demografik veriler kaydedildi. Tüm hastalar bilgilendirilmiş onam formunu imzaladı.

Vücut sıcaklığı 37,5°C'nin üzerinde, feokromasitoma, tiroid fonksiyon bozukluğu, malign hipertermi öyküsü veya riski olan, gebe, vücut kitle indeksi (VKi) 18-40 aralığında olan, onam formunu okuma-anlama-imzalama yetisi olmayan ya da imzalamak istemeyen hastalar çalışma dışı bırakıldı.

Normal sıcaklığı 20-23°C olan preoperatif hazırlık odasında her iki grubun timpanik sıcaklıkları ölçüldü.

Önceden ısıtma grubu; preoperatif hazırlık odasında olguların timpanik sıcaklığı (Braun Thermoscan® 3 timpanik ısı ölçer, Almanya) ölçüldükten sonra tek kullanımlık örtü yardımıyla 15 dakika süresince eksternal basınçlı hava ısıtıcısı (Covidien Warm Touch, İrlanda) kullanılarak 40°C ile olgular ısıtılmaya başlandı. Kullanılan ısıtıcı cihazın maksimum yüksekliği 40°C idi. Ameliyat odasına transfer esnasında da ısıtma devam etti.

Kontrol grubu; preoperatif hazırlık odasında olguların timpanik sıcaklığı (Braun Thermoscan® 3 timpanik ısı ölçer) ölçüldükten sonra olguların üzerine bir pamuklu pike örtüldü ve bu hastalarda eksternal ısıtma cihazı kullanılmadı.

Operasyon odasına geldikten sonra her iki grup da eksternal basınçlı hava ısıtıcısıyla aktif olarak ısıtıldı.

Entübasyon öncesinde tüm hastalara standart monitörizasyona ek olarak invaziv arteryel kan basıncı ölçümü uygulandı ve bispektral indeks (BİS) elektrodu takıldı.

Uygun preoksijenizasyon (6 L dk-1 %80 O_2) sonrası 0,02 mg kg-1 midazolam, 2 µg kg-1 fentanil, 1 mg kg-1 lidokain, 2-3 mg kg-1 propofol ve 0,6 mg kg-1 roküronyum ile anestezi indüksiyonu ve entübasyon gerçekleştirildi.

İntraoperatif akım 2 L dk-1, %50 O_2 ve %50 hava olarak ayarlandı. Entübasyonu takiben özofageal ısı probu yerleştirildi. İntraoperatif dönemde hastaya propofol ve remifentanil infüzyonu ile total intravenöz anestezi (TIVA) uygulandı. Propofol ilk 15 dakika 10 mg kg-1 saat -1 ikinci 15 dakika 8 mg kg -1 saat-1 ve idamede 6 mg kg-1 saat-1 infüzyon ve remifentanil 0,1-1 µg kg-1 dk-1 infüzyon uygulandı. BİS 20-40 aralığında ve ortalama arter basıncı 60 mmHg'nın üzerinde olacak şekilde propofol ve remifentanil doz titrasyonu sağlandı. Dominant olmayan elin radyal arteri kanüle edilerek invaziv kan basıncı monitörizasyonu yapıldı , 1 saat aralıklarla arter kan gazından laktat takibi yapıldı. İdrar çıkışı takip edildi. Subklavyen ven kateterizasyonu ile santral venöz basınç (SVB) ölçümü yapıldı. Hasta hazırlığı tamamlandıktan sonra uygun pozisyona alınarak silikon yastıklarla vücudu desteklendi. Operasyon süresince aktif ısıtma devam etti. Operasyon odasının sıcaklığı 20-22 ^{0}C aralığında sabit tutuldu. Operasyon süresince kor sıcaklığının maksimum 37°C olmasına izin verildi. Maksimum sıcaklığa ulaşıldığında eksternal ısıtıcı 34°C'ye düşürüldü. Tüm intravenöz sıvılar oda sıcaklığında verildi. Tüm hastalara operasyon bitiminden 15 dakika önce intravenöz olarak 4 mg ondansetron, 15 mg kg-1 parasetamol uygulandı. Operasyon bitiminde intraoperatif tüketilen remifentanil ve propofol dozu, toplam intravenöz mayi ve kanama miktarı kayıt edildi. Uygun ekstübasyon ve uyanıklık sonrası hastalar ilk olarak 30 dakika takip için derlenme ünitesine eksternal basınçlı hava ısıtıcısı ile transfer edilerek ısıtılmaya devam edildi. Postoperatif 30. dakikada takip sonlandırıldı.

Hastalar daha sonra 24 saat boyunca takip edilecekleri beyin cerrahi yoğun bakım ünitesine transfer edildi.

Bakılan parametreler şunlardır: Preoperatif dönemde; timpanik sıcaklık (^{0}C), kan basıncı (mmHg) (KB), kalp hızı (atım dk.-1) (KH), oksijen satürasyonu (SpO_2) (%) ve BİS.

İntraoperatif dönemde; 15 dakika arayla KB, KH, SpO_2, BİS, 30 dakika arayla özofageal sıcaklık (^{0}C), idrar miktarı (mL), santral venöz basınç (SVB - mmHg) ve saatlik arter kan gazından laktat değeri.

İntraoperatif toplam tüketilen remifentanil (µg), propofol miktarı (mg), verilen toplam intravenöz mayi (mL), toplam kanama miktarı (mL) , operasyon ve anestezi süresi (dakika).

Postoperatif derlenme odasında; 15 dakika arayla KB, KH, SpO_2, postoperatif 0. ve 30. dakika timpanik sıcaklık ve titreme skoru (0: yok, 1: sadece baş ve boyun, 2: üst ekstremiteler de dahil, 3: tüm vücut).

İntraoperatif dönemde özofageal ısının, preoperatif ve postoperatif dönemde timpanik sıcaklığın ölçülme nedeni hastanın özofageal ısı probundan rahatsız olmasını önlemektir.

İstatistiksel analiz

%91 güçle hasta sayısı her grup için 36 olarak belirlendi. Verilerin analizi IBM SPSS 25.0 (Armonk, NY: IBM Corp.) istatistik paket programı kullanılarak yapıldı. Çalışma verileri değerlendirilirken tanımlayıcı istatistiksel metotların (frekans, yüzde, ortalama, standart sapma, medyan, minimum-maksimum, çeyrekler arası aralık) yanı sıra niteliksel verilerin karşılaştırılmasında Ki-Kare (χ^2) testi kullanıldı. Verilerin normal dağılıma uygunluğu Kolmogorov-Smirnov testi ve grafiksel yöntemler ile değerlendirildi. Araştırmada, normal dağılım gösteren niceliksel verilerin değerlendirilmesinde bağımsız değişkenler t testi kullanıldı. Normal dağılım göstermeyen verilerin değerlendirilmesinde Mann-Whitney U testi kullanıldı. İstatistiksel anlamlılık düzeyi a=0,05 olarak kabul edildi.

Bulgular

Çalışmamız preoperatif dönemden itibaren ısıtılan (ön ısıtma yapılan) ve ısıtmaya operasyon odasına geldikten sonra başlanan (ön ısıtma yapılmayan) 36'şar hastadan oluşan toplam 72 hasta üzerinde gerçekleştirilmiştir.

Araştırmaya katılanların özellikleri Tablo 1'de verilmiştir. Gruplar arasında yaş, cinsiyet, VKİ, ASA sınıflaması, anestezi süresi açısından fark yoktur.

Tablo 1. Hasta Özelliklerinin Karşılaştırılması				
		Ön ısıtma		
		Yok (n=36)	Var (n=36)	p
Cinsiyet	Kadın Erkek	21 (58,3%) 15 (41,7%)	19 (52,8%) 17 (47,2%)	0,813[a]
Yaş (yıl)		48,8 ± 13,8	44,9 ± 10,3	0,175[b]
Boy (m)		1,7 ± 0,1	1,7 ± 0,1	0,585[b]
Ağırlık (kg)		75,5 ± 12,8	76,3 ± 13,5	0,802[b]
Vücut kitle indeksi (kg m-2)		27,6 ± 5,1	27,4 ± 4,7	0,835[b]
ASA Skoru	I II	6 (16,7%) 30 (83,3%)	6 (16,7%) 30 (83,3%)	1,000[a]
Operasyon süresi (dakika)		167,5 (150,0-207,5)	180 (148,8-235,0)	0,513[c]
Anestezi süresi (dakika)		240,0 (216,3-273,8)	255 (220,0-303,8)	0,234[c]
Göz açma zamanı (dakika)		12,9 ± 4,3	11,1 ± 4,5	0,096[b]
Kitle yeri	Supratentoryal Infratentoryal	31 (86,1%) 5 (13,9%)	31 (86,1%) 5 (13,9%)	1,000[a]

a:Ki-kare Testi, b:Bağımsız Örneklem t Testi (Ort ± SS), c:Mann-Whitney U Testi ,ASA: Amerikan Anestezistler Derneği Skoru, n:Hasta sayısı

Gruplar arasında yapılan karşılaştırmalarda; 15. dakikadan 255. dakikaya kadar olan tüm eş zamanlarda ölçülen sıcaklık değerleri yönünden istatistiksel olarak anlamlı bir fark olduğu (p<0,05), fark bulunan tüm durumlarda ön ısıtma yapılmayan hasta grubunda <36 ^{0}C olma oranının daha yüksek olduğu bulunmuştur (Tablo 2). Ön ısıtma yapılmayan hastaların tümünde en az bir defa hipotermik vücut sıcaklık değeri vardı. Önceden ısıtılan grupta ise yalnızca %11,1 hastada hipotermi saptandı. Gruplar arasında yapılan karşılaştırmalarda; verilen total iv mayi (mL), remifentanil, propofol dozları (mg) ve kanama miktarları (mL) arasında istatistiksel olarak anlamlı bir fark yoktur (p>0,05) (Tablo 3). Hiçbir hastada kan transfüzyonuna gerek duyulmamıştır.

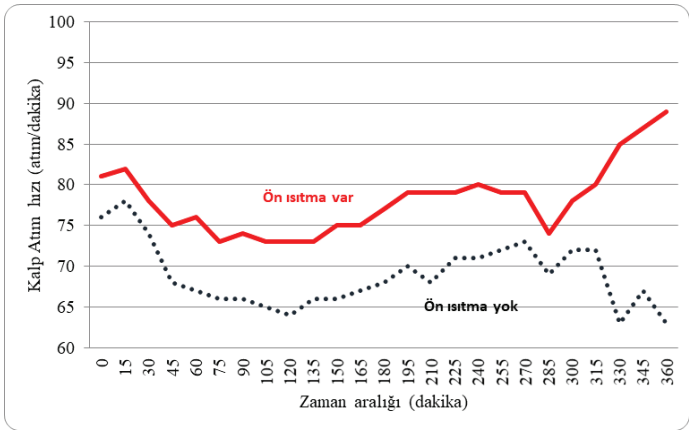
Tablo 2. Sıcaklığın Gruplar Arası Karşılaştırılması					
	Ön ısıtma Yok		Ön ısıtma Var		
Zaman (dakika)	Sıcaklık (0C)	n	Sıcaklık (0 C)	n	p *
Preindüksiyon	36,5 ± 0,3	36	36,5 ± 0,3	36	0,821
15. dakika	36,0 ± 0,4	36	36,4 ± 0,3	36	0,000
45. dakika	35,7 ± 0,3	36	36,3 ± 0,3	36	0,000
75. dakika	35,7 ± 0,3	36	36,3 ± 0,3	36	0,000
105. dakika	35,8 ± 0,3	36	36,4 ± 0,3	36	0,000
135.dakika	35,9 ± 0,3	36	36,5 ± 0,3	36	0,000
165. dakika	36,0 ± 0,4	35	36,6 ± 0,3	35	0,000
195. dakika	36,1 ± 0,5	29	36,7 ± 0,3	31	0,000
225. dakika	36,1 ± 0,5	21	36,8 ± 0,3	26	0,000
255. dakika	36,1 ± 0,6	12	36,8 ± 0,3	16	0,002
285. dakika	36,3 ± 0,9	5	36,9 ± 0,2	10	0,212
315. dakika	36,5 ± 0,6	5	36,8 ± 0,3	5	0,375
345. dakika	36,7 ± 0,0	1	36,9 ± 0,2	3	--
Postop. 0. dakika	36,3 ± 0,4	36	36,6 ± 0,4	36	0,002
Postop.15. dakika	36,4 ± 0,3	36	36,5 ± 0,5	36	0,157
Postop.30. dakika	36,4 ± 0,4	36	36,6 ± 0,4	36	0,067

*Bağımsız Örneklem t Testi (Ort±SS), n hasta sayısı

Tablo 3. Total iv mayi, Remifentanil, Propofol ve Kanamanın Gruplar Arası Karşılaştırılması.			
	Ön ısıtma Yok (n=36)	Ön ısıtma Var (n=36)	p*
Total iv mayi (mL)	1679,2 ± 627,7	1738,9 ± 461,5	0,647
Remifentanil (µg)	1,6 ± 0,6	1,8 ± 0,8	0,265
Propofol (mg)	2003,3 ± 629,3	2258,3 ± 798,7	0,137
Total kanama (mL)	216,0 ± 174,4	209,7 ± 139,8	0,867

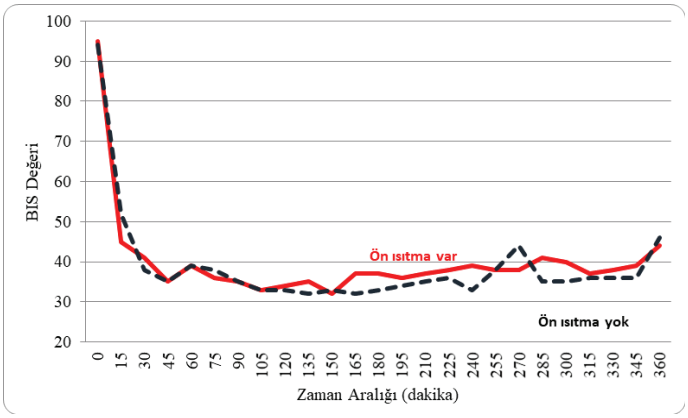
*: Bağımsız Örneklem t Testi (Ort ± SS), n hasta sayısı, iv intravenöz

Gruplar arasında yapılan karşılaştırmalarda; 45. dakika, 75.-225. dakikalar arası ve tüm postoperatif KH değerleri yönünden gruplar arasında istatistiksel olarak anlamlı bir fark olduğu (p<0,05), fark bulunan tüm durumlarda ön ısıtma yapılan hasta grubunun değerlerinin daha yüksek olduğu bulunmuştur. Diğer eş zamanlarda ölçülen KH değerleri yönünden gruplar arasında istatistiksel olarak anlamlı bir fark olmadığı (p>0,05) bulunmuştur (Şekil 1). Sistolik ,diyastolik ve ortalama arter basıncı ile SpO2 değerleri açısından fark yoktur.



Şekil 1. Kalp Hızının Gruplar Arası Karşılaştırılması.

Gruplar arasında yapılan karşılaştırmalarda; 15. ve 165. dakikalarda ölçülen BİS değerleri yönünden gruplar arasında istatistiksel olarak anlamlı bir fark olduğu ($p<0,05$), 15. dakikada ön ısıtma yapılmayan hasta grubunun, 165. dakikada ön ısıtma yapılan hasta grubunun değerlerinin daha yüksek olduğu bulunmuştur. Diğer eş zamanlarda ölçülen BİS değerleri yönünden gruplar arasında istatistiksel olarak anlamlı bir fark olmadığı ($p>0,05$) bulunmuştur (Şekil 2).



Şekil 2. BİS'in Gruplar Arası Karşılaştırılması.

Gruplararası laktat düzeyi, SVB ve titreme skorları (Tablo 4) açısından istatistiksel fark bulunmamıştır. İdrar çıkışı ise yalnızca ısıtılan grupta cerrahinin 15.dk ölçümünde anlamlı ($p<0,05$) çıkmakla birlikte gruplar arasında benzer olarak bulunmuştur.

Tablo 4. Titreme Skorunun Gruplar Arası Karşılaştırılması

	Ön ısıtma		
Titreme Skoru	Yok	Var	p değeri*
0. Dk.	0,4 ± 0,8	0,3 ± 0,8	0,769
15.Dk.	0,2 ± 0,6	0,1 ± 0,4	0,485
30.Dk	0,1 ± 0,5	0,0 ± 0,2	0,365

*Bağımsız Örneklem t Testi (Ort±SS)

Tartışma

Bu çalışmada preoperatif dönemden başlayan ısıtmanın intrakraniyal kitle cerrahisi geçiren hastalarda hipotermiyi önlemedeki etkisi değerlendirilmiş olup, önceden ısıtılan grupta hipotermi insidansının anlamlı derecede düşük olduğu tespit edilmiştir.

Preoperatif dönemden itibaren yapılan ısıtmanın hipotermiyi önlemedeki etkisiyle ilgili literatürde birçok çalışma bulunmaktadır. Ancak intrakraniyal kitle cerrahisinde yapılmış detaylı bir çalışmaya rastlanmamıştır. Bu hasta grubunun çalışmamızda seçilmesinin nedenlerinden biri hastaların vücut alanının çok geniş bir kısmını aktif olarak ısıtmamıza olanak sağlamasıdır. Bir diğer neden ise Galvin ve ark.nın [3] da belirttiği gibi hipoterminin serebral fonksiyonlar üzerine etkisinin tartışmalı olmasıdır.

Çalışmamızda seçmiş olduğumuz ısıtma yöntemi tek kullanımlık örtüler ile birlikte sıcak hava üflemeli sistemlerdir. Birçok çalışmada sıcak hava üflemeli cihazların hipotermiyi önlemede ve postoperatif komplikasyonları azaltmada etkin olduğu belirtilmiştir [5,6]. Çalışmamızda intraoperatif ve postoperatif vücut sıcaklık değerleri arasında istatistiksel anlamlı fark bulunmuştur. Önceden ısıtılan grupta hipotermik ölçümlerin sayısı daha azdır. Bu hastalarda ısı kaybının önlenmesi yanında ciltten ısı transferi ile de sıcaklık düşmemiştir.

Literatürde preoperatif dönemde 10, 15, 20, 30 ve 45'er dakikalık ısıtma süreleri ile hipoterminin önlendiğine dair yayınlar [7,8] olmakla birlikte, çalışmamızda preoperatif dönemdeki ısıtma süresi 15 dakika olarak belirlenmiştir. İntrakraniyal kitle cerrahisi geçirecek hastalar sedatiflere karşı oldukça duyarlıdır ve bu hasta grubunda premedikasyon yapılması riskli olduğundan preoperatif hazırlık odasındaki bekleme süresinin kısaltılması, preoperatif anksiyete ve etkilerini önlemek adına süre kısa olarak belirlenmiştir.

Jun JH ve ark. [9] yüksek derecelerde (44°C), 20 dk ön ısıtma yapmanın da perioperatif hipotermiyi engellediğini bildirmişlerdir. Biz; ısıtıcı cihazımızın maksimum derecesi 40 olduğu için 15 dk. boyunca maksimum 40°C'de çalışmamızı gerçekleştirdik.

Darvall ve ark. [10] preoperatif ısıtmanın hipotansiyon üzerine etkilerine bakmışlar ve sistolik ya da ortalama arter basıncında herhangi anlamlı bir değişikliğe yol açmadığını fakat kalp hızlarında anlamlı bir şekilde yükseklik olduğunu belirtmişlerdir. Bunun nedeni olarak da kutanöz kan akışının artması, arteriyovenöz şantlaşma ve kardiyak outputun artışına sekonder kompanzasyon mekanizmasını göstermişlerdir. Bu açıdan sonuçlar bizim çalışmamızda da benzer bulunmuştur.

Çalışmamızda iki grup arasında intraoperatif dönem kor sıcaklıkları arasında belirgin istatiksel anlamlı fark bulunmuştur. Yapılan benzer çalışmalarda da sonuçlar bizim çalışmamızla uyumludur. Shin ve ark. [11] serebral anevrizmaların endovasküler tedavi girişimlerinde yapmış oldukları çalışmada da entübasyon ardından sıcaklık ölçülen tüm zamanlarda önceden ısıtılan grupta vücut sıcaklıkları daha yüksek bulunmuştur.

Cerrahi süresi oldukça uzun olmasına ve her iki grup intraoperatif ısıtılmasına rağmen postoperatif dönemde de vücut sıcaklıkları arasında anlamlı fark saptanmıştır. Kaufner

ve ark. [12] da over kanserinde sitoredüktif cerrahi uygulanan hastalarda epidural kateter takılırken önceden ısıtma uygulanan ve uygulanmayan grupları karşılaştırdıklarında indüksiyon sonrası, intraoperatif, postoperatif ve hatta yoğun bakıma transferinden 2 saat sonra iki grup arasında vücut sıcaklıkları açısından anlamlı fark saptamışlardır.

Literatürden bilindiği üzere hipotermi ilaç metabolizmasını etkilemektedir ve propofolün plazma konsantrasyonunu artırmaktadır. Propofol tüketimini etkileyecek bir durum anestezi derinliğidir ancak bizim çalışmamızda iki grup arasında BİS değerleri açısından fark saptanmamıştır. Propofol tüketiminde fark saptanmamasının önemli bir nedeninin bu hastaların hafif hipotermik seyretmiş olması olabilir. Daha yüksek derecede ve uzun süreli ısıtma yapmış olsaydık BİS değerleri daha anlamlı olarak bulunabilirdi.

Andrzejowski ve ark. [13] da önceden ısıtmayı spinal cerrahi geçirecek hastalarda uygulamışlar ve literatürle uyumlu şekilde bu çalışmada da önceden ısıtılan grupta istemsiz intraoperatif hipotermi insidansının anlamlı bir şekilde daha düşük olduğunu bulmuşlardır.Bu hastalar intraoperatif ilaç tüketimi açısından değerlendirildiğinde propofol ve remifentanil tüketimi açısından anlamlı fark saptanmamıştır.

Aynı şekilde Xiao ve ark. [14] video yardımlı toraks cerrahisi (VATS) geçiren hastalarda yaptıkları çalışmada da intraoperatif anestezik tüketiminde anlamlı fark bulmamışlardır.

Hipoterminin olumsuz etkilerinden bir diğeri de koagülasyonun bozulmasına sekonder kanamadır. Çalışmamızda kanama miktarı açısından iki grup arasında anlamlı fark saptanmamıştır. Çalışmamızda seçmiş olduğumuz hasta grubunda kanama sık görülen bir komplikasyon olmamakla birlikte kitlenin tipi de kanama oranını değiştirmektedir. Bizim çalışmamızda majör kanama veya transfüzyon ihtiyacı gözlenmemiştir. Ayrıca hastalarımız derin hipotermiye girmemiş ve intraoperatif ısıtılmaya devam edildiği için vücut sıcaklıkları zaman içerisinde normalize olmuştur.

Kardiyak dışı cerrahide Lau ve ark. [15], off-pump koroner arter bypass cerrahisinde Cho ve ark. [16] bizim sonuçlarımızla benzer olarak kanama miktarı ve intraoperatif transfüzyon açısından anlamlı fark bulamamışlardır.

2013 yılında yayınlanmış olan ASA kılavuzunda da sıcak hava üflemeli sistemlerin hasta ısısını normalleştirdiği ve titremeyi azalttığı belirtilmiştir [17].

Literatürdeki sonuçlara benzer olarak [18,19] çalışmamızda postoperatif titreme değerlendirilmiş ancak titreme skorları arasında anlamlı fark saptanmamıştır.

Bu çalışmalarda genel olarak perioperatif dönemdeki ısıtma temel alınmıştır. Bizim çalışmamızda her iki grup da intraoperatif ısıtılmaya devam edilmiştir. Operasyon süresi de oldukça uzun olduğu için hastaların postoperatif döneme kadar vücut sıcaklığı normal aralığa yükselmiştir. Çalışmamızda titremenin anlamlı çıkmamasının nedenlerinden birisinin bu olabileceği düşünülmüştür. Ayrıca hastalarımız postoperatif dönemde de ısıtılmaya devam edilmiştir.

Çalışmamızın bazı kısıtlamaları mevcuttur. Bunlardan ilki hastanemizde mevcut olmadığı için TİVA yönetiminde hedef kontrollü infüzyon cihazı kullanmamış olmamızdır. Hedef kontrollü cihazlar ile daha etkin bir anestezi derinliği ve daha detaylı bir ilaç tüketimi hesaplanması mümkündür. Bir diğer kısıtlayıcı neden kitlelerin yerleşimi, tipi, cerrahi pozisyonun farklı olması ve bu faktörlerin sonuçlarına etki edebilmesidir. Bunlar da göz önüne alındığında daha fazla hasta sayısı ile prospektif randomize kontrollü çalışmalara ihtiyaç duyulmaktadır.

Sonuç

İntrakraniyal kitle cerrahisi geçiren hastalarda hava üflemeli ısıtma sistemleri ile perioperatif dönemde (preoperatif 15 dk, intraoperatif ve postoperatif) uygulanan 40 derecedeki ısıtmanın intraoperatif ve postoperatif hipotermiyi önlediği ve bu uygulamanın ön ısıtma yapılmayan ancak intraoperatif ve postoperatif ısıtma yapılan gruba göre üstün olduğu sonucuna varılmıştır. Ayrıca bu çalışma ile birlikte vücut sıcaklığı monitörizasyonu yapılması ve hastaların preoperatif dönemden itibaren ısıtılmasının günlük anestezi pratiğinde oldukça önemli olduğu bir kez daha vurgulanmıştır.

Çıkar tatışması / Finansal destek beyanı

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

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Turkish Journal of Clinics and Laboratory

To cite this article: Toksoz Yildirim AN, Korkmaz O, Ozkan K, Akyurek M, Tataroglu Ozyukseler D. Video consultations for soft tissue and bone tumor pathology during the Covıd-19 pandemic: A single center experience in a developing country. Turk J Clin Lab 2023; 4: 685-689

Research Article

Video consultations for soft tissue and bone tumor pathology during the Covid-19 pandemic: A single center experience in a developing country.

COVID-19 salgını sırasında yumuşak doku ve kemik tümör patolojisi için video konsültasyonlar: Gelişmekte olan bir ülkedeki tek merkez deneyimi.

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Abstract

Aim: Consultation in medical practice is an indispensable practice in all branches of medicine. In pathology in particular, it was mainly done face-to-face until the recent Covid-19 pandemic which necessitated physical distancing measures, lockdowns, and work-from-home arrangements.

We had to embrace consultation via videoconferencing using Zoom® in our hospital during the peak of lockdown and beyond. This study describes our experience in Istanbul Medeniyet University Training and Research Hospital Goztepe, Istanbul.

Material and Methods: One hundred bone and soft tissue slides received from the orthopedic oncology unit between March 2020 and January 2021 were reviewed by the hospital's musculoskeletal pathologist (hosts) with an external pathologist (consultant) via Zoom® video conferencing.

Results: Mean age of the patients was 32. 51 cases were male and 49 were female. Seventy cases were bone tissue lesions and 30 were soft tissue lesions. 36 specimens were resection materials, 42 of them were curettage materials and 22 of them were tru-cut biopsy materials. The number of slides examined per case ranged between 1 to 28.

Conclusion: The most important advantage of dynamic nonrobotic telemicroscopy is the simultaneous interaction between the consultant, host pathologist, and other participants, effectively serving as a medium for teaching.

Keywords: Consultation, Telepathology, Bone & Soft Tissue Tumors

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Recevied: 14.08.2023 accepted: 20.10.2023

Öz

Amaç: Tıp pratiğinde konsültasyon, tıbbın tüm dallarında vazgeçilmez bir uygulamadır. Özellikle patolojide, yakın zamana kadar genellikle yüz yüze yapılmıştır; ancak yakın zamandaki COVID-19 salgını, fiziksel mesafe önlemleri, karantinalar ve evden çalışma düzenlemelerini zorunlu kıldı.

Biz de hastanemizde kapanmanın ve sonrasının yoğun olduğu dönemde Zoom® video konferansı kullanarak konsültasyonu benimsemek zorunda kaldık. Bu çalışma ile İstanbul Medeniyet Üniversitesi Göztepe Eğitim ve Araştırma Hastanesi'ndeki deneyimimizi aktarmak istedik.

Gereç ve Yöntemler: Mart 2020 ile Ocak 2021 tarihleri arasında ortopedik onkoloji biriminden alınan 100 kemik ve yumuşak doku tümörü, hastanenin patoloğu ve konsültan patolog tarafından Zoom® video konferansı aracılığıyla gözden geçirildi.

Bulgular: Hastaların yaş ortalaması 32 idi. 51'i erkek, 49'u kadındı. 70 vaka kemik lezyonu, 30 vaka ise yumuşak doku lezyonları idi. Spesmenlerin 36'sı rezeksiyon materyali, 42'si küretaj materyali ve 22'si tru-cut biyopsi materyaliydi. Vaka başına incelenen kesit sayısı 1 ila 28 arasında değişmekteydi.

Sonuç: Dinamik olmayan robotik olmayan telemikroskopinin en önemli avantajı, danışman, ev sahibi patolog ve diğer katılımcılar arasında aynı anda gerçekleşen etkileşimdir; bu etkileşim, etkili bir şekilde öğretim aracı olarak hizmet etmektedir.

Anahtar kelimeler: Konsültasyon, Telepatoloji, Kemik ve Yumuşak Doku Tümörleri

Introduction

Consultation in medical practice can be described as an act of seeking assistance/opinion from other physicians or healthcare professionals for diagnostic studies, therapeutic interventions, or other services that may benefit the patient [1]. It is an indispensable practice in all branches of medicine including pathology. Until the pandemic, surgical pathology in our institution, mainly relies on the evaluation of physical glass slides, while consultations were mainly held face-to-face in the same physical environment.

During the recent COVID-19 pandemic, several lockdowns, work-from-home arrangements, and social distancing precautions largely eliminated the usual face-to-face consultation. We had to embrace Telepathology, which is a relatively new technology that is developing rapidly and is being widely used by pathologists, especially during the pandemic when face-to-face consultation is not available. It refers to the remote practice of pathology by utilizing telecommunication facilities to facilitate the transfer of pathology data between two different locations for the purpose of diagnosis, research, and education [2]. The term was first coined by Weinstein et al in 1986, who is also known by many as the 'Father of telepathology' [2,3]. Telepathology is defined as a form of communication between medical professionals that includes the transmission of pathology images and associated clinical information for various clinical applications including, but not limited to, primary diagnoses, rapid cytology interpretation, intraoperative and second opinion consultations, ancillary study review, archiving, and quality activities [4].

Whole slide imaging (WSI) is a frequently used telepathology method for consultation in surgical pathology, however, it needs an advanced infrastructure for its deployment. It utilizes the use of a digital scanner for high resolution scanning of the glass slides [2,5,6]. Not all institutions can afford this massive investment in a short time, especially under the pandemic restrictions. Equipment cost emerges as another negative impediment. A cheaper option is static imaging (SI) of slides which is also widely used. It involves using a digital camera to capture multiple images from different but relevant areas of a glass slide and transmitting the same to the consulting pathologist for review. Its main drawback is the inability of the consultant to freely navigate the entire glass slide and overall dependence on only the captured images for interpretation. Therefore, static images should be taken by an experienced pathologist and must show critical parts relevant to diagnosis, or there should be numerous images of all parts of the slide. Both WSI and SI also generate lots of data load [2,5,6].

One of the most important factors that facilitate consultation in surgical pathology is to create an environment for mutual discussion and education through active participation. This is lacking in consultation through the traditional telepathology methods of WSI and SI, and the whole process becomes passive information transmission [5,6]. In our institution we

aimed to eliminate these handicaps by using the Zoom Cloud Meetings (Zoom Video Communications Inc. San Jose, CA) for consultation, effectively enjoying both slide-sharing ability as well as the opportunity for active discussion, effectively deploying dynamic nonrobotic telemicroscopy (DNTM) [5,6]. This study presents our experience in telepathology consultation via Zoom®.

Material and Methods

The study was conducted at Istanbul Medeniyet University Goztepe, Training & Research Hospital, Istanbul, a 758-bedded referral hospital with a fully functional orthopedic oncology unit among many other different subspecialties of medicine.

Equipment used for the consulting sessions was a microscope camera (DP72; Olympus®) mounted on a single-headed microscope (Bx-51; Olympus®). This microscope camera was attached to an internet-enabled computer via a HDMI cable. A computer program that could receive the view of the microscope camera (Olympus cell Sens standard), as well as the Zoom® Desktop Application (https://zoom.us/download), were installed on the internet-enabled computer. This would allow the glass slide seen through the microscope camera to be viewed on the computer screen, which would then be screen-shared on the Zoom® Desktop Application.

Only cases that were thought to be radiologically and clinically malignant or lesions with secondary changes due to coexisting bone fractures or had a preliminary diagnosis of benign lesion but also have a few atypical changes, were selected for the telepathology consultation. One hundred bone and soft tissue slides received from the orthopedic oncology unit between March 2020 and January 2021 were reviewed by two of the hospital's musculoskeletal pathologists (hosts) together with an external pathologist (consultant) via Zoom® video conferencing. Consultation sessions ranged from 2 to 3 hours, with the residents also as participants in the Zoom® sessions. The host would screen-share the Olympus cell Sens standard program, allowing the consultant to see the same microscope view as the host. The host usually would show the whole glass slide and highlight certain important areas for diagnosis. Since the Zoom® application provides an active interaction, the consultant pathologist can choose certain important areas to zoom in or to emphasize. The consultant, the host, and also the residents or other participants can share ideas simultaneously. The study has been approved by the Ethics Committee of Istanbul Medeniyet University Training and Research Hospital and conducted in accordance with the Helsinki Principles Declaration.

Results

Tissue specimens of 100 patients sent from the orthopedic oncology unit between March 2020 to January 2021 and reviewed with the consultant pathologist, who is experienced in the pathology of bone and soft tissue tumors, via Zoom® Desktop application were evaluated. The mean age of the patients was 32. 51% of the cases were male and 49% were female. Seventy cases were bone tissue lesions and thirty were soft tissue lesions. The final pathological diagnoses of the submitted tissue specimens are summarized in Table 1. Thirty-six of the consulted cases were resection materials, forty-two of them were curettage materials and twenty-two of them were tru-cut biopsy materials. The number of slides examined per case ranged between 1 to 28. Each slide showing similar morphological features for each case was marked. The relationships of bone lesions with bone and soft tissue were assessed. Due to the decalcification process and the nature of the curettage, a large number of serial sections were required for bone tissues. The relationship with surrounding tissues was evaluated in soft tissue tumors. The presence of mitosis and necrosis was marked by the host pathologist and presented during the consultation. Subsequent immunohistochemical stains were ordered for most of the cases and for certain cases, more than one round of immunostains was needed. For cases where immunohistochemistry or special stains were requested, the mean number of slides was 10. Patient information was shared via Zoom® during the consultation session and radiological images were evaluated by both the consultant and the host via screen sharing.

Table 1. Distribution of specimen tissue types

S/No	Tissue types	Percentage	
	Bone lesions		70
1.	Undifferentiated round cell sarcoma	9	
2.	Chondrogenic tumors	17	
3.	Osteogenic tumors	11	
4.	Osteoclastic giant cell rich tumors	9	
5.	Other mesencymal tumors of bone	19	
6.	Hematopoetic neoplasms of bone	1	
7.	Fibrogenic tumors	2	
8.	Nontumoral infectious lesions	2	
	Soft tissue lesions		30
1.	Adipocytic tumors	4	
2.	Fibroblastic and myofibroblastic tumors	15	
3.	Vascular tumors	4	
4.	Tumors of uncertain differentiation	4	
5.	Peripheral nerve sheath tumors	2	
6.	Skeletal muscle tumors	1	
	Totals	100	100

Discussion

With the COVID-19 pandemic, face-to-face consultation opportunities nearly vanished, and consultations became mostly via telepathology. Several studies were published that evaluated the different telepathologic methods and their adaptation to daily practice [7,8,9]. Through the peak of the COVID-19 pandemic, telepathology thrived in Turkey too. This study reports our experience in telepathology, a relatively new practice that we have started to implement frequently recently.

The challenges we encountered were similar to those in face-to-face consultations, such as macroscopically small tissues. This led to difficulty in evaluating atypical mitosis, necrosis, and increased mitotic index on small tissue size. However, the most challenging cases were the small round blue cell tumors, for which molecular tests are of great importance in the diagnosis (e.g., Ewing's Sarcomas).

Another challenge is with especially, the cartilage tumors in which the specimen was taken by curettage and providing many samples. Lipomas also may pose a challenge especially when atypical lipomatous tumors were included in the differential diagnosis, due to their diameter/localization and the need for large numbers of samples. Small round cell tumors were interpreted as malignant small round cell tumors without further differentiation, after rhabdomyosarcoma, lymphoma, synovial sarcoma, and mesenchymal chondrosarcoma were excluded by preliminary immunohistochemical examinations. Genetic tests were requested for these in accordance with the new World Health Organization (WHO) classification of soft tissue and bone tumors [10]. Since many samples were taken in the resections of lipomatous lesions larger than 10 cm in diameter or in deep localization, it was practically not possible to show all the slides via Zoom®. For this reason, slides were evaluated, and relevant areas were marked by two pathologists and these areas were selected for consultation. The diagnosis was supported immunohistochemically with MDM2 and CDK4 stains which were usually applied before the consultation. Since not all hematoxylin and eosin (H&E) stained glasses of such lesions can be presented for consultation, it was concluded that the host pathologist should have a certain experience with bone and soft tissue lesions.

One of the cases was a multifocal malignant mesenchymal tumor with permeative spread, in which atypical osteoblastic cells were observed microscopically, it was initially evaluated as osteosarcoma. A subsequent face-to-face consultation was requested for only this case when the diagnosis of synchronous osteosarcoma was confirmed.

For a successful telepathology, the following measures are important:

- Immunohistochemical/histochemical stains or molecular tests should be adequate.

- Radiologic findings and patient clinical history should be evaluated before the consultation session.

- In cases where a large number of samples are required (e.g. atypical lipomatous tumor, cartilaginous tumors), the host pathologist should be experienced.

However, these above items do not require to be as strict as in other telepathology arrangements.

The most important advantage of dynamic nonrobotic telemicroscopy is the simultaneous interaction between the consultant, the host pathologist, and other participants [5,6]. This advantage allows dynamic nonrobotic telemicroscopy to also be used for teaching since it supports real-time engagement from both ends.

Participants were able to actively participate during teaching sessions to formulate their own approach to the diagnosis or their differentials and to learn from each other's points of view. The consultant was able to give immediate feedback, point out the strength and weaknesses of any argument, and clarify any confusing points. A further benefit is the number of participants. Since the Zoom® application allows multiple participants, residents or other pathologists can actively participate in these consulting sessions. Simplicity is an added advantage as any smartphone with internet access can log in to Zoom®. Data load was also considerably reduced compared to WSI. There was usually a short turnaround time since this method is based on simultaneous interactions and can even be used for frozen section interpretation.

Another advantage was for cases requiring large numbers of sampling, dynamic nonrobotic telemicroscopy consultation provided the possibility to view more areas than static images.

One of the major weaknesses of this method of consultation is that it does not provide free navigation capability to the consultant like in WSI and dynamic robotic telemicroscopy [5,6]. Time constrain is another disadvantage, since the consultant should evaluate and interpret the lesions instantly during the session, which may result in diagnostic errors from oversight.

Today, this method can be used comfortably for diagnosis in centers that do not have digital slide-scanning systems. It also has the potential to be used as an adjunct to the usual physical face-to-face teaching, allowing the participation of residents

and a larger number of pathologists. Telepathology is a popular concept now and will probably become more popular over the next decades. Hence, it is important for all pathologists to be familiar with these methods as they may be the major development in the field of pathology in the 21st century.

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To cite this article: Ucaner B, Cifci MS. Symptomatic Meckel's Diverticulum in Adult Patients: Our Single Center 6-Year Clinical Experience and Results. Turk J Clin Lab 2023; 4: 690-695

Research Article

Symptomatic Meckel's Diverticulum in adult patients: our single center 6-year clinical experience and results

Erişkin hastalarda semptomatik Meckel Divertikülü: Tek merkez 6 yıllık klinik deneyim ve sonuçlarımız

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Abstract

Aim: Meckel's diverticulum (MD) is an embryological remnant that results from the incomplete obliteration of the omphalomesenteric or vitelline duct after birth and it is the most common congenital anomaly of gastrointestinal tract. MD is usually asymptomatic and presents in the pediatric population. In this study, it was aimed to analyze the clinicopathological characteristics of MD, which has an important place in the differential diagnosis of acute abdomen and is difficult to diagnose in the preoperative period, in the light of current literature and to examine the results

Material and Methods: Patients diagnosed with Meckel's diverticulum and underwent surgery between January 2017 and January 2023 in the general surgery clinic were retrospectively scanned. Preoperative, intraoperative and postoperative data of the patients were examined and analyzed.

Results: Sixteen of the cases were male and 6 of them were female. Comorbid disease was present in 7 cases. Abdominal pain (72.7%) was the most common symptom, while heterotopic tissue was observed in 9 cases in histopathological evaluation. Postoperative surgical complication was observed in 6 patients and the most common complication was found to be ileus (3 patients). Mortality was observed in one patient in the postoperative period.

Conclusion: Meckel's diverticulum should always be kept in mind in the differential diagnosis of acute abdominal pain. Delay in diagnosis and going unnoticed during surgery increase mortality and morbidity rates, especially in symptomatic patients and pathologies associated with other causes of acute abdomen.

Keywords: Meckel's diverticulum, diverticulitis, acute abdomen, small bowel resection

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Doi: 10.18663/tjcl.1321925
Recevied: 03.07.2023 accepted: 27.09.2023

TJCL Volume 14 Number 4 p: 690-695

Öz

Amaç: Meckel divertikülü (MD), doğum sonrasında omfalomezenterik veya vitellin kanalın tam olmayan obliterasyonu sonucunda oluşan embriyolojik bir kalıntıdır ve gastrointestinal sistemin en sık gözlenen konjenital anomalisidir. MD genellikle asemptomatik olup; genellikle çocuk hasta popülasyonunda semptom vermektedir. Bu çalışmada; akut batının ayırıcı tanısında önemli yeri olan, preoperatif dönemde tanı konulmasının zor olduğu MD'nin güncel literatür bilgileri eşliğinde klinikopatolojik özelliklerinin analizi ve sonuçların incelenmesi amaçlandı.

Gereç ve Yöntemler: Ocak 2017 - Ocak 2023 tarihleri arasında genel cerrahi kliniğinde Meckel divertikülü tanısı alan ve ameliyat edilen hastalar retrospektif olarak tarandı. Çalışmaya 18 yaşın altındaki hastalar ve inflamatuar bağırsak hastalığı tanısı olan hastalar dahil edilmedi. Hastaların preoperatif, intraoperatif ve postoperatif verileri incelenerek analiz edildi.

Bulgular: Çalışmaya dahil edilen 22 olgunun yaş ortalaması 44,6 ± 14,6 yaş (20-74 yaş) idi. 16 olgu erkek, 6 olgu ise kadındı. Erkek/kadın oranı 2,7/1 idi. 7 olguda komorbid hastalık mevcuttu. Karın ağrısı (%72.7) en sık gözlenen semptom iken histopatolojik değerlendirmede 9 olguda heterotopik doku izlendi. Postoperatif cerrahi komplikasyon 6 hastada izlenirken en sık gözlenen komplikasyonun ileus (3 hasta) olduğu saptandı. Postoperatif süreçte bir hastada mortalite gözlendi.

Sonuç: MD akut batında ayırıcı tanıda her zaman akılda bulundurulması gereken patolojilerdendir. Tanıda gecikilmesi ve ameliyat esnasında gözden kaçması özellikle semptomatik olan hastalarda ve başka akut batın sebepleri ile ilişkilendirilebilen patolojilerde mortalite ve morbidite oranlarını artırmaktadır.

Anahtar kelimeler: Meckel divertikülü, divertikülit, akut batın, ince bağırsak rezeksiyonu

Introduction

Meckel's diverticulum (MD) is an embryological remnant, resulting from the incomplete obliteration of the omphalomesenteric or vitelline duct after birth and it is the most common congenital anomaly of gastrointestinal tract. [1]. MD contains all three layers of the intestinal wall and is thus a true diverticulum. While true diverticulum can be congenital in the gastrointestinal tract in general, false diverticulum appears as acquired lesions [2].

The "rule of 2s" is used in the diagnosis of Meckel diverticulum. According to the rule of 2s; the distance of the diverticulum from the ileocecal valve is 2 feet (60 cm). Meckel's diverticulum occurs in about 2% of the population. The length of the diverticulum is approximately 2 inches (5 cm). The majority of patients are usually under 2 years of age [3]. Microscopically, the diverticulum usually contains 2 types of heterotopic tissues; gastric and pancreatic. Approximately 2% of patients develop complications. Although it was reported that the disease is 2 times more common in men than women, in current studies this rate was stated to be observed up to 4 times. [4, 5].

MD is usually asymptomatic and usually causes symptoms in pediatric patient population. Symptoms occur as a result of complications that might develop due to the disease. The most common complications include intestinal obstruction, bleeding and diverticulitis [6, 7]. Symptoms of the disease are usually nonspecific; a significant portion of the patients were operated due to acute appendicitis and diagnosed with MD during surgery [8, 9].

In this study, it was aimed to examine and analyze the clinicopathological characteristics of patients with MD, which has an important place in the differential diagnosis of acute abdomen and is difficult to diagnose in the preoperative period, and to evaluate the results in a single-center experience in the light of current literature.

Material and Methods

Patients who were diagnosed with Meckel's diverticulum and operated in a tertiary hospital general surgery clinic between January 2017 and January 2023 were screened retrospectively. Patients under the age of 18 and patients diagnosed with inflammatory bowel disease were not included in the study. A total of 22 patients were included in the study. Medical file records, laboratory results, and pathology reports of the patients were examined. Demographic and clinicopathological characteristics of the patients were recorded. This study was approved by XXXXXXXX: University of Health Sciences Gülhane Training and Research Hospital , Clinical Research

Ethics Committee (Date: June 7, 2023, Decision No: 2023/126). This study was conducted in accordance with the World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.

Statistical Analysis

Statistical analyzes were performed using SPSS package program version 22.0. Conformity of the variables to the normal distribution was examined using visual (histograms and probability graphs) and analytical methods ("Shapiro-Wilk tests"). Continuous variables with normal distribution were presented as mean ± standard deviation; non-normal variables were reported as median (minimum-maximum value). Categorical data were shown as numbers (percentages). $p < 0.05$ was considered statistically significant.

Results

Mean age of 22 cases included in the study was 44.6 ± 14.6 years (20-74 years). 16 patients were male and 6 were female. Male/female ratio was 2.7/1. ASA scores of the cases varied between I-III. Comorbid disesases were present in seven cases (Table 1).

Table 1. Descriptive characteristics of patients

Characteristic	Number (percentage)
Age*	44.6 ± 14.6
Gender	
Male	16 (72.7)
Female	6 (27.3)
ASA	
I	9 (40.9)
II	11 (50.0)
III	2 (9.1)
BMI (kg/m2)*	26.8 ± 4.3
Smoking (+)	13 (59.1)
Alcohol (+)	7 (31.8)
Comorbidity **	7 (31.8)

*Mean ±SD
* *Comorbidity= Hypertension (n=5), Diabetes mellitus (n=2), Coronary artery disease (n=2), Chronic renal failure (n=1)
***ASA; American Society of Anesthesiologists

The most common symptoms observed in the general symptom questioning were abdominal pain (72.7%), nausea/vomiting (50.0%), constipation (31.8%) and bleeding (22.7%). All patients had symptoms associated with Meckel's diverticulum. Eight patients had Meckel's diverticulitis, 7 patients had intestinal obstruction, 5 patients had bleeding, 2 patients had invagination, and intrabadominal abscess was present in 1 patient (Table 2). In the process of diagnosing patients in the preoperative period; Ultrasonography (USG) was performed in 6 (27%) patients, computed tomography was performed in 5 (23%) patients, and both imaging methods were performed in 11 (50%) patients.

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Preoperative laboratory results of the cases are given in Table 3.

Table 3. Preoperative laboratory findings of the patients

Laboratory	Mean ± SD
CRP (mg/dL)*	28.4 (6.7-120.4)
WBC (103/µl)	14.4 ± 3.9
Neutrophil count (103/µl)	12.5 ± 3.7
Lymphocyte count (103/µl)*	1.2 (0.3-3.2)
Platelet count (103/µl)	283 ± 51
Albumin (g/dl)	4.1 ± 0.3
Hemoglobin (g/dl)	12.7 ± 1.6
Hematocrit (%)	37.7 ± 3.6
BUN (mg/dl)	32.0 ± 7.6
Creatinine (mg/dl)*	0.86 (0.56-2.15)

*Median (min-max)
**CRP; C-Reactive protein, WBC; white blood cell count, BUN; blood urea nitrogen
***Min-max: Minimum-maximum.

When the cases were evaluated as surgical method, segmental small bowel resection and side-to-side anastomosis were preferred in 12 cases, diverticulectomy was preferred in 6 cases, ileocecal resection and ileocolic end-to-side anastomosis were preferred in 2 cases, and right hemicolectomy and ileocolic end-to-side anastomosis were preferred in 2 cases. Diverting ostomy was not preferred in any operated patient. The median surgery duration was 85 minutes (65-185 minutes). In histopathological evaluation, heterotopic tissue was observed in 9 cases (gastric mucosa in 7 cases, pancreatic tissue in 1 case, and both

gastric and pancreatic tissues in 1 case). The mean Meckel's diverticulum size was 3.0 ± 0.7 cm (2.0-4.5 cm). The median length of the resected intestine was 17.5 cm (2.0-120 cm). The mean hospital stay of the cases was 3.7 ± 1.9 days (2-8 days). 8 patients were admitted to the ICU postoperatively. Five of these cases stayed in the ICU for 1 day and three of them for 2 days. 1 (12%) of the patients was followed in the ICU due to a history of immunodeficiency, 5 (62%) due to advanced age and coronary artery disease, and 2 (26%) due to poor general condition. Postoperative surgical complications were observed in 6 patients. Three patients had ileus, 2 patients had wound infection, and 1 patient had bleeding. One patient died in the postoperative period (Table 4).

Table 4. Histopathological, prognostic characteristics and postoperative results of the patients

Laboratory	Mean ± SD
Heterotopic tissue in pathology	9 (40.9)
Gastric mucosa	7 (31.8)
Pancreatic tissue	1 (4.5)
Gastric + pancreatic tissue	1 (4.5)
Meckel size (cm)	3.0 ± 0.7
Resected bowel length (cm)	17.5 (2.0-120.0)
Length of hospital stay (days)	3.7 ± 1.9
ICU hospitalization*	8 (36.4)
Length of Stay in ICU	1.3 ± 0.5
Postoperative surgical complication	6 (27.3)
Ileus	3 (13.6)
Wound site infection	2 (9.1)
Bleeding	1 (4.5)
Mortality	1 (4.5)

*ICU: Intensive care unit

According to the anamnesis taken from the patients; It was observed that patients who developed complications in the postoperative period were admitted to the hospital on average 3.5 (2-4) days after the complaints started, and patients who did not develop complications in the postoperative period were admitted to the hospital in 1.2 (1-2) days. The patients were operated on urgently on the day they were admitted to the hospital.

Discussion

MD is a true diverticulum that contains all three layers of the intestinal wall; it is the most common diverticulum in the gastrointestinal tract and should be considered in the acute abdominal differential diagnosis [2]. Although it is seen in approximately 2% of the general population, it was detected at a rate of 0.15%-4.4% in autopsy series. [10]. The disease is usually diagnosed during surgery in patients who were operated on with the suspicion of acute abdomen. People with MD develop 4% to 6.5% diverticular-associated complications during their lifetime [6]. MD is more common in men and the male/female ratio varies between 2:1 and 4:1 [4, 5]. In this study, male/female ratio was found to be approximately 2.5/1, and these ratios were observed to be similar with the literature.

In the preoperative diagnosis process of MD; One of the most basic imaging methods that can be preferred is USG. However; In cases of clinical suspicion, CT may also be preferred if necessary. CT is recommended, especially in complicated diverticula [11]. In our study; While approximately one-third of the patients only underwent USG; Approximately half of the patients underwent combined USG and CT.

The most common complications of MD have been described in various studies in the literature as intestinal obstruction (30-35%), bleeding (32-40%) and diverticulitis (17-22%) [12, 13]. In this study, 36.4% diverticulitis, 31.8% intestinal obstruction and 22.7% intestinal bleeding were reported. While the rate of patients with intestinal obstruction complications in the study was similar to the literature data, it was determined that there was no similarity to the literature data when the patient population with diverticulitis and intestinal bleeding was evaluated.

It is reported in the literature that risk of developing diverticulum-associated complications in MD is related to the length of the diverticulum and that more complications may develop in cases with a diverticulum length above 2 cm [14]. In this study, patients' mean diverticular length was calculated as 3.0 ± 0.7 cm. Presence of heterotopic tissue is another complication-associated factor. When the literature data were examined, ectopic gastric mucosa was observed at a rate of 25-50% and ectopic pancreatic tissue at a rate of 5-15%. In the presence of these two tissues together, the complication rate increases even more. In particular, it has been reported in studies that it might be associated with intestinal bleeding and ulceration [15-17]. In this study, gastric mucosa was reported in 31.8% of the patients and pancreatic tissue in 4.5% of the patients, and the results were found to be similar to the literature data.

When the literature data were investigated, postoperative complication rate was reported to be approximately 8% in patients operated for MD [18,19]. In this study, postoperative surgical complication rate was calculated as 27.3% and it was found to be higher than postoperative surgical complication rates in similar studies. We are of the opinion that late admission of the patients to the hospital and the presence of diffuse

peritonitis due to perforation in the preoperative period in some patients may be related to this result. As a matter of fact, while the average admission time to the hospital for patients who developed complications in the postoperative period was 3.5 days; The average hospital admission time for patients who did not develop complications in the postoperative period was 1.2 days. In patients who develop complications; We believe that the longer average hospital admission time and the presence of more than one comorbid disease in these patients are effective. Additionally, while no mortality was reported in case series in recent years, a patient in this study died due to septic shock associated with intraabdominal sepsis [20].

Surgical procedure to be preferred in MD is determined according to the general condition of the patient and whether the diverticulum is complicated or not. Diverticulectomy is preferred in uncomplicated diverticula [21]. Small bowel resection was performed in 12 of the patients, 6 patients underwent diverticulectomy and 2 underwent right hemicolectomy, in this study. As seen in the results of our study; Except for uncomplicated diverticulitis cases; Intestinal resection was mostly preferred for patients.

Retrospective design of the study, relatively small patient population, and heterogeneous population that may occur due to the fact that patients are not operated by a single surgeon can be considered among the main limitations.

Consequently, MD is one of the pathologies that should always be kept in mind in the differential diagnosis in acute abdomen. Delay in diagnosis and going unnoticed during surgery increase mortality and morbidity rates, especially in symptomatic patients and pathologies associated with other causes of acute abdomen. MD should always be kept in mind by clinicians in the differential diagnosis of acute abdomen.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

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To cite this article: Öztürk D, Oral S. Evre III-B meme kanserli hastalarda CEA ve CA 15-3 düzeylerinin takipteki önemi. Turk J ClinLab 2023; 4: 696-702

Araştırma Makalesi

Evre III-B meme kanserli hastalarda CEA ve CA 15-3 düzeylerinin takipteki önemi

The importance of monitoring of CEA and CA 15-3 levels in patients with stageIII-B breastcancer

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Öz

Amaç: Meme kanserinin ilk tanıda%10-15'i lokal ileri meme kanseridir. Meme kanserinde tümör belirleyicileri grubunda karsinoembriyonik antijen (CEA) ve kanser antijeni 15-3 (CA 15-3) büyük önem taşır. Biz bu çalışmada evre IIIB meme kanserlerinde tümör belirleyicilerinin hastaların takibinde lokal nüks ve uzak organ metastaz ile ilişkisini ortaya koymaya çalıştık.

Gereç ve Yöntemler: Ankara Onkoloji Hastanesi'ne 4 yıllık süre içerisinde başvuran evre IIIB meme kanseri olup neoadjuvan kemoterapi sonrası operabl olan 140 hasta retrospektif olarak incelendi.

Bulgular: Çalışmaya 140 hasta dahil edildi. Başvuru anında; 54'ünde (%38,5) CEA düzeyi normal sınırlarda iken, CA 15-3 düzeyi 72'sinde (%51,4) normal sınırlarda idi. Kemoterapi sonrası ve bu hastaların 60'ında (%69,7) CEA düzeyleri normal, 46'sında (%67,6) CA 15-3 düzeyi normal sınırlarda idi. Kemoterapi sonrası CEA düzeyindeki düşüş oranı ile CA 15-3 düzeyindeki düşüş oranı p'ye göre <0,05 olup anlamlı bulunmuştur.

Hastaların 116'sında (%82,8) CA 15-3 düzeyleri normalleşti. 3 yıllık takip süresinde lokal nüksü olan 48 hastanın 26'sında (%54,1) CEA düzeyi yüksek, 33'ünde (%68,7) CA 15-3 düzeyi yüksek, 37 'sinde (%77) ise CEA veya CA 15-3'ten herhangi birisinde yüksek değer saptandı.

Sonuç: Postoperatif takip döneminde tümör belirleyici düzeylerinde artış oluşan hastalarda 4-6 ay sonrasında lokal nüksün ve/veya uzak organ metastazının ortaya çıkması ihtimalinin anlamlı olarak arttığını bulduk.

Anahtar Kelimeler: Meme kanseri, ileri evre, CEA, CA 15-3, lokal nüks, uzak metastaz

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Doi: 10.18663/tjcl.1369602
Geliş Tarihi: 02.10.2023 Kabul Tarihi: 10.11.2023

TJCL Volume 14 Number 4 p: 696-702

Abstract

Aim: 10-15% of breast cancer is locally advancedbreastcancer at the time of initial diagnosis. Intergroup of tumor markers in breast cancer, carcinoembryonic antigen (CEA) andcancerantigen 15-3 (CA 15-3) are of great importance. Inthisstudy,we tried to reveal the relationshipbetweentumormarkers in stage IIIB breastcancerwithlocalrecurrenceanddistant organ metastasis in the follow-up of patients.

Material and Methods: 140 patientswithstage IIIB breastcancerwhowereadmitted to Ankara OncologyHospitalwithin4yearsandwereoperableafterneoadjuvantchemotherapywhere retrospectively analyzed.

Results: 140 patientswereincluded in thestudy. At the time of application, CEA levelwaswithinthe normal range in 54 (38.5%), the CA 15-3 levelwaswithinthe normal range in 72 (51.4%). Afterchemotherapyand in 60 (69.7%) of thesepatients, the CEA levelswere normal. In 46 (67.6%) of them, CA 15-3 levelwaswithin normal limits. The rate of decrease in CEA levelandthe rate of decrease in CA 15-3 levelafterchemotherapywas<0.05, and it wassignificant. CA 15-3 levelswerenormalized in 116 (82.8%) of thepatients. Duringthe 3-year follow-up period of 48 patientswithlocal recurrence, 26 (54.1%) had high CEA levels, 33 (68.7%) had high CA 15-3 levels, and 37 (77%) had high CEA or CA 15-3.

Conclusion: Wefound that the probability of occurrence of localrecurrenceand / or distant organ metastasisincreasedsignificantlyafter 4-6 months in patientswhosetumor marker levelswereincreased in thepostoperativefollow-upperiod.duringthepostoperativefollow-upperiod.

Keywords: Breastcancer, advanced stage, CEA, CA 15-3, local recurrence, distant metastasis

Anahtar Kelimeler: Meme kanseri, ileri evre, CEA, CA 15-3, lokal nüks, uzak metastaz

Giriş

Kadınlarda görülen kanserlerin %31'ni oluşturan meme kanseri en sık görülen kanser türlerindendir (1). Yaşamları boyunca her 100 kadından 8'inde meme kanserine yakalanma ihtimali olduğu ve dünyada her yıl 500.000'e yakın kadının hayatını bu nedenle kaybettiği hesaplanmaktadır (2).

Tanı yöntemlerindeki gelişmelere, kitle taramalarına, toplumun ve hekimlerin meme kanseri konusunda bilgilerinin artmış olmasına rağmen ilk tanı anında tüm meme kanserlerinin %10-15'i lokal ileri meme kanseridir. Evre IIIB meme kanserleri; memede lokal olarak aşırı büyümüş ve gecikmiş tümörleri (T4) veya küçük tümör olmasına rağmen aynı taraftaki mammariainterna lenf bezlerine metastazı (N) içeren heterojen bir kanserdir.

Evre IIIB meme kanserli hastaların büyük bir kesiminin uzak metastaz nedeniyle ölümleri, lokorejyonel tedavi dışında başka seçenekleri aramayı gündeme getirmiştir. Bu amaçla primer kemoterapi uygulamaya konulmuştur. Neoadjuvan kemoterapisinin başlıca amacı tümör yükünün azaltılması, lokal kontrolün sağlanması ve inoperabl olan tümörlerde evre düşümü sağlanarak operabl hale getirilebilmesidir (3).

Kanserde tümör belirleyicilerinin rolü çok önemlidir.Bu değerler tedavi öncesi tümör yükünü, tedaviye yanıtın takibini, nüks ve metastazı göstermesi açısından önemlidir. Meme kanserinde tümör belirleyicileri grubunda tümöre bağlı antijenler olan karsinoembriyonik antijen (CEA) ve kanser antijeni 15-3 (CA 15-3) büyük önem taşır (4).

Tedavi süresince ve tedaviye yanıtın belirlenmesinde CEA ile CA 15-3 tümör belirleyicilerinin birlikte değerlendirilmeleri daha sağlıklı sonuç vermektedir (5). Bu yüzden meme kanserinde CEA ve CA 15-3 tümör belirleyicilerinin birlikte kullanılması hastaya mali külfet yüklese bile klinikte tanıya ve tedaviye kolaylık sağlamaktadır.

Gereç ve Yöntemler

Bu çalışma Ankara Onkoloji Hastanesi 2002-742990 sayısı ile Ocak 1995-Aralık 1998 yılları arasında başvuran evre IIIB meme kanseri olup neoadjuvan kemoterapi sonrası operabl olan 140 hasta retrospektif olarak incelendi. Bu hastalar uygulanan tedavi prosedürü sonrası tümör belirleyicilerinin düzeyleri, lokorejyonelnüks, uzak organ metastazı açısından değerlendirildi.

Hastaların hepsinde doku tanısı İnvazivduktal karsinom idi. Tanı sonrası tüm hastalarda rutin tümör belirleyicileri Ankara Onkoloji Hastanesi Nükleer Tıp bölümünde; ImmuliteAutomated Analyzer (I.A.A) yöntemiyle çalışıldı. Bu yöntemde CA 15-3 için BR-MA test üniti, CEA için ise CEA test üniti kullanıldı. Bu testlerde kabul edilen referans aralıkları;

• CEA (sigara içen kadın): 0-4.9 ng/ml

• CEA (sigara içmeyen): 0-2,5 ng/ml

• CA 15-3: 7,5-53 U/ml şeklindedir.

Uzak organ taramalarında metastaz saptanmayan T4 tümörler evre IIIB olarak kabul edilip 3 kür evre düşümü amacıyla neoadjuvan kemoterapi verildi. Verilen kemoterapi protokolleri antrasiklinli antibiyotik içeren kombine kemoterapi şeklindeydi (FEC veya FAC). FEC ve FAC kemoterapi protokolleri 1 gün süreliydi ve kürler arası zaman 21 gün idi.

FEC: 5- flourourasil 500mg/m2/gün

Epirubisin 60mgjm"/gün

Siklofosfamid 500mg/m 2/gün

FAC: 5-flourourasil 500mg/m 'gün

Adriamisin 60mg/m2igün

Siklofosfamid

Hastalardaneoadjuvan kemoterapi sonrası Tümör belirleyicilerine bakıldı. Fizik muayene ile evre düşümü tespit edilen 140 hastaya modifiye radikal mastektomi yapıldı. Bu hastalarda preoperatif tümör belirleyicilerine bakıldı.

Operasyon sonrası dönemde hastalara adjuvan olarak 3 kür FEC veya FAC kemoterapisi uygulandı. Postoperatif 3 kür kemoterapi sonrasında meme flepleri, göğüs ve aynı taraf internalmammaria lenf bezlerine 5000-6500cGy, aynı taraf aksilla ve supraklavikuler bölgeye 4500-6500 cGy, 5-6,5 haftalık sürelerde fraksiyone dozlar halinde radyoterapi uygulandı. Postoperatif takip döneminde hastalar 3'er ay ara ile rutin kontrollere çağrıldı. Rutin kontrollerde; fizik muayene ile kan biyokimyasına ve tümör belirleyici düzeylerine bakıldı. Ek olarak 6 ayda bir tüm abdomen ultrasonografisi ve yılda 1 kez de tüm vücut kemik sintigrafileri yapıldı. 2. yıldan itibaren 6 aylık periyotlar şeklinde kontrolleri yapıldı.

İstatistiksel yöntem

Bu çalışmada tüm parametrelerin istatistiksel analizleri SPSS V. 10 paket programı ile yapılmıştır. 140 hastaya ait verilerin dağılımları alınmıştır. Dökümlerde κ^2 ve Fischer'sExact Testi kullanılmıştır.

Bulgular

140 hastanın tanı anındaki yaş ortalaması 53,4 idi. Çalışmamıza dahil olan 140 hastanın; 64'ü (%45) premenopozal ve 76'sı (%55) postmenopozal idi (Tablo-I).

Tablo1. Hastalarda tümör markerlarının oranları ve kemoterapi sonrasındaki değişimleri

	Hasta sayısı (140)	%
CEA ve CA15-3 NORMAL	38	27,1
CEA normal olanlar	54	38,5
CEA yüksek olanlar	86	61,5
CA 15-3 normal olanlar	72	51,4
CA 15-3 yüksek olanlar	68	48,6
CEA ve CA15-3 yüksek olanlar	62	44,2
3 KÜR KT SONRASI CEA normal olanlar	114	81,4
3 KÜR KT SONRASI CEAyüksek olanlar	26	18,6
3 KÜR KT SONRASI CA 15-3 normal olanlar	118	84,2
3 KÜR KT SONRASI CA 15-3 yüksek olanlar	22	15,8

Çalışmamızda olan 140 hastanın başvuru anında; 54'ünde (%38,5) CEA düzeyi normal sınırlarda iken 86'sında (%61,5) normalden yüksek bulunmuştur. Çalışmamızda olan 140 hastanın başvuru anında; 38'inde (%27,1) hem CEA hem de CA 15-3 düzeyleri normal sınırlarda iken, 62'sinde (%44,2) hem CEA hem de CA 15-3 düzeyleri yüksek olarak bulunmuştur. 3 kür FEC veya 3 kür FAC kemoterapisi uygulanıp evre düşümü sağlanarak operasyona uygun hale gelen 140 hastanın preoperatif CEA düzeylerine bakıldığında; 114'ünde (%81,4) normal sınırlarda iken 26'sında (%18,6) normalden yüksek bulunmuştur. 3 kür FEC veya 3 kür FAC kemoterapisi uygulanıp evre düşümü sağlanarak operasyona uygun hale gelen 140 hastanın preoperatif tümör belirleyici düzeylerine bakıldığında; 95'inde (%67,8) hem CEA hem de CA 15-3 düzeyleri normal sınırlarda iken, 18'inde (%12,8) hem CEA hem de CA 15-3 düzeyleri yüksek olarak bulunmuştur.

Hastaların başvuru anındaki tümör belirleyici düzeyleri yüksek olanlarda 3 kür neoadjuvan FEC veya FAC kemoterapisini takiben bakılan preoperatif tümör belirleyici düzeyleri normal] sınırlarda ölçüden hastaların değerlendirilmesi

A* : Başvuru anındaki CEA yüksek olan hasta sayısı 86

B** : Preoperatif CEA normal olan hasta sayısı 60

p değeri*** : Başvuru anı ile preoperatif CEA için p değeri <0,05

C**** : Başvuru anındaki CA 15-3 yüksek olan hasta sayısı 68

D***** : Preoperatif CA 15-3 normal olan hasta sayısı 46

p değeri******: Başvuru anı ile preoperatif CA 15-3 için p değeri <0,05

140 hastanın 86'sında başvuruda CEA yüksek bulunmuştur. Bu hastalar evre düşümü için kemoterapi aldı ve bu hastaların 60'ında (%42,8) CEA normal olarak bulundu. Aynı şekilde hastaların 68'inde başvuru anındaki CA 15-3 yüksek iken kemoterapi sonrası 46'sında (%32,8) CA 15-3 normal sınırlarda idi.

Kemoterapi sonrası CEA düşüş oranı ile CA 15-3 düşüş oranı p'ye göre <0,05 olup anlamlı bulunmuştur. Bu kısımdaki amacımız kemoterapi sonrası tümör yükünde azalma meydana geldikten sonra bu durumun tümör belirleyicilerine nasıl yansıdığını göstermeye çalışmaktı. Başvuru anında CEA yüksek olup neoadjuvan kemoterapi sonrası CA 15-3 normal olanlardakine oranı kıyaslandığında p<0,05 olup CA 15-3'ün CEA'ya göre daha anlamlı olduğunu göstermektedir.

Hastalara postoperatif dönemde 3 kür daha FEC ve FAC kemoterapi ve radyoterapi uygulandı. Hastalar postoperatif dönemde tedavi sonrasında kontrole çağrıldı ve tümör belirleyicileri çalışıldı (Tablo-2).

Tablo2. Tümör belirleyicilerinin başvuru anı, preoperatif ve postoperatif dönemlerdeki düzeylerine göre hasta dağılımı

	Başvuru	Preoperatif	Postoperatif	
CEA	Normal	54(%38,5)	114(%81,4)	92(%65,7)
	Yüksek	86(%61,5)	26 (%18,6)	48(%34,3)
CA 15-3	Normal	72(%51,4)	118(%84,2)	116(%82,8)
	Yüksek	68(%48,6)	22(%15,8)	24(%17,2)

140 hastanın başvuru anında tümör belirleyicileri yüksek olanlardan neoadjuvan kemoterapi ile evre düşümü sağlandıktan sonra opere edilip, postoperatif dönemde kemoterapi ve radyoterapi aldıktan sonra tümör belirleyicileri normal sınırlarda olan hastaları incelemeyi uygun gördük. Bu grup hastalar retrospektif olarak incelendi. 3 yıllık takip süremizde bu hastalar; lokal nükslerine, uzak organ metastazlarına ve her iki durumun beraber ortaya çıkmasına göre gruplandırıldı. Daha sonra bu 3 durumun her birinin nüks veya metastaz ortaya çıktıktan 4-6 ay öncesindeki tümör belirleyicileri retrospektif olarak incelendi.

Postoperatif dönemde hastalar 3 yıl boyunca takip edildi. Takip döneminde 48 hastada sadece lokal nüks, 24 hastada uzak organ metastazı ve 18 hastada ise hem lokal nüks hem de uzak organ metastazı eş zamanlı olarak tespit edildi.

Lokal nüks gelişmiş olan hastaların 4-6 ay önceki tümör belirleyicileri incelendi. Lokal nüksü olan 48 hastanın 26'sında (%54,1) CEA yüksek, 33'ünde (%68,7) CA 15-3 yüksek, 17 'sinde (%35,3) ise CEA ve CA 15-3'de yüksek değer saptandı.

Uzak organ metastazı gelişmiş olan hastaların 4-6 ay önceki tümör belirleyicileri incelendi. Uzak organ metastazı olan 24 hastanın 14'ünde (%58,3) CEA düzeyi yüksek, 18'inde (%75) CA 15-3 düzeyi yüksek 8'inde (%33,3) ise CEA ve CA 15-3'de yüksek değer saptandı.

Lokal nüks ve uzak organ metastazı aynı zamanda ortaya çıkan hastaların 4-6 ay önceki tümör belirleyicileri incelendi. Lokal nüks ve uzak organ metastazı aynı zamanda meydana gelen 18 hastanın 11'inde CEA (%61,1),14'ünde (%77,7) CA 15-3 yüksek, 15'inde (%83,3) ise CEA veya CA 15-3'den herhangi birisinde yüksek değer saptandı.

Hastaların dağılımı Tablo 3'te birarada gösterilmiştir (Tablo-3).

Tablo 3. Hastaların lokal nüks, uzak organ metastaz ve lokal nüks ile uzak organ metastazın bir arada görüldüğü dönemlerdeki tümör belirleyici düzeylerindeki yüksekliğin tümör belirleyici tipine göre hastalardaki dağılımı.

	Lokal nüks (n=48)		Uzak metastaz (n=24)		Lokal nüks ve uzak metastaz (n=18)	
	n	%	n	%	n	%
CEA yüksek olanlar	26	54,1	14	58,3	11	61,1
CA 15-3 yüksek olanlar	33	68,7	18	75	14	77,7

Hastaların lokal nüks ve/veya uzak metastaz geliştiği andan 4-6 ay önce tümör belirleyicilerinin düzeylerinde anlamlı olarak artış olduğu görüldü. Tümör belirleyici tipine göre de anlamlı fark olduğu görüldü. Ayrıca her iki tümör belirleyicisinden herhangi birinde yükseklik olması durumu da anlamlı bulundu. Fakat bunun yanında lokal nüks olan hastaların 4-6 ay öncesindeki tümör belirleyici düzeyleri arasında anlamlı bir fark bulunmadı (p>0,05). Yani tümör belirleyici düzeylerdeki artış 4-6 ay sonra ortaya çıkacak olan lokal nüks veya uzak organ metastazı hakkında fikir vermektedir ama tümör belirleyici düzeyindeki yüksekliğe bakılarak hangisinin oluşacağı tahmin edilememektedir (Tablo 4).

Tablo 4. CEA düzeyi değişikliklerine göre sağkalım oranları

	n	3 yıllık sağkalım	%
Tanı anında N, post-op N CEA	40	30	75
Tanı anında N, post-op Y CEA	14	9	64,2
Tanı anında Y, post-op N CEA	38	28	73,6
Tanı anında Y, post-op Y CEA	48	30	62,5
CA 15-3 değişikliklerine göre Tam anında N, post-op N CA 15-3	60	43	71,6
CA 15-3 değişikliklerine göre Tanı anında N, post-op Y CA 15-3	12	7	58,3
CA 15-3 değişikliklerine göre Tanı anında Y, post-op N CA15-3	26	17	65,3
CA 15-3 değişikliklerine göre Tanı anında Y, post-op N CA15-3	42	26	61,9
N: Normal, Y: Yüksek			

Başvuruda CEA düzeyleri normal olup tedavi sonrasında da normal sınırlarda kalan hastaların 3 yıllık sağkalımı %75

bulunmuştur. Başvuruda CEA düzeyleri normal olup, tedavi sonrası yüksek olanlarda ise 3 yıllık sağkalım oranı %64,2 olarak bulunmuştur. Yine hastalardan başvuruda CEA yüksek olup tedavi sonrası CEA oranları normal sınırlarda olanlarda 3 yıllık survi %73,6 bulunmuştur. Tanı anında CEA yüksek olup tedavi sonrası da yüksek kalanlarda ise 3 yıllık survi oranı % 62,5 olarak bulunmuştur. Gruplar arasında istatistiksel fark bulunamadı (p>0,05).

Başvuruda CA 15-3 normal olup tedavi sonrasında da normal kalan hastaların 3 yıllık sağkalımı %71,6 bulunmuştur. Başvuru anında CA 15-3 normal olup, tedavi sonrası yüksek olanlarda ise 3 yıllık sağkalım oranı %58,3 olarak bulunmuştur. Yine hastalardan başvuruda CA 15-3 yüksek olup tedavi sonrası CA 15-3 oranları normal olanlarda 3 yıllık survi %65,3 bulunmuştur. Tam anında CA 15-3 yüksek olup tedavi sonrası da yüksek kalanlarda ise 3 yıllık survi oram %61,9 olarak bulunmuştur. Gruplar arasında istatistiksel fark bulunamadı (p>0,05).

Tartışma

Tümör belirleyicileri klinik uygulamada kanser tanısının konmasından ziyade tümör yükünü, tedaviye yanıtın takibini, nüksü ve rezidü dokuyu göstermesi açısından önemlidir(6-7). Çalışmamızdapostoperatif dönemde nüks ve uzak organ metastazlarında tümör belirleyicilerinin erken dönemde yükselişlerini gözlemleyerek daha erken tanıda yardımcı parametreler olabileceği konusunu irdeledik.

CEA. CA 15-3. beta-2 mikroglobulin, CRP, doku polipeptit antijen gibi birçok tümör belirleyicisi meme kanserli hastalarda incelenmiştir, fakat hunlardan en çok CEA ve CA 15-3 klinikle kullanım alanı bulmuştur (8-9).

Seçilen hasta grubumuzu evre IIIB meme kanserli hastalar oluşturmaktadır. Meme kanserinde evre IIIB operabilite-inoperabilite arasında ince bir sınır olan dönem olduğu için bu hastalarda tedavi öncesi ve sonrası tümör belirleyici düzeylerindekideğişimlere bakarak hastalarıntedaviye cevaplarını, tedavi sonrası oluşabilecek nüks ve organ metastazları öncesinde yardımcı olabileceğini düşündük.

Konunun daha iyi anlaşılması için başvuruda tümör belirleyicileri yüksek olan grubu seçtik. Bunlara uygulanan 3 kür kemoterapi sonrası tümör belirleyicileri tekrar gözlemledik. Buradaki amacımız kemoterapinin tümör yükünü azaltıp azaltmadığını ve bu durumun tümör belirleyici düzeyi ile korelasyonunu araştırmaktı. Başvuru anında tümör belirleyici düzeyi yüksek olan hastaların neoadjuvankemoterapi sonrasında CEA%69,7'sinde normal sınırlarda bulunurken, CA 15-3 ise %67,6'sında normal sınırlarda tespit edilmiştir. Tümör belirleyicilerindeki düşüş kemoterapi etkisiyle tümör yükündeki azalma ile orantılı olmaktadır. Literatürde ise kemoterapi sonrası tümör belirleyicilerdeki düşüş ortalama %63 oranında bulunmuştur (9-10-11).

Literatürde tedavi sonrası tümör belirleyicilerin düşüş meydana gelip takipte tutulan hastaların tümör belirleyicilerinde olan ikinci bir yükseliş hastalığın nüks ettiğini veya çok kısa zaman içerisinde klinik ve radyolojik olarak belirgin olmayan nüksün ortaya çıkacağını gösterdiği belirtilmektedir (10-12). Lokal nüksü olup retrospektif olarak incelenen hastaların %45'inde 4-6 ay öncesine ait CEAartışıgörülmüştür(10-12-13). Bizim çalışmamızda ise lokal nüks gelişen hastaların %54,1'de 4-6 ay öncesine ait CEA bakıldığında yüksekliğin olduğu görülmüştür. Aynı şekilde CA 15-3 bakıldığında ise hastaların %63'ünde yüksek iken (10-11-12), çalışmamızda bu durum hastaların %68,7'sinde görülmüştür. Yine literatürde her iki tümör belirleyicisinden herhangi birinde 4-6 ay öncesinde görülen artış hastaların %72'sinde mevcut iken (8-10-14), çalışmamızda ise bu oran %77 olarak bulunmuştur.

Literatürde uzak organ metastazı olup retrospektif olarak incelenen hastaların %52'sinde 4-6 ay öncesine ait CEA artışı görülmüştür (9-12-15). Bizim çalışmamızda ise uzak organ metastazı gelişen hastaların %58,3'ünde 4-6 ay öncesine ait CEA bakıldığında yüksekliğin olduğu görülmüştür. Aynı şekilde literatürde CA 15-3 durumuna bakıldığında ise hastaların %69'unda yüksek iken (9-12) bizim çalışmamızda bu durum hastaların %75'inde görülmüştür. Literatürde her iki tümör belirleyicisinden herhangi birinde 4-6 ay öncesinde görülen artış hastaların %77'sinde mevcut iken (5-12),bizim çalışmamızda ise bu oran %83,3 olarak bulunmuştur(21).

Literatürde lokal nüks ve uzak organ metastazı olup retrospektif olarak incelenen hastaların %63'ünde 4-6 ay öncesine ait CEA düzeylerinde artış görülmüştür (6-12)Bizim çalışmamızda ise lokal nüks gelişen hastaların %61,1'inde 4-6 ay öncesine ait CEA düzeylerine bakıldığında yüksekliğin olduğu görülmüştür. Aynı şekilde literatürde CA 15-3 durumuna bakıldığında ise hastaların %79'da yüksek iken (6-12-16), bizim çalışmamızda bu durum hastaların %77,7'sinde görülmüştür. Literatürde her iki tümör belirleyicisinden herhangi birinde 4-6 ay öncesinde görülen artış hastaların % 81'inde mevcut iken (10-11), bizim çalışmamızda ise bu oran % 83,3 olarak bulunmuştur. (19-20)

Literatürde lokal nüks veya uzak metastaz olan hastaların CEA ve CA 15-3 düzeylerindeki artışlar birbirleriyle mukayese edildiğinde CA 15-3 düzeyi CEA değerine göre daha anlamlı

bulunmuştur (11-15). Bizim çalışmamızdaki sonuçlarda da CA 15-3'ün CEA'ya oranla artışı daha fazla bulunmuş olup sonuçlar istatiksel olarak anlamlıdır. Ayrıca CEA veya CA 15-3'ten herhangi birisindeki artış lokal nüks ve uzak organ metastazlarında bakıldığında, bu tümör belirleyicilerinin tek tek bakılmasına oranla anlamlı bulunmuştur ve bu durum da literatür ile uyumludur (11-17-18).

Sonuç

Meme kanseri, kadınlarda en sık görülen kanserlerden biri olmaya devam etmekte ve görülme sıklığı giderek artmaktadır. Tümör belirleyicilerinin keşfinden günümüze çok aşamalar geçilmiş ama hala tam anlamıyla sonuç veren tümör belirleyicileri geliştirilememiştir. Tümör belirleyicileri tanı konulmasından ziyade tedavinin başarısını ve tedavi sonrası olası relapsları hakkında fikir verebilmektedir.

Bu düşünceden yola çıkarak biz de çalışmamızda özellikle operabilite-inoperabilite sınırında hassas bir nokta olan evre IIIB meme kanserli hastalarda tümör belirleyicilerinin önemini ortaya koymaya çalıştık. Evre IIIB meme kanserine yaklaşımda yaklaşım olarak önce 3 kür neoadjuvan kemoterapiyi takiben evre düşümü sağlanan hastalarda modifiye radikal mastektomi prosedürü tarzında operasyon yapıldı. Hastalarımıza postoperatif dönemde 3 kür daha adjuvan kemoterapi ve radyoterapi verip takibe aldık. Bu evreye sahip hastalarda lokal nüksün ve uzak organ metastazının gelişme ihtimalinin fazla olması nedeniyle sıkı takip gerektiğini göz önünde bulundurup 3'er ay aralıklarla hastaları kontrollerden geçirdik. Her dönemde hastaların yüksek risk grubunda olmaları nedeniyle tümör belirleyici düzeylerine baktık. Yaptığımız çalışmada literatür ile uyumlu olarak postoperatif takip döneminde tümör belirleyici düzeylerinde artış oluşan hastalarda 4-6 ay sonrasında lokal nüksün ve/veya uzak organ metastazının ortaya çıkması ihtimalinin anlamlı olarak arttığını bulduk. Ayrıca tümör belirleyicilerinin düzeyinin seyrine göre sağkalım oranlarını da araştırdık. Araştırma sonucunda tümör belirleyici seyrindeki değişikliklerin sağkalım oranlarında anlamlı bir fark oluşturmadığını bulduk.

Gelecekte tümör belirleyicilerin sensitivite ve spesifitelerinin artması halinde kanser hastalarını daha erken evrelerde yakalayabilecek böylece daha fazla fayda getirebilecek tedavi yaklaşımları olabilecektir. Bu sayede kanserli hastaların tedavisinde daha yüz güldürücü sonuçlar elde edilebileceğini umut ediyoruz.

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To cite this article: Yakupoglu A. Correlation of ultrasound and cytological diagnosis of thyroid nodule using TIRADS and Bethesda classifications. Turk J Clin Lab 2023; 4: 703-708

Research Article

Correlation of ultrasound and cytological diagnosis of thyroid nodule using TIRADS and Bethesda classifications

TIRADS ve Bethesda sınıflandırmaları kullanılarak tiroid nodülünün ultrason ve sitolojik tanısının korelasyonu

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Abstract

Aim: The objective of this study was to evaluate the compatibility between the two diagnostic methods used in the initial evaluation of individuals with a thyroid nodule, the TIRADS and Bethesda systems.

Material and Methods: Between January 2020 and December 2022, FNA biopsies performed by a single interventional radiologist on 414 patients with thyroid nodules under US guidance were retrospectively reviewed. Demographic information of the patients, size of the nodules, echogenicity, TIRADS and Bethesda scores were recorded and analyzed.

Results: The mean age of the study population was 50.4 ± 14.2 years and the majority were female patients (74.9%). When thyroid nodules were classified according to TRIADS criteria, it was TIRADS TR2 in 29 (7%) patients, TIRADS TR3 in 147 (35.5%) patients, TR4 in 166 (40.1%) patients, and TR5 in 72 (17.4%) patients. The probability of malignant FNAC (Bethesda Class V and Class VI) in TIRADS classes 2, 3, 4, and 5 was 0%, 3.4%, 31.3%, and 66.7%, respectively. The probability of a benign FNAC (Bethesda Class II) in TIRADS category 2 was 100%, while for TIRADS classes 3, 4 and 5 it was 81.6%, 34.9% and 25%, respectively.

Conclusion: Our study shows a good correlation between the Bethesda Classification of thyroid nodule FNAC and thyroid ultrasound reporting using the TIRADS classification. Correct interpretation of the two findings helps the clinician reduce the risk of unnecessary invasive procedures in patients who are unlikely to demonstrate thyroid cancer, while facilitating the identification of patients at high risk of cancer.

Keywords: Fine-needle aspiration cytology, Thyroid nodules, TIRADS, Bethesda, Ultrasonography

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Recevied: 23.08.2023 accepted: 03.11.2023

Öz

Amaç: Tiroid nodülü olan bireylerin ilk değerlendirmesinde kullanılan iki tanı yöntemi TIRADS ve Bethesda sistemleri arasındaki uyumu değerlendirmektir.

Gereç ve Yöntemler: Ocak 2020 ve Aralık 2022 yılları arasında tek bir girişimsel radyolog tarafından US kılavuzluğunda yapılan 414 tiroid nodüllü hastaya yapılan İİA biyopsileri retrosepektif olarak incelendi. Hastaların demografik bilgileri, nodüllerin boyutu, ekojenitesi ve kontur durumu, TIRADS ve BETHESDA skorları kaydedildi ve analiz edildi.

Bulgular: Çalışma popülasyonunun ortalama yaşı 50.4 ± 14.2 idi ve çoğunluğu kadın hastalardı (%74.9). Hastaların ortalama nodül boyutu 18.36 ± 12.96 mm olarak ölçüldü. Tiroid nodülleri TIRIADS kriterlerine göre sınıflandırıldığında 29 (%7) hastada TIRADS TR2, 147 (%35.5) hastada TIRADS TR3, 166 (%40.1) hastada TR4 ve 72 (%17.4) hastada TR5 idi. TIRADS 2, 3, 4 ve 5 sınıflarında Bethesda Class V ve Class VI olasılığı sırasıyla %0, %3.4, 31.3 ve %66.7 idi. TIRADS kategori 2'de Bethesda Sınıf II olasılığı %100 iken, TIRADS 3, 4 ve 5 sınıfları için sırasıyla %81.6, %34.9 ve %25 idi.

Sonuçlar: Çalışmamız, tiroid nodülü İİAS'nin Bethesda Sınıflandırması ile TIRADS sınıflandırmasını kullanan tiroid ultrason raporlaması arasında oldukça iyi bir korelasyon olduğunu göstermektedir. İki bulgunun doğru yorumlanması, klinisyenin tiroid kanseri gösterme olasılığı düşük olan hastalarda gereksiz invaziv prosedür riskini azaltmasına yardımcı olurken, yüksek kanser riski taşıyan hastaların belirlenmesini kolaylaştırır.

Anahtar Kelimeler: İnce iğne aspirasyon sitolojisi, Tiroid nodülleri, TIRADS, Bethesda, Ultrasonografi

Introduction

Thyroid nodules are defined as lesions of the thyroid gland that are radiologically different from the surrounding parenchyma [1]. The prevalence of thyroid nodules varies between 4% and 7% by palpation alone, and it increases to 20% and 76% in the adult population using imaging modalities such as high-resolution ultrasonography [2-4]. Nodules detected on radiographic examinations are called "thyroid incidentalomas" [2-5]. The main concern in the evaluation of thyroid nodules is the possibility of malignancy. Therefore, the distinction between benign and malignant nodules is of great importance in clinical evaluation. When invasive procedures are evaluated, the mean prevalence of malignancy rates in thyroid nodules worldwide ranges from 4.0% to 6.5% [6,7]. The incidental diagnosis of thyroid nodules is increasing in parallel with the widespread use of ultrasound, fine needle aspiration cytology (FNAC), and developments in 18 FDG-PET imaging.

Some evidence-based guidelines have been developed for the evaluation of patients presenting with thyroid nodules. The American Thyroid Association (ATA) recommends thyroid US along with cervical lymph node examination in patients with suspected thyroid nodules [8]. Similarly, the National Comprehensive Cancer Network (NCCN) recommends lateral neck compartment ultrasound along with thyroid US in all patients with suspected thyroid nodules. recommends that lymph nodes be evaluated as well. It is a neck mass detected incidentally [9]. The clinical purpose of thyroid USG is to detect nodules with a high risk of thyroid cancer. The presence of findings such as microcalcifications, irregular edges, and significant hypoechogenicity indicates a higher risk of malignancy. Current guidelines divide thyroid nodules into risk categories based on the above-mentioned suspicious features and recommend biopsy.

Thyroid Imaging Reporting and Data Systems (TIRADS) is a classification system based on ultrasound characteristics proposed by Horvath et al. TIRADS Scoring is determined by ultrasound findings in five categories. Ultrasound features assessed for each nodule were composition (solid, cystic, mixed), echogenicity (hyperechoic, isoechoic, hypoechoic), margins (well defined with or without halo sign, microlobulated, ill-defined, irregular), presence of calcification (microcalcification, macrocalcification), and shape of the nodule (round, oval). The higher the cumulative score and the TR (TI-RADS) level increase the probability of malignancy. The findings in each category were detailed in the American College of Radiology (ACR) committee's in 2015 [10]. The primary aim of TIRADS is to improve patient management and cost-effectiveness by avoiding unnecessary fine needle aspiration (FNA) biopsies in patients with thyroid nodules [11]. This system also unifies the language among radiologists and endocrinologists all over the world.

In the classification of thyroid nodules, sensitivity and specificity values for TIRADS have been reported as 88% and 49%, respectively [12]. However, its clinical use is still very limited and its application in clinical practice is questioned. FNA biopsy is the most accurate method for detecting malignancy and is an essential part of current thyroid nodule evaluation. The Bethesda System is a standard reporting system based on six criteria used to classify thyroid FNA biopsy results and includes recommendations for clinical management. A recent

meta-analysis evaluated the validity of the Bethesda reporting system and found 97% sensitivity, 50.7% specificity, and 68.8% diagnostic accuracy; negative and positive predictive values were 96.3% and 55.9%, respectively [13,14]. Although both ultrasonography (US) and FNA biopsy are commonly recommended procedures for examining patients with thyroid nodules, the compatibility between the two methods is still controversial. In conclusion, the aim of this study was to evaluate the compatibility between two diagnostic methods (TIRADS and Bethesda systems) used in the initial evaluation of individuals with thyroid nodules.

The Ankara Bilkent City Hospital Clinical Researches Ethics Committee, (No: E2-23-3988, Date: 25/04/2023) has authorized all techniques used in this work. The authors declare that they adhered to the ethical norms of the 1975 Helsinki Declaration, as revised in 2008.

Material and Methods

The study included 414 consecutive patients who were referred to the interventional radiology department of our hospital from the departments of endocrinology, internal medicine, or general surgery with the diagnosis of nodular or non-nodular "thyroid dysfunction" for neck imaging and who underwent thyroid biopsy after detecting a suspicious thyroid nodule in ultrasonography between January 2020 and December 2022. Patients with normal thyroid imaging (TIRADS 1), Graves-Basedow-associated hyperthyroidism, patients with toxic thyroid nodular disease, and patients with a history of surgically resected thyroid cancer were not included in the study.

Ultrasonography reports and cytology results of all patients were reviewed retrospectively using the hospital data system. Demographic information such as age and gender, ultrasound characteristics such as size and echogenicity of nodules, lesion structure, and pathological results were recorded.

Sonographic evaluation

All procedures were performed using a high-resolution ultrasound device (Acuson Juniper, Siemens Healthineers, Erlangen, Germany) with a 6.7-10 MHz linear transducer probe. TIRADS classification based on sonographic features was performed by an experienced radiologist prior to FNA cytology (Table 1).

Table 1. Thyroid imaging reporting and data system (TIRADS) and the Bethesda System for Reporting Cytopathology	
TIRADS 1: Normal thyroid gland.	I. Nondiagnostic or unsatisfactory.
TIRADS 2: Benign conditions (0% malignancy).	Cyst fluid only.
TIRADS 3: Probably benign nodules (5% malignancy).	Virtually acellular specimen.
TIRADS 4: Suspicious nodules (5–80% malignancy rate). A subdivision into 4a (malignancy between 5 and 10%) and 4b (malignancy between 10 and 80%) was optional.	Other (obscuring blood, clotting artifact, etc.).
TIRADS 5: Probably malignant nodules (malignancy >80%).	II. Benign.
TIRADS 6: Category included biopsy proven malignant nodules	Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.).
	Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context.
	Consistent with granulomatous (subacute) thyroiditis.
	III. Atypia of undetermined significance/follicular lesion of undetermined significance.
	IV. Follicular neoplasm/"suspicious" for follicular neoplasm. Specify if Hürthle cell type.
	V. Suspicious for malignancy.
	Suspicious for papillary carcinoma.
	Suspicious for medullary carcinoma.
	Suspicious for metastatic carcinoma.
	Suspicious for lymphoma.
	VI. Malignant.
	Papillary thyroid carcinoma.
	Poorly differentiated carcinoma.
	Medullary thyroid carcinoma.
	Undifferentiated (anaplastic) carcinoma.
	Squamous cell carcinoma.
	Carcinoma with mixed features.
	Metastatic.

FNAC procedure

Informed consent for the procedure was obtained from all patients. FNAC was performed by an experienced interventional radiologist under US guidance. FNAC was not performed for completely cystic lesions. An immediate sample adequacy assessment was performed by a cytopathologist, and smears were interpreted and categorized according to the Bethesda system by an experienced pathologist.

All personal data were confidential and managed exclusively by the principal investigator, according to the legal standards on the confidentiality of the medical record and adhering to the rules of the Institutional Review Committee of Human Ethics (reference number: 05.01.2023- 70).

Results

A total of 414 patients who underwent thyroid nodule biopsy were included in the study. The mean age of the study population was 50.4 ± 14.2 years and the majority were female patients (74.9%). The mean nodule size of the patients was measured as 18.36 ± 12.96 mm. Demographic characteristics of the patients are given in Table 2. Malignancy was more common among male patients presenting with a thyroid nodule (P = 0.001). There was significant difference in the mean age of patients with benign (mean age was 51.5 ± 14.1 years) and malignant thyroid nodules (mean age was 44.6 ± 13.1 years) (P = 0.001). There was significant difference in the age of male and female patients with benign nodules (P = 0.014) and patients with malignant thyroid nodules, men (mean age was 50.6 years) were significantly older than women (mean age was 39.4) (P = 0.001). There was no significant difference in the mean size of benign nodules (mean of 18.7 ± 12.1 mm, range 4.6-56.7 mm) and malignant thyroid nodules (mean of 16.4± 17 mm, range 6-67.9 mm) (P = 0.160)

Table 2. Demographic features of the patients

Age (years)	50.4 ± 14.2
Sex	
male	104 (25.1%)
female	310 (74.9%)
Size (mm)	18.36 ± 12.96
Composition	
solid	292 (70.5%)
semi-solid	122 (29.5%)
Echogenicity	
isoechoic	36 (8.7%)
hypoechoic	274 (66.2%)
hyperechoic	104 (25.1%)

When thyroid nodules were classified according to TRIADS criteria, it was TIRADS TR2 in 29 (7%) patients, TIRADS TR3 in 147 (35.5%) patients, TR4 in 166 (40.1%) patients, and TR5 in 72 (17.4%) patients. Cases with an already proven case of malignancy (TIRADS 6) were not included in the study. When the Bethesda categories of the patients were evaluated according to the pathological examination, Bethesda II category in 225 (54.4%) patients, Bethesda III category in 40 (9.7%) patients, Bethesda IV category in 44 (10.6%) patients, Bethesda V in 42 patients (10.1%), and Bethesda VI in 63 patients (15.2%) was found. There were no inadequate or insufficient samples (Bethesda Class I) (Table 3).

Table 3. Thyroid imaging reporting and data system (TIRADS) and Bethesda correlation

	Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI	Total
TIRADS 2	29 (100%)	0	0	0	0	29
	(100%)					
TIRADS 3	120 (81.6%)	17 (11.6%)	5 (3.4%)	0	5 (3.4%)	147
TIRADS 4	58 (34.9%)	23 (13.9%)	33 (19.9%)	36 (21.7%)	16 (9.6%)	166
TIRADS 5	18 (25%)	0	6 (8.3%)	6 (8.3%)	42 (58.3%)	72
Total	225	40	44	42	63	414

The probability of malignant FNAC (Bethesda Class V and Class VI) in TIRADS classes 2, 3, 4, and 5 was 0%, 3.4%, 31.3%, and 66.7%, respectively. The probability of a benign FNAC (Bethesda Class II) in TIRADS category 2 was 100%, while for TIRADS classes 3, 4 and 5 it was 81.6%, 34.9% and 25%, respectively.

Of the 166 cases classified as TIRADS 4, cytology showed that 58 were benign (Bethesda Class II), 33 were follicular neoplasms (Bethesda Class IV), and 23 were indeterminate (Bethesda Class III). Among the 72 cases suspected to be malignant on ultrasound (TIRADS 5), 48 patients had biopsy (FNAC)-proven cancer (66.7% concordance), but 18 cases were cytologically benign (false positive sonographic impression).

Of 225 patients in the Bethesda II category, 120 (53.3%) likely had benign nodules (TR3), 58 (25.7%) suspected nodules

(TR4), and 18 (8%) likely malignant nodules (TR5) was found. When 44 patients in the Bethesda IV category were analyzed, 5 (11.4%) probably had benign nodules (TR3), 33 (75%) had suspicious nodules (TR4), and 6 (13.6%) had possibly malignant nodules (TR5). In Bethesda category V-VI 5 of 105 patients (4.8%) had possibly benign nodules (TR3), 52 patients (49.5%) had suspicious nodules (TR4), and 48 patients (45.7%) had possibly malignant nodules (TR5).

Discussion

A four-step process is used to evaluate a thyroid nodule, which includes clinical examination, thyroid function tests, thyroid ultrasound, and US-guided aspiration cytology, respectively. However, the most important parameter that enables us to reach a pathological diagnosis is cytological diagnosis with FNA biopsy. FNAC is a useful and cost-effective method for detecting thyroid malignancies. However, it is still controversial which patients should be offered FNAC because of the very high prevalence of thyroid nodules and the minimally invasive nature of FNAC [4]. Various classifications based on sonographic features have recently been proposed to aid this selection.

The American College of Radiologists has accepted the suitability of the TIRADS classification system in the ultrasonographic clinicopathological evaluation of thyroid nodules. The TIRADS scoring system consists of six categories. Horvath et al. reported the malignancy risk of the TIRADS scoring system as 0% in TIRADS 2, 14.1% in TIRADS 3, 45% in TIRADS 4, and 89.6% in TIRADS 5 [11]. After 2009, many studies have been conducted to evaluate the reliability of the TIRADS classification system in distinguishing benign thyroid nodules from malignant ones. Reported rates of malignancy for TIRADS 2–5 categories, respectively, were 9.6% (TRIADS 2), 31.1% (TRIADS 3), 76.8% (TRIADS 4) and 100% (TRIADS 5) by Park et al. [15]. In a single-center study evaluating a total of 184 patients, 156 of whom were women, it was reported as 0% (TRIADS 2), 2.2% (TRIADS 3), 38.5% (TRIADS 4) and 77.8 % (TRIADS 5) [16]. In another study including patients with solitary thyroid nodules and clinical maximum size exceeded 1 cm, the thyroid nodules for malignancy was 6.6%, 32%, 36%, 64%, 59%, and 91% for TIRADS 2, 3, 4a, 4b, 4c, and 5 categories, respectively [17]. In these two studies, nodules classified as Bethesda I and II were considered benign, and nodules classified as Bethesda IV-VI were considered malignant. Kwak et al. proposed a TIRADS classification based on retrospective analysis of thyroid nodules on ultrasound and FNA [18]. This article describes that a malignancy risk of 0% is expected for TIRADS 2, 1.7% for TIRADS 3, 3.3-72.4% for TIRADS 4 and 87.5% for TIRADS 5. The main limitation of this study was that each suspicious sonographic feature was given the same importance, even though in reality each ultrasound feature has a different probability for malignancy. For example, a nodule with marked hypoechogenicity/microcalcifications has a higher risk of malignancy than other nodules with irregular margins. In our study, the risk of malignancy for the different TIRADS categories was 0% (TIRADS 2), 3.4% (TIRADS 3), 31.3% (TIRADS 4) and 66.7% (TIRADS 5). There appears to be significant differences between studies in the reported proportions of TIRADS categories. These differences may be due to the inclusion of other TIRADS categories (especially TR1 and TR2) in some studies. Additionally, in our study, follicular neoplasm or susceptible for a follicular neoplasm (Bethesda IV) was not included in the malignant category. Also, general inclusion and exclusion criteria can cause these differences.

Our study shows that there is strong agreement between the TRIADS and Bethesda categories [12,19], both between the lowest risk (TIRADS 2 and Bethesda II) and higher risk groups (TIRADS 5 and Bethesda V), consistent with previously published studies. This indicates that US features suggesting a higher or lower risk of malignancy will be associated with a higher or lower probability of malignancy, respectively, according to the FNA biopsy report (Bethesda).

Our study has several limitations. First, our report is a single institutional study. An inherent weakness of this study is its retrospective nature. Despite having an experienced radiologist, the use of more than one radiologist for the interpretation of ultrasonographic imaging may be helpful because image analysis may differ between radiologists and the extent of interobserver variability in TIRADS classification is unknown. In addition, the fact that the cytopathological evaluation was performed by more than one cytopathologist affects the reliability of the data; however, we have a team of cytopathologists who are experienced in the field and often consult a senior cytopathologist.

Our study shows a good correlation between the Bethesda Classification of thyroid nodule FNAC and thyroid ultrasound reporting using the TIRADS classification. Correct interpretation of the two findings helps the clinician reduce the risk of unnecessary invasive procedures in patients who are unlikely to demonstrate thyroid cancer, while facilitating the identification of patients at high risk of cancer.

Ethics Committee Approval

Ethics committee approval was received for this study from the ethics committee of İstanbul Memorial Şişli Hospital Ethics Committee (References number: 05.01.2023- 70).

Informed Consent

Written informed consent was obtained from all participants who participated in this study.

Author Contributions

Concept, Design, Materials, Data Collection and/or Processing, Literature Search, Writing Manuscript – A.Y.

Declaration of Interests

The authors have no conflicts of interest to declare.

Funding

The author declared that this study have received no financial support.

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Turkish Journal of Clinics and Laboratory

To cite this article: Sayın M. Hormon reseptörü pozitif meme kanseri tanılı hastalarda tamoksifen sitrat kullanımının ortalama trombosit hacmi üzerine etkisi. Turk J Clin Lab 2023; 4: 709-714

Araştırma Makalesi

Hormon reseptörü pozitif meme kanseri tanılı hastalarda tamoksifen sitrat kullanımının ortalama trombosit hacmi üzerine etkisi

The effect of tamoxifen citrate on average platelet in hormone receptor-positive patients with breast cancer

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Öz

Amaç: Meme kanseri tedavisinde kullanılan tamoksifen sitratın sık görülen yan etkilerinden biri derin ven trombozudur. Daha önce literatürde bildirildiği şekilde, tamoksifen kullanımına bağlı olarak ortalama trombosit hacmi artıyor ve derin ven trombozuna neden oluyor. Bu yan etkinin ortalama trombosit hacmi (MPV) ile ilişkisini araştırdık.

Gereç ve Yöntemler: Çalışma Ankara Eğitim ve Araştırma Hastanesinde, Ocak 2015- Aralık 2016 yılları arasında tedavisinde, tamoksifen sitrat kullanılan 210 meme kanseri tanılı hastanın dosyaları retrospektif olarak tarandı. Tamoksifen sitrat tedavisinin 60. ayını doldurmuş hastaların hepsi çalışmaya dahil edildi. Hastaların çalışma boyunca takip süreleri 6 yıldır. Hastalarda tedaviden önce (bazal seviye), 3. ayda,12. ayda ve 60. ayda bakılan kontrol hemogramlarda MPV seviyeleri tarandı. Retrospektif gözlemsel tarama sonuçları için SPSS 25 ile Microsoft Excel 2007 programı kullanıldı.

Bulgular: Toplam 210 hasta dosyası incelendi. Hastaların yaşları ile zamansal MPV değerleri arasında istatistiksel olarak anlamlı bir ilişki yoktur. (p>0,05). Hastaların menopoz durumları ile zamansal MPV değerleri bakımından istatistiksel olarak anlamlı bir fark yoktur. (p>0,05). Hastaların bazal, 3, 12. ve 60. ay (zamansal olarak) MPV değerleri arasında istatistiksel olarak anlamlı bir fark vardır. (p=0,0001). Evre I-II-III ile evre IV arasında bazal MPV değerleri açısından istatistiksel olarak anlamlı bir fark yoktur. (p>0,05). Evre I-II-III ile evre IV arasında 3.ay 12.ay ve 60.ay MPV değerleri açısından istatistiksel olarak anlamlı bir fark vardır (sırasıyla p=0,005, p=0,002, p=0,002). Evre IV te ölçülen tüm zamanlardaki MPV değerleri Evre I-II-III te ölçülen MPV değerlerinden anlamlı olarak daha düşüktür.

Sonuç: Tamoksifen sitrat meme kanseri tedavisinde kullanılan çok değerli bir ilaç. Tamosifen bazal seviyede ölçülen ve dağılımları normal olan tüm MPV değerlerini zamanla arttırdı. Tamoksifenin menapoz durumuna göre, MPV değerleri üzerine etkisinin değişmediği görüldü. Tamoksifenin evre I,II,III grubundaki MPV değerlerini arttırdığı ancak metastatik evrede MPV üzerine etkisinin olmadığı görüldü.

Anahtar kelimeler: Tamoksifen sitrat, Derin ven trombozu, Ortalama trombosit hacmi

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Geliş Tarihi: 10.07.2023Kabul Tarihi: 06.12.2023

Abstract

Aim: One of the common side effects of the drug containing the active ingredient tamoxifen citrate, used in the treatment of breast cancer, is deep vein thrombosis. As previously reported in the literature, mean platelet volume increases with tamoxifen use and causes deep vein thrombosis. We investigated the relationship of this side effect with mean platelet volume (MPV).

Material and Methods: We retrospectively reviewed the files of 210 breast cancer patients treated with tamoxifen citrate between January 2015 and December 2016 at Ankara Training and Research Hospital. All patients who completed the 60th month of tamoxifen citrate treatment were enrolled in the study. The study follow-up period was 6 years. MPV levels were screened in control hemograms performed before treatment (baseline level), at 3 months, 12 months, and 60 months. SPSS 25 and Microsoft Office Excel 2007 were used for the results of the retrospective observational screenings.

Results: A total of 210 patient files were examined. There is no statistically significant association between the age of the patients and temporal MPV values ($p>0.05$). There is no significant difference between patients' menopausal status and temporal MPV values ($p>0.05$). There is a statistically significant difference between baseline, 3, 12, and 60 months (temporal) MPV values ($p=0.0001$). There is no statistically significant difference between stages I-II-III and stage IV in baseline MPV values ($p>0.05$). There is a statistically significant difference between stage I-II-III and stage IV in terms of 3rd month, 12th month, and 60th month MPV values ($p=0.005$, $p=0.002$, $p=0.002$, respectively). All-time MPV values obtained in stage IV were significantly decreased compared to the MPV values obtained in stages I-II-III.

Conclusion: Tamoxifen citrate is a very valuable drug used in the treatment of breast cancer. Tamosifen increased over time all MPV values measured at baseline and whose distributions were normal. It was observed that the effect of tamoxifen on MPV values did not change depending on menopause status. It was observed that tamoxifen increased MPV values in the stage I, II, III groups, but had no effect on MPV in the metastatic stage.

Keywords: Tamoxifen citrate; Deep vein thrombosis; Mean platelet volume

Giriş

Tamoksifen sitrat (TMX), östrojen agonist etkileri zayıf, non-steroid anti-östrojenik bir ajandır. Meme kanserinin palyatif ve adjuvan tedavisinde kullanılır. Ayrıca yüksek risk altındaki in situ duktal karsinomalı kadınlarda meme kanseri insidansını ve invaziv meme kanseri riskini azaltır. TMX ve östrojen, memedeki östrojen reseptörlerine bağlanma rekabetine girer ve östrojen yerine bağlanır. Böylece östrojenin meme kanserini arttırıcı etkisini ortadan kaldırır [1].

Tedavi edici etkisinin yanısıra TMX'in kullanımını kısıtlayan bazı yan etkileri de bulunmaktadır. Derin ven trombozu ve pulmoner emboli gibi tromboembolik olaylar, hiperkalsemi, endometrial hiperplazi, artmış endometriyal karsinom riski, karaciğer fonksiyon testlerinde artış ve eritemli deri lezyonları, TMX'in yan etkilerinden bazılarıdır [1].

Tromboz, anormal homeostaz ile oluşan patolojik bir durumdur. Derin ven trombozu (DVT) tanımı genellikle derin bacağın, özellikle ilio-femoral damarların trombozu için kullanılır. İleri yaş, cerrahi (özellikle majör cerrahi prosedür), travma, uzamış immobilizasyon, malign hastalık, nörolojik hastalık, santral venöz kateter, gebelik ve lohusalık DVT için kazanılmış risk faktörleridir [2-5]. Bazı hastalarda kalıtsal risk faktörleri olabilir, örn. antitrombin III eksikliği, antifosfolipid sendromu [6].

Ortalama trombosit hacminin (MPV) yükselmesi, daha reaktif ve daha büyük trombositlerin varlığını gösterir ve bu miyokard enfarktüsü (MI) için bir risk faktörü olabilir [7]. Trombosit hacmi arttıkça homeostazda aktif hale gelirler [8]. Akut koroner sendromlarda MPV'nin arttığı ve MPV ile DVT arasında ilişki olduğu bilinmektedir [9,10].

Gereç ve Yöntemler

Sağlık Bakanlığı Ankara Eğitim ve Araştırma Hastanesi 11.05.2022 tarihli E-93471371-514.99 sayılı etik kurul kararı alınmıştır. Çalışmaya dahil edilen tüm hastaların bilgilendirilmiş onam formu alınmıştır. Çalışma Helsinki İlkeler Deklarasyonuna uygun hazırlanmıştır.

TMX, meme kanseri hastalarının adjuvan tedavisinde kullanılan önemli bir ilaçtır ve ciddi yan etkilerinden biri de DVT'dir. Artmış MPV, DVT ve MI arasındaki ilişkiyi gösteren çalışmalar mevcuttur. Bu bulgular üzerine; TMX'in MPV'yi yükselterek DVT'ye neden olduğu ile ilgili hipotezimiz 2011 yılında makale şeklinde sunulmuştu [11]. Bu hipotezden yola çıkarak çalışmaya başlandı ve 5. yılını doldurmuş tüm hastaların dosyaları tarandı.

Çalışmaya Ankara Eğitim ve Araştırma Hastanesinde, Ocak 2015- Aralık 2016 yılları arasında, tedavisinde tamoksifen sitrat 20 mg /gün kullanan 210 meme kanseri tanılı hasta dahil edildi.

Araştırmaya dahil edilme kriterleri

18 yaş üstü,

Meme kanseri tanısı almış,

Herhangi bir evredeki (evre I-II-III ve IV),

Hormon reseptörü (östrojen (ER) ve/veya progesteron (PR)) pozitif,

Kadın hastalar,

Metastatik veya adjuvan dönemdeki hastalar,

Premenapoze veya postmenapoze hastalar,

Tamoksifen sitrat kullanan tüm hastaların dosyası alındı.

Araştırma dışında bırakılma kriterleri:

18 yaş altı,

Hormon reseptörleri ikisi de negatif olan,

Erkek hastalar,

TMX dışında ilaç kullanan hastalar veya 5 yıl içinde ilacı aromataz inhibitörlerine (anastrazol, letrazol veya exemestan) değiştirilen hastalar.

Hastaların TMX tedavisine başlamadan önce yani 0.ay, 3.,12. ve 60. aylarında ki kontrollerinde bakılan tam kan sayımları sonuçları tarandı ve tümünün MPV seviyeleri not alındı.

İstatistiksel Analiz

Tüm veriler SPSS 25 ile Microsoft Excel 2007 kullanılarak analiz edildi. Kategorik değişkenler sayı ve yüzde olarak verildi. İlaç kullanımı öncesi ve sonrası parametrelerin karşılaştırılmasında, değişkenlerin normal dağılıp dağılmadığını belirlemek için Shapiro Wilk testi kullanıldı. İlaç kullanımı öncesi ve sonrası parametrelerin karşılaştırılmasında en az bir değişkenin öncesi ve sonrası normal dağılmaması durumunda Wilcoxon Signed Ranks testi ve Fiedman test kullanıldı. Katılımcıların yaşları ile zamansal MPV değerleri arasındaki ilişki için Spearman Korelasyon Analizi, evreler ile MPV arasındaki ilişki için ise Mann-Whitney U test ve Independent Samples test uygulandı. P<0.05 değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular

Hastaların yaşlarına göre MPV dağılımları Tablo 1 de verilmiştir.

Katılımcıların yaşları ile zamansal MPV değerleri arasında istatistiksel olarak anlamlı bir ilişki yoktur. (Spearman Korelasyon Analizi; p>0,05)

Tablo 1. Hasta yaşları ile MPV ölçümlerinin zamansal değerleri arasındaki ilişki

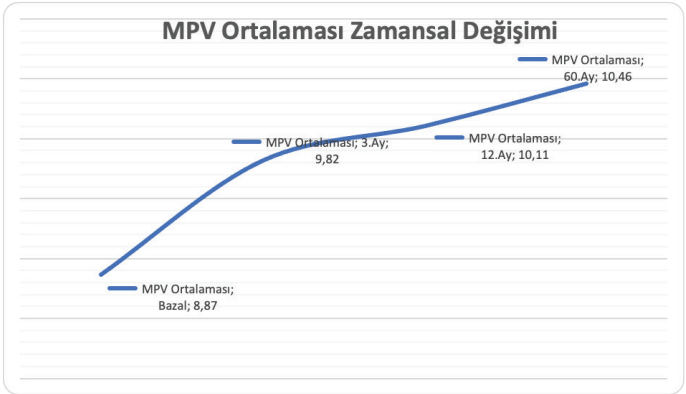
		Yaş	0.Ay	3.Ay	12.Ay	60.Ay
Yaş	r	1,000	0,034	-0,026	0,025	0,072
	p		0,625	0,712	0,724	0,302
	N	210	210	210	210	210
0.ay	r		1,000	0,675**	0,588**	0,468**
	p			0,0001	0,0001	0,0001
	N		210	210	210	210
3.Ay	r			1,000	0,826**	0,627**
	p				0,0001	0,0001
	N			210	210	210
12.Ay	r				1,000	0,796**
	p					0,0001
	N				210	210
60.Ay	r					1,000
	p					
	N					210

**: p<0,01 Spearman Korelasyon Analizi; p>0,05 MPV: Ortalama Trombosit Hacmi

Hastaların MPV ölçümlerinin zamansal olarak karşılaştırmasında 0.ay ve 60. ay MPV değerleri normal dağılmazken (Sırasıyla p=0,0001 ve p=0,039), 3. ve 12. ay MPV değerleri normal dağılmıştır. (p>0,05). İstatiksel sonuçlar Tablo 2'de verilmiştir.

Çalışmaya katılanların 0., 3., 12. ve 60. ay MPV değerleri arasında istatistiksel olarak anlamlı bir fark vardır. (p=0,0001) Bu fark; 0.ay ile 3.ay (p=0,0001), 0.ay ile 12. ay (p=0,0001), 0.ay ile 60. ay (p=0,0001), 3.ay ile 12. ay (p=0,0001), 3. ay ile 60.ay (p=0,0001) ve 12. ay ile 60. Ay (p=0,0001) MPV değerleri arasındaki farklardan kaynaklanmıştır (Şekil 1).

Hastaların evresine göre MPV dağılımları Tablo 3'te verilmiştir.



Şekil 1: MPV'nin zaman içindeki değişimi

MPV: Ortalama Trombosit Hacmi

Tablo2. Hastaların MPV ölçümlerinin zamansal olarak karşılaştırılması								
MPV; n=210	Ortanca	Ort.	SS	Min.	Maks.	Sıra Ortalaması	x^2	p
0.ay	9	8,87	1,05	6,7	13,0	1,29	332,207	0,0001**
3.Ay	9,7	9,82	1,11	7,0	12,7	2,4		
12.Ay	10	10,11	1,08	7,2	12,8	2,85		
60.Ay	10,4	10,46	1,15	7,1	13,4	3,46		
**: p<0,01 MPV: Ortalama Trombosit Hacmi								

Tablo3. Evreye göre MPV ölçümleri							
Evre	Evre I-II-III (n=151)			Evre IV (n=59)			p
	Ortanca	Min.-Maks.	Ort.±SS	Ortanca	Min.-Maks.	Ort.±SS	
0.ay	8,8	6,7-13	8,92± 1,07	8,6	7-11,6	8,72± 1	0,206
3.Ay	9,9	7-12,7	9,93± 1,1	9,3	7,5-12,7	9,53± 1,1	0,005**
12.Ay	10,2	7,2-12,8	10,24± 10,07	9,6	8,2-12,7	9,77± 1,05	0,002**
60.Ay	10,6	7,1-13,4	10,61± 1,11	10,1	7,7-12,4	10,08± 1,17	0,002**
**: p<0,01 MPV: Ortalama Trombosit Hacmi							

Evre I-II-III ile Evre IV arasında bazal MPV değerleri açısından istatistiksel olarak anlamlı bir fark yoktur. (p>0,05)

Evre I-II-III ile Evre IV arasında 3.ay MPV değerleri açısından istatistiksel olarak anlamlı bir fark vardır. (p=0,005) Evre IV te ölçülen 3.ay MPV değerleri Evre I-II-III te ölçülen 3.ay MPV değerlerinden anlamlı olarak daha düşüktür.

Evre I-II-III ile Evre IV arasında 12.ay MPV değerleri açısından istatistiksel olarak anlamlı bir fark vardır. (p=0,002) Evre IV te ölçülen 12.ay MPV değerleri Evre I-II-III te ölçülen 12.ay MPV değerlerinden anlamlı olarak daha düşüktür.

Evre I-II-III ile Evre IV arasında 60.ay MPV değerleri açısından istatistiksel olarak anlamlı bir fark vardır. (p=0,002) Evre IV te ölçülen 60.ay MPV değerleri Evre I-II-III te ölçülen 60.ay MPV değerlerinden anlamlı olarak daha düşüktür.

Hastaların menapoz durumuna göre MPV dağılımı Tablo 4'te verilmiştir.

Tablo 4. Menopoz durumuna göre MPV ölçümleri							
Menopoz durumu	Premenapoze (n=98)			Postmenapoze (n=112)			p
	Ortanca	Min.-Maks.	Ort.±SS	Ortanca	Min.-Maks.	Ort.±SS	
0.ay	8,7	6,7-13	8,9± 1,15	8,7	6,8-11,7	8,83± 0,97	0,995
3.Ay	9,7	7,6-12,7	9,88± 1,07	9,75	7-12,3	9,76± 1,14	0,585
12.Ay	10	7,8-12,8	10,1± 1,05	10,15	7,2-12,5	10,12± 1,11	0,705
60.Ay	10,2	8-13	10,41± 1,13	10,6	7,1-13,4	10,5± 1,17	0,33
MPV: Ortalama Trombosit Hacmi							

Çalışmaya katılan hastaların menopoz durumlarına göre aralarında 0.ay, 3.ay, 12.ay ve 60.ay MPV değerleri bakımından istatistiksel olarak anlamlı bir fark yoktur. (p>0,05)

Tartışma

Keskin ve arkadaşları ateroskleroz risk faktörleri ile MPV arasında ilişki olmadığını ve MPV'nin koroner arter hastalığı için bir risk faktörü değil, patogenezde önemli bir basamak olduğunu vurgulamıştır. Ayrıca akut iskemik olaylarda MPV'nin arttığını ve iskemik olaylar düzelirken normale döndüğünü öne sürmüşlerdir [9].

TMX vasküler endotelyal büyüme faktörünü (VEGF) ve trombosit aktivasyonunu yükseltir [12].

Tromboemboli ve pulmoner emboli, mitral stenozu olan hastalarda önemli komplikasyonlardır ve MPV'si yüksek olan hastalarda komplikasyon riski artar [13].

Başka iki çalışmada MI'nın akut fazında, trombositopeni ve

artmış MPV pretrombotik durumun bir göstergesi olarak belirlenmiş ve MI için risk faktörü olabileceği ileri sürülmüştür. MPV'nin tıkayıcı trombüs ve trombotik emboli oluşumuyla MI'ya neden olduğu ileri sürülmüştür [14-15].

Bir çalışmada meme kanseri tanılı hastaların TMX ve aromataz inhibitörleri kullanımına bağlı oluşan tromboembolik yan etkiler araştırılmış ve TMX kolunda DVT ve tromboembolinin istatiksel olarak anlamlı bulunmuş [16].

Karagöz ve arkadaşları meme kanseri hastalarını iki tedavi grubuna randomize etti ve MPV değerlerini inceledi. TMX ile tedavi edilen hastalarda MPV'de bir artış belirlenirken, aromataz inhibitörleri ile tedavi edilen hastalarda fark görülmedi [17].

Bir steroidal aromataz inhibitörü olan eksemestan, TMX'den daha az tromboembolik olaya neden olmuştur [18].

Çalışmamızda, aromataz inhibitörlerini kullanan hastalar çalışma dışında tutulmuştur. Bu nedenle aromataz inhibitörlerinin MPV üzerindeki etkisini bilmiyoruz.

Taşkaynatan ve arkadaşlarının yapmış olduğu çalışmada ise TMX ve aromataz inhibitörü alan tüm hastalarda zamanla MPV değerlerinin arttığı gözlenmiş. MPV artışının TMX'e özel bir etki olmadığı belirtilmiş. Tüm hormon ilaçlarının dikkatli kullanılması gerektiği belirtilmiş [19].

TMX bazal seviyede ölçülen ve dağılımları normal olan tüm MPV değerlerini zamanla arttırdı. 3.aydan itibaren bakılan tüm ölçümlerde giderek MPV değerlerinin arttığı ve bunlar arasında istatiksel olarak anlamlılık olduğu görüldü.

Çalışmada ayrıca hastaların menapoz durumuna göre, MPV değerlerine etkisi olup olmadığına bakıldı ancak istatiksel olarak anlamlı bulunmadı. Literatürde menapoz durumuyla ilgili herhangi bir çalışmaya rastlanmadı.

Çalışmada hastalar evre I-II-III ile evre IV şeklinde 2 ayrı gruba ayrıldı ve incelendi. Bazal seviyede hiçbir evrede MPV değerlerinde anlamlı değişiklik yoktu. Ancak 3.aydan itibaren bakılan tüm ölçümlerde (3, 12, 60. ayda) evre IV'teki hasta grubunda MPV değerlerinin evre I,II,III grubundaki MPV değerlerinden istatiksel olarak anlamlı bir düşüklük saptandı. Çalışmamızda TMX'in metastatik evrede, MPV üzerine etkisinin olmadığı görüldü. Literatürde bu bulguyla ilgili herhangi bir çalışmaya ve sonuca rastlanmadı.

Sonuç

Meme kanseri adjuvan tedavisi için monoterapi alacak hastalarda DVT veya tromboemboli öyküsü dikkatle sorgulanmalıdır. Tamosifenin bazal seviyede ölçülen ve dağılımları normal olan tüm MPV değerlerini zamanla arttırdığı görüldü. Menapoz durumuna göre, MPV değerleri üzerine etkisinin değişmediği görüldü. Tamoksifenin evre I,II,III grubundaki MPV değerlerini arttırdığı ancak metastatik evrede MPV üzerine etkisinin olmadığı görüldü.

Konuyla ilgili daha ileri çalışmalara ihtiyaç vardır.

Etik kurul kararı

Ankara Eğitim ve Araştırma Hastanesi 11.05.2022 tarihli E-93471371-514.99 sayılı etik kurul kararı alınmıştır.

Teşekkür

İstatiksel analiz için sayın Murat Mutlu beye teşekkür ediyorum.

Finansal Destek

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

Yazarlık katkıları

Konsept ve tasarım, veri toplama, analiz, literatür derleme ve makalenin yazımı: Meral Sayın.

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Turkish Journal of Clinics and Laboratory

To cite this article: Kescioglu F, Arslan I, Cakit MO, Yengil Taci D. Evaluation of attitudes and behaviors of family medicine residency students regarding academic literacy. Turk J Clin Lab 2023; 4: 715-722

Research Article

Evaluation of attitudes and behaviors of family medicine residency students regarding academic literacy

Aile hekimliği uzmanlık öğrencilerinin akademik okuryazarlık hakkındaki tutum ve davranışlarının değerlendirilmesi

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Öz

Amaç: Bu çalışma ile; Ankara ilinde Aile Hekimliği uzmanlık eğitimi alan hekimlerin akademik okuryazarlık ile ilgili tutum ve davranışlarını belirlemek ve bunları etkileyen faktörleri ortaya koymak amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya 188 aile hekimi uzmanlık öğrencisi katılmıştır. Ankara'da eğitim alan Aile Hekimliği uzmanlık öğrencileri çalışmaya dahil edilmiştir. Elektronik ortamda katılımcılara 23 soruluk anket ve Akademik Okuryazarlık Ölçeği (AOÖ) formları gönderilmiştir.

Bulgular: Katılımcıların %68,62'sı kurumlarında, %36,18'si kurumları dışında bilimsel araştırma konusunda eğitim almıştır. Çalışmaya katılan hekimlerin %59'u uzmanlık eğitimleri süresince hiç kongreye katılmamış, %67,61'sı hiç bilimsel araştırmada araştırmacı olarak bulunmamıştır. Çalıştıkları kurumda veya kurumları haricinde kurs, kongre ya da sempozyumda bilimsel araştırma konusunda eğitim alanların AOÖ puanları yüksek bulundu ($p<0,05$). Makale okuma sıklığı arttıkça ölçek puanlarında artış olduğu görüldü ($p<0,05$).

Sonuç: Uzmanlık öğrencilerinin kongre, kurs gibi bilimsel toplantılara katılım oranları, makale okuma sayılarının düşük olduğunu saptadık. Akademik okuryazarlığın Aile Hekimliği eğitimindeki önemine dikkat çekmek ve asistanlığın ilk yıllarından itibaren asistanların bilimsel aktivitelerde bulunmalarının önemini vurgulamak istiyoruz.

Anahtar kelimeler: Aile Hekimliği, Asistan, Uzmanlık eğitimi, Akademik okuryazarlık

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Recevied: 21.07.2023 accepted: 04.12.2023

Abstract

Aim: OIt is aimed to determine the attitudes and behaviors of physicians who receive family medicine research assistant training in Ankara province regarding academic literacy and to reveal the factors affecting them.

Material and Methods: 188 Family Medicine research assistants studying in Ankara were included in the study. A 23-question survey and Academic Literacy Scale (ALS) forms were sent to the participants electronically.

Results: 68.62% of the participants got educated on scientific research in their institution and 36.18% outside their institution, 59.0% of physicians have never attended a congress during their residency training and 67.61% of them had never been a researcher in scientific research. ALS scores of those who were trained in scientific research in a course, congress and symposium or at the hospital they work in were found to be significantly higher ($p<0.05$). As the frequency of article reading increased, it was observed that the scale scores increased significantly ($p<0.05$).

Conclusion: We found that the participation rates of the research assistants in scientific meetings such as congresses and courses, the number of articles they read, and the number of those who obtained information by using scientific databases were low. We would like to draw attention to the importance of academic literacy in Family Medicine education and to emphasize the importance of assistants to engage in scientific activities from the first years of residency.

Keywords: Family Practice, Residency, research assistant, Academic literacy

Introduction

Family Medicine is the backbone of primary health care providers and the discipline in which the first contact with the patient is established. Family physicians have a deep and broad knowledge curriculum as they serve a large and diverse patient population [1]. Due to the scope of the family medicine job description, it requires intensive and extensive medical knowledge. Physicians should constantly renew themselves in terms of learning medical knowledge, updating the acquired knowledge and following the literature [2,3].

Today, medical knowledge is constantly increasing and renewing due to the developing and changing technology and world order. At the same time, as a result of technological developments, information sharing is now faster and easier. In addition to the advantage of this, there is also the possibility of accessing incorrect, unproven and scientifically invalid information. The concept of evidence-based medicine has emerged at the point of access to accurate and scientific information. It is necessary to have academic literacy skills in order to develop the ability to access, read, evaluate and be aware of evidence-based medical resources [4,5].

Although there is no quantitative evaluation method for having academic literacy skills, it is possible to have information about the attitudes and behaviors of the residents in this regard. In terms of gaining academic literacy skills, scientific training can be given to specialty students and they can be encouraged to attend organizations such as congresses or courses on this subject. At the same time, in order to increase the interest of specialty students in scientific academic activities and to raise their awareness and knowledge levels on this subject, they can be supported by their trainers in the institutions where they receive training to conduct scientific research. In this way, family physicians can increase their evidence-based medical knowledge, learn methods of acquiring new knowledge when needed, and distinguish between scientific and non-scientific knowledge. Specialty students with academic tendency will also be encouraged and the academicians of future generations will be brought to the society [6-9].

In our study, we aimed to learn the attitudes and behaviors of Family Medicine research assistants studying in training research hospitals and medical faculties in Ankara province about academic literacy. We think that obtaining information about the attitudes and behaviors of research assistants about academic literacy may help to identify the problems in the residency training process and the points that need to be developed and encouraged.

Material And Methods

The research is an observational, prospective and analytical study. Questionnaire forms were prepared via Google Forms in …….. Hospital Family Medicine Clinic and delivered to the participants in the digital environment. All Family Medicine research assistants who were receiving training in university hospitals and training and research hospitals in Ankara province and who agreed to participate in the study were included in the

study, except for research assistants who started Family Medicine recidency training less than 3 months as of the date of completing the questionnaire. From the sample calculation system whose universe is certain; The universe was accepted as 604 and the confidence interval was 95% and the margin of error was 5%, and it was calculated as 188 people at the 90% confidence level. The protocol of our study approved by The …..local Ethics Committee (decision number 22/881 dated 26.01.2022). The study have been conducted in accordance with the Helsinki Declaration of Principles (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/). All participants included in the study signed the Informed Consent Form online.

A 24-question questionnaire and an Academic Literacy Scale evaluation form prepared on the electronic platform (Google Forms) were presented to the participants by the researcher. The questionnaire and scale form were delivered to the participants via e-mail and filled in electronically.

Nineteen questions were asked to evaluate the attitudes, behaviors and thoughts of research assistants about academic literacy.

After the twenty-four-question questionnaire, the Academic Literacy Scale was used [10].

Academic Literacy Scale (ALS): The ALS has a 5-point Likert type. It consists of 23 items. It has 3 dimensions: Academic Disposition (Tendency), Research Process, and Information Use. Items 10, 11, 12, 13, 14, 15, 16, 17, 20, 23, 24 and 25 belong to academic disposition; items 1, 2, 3, 4, 5, 6, 7 and 8 belong to research process; and items 9, 18, 19 and 22 belong to knowledge utilization sub-dimension. Explanatory factor analysis, test-retest process and confirmatory factor analysis were performed for the validity and reliability of the scale. As a result of the exploratory factor analysis, the three-factor structure of the ALS was confirmed by confirmatory factor analysis (X2=457.55, sd=226, RMSEA=.045, SRMR=.053, NFI=.91, NNFI=.95, CFI=.95, GFI=.92, AGFI=.91). As a result of the test-retest process, Cronbach's Alpha internal consistency coefficient was 0.87 for the overall scale, 0.84 for Factor 1, 0.78 for Factor 2, and 0.76 for Factor 3. Accordingly, it can be said that the scale is reliable and valid. A maximum score of 115 and a minimum score of 23 can be obtained from the scale. A high score indicates a high level of academic literacy, while a low score indicates a low level of academic literacy.

Statistical Analysis

Data were analyzed with SPSS Package Program version 20.0. Number, percentage, mean, standard deviation, median, minimum, maximum, median, minimum, maximum were used in the presentation of descriptive data. Chi-square test was used to compare categorical data. The conformity of continuous variables to normal distribution was evaluated by Shapiro Wilk Test and Kolmogorov Smirnov Test. The Mann Whitney U Test and Kruskal Wallis Test were used for the comparison of variables that conformed to normal distribution, and the Mann Whitney U Test and Kruskal Wallis Test were used for the comparison of variables that did not conform to normal distribution. Spearman Correlation Analysis was used for correlation analysis of variables. $p < 0.05$ was accepted for statistical significance.

Results

The study included 188 family medicine research assistants, of which 61.70% (n=116) were female and 38.30% (n=72) were male. The mean age of the participants was 29.51 ± 4.72 years, and the mean years of occupation was 4.83 ± 4.24 years.

Table 1 shows the percentages of positive (yes) responses of the participants to the nineteen questions about the attitudes, behaviors and thoughts of residents about academic literacy. The total score and subscale scores of the participants are shown in Table 2. In general, it was observed that the scale scores of the participants were high.

There was no statistically significant difference between the groups in terms of the answers given to the questionnaire questions, the total ALS score and the subscale scores according to gender ($p>0.05$).

Those who answered yes to the question "Have you received training on conducting scientific research at the institution where you are currently working?" had higher scale scores than those who answered no ($p<0.05$) (Table 3).

The total score and subscale scores of those who answered yes to the question " Have you received training on conducting scientific research outside your institution " were higher than those who answered no ($p<0.05$) (Table 4).

The total score and sub-scale scores of those who answered yes to the question "Did you attend a scientific congress during your specialty training" were higher than those who answered no ($p<0,05$) (Table 5).

It was observed that the scale scores increased as the number of scientific articles read per week increased ($p<0.05$) (Table 6).

Table 1. Proportions of YES answers given by the participants to the questions on evaluating their attitudes, behaviors and thoughts about academic literacy

	n	%
The time allocated for academic and scientific activities in my institution is sufficient.	112	59.57
Scientific and academic activities at my institution are supported by lecturers	149	79.25
I think that participating in scientific and academic activities is important for my education	169	89.89
I think that participating in scientific and academic activities increases my knowledge and experience in the profession of medicine	170	90.42
Have you received training on conducting scientific research at the institution where you are currently working?	129	68.61
Do you want to receive training in conducting scientific research?	148	78.72
Have you received training on conducting scientific research outside your institution (Symposium, course, congress, etc.)?	68	36.17
Did you attend a scientific congress during your specialty training?	77	40.95
Have you been a researcher in any scientific research at your institution (Case presentation, Case series, Research article, etc.)?	61	32.44
I think thesis studies are scientific researches	147	78.19
Has your thesis topic been determined?	73	38.82
*I think I have allocated enough time for my thesis.	54	28.72
*I have no problems in collecting data for my thesis.	40	21.27
*I think that my thesis is related to the aims and learning objectives of family medicine	61	32.44
*I think my thesis will make a scientific contribution to family medicine	54	28.72

*Those who answered no to the question "Has your thesis topic been determined?" did not answer these questions.

Table 2. Participants' Academic Literacy Scale total score and subscale scores

	mean±SD	median (min-max)
Academic Literacy Scale	82.31±14.83	82.52(39.0-115.0)
Academic tendency	42.95±7.37	44.0 (21-55)
Knowledge utilization	14.99±2.71	15.0 (8.0-20.0)
Research process	24.52±6.94	25.0 (8.0- 40.0)

min: minimum, max: maximum, SD: standard deviation

Table 3. Comparison of the scale scores of the groups according to the question 'Have you received training on conducting scientific research at your current institution?

	Have you received training on conducting scientific research at the institution where you are currently working?				
	Yes (n=129)		No (n=59)		
Academic Literacy Scale	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	p
Total score	85.11±13.92	87.0 (47.0-115.0)	75.91±14.73	77.0 (39.0-106.0)	<0.001
Academic tendency	43.94±6.85	44.0 (25.0-55.0)	40.55±7.87	41.0 (21.0-54.0)	0.009
Knowledge utilization	15.32±2.57	15,0 (10.0-20.0)	14.0±2.79	14.0 (8.0-19.0)	0.002
Research process	25.83±6.64	26.0 (10.0-40.0)	21.42±6.55	22.0 (8.0-34.0)	<0.001

min: minimum, max: maximum, SD: standard deviation, p: Mann Whitney U Test

Table 4. Comparison of the scale scores of the groups according to the question 'Have you received training on conducting and conducting scientific research outside your institution?'

	Have you received training on conducting scientific research outside your institution (symposium, course, congress, etc.)?				
	Yes (n=68)		No (n=120)		
Academic Literacy Scale	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	p
Total score	89.71±12 33	91.0 (56.0-115.0)	78.0±14.8	78.0 (39.0-115.0)	<0.001
Academic tendency	45.65±6.47	46.0 (26.0-55.0)	41.31±7.33	42.0 (21.0-55.0)	<0.001
Knowledge utilization	15.89±2.62	16.0 (10.0-20.0)	14.45±2.67	15.0 (8.0-20.0)	<0.001
Research process	28.24±5.36	28.0 (18.0-40.0)	22.39±6.82	23.0 (8.0-40.0)	<0.001
min: minimum, max: maximum, SD: standard deviation, p: Mann Whitney U Test					

Table 5. Comparison of the scale scores of the groups according to the question 'Have you attended a scientific congress during your specialty training?'

	Did you attend a scientific congress during your specialty training?				
	Yes (n=77)		No (n=111)		
Academic Literacy Scale	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	p
Total score	86.24±15.36	88.0 (41.0-115.0)	79.42±13.74	79.0 (39.0-107.0)	0.001
Academic tendency	43.98±7.11	45.0 (23.0-55.0)	42.16±7.28	43.0(21.0-55.0)	0.090
Knowledge utilization	15.43±2.75	16.0 (8.0-20.0)	14.61±2.53	15.0 (8.0-20.0)	0.026
Research process	26.97±6.99	27.0 (9.0-40.0)	22.75±6,37	23.0 (8.0-39.0)	<0.001
min: minimum, max: maximum, SD: standard deviation, p: Mann Whitney U Test					

Tablo 6. Comparison of scale scores of groups according to the number of scientific articles read weekly

	Number of scientific articles read per week				
	0 (n=36)		Above 0 (n=152)		
Academic Literacy Scale	Mean±SD	median (min-max)	Mean±SD	median (min-max)	p
Total score	73.69±14.92	77.0(39.0-106.0)	84.25±14.0	86.0(41.0-115.0)	<0.001
Academic tendency	39.74±7.96	40.0(21.0-53.0)	43.57±6.99	44.0(23.0-55.0)	0.004
Knowledge utilization	14.0±2.68	15.0(8.0-19.0)	15.12±2.64	15.0(9.0-20.0)	0.051
Research process	19.81±7.53	26.0(9.0-40.0)	25.56±6.38	26.0(9.0-40.0)	<0.001
min: minimum, max: maximum, SD: standard deviation, p: Mann Whitney U Test,					

Discussion

In this study, we found that Family Medicine research assistants' thoughts about academic and scientific activities were positive, and that they were satisfied with the education they received in their institutions and the support of their trainers and considered them sufficient. However, although they were positive in their thoughts, we found that their participation rates in scientific meetings such as congresses and courses and the number of articles they read were low. Receiving research training and reading scientific articles, increased the academic literacy of family medicine residents.

In a study conducted with residents, Aysan et al. reported that

two thirds of the residents believed that theoretical training was inadequate and one third believed that practical training was also inadequate. The majority found the duration and number of educational meetings inadequate. In the same study, in 53% of the departments where regular educational meetings were held, the duration of the meetings was less than 2 hours per week and only 44% of these meetings were in the form of case meetings [7]. In the study by Yılmaz et al. two thirds of the specialty students reported that their universities did not provide them with the necessary opportunities to write articles and two out of three residents did not receive training on publication ethics during their specialty training [8]. Sayek et al. reported that 67% of specialty students received 2 hours or less of formal education per week in the Turkish Medical Association's Medical Specialty Education report [9]. In this study, 60% of the participants stated that they found the time allocated to academic and scientific activities in their institutions sufficient. This made us think that family medicine clinics give more importance to academic and scientific activities.

In this study, it was observed that approximately 70% of the participants did not receive training on conducting scientific research at the institution where they worked. Approximately 64% of them did not receive training in an organization such as a course or symposium outside their institution. Similarly, those who attended a scientific congress were less in number than those who did not. Aysan et al. reported in a multicenter study that 78 percent of the participants received no training in planning and conducting scientific research and 52 percent were not encouraged to conduct scientific research [7]. In a study by Emre et al. evaluating residents' anxiety about scientific research, 51.6% of the residents had received research training and 39.7% had taken part in the preparation of a scientific research [11]. In a study conducted with specialty students in India, the knowledge and attitudes of the participants towards medical research were investigated and it was reported that 60% of them had knowledge about conducting research [12]. In another study conducted in Japan, it was reported that less than 20% of the participants had training on clinical research and the majority had insufficient skills and knowledge about statistics [13]. Yet another study conducted by Uzuner et al. with family medicine residents, reported that 90% of the participants stated that courses and congresses were necessary [14]. In the literature, although the status of receiving training related to scientific activities varied, it was approximately similar to our study. Similarly, those who wanted to receive training were in the majority. The low rate of receiving training outside the institution of employment in our study may be due to financial reasons as these courses usually require a participation fee and congresses cannot be organized as frequently as before during the pandemic period.

In our survey, when physicians were asked whether they had been involved in any scientific research as a researcher, it was observed that 32% of the assistants had conducted a scientific research. Aysan et al. showed that 54% of residents in Turkey did not have a scientific publication, 71% did not have an article, 84% did not have an article in an international journal and as a general comment, the number of scientific publications of residents was very low [7]. Yıkılkan et al. In the study in which the educational needs of family medicine residents receiving education in Ankara province were evaluated, 28.6% had at least one article, oral presentation or poster, provided that it was published in a journal or presented at a congress [15]. In the medical specialty education report, it was stated that 41% of specialty students did not participate in scientific research and this rate was 35% in university hospitals and 51% in training and research hospitals [9]. In the literature, as in our study, it is seen that less than half of the specialty students have a scientific study. The excessive workload and the lack of knowledge and experience of residents in conducting scientific research may have caused this. In addition, the inability to organize congresses and courses during the pandemic period and the opening of new services and outpatient clinics within the scope of the fight against the pandemic and the emergence of extra work areas such as filiation services may have increased the workload. We think that academic and scientific activities may have been disrupted for these reasons.

When we assessed the article reading status of our participants, we found that 19% of them did not read any articles at all and in general, the number of articles read was low. In a study, 83% of specialty students stated that they did not read enough articles and when the number of articles read was analyzed, it was found that 33% read once a week, 35% read once a month and 27% read less frequently [15]. Mandhare et al. reported that the knowledge, attitudes and behaviors of participants who received training on medical research were significantly better than those who did not receive training [12]. Similarly, in our study, we found that the scale scores of those who stated that they received training in organizations such as

courses and symposiums at the institution where they worked or outside their institutions were high. In a study conducted on family physicians in the USA, it was found to be related with developing a positive attitude towards research, using guidelines more frequently in treatment decision-making and the habit of scanning medical literature more frequently [16]. In a study conducted in Canada, it was observed that physicians trained in specialties where special time was allocated for research published more articles [17]. When the total mean scores of the participants who did not receive training in our study were examined, it was found that the participants who received training scored approximately ten points less than the participants who received training, indicating that there was a significant difference when the maximum score that could be obtained from the scale was taken into consideration. In our study, similar to the literature, it was observed that having received training had a direct effect on academic literacy skills.

In a study conducted in Türkiye, the mean number of publications per participant was 2.2, which was lower than those reported in the literature, although a precise comparison could not be made [18]. Namdari et al. found that among orthopaedic residents in the United States, those who were academicians after their training had an average of 4.8 publications and those who were not academicians had 2.4 publications, and that the number of studies conducted was associated with academician status [19]. In Germany, where conducting scientific research is part of the medical curriculum, students were involved in 28% of publications at a specific institution [20]. In Croatia, 23% of undergraduate students were involved in a research Project [21]. In our study, it was observed that those who had previously conducted scientific research (n:61, 32%) had higher scores on the Research Process, a subheading of the Academic Literacy Scale. This result shows that similar to the literature, previous studies provide familiarity with the scientific literature and a better command of the technical knowledge in the research process. However, it should be noted that in our study, we did not ask the participants what type of publications they published or how many studies each of them had. For this reason, we could not compare the scale score with the number of studies conducted by the individuals. This is one of the drawback of our study.

Conclusion

We observed that research assistants had positive opinions about academic and scientific activities, were satisfied with the education they received at their institutions and the support of their instructors, and considered them adequate. However, their participation rates in scientific meetings such as congresses and courses and the number of articles they read were low. We found that the education received and reading scientific articles positively affected academic literacy. We would like to draw attention to the importance of academic literacy in Family Medicine education and emphasize the importance of scientific activities for residents from the first years of residency before they reach the thesis stage.

Ethics Committee Approval

The study was conducted with the approval of the XXXXXXX Hospital Clinical Researches Ethics Committee (Date: 26/1/2022, Decision No: 22-881).

Informed Consent

Written consent was obtained from the participants in this study electronically.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

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Turkish Journal of Clinics and Laboratory

To cite this article: Halipçi Topsakal HN, Dündar B. Comparison of Procalcitonin Test Performance Measured in Different Methods and Devices. Turk J Clin Lab 2023; 4: 723-728

Research Article

Farklı yöntem ve cihazlarda ölçülen prokalsitonin test performansının karşılaştırılması

Comparison of procalcitonin test performance measured in different methods and devices.

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Öz

Amaç: Bu çalışmada prokalsitonin test performansının ayrı kit ve cihazlarda karşılaştırması incelenmiştir. Prokalsitonin (PCT), Kalsitoninin 116 amino asitten oluşan prohormonudur. Serumda PCT seviyelerindeki yükselmeler ciddi sepsis ve viral enfeksiyonlar ile ilişkilidir. Serumdaki PCT seviyesi genellikle bakteriyel enfeksiyonu olan hastalarda görülür, bu nedenle bakteriyel ve viral bulaşıcı hastalıkları ayırt etmek için güvenli bir biyobelirteç olarak kullanılmaktadır. PCT' nin kantitatif ölçümünün sepsisin prognozunu değerlendirmeye ve antibiyotik başlatma ve sonlandırmaya rehberlik etmeye yardımcı olabileceği bilinmektedir. Serum PCT' nin kantitatif ölçümü için yöntemler esas olarak floresan, kemilüminesan ve elektrokemilüminesan immünoanaliz gibi yöntemleri içermektedir.

Gereç ve Yöntemler: Hastaneden alınan 40 hasta örneği Prokalsitonin ölçümü için toplandı ve etik kurul onayı alındı.

Prokalsitonin ölçümleri biyokimya laboratuvarında ARCHITECT ci4000 system (CMIA, Abbott Diagnostic) ile Autolumo A2000 Plus (CLIA, Autobio Diagnostic) sistem cihazlarda ardışık olarak yapıldı. Yöntem karşılaştırma çalışmaları Clinical Laboratory Standards Institue tarafından yayımlanan National Committee for Clinical Laboratory Standards (NCCLS)'in EP15-A2 protokolüne göre gerçekleştirildi.

Bulgular: Çalışmamızda hasta örneklerinin prokalsitonin konsantrasyonları 0,01-53,1 ng/ml arasındaydı. Hasta sonuçlarının her iki cihaz için ortalama ve standart sapma değerleri X=7,71±1,22 ve Y=8,4±1,32 idi. Her iki yöntem ile ölçülen hasta sonuçları karşılaştırıldığında istatistiksel olarak anlamlı bir fark elde edilmedi (p>0,05).

Sonuç: Prokalsitonin için her iki cihazda da ölçüm sonuçlarının korelasyonunu inceledik ve sonuçların birbiriyle korale olduğunu tespit ettik.

Anahtar kelimeler: Prokalsitonin, kemilüminesan immunassay, CLIA, analitik performans

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Recevied: 28.08.2023 Accepted: 07.11.2023

Abstract

Aim: In this study, the comparison of procalcitonin test performance in different kits and devices was examined. Procalcitonin (PCT) is the prohormone of Calcitonin, consisting of 116 amino acids. Elevations in PCT levels in serum are associated with severe sepsis and viral infections. PCT level in serum is often observed in patients with bacterial infection, so it is used as a safe biomarker to distinguish bacterial and viral infectious diseases. It is known that quantitative measurement of PCT can help assess the prognosis of sepsis and guide antibiotic initiation and discontinuation. Methods for quantitative measurement of serum PCT mainly include methods such as fluorescent, chemiluminescent and electrochemiluminescent immunoassay.

Material and Methods: 40 patient samples collected from the patients were collected for procalcitonin measurement and ethics committee approval was obtained.

Procalcitonin measurements were made consecutively in the biochemistry laboratory on ARCHITECT ci4000 system (CMIA, Abbott Diagnostic) and Autolumo A2000 Plus (CLIA, Autobio Diagnostic) system devices. Method comparison studies were carried out according to the EP15-A2 protocol of the National Committee for Clinical Laboratory Standards (NCCLS) published by the Clinical Laboratory Standards Institute.

Findings: In our study, procalcitonin concentrations of patient samples were between 0.01-53.1 ng/ml. The mean and standard deviation values of patient results for both devices were X=7.71±1.22 and Y=8.4±1.32. When patient results measured by both methods were compared, no statistically significant difference was obtained (p>0.05).

Results: We examined the correlation of measurement results for procalcitonin in both devices and found that the results were correlated with each other.

Keywords: procalcitonin, chemiluminescent immunoassay, CLIA, analytical performance

Giriş

Prokalsitonin (PCT) 116 amino asitten oluşan prohormondur. Sepsis ve solunum yolu enfeksiyonlarında kullanılan geçerli bir prognostik biyobelirteçtir [1]. Serumdaki PCT seviyesi genellikle ciddi bakteriyel enfeksiyonu olan hastalarda yükselir. Viral enfeksiyonlarda plazma PCT düzeyinde önemli bir artış olmaz. Bu nedenle plazma PCT ölçümü bakteriyel enfeksiyon ve viral enfeksiyonların ayırt edilmesinde kullanılır [2]. Ayrıca PCT ölçümünün antibiyotik tedavisine başlama ve sonlandırmaya rehberlik etme konusunda da fikir vermektedir [3]. PCT'nin önemli bir prognostik belirteç olması, doğru analitik yöntemlerle ölçülmesi gerektiğini göstermektedir [4]. Serum PCT' nin kantitatif ölçümü için yöntemler esas olarak floresan, kemilüminesan ve elektrokemilüminesan immünoanaliz yöntemleridir [5]. Analiz sonuçlarının farklı laboratuvarlar arasında karşılaştırılabilir olması gerekmektedir. Günümüzdeki tıbbi laboratuvarlarda standardizasyon bakımından önemli eksiklikleri vardır [6]. Hem uygulanan test ve kit sayısı az hem de cihazların çalıştırılmasıyla ilgili prensibler benzerdir [7].

PCT'nin miktarının belirlenmesi için şu anda mevcut olan tüm analizler immünolojik test tekniklerine dayanmaktadır. Ticari olarak ilk mevcut PCT testi BRAHMS PCT LIA® (Thermo Fisher, Hennigsdorf, Almanya), manuel bir luminometrik immünolojik tahlildir. Daha hassas ve hızlı bir otomatik analiz olan

BRAHMS PCT Kryptor® (Thermo Fisher, Hennigsdorf, Almanya) ise daha sonra geliştirildi ve ilk defa şiddetli sepsis tanısında kullanılmak üzere 2008 yılında FDA tarafından onaylandı.

Prokalsitonin, sepsis gibi önemli enfeksiyon durumlarıyla ilişkilendirildiğinden çalışılan testlerin çeşitliliği, ekonomik olması ve altın standart olarak kabul edilen testlerle de uyumlu sonuçlar vermesi oldukça önemlidir. Biz bu çalışmada ARCHITECT BRAHMS PCT kemilüminesan mikropartikül immünolojik yönteme dayalı analiz yapan ARCHITECT ci4000 system (CMIA, Abbott Diagnostic) marka cihaz ile PCT CLIA Microparticles ve Chemiluminescent microparticle immunoassay (CLIA Microparticles) yöntemi ile çalışan AutoLumo A2000 Plus marka cihazın PCT test performans sonuçlarını karşılaştırdık.

Gereç ve Yöntemler

Hasta Örneklerinin Toplanması ve Etik Kurul Onayı

Hastalardan alınan venöz kan numunelerinden elde edilen serum örnekleri hiç bekletilmeden her iki cihazla ölçüldü. Elde edilen sonuçlar MedCalc programına kaydedildi. Bu çalışma, Helsinki Bildirgesi'ne uygun olarak İstanbul Atlas Üniversitesi Etik Kurulu (No:E-22686390-050.99-26196) tarafından onaylandı. Bu araştırmada örneklerin kullanılmasından önce hastalardan yazılı bilgilendirilmiş onam alındı.

Kemiluminesan İmmunoassay Sistem Testi

Prokalsitonin ölçümleri hastanemiz biyokimya laboratuvarında ARCHITECT ci4000 system (CMIA, Abbott Diagnostic) ile Autolumo A2000 Plus (CLIA, Autobio Diagnostic) system cihazlarda ardışık olarak yapıldı [8]. Yöntem karşılaştırma çalışmaları Clinical Laboratory Standards Institue tarafından yayımlanan National Committee for Clinical Laboratory Standards (NCCLS)'in EP15-A2 protokolüne göre gerçekleştirildi. Bu protokolde, yöntem karşılaştırma için en az 40 olgu toplanması, bunların bir kısmının referans aralığın dışında olması ve çalışmanın en az beş günde yapılması önerilmektedir [9,4]. Bu öneriler doğrultusunda, çalışmamız düşük ve yüksek düzey kontroller ile 40 hasta örneği kullanılarak 10 günde yapıldı. Bknz tablo 1 [10].

Çalışmaya başlamadan önce her iki cihaz kalibratörleri ile kalibre edildi. Çalışmamızın birinci aşamasında, düşük ve yüksek düzey kontrol çalışmaları yapıldı [11]. Çalışmamızın ikinci aşamasında, hastanemiz biyokimya laboratuvarına prokalsitonin ölçümü için gönderilen 40 hasta örneği çalışmaya dahil edildi. Pearson korelasyon analizi ve regresyon analizi yapıldı [12].

Bulgular

Çalışmamızda hasta örneklerinin prokalsitonin konsantrasyonları 0,01-53,1 ng/ml arasındaydı. Hasta sonuçlarının her iki cihaz için ortalama ve standart sapma değerleri X=7,71±1,22 ve Y=8,4±1,32 idi. Her iki yöntem ile ölçülen hasta sonuçları karşılaştırıldığında istatistiksel olarak anlamlı bir fark elde edilmedi (p>0,05). (bknz tablo 2, ve tablo 3).

İki yöntem arasındaki korelasyon (r =0,999, p<0,0001) ve regresyon denklemi

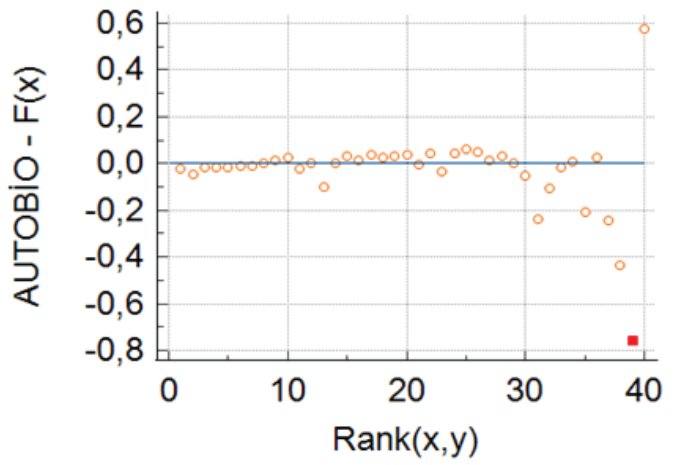
(y =0,03+1,07x) hesaplandı. Korelasyon katsayısı r =0,999 değeri iki cihaz arasında korelasyon olduğunu gösterdi (bknz şekil 1, ve şekil 2).

Tablo 1. Kullanılan reaktif=kit reaktiflerin özellikleri. RLU: relative light units B.R.A.H.M.S PCT-Q Instruction manual.

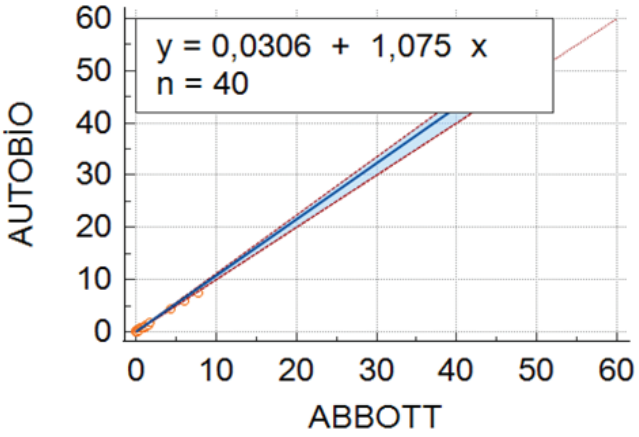
	ARCHITECT Brahms PCT, ci4000 system (CMIA, Abbott Diagnostic)	PCT CLIA Microparticles AutoLumo A2000 Plus
Test sayısı	100 ve 500 test sayısı seçenekleri	50x1, 50x2, 100x5 test sayısı seçenekleri
Prensip	İki adım-Sandviç	Tek adım-Sandviç
Sinyal	RLU	RLU
Örnek tipi	Serum, plazma	Serum, plazma
Örnek hacmi	100	25
Kalibrasyon sıklığı	30 gün	28 gün
Tayin sınırı (LoQ)	0.01 ng/mL	0.06 ng/mL
Taramada kısıtlama (LoD)	0.00 ng/mL	≤0.05ng/mL
Ölçüm aralığı	0.02-100.00 ng/mL	0.03-100 ng/mL
Örnek dilusyonu	Otomatik, 1:10	Manuel, 1:25
Kalibratör ve integral stabilitesi	30 gün	28 gün
İlk sonuçların alınma süresi	15-20 dk arası	15-20 dk arası

Tablo 2. Passing ve Bablok regresyon tablosu, Veri setinin özeti		
X değişkeni		ABBOTT
Y değişkeni		AUTOBIO
Örneklem sayısı		40
	X değişkeni	Y değişkeni
En düşük değer	0,02000	0,01000
En yüksek değer	48,5600	53,1000
Aritmetik ortalama	2,0340	2,1708
Medyan	0,2450	0,3150
Standart sapma	7,7158	8,4008
Ortalamanın standart hatası	1,2200	1,3283
y=0,0305660+1,075472x		
Sistematik farklılıklar		
İntersept A		0,03057
%95 CI		0,008667'ye 0.04500
Proporsiyonel farklılıklar		
Slope B		1,0755
%95 CI		1,000'e 1,1152
Rastgele farklılıklar		
Rezidual Standart deviasyonlar		0,1852
Lineer model geçerliliği		-0,3629'a 0,3629

Tablo 3. Korelasyon eğrisi verileri	
Y değişkeni	Autobio
X değişkeni	Abbott
Örneklem Sayısı	40
Korelasyon katsayısı	0,9996
Anlamlı olduğu seviye	P<0,0001
%95'lik güven aralığı	0,9992 den 0,9998



Şekil 1. Autobio ve Abbott cihazları arasındaki korelasyonu gösteren rezidüel çizelgesi.



Şekil 2. Analiz sonuçları. Autobio ve Abbott cihazları arasındaki korelasyon.

Tartışma

Prokalsitonin ölçümünde en sık tercih edilen cihazlardan birinin Brahms reaktifiyle çalışan ARCHITECT ci4000 sistemi olduğu bilinmektedir. Araştırmamızın sonucuna göre hem ARCHITECT ci4000 hem de Autolumo A2000 Plus platformlarında PCT' nin belirlenmesi, duyarlılık ve özgüllük açısından iyi performans sunmaktadır. Elde edilen sonuçlara göre iki analizörde de gerçekleştirilen testler arasında yüksek bir korelasyon bulunmaktadır. Ancak mevcut PCT'yi ölçmek için mevcut farklı yöntemlerin standardizasyon eksikliği karşılanmamış bir hedef olmaya devam etmektedir. Şu anda PCT kantitasyonu enzimatik, lüminometrik, kemilüminesans olarak belirlenmektedir [13]. Son yıllarda kısa sürede hızlılık ve kesinlik içeren sonuçlar elde edilmesi nedeniyle kemilüminesans yöntemler ile çalışan otoanalizörler laboratuvarlarda sıklıkla kullanılmaktadır. Prokalsitonin ölçümünde de en sık Brahms reaktifi ve kemilüminesans yöntem ile çalışan cihazlar tercih edilmektedir. Bu amaçla ARCHITECT ci4000 sistemi sıklıkla kullanılmaktadır. Ancak Brahms PCT reaktifinin maliyeti yüksektir. Maliyetin yüksek olması laboratuvarları maliyeti düşük başka yöntem ve reaktifleri tercih etmeye zorlamaktadır. Buradan yola çıkarak yapmış olduğumuz cihaz ve yöntem karşılaştırmasında hem ARCHITECT ci4000 hem de Autolumo A2000 Plus PCT ölçümünde korelasyon olduğunu belirledik. Ayrıca Autolumo A2000 Plus cihazında PCT dışında farklı testler ve cihazlar ile karşılaştırma yapılmıştır. Farzami ve Aliasgharpour' nin yaptığı araştırmada aynı cihazda Prolaktin (PRL) ölçümü yapılmıştır. Laboratuvarların kendi ölçüm aralığını belirlemesi sonucuna varmışlardır. Prolaktin ölçümlerinin takibinde hep aynı cihaz

ve reaktif kullanılması önerilmektedir. [14].

Bu bağlamda nihai laboratuvar raporlarında yöntem ve sistem tipinin belirtilmesi önemli hale gelir ve laboratuvarda kalitenin yanı sıra laboratuvar talebinin klinik yönlerini de dikkate aldığını doğrular.

2015 yılında yapılan çok merkezli bir çalışmada Dipalo ve arkadaşları BRAHMS PCT Kryptor'un sonuçlarını dört farklı test düzeneğinde (DiaSorin Liaison, Vidas, Roche E601; Siemens Advia Centaur, ve Diazyme immünoturbidimetrik tahlili; Abbott Architect c16000, Siemens Advia 2400 üzerinde, Roche Cobas C501 ve Beckman Coulter AU5800) PCT ölçümünü karşılaştırdı. Sonuçlar arasında istatistiksel olarak anlamlı farklılıklar gözlendi. Vidas, Advia Centaur, Architect, Cobas C501 ve AU5800 BRAHMS PCT Kryptor ile karşılaştırıldığında tatmin edici korelasyon katsayıları (r = 0,899 ve 0,988) elde edilmiştir. Vidas dışındaki tüm yöntemler için ortalama sapma: ±1,02 µg/L'den az olduğu tespit edildi. Daha da önemlisi, ilgili üç PCT'de bakteriyel enfeksiyonlar için tanısal eşikler, diğer yöntemler ile BRAHMS PCT Kryptor arasında uyum gösterdi. Kullanılan reaktifler için optimum değerler: 0.50 µg/L'de, 83–98% , 2.0 µg/L'de 90–97%, ve 10 µg/L'de 98% olarak kaydedildi.

ARCHITECT BRAHMS PCT yöntemi, PCT ile izlenen antibiyotik tedavisi ve bakteriyel enfeksiyonun ilk tanısı için, iyi kalitenin yanı sıra antibiyotik tedavisi ve bakteriyel enfeksiyonun ilk tanısı için, hem hassas hem de doğru sonuçlar sunan önemli bir bileşen yada kabul olmalı PCT ölçümleri sağlayabilir. Bununla birlikte, ticari olarak temin edilebilen diğer PCT belirleme testlerinde olduğu gibi, PCT seviyelerindeki artışın her zaman enfeksiyonla ilişkili olmadığı ve düşük PCT seviyelerinin enfeksiyonla ilişkili olmadığı göz önüne alındığında, sonuçların tıbbi öykü, fiziksel muayene ve mikrobiyolojik değerlendirme bağlamında da dikkatle yorumlanması gerekir. Pct ölçümü bakteriyel enfeksiyonu gösterir viral enfeksiyonu dışlar [15, 16, 17]. Bu nedenle, test sonuçları klinik son kararın yerini almamalı, sonuçlar daha iyi bir teşhis performansı elde etmek için daha geniş bir bağlama entegre edilmelidir [18].

Yazarların katkısı

Her iki yazar da makalenin içeriğine eşit katkıda bulunmuşlardır. İki yazar da gönderilen bu makalenin ve onaylanmış gönderimin tüm içeriğinin sorumluluğunu kabul etmişlerdir.

Finansal Destek

Bulunmamaktadır.

Çıkar Çatışmaları

Yazarlar herhangi bir çıkar çatışması beyan etmemektedir.

Kaynaklar

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Turkish Journal of Clinics and Laboratory

To cite this article: NURKOC SG. The role of atherogenic index of plasma in coronary artery patients with high SYNTAXII score. Turk J Clin Lab 2023; 4: 729-735

Research Article

The role of atherogenic index of plasma in coronary artery patients with high SYNTAXII score

Yüksek SYNTAXII skoru olan koroner arter hastalarında plazma aterojenik indeksinin rolü

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Abstract

Aim: We tried to evaluate the best diagnostic threshold value of the atherogenic index of plasma (AIP) with respect to coronary artery disease (CAD) and its relationship with SYNTAX II (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) score (SSII).

Material and Methods: The research encompassed 280 consecutive patients with non-ST-segment elevation myocardial infarction (NSTEMI) undergoing coronary angiography, through which SSII was calculated based on initial coronary angiography by at least two independent cardiologists. The patients were separated into two groups low SSII (<23, n=116) and high SSII (≥23, n=164), while AIP was calculated by logarithmic conversion of triglyceride to high-density lipoprotein-to-cholesterol ratio.

Results: We determined some differences between the study groups in point of age, gender, smoking, hypertension, family history, diabetes mellitus, serum urea, C-reactive protein, hemoglobin level, left ventricular ejection fraction, and AIP (P <.05), which indicates a positive connection found between high SSII and AIP (r=0.343; p<0.001; statistically significant p<.05). As a result of multivariate logistic regression analysis, AIP was determined to be an independent risk factor for CAD and high SSII. In addition, we found that AIP values of 0.54 ng/ml and above could estimate the severity of coronary artery disease with 62.8% sensitivity and 60.5% specificity (area under the curve:0.676, %95 confidence interval, 0.613 – 0.739%; p<0.001).

Conclusion: AIP ratios were detected to be increased in patients with high SSII in comparison to those with low SSII. In addition, AIP was significantly independently connected with CAD and high SSII in the group with high SSII. In light of these findings, AIP, as a biomarker, may help prevent CAD.

Keywords: Atherogenic index of plasma, SYNTAX score II, acute coronary syndrome.

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Recevied: 15.07.2023 accepted: 15.12.2023

Öz

Amaç: Koroner arter hastalığına (KAH) göre aterojenik plazma indeksinin (AIP) en iyi tanısal eşik değerini ve bunun SYNTAX II (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) skoru (SSII) ile ilişkisini değerlendirmeye çalıştık.

Gereç ve Yöntemler: Araştırma, koroner anjiyografi uygulanan, ST segment yükselmesiz miyokard enfarktüsü (NSTEMI) olan ve en az iki bağımsız kardiyolog tarafından ilk koroner anjiyografiye dayalı olarak SSII'nin hesaplandığı ardışık 280 hastayı kapsamıştır. Hastalar düşük SSII (<23, n=116) ve yüksek SSII (≥23, n=164) olarak iki gruba ayrıldı. AIP, trigliseritin yüksek yoğunluklu lipoprotein-kolesterol oranına logaritmik dönüştürülmesiyle hesaplandı.

Bulgular: Çalışma grupları arasında yaş, cinsiyet, sigara kullanımı, hipertansiyon, aile öyküsü, diyabet, serum üre, C-reaktif protein, hemoglobin düzeyi, sol ventriküler ejeksiyon fraksiyonu ve AIP açısından bazı farklılıklar belirledik (P<.05), bu da yüksek SSII ile AIP arasında pozitif bir bağlantı bulunduğunu göstermektedir (r=0,343; p<0,001; istatistiksel olarak anlamlı p<0,05). Çok değişkenli lojistik regresyon analizi sonucunda AIP'nin KAH ve yüksek SSII için bağımsız bir risk faktörü olduğu belirlendi. Ayrıca 0,54 ng/ml ve üzerindeki AIP değerlerinin koroner arter hastalığının ciddiyetini %62,8 duyarlılık ve %60,5 özgüllükle tahmin edebildiğini bulduk (eğri altında kalan alan:0,676, %95 güven aralığı, %0,613 – 0,739; p <0,001).

Sonuç: Yüksek SSII'li hastalarda AIP oranlarının düşük SSII'li hastalara göre arttığı tespit edildi. Ayrıca yüksek SSII'li grupta AIP'nin KAH ve yüksek SSII ile anlamlı derecede bağımsız olarak ilişkili olduğu görüldü. Bu bulgular ışığında, bir biyobelirteç olarak AIP, KAH'ın önlenmesine yardımcı olabilir.

Anahtar kelimeler: Plazmanın aterojenik indeksi, SYNTAX II skoru, akut koroner sendrom.

Introduction

Acute myocardial infarction is a significant agent of mortality and morbidity, as well as one of the common public health problems seen worldwide. Atherosclerosis plays an important role in the emergence of most cardiovascular (CV) disorders [1,2], causing a progressive accumulation of fibrous tissue and cholesterol in the type of plaque, both resulting in contracting of the arterial lumen and being the primary factor of non-ST-segment elevation myocardial infarction (NSTEMI). Taking into consideration the fact that inflammation emerges as a constituent of the atherosclerotic process [3,4], it is now widely accepted that all developmental stages of atherosclerosis, including increased plaque instability, are mediated by inflammatory factors, resulting in clinical events such as unstable angina, myocardial infarction (MI), sudden death, and stroke [5,6].

Many types of research have revealed that dyslipidemia and inflammation are closely linked by the pathogenesis of atherosclerosis [7-9]. Low-density lipoprotein cholesterol (LDL-C) is considered an independent element and can be evaluated as a primary intervention target for coronary artery disease (CAD) [10-12], though the LDL-C target value has been an issue of discussion for a long [13,14]. Therefore, it is recommended to reduce LDL-C levels by 50% in clinical practice so as to eliminate CV risks [15].

The size of small, dense low-density lipoprotein (sdLDL), a subfraction of the LDL-C, has been widely investigated through research dealing with lipid metabolism [16,17]. Since sdLDL is assessed to be more atherogenic than floating LDL-C [17], it is widely evaluated as a risk agent for atherosclerosis and an indicator of CV disease [17,18]. However, its assessment is inadequate in clinical practice due to its complexity and high test cost. The logarithm of the molar ratio of triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) levels (log [TG/HDL]) was determined as the atherogenic index of plasma (AIP). Because AIP is indirectly strongly connected and reversely proportional to the diameter of LDL-C fragments and reflects sdLDL levels, it is referred to and used as a marker to predict cases of CAD and plasma atherosclerosis [19-21].

The SYNTAX II (SYNergy between cardiac surgery and percutaneous coronary intervention with TAXus) score (SSII) includes clinical variables, in addition to anatomical factors, to assess the extent and chance of developing CAD, and is mostly referred with the purpose of both coronary risk classification and evaluation of CAD prognosis [22]. Within this context, we evaluated the level of SSII and AIP in patients with NSTEMI encompassed in this study.

Material and Methods

Study Population

Totally 280 consecutive patients who applied to our emergency department with a first episode of NSTEMI were involved in the cross-sectional, single-center study from January 2021 to June 2022. Exclusion criteria include previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting history, statin use, no fasting lipid blood results, presence of decompensated heart failure, severe liver and kidney diseases, autoimmune diseases, malignancies, hematological disorders, severe valve disease, inflammatory or infectious diseases. NSTEMI was diagnosed according to current guidelines [23,24].

Each patient was required to sign a written informed consent form, followed by the confirmation of the study protocol by the Bozok University Ethics Committee, Yozgat, Turkiye (Date/No:22 September 2017/189_2022.09.22_05). Thereby, we began to conduct the study protocol in line with the ethical guidelines of the 1975 Declaration of Helsinki.

The patients' age, gender, CV risk factors, and history of CAD were added to their files. Hypertension (HT) was determined as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg through two separate measurements or by means of any antihypertensive medication. In addition, we determined diabetes mellitus as fasting plasma glucose > 126 mg/dl or > 200 mg/dl via any antidiabetic drug use or any measurement.

Laboratory Measurements

Age, gender, CV risk factors, and laboratory analyses of all patients were received retrospectively from hospital medical documents [including complete blood count and standard biochemical parameters]. Values of lipid parameters were detected by means of the Beckman Coulter AU 5800 autoanalyzer subsequent to at least 12 hours of fasting, while AIP was calculated by the logarithmic transformation of the value of TG and HDL-k concentrations: log10[(TGx0,0113)/(HLDL-Cx0,0259)].

Angiographic Analysis

We also performed coronary angiography via the Standard Judkins technique (Expo; Boston Scientific Corporation, Natick, Massachusetts, USA) and Siemens Axiom Sensis XP device (Munich, Germany), displaying each coronary artery on at least two perpendicular planes. As well as performing PCI according to clinical practice standards through iopromide (low osmolarity and nonionic contrast agent), we digitally documented all coronary angiographic images so as to make a quantitative analysis.

Digital angiograms were evaluated by at least two detached and qualified interventional cardiologists, along with calculating SSII scores, which indicated no difference between interventional cardiologists in terms of value. They also used the online SSII Calculator version 2.1 (www.syntaxscore.com) in order to score each lesion in epicardial arteries ≥1.5 mm in diameter and producing ≥50% stricture. According to this scoring system, the study groups were separated into two groups the low SSII group with values below SSII 23 and the high SSII group with an SSII value of 23 and above.

Statistical Analysis

We also conveyed statistical analyses by means of IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA), while assessing the normality of the distribution of continuous variables via the Kolmogorov-Smirnov test. Based on the distribution pattern, Mann–Whitney U test or independent sample t-test was applied to compare continuous variants between both groups. Categorical variants were given as frequency (percentage), while their comparisons were made via the Chi-Square test. We performed univariate and multiple variable logistic regression analyses in order to detect the independent markers of the emergence of high SxS II. Two-tailed Pearson correlation analyses were performed to analyze correlations between Syntax score II and AIP. The results were expressed as correlation coefficient (r) and p values. We evaluated the value of AIP via receiver operating characteristic curve (ROC) analysis, along with diagnosing the values of high SxS II. Two-tailed p-value <0.05 was assessed to be remarkably significant.

Results

Demographic, basic clinical, and laboratory characteristics of the study groups, consisting of 280 patients in total, are displayed in Table 1. A statistical AIP significant difference was detected between the two groups with respect to age, gender, smoking, HT, family history, diabetes mellitus (DM), serum urea, hemoglobin, serum C-reactive protein (CRP), left ventricular ejection fraction (LVEF) and AIP. However, according to univariate logistic regression analysis, age, gender, smoking, HT, family history, DM, serum urea, hemoglobin level, LVEF, and AIP levels were detected to be independent markers for the high SSII group. On the other hand, age, gender, LVEF, and AIP were determined as independent determinant values in the high SSII group based on the multivariate logistic regression analysis (Odds Ratio respectively (OR): 1.325, %95 confidence interval (CI): 1.178-1.490; p<0,001; OR: 0.164, %95 GA: 0.033-0.807; p=0.026; OR: 0.747, %95 CI: 0.658-0.849; p<0.001; OR: 2.683, %95 CI: 1.552-4.369; p<0.001; Table 2). It was also detected that there was a positive correlation between AIP and high SSII (r=0.343; p<0.001; Figure 1). In addition, we found that AIP values of 0.54 ng/ml and above could estimate the severity of coronary artery disease with 62.8% sensitivity and 60.5% specificity (area under the curve:0.676, %95 confidence interval, 0.613 – 0.739%; p<0.001); figure 2).

Table 1. Baseline clinical and laboratory parameters of the study population.

	SxS II < 23 (n=116)	SxS II ≥ 23 (n=164)	P
Age, years	52 (46-58)	64.50 (56-69.75)	<0.001
Gender, male, n (%)	102 (87.9)	112 (68.3)	<0.001
Smoking, n (%)	101 (87.1)	105 (64)	<0.001
Hypertension, n (%)	29 (25)	69 (42.1)	0.003
Family history, n (%)	34 (29.3)	30 (18.3)	0.031
Diabetes, n (%)	16 (13.8)	55 (33.5)	<0.001
Urea, (mg/dl)	30 (26-36)	38 (28.50-46)	<0.001
Creatinine, (mg/dl)	86 (72-98.75)	0.85 (0.71-1.02)	0.568
Uric acid, (mg/dl)	5.30 (4.60-6.30)	5.60 (4.60-6.50)	0.464
Sodium, (mEq/L)	135 (134-137)	136 (133-138)	0.834
WBC count, x103	10.45 (8.60-13.40)	10.45 (8.10-12.37)	0.344
Neutrophil count, x103	7.10 (5.22-10.05)	7.70 (5.32-9.70)	0.898
Lymphocyte count, x103	1.80 (1.30-2.80)	1.70 (1.12-2.40)	0.240
Monocyte count, x103	600 (500-800)	600 (400-800)	0.277
Hemoglobin, g/dl	14.55 (13.52-15.20)	13.90 (12.90-15.10)	0.005
Platelet count, x103/mm3	235.50 (202-277)	228.50 (195-269.75)	0.400
Total cholesterol, (mg/dl)	187.50 (163.25-280.75)	190 (157-215)	0.837
Triglyceride, (mg/dl)	136.50 (77.25-182.50)	132.50 (84-194)	0.141
LDL, (mg/dl)	117.50 (103.75-141)	122.50 (100-152)	0.685
HDL, (mg/dl)	44.50 (40-52)	32 (25-37)	0.115
CRP, (mg/L)	0.42 (0.20-0.67)	0.48 (0.32-1)	0.017
EF, (%)	50 (48-55)	44 (35-50)	<0.001
AIP	0.44 ± 0.30	0.64 ± 0.32	0.003

Results are expressed as mean ± SD or median (IQR) or frequency (%), SS, SYNTAX score, WBC: white blood cells, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol, CRP: C-reactive protein, EF: Ejection fraction, AIP: atherogenic index of plasma (log(TG/HDL-C).

Table 2. Univariate and multiple variate logistic regression analysis shows the independent predictors of the presence of Syntax Score II ≥23.

	Univariate				Multiple variate			
		95% CI				95% CI		
	OR	Lower	Upper	P	OR	Lower	Upper	P
Age	1.145	1.107	1.185	<0.001	1.325	1.178	1.490	<0.001
Gender (male)	0.314	0.163	0.602	<0.001	0.164	0.033	0.807	0.026
Smoking	0.264	0.141	0.496	<0.001	0.761	0.137	4.233	0.755
Hypertension	2.179	1.293	3.673	0.003	0.360	0.090	1.442	0.149
Family history	0.540	0.308	0.948	0.032	0.779	0.183	3.318	0.736
Diabetes	3.154	1.698	5.859	<0.001	0.774	0.185	3.240	0.725
Urea	1.072	1.043	1.102	<0.001	0.983	0.905	1.068	0.683
Hemoglobin	0.801	0.684	0.938	0.006	0.903	0.588	1.386	0.641
CRP	1.479	0.928	2.359	0.100	1.284	0.546	3.019	0.567
EF	0.871	0.837	0.905	<0.001	0.747	0.658	0.849	<0.001
AIP	4.132	1.963	8.438	<0.001	2.683	1.552	4.369	<0.001

CRP: C-reactive protein, EF: Ejection fraction, AIP: atherogenic index of plasma (log(TG/HDL-C).

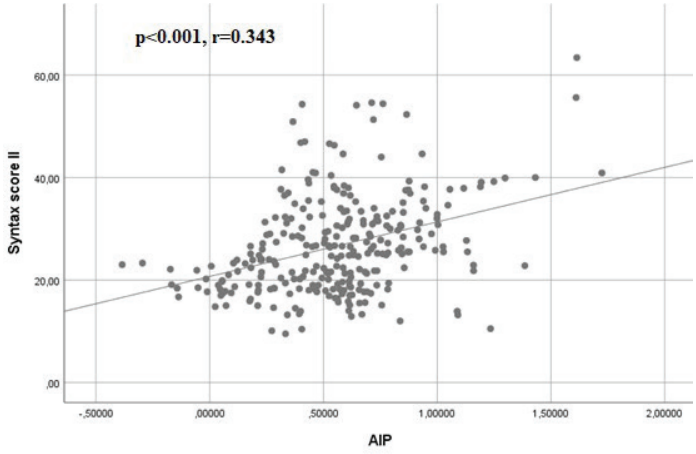

Figure 1. Relationship between Syntax score II and atherogenic index of plasma (AIP)

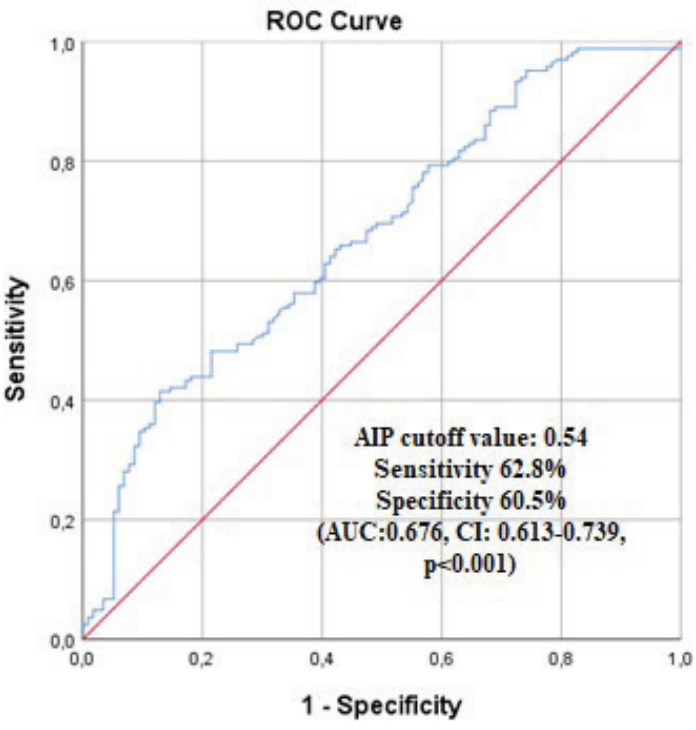

Figure 2. Receiver operating characteristic (ROC) curve for atherogenic index of plasma as a predictor of high syntax score II.

Discussion

AIP and high SSII were shown to be positively correlated according to the findings of the study. In addition, AIP was determined as the independent predictive value for High SSII. This study revealed that AIP as a comprehensive lipid index can be a strong marker for the risk of CAD. In light of these data, AIP may provide clinical utility in terms of examining the emergence of CAD in the following studies.

Since lipid metabolism disorder is considered a significant mechanism for the emergence and progress of CAD [10], most cases of dyslipidemia are triggered by low LDL-C and high TG. The fact that AIP is indirectly closely related to the diameter of LDL-C particles and indicates sdLDL levels makes it a more compatible index with the properties of blood lipids [19].

Studies show that smaller particle size promotes arterial wall penetration and deposition as an efficient cause of atherosclerosis. Therefore, the occurrence of plaque is considered a significant sensitive marker of CAD and atherosclerosis [17]. However, due to high costs and complicated techniques, measuring the ratios of sdLDL is rarely applied in today's medical treatments. AIP has been suggested to be adversely linked to the size of LDL particles. Thus, AIP can, in part, help as a proxy for sdLDL to evaluate potential plasma atherogenicity [19,25,26].

Moreover, numerous relevant studies have revealed that AIP is associated with obesity, HT, DM, insulin resistance, metabolic syndrome, the severity of CAD, and the incidence of acute coronary syndrome [27-29]. AIP may therefore provide a potential direction for CV risk research and the development of early detection, treatment, and intervention strategies for CAD in such patients.

It is confirmed through this study that AIP can be remarkably increased in high-risk CAD patients. Moreover, multivariate logistic regression analysis suggested that AIP can serve as an independent risk agent for CAD, as long as adjusted about age, gender, smoking, HT, family history, DM, serum urea, hemoglobin, serum CRP level, and LVEF (OR: 2.683, %95 CI: 1.552-4.369; P < 0.001). Çerik et al. In his study, CRP was found to be significantly higher in obstructive coronary ectasia than in isolated coronary ectasia [30]. CRP, an inflammatory marker, was also found to be statistically significant in our study (p=0.017).

The SSII is used for risk stratification of patients with CAD and to lead clinic staff into conducting an improved revascularization process. It also provides support for individualized treatment. Since AIP was detected to be remarkably increased in the high SSII group in comparison to the low SSII group, it may allow physicians to assess coronary artery severity early and non-invasively in CAD.

Study Limitations

Although AIP was determined to be positively correlated with high SSII in patients with acute coronary syndrome, this research has some limitations, such as the existence of a single center and therefore a small sample size, no follow-up data available due to its cross-sectional design, not being prospective and multi center, and not including other individual risk factors.

Conclusion

The atherogenic index of plasma can be suggested as an independent risk agent for CAD and high SSII. Therefore, it can be used as a diagnostic biomarker for early diagnosis of CAD and initiation of preventive treatment methods.

Declaration of Conflicting Interests

None.

Funding

The authors did not receive any financial funds for the study's conduct, authorship, and/or publication.

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Turkish Journal of Clinics and Laboratory

To cite this article: Yavrum F, Ilhan C. Investigation of the effects of sociodemographic conditions on adherence to spectacles treatment in adolescents. Turk J Clin Lab 2023; 4: 736-743

Research Article

Investigation of the effects of sociodemographic conditions on adherence to spectacles treatment in adolescents

Sosyodemografik koşulların genç erişkinlerdeki gözlük tedavisine uyum üzerine etkilerinin incelenmesi

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Abstract

Aim: To investigate the effects of several sociodemographic conditions on adherence to spectacles treatment in adolescents.

Material and Methods: 10-19-year-old otherwise healthy adolescents who had been prescribed spectacles at least one year ago were included in this study. To quantitatively evaluate adherence to spectacles treatment, patients were asked to mark along a visual analog scale and the result was noted as an adherence score (AS). Sociodemographic conditions that have potential to affect adherence to spectacles treatment were questioned.

Results: This study includes 107 patients and the mean age of patients was 14.83 ± 2.75 years (10-19). The mean AS was 8.59 ± 2.21 (3-10) for mothers with a higher educational degree, and 6.85 ± 3.14 (0-10) for mothers with a lower educational degree (p =0.018). Similarly, the mean AS was 8.45 ± 2.40 (3-10) for fathers with a higher educational degree and 6.94 ± 3.08 (0-10) for fathers with a lower educational degree (p =0.033). According to logistic regression analysis, a higher educational degree in fathers was associated with 8 and more AS (odds ratio: 4.17, 95% confidence interval 1.14-15.25, and p =0.031). There was no significant difference in AS according to conditions regarding whether or not to use spectacles in a family and social environment (p >0.05, for all).

Conclusion: It was concluded that higher parental educational level is associated with higher adherence to spectacles treatment in adolescents.

Keywords: Adolescent, children, glasses, refractive error, spectacles.

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Recevied: 17.10.2023 accepted: 15.12.2023

Öz

Amaç: Genç erişkinlerde çeşitli sosyodemografik koşulların gözlük tedavisine uyum üzerindeki etkilerini araştırmak.

Gereç ve Yöntemler: Bu çalışmaya en az bir yıl önce gözlük reçete edilmiş 10-19 yaş arası sağlıklı genç erişkinler dahil edildi. Gözlük tedavisine uyumu niceliksel olarak değerlendirmek için hastalardan vizüel analog skala uygulamaları istendi ve sonuç uyum skoru (US) olarak not edildi. Gözlük tedavisine uyumu etkileme potansiyeli olan sosyodemografik koşullar sorgulandı.

Bulgular: Bu çalışmaya 107 hasta dahil edildi ve hastaların yaş ortalaması 14,83 ± 2,75 (10-19) idi. Ortalama US annede eğitim düzeyinin yüksek olduğu durumda 8,59 ± 2,21 (3-10), eğitim düzeyinin düşük olduğu durumda 6,85 ± 3,14 (0-10) idi (p =0,018). Benzer şekilde, babada eğitim düzeyinin yüksek olduğu durumda 8,45 ± 2,40 (3-10), eğitim düzeyinin düşük olduğu durumda 6,94 ± 3,08 (0-10) idi (p =0,033). Lojistik regresyon analizine göre, babada eğitim düzeyinin yüksek olması koşulu, 8 ve daha fazla US ile ilişkiliydi (odds oranı: 4.17, %95 güven aralığı 1.14-15.25 ve p =0.031). Aile ve sosyal çevrede gözlük kullanan birey olması veya olmaması durumuna göre US'de anlamlı fark yoktu (tümü için p >0,05).

Sonuç: Genç erişkinlerde anne ve baba eğitim düzeyinin yüksek olmasının gözlük tedavisine uyumun artmasıyla ilişkili olduğu sonucuna varıldı.

Anahtar kelimeler: Çocuk, genç erişkin, gözlük, kırma kusuru.

Introduction

The World Health Organization (WHO) reported that there are 2.2 billion people who have visual impairment, and uncorrected refractive error is one of the most important causes. [1] The prevalence of refractive errors is associated with age, sex, geographic location, education level, and duration of closeup work. [2] Studies from China and India have reported that uncorrected refractive error is the leading cause of vision loss in school aged children. [3,4]

Uncorrected refractive error can cause reduced academic, social, and economic performance. From the public health perspective, one of the most important features of the refractive error that causes visual loss in an individual who is otherwise healthy is being easily rehabilitated by wearing spectacles. Adherence to spectacles treatment can be low for various reasons. Studies from several developing and developed countries report that the rate of adherence to spectacles treatment in children and adolescents is far from desirable. [5-8] So, an important amount of the population in this age group is quite prone to uncorrected refractive error associated developmental and functional impairment. It is vital to understand why adherence to spectacles treatment in children and adolescents is low and what conditions affect the adherence. It is hypothesized that positive behavioral development of adherence to spectacles treatment in children and adolescents can be affected by perceptions and attitudes of family, school, and social environment. The purpose of this study is to investigate the effects of sociodemographic conditions on adherence to spectacles treatment in adolescents.

Material and Methods

This cross-sectional study was carried out at a tertiary referral center during 2021-2022, in Turkey. The study protocol was prepared per the ethical standards of the 1964 Declaration of Helsinki and was approved by the Hatay Mustafa Kemal University Faculty of Medicine Research Ethics Committee (Protocol no: 2022/33; Date: 14/03/2022). Informed consent was obtained from all participants.

10-19-year-old Turkish adolescents who had been prescribed spectacles at least one year ago were included in this study. Patients that had the following conditions were excluded from the study: 1) amblyopia; 2) other ocular co-morbidities related to low vision (e.g., strabismus, cataract, glaucoma, or neuroophthalmological diseases); 3) <20/20 the best-corrected visual acuity; 4) >6.0 diopters of manifest refraction spherical equivalent; 5) systemic diseases or developmental abnormalities that could affect the eye (e.g., Down's syndrome, Marfan syndrome, neurofibromatosis, dyslexia, or autism spectrum disorders).

All patients underwent a detailed ophthalmological examination including autorefractometry and tonometry (TONOREF III; Nidek Co., Ltd., Aichi, Japan), the best-corrected

visual acuity with Snellen chart, and anterior and posterior segment with slit-lamp biomicroscopy. Manifest refraction was determined using a combination of objective and subjective refraction techniques. Ocular motility was also evaluated with nine gazes and cover-uncover tests for both near and far. After noting demographic and clinical data, patients were asked to mark along a visual analog scale their adherence to spectacles treatment in the last month [ranging from 0 to 10 (0 for I never use, 10 for I use all time I am awake)] and the result was also noted as adherence score (AS). The patients were informed if their spectacles had been broken or lost; the last month before the event should be considered. Then some questions related with sociodemographic conditions that have the potential to affect adherence to spectacles treatment were directed to patients by the same physician (Dr. C.I.) and the answers were noted. The details of the questions are given in Table 1.

Table 1. Details of questions directed to patients.
When was prescribed spectacles for the first time?
Do you know your disease (myopia, hyperopia, or astigmatism) that is required spectacles treatment?
How many people (including you) do you live in your house?
How many people (other than you) use spectacles in your house?
If your mother is alive, does she use spectacles?
If your father is alive, does he use spectacles?
If you have one or more siblings, do any of them use spectacles?
Do any of your other relatives (uncles, aunts, and cousins) use spectacles?
If you go to school, do any of your close friends at school use spectacles?
If you go to school, do any of your teachers who frequently attends your class use spectacles?
If you followed one or more social media phenomenon, do any of them use spectacles?
In your spare time, do you use a smart device (phone, tablet, or computer)?
In your spare time, do you surf on social media?
In your spare time, do you read a book?
In your spare time, do you watch television?
In your spare time, do you do outdoor activities?
On a typical day, how many hours do you spend in front of screen?
On a typical day, how many hours do you spend with near working?
On a typical day, how many hours do you spend outdoor?
Does your mother have a permanent job?
Does your father have a permanent job?
What school did your mother graduate from?
What school did your father graduate from?

Results

This study included 107 patients, 24.17% were male and 75.83% were female. The mean age of patients was 14.83 ± 2.75 years (10-19). 37.24% of patients had at least one companion (parents, siblings, or other relatives) during evaluation. 85.86% of patients stated that they had information about their disease that made spectacles treatment necessary. The mean AS was 7.45 ± 3.23 (0-10) in males and 7.29 ± 2.90 (0-10) in females, 7.45 ± 3.08 (0-10) in patients aged 10-14 and 7.25 ± 2.87 (0-10) in patients aged 15-19, 7.80 ± 3.07 (0-10) in patients who had a companion and 7.10 ± 2.86 (0-10) in patients who had no companion, and 7.46 ± 2.82 (0-10) in patients who had information about the disease and 6.92 ± 3.71 (0-10) in patients who had no information ($p > 0.05$, for all).

The mean AS was 6.94 ± 3.21 (0-10) in patients who stated that their mothers used spectacles and 7.57 ± 2.80 (0-10) in patients who stated that their mothers did not use spectacles; 6.88 ± 2.94 (0-10) in patients who stated that their fathers used spectacles and 7.52 ± 2.96 (0-10) in patients who stated that their fathers did not use spectacles; and 7.45 ± 2.88 (0-10) in patients who stated that their teachers used spectacles and 7.23 ± 3.06 (0-10) in patients who stated that their teachers did not use spectacles. There was no significant difference in AS according to conditions regarding whether or not spectacles were used in the family and social environment ($p > 0.05$, for all), and the details are given in Table 2.

The mean AS was 7.31 ± 3.05 (0-10) in patients who stated that they used a smart device and 7.55 ± 2.61 (3-10) in the others; 7.32 ± 2.77 (0-10) in patients who stated reading and 7.46 ± 3.41 (0-10) in the others; and 7.09 ± 3.13 (0-10) in patients who stated doing outdoor activities and 7.50 ± 2.86 (0-10) in the others. The differences in AS between patients doing the aforementioned activities or not were not statistically significant ($p > 0.05$, for all), and the details are given in Table 2.

The mean value of spherical equivalents was 2.56 ± 1.57 diopters (0.75-6.00), duration of spectacles use 2.75 ± 2.24 years (1-10), population of households 4.85 ± 1.10 persons (2-9), and number of households using spectacles 1.17 ± 1.13 person (0-4). On a typical day, the mean time spent in front of a screen was 3.70 ± 2.05 hours (0-10), with closeup working 3.76 ± 2.40 (0-8), and outdoors 1.73 ± 1.84 (0-6). There was no significant relationship between AS and magnitudes of other continuous variables ($p > 0.05$, for all), and the details are given in Table 3.

Table 2. Comparisons of adherence scores according to different conditions.

		Frequency (%)	Adherence scores			p value*
			Mean	Median	Min-Max	
Spectacles using conditions in family and social environment	Mother					
	Yes	35.48	6.94 ± 3.21	7	0-10	0.386
	No	64.52	7.57 ± 2.80	9	0-10	
	Father					
	Yes	27.95	6.88 ± 2.94	7.50	0-10	0.315
	No	72.05	7.52 ± 2.96	9	0-10	
	Sibling					
	Yes	37.63	6.74 ± 3.07	7	0-10	0.146
	No	62.37	7.71 ± 2.84	9	0-10	
	Other relative					
	Yes	88.17	7.26 ± 2.96	8	0-10	0.429
	No	11.83	8.00 ± 2.93	10	2-10	
	School friend					
	Yes	72.04	7.40 ± 2.91	8	0-10	0.734
	No	27.96	7.15 ± 3.07	8	0-10	
	Teacher					
	Yes	58.51	7.45 ± 2.88	8	0-10	0.706
	No	41.49	7.23 ± 3.06	8	0-10	
	Social media phenomenon					
	Yes	44.00	7.45 ± 2.95	9	0-10	0.704
	No	56.00	7.31 ± 2.92	8	0-10	
Free time activities	Using a smart device					
	Yes	76.59	7.31 ± 3.05	8.50	0-10	0.808
	No	23.41	7.55 ± 2.61	8	3-10	
	Surfing on social media					
	Yes	61.70	7.19 ± 2.95	8	0-10	0.484
	No	38.30	7.64 ± 2.95	9	0-10	
	Reading					
	Yes	72.34	7.32 ± 2.77	8	0-10	0.463
	No	27.66	7.46 ± 3.41	10	0-10	
	Watching television					
	Yes	51.06	7.27 ± 3.07	8.50	0-10	0.837
	No	48.94	7.46 ± 2.83	8	0-10	
	Outdoor activities					
	Yes	34.04	7.09 ± 3.13	7.50	0-10	0.587
	No	65.96	7.50 ± 2.86	9	0-10	
Parents' working in a permanent job	Mother					
	Yes	15.39	8.00 ± 2.87	9.50	2-10	0.853
	No	84.61	7.71 ± 2.85	10	0-10	
	Father					
	Yes	84.61	7.87 ± 2.57	9	0-10	0.922
	No	15.39	7.10 ± 4.10	10	0-10	
Parents' education level	Mother					
	High school or higher	48.49	8.59 ± 2.21	10	3-10	0.018
	Lower than high school	51.51	6.85 ± 3.14	7.50	0-10	
	Father					
	High school or higher	50.00	8.45 ± 2.40	10	3-10	0.033
	Lower than high school	50.00	6.94 ± 3.08	7	0-10	

* Statistical analysis was made with Mann Whitney-U test.

Table 3. Correlations between adherence scores and other continuous variables.

	Mean	Median	Min-Max	p value*	r value*
Age (year)	14.83 ± 2.75	15	10-19	0.348	-0.099
Spherical equivalent (diopter)	2.56 ± 1.57	2	0.75-6.00	0.139	0.162
Duration of spectacles using (year)	2.75 ± 2.24	2	1-10	0.145	0.158
Population of households (person)	4.85 ± 1.10	5	2-9	0.662	-0.046
Number of households using spectacles (person)	1.17 ± 1.13	1	0-4	0.059	-0.200
Time spent in front of screen (hour)	3.70 ± 2.05	3	0-10	0.668	-0.045
Time spent in near working (hour)	3.76 ± 2.40	3	0-8	0.471	0.076
Time spent outdoor (hour)	1.73 ± 1.84	1	0-6	0.471	-0.076

* Correlation analysis was made with Spearman correlation test.

The mean AS was 8.00 ± 2.87 (2-10) in patients who stated that their mothers worked in a permanent job and 7.71 ± 2.85 (0-10) in patients who stated that their mothers did not; 7.87 ± 2.57 (0-10) in patients who stated that their fathers worked in a permanent job and 7.10 ± 4.10 (0-10) in patients who stated that their fathers did not. There was no significant difference in AS between mother/father of patients working in a permanent job or not (p >0.05, for both). The mean AS was 8.59 ± 2.21 (3-10) in higher educational degree for mothers and 6.85 ± 3.14 (0-10) in lower educational degree for mothers. Similarly, the mean AS was 8.45 ± 2.40 (3-10) in higher educational degree for fathers and 6.94 ± 3.08 (0-10) in lower educational degree for fathers. The differences in AS between higher and lower educational degrees for both of mothers and fathers were statistically significant (p =0.018 and p =0.033, respectfully). The details of comparisons of AS according to parents working and education conditions are given in Table 2. The demonstration of AS of patients according to educational levels of parents is given in Figure 1.

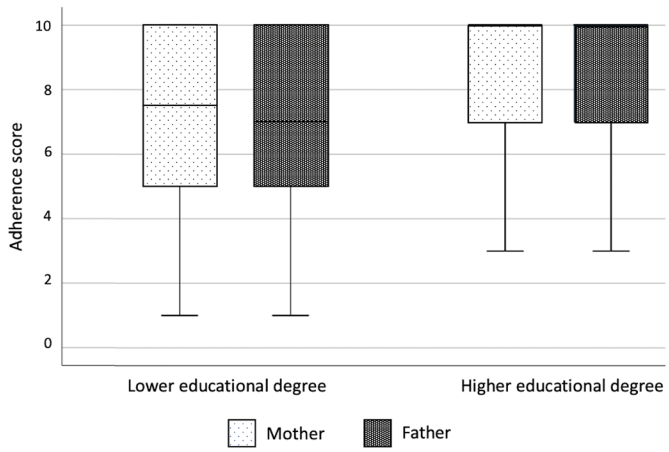

Figure 1. The demonstration of adherence scores of patients according to educational levels of parents.

According to logistic regression analysis, higher educational degree in fathers was associated with 8 and more AS (odds ratio :4.17, 95% confidence interval 1.14-15.25, and p =0.031) while other analyzed parameters (magnitude of spherical equivalent, duration of spectacles using, number of households using spectacles, and mother's education level) were not significantly associated (p >0.05, for all), and the summary of the analysis is given in Table 4.

Discussion

This study contributes to the literature in many different aspects. Some of the previous studies have focused on adherence to spectacles treatment in amblyopic children. [9-11] Spectacles use was not considered as only visual rehabilitation for amblyopic children, and adherence to treatment can be more reinforced by family and social environment because of amblyopia treatment/prevention by using spectacles. So, the results of studies conducted on amblyopic children are not representative of the otherwise healthy population with refractive error. Large sample sized population-based or school-based screening programs were the methods of many previous studies, and contained many children and adolescents who had never used spectacles despite having refractive error. [1,4,6,7,12] This is not an ideal way to investigate conditions that had the potential to affect adherence to treatment because adherence has been decided as very low, with surprise visits for reasons like losing spectacles, breaking the spectacles, or forgot the spectacles and left them at home. [1,4,6,7,12] It was also reported that patients who were not used to spectacles are less likely to be using spectacles than the others. [6] So, the patients who wear spectacles for at least one year and who were admitted to an ophthalmology clinic for spectacles correction are more eligible subjects to investigate. In some studies, standard spectacles were provided under public

Table 4. Summary of the logistic regression analysis for some conditions* that have potential to effect adherence score.

	Odds ratio	95% confidence interval		p value*
		Lower limit	Upper limit	
Duration of spectacles using	1.259	0.940	1.685	0.122
Spectacles use condition in siblings (ref :yes)	4.345	0.982	19.221	0.053
Father's education level (ref :lower than high school)	4.172	1.141	15.257	0.031

* Logistic regression analysis was made with Backward-LR test. Magnitude of spherical equivalent, duration of spectacles using, number of households using spectacles, mother's education level, and father's education level were conditions included into the logistic regression analysis, and the final comparison (given in the table) was reached after six steps. Fitting for logistic regression model was checked with Hoshmer-Lemeshow test.

health promotional programs. Despite this method providing a greater opportunity to remove the barriers prior to the availability of treatment, one size/color/design standardized spectacles could not be deemed as being acceptable for all children and adolescents, and some of them have never used these spectacles that were provided free of charge. [12] Many of the previous studies determine the adherence using a binary format (0 for non-adherence and 1 for adherence). In this study, another method, a visual analogue scale was used to determine adherence to spectacles treatment. A Visual analogue scale allows a more comprehensive evaluation to the adherence. Grading of adherence to spectacles treatment is a more appropriate method than binary format because Gajiwala et al.13 reported only less than a third of students use spectacles for the whole day. The scale was not conducted on very young children, only adolescents were included, and an older family member accompanied then for some of the time during the evaluation.

Many studies reported parental disapproval, teasing by peers, unattractive frames/poor appearance, and a negative attitude from society as important factors for low adherence to spectacles treatment. [14-17] In their meta-analysis, Dhirar et al. [18] classified the reasons for low adherence as personal factors 25.78%, social factors 13.18%, visual problems/ headache 5.47%, and breakage/loss/forgetfulness 23.34%. They reported that sociocultural factors are more important contributors in adherence to spectacles treatment, especially for upper/middle income countries. [18] They also emphasized the importance of positive reinforcement at both school and household levels. [18] Similarly, Morjaria et al. [19] investigated the attitudes of parents and teachers to clarify the reasons for low adherence to treatment in students. Classmates, teachers, parents, other family members, and community perceptions regarding spectacles were described as sociodemographic factors by Morjaria et al., [20] and they stated that the reasons for low adherence are more complex. It is thought that the presence of individuals who used spectacles within a close circle of adolescent friends can contribute to developing positive behavioral development of spectacles use. In this study, comprehensive questioning was conducted, including family members, school friends, teachers, and social media phenomena. According to the results of this study, the presence of individuals who used spectacles within a close circle of adolescents has no significant effect on adherence to spectacles treatment.

In the literature, conflicting results had reported the relationship between adherence to spectacles treatment and age/sex/magnitude of refractive error. [8,12,18,21-24] According to the results of this study, demographic conditions including age and sex have no significant effect on adherence to spectacles treatment in adolescents. Albeit there is a tendency to think the adherence to spectacles treatment should be higher in the adolescents who have information about their disease, had a higher magnitude of refractive error, and used spectacles for a longer duration; the results of statistical analysis did not support this theory. So, it can be concluded that clinical conditions have a limited effect on adherence to spectacles treatment in adolescents.

Varieties of daily habits or free time activities like using a smart device, reading, surfing on social media, watching television, and doing outdoor activities was another parameter investigated; however, whether or not these activities were carried out had no significant effect on adherence to spectacles treatment. Additionally, there was no significant relationship between adherence to treatment and the time spent in front of a screen, closeup working, and outdoor activities. In the literature, there is not enough data to compare the results of this study and it can be easily thought that there is a negative effect of doing outdoor activities or the magnitude of the time spent outdoors on adherence to spectacles treatment in adolescents; however, this study clearly demonstrates that there is not a significant

relationship. To conclude, the effects of daily habits or free time activities on adherence to spectacles treatment in adolescents is one of the most important aspects of this study.

The relationship between adherence to spectacles treatment and parents' education level was not clear enough. Messer et al. [6] reported that the education level of the father was not associated with the adherence to spectacles treatment. Gogate et al. [12] reported that low adherence to spectacles treatment in children is related to low education in the father, and the worst adherence occurs in children with illiterate fathers. On the other hand, a similar relationship with mother's education was not reported. [12] Another study demonstrated that adherence to spectacles treatment increases with the education level of the parents. [25] According to the results of this study, both father's and mother's education levels are significantly related to adherence to spectacles treatment in adolescents, and better adherence was found in higher educational degree for both father and mother. To clearly separate working status and education degree, the condition of parents' working in a permanent job was questioned and there was no significant relationship between adherence to treatment and working status of parents. Additionally, logistic regression analysis used in this study clearly revealed the strong relationship between increased adherence to spectacles treatment in adolescents and higher educational level of father. A study from India associated a similar result with patriarchal social structure. [12] This cause-and-effect relationship can apply to the social structure which was conducted in this study to some degree; this study does not provide objective data to support this hypothesis. Maybe, educated women having equal or more educated husbands can be a reason affecting the results of statistical analysis that presents the father's education level as more important than the mother's.

When compared with similar studies, having a small sample size and being a single center study are limitations of this study. Despite not being technically difficult, not doing an objective evaluation of AS obtained with visual analog scale was another important limitation. On the other hand, this study is one of the most important reports that has detailed and investigated the effects of sociodemographic conditions on adherence to spectacles treatment in adolescents.

Conclusion

In conclusion several clinical conditions were investigated in this study (magnitude of refractive error or duration of spectacles use): social (spectacles use in conditions within a close circle of friends), and personal (daily habits or free time activities). There was no important effect on adherence to spectacles treatment in adolescents. On the other hand, it was found that higher parental educational level is related to higher adherence to spectacles treatment.

Acknowledgements

Disclaimer on financial support (grants): None

Potential conflicts of interest: None

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. The authors have indicated they have no financial relationships with any company and no external funding. Involved in design and conduct of this study (FY, CI); involved in collection, management, analysis, and interpretation of the data (CI); involved in preparation, review, or approval of the manuscript (FY, CI).

Acknowledgments

Disclaimer on financial support (grants): None

Potential conflicts of interest: The authors declare that they have no competing interests.

All persons named in the Acknowledgment section have provided me with written permission to be named

Funding

None. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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To cite this article: Tekeli A, Gorgulu S, Alakus Sabuncuoglu F, Duran GS. Evaluation of orthodontic bracket bonding strength on demineralized enamel: Effects of remineralization agents and SEM examination. Turk J Clin Lab 2023; 4: 744-752

Research Article

Evaluation of orthodontic bracket bonding strength on demineralized enamel: Effects of remineralization agents and SEM examination

Farklı yöntemlerle tedavi edilen erozyonlu mine yüzeyine uygulanan ortodontik braketlerin bağlanma dayanımlarının karşılaştırılması

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Abstract

Aim: To evaluate the shear bond strength (SBS) of orthodontic brackets bonded to demineralized enamel treated with four different remineralization agents and examine enamel surfaces using scanning electron microscopy (SEM).

Material and Methods: In this in vitro study, 120 premolar teeth were examined. The premolars were divided into six groups as; negative control (Group NC) with erosion remineralization cyclus were applied without any treatment agent, positive control (Group PC), treated with fluoride (Group F), with combined fluoride and diode laser (Group F+D), with CPP-ACP (Group M) and treated with nano-hydroxyapetite (Group B). Erosion remineralization cycle were applied to all samples except PC group. For each group, 20 samples were tested in SBS and examined using scanning electron microscopy (SEM).

Results: There was a statistically significant difference between groups in terms of the SBS values of the orthodontic brackets ($p<0.001$). There was no statistically significant difference between Group M and Group B ($p = 0.375$). There was a significant difference in all other binary comparisons ($p<0.001$). The sequence in terms of the SBS values of orthodontic brackets applied after erosion remineralization cycle of the groups were; Group NC (sound enamel)>Group B~Group M >Group F+D >Group F >Group PC (eroded enamel). SEM examinations corroborated the findings.

Conclusions: It was determined that remineralization materials applied in all study groups significantly increased the shear bond strength values of the eroded tooth surfaces. Group M and Group B were more efficient than other groups providing clinically acceptable SBS values for the bonding of orthodontic brackets to previously treated demineralized enamel surfaces.

Keywords: Enamel, erosion, remineralization, shear bond strength.

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Doi: 10.18663/tjcl.1380618
Recevied: 24.10.2023 accepted: 04.12.2023

TJCL Volume 14 Number 4 p: 744-752

Öz

Amaç: Çalışmanın amacı ortodontik braketlerin, dört farklı remineralizasyon ajanı ile işlenmiş demineralize mineye bağlanma dayanımının (Shear Bond Strength- SBS) değerlendirmesi ve taramalı elektron mikroskobu (SEM) kullanarak mine yüzeylerinin incelenmesidir.

Gereç ve Yöntemler: Bu in vitro çalışmada, 120 premolar diş incelenmiştir. Premolar dişler 20'şer dişin olduğu altı gruba ayrıldı: negatif kontrol (Grup NC)- herhangi bir tedavi ajanı uygulanmadan erozyon remineralizasyon döngüsü uygulanan grup, pozitif kontrol (Grup PC), florür ile tedavi edilen grup (Grup F), kombinasyon halinde florür ve diyot lazer ile tedavi edilen grup (Grup F+D), CPP-ACP ile tedavi edilen grup (Grup M) ve nano-hidroksiapatit ile tedavi edilen grup (Grup B). PC grubu hariç tüm örneklerde erozyon remineralizasyon döngüsü uygulandı. Her bir grup için 20 örnek, yapışma dayanımı SBS testine tabi tutuldu ve SEM kullanılarak incelendi.

Bulgular: Ortodontik braketlerin SBS değerleri açısından gruplar arasında istatistiksel olarak anlamlı fark tespit edildi ($p<0.001$). Grup M ve Grup B arasında istatistiksel olarak anlamlı bir fark bulunmamaktaydı ($p = 0.375$). Diğer tüm ikili karşılaştırmalarda önemli bir fark vardı ($p<0.001$). Grupların erozyon remineralizasyon döngüsü sonrasında uygulanan ortodontik braketlerin SBS değerleri sırası şu şekildeydi; Grup NC (sağlam mine)> Grup B ~ Grup M> Grup F+D> Grup F> Grup PC (erozyona uğramış mine). SEM incelemeleri SBS bulgularını destekler niteliteydi.

Sonuç: Çalışmamızdaki tüm gruplara uygulanan remineralizasyon materyallerinin, erozyona uğramış diş yüzeylerinin yapışma dayanım değerlerini önemli ölçüde arttırdığı belirlendi. Grup M ve Grup B, demineralize mine yüzeylerine ortodontik braketlerin yapıştırılması için klinik olarak kabul edilebilir SBS değerleri sağlama konusunda diğer gruplardan daha etkili bulundu.

Anahtar kelimeler: Mine, erozyon, remineralizasyon, bağlanma dayanımı.

Introduction

Dental erosion is the loss of hard tissue caused by a chemical factor without bacterial involvement.1 Erosion has been a condition in dentistry that received little attention for years and was often overlooked in its early diagnosis. With changes in lifestyle, the consumption frequency, and quantity of acidic foods and beverages have increased in recent times. As a result, the etiology, prevalence, and approaches to the treatment of dental erosion have become increasingly important.2

In orthodontic treatment, brackets are attached to the enamel surface of teeth using various adhesives. Studies in this area have mostly focused on determining the optimal bracket-adhesive combination for bonding in orthodontic treatment. Although there have been studies on the retention of brackets applied to enamel surfaces whose morphological structure has changed due to erosion, there is no complete consensus on this matter. Therefore, it is important for clinical applications to determine to what extent various remineralization agents applied to eroded tooth enamel before orthodontic treatment prevent erosion and affect bracket retention.

The use of fluoride-containing preparations is recommended to protect teeth against acid attacks.3,4 When fluoride is applied to the teeth, it forms weakly bound calcium fluoride (CaF_2) crystals on the tooth surface, protecting it against repeated demineralization and serving as a fluoride reservoir. At the same time, it facilitates the reattachment of minerals to the surface through the formation of fluoroapatite and fluorohydroxyapatite.5 This attachment is further enhanced when the fluoride preparation is acidic, such as acidulated phosphate fluoride (APF). Due to its low pH, APF gel forms submicron CaF_2 and less soluble forms of calcium, reducing enamel permeability for a longer period and strengthening surface precipitation.6 In addition to fluoride agents, laser applications, calcium and phosphate-containing toothpastes, casein glycopeptide, casein phosphopeptide, and preparations containing amorphous calcium phosphate have been investigated for remineralization purposes.7,8

Laser application has been reported to result in morphological changes such as surface melting and recrystallization, making the surface less susceptible to acid attacks.9,10 Laser treatment is thought to decrease the Calcium/Phosphorus ratio on the tooth surface, change the calcium-phosphate ratio, create a thin layer of dissolution, and then re-precipitate and solidify inorganic material, making the teeth more resistant to decay.11 It has also been reported that the critical pH (5.5), at which enamel dissolution begins, decreases to 4.8 after laser application.12 Some studies have shown that the effectiveness

of fluoride is enhanced when applied in combination with laser treatment.13,14 The mechanism of increasing fluoride retention by the laser is explained by the thermal effect of the laser beam, creating changes such as pits, microcavities, and roughness on the surface, increasing fluoride retention.

Another remineralization agent used to prevent dental erosion as an alternative to fluoride is casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). Phosphopeptides in CPP-ACP's structure are protective factors found in milk. CPP is obtained by breaking down casein with trypsin enzyme using selective precipitation methods and can stabilize calcium phosphate as a CPP-amorphous calcium phosphate (ACP) complex.15

CPPs prevent ACP from precipitating in the solution by binding it in small clusters with phosphoserine extensions. This results in the formation of saturated, basic nanocomplexes with calcium phosphate. CPP-ACP can bind to tooth surfaces and dental plaque, functioning as a reservoir for calcium and phosphate.16 It is reported that when compared to fluoride toothpaste, CPP-ACP treatment reduced the lesion depth more on enamel surfaces.17

The remineralization effect of nano-hydroxyapatite added to the contents of toothpaste and mouthwashes has been reported.18 It is determined in a study that samples treated with toothpaste containing carbonate-hydroxyapatite nanocrystals, SEM images showed a thick, homogeneous apatitic structure which is formed by nanocrystals, completely covering interprismatic and prismatic enamel structures.19

The aim of our in vitro study is to evaluate which treatment method is more effective in terms of bonding strength of applied orthodontic brackets, based on the data obtained after the treatment of eroded tooth enamel surfaces with four different remineralization agents namely, Fluoride, Fluoride and Diode Laser combination, CPP-ACP and a toothpaste that includes nano-hydroxyapatite.

Material and Methods

The study is designed as an in vitro study. The sample size for each study group was determined statistically through a power analysis with Power: 0.95 and α: 0.05. As a result, the sample size was determined as n=20 for each group. Teeth included in the study are the lower and upper jaw first and second premolar teeth, which have completed root development and exhibit no signs of decay, hypomineralization, cracks, erosion, abrasion, restoration, core damage, etc. These teeth are non-amorphous and have not been subjected to any chemical agents.A total of 120 extracted human premolar teeth were collected, cleaned of soft tissue, stored in a 0.1% thymol solution, and utilized within a 2-month period. These teeth were obtained from patients with their informed consent, and the extractions were unrelated to the objectives of this study. The research project received approval from the scientific council of the Keçiören Education and Research Hospital Clinical Research Ethics Committee (decision no: 1369, decision date: 08.03.2017). The research project received approval from the local ethical commitee (decision no: 1369, decision date: 08.03.2017). The samples were divided into six groups as illustrated in Figure 1.

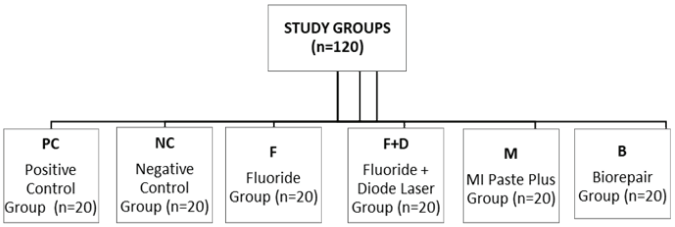

Figure 1. Study groups

Study Groups

a) Positive Control Group (PC): Throughout the experiment, apart from the removal of debris, the bracket bonding procedure with a 1% Citric acid solution (pH 2.4), and the erosion remineralization cycle, no additional surface treatment was conducted.

b) Negative Control Group (NC): During the experiment, apart from debris removal, the teeth were immersed in artificial saliva solution with a pH of 7, and no additional surface treatment was performed before the bracket bonding procedure.

c) Fluoride Group (F): In this group, in addition to erosion-remineralization cycle, fluoride gel (1.23% APF gel) was applied to the exposed enamel surfaces, including the bracket boundaries, using a cotton-tipped applicator and left for 2 minutes before bracket bonding.

d) Fluoride + Diode Laser Group (F+D): In this group, in addition to erosion-remineralization cycle, fluoride gel (1.23% APF gel) was applied to the enamel surface, followed by diode laser treatment following the manufacturer's recommendations (4 Watts, 60 Joules, 15 seconds). The diode laser beams, with pulse duration of 1 ms-1s and repetition rate of 0.5 Hz-0.5 kHz, were delivered to the sample surfaces via a fiber transport system before bracket bonding.

e) CPP-ACP Group (M): In this group, in addition to the erosion-remineralization cycle, CPP-ACP + 900 ppm fluoride (GC MI Paste Plus, RECALDENT™) was applied to the exposed enamel

surfaces, including the bracket boundaries, using a cotton-tipped applicator and left for 2 minutes before bracket bonding.

f) Nano-Hydroxyapatite Group (B): In this group, in addition to erosion-remineralization cycle, a toothpaste containing nano-hydroxyapatite (BioRepair®, Coswell S.p.a, Bologna, Italy) was applied to the exposed enamel surfaces, including the bracket boundaries, using a cotton-tipped applicator and left for 2 minutes before bracket bonding.

Demineralization-Remineralization Cycle

During the erosion-remineralization cycle, for erosion, teeth were immersed in a 1% citric acid solution (pH 2.4) for 2 minutes, six times a day. For remineralization, the teeth were removed from citric acid solution, rinsed with distilled water, and then specific remineralization agents for each group, except for the control groups, were applied and afterwards the teeth were placed in an artificial saliva solution with a pH of 7, and this erosion-remineralization cycle was repeated for 10 days.

Bracket Bonding

Bracket bonding was performed using the same standards by a single operator. Firstly, a 37% orthophosphoric acid gel was applied to the buccal surface of each tooth for 20 seconds. Afterward, the teeth surfaces were cleaned and dried, and adhesive primer Transbond XT primer (3M Unitek, USA) was applied. Following this step, the adhesive bracket base was applied and attached to the tooth surface. In the study, brackets were attached to tooth enamel surfaces treated with different remineralization agents using light-cured Transbond XT resin (3M Unitek, USA).

Mini Master 0.018 slot stainless steel brackets (American Orthodontics, USA) were used as brackets. The base area of the brackets is 10 mm2. A Light Emitting Diode (LED) machine that emits blue light in the range of 430-480 nm was used as the light source (3M Elipar FreeLight 2, 3M ESPE, USA). Light was applied to the attached brackets for 20 seconds, with 10 seconds from the mesial and 10 seconds from the distal direction.

Thermal Cycling Process

Samples for evaluating bond strength were placed in a thermal cycling device (Dentester, Salubris Technica, Istanbul, Turkey) to simulate intraoral temperature changes after the brackets were bonded. The prepared samples were immersed 500 times in water baths at temperatures of 5°C and 55°C, respectively. Each time the samples were immersed in the bath, they remained inside for 20 seconds, and the transfer time between baths was set to 10 seconds by the device.

Shear Bond Strength Test

Shear bond strength (SBS) tests of the bonded brackets were conducted using a universal testing machine (Instron Universal Testing Machine, Elista, Istanbul, Turkey). Within the machine, there is a setup to hold the sample securely. The loading tip, which tapers to a sharp edge like a blade, was positioned parallel to the surface where the bracket was bonded. A shear force was applied to the tooth-bracket interface at a rate of 0.5 mm/minute until the bracket separated. The resulting data was recorded in Newtons using a computer connected to the machine. The results were later converted to Megapascals (Mpa) using the equation Mpa(N/mm2) = Force (Newton)/Bracket area (mm2).

Scanning Electron Microscopy Examination

Samples for Scanning Electron Microscopy (SEM) were embedded in special acrylics (SamplKvick Acrylic System, Buehler Lake Bluff, Illinois, USA). Images were acquired at different magnifications after being coated with a 100 Angstrom (A°) thick layer of platinum and were evaluated.

Statistical Analysis

Statistical analyses were conducted using the SPSS software (Statistical Package for Social Sciences, SPSS for Windows 17.0, IBM, USA). Descriptive statistics, including the mean, standard deviation, minimum, and maximum values of the force data in Mpa obtained from six groups, were calculated. Group comparisons were performed using Analysis of Variance (ANOVA) and Tukey post hoc tests, and $p<0.05$ was considered statistically significant.

Results

The descriptive statistics and statistical comparisons of the SBS values for six groups are presented in Table 1 and Table 2. The lowest SBS values were obtained in the PC group (6.56 ± 0.74 MPa), whereas the highest values were obtained in the NC group, (14.32 ± 1.66 MPa) .

Table 1. The descriptive statistics of the SBS values.

Group	SBS values (mean±SD Mpa)	SBS values (minimum,Mpa)	SBS values (maximum,Mpa)
NC	14.32±1.66	10.62	16.85
PC	6.56±0.74	5.13	7.90
B	11.67±1.56	8.59	14.48
M	10.85±1.10	9.48	13.77
F+D	9.49±1.00	7.73	11.71
F	7.95±1.59	5.58	11.40

SBS: Shear Bond Strength, NC: Negative control group, PC: Positive control group, B: Biorepair group, M: MI Paste Plus group, F+D: Fluoride + Diode laser group, F: Fluoride group, SD: standard deviation.

Table 2. Comparison of the means of SBS values among groups. Tukey multiple comparison test.

Groups	Significance
NC/ B	<0.001
NC / M	<0.001
NC / F+D	<0.001
NC / F	<0.001
PC / B	<0.001
PC / M	<0.001
PC / F+D	<0.001
PC / F	0.016
B / M	0.375
B / F+D	<0.001
B / F	<0.001
M / F+D	0.018
M / F	<0.001
F+D / F	0.005

SBS: Shear Bond Strength, NC: Negative control group, PC: Positive control group, B: Biorepair group, M: MI Paste Plus group, F+D: Fluoride + Diode laser group, F: Fluoride group. The mean difference is significant at the 0.05 level.

According to the ANOVA, there were significant differences between the SBS values of the groups ($p<0.001$). Comparison of the means of SBS values among groups with Tukey multiple comparison test showed statistically significant differences between all groups, except for groups B and M ($p=0.375$).

SEM images of intact, demineralized, and treated enamel surfaces are presented in Figure 2. In SEM images taken from the sound enamel surface, it is observed that the surface is smooth and due to the regular arrangement of enamel prisms, it has a homogeneous appearance. Typical enamel structures such as grooves and perikymata lines are distinct on the sound enamel surface. Additionally, small indentations or pits, indicative of cumulative mechanical effects on teeth, were observed (Figure 2a). SEM images of the demineralized enamel (Group PC) presented a porous structure, with the prisms increasing in size and distributing irregularly (Figure 2b). In F and F+D groups, demineralized areas were still observed, however, structures resembling CaF2, similar to those seen in sound enamel morphology, were also observed (Figure 2c and 2d). On the surfaces of enamel samples treated with CPP-ACPF paste, remineralization was smoother and more homogeneous (Figure 2e). SEM image of Group B showed acicular nano-hydroxyapatite crystals deposited on the enamel surface, resulting in reductions in voids and erosion areas (Figure 2f).

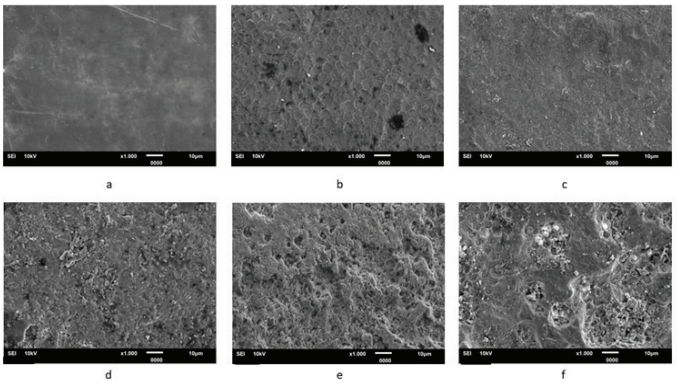

Figure 2. Scanning Electron Microscopy (SEM) images of the groups tested. Scanning Electron Microscopy (SEM) images of the groups tested with 1000x magnification. **2a:** sound enamel surface (Group NC), **2b:** demineralized enamel (Group PC), **2c:** Group F**, 2d:** Group F+D, **2e:** Group M, **2f:** Group B.

Discussion

In recent years, changes in lifestyles and conditions, along with an increase in the consumption of acidic foods and beverages, have led to an increased incidence of erosion in teeth. In our in-vitro study we used citric acid solution to simulate enamel erosion, samples were immersed in lemon 1% citric acid solution with a pH of 2.4 for 2 minutes, six times a day and then in artificial saliva solution with a pH of 7. It has been shown that when the teeth which were exposed to an erosive solution were stored in saliva, there were less erosion. Artificial saliva is based on the electrolyte composition of natural saliva. It does not contain saliva proteins that bind calcium and is highly saturated. Some proteins in natural saliva, such as statherin, tend to inhibit calcium phosphate precipitation. Artificial saliva, which lacks these proteins, causes excessive calcium phosphate precipitation.20 Therefore, in vitro remineralization provided is higher than that occurring in vivo with artificial saliva.20,21 In our study, 10 ml of artificial saliva was used for each sample, and the samples were kept in artificial saliva during each cycle.

Shear Bond Strength Testing

In fixed orthodontic treatment, it is crucial for brackets not to dislodge and to withstand chewing forces. In a study conducted by Reynolds in 1975, it was suggested that the minimum bond strength should be in the range of 5.9-7.8 MPa.22

Our results showed that all the applied remineralization treatment agents significantly increased the SBS values and the SBS values of demineralized specimens were lower than those of the other groups. The highest mean SBS value was

obtained in the NC group (14.32±1.66 MPa). This was followed by Group B (11.67±1.56 MPa), Group M (10.85±1.10 MPa), Group F+D (9.49±1.00 MPa), Group F (7.95±1.59 MPa) and Group PK (6.56±0.74 MPa). There were no statistically significant differences between Group B and Group M (p=0.375).

There are several studies in the literature regarding fluoride use for demineralized teeth on SBS.23–25 This is because many patients use fluoride-containing toothpaste to clean their teeth before bonding brackets. The results of these studies showed that, fluoride increases the SBS values compared to the control groups which were the demineralized specimens. In our study, we found higher SBS values on erosive enamel surfaces treated with fluoride compared to our PC group, which was only subjected to demineralization.

Studies in the literature regarding Fluoride + Diode laser applications have mostly focused on measuring the level of microhardness or the decrease in Ca+2 and Ca+2/P ratios on the erosion surface. It is reported in the literatüre that when flüoride is used in combination with laser.26,27

The results of our study indicate that the Fluoride + Diode laser irradiation of the demineralized specimens significantly increased the SBS values compared to fluoride gel application alone.

CPPs have been shown to stabilize ACP, localize ACP in dental plaque, and have anti-cariogenic effects in animal and in situ human dental caries models.28,29 The increasing number of patients receiving CPP-ACP as a prophylactic agent before orthodontic treatment has led to an increase in studies on the effects of CPP-ACP on the bond strength of orthodontic brackets. The first ACP-containing orthodontic composite adhesive available on the market received FDA approval in 2002, and the results of a study conducted by Dunn30 were published. In this study, the bond strengths of orthodontic brackets attached to enamel surfaces using conventional resin-based orthodontic adhesive and ACP-containing orthodontic adhesive were compared. The results showed that the bond strength of orthodontic brackets attached with ACP-containing adhesive to teeth was significantly weaker than that of conventional resin-based orthodontic adhesive. Kecik et al.31, reported that the shear bond strength was positively affected when enamel surfaces were treated with 1.23% APF, CPP-ACP, or their combination. All bond strength values obtained in the study were well above the range of values recommended by Reynolds, providing preliminary data about the effect of CPP-ACP on the SBS of brackets. In the study by Al-Kawari et al.32, CPP-ACP+F (MI Paste Plus) was applied to enamel surfaces after acid erosion, and it was found that it significantly increased bond strength when compared to the control group before acid erosion and the results after application. Uysal et al.23 compared the effects of fluoride and CPP-ACP on the SBS of orthodontic brackets bonded to demineralized enamel and found no significant differences between the control and CPP-ACP groups. In our study, we used MI Paste Plus, one of the current products, as one of the remineralization agents we applied after erosion. We found that the MI Paste Plus group in our study significantly increased SBS values but not to the level of sound enamel, which was the negative control group.

Nano-hydroxyapatite (HA) crystals, one of the most popular remineralization agents in recent years, have the ability to penetrate the enamel surface, reform stronger crystals, and distribute freely available ions, thus exerting an effect on the tooth surface.33 Synthetic apatite or hydroxyapatite has been proven to be beneficial in enamel remineralization.34 HA crystals exhibit high biomimetic properties due to their composition, structure, morphology, mass, and surface physical-chemical properties. Cossellu et al.33, analysed the effects of six different prophylactic agents on the bond strength of orthodontic brackets. They compared commonly used prophylactic techniques (fluoride, CPP-ACP, ozone) with a new material, toothpaste containing nanohydroxyapatite (BioRepair®). Considering the limitations of this in vitro study, the results showed that the use of fluoride varnish before acid etching and bonding negatively affected the SBS of brackets, but no differences were observed in teeth treated with BioRepair®, ozone, and CPP-ACP.

In our study, BioRepair® (Coswell S.p.A., Bologna, Italy), which is a fluoride-free toothpaste made from hydroxyapatite nanoparticles. Showed the highest SBS values. Although this value was not statistically significantly higher than the MI Paste Plus group, it was significantly higher than all other treatment groups.

SEM Examination

The findings obtained from the SEM images support the SBS results. In the SEM images of F and F+D groups, demineralized areas were still somewhat visible in a honeycomb-like structure, and a mild irregular erosion pattern was observed. At the same time, structures resembling CaF2, similar to those seen in enamel morphology, were also observed. In the F+D group, the structures resembling CaF2 were observed in various regions of the enamel surface to a greater extent compared to SEM images of F group. It is reported in the

literature that SEM images of fluoride treated groups, although less in amount, presented exposion of enamel prisms, similar to the demineralized control group. and also a more robust surface appearance35 that are consistent with our findings.

Magalhaes and colleagues36 examined the effect of using sodium fluoride and titanium tetrafluoride (TiF4) preparations in conjunction with Nd:YAG laser on enamel erosion, using SEM. They reported that in the group where TiF4 and Nd:YAG laser were used together, there were fewer pores and microcracks on the enamel surface compared to other groups. They concluded that TiF4 varnish protected against enamel erosion, without the influence of laser irradiation. Alsherif et al26 suggested in their in vitro study that the group that was treated with combined use of nanosilver fluoride and diode laser, displayed a homogenous subsurface enamel, that is similar to normal enamel mineralization. The SEM findings of our study was similar to the findings of Alsherif et al.26

Our results revealed that on the surfaces of enamel samples treated with CPP-ACPF paste (MI Paste Plus), remineralization was smoother and more homogeneous compared to the F and F+D groups. This difference can be attributed to the inclusion of casein, which contributes to the smoother and more uniform remineralization. It was shown that the SEM images of specimens that treated with CPP-ACP, the remineralized enamel surface was more resistant to acid attacks compared to normal enamel surfaces. CPP-ACP acts as a reservoir for calcium and phosphate by breaking down in the presence of low pH and helps reduce demineralization and Hemingway et al.37 showed that citric acid modified with casein, significantly prevented erosion, and SEM images revealed the presence of an approximately 5µm thick amorphous layer covering the surface. Oshiro et al.29 examined the results of applying CPP-ACP-containing paste by comparing SEM images and reported that in the control group images, significant demineralization was observed in the enamel surface layer, whereas in the group where CPP-ACP paste was applied, only very mild porosity was present in the enamel, indicating that demineralization was prevented.

The SEM findings of our study also revealed the presence of a remineralization layer, and it was observed that the remineralization was smoother and more homogeneous in F+D group.

The SEM images of our results demonstrated that the enamel surface treated with a toothpaste containing nano-hydroxyapatite after demineralization (Group B) showed acicular nano-hydroxyapatite crystals that deposited on the enamel surface, leading to a reduction in voids and erosion areas. The results of a study comparing the remineralization effect of a 10% nano-hydroxyapatite solution with a 2% sodium fluoride solution on initial enamel lesions were showed that nano-hydroxyapatite particles adhered to the pores resulting from demineralization in SEM images. These adhered nanocrystals grew at the sites of deposition and formed microclusters, creating a uniform apatitic layer on the demineralized enamel surface.38 Jeong et al.39 reported that SEM examinations performed after toothpaste application revealed that hydroxyapatite particles interacted with the enamel surface. that increased the concentration of Ca and P ions, resulting in the repair of the demineralized surface. In another study assessing the remineralization efficacy of nano-hydroxyapatite + fluoride, bioactive glass, and strontium acetate-fluoride-containing toothpaste, the results showed that in the group where nano-hydroxyapatite + fluoride toothpaste was applied, demineralization on the surface disappeared, and the surface was covered with a protective layer.40

In our study, it was observed that the enamel surface treated with toothpaste containing nano-hydroxyapatite was covered with a newly formed apatitic layer that extended over both the prismatic and interprismatic enamel structures. However, it was noted that the remineralization layer did not have a homogeneous surface. This lack of homogeneity was believed to be due to the absence of fluoride in our remineralization agent, which we used.

The main limitation of our study was calculation of the SBS values were in vitro, and more clinical research is needed to confirm the findings in clinical settings.

Conclusions

- Enamel demineralization significantly reduces the SBS of orthodontic brackets.
- SBS values in all groups met the bonding strength values required for clinical success, as determined by Reynolds (5.9-7.8 MPa).
- Fluoride, combined fluoride and diode laser, CPP-ACP and nano-hydroxyapatite applications, used after demneralization, increased SBS of orthodontic brackets and resulted in SEM findings nearly similar to normal enamel surfaces.
- There was no statistically significant difference between Group M and Group B and they were more efficient than other groups providing clinically acceptable SBS values for the bonding of orthodontic brackets to previously treated demineralized enamel surfaces.

Conflict of interest

The authors have no conflict of interest to declare.

Financial Disclosure

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

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Turkish Journal of Clinics and Laboratory

To cite this article: Uyar B, Salman CB, Aydar S, Batihan G, Savga K, Balikci B, Baran H, Cankaya Inan E, Arslan A, Gunes M, Kaya MC, Bulut M. Retrospective evaluation of post-traumatic stress disorder data of healthcare workers who received counseling from psychosocial support unit after the kahramanmaraş earthquake.Turk J Clin Lab 2023; 4: 753-759

Research Article

Retrospective evaluation of post-traumatic stress disorder data of healthcare workers who received counseling from psychosocial support unit after the kahramanmaraş earthquake

Kahramanmaraş depremi sonrası psikososyal destek biriminden danışmanlık alan sağlık çalışanlarının travma sonrası stres bozukluğu verilerinin retrospektif değerlendirilmesi

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Abstract

Aim: Healthcare workers seem to be a neglected professional group when helping other people during disasters. This study aimed to determine the Post-Traumatic Stress Disorder(PTSD) levels of healthcare workers and the risk factors for PTSD after the Kahramanmaraş Earthquake.

Material and Methods: Sociodemographic, clinical, National Stressful Events Survey Short Scale (NSESSS) ASD (Acute Stress Disorder) and PTSD data of healthcare professionals working at Dicle University Hospital who applied to the psychosocial support unit after the February 6 Kahramanmaraş earthquake were examined retrospectively. Data from 102 people who were evaluated twice in the first and second 30 days after the earthquake were included in our study.

Results: Participants' mean age was 32.70±8.26 years. 52% of the participants were women, 49% were married, and 42.2% had a child/children. The rates of professions were distributed as follows: 38.2% physician, 35.3% nurse, and 26.5% other healthcare workers. PTSD scores were significantly higher in those with children than in those without, in nurses than in doctors, and in those with a psychiatric history than in those without. Gender, marital status, and psychiatric family history did not significantly affect the scale scores. According to simple linear regression analysis, ASD scores predicted PTSD scores %40.6.

Conclusion: High NSESSS-ASD scores, having a child/children, being a nurse, and having a psychiatric history were found to be risk factors for developing PTSD in healthcare workers. Risk groups for PTSD in healthcare workers should be identified through studies with larger samples and more extended follow-up periods, and protective measures should be taken.

Keywords: Post-Traumatic Stress Disorder, Acute Stress Disorder, Healthcare Workers, Psychological Trauma, Earthquake

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Recevied: 31.10.2023 accepted: 10.11.2023

Öz

Amaç: Sağlık çalışanları felaket dönemlerinde diğer insanlara yardım ederken ihmal edilen bir meslek grubu gibi görünmektedir. Bu çalışmada Kahramanmaraş Depremi sonrasında sağlık çalışanlarının Travma Sonrası Stres Bozukluğu (TSSB) düzeyleri ile risk faktörlerinin belirlenmesi amaçlandı.

Gereç ve Yöntemler: Dicle Üniversitesi Hastanesi'nde çalışan, 6 Şubat Kahramanmaraş depremi sonrası psikososyal destek ünitesine başvuran sağlık çalışanlarının sosyodemografik, klinik, Ulusal Stresli Olaylar Araştırması Kısa Ölçeği (NSESSS) ASB ve TSSB verileri geriye dönük olarak incelendi. Çalışmamıza depremi sonrası ilk 30 gün ve ikinci 30 günde iki kez değerlendirmeye alınan 102 kişinin verileri dahil edildi.

Bulgular: Katılımcıların yaş ortalaması 32,70±8,26 yıldı. %52'si kadın, %49'u evliydi ve %42,2'sinin çocuk sahibiydi. %38,2'si hekim, %35,3'ü hemşire ve %26,5'i diğer sağlık çalışanıydı. TSSB skorları çocuğu olanlarda olamaynalara göre, heşmşirelerde doktorlara göre, psikiyatrik özgeçmişi olanlarda olmayanlara göre anlamlı düzeyde yüksekti. Cinsiyet, medeni durum, psikiyatrik soygeçmişin ise ölçek skorlarına anlamlı etkisi yoktu. Basit doğrusal regresyon analizine göre ASB puanları TSSB puanlarını %40,6 yordamaktaydı.

Sonuçlar: Yüksek NSESSS-ASB skorları, çocuk sahibi olmak, hemşire olmak, psikiyatrik özgeçmişi olmak sağlık çalışanlarında TSSB geliştirmek için risk faktörleri olarak bulundu. Daha geniş örneklemli, daha uzun takip süreli çalışmalarla sağlık çalışanlarında TSSB için risk grupları tespit edilmeli ve koruyucu önlemler alınmalıdır.

Anahtar Kelimeler: Travma Sonrası Stres Bozukluğu, Akut Stres Bozukluğu, Sağlık Çalışanları, Psikolojik Travma, Deprem

Introduction

On 06.02.2023, two earthquakes of magnitude M7.7 and 7.6 occurred at 04:17 and 13:24 local time, with the epicenter in Kahramanmaraş. The earthquake affected a wide geographical area and caused great destruction in 11 provinces (Kahramanmaraş, Hatay, Adıyaman, Gaziantep, Malatya, Kilis, Diyarbakır, Adana, Osmaniye, Şanlıurfa and Elazığ) in Turkey. More than fifty thousand people lost their lives, and more than 100 thousand people were injured (1).

Trauma is defined as experiencing actual or threatened death, serious injury, or sexual assault in one of the following ways: i) Directly experiencing a traumatic event, ii) Seeing directly what happens to others, iii) Learning that a traumatic event has happened to a family member or close friend iv) Recurrent or excessive exposure to unpleasant details of the traumatic event (2).

Acute Stress Disorder (ASD) is defined as involuntary symptoms, negative mood, dissociative, avoidance, and arousal symptoms occurring within 3 to 30 days after a traumatic event. If these symptoms persist for more than 30 days, the diagnosis is Post-Traumatic Stress Disorder (PTSD) (2).

Factors such as the type of trauma, diagnosis of ASD, gender, marital status, history of psychiatric disorder, and family history of psychiatric disorder affect the development of PTSD (3).

There is evidence to suggest that survivors of exposure to traumatic events such as physical or sexual assault and natural disasters are at risk of suffering from post-traumatic stress symptoms. Previous studies have shown that 57-83% of cases with ASD develop PTSD in the subsequent period and that ASD is a risk factor for PTSD. In a study that evaluates the ability of ASD to predict PTSD in China, the severity of ASD symptoms was found to correlate with later PTSD symptoms in a sample of 197 people who experienced the Lushan earthquake (4).

Early intervention in cases of ASD may reduce the likelihood of developing long-term psychiatric disorders, according to several studies (5). Therefore, it is crucial to identify patients with ASD after traumatic events.

Since Turkey is an earthquake country, PTSD has been studied in many groups after the earthquakes, but it has been determined that there is no study related to healthcare workers. Healthcare professionals seem to be neglected while helping other people in these processes.

In this study, we aimed to determine the PTSD levels of healthcare workers and the risk factors for PTSD after the Kahramanmaraş Earthquake.

Material and Methods

1.Sample selection

Criteria for inclusion in the study: i. Having been working at Dicle University Faculty of Medicine Hospital for at least 6 months, ii. Having received counseling from our psychosocial support clinic after the Kahramanmaraş Earthquake, iii. Being evaluated twice between the first 30 days and the second 30 days after the earthquake

Exclusion criteria from the study: i. Having been working at Dicle University Faculty of Medicine Hospital for less than 6 months, ii. Being evaluated outside the specified dates, iii. Been evaluated less than two times

Data from 102 healthcare professionals were included. All participants included in the study signed the informed consent form. The study was carried out following the Declaration of Helsinki Principles.

2.Data Collection Tools

The sociodemographic data and scales for evaluating ASD and PTSD of the participants were recorded by the clinicians in the hospital data recording system. The data of participants were examined retrospectively.

2.1.Sociodemographic Data Form: This form, which was prepared to record the sociodemographic characteristics of healthcare professionals applying to the psychosocial support clinic, includes information such as age, gender, marital status, and education information.

2.2.The National Stressful Events Survey Acute Stress Disorder Short Scale (NSESSS): This scale measures the severity of ASD symptoms in individuals over 18 years following a highly stressful event or experience. It has seven items which rate the severity of acute stress disorder during the past seven days on a 5-point (0=Not at all; 1=A little bit; 2=Moderately; 3=Quite a bit, and 4=Extremely) Likert scale. The total score can range from 0 to 28, and higher scores indicate greater severity. The scale was structured and published according to the ASD DSM-V diagnostic criteria by the American Psychiatric Association (APA), and its Turkish reliability and validity study was conducted by Aşçıbaşı et al. in 2017 (6). In the Turkish validity and reliability study, Cronbach's alpha coefficient for internal consistency was 0.95.

2.3.The National Stressful Events Survey Post-traumatic Stress Disorder Short Scale (NSESSS): This scale measures the severity of PTSD symptoms in individuals over 18 years following a highly stressful event or experience. It has nine items which rate the severity of acute stress disorder during the past seven days on a 5-point (0=Not at all; 1=A little bit; 2=Moderately; 3=Quite a bit, and 4=Extremely) Likert scale. The total score can range from 0 to 28, and higher scores indicate greater severity. The scale was structured and published according to the PTSD DSM-V diagnostic criteria by the APA, and its Turkish reliability and validity study was conducted by Evren et al. in 2016 with Cronbach's alpha of 0.87 (7).

3.Ethics Committee Permission

Since the study was designed retrospectively, academic review board permission was obtained from Dicle University Faculty of Medicine, Department of Psychiatry. Ethics committee permission for the study was received from Dicle University Medical Faculty Non-Interventional Clinical Research Ethics Committee (Date: 13.09.2023/Permission number: 240).

4.Statistical Methods

SPSS (Statistical Package for Social Sciences) 26.0 program was used to analyze the data. Frequencies, means, and standard deviations were calculated for descriptive statistics. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. To compare two sample means, for normal distributed data Independent-T test and non-normal distributed data Mann-Whitney U test was used. Kruskal Wallis test was used to compare three sample means for non-normal distributed data, and Post Hoc test was used to identify which groups differ from each other. Simple linear regression analysis was used to examine the relationship between a dependent and an independent variable. P-value of <0.05 was taken for statistical significance.

Results

Participants' mean age was 32.70±8.26 years, and the mean education duration was 15.81±3.26 years. 52% of the participants were women, 49% were married, and 42.2% had a child/children. The rates of professions were distributed as follows: 38.2% physician, 35.3% nurse, and 26.5% other healthcare workers. While 25.5% had a history of psychiatric disorder, 17.6% had a family history of psychiatric disorder (Table 1).

Table 1. Sociodemographic characteristics and psychiatric disorder history of participants	
	X̄±SD
Age	32.70±8.26
Education duration (years)	15.81±3.26
	N (%)
Gender Female Male	53 (52) 49 (48)
Marital status Single Married	52 (51) 50 (49)
Having a child/children Yes No	43 (42.2) 59 (57.8)
Proffession Medical doctor Nurse Other healthcare workers	39 (38.2) 36 (35.3) 27 (26.5)
History of psychiatric disorder Yes No	26 (25.5) 76 (74.5)
Family history of psychiatric disorder Yes No	18 (17.6) 84 (82.4)
X̄; Mean, SD; Standart Deviation, N; Number, %; Percent	

Gender, marital status, and having a child/children did not significantly affect NSESSS-ASD scores. While NSESSS-PTSD mean scores were significantly higher in the participants who have a child/children than the ones who have not (p<.05), there were no statistical differences by gender and marital status (Table 2).

Table 2. Scale scores by sociodemographic characteristics				
Gender	Female (N=53)	Male (N=49)	Independent T-Test	
	X̄±SD	X̄±SD	t	p
NSESSS-ASD	12.00±6.94	9.78±5.99	1.727	.087
NSESSS-PTSD	12.58±8.85	12.49±7.72	.058	.954
Marital Status	Single (N=52)	Married (N=50)		
NSESSS-ASD	10.40±6.23	11.48±6.91	-.826	.411
NSESSS-PTSD	11.79±7.44	13.32±9.09	-.933	.353
Having a child/children	Yes (N=43)	No (N=59)		
NSESSS-ASD	11.98±7.23	10.17±5.98	1.379	.171
NSESSS-PTSD	14.65±9.27	11.00±7.18	2.154	.034*
X̄; Mean, SD; Standart Deviation, N; Number, NSESSS; The National Stressful Events Survey Short Scale, ASD; Acute Stress Disorder, PTSD; Post-traumatic Stress Disorder *; p< .05				

Nurses had significantly higher scores than physicians for both ASD and PTSD scales (p<.05), while there was no statistical difference between other binary comparisons (Table 3).

Table 3. Scale scores by profession						
Profession	Physician (N=39)	Nurse (N=36)	Other HW (N=27)	Kruskal Wallis test		Post hoc
	±SD	X̄±SD	X̄±SD	X 2	p	
NSESSS-ASD	8.31±4.91	13.61±6.63	11.15±7.26	11.565	.003**	2>1
NSESSS-PTSD	9.05±4.95	16.31±8.57	12.56±9.70	12.411	.002**	2>1
X̄; Mean, SD; Standart Deviation, N; Number, NSESSS; The National Stressful Events Survey Short Scale, ASD; Acute Stress Disorder, PTSD; Posttraumatic Stress Disorder, HW; Healhcare Worker**; p< .01						

Participants with history of psychiatric disorder had significantly higher scores than the ones with no history of psychiatric disorder for both scales (p<.05). Family history of psychiatric disorder did not significantly affect scale scores (Table 4).

Table 4. Scale scores by having history and family history of psychiatric disorder				
History of psychiatric disorder	Yes (N=26)	No (N=76)	Mann-Whitney U	
	X̄±SD	X̄±SD	U	p
NSESSS-ASD	13.85±6.71	9.93±6.25	659.000	.011*
NSESSS-PTSD	16.23±9.19	11.28±7.61	667.000	.014*
Family history of psychiatric disorder	Yes (N=18)	No (N=84)		
NSESSS-ASD	12.83±5.03	10.52±6.80	568.000	.098
NSESSS-PTSD	13.11±7.74	12.42±8.44	691.000	.568
X̄; Mean, SD; Standart Deviation, N; Number, NSESSS; The National Stressful Events Survey Short Scale, ASD; Acute Stress Disorder, PTSD; Post-traumatic Stress Disorder *; p< .05				

According to simple linear regression analysis, ASD score predicts PTSD score by 40.6% (R2=.406) (Table 5).

Table 5. Simple linear regression analysis results on the effect of NSESSS-ASD on NSESSS-PTSD						
Dependent variable	Independent variable	B	SE	Beta	t	Regression results
NSESSS-PTSD	NSESSS-ASD	.805	.097	.637	8.273	R=.637 R2=.406 F=68.447 p=<.001***
Durbin Watson: 1,612						
NSESSS; The National Stressful Events Survey Short Scale, ASD; Acute Stress Disorder, PTSD; Post-traumatic Stress Disorder						

Simple linear regression chart is given in Figure 1. The regression formula is "PTSD Score= 3.74+0.8 (ASD Score)".

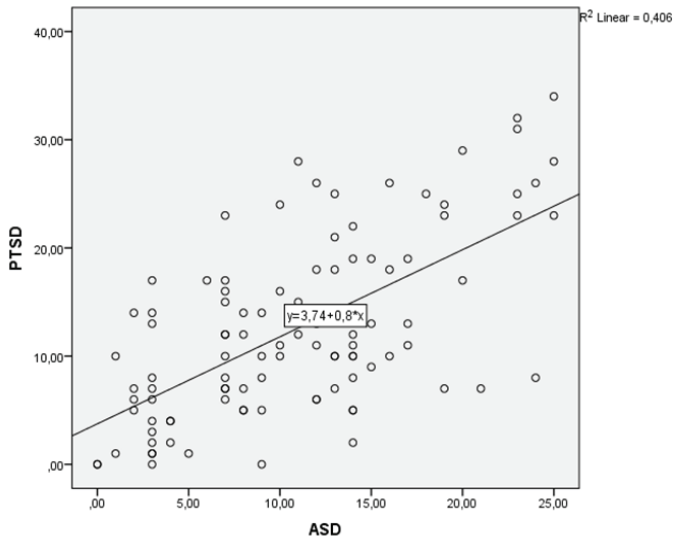

Figure 1. Simple linear regression chart of NSESSS-ASD's effect on NSESSS-PTSD

ASD; Acute Stress Disorder, PTSD; Post-traumatic Stress Disorder

Discussion

The main findings of our study were:

1.While having children was a factor that significantly increased the PTSD scale score, it did not significantly affect ASD scores. Additionally, scale scores were not significantly affected by gender and marital status.

2.Since healthcare workers were compared threefold as physicians, nurses, and others, both scale scores of nurses were found to be significantly higher than medical doctors.

3.While having history of psychiatric disorder significantly increased both ASD and PTSD scale scores, having family history of psychiatric disorder did not significantly affect either scale.

4.NSESSS ASD scores were predicting PTSD scores by regression formula of "PTSD Score= 3.74+0.8 (ASD Score)".

The fact that healthcare workers are a front-line professional group in disasters such as epidemics and earthquakes brings healthcare workers more face-to-face with psychological trauma (8, 9). For this reason, this particular group needs to be studied.

1.While having children was a factor that significantly increased the PTSD scale score, it did not significantly affect ASD scores. Additionally, scale scores were not significantly affected by gender and marital status.

A study conducted in the United States with emergency physicians showed no statistically significant difference between mean PTSD severity score by age, gender, marital status, and having children (10). It is noteworthy that there are not enough studies in the literature investigating the effect of having a child/children on PTSD. The magnitude of the earthquakes experienced, two consecutive main earthquakes, and thousands of aftershocks did not make it possible to create a safe living space for earthquake victims after the earthquake. Healthcare workers who had to be on duty had difficulty finding suitable places to leave their children, and they could not stop themselves from worrying about their children. For these reasons, the Kahramanmaraş earthquake may have had different effects than other traumas and even other earthquakes.

Previous studies showed that women have higher risk for PTSD than men. These studies indicate that their results may be related to greater fear conditioning in women (11, 12). In a large sample post-earthquake PTSD study conducted in Iran, it was stated that women had more PTSD than men in regions moderately affected by the earthquake. Still, such gender differences were not found in severely affected areas (13). Our non-significant result may be due to the severity of the earthquake.

In a study with 2004 sample after an earthquake in China, being unmarried/divorced/widowed was found to be an independent risk factor for PTSD (14). On the contrary, Guo J. et al. found that being married in the early period after the earthquake was significantly associated with PTSD (15). Being married may be a factor that causes higher anxiety in the early post-traumatic period and increases PTSD. It may turn into a protective factor in terms of social support in later periods after trauma. In a review of 46 articles, parallel to our result, it was found that marital status did not significantly affect the incidence of PTSD (16). How long after the trauma the study was conducted and the sample size may affect the results. Our results may have been affected by similar factors.

2.Since healthcare workers were compared threefold as physicians, nurses, and others, both scale scores of nurses were found to be significantly higher than physicians.

There is only one study about the comparison of PTSD between nurses and physicians after an earthquake. This study was conducted following an earthquake measuring 7.0 that occurred in Southern Taiwan in 2016 and resulted in 117 deaths and 513 people wounded disaster. In this study, nurses tended to have higher rates of PTSD than physicians, similar to our study (17).

In studies after pandemics and epidemics, nurses were found to be more at risk for PTSD than other healthcare professionals

and physicians. Some of these studies focused on positive coping styles of physicians associated with better outcomes (18, 19). Other authors stressed the effect of maladaptive coping styles in predicting PTSD (20).

In a study evaluating physicians and nurses in China, it was found that negative life events were associated with anxiety and depression, physicians experienced more work-related negative events than nurses, but nurses had higher anxiety and depression symptoms than physicians (11).

In a study conducted during the COVID-19 epidemic in Turkey, parallel to our study, nurses' NSESSS-ASD scale levels were significantly higher than physicians (21). This study commented that the NSESSS levels of nurses who are in contact with patients for a long time and provide primary care are significantly higher than physicians and other healthcare professionals, which is an expected and consistent finding with the literature (22, 23).

3.While having history of psychiatric disorder significantly increased both ASD and PTSD scale scores, having family history of psychiatric disorder did not significantly affect either scale.

In a review, it was mentioned that individuals who reported psychological adjustment problems before the trauma showed higher levels of PTSD symptoms than those who did not report psychological adjustment problems before the trauma (24). It has been suggested that the individual's pre-traumatic psychopathology also poses a risk for the development of PTSD (25). In this context, our results are parallel to the literature.

Evidence supporting the association between family psychiatric history and PTSD is inconsistent. Individual studies have shown that parents' mental health disorders are associated with an increased risk of PTSD. Maternal depression has also been shown to be associated with an increased risk of PTSD. Statistically significant associations between PTSD and family history of psychiatric depression, anxiety, and psychosis have also been reported (26). However, a meta-analysis including 77 studies investigating PTSD risk factors showed that the relationship between family psychiatric history and PTSD was not significant (27).

4.NSESSS-ASD score was a predictor of PTSD score.

Previous studies have shown that 57-83% of cases with ASD develop PTSD in the subsequent period and that ASD is a risk factor for PTSD. A study assessing the ability of ASD to predict PTSD found that the severity of ASD symptoms was associated with later PTSD symptoms in a sample who experienced the Lushan earthquake (4).

Having a longitudinal design is a strong aspect of our study. Unlike most previous reports addressing the long-term consequences of traumatic events, our study's early assessment of PTSD, ASD, and related risk factors can be mentioned as a strength of our research. However, the fact that the mental status evaluations of the people were not continued in the subsequent period is a limitation of the study. The small number of samples can also be considered a limitation of the study.

Conclusion

Having a child/children, being a nurse, and having a psychiatric history were found to be risk factors for developing PTSD in healthcare workers. Gender, marital status, and family history of psychiatric disorder did not statistically affect the development of PTSD. Higher NSESSS-ASD scores were predicting higher NSESSS-PTSD scores.

Risk groups for the development of PTSD in healthcare workers should be identified through studies with larger samples and more extended follow-up periods.

Protective measures should be taken for all healthcare workers and risk groups. The working conditions of healthcare workers should be improved. It should not be forgotten that healthcare professionals may also need support while helping other people.

Financial support and conflict of interest

No person/organization financially supports the study, and the authors do not have any conflict of interest.

Declaration of Author Contribution

All authors contributed to the design of the study, collection, analysis or expression of data, designing the article, reviewing the scientific content, or approving the preprint version of the article.

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Turkish Journal of Clinics and Laboratory

To cite this article: Esendagli D, Koc E, Ercan MB, Teksam B, Turkay BE, Yagci ZD. Can we predict lung sequelae in post-COVID-19 patients?. Turk J Clin Lab 2023; 4: 760-766

Research Article

Can we predict lung sequelae in post-COVID-19 patients?

COVID-19 sonrası hastalarda akciğer sekelini baştan tahmin edebilir miyiz?

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Abstract

Aim: Patients hospitalized with COVID-19 pneumonia can progress to lung fibrosis after the infection even though given the standard treatment or the anti-inflammatory regimen for the long term. It is hard to predict which group of patients is going to have a progressive lung disease thus this study aims to define possible biomarkers at the acute onset of infections that might predict lung fibrosis afterwards.

Material and Methods: Patients hospitalized between January - December 2020 with pneumonia and a positive PCR for COVID-19 infection were included in the study. They were followed up for 12 months for post-COVID-19 symptoms and lung sequelae formation.

Results: A total of 64 patients were included with a median age of 62 (R: 17-93) and 42.2% were women (n=27). 35 patients (54.7%) had post-COVID symptoms, 8 (12.5%) of them died and 22 (34.4%) were re-hospitalized. 76.6% had a good clinical course but 54.7% of the patients developed sequelae after infection. The pneumonia score, blood oxygen saturation level, CRP, and troponin levels at admission were significantly related to sequelae development ($p<0.05$). Male gender, elderly age, hospitalization period duration, bad clinical prognosis, and intensive care unit admission together with the presence of Hypertension and post-COVID symptoms were correlated with sequelae formation ($p<0.05$). Age above 63.5, CRP higher than 24.1 and pneumonia score greater than 0.15 were significant cut-off values for lung sequelae prediction.

Conclusion: This study shows that lung sequelae after COVID-19 infection can be predicted from the start of infection and measures might be taken afterwards.

Keywords: Biomarkers, COVID-19, lung sequelae, monitoring

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Recevied: 02.11.2023 accepted: 04.12.2023

Öz

Amaç: COVID-19 pnömonisi ile hastaneye yatırılan hastalar, uzun süreli standart tedavi veya antienflamatuar rejim uygulansa bile enfeksiyon sonrası akciğer fibrozisine ilerleyebilir. Hangi hasta grubunun ilerleyici akciğer hastalığına sahip olacağını tahmin etmek zordur. Bu çalışma enfeksiyonun başlangıcından itibaren daha sonra akciğer fibrozisini öngörebilecek olası biyobelirteçleri tanımlamayı amaçlamaktadır.

Gereç ve Yöntemler: Ocak-Aralık 2020 tarihleri arasında COVID-19 pnömonisi nedeniyle yatan ve PCR pozitif olan hastalar çalışmaya alındı. COVID-19 sonrası semptomlar ve akciğer sekel oluşumu açısından hastalar 12 ay boyunca takip edildi.

Bulgular: Çalışmaya ortanca yaşı 62 (R: 17-93) olan toplam 64 hasta dahil edildi ve %42.2 kadındı (n=27). 35 hastada (%54.7) COVID sonrası semptomlar mevcuttu, 8 hasta (%12.5) kaybedildi ve 22'si (%34.4) yeniden hastaneye yatırıldı. Hastaların %76.6'sının klinik seyri iyiydi ancak hastaların %54.7'sinde enfeksiyon sonrası sekel gelişti. Pnömoni skoru, kan oksijen satürasyon düzeyi, CRP ve başvuru sırasındaki troponin düzeyleri sekel gelişimi ile anlamlı olarak ilişkiliydi ($p<0.05$). Erkek cinsiyet, ileri yaş, hastanede yatış süresi, kötü klinik prognoz ve yoğun bakım ünitesine yatış ile birlikte hipertansiyon varlığı ve post-COVID semptomları sekel oluşumu ile korelasyon gösterdi ($p<0.05$). Yaş 63.5'in üzerinde, CRP'nin 24.1'den yüksek olması ve pnömoni skorunun 0.15'in üzerinde olması akciğer sekel tahmini için anlamlı bulundu.

Sonuç: Bu çalışma, COVID-19 enfeksiyonu sonrası akciğer sekellerinin enfeksiyonun başlangıcından itibaren tahmin edilebileceğini ve sonrasında önlem alınabileceğini göstermektedir.

Anahtar kelimeler: Biyobelirteçler, COVID-19, akciğer sekelleri, monitorizasyon

Introduction

COVID-19 (Coronavirus disease 19) which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic with approximately 692 million people infected and around 6.9 million deaths worldwide (1). The widespread of infection and the variety of clinical presentation and outcomes made it difficult to manage patients and raised a need for continuous development of strategies regarding the diagnosis, treatment and follow-up of these patients. COVID-19 disease is also challenging regarding its multisystem involvement and can lead to multi organ failure (2). Lung is the main organ affected and patients usually present with respiratory related symptoms like cough and dyspnea. Even though the majority of patients presented with mild or even asymptomatic disease a significant number with moderate or severe disease had a need for hospitalization and intensive care unit admission and this group of patients was especially at risk for development of post-COVID symptoms and complications (3,4).

One of the most important issues that pulmonologists are dealing with is the lung sequelae and fibrosis which has caused an impairment of functional status of lung and presence of symptoms that remain even after the virus has been cleared and is not detected by PCR. Many studies have analyzed clinical, radiological and laboratory parameters that can be related with the COVID-19 disease outcome and prognosis, but the data regarding parameters to foresee the lung sequelae are scarce (5-7). One study developed a risk assessment score to predict the pulmonary sequelae, which included many parameters like age, BMI, comorbidities, patient performance and dyspnea perception according to the thorax computed tomography of patients at four months after infection taking in consideration a lung involvement higher than 10 % (8).

The aim of this study was to determine clinical and laboratory parameters that might be used to predict the group of patients that are at risk for lung sequelae development from the diagnosis of disease. The usage of CT for the one-year follow-up of post-COVID-19 patients was used for possible correlations of these parameters and the cut-offs were investigated for practical usage in clinical management of these patients.

Material and Methods

Statement of Ethics

This study was performed in accordance with the Declaration of Helsinki. This human study was approved by the institutional review board of Baskent University Hospital – KA22/92. Adult participant consent was not required because of retrospective study design.

Study population

A total of 64 patients with a positive reverse-transcriptase-

polymerase-chain-reaction (RT-PCR) result for COVID-19 and presence of pneumonia in the thorax computed tomography (CT) who were admitted to the isolated ward of our hospital were included in the study. The patients were recruited by retrospective data collection for patients that were hospitalized from 01/01/2020 to 30/12/2020. 158 patients' data was collected first and only 64 of them were included for analysis. The reason for this was absence of CT or lack of follow up of the patients that were excluded. All the included ones had at least one CT at diagnosis and one CT at the follow-up starting from the first month until 12 months after COVID infection.

Study protocol

Demographic data, past history, clinical symptoms and laboratory parameters at admission together with the CT findings were analyzed. The pneumonia score was calculated by an automated system (Siemens Healthineers, Forchheim, Germany) which provided the lung involvement as a percentage value thus it was expressed as values from a range 0-1 which stands for 0 -100%.

The hospitalization duration, clinical course, together with the development of lung sequelae in the first year after infection were analyzed and their correlations were investigated. The conformity of numerical variables to normal distribution was examined with the Shapiro-Wilk and Kolmogorov-Smirnov normality tests. Numerical variables were presented as mean ± standard deviation and median values (with minimum-maximum), and categorical variables as the number and percentage. Since the variables were not normally distributed, the Mann-Whitney U test was used to compare the differences between groups. Categorical variables were compared using Pearson Chi-square and Fisher Exact test. Receiver Operating characteristic (ROC) curve analysis were performed to determine the cut-off values for the significant variables. Analyzes were performed using SPSS version 25.0 software for Windows. Hypothesis was tested at a= 0.05 significance level.

Results

Baseline characteristics

A total of 64 patients were included in the study with a median age of 62 (R: 17-93). 42.2% (n=27) were women, 57.8% (n=37) were men. The most common comorbidities were: hypertension (60.9%), diabetes mellitus (31%), cancer (20.3%), cardiac disease (25%), solid organ transplant (14%). The most common symptoms at admission were fever, cough and fatigue. The baseline characteristics and laboratory parameters at admission (day 0) are summarized at table 1.

Table 1. Baseline characteristics of patients at hospital admission

Number of patients (n)	64
Sex	
Male (n, %)	37 (57.8%)
Female (n, %)	27 (42.2%)
Age in years	62.0±16.25 (17-93)
Comorbidity	
Hypertension	39 (60.9%)
Diabetes mellitus	20 (31.3%)
Cancer	16 (25.0%)
Cardiac disease	16 (25.0%)
Solid organ transplant	9 (14.1%)
Chronic respiratory disease	7 (10.9%)
Chronic kidney disease	6 (9.4%)
Chronic liver disease	4 (6.3%)
Hyperthyroidism	4 (6.3%)
Hypothyroidism	2 (3.1%)
Symptoms at admission	
Fever	30 (46.9%)
Cough	29 (45.3%)
Fatigue	28 (43.7%)
Dyspnea	14 (21.9%)
Diarrhea	8 (12.5%)
Sore throat	6 (9.4 %)
Chest pain	2 (3.1%)
Loss of smell or taste	2 (3.1%)
Laboratory results	
CRP (mg/dL)	33.6 (2-285.5)
D-dimer (mg/dL)	0.97 (0.19-35)
Leucocyte count (x1000)	6.67 (1.67-19.09)
Lymphocyte count (x1000)	1.4 (0.07-10.71)
Neutrophil/lymphocyte	3.49 (0.63-88.28)
Ferritin (µg/L)	417 (2-3659)
CK (U/L)	63 (7-507)
Procalcitonin (µ g/L)	0.18 (0.02-100)
Troponin (ng/L)	6 (1-747)
Pneumonia score	0.2 (0-0.08)
SpO2	95 % (38-100)

(CRP: C-reactive protein, CK: creatine kinase, SpO2: oxygen saturation as measured by pulse oximetry)

CT findings and lung sequelae

The CT findings regarding the lung sequelae were analyzed at intervals: 1st, 3rd, 6th, 9th and 12th months. 22 patients had a sequelae detected from the first month, 5 patients at 3rd month, 5 patients at 6th month, 1 patient at 9th month and 2 of them at 12th months. Once the sequelae findings were detected, they were also present at the other CTs afterwards, but for 2 patients the lung findings regressed at 3rd and 6th month at control CTs. The most common CT findings were: atelectasis and sub pleural bands (n=30, 46.8%), mediastinal lymphadenopathy

(n=22,34.4%), fibrosis (n=19,29.7%), ground glass opacity (GGO) (n=19,29.7%), bronchiectasis (n=10,15.6%), consolidation and nodules (n=10,15.6%), honeycombing (n=5,7.8%) and cavitary lesions (n=2,3.1%).

Analysis of routine tests regarding the sequelae formation prediction

At the end of the study 35 patients (54.7%) had post-COVID-19 symptoms. Only 8 patients (12.5%) died whereas 22 patients (34.4%) were re-hospitalized within one year period of follow up. Lung sequelae was present at 35 patients as detected by changes in thorax CT within one year period after COVID-19 infection. Lung sequelae was significantly related to gender and was more common in males (p=0.015) when compared to females. HT was the only comorbidity to be related to lung sequelae (p=0.016). A bad clinical prognosis which was defined mainly as need for intensive care unit admission (p=0.004) together with presence of post-COVID symptoms (p=0.015) were also in correlation with sequelae formation. The lung sequelae could be detected as early as the 1st month post-COVID infection (p=0.013). The changes were usually permanent but 2 patients showed resolution at the end of 3rd and 6th month. Regarding the laboratory, radiological score and clinical parameters age, pneumonia score, blood oxygen saturation level, C-reactive protein (CRP) and troponin levels at admission and the hospitalization duration were significantly related to sequelae development (p<0.05) and are shown in details in table 2.

Table 2. Comparison of clinical, radiological and laboratory parameters of both lung sequelae + and – patients.

Variables	Lung sequelae + (n=35)	Lung sequelae – (n=29)	p value
Age (years)	69 (17-93)	53 (17-73)	0.001*
Pneumonia score (0-1)	0.3 (0.0- 0.8)	0.1 (0.0-0.6)	0.001*
Leucocyte count /μL	6.7 (1.6-19.1)	5.7 (2.9-12.2)	0.735
Lymphocyte count/μL	1.32 (0.07-4.39)	1.41 (0.13-10.7)	0.595
NLR	3.44 (1-88.28)	3.49 (0.63-21.31)	0.720
D-dimer (mg/L)	1 (0.23-35)	0.89 (0.19-9.39)	0.572
CRP (mg/L)	62.2 (3.5-285.5)	14.6 (2-364.9)	0.004*
Ferritin (μg/L)	574.5 (13.8-3659)	212 (2-1676)	0.106
Procalcitonin (μg/L)	0.2 (0.12-100)	0.12(0.02-6.9)	0.268
CK (U/L)	58 (7-331)	64 (19-507)	0.761
Troponin (ng/L)	8.5 (2-747)	3 (1-360)	0.036*
SpO2 (%)	94 (38-100)	95 (89-100)	0.028*
Duration of hospitalization (days)	11 (0-52)	4 (0-30)	0.039*

(NLR: neutrophil to lymphocyte ratio, CRP: C-reactive protein, CK: creatine kinase, SpO2: oxygen saturation as measured by pulse oximetry)

3.3 ROC curves for possible biomarkers

The continuous parameters that were found to be significant for the lung sequelae prediction were further analyzed for a cut off value that can be used to follow-up the patients. Regarding the ROC curves CRP with a cut off value of 24.1 mg/L (AUC=0.713), age above 63.5 years (AUC=0.794) and pneumonia score of 0.15 (AUC= 0.732) were significant and could be used as biomarkers to predict the lung sequelae formation from the start of COVID-19 infection (Figure 1).

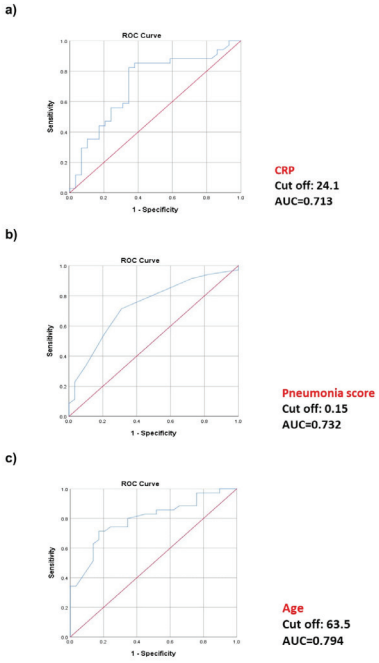

Figure 1. ROC curves for a) CRP, b) Pneumonia score and c) Age

Discussion

This study reports that lung sequelae after COVID-19 infection can be predicted by simple laboratory and radiological techniques that have been routinely used for this group of patients at the admission. A long follow-up period of one year post-COVID has shown that a large group of patients (54.7%) develop changes at lungs after infection and should be closely monitored. CRP, older age and pneumonia score at admission together with male gender predominance, persistence of symptoms even after discharge, length of hospitalization and need for intensive care unit were all significantly correlated with pulmonary sequelae.

Up to date there have been many studies that have reported factors which are related to the COVID-19 disease progression, outcome and severity, but the data regarding the relationship of such risk factors to the lung sequelae formation are scarce (3, 5-9).

Advanced age, severe illness, prolonged ICU stay, smoking, presence of acute respiratory distress syndrome (ARDS) and higher inflammatory markers have all been associated with a worse outcome (3-4,9-10). Biomarkers are helpful as they can provide an objective information about the disease status and can also be evaluated at many different centers as well. Lymphocyte count, neutrophil to lymphocyte ratio (NLR), CRP, erythrocyte sedimentation rate (ESR), procalcitonin , interleukin-6 (IL-6), D-dimer, troponin and creatine kinase (CK) have been found to be related with progression of COVID-19 disease (5). As the development of lung sequelae cannot be predicted from the start we analyzed if such parameters related to disease progression could also be used to predict lung changes afterwards in order to enable earlier intervention to prohibit the permanent changes that might lead to both functional capacity impairment and persistent symptoms in long-term. We could find that similarly to the disease severity and outcome parameters like CRP and troponin could be also used to predict lung sequelae formation as well. Especially for CRP with a cut off 24.1 mg/L and higher had a stronger correlation when compared to troponin levels.

The main tool that was used to detect lung changes both at diagnosis and at the follow-up was the radiological techniques like x-ray, CT, high resolution CT (HRCT) and lung ultrasound (11). A meta-analysis showed that the CT severity score (CTSS) and consolidations were the most common predictors among the studies for the post-COVID-19 sequelae (11). Lung ultrasound score (LUS) could also be used to diagnose and track changes of lungs in patients where CT could not be used (11).

There are different studies that have assessed lung changes at variable times after COVID-19 infection mainly at 3, 4, 6, 7 and 12 months (12-16). Froidure A. et al (12) have reported that up to 35 % of patients still have symptoms after COVID-19 and that 21 % of them developed lung fibrosis. Interestingly the pulmonary function tests and radiological changes were not related to the degree of post-COVID symptoms (12). In our study 29.7 % of patients had fibrosis and there was a relation of post-covid symptoms with lung sequelae formation (p=0.015), but 17 patients that did not have any radiologically detected sequelae still had post covid symptoms. This phenomenon may be explained with the extrapulmonary involvement and multi organ disease which might have an effect to mainly dyspnea and fatigue development afterwards at long term (17).

According to the other studies 21 % had fibrosis and 44% of patients had GGO changes at 4th month, whereas another study showed that up to 72 % of patients had fibrosis like changes at the 6th month after infection (13-14). Another study showed that 29 % had fibrosis at 7th month and that elderly patients were the most effected ones (15). Our study also had a similar percentage (29.7%) and the patients included were mainly the elderly ones as the median was 62 years which explains the higher rate of lung sequelae up to 54.7%. At one year after COVID-19 infection fibrotic –like changes could be detected up to 22.7 % of patients and the radiological lung involvement at admission was one risk factor related to these long-term changes (16). In our study the pneumonia score at admission was also significantly related and the cut off 0.15 (15% of lung parenchyma) or higher could predict the lung sequelae with an AUC of 0.732.

There are also studies that have shown that radiological findings can be improved with time (18) and that the risk of fibrosis is not very high thus no hurry for immediate treatment is needed especially for the first 3 months (4,18). On the other hand other studies showed that up to 90% of patients can experience sequelae after COVID-19 and even though the recovery rate is around 50 % at first 3 months it decreases to 35 % between 6 to 9 months and down to 15 % afterwards (19). In our study the majority of patients that developed lung sequelae had radiological findings from the first month and only 2 cases could recover afterwards at 3rd and 6th months respectively, which suggests a low rate of improvement and regression of radiological findings that might have been related to the elderly population included in the study. Regarding the high number of infected people globally it is also hard to detect lung changes if patients are not followed up, thus chest radiography should be recommended within 3 months after discharge and also oxygen saturation measurements should be performed in the primary care so that patients can then be referred to the pulmonologists (20).

Biomarkers which have been related to the oxidative stress like TNF–alpha have been associated with prediction of pulmonary complications and could be used as therapeutic targets as well (21). The usage of such biomarkers might not be practical for routine usage and might not be performed widely in different centers. Thus a need for biomarkers that are often used and sometimes a combination of them to develop risk assessment scores for pulmonary sequelae in COVID-19 have been developed to help physicians in their daily practice (8). Yet further studies and multicenter involvement is needed to draw definite conclusions and implementation of them in patient care.

Early detection of lung sequelae might help to treat patients promptly and slow the progression or functional impairment. Early treatment with corticosteroids have been shown to improve both functional and radiological findings in post-COVID patients (22). It is suggested to think about anti-fibrotic drugs especially after the 3rd month after which the improvement rate falls significantly (3). The pulmonary sequelae of COVID-19 include also the thromboembolic disease and 2 patients in our study also had a pulmonary embolism detected thus appropriate treatment regarding vascular disease should also be given if necessary (17). There is also a need for new therapies for patients that progress and have a decreased functional capacity and also pulmonary rehabilitation should be offered to manage the post-COVID -19 breathlessness (17,19).

Study limitations

This study has some limitations regarding the few numbers of patients as it was mainly performed in one center. Another limitation is the retrospective nature of the study which also reduced the number of patients included, as the data could not be achieved. Finally, because at our center during pandemics we did not utilize the spirometry laboratory we could not make a functional assessment of the lungs at these patients thus we mainly concentrated at clinical, laboratory and radiological results.

Conclusion

Since the burden of COVID-19 infection will continue for a long term regarding the high number of infected patients and the diverse clinical outcome together with development of lung sequelae afterwards, a need for biomarkers is still present nowadays. It is essential to develop easily achievable and widely accessed parameters that might help to define the population at risk for lung sequelae in order to follow and treat these patients properly. This study has shown that laboratory, clinical and radiological measurements that are performed at admission can predict the lung sequelae from the initial stage of the infection.

Ethics permission

This study was performed in accordance with the Declaration of Helsinki. This human study was approved by the institutional review board on 18/02/2022 by No: KA22/92.

Informed consent: Adult participant consent was not required because of retrospective study design.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Concept: D.E, Design: D.E., Data Collection or Processing: all authors, Analysisor

Interpretation: D.E, Literature Search: all authors, Writing: D.E.

Conflict of Interest: There is no conflicts of interest with respect to the authorship and/or publication of this article.

Financial Disclosure: The authors declared that they did not receive any financial support during the research and authoring of this article.

Thank you to Eylem Gül Ateş for giving a support to statistical analysis and interpretation.

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Turkish Journal of Clinics and Laboratory

To cite this article: Ozturk D, Ozturk B. Predictive factors causing complications in abdominoplasty after bariatric surgery. Turk J Clin Lab 2023; 4: 777-781

Research Article

Predictive factors causing complications in abdominoplasty after bariatric surgery

Bariatrik cerrahi sonrası abdominoplastide komplikasyonlara neden olan prediktif faktörler

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Abstract

Aim: Abdominoplasty has become increasingly popular in recent times. While it yields pleasing results for the patient, it can also lead to certain undesired outcomes post-operatively. The aim of this study is to examine complications arising after abdominoplasty and to identify potential risk factors associated with these complications. Factors affecting the local and systemic complications of abdominoplasty have not been adequately defined in the literature. Abdominoplasty is a radical cosmetic surgical procedure aimed at improving body contours by removing excess skin, subcutaneous fat, and soft tissue from the anterior abdominal wall while restoring muscle-fascia integrity and skin elasticity. Despite abdominoplasty being safe and highly popular, it is a procedure prone to complications when compared to other body contouring methods.

Material and Methods: Data from 95 patients (81 female and 14 male) who underwent abdominoplasty after bariatric surgery at Atatürk Sanatorium Education and Research Hospital between February 2020 and February 2022 were retrospectively reviewed. The patients' age, gender, BMI, weight loss, history of diabetes mellitus, hypertension, smoking status, and their association with complications were analyzed. The potential risk factors and their relationship with developed complications were investigated using Independent Sample T Test and Chi-square analysis. The examined risk factors included age, gender, body mass index, history of smoking, history of diabetes mellitus, history of hypertension, and abdominoplasty surgical technique.

Results: Among the 95 patients who underwent abdominoplasty, 27 (28.42%) experienced both local and systemic complications. The most frequent complication was seroma observed in 16 patients (16.84%). Subsequently, wound infection occurred in 4 patients (4.21%), skin necrosis in 1 patient (1%), wound dehiscence in 2 patients (2.1%), hematoma in 2 patients (2.1%), and pulmonary thromboembolism in 2 patients (2.1%).

Conclusion: Factors significantly increasing the complication rate were increased body mass index ($p = 0.002$) and a history of smoking ($p = 0.004$). However, statistical significance was not observed for other parameters.

Keywords: Abdominoplasty, complication, BMI, obesity, hypertension, diabetes mellitus.

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Recevied: 19.11.2023 accepted: 15.12.2023

Öz

Amaç: Abdominoplasti günümüzde giderek popüler bir prosedür haline gelmiştir. Hasta için yüz güldürücü sonuçları olmasının yanında, operasyon sonrası bazı istenmeyen sonuçlar da ortaya çıkabilmektedir. Bu çalışmanın amacı, abdominoplasti sonrası gelişen komplikasyonları irdelemek ve olası risk faktörlerinin komplikasyonlarla ilişkisini ortaya koymaktır.

Abdominoplastinin lokal ve sistemik komplikasyonlarını etkileyen faktörler literatürde yeterince tanımlanmamıştır Abdominoplasti güvenli ve çok popüler olmasına rağmen, bu prosedür diğer vücut şekillendirme yöntemleriyle karşılaştırıldığında komplikasyonlara açık bir yöntemdir.

Gereç ve Yöntemler: Atatürk Sanatoryum Eğitim ve Araştırma Hastanesinde Şubat 2020 ile Şubat 2022 tarihleri arasında bariatrik cerrahi sonrası abdominoplasti uygulanan 95 hastanın (81 kadın ve 14 erkek) verileri retrospektif olarak incelendi. 95 hastanın yaş,cinsiyet, BMİ, verilen kilo, diabetetesmellitus,hipertansiyon, sigara içimi mevcudiyeti ve bunların komplikasyonlarla ilişkisi analiz edildi. Olası risk faktörleri ve gelişen komplikasyonlar arasındaki ilişki İndependent Sample T Test ve Ki-Kare analizi kullanılarak araştırılmıştır. İncelenen risk faktörleri yaş, cinsiyet, vücut kitle indeksi, sigara içme öyküsü, diabetesmellitus öyküsü, hipertansiyon öyküsü, abdominoplasti ameliyat tekniğidir.

Bulgular: Abdominoplasti yapılan 95 hastanın 27'sinde (%28,42) lokal ve sistemik komplikasyonlar gelişti. En sık görülen komplikasyon, 16 hastada saptanan seromaydı (%16.84). Sırasıyla 4 hastada yara yeri enfeksiyonu (%4.21), 1 hastada cilt nekrozu (%1), 2 hastada yara ayrılması (%2.1) ve 2 hastada hematom (%2.1), 2'sinde de pulmonertromboemboli (%2.1) gelişti.

Sonuçlar: Komplikasyon oranını önemli ölçüde artıran faktörler, artmış vücut kitle indeksi (p =0.002) ve sigara içme öyküsüydü (p = 0.004). Bu parametreler komplikasyon oluşumunda istatiksel olarak anlamlıydı. Diğer parametrelerde ise istatiksel anlamlılık saptanamadı.

Anahtar Kelimeler: Abdominoplasti, komplikasyon, BMI, obezite, HT, DM gelişti.

Introduction

Abdominoplasty is one of the most popular body contouring procedures, considered as a safe and reliable surgical technique. It ranks among the top five procedures in plastic surgery in the United States [1]. However, it is associated with a significant number of complications (32–37.4%) [2, 3], with the most common being seroma, hematoma, infection, wound healing issues, and skin flap necrosis [4, 5]. The aim of abdominoplasty after bariatric surgery is to remove excess, sagging skin, and subcutaneous fat tissue [6]. Despite significant weight loss, high BMI commonly persists in the bariatric population [7], known as a risk factor for complications.

Material and Methods

This study includes 95 patients who underwent abdominoplasty after bariatric surgery at Ankara Atatürk Sanatorium Education and Research Hospital between February 2020 and February 2022. The study commenced following the approval of the Ankara Atatürk Sanatorium Education and Research Hospital Ethics Committee with reference number 2012-kaek-15/2680 on March 22, 2023.

The study included a total of 95 patients (81 female, 14 male) with an average age of 38 and a BMI of 31 kg/m^2. Abdominoplasty surgery was performed on patients who presented at Ankara Atatürk Sanatorium Education and Research Hospital after approximately 2 years following bariatric surgery and became suitable for functional surgery. All procedures were conducted under general anesthesia.Preoperative marking of the abdominal skin was performed while the patient was standing. The skin incision started with an elliptical cut joining both iliac prominences. Subsequently, the upper flap was raised and advanced to the xiphoid and costal edges. Excess skin and subcutaneous fat tissues were excised, and the fatty layer beneath the superficial fascia was sharply removed. The umbilicus was excised in a round shape, attempting to preserve subcutaneous blood supply. The umbilicus was reconstructed again through an opening created in the upper abdominal flap. Following surgical incision of the skin, suprafascial dissection was carried out up to the xiphoid. A medial skin

incision was applied with a lateral extension depending on the desired size. Myofascial plication was performed to correct the diastasis of the rectus muscles in cases of significant diastasis, incisional hernias, and/or hernias. If there was a large defect, a polypropylene mesh could be placed.

The skin resection, repositioning of the umbilicus, and closure of the skin were conducted using absorbable monofilament (Vicryl 2/0) and 2/0 Monosin sutures. Routinely, two negative pressure drains were placed. Drains were removed if fluid output was less than 30 ml in the last 24 hours postoperatively. All patients received prophylactic antibiotics immediately before surgery and continued for 10 days. Low molecular weight heparin was used for 10 days postoperatively to prevent deep vein thrombosis and pulmonary embolism. Daily dressing changes were performed during the wound healing period. Two patients experienced thromboembolism. They received low molecular weight heparin for one month. In four patients with infection, Staphylococcus aureus and Escherichia coli were cultured from wound cultures and treated with appropriate antibiotic therapy. One patient with skin necrosis underwent necrosis debridement and dressing. Sixteen patients developed seroma, which was monitored with negative pressure drains and removed when drainage decreased to below 30 ml per day.

Statistical Analysis

The statistical analysis was performed as follows:

Independent Samples T Test

** Chi-square Test

A P-value less than 0.05 was considered statistically significant in assessing the relationship between patients' age, gender, BMI, history of smoking, diabetes mellitus, hypertension, and complications.

Results

It shows that out of the patients, 81 were female (85.5%) and 14 were male (14.7%). The mean age of the patients was 38.0 (ranging from 22 to 58). Eleven patients had diabetes mellitus (11.57%), 9 patients had hypertension (9.4%), and 25 patients had a history of smoking (26%). Regarding the surgical technique, 18 patients underwent the procedure using the harmonic technique (18.94%), while 77 patients underwent the standard technique (81%) Table 1,Table 2.

Table 1. Demographic and operative data

Gender	
Female	81 (%85,5)
Male	14(%14,7)
Age (years)mean (range)	38(22-58)
BMI; mean (range)	30,28(22-47)
Diabetes Mellitus	11(%11,57)
Hypertension	9(%9,47)
Smoking	25(%26)
Hernial Repair	17(17.89)
Operation time (h)	2.56±0.76
Surgical technique-Harmonic	18(%18,94)
Surgical technique-Standard	77 (%81)
BMI:Body Mass Index	

Table 2. Preoperative Characteristics and Complications

Characteristics	n (%)
Gender	
Female	81 (85.3)
Male	14 (14.7)
Diabetes Mellitus	11 (%11,57)
Hypertension	9 (%9,47)
Complication-total	27 (%28,42)
Complication-Infection	4(%4,21)
Complication-Dehiscence	2 (%2,1)
Complication-Necrosis	1 (%1)
Complication-Seroma	16((16,84)
Complication-Thromboemboli	2(%2,1)
Complication-hematom	2(%2,1)

A total of 27 complications (28.48%) occurred. The most frequent complication was seroma, observed in 16 patients (16.84%). Four patients (4.21%) had wound infections, treated with intravenous antibiotics. One patient (1%) developed skin necrosis, managed with necrosis debridement and prolonged dressing. Hematoma was observed in 2 patients (2.1%) and was drained. Two patients (2.1%) developed thromboembolism and were treated with low molecular weight heparin for one month Tablo 3.

Tablo 3. The statistical analysis of the parametres

	p*
Age (years)	0.005
Gender	0,429
BMI (kg/m2)	0.002
Smoking	0,003
Operation time (h)	0,378
Follow-up time (m)	0.454*
Diabetes Mellitus	0.612
Hypertension	0.542
Hernial repair	0.715
Surgical technique	
Harmonic Standard	0.907**

* Independent Samples T Test ** Chi-square Test

Out of the 95 patients, the average BMI was 30.28 kg/m² (mean (range)). The recorded overall complication rate was 27 (28.48%). The most prevalent complication was seroma, accounting for 16 (16.84%) cases. Seroma emerged as a significant factor significantly increasing the likelihood of complications (p=0.002), demonstrating statistical significance. The BMI value was associated with an increased risk of wound healing issues (p=0.002). The overall frequency of complications was significantly correlated with age (p=0.005) and BMI (p=0.002). The abdominoplasty technique did not significantly impact total complications (p=0.907). The relationship between patient age during surgery and total complications was evident. Increasing patient age was associated with a rise in general complications, indicating age as a significant risk factor (p=0.005). However, the duration of the operation did not increase complications (p=0.378). Co-existing conditions such as hypertension (HT) and diabetes mellitus (DM) did not escalate complications. Nevertheless, a history of smoking significantly increased the risk of total complications, showing statistical significance (p=0.003).

Discussion

Abdominoplasty or abdominal dermolipectomy is a fundamental procedure in plastic surgery aimed at enhancing body contours and has been practiced for over a century. Its first publication dates to 1899 by Kelly [7]. Numerous risk factors have been suggested in plastic surgery literature, demonstrating associations between complications and factors such as smoking [13], obesity [8], hypertension [14], and prior abdominal surgeries (gynecologic) [15]. Complication rates tend to increase in obese patients (BMI >30 kg/m²) compared to non-obese patients (BMI <30 kg/m²) [7, 16]. These obese patients are individuals who remained obese despite previous weight loss surgery, sometimes leading to underestimated expectations, dissatisfaction, and increased follow-up issues.

As it is mentioned in literatureour most frequently observed complication was seroma [4], predominantly seen in overweight patients or those who have undergone significant weight loss. In cases with a dead space between fasciae or postoperative abdominal flaps [17], consecutive aspirations may be necessary for treating this complication. Seroma is considered a minor complication and therefore often disregarded by patients. It occurs in approximately 38% to 42% of patients. In our series, it was the most common complication, occurring in 16 patients (16.84%). The incidence of seroma after abdominoplasty varies, ranging from 1% to 26% [15,18]. Hematomas pose potential complications. While their occurrence in any surgery, including abdominoplasty, is less frequent than seromas, constituting around 0.8% of cases, they occur in about 3% of patients undergoing abdominoplasty. However, the outcomes were more severe. Hematomas were identified during clinical examination and abdominal inspection. They were detected via ultrasound and subsequently drained through aspiration.

Issues with wound healing in abdominal incisions can more easily arise in individuals with a history of obesity. This can be due to insufficient subcutaneous coverage. Various factors may contribute to the increase in this complication: preoperative BMI > 25 kg/m², concomitant diabetes, and tobacco use (smokeless) [16]. Moreover, excessive tissue manipulation during surgery affects both clotting and complement activity, leading to excessive cytokine activation and subsequent postoperative complications, altering the healing process. Excessive release of cytokines also increases the risk of wound site infections [8-13]. Based on our experience, the commonly isolated organisms were Staphylococcus epidermidis. Staphylococcus aureus and Escherichia coli were detected with less frequency [19]. Treatment involved appropriate antibiotic therapy, abscess drainage, necessary debridement, and alterations in dressing changes. There were no postoperative mortalities. It mainly focuses on complications and risk factors without discussing the success rates, patient satisfaction, or advancements in abdominoplasty techniques over time.

Conclusion

After abdominoplasty,postoperative complications such as seroma and wound infection are common.Previous bariatric surgical procedures might play a role similar to other commonly researched risk factors such as smoking and BMI, even within specific patient categories. In abdominoplasty surgery,,more attention should be paid to preoperative, intraoperative, and postoperative management. Therefore, we strongly believe that informing patients with high expectations before abdominoplasty is extremely important. Obtaining their consent and providing necessary enlightenment during the preoperative period is crucial due to the potential risk of complications.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

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Turkish Journal of Clinics and Laboratory

To cite this article: Budak AB, Gunertem OE, Tumer NB, Ozısık K, Gunaydın S. Retrograde recanalization for chronic superficial femoral artery occlusion: is it safe and effective as a primary strategy. Turk J Clin Lab 2023; 4: 782-797

Research Article

Retrograde recanalization for chronic superficial femoral artery occlusion: is it safe and effective as a primary strategy

Kronik yüzeyel femoral arter tıkanıklığında retrograd rekanalizasyon: Birincil strateji olarak güvenli ve etkili mi?

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Abstract

Aim: Peripheral arterial disease (PAD) is one the most common cause of mortality and morbidity after coronary artery disease and serebrovascular event worldwide. Endovascular treatment (EVT) of chronic occluded superficial femoral artery SFA is generally managed by antegrade approach. Retrograde popliteal access (RPA) is a valuable option when antegrad attempt fails or has also been preferred as a primary choice. We aim to compare patients in whom RPA in prone position was chosen as a first-line strategy and percutaneous intentional extraluminal angioplasty (PIER) technique was used for recanalization, with patients in whom antegrade attempt had failed and RPA in supine position with either endoluminal or bidirectional "randevous" technique was used for recanalization with 15-month follow-up.

Material and Methods: We retrospectively studied consecutive EVTs between February 2017 and April 2019, and selected all EVTs in which RPA was used for the recanalization of CTO of SFA lesions were included. The study divided patients into two groups as Group 1 (n=24): patients in whom RPA in the prone position was chosen as a first-line strategy and PIER technique was used for recanalization (with 6F Sheat) and Group 2 (n=22): patients in whom antegrade attempt had failed and RPA in the supine position with endoluminal recanalization or if the wire failed while crossing the lesion, a bidirectional "double-balloon (rendezvous)" technique was used for recanalization (Sheatless).

Results: Technical success rate was %100. RCC and ABI were improved post procedurally in both groups significantly. Primary stenting was required in more patients in group 1(70.8% vs. 45.4%; p<0.05). In group 2, randevous technique was used in 9 patients (40.9%). There was not any significant difference between the groups in terms of 30-day, and 12-month MACE. There were no major amputations, stent fracture, and death. In the 12th month, no significant differences was found between the groups for amputation-free survival (95.8% vs. 95.4%; p>0.05) .1-year limb-salvage rate was 100 ± 0 for both groups. Primary patency rates of group 2 were higher than group 1, but this difference became significant only at 6th month (95,8%, 87.5%, 79.1% for group 1vs. 100%, 95.4%, 81.8% for group 2, respectively; p<0.05 only for 6th month). The 1-year CD-TLR rate was 17,25% for whole study group, group 1 seems to have more CD-revascularization procedures but it did not reach to a significant difference (95% CI 20.8% to 13.7%).

Conclusion: The RPA techniques has their own advantage and disadvantages. Considering safety and effectiveness, either planned as a primary strategy or needed as a back-up plan, it should be in the portfolio of vascular surgeons.

Keywords: peripheral arterial disease; chronic total occlusion; retrograde popliteal access.

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Recevied: 08.12.2023 accepted: 20.12.2023

Öz

Amaç: Periferik arter hastalığı (PAH), dünya çapında koroner arter hastalığı ve serebrovasküler olaylardan sonra en sık görülen mortalite ve morbidite nedenlerinden biridir. Kronik tıkalı yüzeyel femoral arter (SFA)'in endovasküler tedavisi (EVT) genellikle antegrad yaklaşımla yönetilir. Retrograd popliteal erişim (RPA), antegrad girişimin başarısız olduğu veya birincil seçenek olarak tercih edildiği durumlarda değerli bir seçenektir. Birinci basamak strateji olarak yüzüstü pozisyonda RPA'nın seçildiği ve rekanalizasyon için perkütanöz kasıtlı ekstralüminal anjiyoplasti (PIER) tekniğinin kullanıldığı hastaları, ileriye doğru girişimin başarısız olduğu ve sırtüstü pozisyonda RPA'nın kullanıldığı hastaları karşılaştırmayı amaçlıyoruz. 15 aylık takip ile rekanalizasyon için çift yönlü "randevous" tekniği kullanıldı.

Gereç ve yöntemler: Şubat 2017 ile Nisan 2019 arasında ardışık EVT'leri retrospektif olarak inceledik ve SFA lezyonlarının CTO'sunun rekanalizasyonu için RPA'nın kullanıldığı tüm EVT'leri seçtik. Çalışma, hastaları Grup 1 (n=24) olarak iki gruba ayırdı: Birinci basamak strateji olarak yüzüstü pozisyonda RPA'nın seçildiği ve rekanalizasyon için PIER tekniğinin kullanıldığı hastalar (6F Sheat ile) ve Grup 2 (n= 22): Antegrad girişimin başarısız olduğu ve endolüminal rekanalizasyon ile sırtüstü pozisyonda RPA'nın olduğu veya lezyonu geçerken telin başarısız olduğu hastalar, rekanalizasyon için çift yönlü "çift balon (randevu)" tekniği kullanıldı (Kılıfsız).

Bulgular: Teknik başarı oranı %100 oldu. RCC ve ABI her iki grupta da işlem sonrası anlamlı düzeyde iyileşti. Grup 1'de daha fazla hastaya primer stent gerekti (%70,8 vs. %45,4; p<0,05). Grup 2'deki hastaların 9'unda (%40,9) randevöz teknik kullanıldı. Gruplar arasında 30 günlük ve 12 aylık MACE açısından anlamlı fark yoktu. Büyük bir amputasyon, stent kırılması ve ölüm yaşanmadı. 12. ayda amputasyonsuz sağkalım açısından gruplar arasında anlamlı fark bulunmadı (%95,8 vs. %95,4; p>0,05). 1 yıllık uzuv kurtarma oranı her iki grup için de 100 ± 0 idi. Grup 2'de primer açıklık oranları grup 1'e göre daha yüksekti ancak bu fark ancak 6. ayda anlamlı hale geldi (grup 1'de sırasıyla %95,8, %87,5, %79,1'e karşı grup 2'de sırasıyla %100, %95,4, %81,8); p<0,05 yalnızca 6. ay için). Tüm çalışma grubu için 1 yıllık CD-TLR oranı %17,25 idi, grup 1'de daha fazla CD revaskülarizasyon işlemi yapılmış gibi görünüyor ancak anlamlı bir farka ulaşılamadı (%95 Cl %20,8 ila %13,7).

Sonuç: RPA tekniğinin kendi avantaj ve dezavantajları vardır. Güvenlik ve etkinlik göz önüne alındığında, ister birincil strateji olarak planlanmış, ister yedek plan olarak ihtiyaç duyulmuş olsun, damar cerrahlarının portföyünde yer almalıdır.

Anahtar kelimeler: periferik arter hastalığı; kronik total tıkanıklık; retrograd popliteal erişim.

Introduction

Third leading cause of mortality and morbidity after coronary artery disease and serebrovascular events is peripheral arterial disease (PAD) (1). Symptomatic PAD refractory to medical and exercise therapy needs further planning for treatment. Chronic total occlusion (CTO) of the Superficial femoral artery (SFA) can be defined as a femoropopliteal (FP) disease can be explained as long, diffuse and complex occlusions that include high calcium rates within the plaque and the vascular wall (2). Among patients who were non-revascularized, major amputation rates can be high as 50% in one-year after critical limb threatening ischemia (CLTI) onset (3). Furthermore, the longest artery in the lower extremity was SFA and prone to flexion, compression, and torsion (4). As a result, treatment modalities usually require careful planning and back-up strategies. Although surgical bypass is recommended in the guidelines for long and complicated lesions, bypass surgery is associated with substantial morbidity; instead, endovascular treatment of chronic totally occluded SFA, including the proximal popliteal artery (PA), is successful in >90% of patients (5).

EVTs for CTO of SFA are generally performed via antegrade approach, in which either a contralateral retrograde intervention or ipsilateral antegrade access of the CFA is used (6). If the antegrade attempt with a guidewire fails, reentry catheters are sometimes useful, and Kitrou et and colleagues(7) reported a 93% success rate in usage of Outback catheter, costs and reimbursement criteria of the countries must be taken into consideration. As retrograde popliteal access (RPA) is considered to be a valuable option when the antegrade attempt fails- especially in long TASC D lesions with a reported rate of 2% (8)-, the RPA technique has also been preferred as a primary choice in procedures with CFA

stenosis or occlusion, proximal lesions of SFA without a stump, presence of comorbidities such as severe obesity, concurrent iliac lesions and strong collaterals distal to the CTO.

First time in history, Tonnesen and colleagues described the retrograde popliteal approach(9), but the technique lost its popularity because of severe complications such as rupture, dissections, arteriovenous fistula, hematoma or pseudoaneurysms of the vessel which develop at the puncture site (10). Using ultrasound (US) guidance routinely while puncturing and evaluating PA is curcial to avoid complications, the recent developments in imaging technologies such as digital subtraction angiography which helps to create a roadmap and can be guide for physician while adnvancing the needle and availability of thinner sheats notably decreased the complication rate (12-14).

Since the description of the safest technique to puncture PA by Trigaux et al. (11), several methods for retrograde popliteal access have been reported (15-18), which can basically be classified into two groups according to the patient's position as prone and supine. One should plan the treatment strategy well because the need for the patient to change position during the procedure results in discomfort, anxiety, prolonged procedure duration, and compromising sterility.

Recanalization of long SFA CTOs can be accomplished by a bidirectional femoral-popliteal approach – named as "rendezvous technique (18)" or by percutaneous intentional extraluminal (subintimal) angioplasty (PIER). PIER technique was proven as a successful method in the treatment of long diameter femoropopliteal occlusions (17,19,20).

This study investigates the safety and effectiveness of the RPA in which the technique was successfully used in the revascularization of the patients with SFA CTO. We compared patients in whom RPA in the prone position was chosen as a first-line strategy, and PIER technique was used for recanalization with patients in whom antegrade attempt had failed, and RPA in the supine position with bidirectional "rendezvous" technique was used for recanalization. Besides procedural outcomes, another purpose of this study was to evaluate the 15-month follow-up results. In the current literature, there are very few studies that the same interventionalist performs both techniques, which eliminates the possible technical differences between operators, as well as comparing both techniques in terms of follow-up results.

Material and Methods

Study design

We retrospectively studied consecutive EVTs in Numune Research and Teaching Hospital, Ankara, Turkey between February 2017 and April 2019, and selected all EVTs in which RPA was used for the recanalization of SFA CTO lesions were included. The authors received no financial support from the medical industry for the research and/or authorship of this article. Inclusion and exclusion criterias of the patients are listed in table 1.

Table 1. Inclusion and exclısion criteria of the patients

Inclusion Criteria	Exclusion Criteria
• RCC 3-5 • Persistent symtoms despite medical and physical therapy >2 month • SFA occlusion not including PA regardless of the vessel diameter	• Urgent requirements for revascularization (acute ischemia • Distal lesions inaccessible via a popliteal approach • Pedal access • Patients with concomitant or staged infrapopliteal and iliac interventions.

The study population was divided into two groups as:

Group 1 (n=24): patients in whom RPA in the prone position was chosen as a first-line strategy and PIER technique was used for recanalization-with sheat

Group 2 (n=22): patients in whom antegrade attempt had failed and RPA in the supine position with endoluminal recanalization or if the wire failed to cross the lesion, a bidirectional "double-balloon (rendezvous)" technique (21-23)" technique was used for recanalization - sheatless

We compared both groups in terms of patient demographics and risk factors, procedural findings and outcomes, safety, complication rates, postprocedural outcomes, and follow-up results.

The study protocol was approved by local ethical committee. Consent form was not obtained due to retrospective nature of the study. Procedures were carried out in accordance with the 2013 Helsinki Declaration.

Patient Population and Methodology

We retrospectively studied 451 consecutive EVTs. Of these, EVT of SFA occlusion was performed in 188 patients in which a total of 46 patients who had undergone EVT via RPA were included. The study population was divided into two groups as group 1(n=24) and group 2 (n=22). All patients suffered from stable PAD (Rutherford category 3 to 5) with CTOs of the SFA.

Each patient underwent physical examination, categorized according to the RCC, had an measurement of the ankle-brachial index (ABI) and clinical risks. Demographics, symptoms, comorbidities, and risk factors for atherosclerotic vascular disease were identified for all patients. Duplex ultrasound examination or by computed tomographic angiography was used to obtain complete anatomical overview for each patient. Thus, a lower extremity digital substraction angipgraphy was always available for preprocedural planning.

Procedure Description

Prone Technique

This technique was preferred as an initial strategy for recanalization of SFA CTO in:

• Long-standing occlusions have become hard with time where the intraluminal approach would fail. Subintimal dissection plane is relatively easily created in these situations

• Long occlusions where it is difficult to maintain an intraluminal approach.

• Diffusely diseased vessels, which often have occlusions that are difficult to negotiate intraluminally.

• Flush SFA occlusions where there may be a tiny stump or no stump at all. The intraluminal approach in these situations is difficult, if not impossible.

• Heavily calcified vessels, which are often difficult to treat by conventional angioplasty but are relatively easily managed using Subintimal Angioplasty, as the wire follows the path of least resistance along the subintimal plane.

• Long stenoses which usually provide poor outcome with conventional angioplasty

• The presence of large collateral vessel proximal to the occlusion, which often lacks a stump necessary to engage the guidewire for transluminal angioplasty.

Ultrasound-guided ipsilateral retrograde PA puncture was performed in all patients. With the help of previous tomographic and/or diagnostic angiographic studies and body landmarks, an ideal diameter puncture point without a calcification was chosen after the careful examination of the PA and the surrounding muscles of popliteal fossa with B-mode ultrasound using 3.5 to 5-Mhz transducers. According to the distance from the distal tip of the occlusion, the popliteal access was maintained from popliteal fossa. Popliteal artery and vein were differentiated using a simple compression maneuver. Then the ultrasound probe was placed in a transverse fashion and to avoid the superimposition of the vein probe was tilted approximately 30° cranially. Anesthesic agent was injected locally around the popliteal artery under ultrasound. Successfully puncturing the vessel with an 18-G needle using the single-wall technique, a 6 F sheath was advanced from the PA. An angiogram showing the distal tip of the occlusion, the position of the sheat, the PA, and crural arteries was obtained before starting the procedure. After completing the preprocedural angiogram, unfractionated heparin (100mg/kg) was injected from the sheath. The PIER technique was described previously (6,19,20,24), but our technique includes some differences. The tip of the support catheter (Seeker, BD, Tempe, AZ, USA) with a guidewire inside (Supracore35, Abbott, Cal-USA / Nitrex35, Medtronic, MN-USA / Amplatzer, Boston-Scientific, MA-USA / Roadrunner. CookMedical, IN-USA / V18, Boston-Scientific, MA-USA) was brought up to the distal tip of the occlusion. Then, the subintimal slayer was entered at the distal tip of the occluded segment easily because the wire and support catheter advances into the path of least resistance, which is within a dissection plane, and entry into the subintimal plane was confirmed by injection of a small amount of diluted contrast. After five or six cases, we did not have a necessity to confirm visually, because once the guidewire enters into the subintimal layer, the guidewire advances freely with little resistance. The tip of the guidewire was then flipped to form a large loop with an approximate length of 3 to 5 cm and the loop that was supported by a catheter advanced along the length of the occlusion. Around 1 cm below the proximal tip of the occlusion or after reaching the end, we perform a few different techniques to re-enter the lumen:

· Shorten the length of the loop, make a slight twisting or screwing move

· Pull the wire back and try to find a new dissection plane.

· Change the support catheter with an angled one (Vertebral catheter, MeritMedical, UT-USA) and the screwing maneuver again

• Retract and straighten the guidewire, rotate and reposition the catheter slightly and push the guidewire towards the native vessel

• Change the wire and increase the strength and/or pushability of the wire (did only in one case-care must be taken to prevent perforation – requires experience)

Using either one of them or combination of these maneuvers, re-entry into the true lumen was successful in all cases, which was felt by the free movement of the floppy tip of the wire or confirmed by injection of the contrast medium. The crossing of CTO via a retrograde approach in a prone position is shown in figure 1.

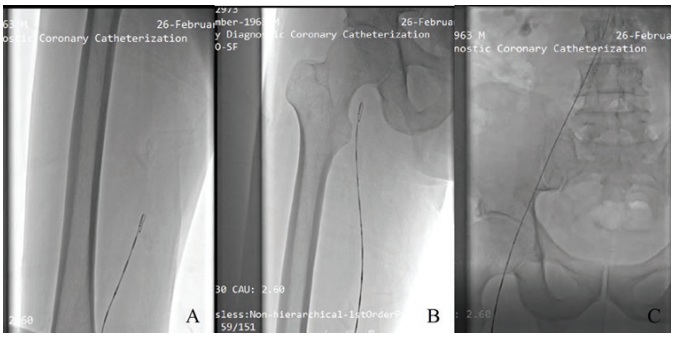

Figure 1: crossing of CTO via retrograde approach in prone position

Figure 1. (A) "loop" wire and supporting catheter. **(B)** Retrograde crossing through the lesion. (C) Guiding wire has passed through the lesion and positioned in the abdominal aorta.

Once the lesion had been crossed, the whole length of the subintimal channel was predilated with a 5F balloon catheter (Bantham, BD, Tempe, AZ, USA) using approximately 10-12 atmospheres of pressure and short segment inflations starting from the distal end of the occluded segment to the proximal segment . Any residual stenosis of more than 30% is repeatedly balloon dilated, possibly with high pressure, until a satisfactory result is achieved. After the vessel preparation was maintained successfully, drug-coated balloon angioplasty with a 6x120-mm balloon catheter (LutonixTM, BD, Tempe, AZ, USA) was performed. Stents (LifeStentTM, BD, Tempe, AZ, USA) were only deployed in the event of a suboptimal angioplasty, acute recoil, or dissection. The patient can feel some pain, especially in local calcified areas during balloon dilatation. The procedure was finished with a control angiogram confirming the technical success.

Supine Technique

All procedures were performed in the angiography laboratory. In supine position, after sterile conditions were achieved, local anesthesia was administered. As we mentioned before, group 2 patients were the patients whose procedures had first started with an antegrade approach for target lesion, which had been either (1) ipsilateral via the CFA with the insertion of a 6F sheat (2) contralateral using a 6F, 45-cm long dedicated crossover sheath (DestinationTM, Terumo, USA), and antegrade recanalization was failed because of morphological characteristics of the lesions

For the retrograde approach, either a 18-G (Terumo) or a 21-G needle cannula (Cook Inc.) was introduced distal to the occluded segment. Contralateral oblique (30°–45°) position for the C-arm was preffered to facilitate fluoroscopically-guided puncture. During the cannulation process, if you want to see the assessment of the angle of the needle as it approached the artery (should be < 70°), 90° ipsilateral position can be used to figüre out the distance of the needle tip from vessel. (Figure 2).

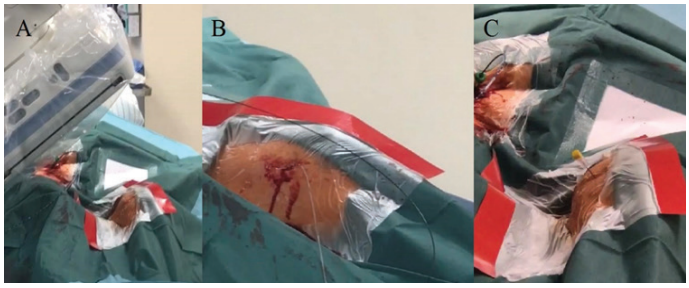

Figure 2: Positioning of C-Arm and retrograde approach via the distal SFA

(A) Position of "C" arm. **(B)** Distal SFA entrance point. **(C)** femoral and popliteal entrance points.

Furthermore, by injecting contrast via the antegrade sheath, we took a roadmap to ease our puncture and visualize the distal SFA target. After successful puncture was confirmed, a 300-cm guidewire advanced into the target vessel, the puncture needle was pulled out, and a support catheter (SeekerTM, BD, Tempe, AZ, USA) was directly introduced through the skin over the wire. The first choices guidewire to initiate the retrograde recanalization were either V-18 Control (Boston) or a 0.035-inch hydrophilic wire (Roadrunner, Cook, or Radifocus, Terumo) supported by SeekerTM. If passage failed, 0.014-inch WINN (WINN 40-80-200, Abbott), V-14 (Boston), Command (Abbott), Astato XS 40 (Asahi Intecc Co Ltd.) wires were used to penetrate the distal cap. After the first crossing goal was achieved and angiograpy confirmed the re-entry into the proximal artery, the wire was used as a guidance into the proximal sheath. Antegrade introduction of a multipurpose assisted this maneuver, Judkins right (JR4, Terumo) or vertebral catheter opposite to the catheter tip to the artery wall, aiding wire engagement into the catheter tip. After this maneuver, the wire was pushed from the distal puncture site further into the antegrade guiding catheter (externalized through the external port of the sheath) (Figure 3).

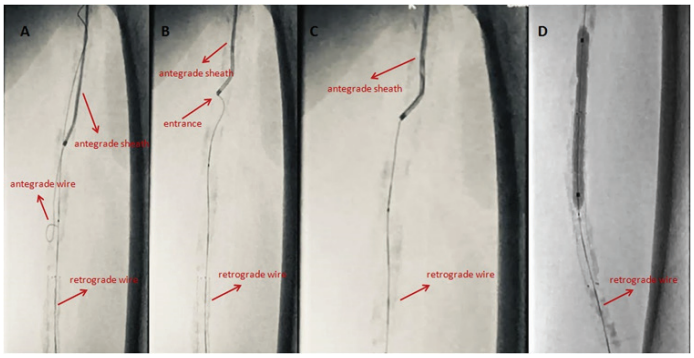

Figure 3: Wire engagement into the catheter tip and balloon angioplasty

(A) Both ante and retrograde wires are in same lumen. **(B)** Retrograde wire is being advanced into the antegrade sheath -touching the JR4 cath. **(C)** Retrograde wire is in the antegrade sheath. **(D)** Balloon angioplasty was performed

In order to re-establish the system as a standard antegrade fashion, a support catheter was withdrawn, and a 5F balloon catheter (Bantham, Bard) was inserted over the antegrade introducer distal to the target lesion. The wire was retrieved out of the balloon; after contrast injection into the balloon to be sure about proper position on the angiogram, the support catheter serving as an introducer sheath was pulled out. Hemostasis at the distal SFA puncture site was immediately achieved by local compression. At the same time, after an angiographic verification, the guiding wire was inserted again from above through the balloon and steered distal to the lesion. A blood pressure cuff was used at the puncture site for hemostasis. Inflation for % minutes of 10 mm Hg more than the systolic blood pressure can be enough. Prolonged low-pressure balloon inflation (5 minutes at 10 ± 4 atmospheres) was administered for persisten bleeding. After the vessel preparation was maintained successfully, drug-coated balloon angioplasty with a 6x120-mm balloon catheter (Lutonix, Bard) was performed. Stents were only deployed in the event of a suboptimal angioplasty, acute recoil, or dissection. The procedure was finished with a control angiogram confirming the technical success without any complication.

If the guidewire would not be able to pass through lesion retrogradely, a "double-balloon" technique was used to create 2 subintimal channels. Two 5- or 6-mm balloons were inserted at the same time antegradely and retrogradely into the occlusion. After these two balloons were positioned, caution was taken for potential ovelapping. Distance between tips of balloons should be less than 5mm. After positioning wires inside the balloons were pulled back, and they were inflated simultaneously. Once the dissection membrane separating the balloons from each other was disrupted, which facilitate the guidewire rendezvous, wire passage was attempted from either antegrade or retrograde direction. Taking all the procedures into consideration, no dedicated device (Snare, GooseNeck, etc…) was used to externalize the wire from the antegrade sheath.

Medical Therapy

The antithrombotic medication was administered as periprocedural anticoagulation with weight-based heparin (100mg/kg) to maintain activated clotting time >250 seconds. If necessary, an additional 2000 units were given every hour. All patients were on chronic single antiplatelet therapy (acetylsalicylic acid 100 mg/d) with cilostazol (200 mg/d), and they were given a single loading dose of clopidogrel 300 mg the day before the intervention.

All patients received 10.000 U Bemiparin (Hibor, Dem İlaç, Istanbul-Turkey) for two days in association with dual antiplatelet therapy as clopidogrel (75 mg/d) for four weeks followed by aspirin (100 mg/d) indefinitely.

Defınitions, Follow-Up And Outcome Measures

Critical limb ischemia (CLI) is defined in the presence of rest pain, ulcer, or gangrene due to arterial occlusive disease (25,26). Severity of PAD is determined according to the Rutherford-Becker classification (RCC) (27).

Anatomic characteristics of the SFA lesion was classified based on the TASC II classification (26). Calcium in the SFA and the popliteal artery was assessed using multiplanar DSA imaging of the vessel segment to accurately determine the extent of calcification. The calcification degree of the stenotic lesion was categorized according to the Proposed Peripheral Arterial Calcium Scoring System (PACSS): if there is no visible calcium at the target lesion site, it is categorized as grade 0 ; Unilateral calcification <5 or ≥5 cm, respectively is defined as grade 1 and 2; In grades 3 and 4 were there are bilateral calcification <5 or ≥5 cm , respectively (18).

The technical success was defined as leaving residual stenosis lower than %30 in the SFA. At least 0.10 increase in the ABI can be used as an objective evidence of increased arterial perfusion distal to the treated site (27). Technical Success of puncture was defined as retrograde placement of a sheath (group1) or support catheter (group2) into the PA without traversing the adjacent anatomical structures and without dissection or rupture. For providing objective evidence of increased arterial perfusion (hemodynamic success), an increase in the ABI of at least 0.10 is an objective parameter.(28)

Patency that is achieved without the need for additional or secondaryy surgical or endovascular procedures is defined as

primary patency (28). Primary conversion refers conversion which is needed within 30 days after initial procedure(28).

Complications

A complication was defined as access-site related when its occurrence and clinical consequences were directly attributable to the puncture (hematoma, pseudoaneurysm, arteriovenous fistula, thrombosis, dissection, neuropathy, and infection) or as intervention-specific when it was directly referable to the EVT procedure (pseudoaneurysm, thrombosis, macroembolization, microembolization, arteriovenous fistula, rupture), or systemic.

Objective performans goals (OPG)

Major adverse limb events (MALE), were defined as above-ankle amputation of the index limb or major reintervention. Major adverse cardiac events (MACE) include myocardial infarction, stroke, or death. Other OPGs were freedom from MALE or postoperative death, limb salvage, survival, amputation-free survival (AFS), clinically-driven target lesion revascularization (CD-TLR), amputation, or stenosis or amputation. These goals were evaluated at 30 days and 12 months after the procedure. The secondary endpoints also included changes in clinical status according to the Rutherford-Becker classification, ABI measurements (28).

DUS imaging was the standard tool for surveillance. DUS was performed, postprocedural 1st day, 3rd month, and every 6 months (29). During follow-up if DUS suggested restenosis and/or occlusion according to the ABI or the patient suffered from recurrent symptoms, an angiograpy can be performed. Median follow- up was 15.8 ± 2.6 months.

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS statistics software version 23 (IBM Corp, USA). Descriptive statistics were used to present the mean ± standard deviation (SD) or median (range) for continuous variables and the counts (percentages) for categorical variables. Cumulative patency rates with their standard errors, including determination of limb salvage rate, amputation-free survival rate, and primary and secondary patency rates were estimated using Kaplan-Meier analysis. The Wilcoxon Signed-Rank test was applied in the comparison of two dependent groups, not conforming to normal distribution. Comparisons of mean ABI and RCC at various time points were made using the Student t-test for dependent samples. A two-sided value of $p < 0.05$ was accepted as statistically significant.

Results

From February 2017 to April 2019, 46 patients with SFA CTO underwent recanalization via a retrograde approach. They were divided into two groups according to the technique of recanalization. Demographic data, risk factors, comorbidities, and procedural details are summarized in table 2. Patients in group1 were older (68.6 ± 8.3 vs. 61.8 ± 7.6 years, respectively<0.05). Mean BMI of the patients in group 2 was significantly higher than group 1 (22.4 ± 3.7 vs. 27.8 ± 4.1 kg/m2, respectively; p<0.05). Taking risk factors into evaluation, DM was more frequent in group 1 (75.0% vs 54.5%; p<0.05), but COPD was more frequent in group 2 (4.1% vs 31.8%; p<0.05). the other risk factors did not show any intergroup difference between the groups. Most of the occlusions in both groups were TransAtlantic Inter-Society Consensus (TASC) II D lesions. RCC and ABI were improved post procedurally in both groups significantly. The length of CTO was longer (26.9 ± 4.1vs. 20.6± 6.5 cm. respectively; p<0.05), and the number of lesions with severe grade 4 calcification were higher (70.8% vs. 54.5%, respectively; p<0.05) in group 1. In two patients from group 2, in-stent occlusion was diagnosed (0.0% vs 9.09%, respectively<0.05). The duration of the procedure and fluoroscopy were longer, and the amount of contrast volume administered in the index procedure was higher in group 2, respectively. Perioperative mortality and mortality occurred in neither of the groups. Primary stenting was required in more patients in group 1(70.8% vs. 45.4%; p<0.05). Mean hemostasis time was longer in group 1, respectively (39.7 ± 14.1vs 7.6 ± 7.3 min; p<0.05).

In group 2, double-balloon technique was used in 9 patients (40.9%). Access site, intervention-specific complications and time of occurrence are listed in table 3.

In 2 cases (8.3%) in group 1, a small residual bleeding were detected from the popliteal access site at postop period, one of them turned into a popliteal hematoma which was managed conservatively. In one patient (4.5%) in group 2, a groin-hematoma was detected around the antegrade CFA sheath and persisted at postop period. A pseudoaneurysm was diagnosed at postop 1st day in the hematoma and treated with DUS-guided compression. A low-flow A-V fistula was detected at the site of the distal puncture between PA and PV in one patient in group 1 (4.1%), and treated successfully with a low-pressure inflation of a plain balloon at the site of the puncture for additional 3 minutes.

Taking account into secondary endpoints, ABI and RCC were remained improved in both groups at 30-days and12th month. 30-day and 1-year MALE and mortality were 0. No significant difference found between the groups in terms of 30-day (0.0% vs 0.0%, p>0.05) and 12-month MACE (8.33% vs 9.09%, p>0.05) (Table 4). There were no major amputations, stent fracture, and death. In the 12th month, there were no differences between the groups for amputation-free survival (95.8% vs. 95.4%; p>0.05) .1-year limb-salvage rate was 100 ± 0 for both groups.

Table 2.			
Variable	Group 1 (n=24)	Group 2 (n=22)	p
Age (years)	68.6 ±8.3		<0.05
Men	21 (87.5%)	19 (86.3%)	NS
Body mass index (kg/m2)	22.4 ±3.7	27.8 ±4.1	<0.05
Risk Factors			
•Hypertension	21(87.5%)	19 (86.3%)	NS
•Diabetes	18 (75.0%)	12 (54.5%)	<0.05
•Active smoking	14 (58.3%)	13 (59.1%)	NS
•Coronary artery disease	10 (41.6%)	10 (45.4%)	NS
•Hemodialysis	4 (16.6%)	3 (13.6%)	NS
•Cerebrovascular disease	4 (16.6%)	4 (18.1%)	NS
•Dyslipidemia	11(45.8%)	10 (45.4%)	NS
•COPD	1 (4.1%)	7 (31.8%)	<0.05
Prior EVT to ipsilateral SFA	3 (12.5%)	4 (18.1%)	NS
•Balloon angioplasty	3 (12.5%)	2 (9.05%)	NS
•Stent	0 (0.0%)	2 (9.05%)	<0.05
Rutherford Class preprocedural / before discharge	3.24 ±0.7 / 2.01± 0.5 (p'<0.05)	3.41 ± 0.4 / 2.14 ±0.4(p'<0.05)	NS
TASC II class D	19 (79.1%)	17 (77.2%)	NS
Lesion			
•CTO length (cm)	26.9 ± 4.1	20.6± 6.5	<0.05
•De novo	21 (87.5%)	18 (81.8%)	NS
•In-stent occlusion	0 (0.0%)	2 (9.09%)	<0.05
ABI preprocedural / before discharge	0.51 ± 0.16 / 0.89 ± 0.12 (p'<0.05)	0.48 ± 0.17 / 0.86 ± 0.17 (p'<0.05)	NS
Technical success	100%	100%	NS
Procedure time (min)	45.6 ± 21.4	91.7 ± 18.6	<0.05
Fluoroscopy time (min)	24.4 ± 15.6	63.5 ± 17.7	<0.05
Mean contrast volume (ml)	41 ± 17.4	69.2 ± 22.9	<0.05
Primary stenting	17 (70.8 %)	10 (45.4%)	<0.05
Perioperative mortality	0 (%0.0)	0 (%0.0)	NS
Perioperative morbidity	0 (%0.0)	0 (%0.0)	NS
Mean hemostasis time (retrograde puncture site) (min)	39.7 ± 14.1 (sheath)	7.6 ± 7.3 (support cath)	<0.05

Abbreviations: COPD: Chronic obstructive pulmonary disease; EVT: Endovascular treatment; SFA: superficial femoral artery; TASC: Trans Atlantic Inter-Society Consensus; CTO: Chronic total occlusion; ABI: Ankle-Brachial Index; PACSS: Proposed Peripheral Arterial Calcium Scoring System; NS: not significant.

Table 3. Complications						
Complication	Group 1(n=24)			Group 2 (n=22)		
Access-site	Intraop.	Postop.	30-days	Intraop.	Postop.	30-days
•Bleeding	0 (0.0%)	2 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Hematoma	0 (0.0%)	1 (4.1%)	0 (0.0%)	1 (4.5%)	1 (4.5%)	0 (0.0%)
•Pseudoaneurysm	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)
•A-V fistula	1 (4.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Thrombosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Dissection	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Intervention-specific						
•Pseudoaneurysm	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Thrombosis	0 (0.0%)	0 (0.0%)	1 (4.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Macroembolisation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•A-V fistula	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
•Rupture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 4. Improvements in ABI and RCC						
Variable	GROUP 1			GROUP 2		
ABI	Baseline 0.51 ± 0.16	30-days 0.87 ± 0.13[a]	12-month 0.83 ± 0.18[a]	Baseline 0.48 ± 0.17[a]	30-days 0.85 ± 0.19[a]	12-month 0.82 ± 0.16[a]
RCC	3.24 ± 0.7	1.81 ± 0.6[a]	1.51 ± 0.2[a]	3.41 ± 0.4	1.84 ± 0.7[a]	1.53 ± 0.6[a]
ap<0.05 versus baseline.						

No statistically significant difference was found in terms of restenosis/reocclusion rates as restenosis occurred in three patients (all of them were ISR) in group 1 at 5th, 7th and 11th months- they were successfully treated with DCB angioplasty, an acute stent thrombus occurred in one patient 18 days after the initial procedure which was treated successfully with catheter-directed thrombolysis and one patient underwent surgical embolectomy at postprocedural 4th month due to cessation of the antiaggregant medication.

Whereas three patients underwent catheter-based for restenosis at postprocedural 5ht, 8ht, and 10th month, and one patient underwent fem-pop bypass because of reocclusion and CLTI at postprocedural 12th month (12.5% vs. 13.6%, p>0.05).

The primary patency rates at 1, 6 and 12 months after interventions was 97,9%, 91.45% and 80.4% for whole study group. As taken intergroup differences into consideration, primary patency rates of group 2 were higher than group 1, but this difference became significant only at 6th month (95,8%, 87.5%, 79.1% for group 1vs. 100%, 95.4%, 81.8% for group 2, respectively; p<0.05 only for 6th month) (figure 4).

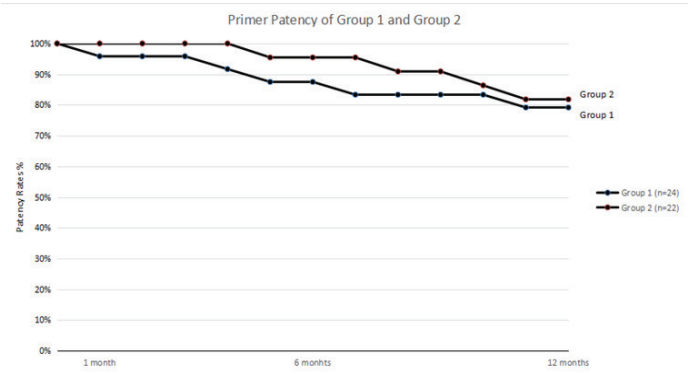

Figure 4: Kaplan-Meier analysis probability estimates of primary patency

Primary surgical conversion rate was 0% for both groups. The difference between secondary conversion rates at 12 months were (4.34 ± 0.2 vs 4.51± 0.18; p>0.05) not statistically significant. The 1-year CD-TLR rate was 17,25% for whole study group, group 1 seems to have more CD-revascularization procedures but it did not reach to a significant difference (95% CI 20.8% to 13.7%).

Discussion

PAD is a serious disease that affects an almost 10–12 million people in the United States (30). EVT is routinely prefered as a primary approach with lower procedural risks for the treatment of PAD. CTO of the SFA is a commonly encountered target lesion in patients with symptomatic lower extremity arterial disease (31), but EVT of SFA CTO is often challenging because of the lesion length and high probability of the presence of severe calcification.

EVT of SFA can be performed either the contralateral retrograde or ipsilateral antegrade CFA access (32-34). The contralateral approach can be tough in the presence of narrow aortic bifurcation. Furthermore, long introducers and devices are required, which impoverishes the pushability like transaxillary or transradial approaches. The antegrade CFA approach offers more productive usage of short instruments. Unfortunately, all these approaches are inappropriate when the SFA occlusion is either flush, or in the presence of lesions involving CFA or proximal stump of SFA. Furthermore, if the antegrade attempt fails, you need a back-up plan. An unsuccessful EVT is most often not the inability to cross the occlusion with the guidewire, but an unsuccessful re-entry of the guidewire into the true lumen distal to the occlusion (15). Devices for re-entry were produced to salvage situations in which a guidewires cross the occluded segment but fails to re-enter the true distal lumen (35,36). But high costs of these devices precludes the usage. Some situations such as wire perforation within an occluded segment or occluded stents make it impossible to pass from the antegrade direction. Furthermore, the re-entry device itself can also fail. Shin et al. (37) recently reported a 35% failure rate. In our study, we did not use any of the re-entry devices.

To summarize and focus on our study, the main indications for retrograde distal SFA or popliteal approach were a short SFA stump, flush occlusion of SFA (like in group 1), and failure of the antegrade approach (like in group 2) (12,14,16, 38).

The reason why retrograde revascularization was more effective than an antegrade approach is not apparent. However, before interpreting the results with two different

techniques, we must admit that an essential limitation of RPA. Atherosclerotic lesions or occlusion extends to the distal popliteal artery is major obstacle. Percutaneous approach from in below-the-knee arteries requires a patent target vessel and has a high risk of iatrogenic injury. Consequent damage to crucial collateral arteries is an another concern(15).

Subintimal Angioplasty (SA) technique that we preferred to use in group 1as a treatment of choice can also be named as "percutaneous intentional extraluminal recanalization (PIER)." It shows a great similarity to surgical endarterectomy by which recanalizes an occluded arterial segment through an extraluminal channel between the intima and media yielding a 'bare' neo-lumen (39).

The development of the technique of PIER has largely been dominated by the extensive work of Bolia and Reekers (19,20). PIER technique aims to obtain a smooth neolumen free from atheromatic area between the tunica intima and media, which produce a possible better patency rate (19,40). But our technique is slightly different because Bolia technique requires an antegrade ipsilateral CFA puncture and the presence of at least a 5-mm stump at the origin of the SFA (19,20,40,41) and they did not use the procedure if the patient has no SFA stump (41). An alternative was brought by Heenan et al. (42). They have reported successful results in three SFA occlusions through ipsilateral RPA like our technique.

In PIER through the retrograde popliteal approach, re-entry is achieved around the deep femoral artery (DFA). Thus, inadvertent occlusion of the ipsilateral DFA while trying to re-enter the true lumen may be dangerous. This can best be avoided by entering the true lumen below or at the level of the origin of the DFA since, in the case of a high re-entry site, PTA of the subintimal space may cause occlusion of the DFA at its origin. This was the reason we preferred to try to re-enter the true lumen by a controlled catheter– guidewire manipulations instead of simple forward pushing of the catheter–guidewire combination toward the patent part of the artery. In 1994 London et al. (41) provided the first significant report of the technique for SA on 200 consecutive femoropopliteal artery occlusions with a median length of 11 cm (range 2-37). The technical success rate was 80% and was not significantly different for occlusions of more than 20 cm. They reported the factors influencing long term patency were smoking, the number of calves runoff vessels, and occlusion length. Laxdal et al. (43) reported the experience with 124 SA accumulated over a 5- year period and reported a technical success rate of 90% with a 42% primary patency at 12 months. Taking the impact of the number of distal runoff vessels on patency and to correctly evaluate both techniques' results, we excluded patients with lesions affecting the distal runoff in our study. Soga et al., (44) employed a bidirectional approach in 37% of the SA group and achieved a technical success rate of 90% (mean occlusion length= 23.5 cm).

This approach is not feasible in patients who are obese, have impaired respiratory function, or have conditions that may interfere with positioning them prone or in lateral decubitus. This factor may explain why BMI and COPD were high in group 2 because they are not suitable candidates for pron technique, and the supine technique is preferred. But before interpreting this result, we should accept that obesity can also be a situation where a CFA puncture will be very difficult or contraindicated.

Since most of the patients in group 1 had TASC D lesions and all of them had a SFA stump of <5 mm, we have chosen RPA as a first choice instead of contralateral or ipsilateral CFA access. Evaluating our results, another advantage of the pron technique has come forward as the lower duration of procedure and fluoroscopy times as well as the amount of contrast medium. This difference can partly be explained by the time passed and the contrast used during the failed antegrade attempt. But also a part of it can be attributed to the use of DUS for cannulation of PA in every case. DUS has the advantage of visualizing the vein to avoid accidental puncture and reduce the risk of arteriovenous fistulas. Performing the puncture with ultrasound guidance reduced the contrast volume used as well as the duration of fluoroscopy.

Yilmaz et al. successfully treated 32 of 39 SFA occlusions (82%) with PIER technique via RPA and reported a cumulative patency rate of 66% at 6 months (17). Noory et al. reported 56 procedures, in which after re-entry to the true lumen failed in the antegrade approach, all patients were turned to a prone position, and a 5-F or 6-F sheath was placed into the mid-segment of the PA and crossed the lesion either subintimal or endoluminal. They reported the reperfusion success as 98%, 12-month primary patency rate as 45.1%, 1- year TLR rate as 45.1% (46). Mert Dumantepe (46) published the results of the endoluminal recanalization of 28 patients with CTO of SFA via RPA with the patient in the prone position using a Rotarex device and reported a significant increase in ABI and a 1-year primary patency rate of 85.7%. Housam et al. reported 16 patients using transpopliteal artery retrograde access with the patient placed in the prone position, reported a 30-day MACE

of 6% without perioperative morbidity, 30-day mortality, and 30-day MALE. The primary patency was 66 ± 9%; limb salvage was 100%, AFS was 92% at 2 years (48). Sangiorgi et al. (8) reported the treatment results of 23 patients requiring RPA for occlusive lesions with an average length of 20.6 ± 8.8 cm. This group demonstrated procedural success in 22 of 23 patients compared with group 1 as we treated longer lesions with 100% success.

Taking supine group in which a retrograde approach was achieved after the failed antegrade attempt, we adopted the sheathless approach, passing the guidewire directly through the puncture needle into the occluded artery followed by the support catheter different from the WBO technique described by Baker et al. (15) (in WBO technique, a balloon used as support catheter gives the opportunity to stepwise dilate the artery in case the wire and/or balloon encounters friction within the occlusion). We prefer to use a support catheter rather than a ballon, because a balloon after inflation has a larger diameter than an unused balloon, potentially increasing the trauma during retrieval. We used fluoroscopic guidance as well as DUS. The vicinity of the radiation source to the hands of the operator during puncturing might be of concern. However, if we decided to use fluoroscopy, we found it feasible after local anesthesia to first just pierce the skin using a roadmap or an angiogram via the proximal sheath, leaving the needle in place as a guide while performing a second angiogram to determine the distance of the needle to SFA or PA. The needle was then guided into the artery without fluoroscopy until back- bleeding was noticed.

The technique for extraction of the retrograde guidewire from the antegrade sheath maneuvered the guidewire into the tip of the catheter inserted antegrade until the guidewire tip appeared outside of the proximal sheath. This technique was successful whenever used. We think that not using the dedicated devices for this issue, potentially help to decrease the costs.

Fanelli et al. (16) published the results of 26 patients who, after the failure of an antegrade attempt, an RPA in the supine position for recanalization of SFA was preferred and reported primary patency of 80.7% at 6 months and 76.9% at 1 year. Shi et al. (48), published the results of 21 patients underwent dual femoral-popliteal recanalization in the supine position for CTO of the SFA, with much shorter mean lesion length as 87.4 mm± 5.8 compared to our study, and reported a 100% technical success, a significant increment in ABI and a primary patency rate of 80% at 6 months. But in their study, further stent stenosis had occurred in 57.1% of the patients after 6 months and decreasing the primary patency to 42% at 12 months. In their study, ABI changed from 0.48 ± 0.17 pre-interventionally to 0.89 ± 0.10 at 1 day, to 0.87 ± 0.10 at 1 month, 0.85±0.11 at 6-months and 0.84 ± 0.11 at 1 year post-interventionally. These results are in line with our study. Schmidt et al. (22), published the results of 50 patients who received retrograde recanalization via distal SFA after failed antegrade recanalization of SFA CTO with a mean lesion length of 205 ±75 mm. They utilized the rendezvous technique in 24% of the patients with a success rate of 96%. Ye M et al. (49), published an approach with infracondylar-plane access to the popliteal artery in the supine position, in which the postinterventional ABI was 0.74 ± 0.23, and the primary patency rate was 84.2% after a 6-month follow-up. In our study, we achieved an increment in ABI and an improvement in RCC post procedurally, and this improvement continued for at least 12-months. Tan et al. (18) reported 20 patients underwent EVT via retrograde access using the anterolateral popliteal puncture technique with the patient in the supine position. Their technique was different from ours' in terms of the cannulation site (P3 segment) and similar in terms of cannulation without a sheat like our group 2, and preferred usage of the rendezvous technique as we did in 9 patients in group 2. In their study, the mean hemostasis time for balloon inflation was 7.73±4.03 min. Similar to our group 2. The low profile of the support catheter made it easier to obtain hemostasis, and the supine technique allows utilization of various techniques in combination including compression, controlled inflation of a blood pressure cuff at the puncture site and a controlled prolonged intraluminal balloon inflation if necessary to provide tamponade after removal of the catheter.

Komshian et al. (50) retrospectively reviewed 148 patients with isolated SFA and PA disease treated with RPA access, compared with antegrade CFA access, and published their results in 2018. They did not give any information about the procedural techniques. They reported technical success as 80.4%, MALE-free survival as 74.5%, and patency as 70.3%, which was significantly lower than the CFA access group and lower than our study. The enormous difference in sizes of the analyzed groups presented a methodologic challenge for statistical analysis of the data (29.926 vs. 148), preventing the correct statistical comparison. Moreover, they did not

standardized the groups in terms of lesion severity as the proportion of TASC II D lesions was more frequent in the RPA group (49.6% vs. 18%), leading the misinterpretation of the results.

Young-Guk Ko (51) published a review comparing SA and endoluminal angioplasty by evaluating several registry studies and concluded that SA appears to achieve a higher technical success rate than EA, whereas mid-term primary patency rates are comparable for both endovascular wiring strategies for SFA CTO. They also reviewed published studies on the primary patency of SA for femoropopliteal artery occlusions from 1994 to 2017. From their review, we can easily show the improvement of patency rates after using stents. But in most cases needs the support of stents for preventing recoil. But also we know that limited efficacy of stents in long lesions. Long stenting may have also contributed to the lower patency rates. Hong et al. (52) showed that primary patency was significantly lower with long stenting than with spot stenting following SA of long femoropopliteal occlusions. Thus, stenting strategies may play a more critical role than the wire passage method in maintaining the patency of recanalized long arterial lesions. Considering the SA technique, during the dissection maneuver, it is conceivable that damage to collateral vessels occurs. In other words, the flow in the artery beyond the occluded segment becomes static. The majority of these situations have been retrieved with the use of self-expanding stents in the site of the occlusion, where the re-coil is supposed to have been maximal. Besides, in our study, we faced more flow-limiting dissection flaps in group 1 than group 2, which mainly can be attributed to the more severe calcific nature of the CTO, which probably increased the frequency of stent deployment. On the other hand, questioning the primary stent difference between the groups, w the two patients in group 2 were treated because of in-stent occlusion, and we did not use a stent in their treatment. Since the number of patients is relatively low, this may have contributed to the intergroup statistical difference. But we always choose spot stenting in both groups for the indications we mentioned before. Since a deployed stent in SFA must deal with strong bending, compression, and torsion forces, dynamic vessel conformability is very important. We preferred The LifeStent™, which is the only FDA-approved stent for the SFA. Palena et al., published their results in PRESTO trial that they used Supera stent (Abbott, CA, USA) which was navigated in a retrograde fashion to position the first crown to be released just at the SFA ostium in 21 patients and concluded that The PRESTO technique (is a feasible and potentially useful strategy to safely and accurately deploy this type of metallic endoprostheses at the SFA ostium (53).

In 2019, Igus and Firat (54) described an alternative treatment of SFA stump occlusion by a direct puncture of occluded SFA and followed by antegrade recanalization when conventional antegrade or retrograde access was not achievable. They achieved technical success in 80% of the patients, and a significant difference between mean Rutherford pre- and post-procedural scores (4,2 ± 0,4 vs. 1,3 ± 0,5). They reported an AFS of 60%, a primary patency rate of 62.5% at 24 months.

The primary patency rates of the patients at 1, 6, and 12 months were 97,9%, 91.45%, and 80.4%. There were no intergroup differences except 6th month, which group2 has better patency. With the number of patients and the reasons for secondary interventions (one of them was a macroemboli requiring surgical intervention because of the patients' cessation of the anticoagulant management), it is difficult and will definitely be wrong to interpret this discrepancy. The 1-year CD-TLR rate was 17,25% for the whole study group without an intergroup difference.

The reason that popliteal access has not become more popular is the risk of access-site complications. However, several case series report low rates of major complications (33,55,56) with prone technique. Several authors have reported complication rates between 2.5% and 5.2% after manual compression of the popliteal artery access (42, 55,56). Possible complications in pron technique are occlusion of PA at the puncture site, distal embolization, and arteriovenous fistula due to unintentional puncture of the popliteal vein. Since the popliteal vein is located posterior to the artery, there is always a high risk of traversing both vessels with the needle when operating the RPA. By using DUS guidance, we significantly prevented these complications as DUS allows the operator a visual control of the needle, the PA, and the vein, lowering the risk of perforation of the vein and consequently, the risk of fistula formation. In our series, we had only 4 complications in group 1, which is a small hematoma in 1 patient and arteriovenous fistula in 1 patient and minor bleeding in 2 patients. But the potential problem with this technique is the usage of a 6F sheat resulting in a long hemostasis time like approximately 40 minutes. Arterial rupture is the most concerning complication associated with SA, but the incidence is relatively low, ranging from 0% to 6% (51). The risk of perforation is increased in older patients, those

with diabetes, and smokers. We did not face this complication in our study. Although distal embolization was thought to occur less frequently in SA than IA due to the absence of atherosclerotic plaques and thrombus in the subintimal channel, the incidence is similar to that of IA and varies from 0% to 7.3% (51).

If we consider our supine technique, we believe that the sheathless technique avoids complications in the retrograde access site related to a large sheat. As Yilmaz and colleagues noted (57), only 3 to 10 minutes of manual compression seems to be enough to obtain complete hemostasis of the popliteal puncture site without any complication, like in our group the duration of complete hemostasis in group 2 patients was approximately 7.5 minutes. Tokuda et al. (58), reported 68 patients whom RPA in the supine position was used and divided the cohort into two groups performed with a 4-F or 6-F sheath and those with a 2.1-F microcatheter and compared the groups in terms of complications, the success of popliteal artery puncture, lesion crossing, and reperfusion. They found a significant difference in terms of mean time to hemostasis as 8.9±8.8 minutes in the microcatheter group vs. 47.7±13 minutes in the sheath group ($p<0.0001$), and the complication rate (22.2% in the sheath group vs. 2.0% in the microcatheter group) advocating the sheathless technique.

As for the shortcomings of this study, we can put forward its retrospective nature and the small number of patients. Also, adding a comparative group of patients with SFA obstructions who underwent recanalization through antegrade approach might have increased the precision. But, most of the published works in the current literature only focused on one technique, its safety and technical success without follow-up results. Comparing the safety and success of two techniques applied by the same operator, having no lost patient in follow-up, standardization of the definitions and reporting them in the same standards, investigating the prior techniques in the literature and discuss our own techniques created by removing the proven problematic parts of prior techniques and try to create an algorithm can be counted our studies' superiorities.

Conclusion

Undoubtedly, endovascular procedures becomes more invasive via bidirectional approach (femoral and popliteal) and prolongs the duration of procedure and fluoroscopy. There are options to provide re-entry into the true lumen in case of subintimal recanalization like our double-balloon maneuver when used as an adjunct to the bi-directional approach, it has been extremely useful in facilitating wire cross in casee of an inability to pass the occlusion from either direction. This is not possible with the patient lying prone for the transpopliteal approach. When the diameters of the balloons are preferred to match the artery and are not smaller, the "double-balloon" technique maneuver brings success mostly. We do not believe that a 5- or 6-mm balloon carries a significant risk of perforation. Moreover, fewer complications in distal puncture site because of not using a large introducer sheath. As we did not find a significant difference in the success rate, the sheathless method resulted in a shorter time to maintain hemostasis and a tendency of lower complication rate as the hematoma and pseudoaneurysm in group 2 occurred in the same patient and in the femoral area. There was no complication in group 2, regarding the retrograde access. On the other hand, by creating a new lumen without atheroma, the pron technique makes the length of the lesion trivial. It offers a proper, clean, uninterrupted, antegrade flow without any atheromatous plaque, shortening the duration of procedure, fluoroscopy, decreasing the amount of radiation exposure, and amount of contrast medium. Nonetheless, either planned as a primary strategy or needed as a back-up plan, it should be in the vascular surgeon's portfolio.

Conflicts of interest

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

Funding

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

Authors Contribution

AB, OEG, NBT, KO and SG contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

*All authors read and approved the final version of the manuscript.

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Turkish Journal of Clinics and Laboratory

To cite this article:Demirdag ED, Adam Erden AC, Ozer Yagci SB, Karakis D. Evaluation of EMG activities of masticatory muscles after reestablishment of vertical dimension in patients with worn dentition: A case series Turk J Clin Lab 2023; 4: 798-806

Case Report

Evaluation of EMG activities of masticatory muscles after reestablishment of vertical dimension in patients with worn dentition: A case series

Diş aşınması olan hastalarda dikey boyutun yeniden yapılandırılması sonrasında çiğneme kaslarının EMG aktivitesinin değerlendirilmesi: Vaka Serisi

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Abstract

Management of the patient with worn dentition has been required the reestablishment of occlusal vertical dimension and comprehensive treatment planning for each case. In the present study, the effect of increased occlusal vertical dimension with dental restoration on the EMG activities and functional indices of masticatory muscles have been evaluated. The rehabilitation of three patients with worn dentition was presented. Before and after the restorative treatment, EMG recordings were taken and the activity index and asymmetry index were measured. The functional indices have been found more related to occlusal contact stability.

Keywords: bruxism, electromyography, occlusal vertical dimension, activity and asymmetry index, masticatory muscles

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Doi: 10.18663/tjcl.1382154
Recevied: 30.10.2023 accepted: 17.11.2023

Öz

Aşınmış diş yapısına sahip hastanın tedavisi, oklüzal dikey boyutun yeniden oluşturulmasını ve her bir vaka için kapsamlı tedavi planlamasını gerektirir. Bu çalışmada diş restorasyonu ile artan oklüzal dikey boyutun çiğneme kaslarının EMG aktiviteleri ve fonksiyonel indeksleri üzerindeki etkisi değerlendirildi. Dişlerinde aşınma olan üç hastanın rehabilitasyonu sunuldu. Restoratif tedavi öncesi ve sonrasında EMG kayıtları alınarak aktivite indeksi ve asimetri indeksi ölçüldü. Fonksiyonel indekslerin oklüzal temas stabilitesi ile daha fazla ilişkili olduğu bulunmuştur.

Anahtar Kelimeler: Bruksizm, elektromiyografi, oklüzal vertikal boyut, aktivite ve asimetri indeksi, çiğneme kasları

Introduction

Occlusal wear has mostly been consisting of the contribution of attrition, erosion, abrasion and parafunctional habits. In patient with excessive wear, esthetic appearance particularly for anterior teeth become a problem. The rehabilitation of these patients with restoration required the reestablishment of occlusal vertical dimension (OVD) [1].

Management of patients with worn dentition requires a careful and comprehensive treatment plan. Depending on the degree of tooth wear, treatment options can change from the range of the placement of bonded composite restoration to full mouth restoration [2]. Diagnostic wax up casts provide detailed information for the desired aesthetics and the determination of the amount of distance to increase and to discuss the treatment options. Adaptation of newly formed OVD confirmed with a diagnostic splint or provisional prosthesis [3]. The best OVD increase has been performed at the patients' satisfied esthetic desires with the most conservative approach [4].

The jaw muscles are the primary determinant of vertical dimension [5]. There is an important relationship between the jaw muscles and the maxillo-mandibular relationship that an increase in OVD leads to the stretching of jaw closing muscles and has a more direct effect on vertically oriented muscle fibers [6]. To evaluate and observe the electro-physiological behavior of the muscles surface electromyography (EMG) is widely used in dentistry [7,8,9]. EMG is a non-invasive and useful assessment of the electrical activity of muscles at rest and during muscle contraction [10-11]. The symmetry of EMG activity between the right and left side may be an indicator of the structural or functional disorders of the stomatognathic system [7]. The activity indices (AcI) indicate the ratio of one muscle group to the other that is used to evaluate the participation of the masseter muscle (MM) and temporalis anterior muscle (TAM) in the clenching activity [7]. The asymmetry index (AsI) determines ratios between the right and left sides that are used to estimate the activity balance for each muscle pair [7]. In the presence of pain [13], changed occlusion parameters [14], or temporomandibular disorders (TMDs) [15], masticatory muscles present abnormal activity patterns [9]. The functional indices provide the evaluation of the integrated EMG activity analysis of masticatory muscles. Therefore, any particular change in functional indices ratios can be related to an abnormal pattern of masticatory muscle activity and an early sign of disturbance [12]. In addition, the functional indices of masticatory muscles could be a useful tool to determine functional improvement and to observe the effects of applied treatment.

There are many studies related to the OVD increase [1-4]. Some authors supposed that the alteration of OVD may damage the physiology and the functional status of the masticatory system and temporomandibular joint (TMJ) structures [16,17], on the other hand, others reported that these symptoms are temporary [16,18,19]. In the literature, there are no studies about the effect of increased OVD on the functional indices of masticatory muscles. Therefore, in the present study, we aimed to investigate the effect of increased OVD with dental restoration on the EMG activities and functional indices of masticatory muscles.

EMG activity recording procedure

Before the start of the restorative treatment EMG recordings were taken from patients. EMG recordings of the MM and TAM were performed in the resting and clenching activity at the maximum intercuspal position. EMG recordings were performed with a BioEMG III (BioPAK, BioResearch Associates Inc., Milwaukee, WI, USA) EMG amplifier connected to a PC running Windows (Microsoft, Redmond, WA, USA) and the BioPAK software program. The signals of EMG recordings were graphically viewed on the computer screen. The eight channel amplifier had a bandwidth of 30-1000 Hz and an input impedance of >100 MU. EMG activity was recorded bilaterally in microvolts (mV) with bipolar electrodes (BioFlex, BioResearch). Before placing the

electrodes on the muscle, the muscles were palpated by using fingers. Initially, the palpation of the MM and TA was performed to define the placement of the electrodes that were positioned parallel to the direction of the muscle fibers. Before the electrode placement, the skin was cleaned with 95 % alcohol. A disposable ground electrode was placed on the neck.

First EMG recordings of patients performed in the rest position. The patients sat in an upright position parallel to the Frankfurt Horizontal Plane and were instructed not the contact teeth and to release the mandibula in the rest position. In the rest position the EMG activities of muscles (MMR: Right masseter muscle; MML: Left masseter muscle; TAR: Right temporalis anterior; TAL: Left temporalis anterior) were recorded. Then in the intercuspal position, the patients performed 3 clenchings in maximum voluntary contraction for 1-3 seconds, and the mean values of these 3 clenchings were recorded as the maximum contraction values of each muscle. After 8 weeks of the completion of restorative treatment, all records were repeated in the same procedures.

The calculation of activity and asymmetry index of muscles

AcI and AsI were measured from the RMS (Root means Square) (20). AcI are used to evaluate the participation of MM and TAM during clenching activity. The AcI is used to measure the ratio of one muscle group to the other [7]. AcI values are set between −100 and +100. The negative (−) values show the predominance of the TAM and the positive (+) values suggest an MM advantage. AcI values range between +100% and −100%, with +100% indicating the involvement of only the MM during activity and −100% of only the TA [20].

$$AcI = (RMS\ MM - RMS\ TA)/(RMS\ MM + RMS\ TA) \times 100$$

The AsI was calculated to determine ratios between the right and left sides based on the equation by Naeije (1989) [20]. This index has been used to estimate the activity balance for each muscle pair. If the muscle activation level is fully symmetrical AsI is 0%, while the full asymmetry corresponds to 100%. The formula is:

Asymmetry index (AsI) = (RMS right - left RMS)/ (RMS right + left RMS) * 100

Case Presentations

Case 1

A 64-year-old female patient applied to the prosthodontic clinics with the complaint of worn dentition, poor esthetic and, difficulty in masticatory function. Medical and dental history was obtained and the patient gave a history of bruxism. On extraoral clinical examination, a reduced lower face height was noted. Dental examination showed a generalized worn dentition, diastemas in anterior teeth, and missed teeth numbers as; 24,26,35,36,37,45,46 (Figure 1). TMJ evaluation revealed no history of dysfunction, no joint sound, and pathology. Masticatory muscle, and head and neck muscles were normal at palpation. The mandibular range of the motion and jaw opening were within the normal limits.

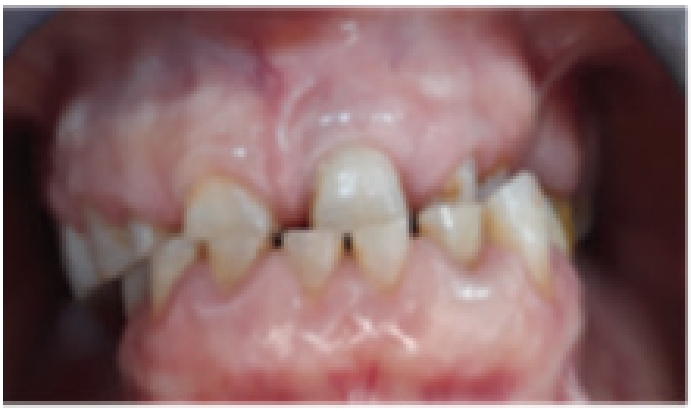

Figure 1. Intraoral view before treatment

To determine the amount of OVD increase a mock up procedure was performed (Figure 2). The impression of upper and lower dentition was taken with hydrocolloid impression material (Hydrocolor 5, Zhermack, Badia Polesine, Italy). Then facebow record (UTS Face-bow, Ivoclar Vivadent, Austria) was performed and casts were mounted on an articulator (Stratos 300, Ivoclar-Vivadent, Austria). Then, mock up waxing was performed and trained in the patient's mouth. A total 6 mm OVD increase was detected in facial measurement (distance between nose and chin tip) with the Niswonger method. Actual increase was determined as 4 mm in the anterior teeth and the incisal guidance of the articulator pin was set.

After the esthetic and functional evaluation of mock up restoration, the patient was informed about the possible restorative treatment options, and also the advantages, disadvantages, and possible risks of the treatment options. The restorative treatment involves the restoration of upper and lower teeth with increasing OVD. Upper fixed restorations (21,22,23, 24,25,26,27,11,12,13,14,15,16,17) and lower fixed restorations (31,32,33,34,41,42,43,44,47) with the removable partial denture (35,36,37,45,46) were planned for the rehabilitation of patients. For the adaptation of the patient to altered OVD, a self-cured acrylic resin (Panacryl, Arma Dental, Istanbul, Turkey) occlusal splint was produced with bilateral anterior and posterior simultaneous contacts in centric relation (Figure 3). The patient

was instructed to wear a splint for 24 hours, for 4 weeks. After the four-week adaptation period, no muscle tenderness and temporomandibular discomfort were reported. The occlusal splint was kept to take bite registration at preparation procedures. After preparation of all anterior and posterior teeth final impressions were made with polyvinylsiloxane impression material (Optosil Comfort/Xantopren VL Plus, Heraeus Kulzer, Hanau, Germany) and provisional restorations were fabricated using a self-cured acrylic resin (Figure 4).

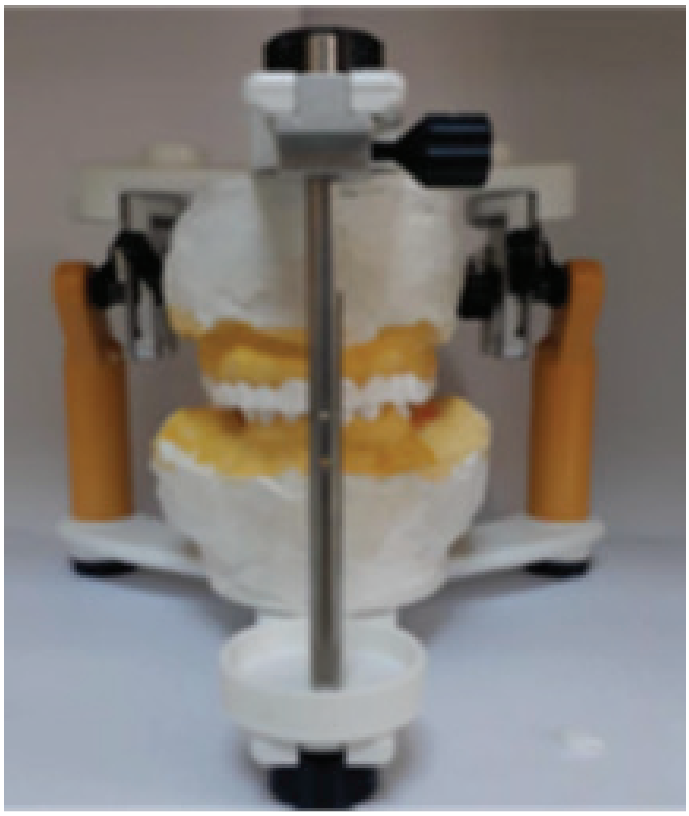

Figure 2. Diagnostic wax up

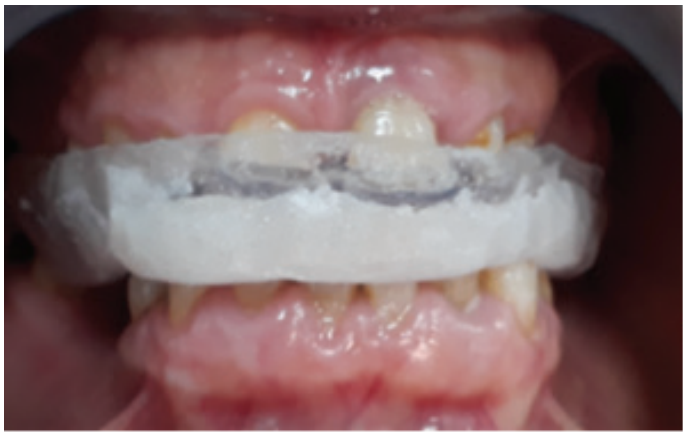

Figure 3. Maxillary occlusal splint

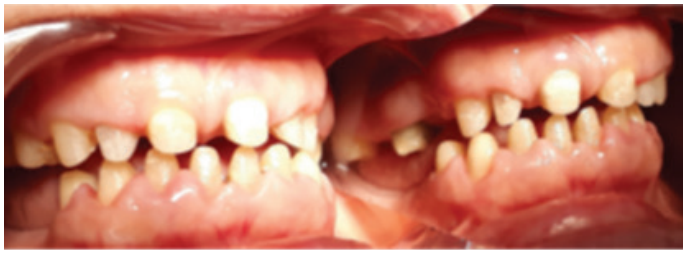

Figure 4. Intraoral view after preparation of teeth

In the following sessions, metal substructures of fixed restorations (Kera N, Dr.-Konrad-Wiegand-Str. 9 - D-63939 Wörth, Germany) were performed (Figure 5) and the trial of ceramic restoration (Ceramco 3, Dentsply, Dreieich, Germany) was accomplished with minor occlusal adjustments. The final restorations were glazed and cemented with zinc polycarboxylate cement (Adhesor-Carbofine, Spofa-Dental, Germany). At the session three days later, a second impression of the mandibular removable denture was taken with alginate impression material. The metal framework of the lower denture and tooth alignment was performed in the following sessions. Then acrylic removable mandibular denture was adjusted in the patient's mouth. The occlusal scheme of definitive restoration was designed as group functional occlusion (Figure 6). The patient was advised to maintain oral hygiene and schedule regular check-ups every six months. Written informed consent was obtained from the patient for the publication of her data.

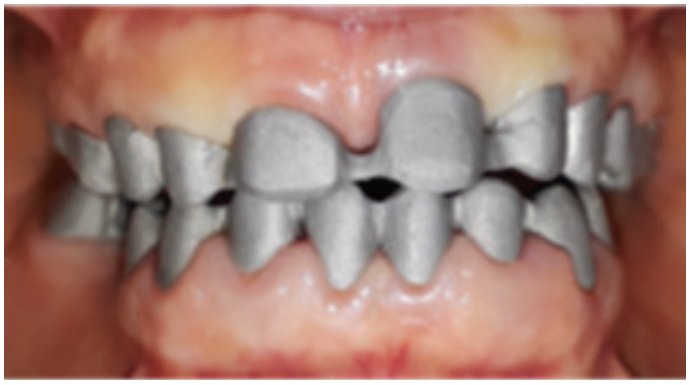

Figure 5. Metal substructure

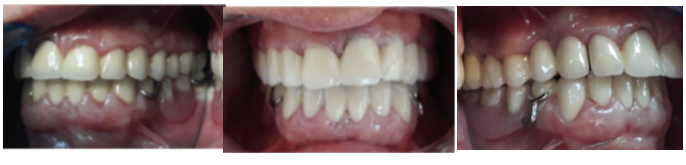

Figure 6. Intraoral view of final restoration

Case 2

A 77-year-old male patient was referred to the clinic with the chief complaint of poor aesthetics, a generalized worn dentition, and missing teeth (12,13,16,17,46) (Figure 7). The patient has a history of bruxism and is wearing a night guard to prevent attrition of dentition. In the periodontal examination, generalized stainings and calculus were observed on teeth. Supragingival scaling was performed to remove plaque and calculus and then polishing was applied. TMJ evaluation showed no history of dysfunction, no joint sound, and pathology. Masticatory, head and neck muscles were normal to palpation. The mandibular range of the motion and jaw opening were within the normal limits.

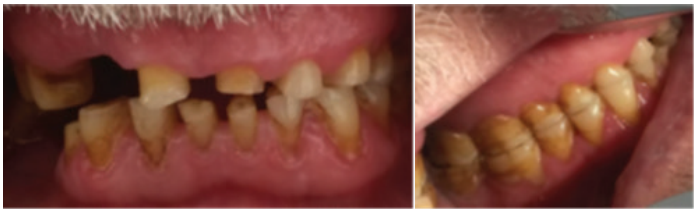

Figure 7. Intraoral view before treatment

As there was not enough space for the rehabilitation of missing anterior teeth with restoration, we needed to increase OVD to create a space for dental materials. To determine the amount of increase a mock up procedure was performed. The impression of upper and lower dentition was taken with hydrocolloid impression material (Hydrocolor 5, Zhermack, Zhermack SpA., Badia Polesine, Italy). Then facebow record (UTS Face-bow, Ivoclar Vivadent, Austria) was performed and casts were mounted on an articulator (Stratos 300, Ivoclar-Vivadent, Austria) with a facebow record (Figure 8). Mock up waxing was performed with the 4 mm increase of anterior dentition (Figure 9). The prepared mock up waxing was trained in the patient's mouth and a 6 mm OVD increase was detected in facial measurement (distance between nose and chin tip) with the Niswonger method. The patient was informed about the possible restorative treatment options. Upper fixed restorations (11,12,13,14,15,21,22,23,24,25,26) with removable partial denture (16,17) and lower fixed restorations (31,32,33,34,35,36, 37,41,42,43,44,45,46,47) with increasing OVD were planned for the rehabilitation of patients. A self-cured acrylic resin (Panacryl, Arma Dental, Istanbul, Turkey) occlusal splint was performed to evaluate the adaptation of the patient to the increased OVD. The patient was instructed to wear a splint for 24 hours for 4 weeks. At the end of the adaptation period, no muscle tenderness and temporomandibular discomfort were reported by the patient. The preparation of all anterior and posterior teeth (Figure 10) was completed, and second impressions were made with polyvinylsiloxane impression material (Optosil Comfort/Xantopren VL Plus, Heraeus Kulzer, Hanau, Germany) and provisional self-cured acrylic resin restorations were inserted. In the next sessions four days the metal substructures (Kera N, Germany) and ceramics (Ceramco 3, Dentsply, Dreieich, Germany) of fixed restorations were adjusted (Figure 11). The definitive restorations were glazed and cemented with zinc polycarboxylate cement (Adhesor-Carbofine, Spofa-Dental, Germany). The group functional occlusion was established. The patient was satisfied with the improved aesthetics and also the function of dentition. Written informed consent was obtained from the patient for the publication of his data.

Figure 8. Diagnostic wax up

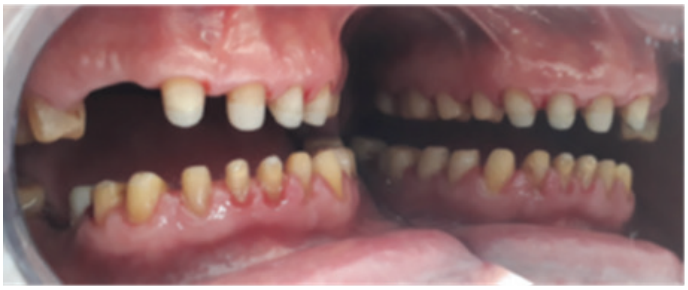

Figure 9. Intraoral view after preparation of teeth

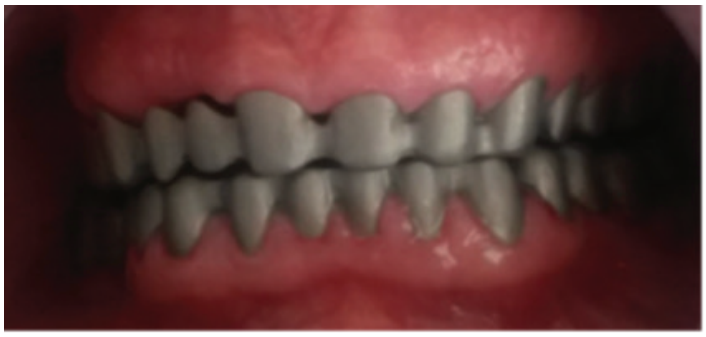

Figure 10. Metal substructure

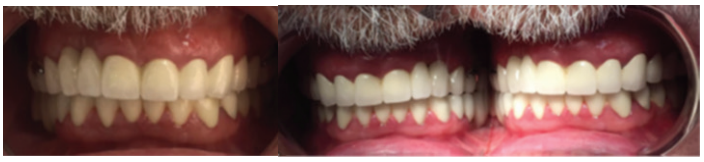

Figure 11. Intraoral view of final restoration

Case 3

A 62-year-old male patient applied to the prosthodontic clinics with complaints of poor aesthetics of anterior teeth. The patient had an apparent worn upper anterior teeth with missing teeth (16,26,36,47) (Figure 12). The plaque accumulation has been examined. The patient did not have any dysfunction in the TMJ evaluation. For the rehabilitation of worn anterior teeth and rehabilitation of posterior missing teeth, upper full mouth restoration (11,12,13,14,15,16,21,22,23,24,25,26,27) and fixed partial bridge restorations for lower missing teeth were planned (45-46-47, 35,36,37). The patient was informed about the potential restorative treatment option and all the advantages, disadvantages and possible risks of treatment have been explained.

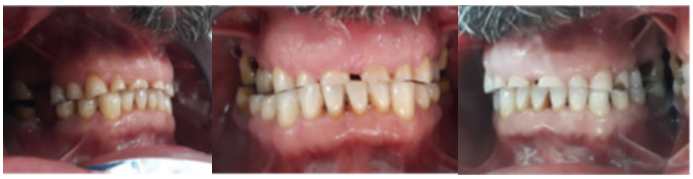

Figure 12. Intraoral view before treatment

To provide enough space for the dental restoration material in the anterior upper teeth, we need to increase the OVD. A mock up waxing was performed (Figure 13). The impression of upper and lower dentition was taken with hydrochloride impression material and facebow registration (UTS Face-bow, Ivoclar Vivadent, Austria) was performed. The casts were mounted on an articulator (Stratos 300, Ivoclar-Vivadent, Austria). The mock-up waxing was tried on the patient and it was decided that the OVD should be increased by 4 mm in the anterior teeth. Following the aesthetic approval by the patient, to evaluate the neuromuscular adaptation to the planned OVD increase, an occlusal splint was prepared (Figure 14). This was used by him for 4 weeks and finally, no muscle tenderness and temporomandibular discomfort were noted. After the functional adaptation to the new OVD, upper and lower teeth were prepared to receive full metal ceramic crowns. The second impressions were obtained and provisional auto-polymerized acrylic resin restorations were prepared and placed. Then, definitive metal (Kera N, Germany) supported ceramic restorations (Ceramco 3, Dentsply, Dreieich, Germany) were fabricated and adjusted in canine guided occlusion (Figure 15). After the glazing procedure, the restorations were cemented (Figure 16). Written informed consent was obtained from the patient for the publication of his data.

Figure 13. Diagnostic wax up

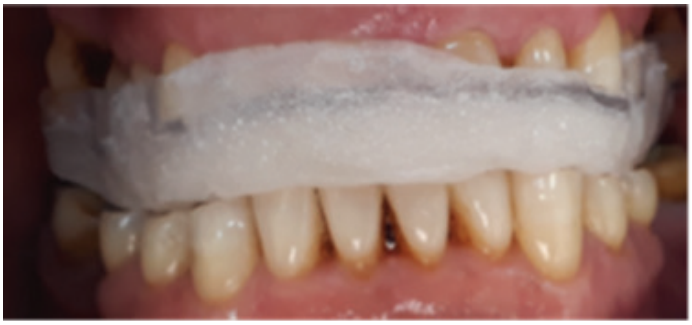

Figure 14. Maxillary occlusal splint

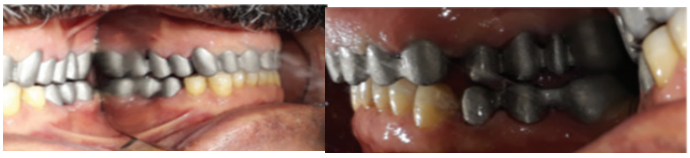

Figure 15. Metal substructure

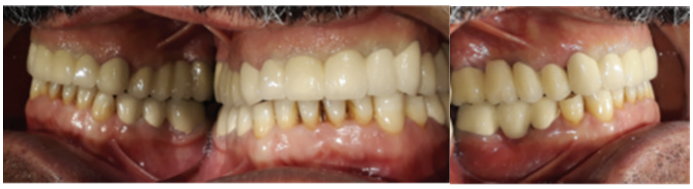

Figure 16. Intraoral view of final restoration

Discussion

The OVD is based on a balance between the hard and soft tissues where any disruption in these components will affect the balance of the forces and result in a change in the form of bony remodeling and/or soft tissue adaptation [5]. As a result of this situation, in the present three case reports patients with the loss of OVD and teeth suffer from the insufficient masticatory efficiency

EMG activity of masticatory muscles is the indicator of masticatory efficiency and is related to the vertical dimension of subjects. In the present study, in the evaluation of the EMG activity of the patients before the restoration of occlusion and OVD, all patients had a normal range of EMG activity in resting, for both masticatory muscle groups (Table 1). However, the functional indices showed impaired balance in the MM and TA activity in three cases (Table 2).

Table 1. Resting EMG activity (mV) of cases before and after treatment.

	Before treatment				After treatment			
	TAR	TAL	MMR	MML	TAR	TAL	MMR	MML
Case 1	1.04	1.32	1.25	0.79	2.76	2.78	1.66	1.22
Case 2	2.05	1.39	1.84	2.74	1.8	2	2.8	2.5
Case 3	1.3	1	1.8	17.6	0.87	0.96	1.28	1.43

Abbreviations: TAR: Right temporalis anterior, TAL: Left temporalis anterior, MMR: Right masseter muscle, MML: Left masseter muscle

Table 2. Activity and asymmetry index values of cases before and after treatment.

	Before treatment				After treatment			
	Activity index		Asymmetry index		Activity index		Asymmetry index	
	TAR-MMR	TAL-MML	TAR-TAL	MMR-MML	TAR-MMR	TAL-MML	TAR-TAL	MMR-MML
Case 1	27	47	66	20	84	96	95	76
Case 2	71	68	79	77	61	78	87	90
Case 3	91	94	49	47	98	70	64	46

Abbreviations: TAR: Right temporalis anterior, TAL: Left temporalis anterior, MMR: Right masseter muscle, MML: Left masseter muscle

The muscle activity pattern of case 1 showed that she has increased EMG activity of MMR. As a result of this predominant MMR activity, there was an increased asymmetry indices of MML and MMR and activity indices in MMR -TAR. After the restoration of occlusion and OVD, all the muscle activity comes to near value of each other which has indicated an increased activity and asymmetry indices values.

In case 2, before treatment, the patient had a relatively increased MML and TAL activity which could be related to the presence and full contact of left side teeth, while there was dis-occlusion on the right side. After the treatment, activity indices didn't show important changes, however, asymmetry indices came to a higher level. It was shown that the re-establishment of occlusion on the left side led to an increase in left side muscles activities.

In case 3, the patient had bruxism and had increased activity in both the MM and TA in clenching. With the restorative treatment of the patient, EMG activities of both muscles decreased, however in the evaluation of asymmetry indices there is still a predominance of EMG activity of MM and TA on the left-side, in the evaluation of activity indices increased activity of MM on the left side was seen.

For all 3 patients before and after the treatment, resting EMG activities were in normal ranges, however when evaluating clenching EMG activity of both muscles there was a decrease after the treatment. Also in functional indices, it was seen that there was an equalization of the balance in the asymmetry and activity indices after the dental restoration.

Manns et al stated that with the increasing of the postural position of the mandibula, the EMG activity of muscles shows a decrease [21]. It has been stated that in the early period the increase of OVD increases the EMG activity of masticatory muscles however after 2 to 3 months, EMG activities of muscles will have returned to the baseline values [22]. With

this result, in the present study one month later after dental restoration presented cases showed a decrease in clenching EMG activity of MM and TA. On the other hand, Widmer et al stated that, two different changes in jaw-closing muscle activity were observed depending on the way the increasing OVD with the freely moving jaw by interocclusal appliance or inter-maxillary fixation by fixed restoration [5]. The increased OVD with appliance appears to lead to the addition of sarcomeres to lengthen the muscle fiber and hypertrophy of the muscle fiber. On the other hand, the increase of OVD with the fixed restoration, leads to an increase in muscle length that results in the formation of new sarcomeres at the ends of the muscle fiber and atrophy of the muscle fibers [5]. In the presented cases the reduced EMG activity of both muscles after restoration could be related to increasing OVD fixed restoration that leads to muscle fiber atrophy.

In all cases, in addition to increasing occlusal vertical dimension, also, occlusion has been restored providing occlusal stability, therefore both of those factors will affect on EMG activity of the anterior temporalis and MM [23]. In many studies, the number of occlusal contacts has been related to the positive correlation of the EMG activity of masticatory muscles [24,25,26]. Among the present cases, the most tooth loss was seen in case 1 with the lack of posterior occlusal support in the mandibula and also after the treatment with the restoration of the missing teeth, the most apparent improvement in functional indices was seen in case 1. This apparent change in the EMG activity of muscles and the functional indices after treatment could be related to ensuring stable occlusal contacts with restoration of dentition. This result was in agreement with the study of Ribeiro et al that the increase in OVD did not alter the electrical activity of the masticatory muscles of asymptomatic participants due to the number of stable occlusal contacts already present [23].

In conclusion, the present clinical reports described the use of occlusal splint to restore occlusal vertical dimension and prosthetic rehabilitation of 3 patients with worn dentition. As a result of the presented 3 cases, it could be stated that functional indices are more related to the occlusal contact stability, however, the EMG activity of related muscles during clenching seems to be more related to the amount of the OVD changing.

Informed consent

Written informed consent was obtained from the patients for publication of this article.

Conflict of Interest

The authors declare no conflict of interest.

Funding

The authors received no financial support for this research.

Authors' Contribution

Elif Didem Demirdağ: Application of treatment and taking records

Ayşe Canan Adam Erden: Application of treatment and taking records

Sıla Burcu Özer Yağcı: Taking records and writing

Duygu Karakış: Desing, writing and reviewing.

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

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

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

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

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

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

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

Dergi adının kısaltması: Turk J Clin Lab

Yazışma adresi: Yazılar e-mail yoluyla sorumlu yazar tarafından, Dergipark ta yer alan Turkish Journal of Clinics and Laboratory linkine girip kayıt olduktan sonra gönderilmelidir.

Makale dili: Makale dili Türkçe ve İngilizcedir. İngilizce makaleler gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanı tarafından düzeltilebilir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu amaçla, Türk Dil Kurumu Sözlük ve Yazım Kılavuzu yazım dilinde esas alınmalıdır.

Makalenin başka bir yerde yayımlanmamıştır ibaresi: Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. 400 kelimeden az özetler kapsam dışıdır. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

Değerlendirme: Dergiye gönderilen yazılar format ve plagiarism açısından değerlendirilir. Formata uygun olmayan yazılar değerlendirilmeden sorumlu yazara geri gönderilir. Bu tarz bir zaman kaybının olmaması için yazım kuralları gözden geçirilmelidir. Basım için gönderilen tüm yazılar iki veya daha fazla yerli/yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayıma kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir. Makalenin dergiye gönderilmesi veya basıma kabul edilmesi sonrası isim sırası değiştirilemez, yazar ismi eklenip çıkartılamaz.

Basıma kabul edilmesi: Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak basım sırasına alınır. Her yazı için bir doi numarası alınır.

Yayın hakları devri: http:/www.dergipark.ulakbim.gov.tr/tjclinlab adresi üzerinden online olarak gönderilmelidir. 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.