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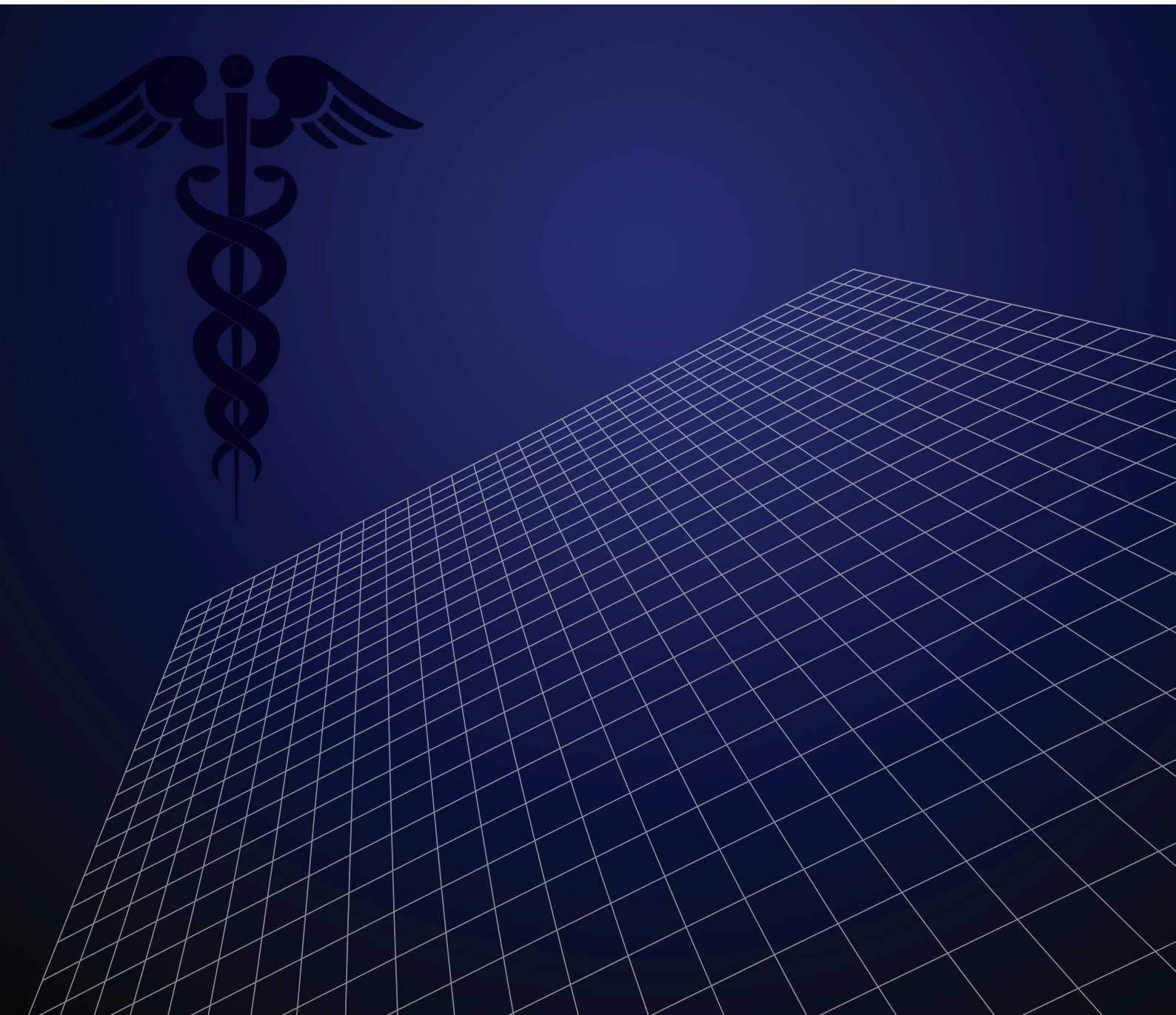

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Research Article

Edoxaban therapy in non-valvular atrial fibrillation patients: Paradoxical effect on mean platelet volüme

Non-valvüler atriyal fibrilasyon hastalarında edoksaban tedavisi: Ortalama trombosit hacmi üzerinde paradoksal etki

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ABSTRACT

Aim: New generation oral anticoagulants (NOACs), which selectively and reversibly block the activity of clotting factor Xa, are now preferred as first-line therapy for preventing ischemic stroke in the treatment of atrial fibrillation (AF). Edoxaban, one of these NOACs, has been shown to be as effective as warfarin in preventing stroke or systemic embolism, while carrying a lower risk of bleeding and cardiovascular death. Mean platelet volume (MPV), as an indicator of platelet activity, is associated with an increased risk of ischemic stroke in patients with AF. Therefore, medical therapies that reduce MPV may play an important role in preventing unwanted ischemic events. The aim of this study is to determine whether edoxaban has an effect on platelet volume and other platelet indices, in addition to its protective anticoagulant effect against ischemic stroke.

Materials and Methods: The study was designed as a retrospective cross-sectional study. Two hundred non-valvular AF patients without a history of oral anticoagulant use were included in the study. Complete blood count (CBC) and basic biochemical parameters (urea, creatinine, electrolytes, etc.) were recorded from the hospital registration system before edoxaban treatment was started, along with basic demographic data. The CBCs of the patients were reevaluated an average of 6 months (184 ± 9 days) after edoxaban treatment initiation, and platelet indices after edoxaban treatment were compared. Results were presented as mean ± standard deviation and percentage. Data were compared using Student's t-test and Wilcoxon test, and $p<0.05$ was considered statistically significant.

Results: The mean age of the patients was 74±9 years. The majority of the patients in the study were female (52.5%). A significant increase in MPV value was observed after treatment [10.0 fL (6.0-13.8) vs. 10.2 fL (7.1-14.9), p=0.023], considering the change in MPV values of the patients. This increase in MPV was not observed in the group using 30mg/day edoxaban (p=0.333), while a significant increase was observed in the group using 60mg/day (p=0.041). In addition, no gender-related change was observed in MPV. No significant changes were observed in platelet count (PLT) (p=0.863), platelet distribution width (PDW) (p=0.085), or plateletcrit (PCT) (p=0.127) values during the six-month period of edoxaban use.

Conclusion: In oral anticoagulant naïve AF patients, edoxaban treatment led to an elevation in MPV levels after 6 months, without causing significant alterations in other platelet indices. These findings highlight the need for further research to explore the clinical implications and potential unknown pleiotropic effects of elevated MPV levels in patients receiving edoxaban therapy.

Keywords: Edoxaban, mean platelet volume (MPV), atrial fibrillation, NOAC

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ÖZ

Amaç: Atriyal fibrilasyon (AF) tedavisinde iskemik inmenin önlenmesi için artık yeni nesil oral antikoagülanlar (NOAK'lar) birinci basamak tedavi olarak tercih edilmektedir. Seçici ve geri dönüşümlü olarak pıhtılaşma faktörü Xa'nın aktivitesini bloke eden yeni nesil oral antikoagülanlardan biri olan edoxabanın, felç veya sistemik embolizmi önlemede varfarin kadar etkili olduğu, kanama ve kardiyovasküler nedenlerden ölüm oranları açısından daha düşük risk taşıdığı gösterilmiştir. Ortalama trombosit hacmi (OTH), trombosit aktivitesinin bir göstergesi olarak, AF'li hastalarda artmış iskemik inme riski ile ilişkilidir. Bu nedenle OTH'yi düşüren medikal tedaviler, iskemik istenmeyen olayları önlemede önemli bir rol oynuyor olabilir. Bu çalışmanın amacı, edoksabanın iskemik inmeye karşı koruyucu antikoagülan etkisinin yanı sıra trombosit hacmi ve diğer platelet indeksleri üzerine etkisinin olup olmadığını belirlemektir.

Gereç ve Yöntemler: Çalışma retrospektif kesitsel çalışma olarak tasarlandı. Çalışmaya daha önce oral antikoagülan ilaç kullanım öyküsü olmayan 200 non-valvüler AF hastası dahil edildi. Hastane kayıt sisteminden edoksaban tedavisi başlanmadan önce çalışılan tam kan sayımı (TKS) ve temel biyokimya parametreleri (üre, kreatinin, kan elektrolitleri vb.) ile temel demografik veriler kayıt altına alındı. Hastaların ortalama 6 ay (184 ± 9 gün) sonra tekrarlanan TKS'leri incelenerek edoksaban tedavisi ve sonrası platelet indeksleri karşılaştırıldı. Bulgular ortalama ± standart sapma ve % oranıyla gösterildi. Veriler Student's t testi ve Wilcoxon testleri kullanılarak karşılaştırıldı. $p<0.05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: Hastaların ortalama yaşı 74±9 yıldı. Çalışmaya katılan hastalarımızın çoğunluğu kadınlardan oluşmaktaydı (%52,5). Hastaların OTH değerlerindeki değişimi göz önünde bulundurarak, tedavi sonrası OTH değerinde anlamlı artış gözlendi [10,0 fL (6,0-13,8) vs. 10,2 fL (7,1-14,9), p=0,023]. OTH'de görülen bu artış 30mg/gün edoksaban kullanan grupta görülmezken (p=0,333), 60mg/gün kullanan grupta anlamlı artış izlendi (p=0,041). Ek olarak, OTH'de cinsiyetle ilgili bir değişiklik gözlenmedi. Edoxaban kullanımının altı aylık sürecinde kan trombosit sayısı (PLT) (p=0,863), trombosit dağılım genişliği (PDW) (p=0,085) veya trombokrit (PCT) (p=0,127) değerlerinde anlamlı değişiklikler gözlenmedi.

Sonuç: Edoksaban tedavisi, oral antikoagülan kullanım öyküsü olmayan AF hastalarında, 6. Ayın sonunda OTH düzeylerinde artışa neden olurken diğer trombosit indekslerinde anlamlı bir değişiklik yaratmadı. Bu bulgular, edoksaban tedavisi alan hastalarda yükselmiş MPV düzeylerinin klinik sonuçları ve potansiyel bilinmeyen pleiotropik etkileri için daha fazla araştırmanın gerekliliğini vurgulamaktadır.

Anahtar Kelimeler: Edoksaban, ortalama trombosit hacmi (OTH), atriyal fibrilasyon, NOAK

Introduction

Atrial fibrillation (AF) is characterized by the most common continuous cardiac arrhythmia in the elderly (1). While the prevalence of AF is 2-4% in the adult population, it increases with a sharp slope after the age of 65 and emerges as one of the most important causes of cerebrovascular mortality and morbidity (2). Furthermore, the increase in the prevalence of comorbidities such as coronary artery disease, heart failure, diabetes and hypertension with aging leads to AF, the most common cause of cardioembolic stroke (3-5).

Anticoagulation is the most effective treatment for stroke prevention in patients with AF. Indeed, cardioembolic stroke studies have demonstrated the superiority of anti-coagulation therapy in stroke prevention in the absence of any contraindications (1). In such cases, warfarin, an anticoagulant with a long clinical history appears to be effective in the prevention of thromboembolic events in patients with non-valvular AF (6). On the other hand, the heterogeneity in the pharmacologic response of different age groups to warfarin or its interaction with some common drugs pose limitations to its clinical use.

In clinical practice, new oral anticoagulants (NOACs) are used as an alternative therapy in patients with nonvalvular AF. This group of anticoagulants is known to prevent stroke in ischemic events in a manner non-inferior or superior to warfarin, resulting in lower intracranial bleeding complications (1-4). A retrospective study of 61678 patients with non-valvular AF who had not previously used oral anticoagulants and had no previous indications for valvular atrial fibrillation showed that NOACs are as effective and safe as warfarin (7).

Platelet volume is a marker of platelet activation that is easily measured as mean platelet volume (MPV) when a complete blood count (CBC) is performed and is positively correlated

with platelet activity. Larger platelets are hemostatically more active than normal-sized platelets and increase the tendency for thrombosis (8-10). It is known that the tendency of platelets to increase in size during ischemic events causes them to be more active and produce more thromboxane A2 (11). There are studies showing that MPV is an independent risk factor in the development of ischemic stroke due to its high granule concentration and secondarily increased thrombopoietic activity (11, 12). Considering that MPV may be an important parameter in predicting the development of ischemic stroke in AF patients (11, 13), it is highly important to prevent acute thrombotic events with the use of agents that reduce platelet volume and activation. Edoxaban, an anticoagulant that work by selectively and reversibly blocking the activity of clotting factor Xa, has been shown to be as effective as warfarin in preventing stroke or systemic embolism and is associated with significantly lower rates of bleeding and death from cardiovascular causes (14, 15). All these findings suggest that the effect of edoxaban on MPV, an important parameter in predicting stroke development in patients with AF, could be clinically important. Therefore, the aim of this study was to determine whether edoxaban has an effect on platelet volume and activation in addition to its protective anticoagulant effect against ischemic stroke.

Materal and Methods

Study population

A cross-sectional study was conducted at the Cardiology Outpatient Clinic of Karabuk University Faculty of Medicine from January 2020 to October 2022. The study involved 200 patients with paroxysmal and permanent non-valvular AF who had not previously received oral anticoagulant (OAC) treatment (16). Comprehensive clinical information was collected from the electronic medical records, including demographic data such as age and sex, medication history, smoking status, and co-existing medical conditions. The diagnosis of AF was confirmed in all patients through a 12-lead surface electrocardiogram at the time of initial presentation. Patients with moderate to severe mitral stenosis, autoimmune diseases, chronic kidney disease, thyroid disorders, acute infections, malignancies, AF related to acute coronary syndrome, and a history of hemorrhagic stroke were excluded from the study. Additionally, patients who required a medication change during the follow-up period, for any reason, were also excluded. Echocardiograms were performed on all patients, and CHA2DS2-VASc scores were calculated. Patients were assigned one point for congestive heart failure (signs/symptoms of heart failure and ejection fraction <40%), hypertension (taking antihypertensive medicine or systolic and diastolic blood pressure ≥140/90 mmHg), diabetes mellitus (defined as a fasting blood glucose level ≥126 mg/dl or blood glucose level ≥200 mg/dl or using anti-diabetic drugs), history of vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65–74 years, female gender, and two points for age 75 years or older and previous stroke or transient ischemic attack (16). Complete blood count, basic biochemistry parameters (urea, creatinine, blood electrolytes, etc.), and International Normalized Ratio (INR) were obtained before initiating edoxaban treatment. Repeated CBC and INR were obtained during routine follow-up visits after a mean period of 6 months (184±9 days). Changes in platelet indices were analyzed separately in patients using 30 mg and 60 mg daily doses of edoxaban. The study was designed in accordance with the 1964 Declaration of Helsinki, the principles of Good Clinical Practice and not contradicting the ethical rules of the subject research. The study was approved by the Bioethics Committee of Karabuk University (No. 2022/1151).

Laboratory analysis

The blood samples were collected from all patients using anticoagulated tubes containing tripotassium EDTA and citrate for CBC and INR measurements, respectively. To prevent platelet swelling, CBC measurements were performed within one hour using the automatic hematology analyzer SYMEX XE-2100 (Kobe, Japan) which utilizes both optical and impedance methods. INR values were measured with the Sysmex CA500 (Sysmex Corporation, Kobe, Japan) auto analyzer. Biochemical parameters were analyzed using the ROCHE COBAS 8000 molecular analyzer (Roche Diagnostics, Mannheim, Germany).

Statistical analysis

The statistical analysis was conducted using the SPSS for Windows 25.0 package program (SPSS Inc., Chicago, IL), while categorical variables were presented as numbers and percentages, and continuous variables were reported as mean ± SD or median, minimum, and maximum. The normality of the data was evaluated using the Kolmogorov-Smirnov test. For normally distributed continuous data, Student's t-test was

used for comparison, while the Wilcoxon test was utilized for non-normally distributed continuous data. A p-value less than 0.05 was considered statistically significant.

Results

The baseline clinical data of the patients are presented in Table 1. The study population had a mean age of 74±9 years, with a predominance of females (52.5%). The findings of this investigation indicate a high prevalence of chronic medical conditions among the participants, notably diabetes mellitus (49.5%) and hypertension (88.5%). Nearly half of the patients presented with dyslipidemia (49.0%), while 48.0% had a history of smoking. Moreover, the prevalence of deep vein thrombosis or pulmonary embolism was 4.0%, and approximately 46.0% of the patients exhibited coronary artery disease (CAD). Additionally, around one-quarter of the participants (23.5%) experienced cerebrovascular events (CVEs). The mean CHA2DS2VASc score was 4.3±1.2.

Table 1. Demographic, clinical and echocardiographic characteristics of the study population.

Parameters (n=200)	Value
Age in years (mean ± SD)	74 ± 9
Gender, male; n (%)	95 (47.5)
Diabetes mellitus, n (%)	99 (49.5)
Hypertension, n (%)	177 (88.5)
Dyslipidaemia, n (%)	98 (49.0)
Smoking (>20 cigarettes/d for more than 5 years) n (%)	96 (48.0)
DVT or PE, n (%)	8 (4.0)
CAD, n (%)	92 (46.0)
CVEs, n (%)	47 (23.5)
HF, n (%)	78 (39.0)
CHA2DS2-VASc score (mean ± SD)	4.3 ± 1.2
LVEF (mean ± SD) (%)	54.3 ± 10.0
LA diameter (mean ± SD) (mm)	43.3 ± 4.1
Drug use, n (%)	
Statin	88 (44.0)
Beta blocker	158 (79.0)
CCB	97 (48.5)
ACEi or ARB	156 (78.0)
Digoxin	50 (25.0)
Furosemide and/or thiazide	117 (58.5)

Abbreviations: SD: Standard deviation, ACEi: Angiotensin-converting-enzyme inhibitors, ARB: Angiotensin Receptor Blocker, CAD: Coronary artery disease, CCB: calcium channel blocker, CHA2DS2-VASc score: risk of stroke (for non-rheumatic atrial fibrillation), CVEs: Cerebrovascular events, DVT: Deep vein thrombosis, HF: Heart failure, LA: Left Atrium, LVEF: Left ventricular ejection fraction, PE: Pulmonary embolism

An increase in MPV values was observed after the treatment with edoxaban [10.0 fL (6.0-13.8) vs. 10.2 fL (7.1-14.9), p=0.023], as shown in Table 2. No significant gender-related changes were observed in MPV values. Additionally, there were no significant changes in blood platelet count (PLT) (p=0.863), platelet distribution width (PDW) (p=0.085), or plateletcrit (PCT) (p=0.127) values during the six-month period of edoxaban use, as illustrated in Figure 1.

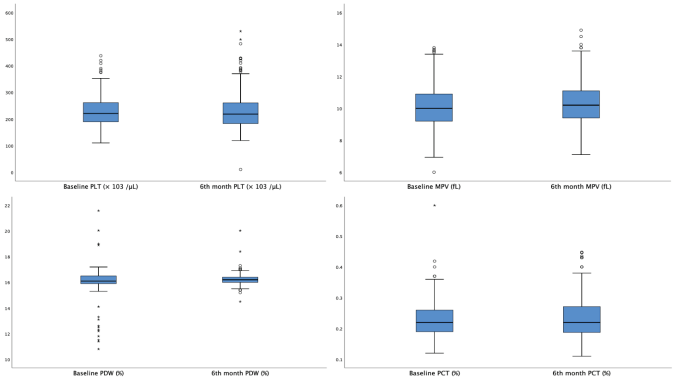

Figure 1. Platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) values before and after treatment with edoxaban.

The study findings demonstrated a significant increase in MPV values in patients, regardless of their comorbid conditions, (p<0.05, for all) (Table 3). Additionally, there was no significant change in MPV values among patients who were administered a daily dose of 30 mg edoxaban [10.4fL (± 1.4) vs. 10.6fL (± 1.5), p=0.333]. However, among those who received a daily dose of 60 mg, a significant increase in MPV was observed [10.0fL (± 1.2) vs. 10.2fL (± 1.2), p=0.041], (Table 4).

Table 2. Platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) values before and after treatment with edoxaban

Variables	Baseline Median (min-max)	6th month Median (min-max)	P
PLT (× 103 /µL)	221.0 (110.0-438.0)	218.3 (10.4-530.0)	0.863
PDW (%)	16.1 (10.9-21.5)	16.2 (14.5-20.0)	0.085
PCT (%)	0.2 (0.1-0.6)	0.2 (0.1-0.4)	0.127
MPV (fL)	10.0 (6.0-13.8)	10.2 (7.1-14.9)	0.023
INR	1.0 (0.8-1.8)	1.1 (0.8-1.9)	0.018

Abbreviations: INR: International Normalized Ratio, MPV: Mean Platelet Volume, PCT: Plateletcrit, PDW: Platelet Distribution Width, PLT: platelet count

Table 3. Comparison of MPV values at baseline and 6 months of edoxaban use in terms of comorbidities

Variable	Categories	Baseline value	6th month value	p
		Median (min-max)	**Median (min-max)**	
DM	(+)	10.1 (6.9-13.8)	10.4 (7.7-14.5)	**0.030**
	(-)	10.0 (6.0-13.6)	10.0 (7.1-14.9)	**0.049**
HT	(+)	10.4 (9.5-13.6)	10.9 (9.2-12.6)	**0.015**
	(-)	10.0 (6.0-13.8)	10.1 (7.1-14.9)	**0.020**
Dyslipidemia	(+)	10.1 (6.0-13.8)	10.3 (7.1-13.8)	**0.030**
	(-)	10.0 (7.4-13.5)	10.0 (7.4-13.5)	**0.049**
PE / DVT	(+)	10.0 (6.0-13.8)	10.2 (7.1-14.9)	**0.003**
	(-)	9.7 (8.8-11.3)	10.6 (8.6-12.2)	**0.025**
CAD	(+)	10.0 (6.0-13.7)	10.2 (7.1-14.9)	**0.001**
	(-)	10.0 (6.9-13.8)	10.1 (7.8-13.8)	**0.037**
CVEs	(+)	10.0 (6.0-13.8)	10.1 (7.7-13.8)	**0.015**
		10.0 (6.9-13.6)	10.3 (7.1-14.9)	**0.014**

Abbreviations: CAD: Coronary artery disease, CVEs: Cerebrovascular events, DM: Diabetes mellitus, DVT: Deep vein thrombosis, HT: Hypertension, PE: Pulmonary embolism

Table 4. Comparison of baseline and 6th month MPV according to daily edoxaban dose

Edoxaban Dosage (mg)	Baseline MPV(fL)	6th month MPV(fL)	p
30 mg	10.4 ± 1.4	10.6 ± 1.5	0.330
60mg	10.0 ± 1.2	10.2 ± 1.2	0.041

Abbreviations: MPV; Mean Platelet Volume

Discussion

To the best of our knowledge, our study is the first to investigate the effects of edoxaban on platelet indices. We found a significant increase in MPV at 6 months compared to baseline in OAC-naïve patients with AF. The results showed that there was no significant change in MPV values among patients who were administered a daily dose of 30 mg edoxaban. However, a significant increase in MPV was observed only among those who received a daily dose of 60 mg. This suggests that edoxaban may affect MPV values in a dose-dependent manner.

Platelets in circulation exhibit variability in size and hemostatic potential. The size of platelets, as MPV, is often considered a reflection of platelet activity (17). However, emerging research suggests that platelet size and density are determined during thrombopoiesis, where megakaryocyte ploidy influences platelet volüme (18). This suggests the existence of a complex megakaryocyte-platelet hemostatic axis that may be disrupted in the presence of certain comorbidities, such as hypertension, hyperlipidemia, and diabetes mellitus (19). While some drugs, such as antihypertensives, antidiabetics, and lipid-lowering agents, may impact MPV, no clear correlation has been established between antiplatelet agents and MPV (20). Indeed, these conditions have been known to alter the regulation of this axis. However, thrombopoiesis and megakaryopoiesis may be regulated by different humoral factors. Thus, a decrease in platelet volume may not occur in situations where active megakaryocyte ploidy induces megakaryopoiesis (19). Higher MPV values have been reported in patients with HT, DM, dyslipidemia, and CAD (18-20). In our study, most of the patients had comorbid conditions, but we observed a significant increase in MPV values following edoxaban use regardless of the presence of comorbidities. In addition, the dose-dependent effect of edoxaban on MPV values suggests that the drug has a pleiotropic effect.

Our study, in line with previous research, has revealed an intriguing phenomenon where certain medications, expected to reduce MPV, can actually lead to an increase in MPV. De Luca et al. observed a paradoxical rise in MPV during the initial five days of dual antiplatelet therapy in patients with acute coronary syndrome (20). Similarly, nicotinic acid, known for its lipid-modifying activity and additional effects in ischemic heart disease, was found to increase MPV while simultaneously decreasing platelet count (21). Another study conducted by Duzen et al. examined the effect of NOACs such as apixaban, rivaroxaban, and dabigatran on MPV in non-valvular AF patients. Remarkably, they did not find a significant decrease in MPV following the use of these medications [(9.36 ± 1.70) vs. (9.63 ± 1.68), p=0.072] (22).

There may be several contributing factors that explain the lack of any functional effect of increased platelet size. The increase in MPV could be a process driven by the increased production of larger reticulated platelets in the bone marrow (23). In fact, it has been shown that MPV correlates with both megakaryocyte ploidy and the percentage of reticulated platelets in circulation. Therefore, larger MPV may not necessarily indicate higher platelet reactivity, but rather larger platelets may be indicative of immature platelets, which may be associated with further decreased aggregation (24). Our hypothesis is that the rise in MPV levels detected after edoxaban treatment could be linked to the pleiotropic effects of the drug on bone marrow, which may have been amplified by the relatively higher dose of 60mg/day.

Platelet Distribution Width is a laboratory test parameter that serves as an indicator of platelet activation. Previous studies

have consistently shown higher levels of both MPV and PDW in diabetic patients compared to healthy individuals, with PDW being particularly elevated in those with microvascular complications (25, 26). Furthermore, elevated PDW has been identified as a significant risk factor for stroke in patients with AF (27). In our study, despite observing an increase in MPV values, we did not find a significant impact of edoxaban on PDW. This suggests that while edoxaban treatment may affect platelet volume, it does not exert a substantial influence on platelet activation as measured by PDW.

Study limitations

Our study has several limitations. Firstly, we had strict exclusion criteria, which may limit the generalizability of edoxaban's effect on MPV to populations beyond AF patients. Secondly, we did not investigate the underlying mechanisms of the observed increase in MPV, which could provide valuable information about the pleiotropic effects of edoxaban. The use of tests such as platelet aggregation could provide more precise data on the clinical significance of the MPV increase. Thirdly, our study patients were receiving treatments for other comorbidities that may affect MPV, and the results may not reflect isolated changes in MPV due to edoxaban. Lastly, we only evaluated the platelet indices at a single time point (6 months after starting edoxaban therapy) and did not assess changes in these indices over time.

Conclusion

Edoxaban treatment led to an increase in MPV levels in anticoagulant OAC naïve AF patients, particularly in those receiving a daily dose of 60 mg, without significant alterations in other platelet indices. This increase in MPV may potentially be attributed to one of the unknown pleiotropic effects of edoxaban. These findings highlight the need for further research to explore the pleiotropic effects of edoxaban and the possible clinical implications of increased MPV levels in patients receiving edoxaban therapy.

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Research Article

YouTube as an information source of Transversus abdominis plane block

Transversus abdominis plan bloğu hakkında bir bilgi kaynağı olarak YouTube

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Abstract

Aim: The YouTube video platform has recently been used by doctors as a source of information. Many studies have evaluated the quality of YouTube videos. Our aim is to review the quality of transfers andominis plane block videos available on YouTube

Material and Methods: Searched the term "Transversus abdominis plane block" on YouTube portal on 20.03.2023. The 50 most clicked videos were included in the study. By two different independent observers; Video durations; number of clicks, likes, dislikes, comments; and publication dates noted. In addition, video contents were reviewed. Video Power Index (VPI) was calculated. Videos were analyzed according to video quality, DISCERN, JAMA (Journal of the American Medical Association), global quality scale (GQS), AND modified DISCERN scores.

Results: The mean DISCERN VALUES of the videos were 59.51 ± 10.53, JAMA scores were 2.8 ± 1.08, GQS scores were 3.54 ± 1.34, and modified DISCERN scores were 3.38 ± 1.24. All videos were "good" according to DISCERN. According to the DISCERN scoring system, 19 videos were excellent, 17 were good, 12 were average, and 2 were poor.

Conclusion: The quality of the TAP block related videos on Youtube was quite adequate. The uploaded videos were considered both informative in terms of literature and videos that could be watched in practice.

Keywords: YouTube, TAP block, quality, DISCERN, JAMA, GQS

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Öz

Amaç: YouTube video platformu son zamanlarda doktorlar tarafından bilgi kaynağı olarak kullanılmaya başlandı. Birçok çalışma, YouTube videolarının kalitesini değerlendirmiştir. Amacımız, YouTube'da bulunan transfer andominis uçak bloğu videolarının kalitesini incelemektir.

Gereç ve Yöntemler: 20.03.2023 tarihinde YouTube portalında "Transversus abdominis plan bloğu" terimini arattı. En çok tıklanan 50 video çalışmaya dahil edildi. İki farklı bağımsız gözlemci tarafından; Video süreleri; tıklama, beğeni, beğenmeme, yorum sayısı; ve yayın tarihleri not edilmiştir. Ayrıca video içerikleri incelendi. Video Güç İndeksi (VPI) hesaplandı. Videolar, video kalitesi, DISCERN, JAMA (Journal of the American Medical Association), küresel kalite ölçeği (GQS), AND modifiye DISCERN puanlarına göre analiz edildi.

Bulgular: Videoların ortalama DISCERN DEĞERLERİ 59,51 ± 10,53, JAMA puanları 2,8 ± 1,08, GQS puanları 3,54 ± 1,34 ve modifiye DISCERN puanları 3,38 ± 1,24 idi. DISCERN'e göre tüm videolar "iyi" idi. DISCERN puanlama sistemine göre 19 video mükemmel, 17 iyi, 12 ortalama ve 2 video kötüydü.

Sonuç: Youtube'daki TAP bloğu ile ilgili videoların kalitesi oldukça yeterliydi. Yüklenen videolar hem literatür açısından bilgilendirici hem de uygulamalı olarak izlenebilecek videolar olarak değerlendirilmiştir.

Anahtar Kelimeler: YouTube, TAP bloğu, kalite, DISCERN, JAMA, GQS

Introduction

YouTube is an online video-sharing platform that reaches billions of users every day. Recently, the number of users and viewers has been increasing as a result of the easy accessibility of social media and the development of internet infrastructure [1]. Several studies have shown that patients and healthcare professionals use the videos uploaded to the Youtube platform as a source of knowledge [2,3].

Recently, uploading videos to the Youtube platform and generating revenue based on the number of views has become a new business model. For this reason, videos are uploaded to increase click-through and view rates rather than the authenticity of the videos [4]. This led to the idea that the quality of the videos should be questioned. Health-related videos are important in this context. According to a study, YouTube has the potential to serve as a resource for young people looking for health information. This study has determined that information published by healthcare professionals can promote learning and improve knowledge [5].

Both specialists and patients actively use social media as a source of information. Since a very large number of videos related to each topic have been shared, many studies in the field of health are investigating YouTube video quality [6-8].

The transversus abdominis plane (TAP) block, one of the abdominal site blocks, was first described by Rafi in 2001 [9]. Then, in 2007, Hebbart et al [10] stated for the first time that ultrasound-assisted TAP block can be applied more effectively and safely. It is noticeable that it has been used in many indications in the literature until today, especially with the spread of applications with the help of USG. Because it is an interventional procedure, it is normal for health workers to try to access videos related to TAP block.

Our aim in this study is to investigate the quality of TAP block-related videos objectively. It started from the idea that the TAP block application, which is frequently used today, can contribute to education by watching Youtube videos.

Material and Methods

On March 20, 2023, a search was made by typing “Transversus abdominis plane block” into the search bar of the Youtube online platform. The results were sorted by the number of views. Only videos uploaded by health professionals were evaluated. Duplicate videos, videos other than those uploaded by health professionals, videos containing ads, non-English videos, and videos shorter than 1 minute were excluded from the study. Two independent auditors reviewed the videos. As an explanatory feature, the structure of the videos, the number of views, the upload date, the number of likes, the number of dislikes, and the comments under the video were recorded.

Videos were analyzed according to DISCERN, JAMA (Journal of the American Medical Association), global quality scale (GQS), AND modified DISCERN scores.

The DISCERN scoring system consists of 16 questions and

is examined in 2 separate sections [11]. The questions are divided into two sections: the first section is about security, and the second section is about video quality [8]. Answers to the sixteenth question are provided for overall review (Table 1). According to the videos score; 16-26 points: poor quality, 27-38 points: low quality, 39-50 points: average quality, 51-62 points: good quality, higher scores are rated as excellent quality.

Table 1. DISCERN Scoring System

Section	Questions	No	Partly			Yes
Reliability	1.Explicit aims	1	2	3	4	5
	2.Aims achieved	1	2	3	4	5
	3.Relevance to patients	1	2	3	4	5
	4. Source of information	1	2	3	4	5
	5.Currency (date) of information	1	2	3	4	5
	6. Bias and balance	1	2	3	4	5
	7. Additional sources of information	1	2	3	4	5
	8. Reference to areas of uncertainty	1	2	3	4	5
Quality	9. How treatment works	1	2	3	4	5
	10. Benefits of treatment	1	2	3	4	5
	11. Risks of treatment	1	2	3	4	5
	12. No treatment options	1	2	3	4	5
	13. Quality of life	1	2	3	4	5
	14. Other treatment options	1	2	3	4	5
	15. Shared decision making	1	2	3	4	5
16. Based on the answers to all of these questions, rate the overall quality of the publication as a source of information about treatment choices		1	2	3	4	5

In addition, the video quality was evaluated with a QRS Score. A 5-point scoring system was used for the overall quality of the videos (Table 2).

Table 2. Global Quality Scale Criteria

Score	Global Score Description
1	Poor quality, poor flow of the site, most information missing, not at all useful for patients
2	Generally poor quality and poor flow, some information listed but many important topics missing, of very limited use to patients
3	Moderate quality, suboptimal flow, some important information is adequately discussed but others poorly discussed, somewhat useful for patients
4	Good quality and generally good flow, most of the relevant information is listed, but some topics not covered, useful for patients
5	Excellent quality and excellent flow, very useful for patients

The JAMA scoring system is an evaluation method that includes description, validity, qualification, and authorship to examine the quality of information. Each question receives 0 or 1 point, which is noted as a maximum of 4 points (Table 3).

Table 3. Journal of the American Medical Association scoring system

Authorship	Authors and contributors, their affiliations, and relevant credentials should be provided
Attribution	References and sources for all content should be listed clearly, and all relevant copyright information should be noted
Disclosure	Website "ownership" should be prominently and fully disclosed, as should any sponsorship, advertising, underwriting, commercial funding arrangements or support, or potential conflicts of interest
Currency	Dates when content was posted and updated should be indicated

Singh et al [12] also used the modified DISCERN scoring system, in which they simplified the DISCERN scoring system. It examines the reliability, openness, bias, referencing, and information uncertainty in this scoring system (Table 4).

Table 4. Modified discern scoring system

1. Are the aims clear and achieved?
2. Are reliable sources of information used? (i.e., publication cited, speaker is board-certified general surgeon)
3. Is the information presented balanced and unbiased?
4. Are additional sources of information listed for patient reference?
5. Are areas of uncertainty mentioned?
*1 point for every "Yes," 0 points for "No"

The Video Power Index (VPI) was used for the popularity of the videos. The VPI score was calculated using the following: (number of likes/ dislikes + number of likes) X 100.

Since there will be a difference in the number of views depending on the uploaded year, the viewing rate of a video on Youtube has been calculated based on the total views/time since uploading for an objective assessment.

Video content was grouped into Presentation/Application videos, video length (over and under 3 minutes), release date [<5 years (new videos) and >5 years (old videos), the first 25 videos and the second 25 videos according to the number of views, the daily number of views (<10 or >10), VPI (<95 or >95). Each group and the video quality were evaluated separately.

SPSS for Mac 26.0 was used to perform statistical analysis(IBM SPSS for Mac, Version 26.0; IBM Corp). The statistical significance level was set as 0.05. Descriptive data were given as mean and standard deviation. The coefficient was calculated to evaluate the relationship between Pearson correlation and Deceleration. Due to the abnormal distribution of the parameters, the Mann-Whitney test was used to compare the Kruskal-Wallis groups. The U-test to determine the group (with Bonferroni's correction) caused this difference. The differences between the groups were compared using one-way ANOVA test.

Ethics committee approval was not required in this study. The study was carried out as the Declaration of Helsinki Principles.

Results

"Transversus abdominis plane block" was entered into the Youtube search bar. Then, the videos were sorted according to the number of views from the filtering section. 180 videos were found, of which 100 and above have been viewed. When the first 50 of these videos were examined, 2 of them were excluded from the study because they were not in English, 3 of them were irrelevant content, and 2 videos were under 1 minute.

The total number of views of the videos was 1,604,400. The least-watched video was watched 2,700 times and the most-watched video was watched 261,000 times (32,088 ± 54,954.31). The average video length was 287.16 ± 258.4. Other descriptive statistics are shown in Table 5.

Table 5. Data of YouTube™ videos

	n	Mean ± Std	Min-Max
Video length (sec)	**50**	287.16 ± 258.4	60-1366
View count	**50**	32088.88 ± 54954.31	2700-261000
View count Daily	**50**	21.48 ± 41.7	1.25-232.87
Like	**50**	177.48 ± 287.57	0-1200
Dislike	**50**	6.98 ± 12.52	0-65
Comment/year	**50**	2.82 ± 8.46	0-4700
VPI	**50**	94.29 ± 80.72	60-100
DISCERN	**50**	59.51 ± 10.53	34-76
JAMA	**50**	2.8 ± 1.08	1--4
GQS	**50**	3.54 ± 1.34	1--5
MODIFIED DISCERN	**50**	3. 38 ± 1. 24	1--5

Sec: Second; n: number of videos; Std: Standard deviation; Min: Minimum; Max: Maximum; VPI: Video Power Index; JAMA: Journal of the American Medical Association; GQS: global quality scale.

The mean DISCERN score of the videos was 59.51 ± 10.53, JAMA scores were 2.8 ± 1.08, GQS scores were 3.54 ± 1.34, and modified DISCERN scores were 3. 38 ± 1.24. According to the DISCERN scoring system, 19 videos were excellent, 17 good, 12 average, 2 poor.

The videos were examined in 2 groups presentation videos and application videos. While 23 (45.1%) videos were uploaded as presentations, the number of application videos was 27 (52.9%).

In multiple regression analysis, only the VPI value showed a positive correlation with DISCERN, JAMA, GQS, and modified DISCERN scores ($p<0.05$, R Square: 0.51). The correlation analysis between scoring systems is shown in Table 6.

Table 6. Correlation Between quality scores

	DISCERN	JAMA	GQS	Modified DISCERN
DISCERN	**1**	0.524	0.518	0.413
JAMA	**0.524**	1	0.871	0.615
GQS	**0.518**	0.871	1	0.803
Modified DISCERN	**0.413**	0.615	0.803	1

JAMA: Journal of the American Medical Association; GQS: global quality scale.

When 6 different parameters were examined in themselves, it was found that only daily viewing affected JAMA and GQS scores, video quality increased as daily viewing increased, and JAMA scores of old videos were significantly lower (Table 7).

Table 7. Relationship between six categoric variables and videos quality

	n	DISCERN (std dev)	p value	JAMA (std dev)	p value	GQS (std dev)	p value	ModifiyeDis-cern (std dev)	p value
Video source									
Presentation	23	59.26 ± 10.51	0.798	2.83 ± 1.02	0.574	3.35 ± 1.30	0.918	3.22 ± 1. 24	0.946
Application	27	59.74 ± 10.74		2.78 ± 1.15		3.37 ± 1.38		3.52 ± 1.25	
Old videos(>5 years)	25	59.52 ± 10.63	0.544	2.52 ± 1.19	0.016	3.24 ± 1.48	0.39	3.16 ± 1.28	0.837
New videos (≤5 years)	25	59.52 ± 10.65		3.08 ± 0.9		3.84 ± 1.14		3.60 ± 1.19	
View count first 25	25	61.88 ± 9.78	0.353	2.92 ± 0.95	0.69	3.52 ± 1.19	0.166	3.24 ± 1.05	0.124
View count second 25	25	57.16 ± 10.92		2.68 ± 1.21		3.56 ± 1.5		3.52 ± 1.41	
View count daily (>10)	23	61.70 ± 57.67	0.934	3.17 ± 0.77	0.01	4.04 ± 0.97	0.003	3.74 ± 0.96	0.077
View count daily (≤10)	27	57.67 ± 10.29		2.48 ± 1.22		3.11 ± 1.47		3.07 ± 1.38	
Video length(>3 minutes)	22	59.45 ± 12.08	0.305	2.77 ± 1.02	0.47	3.59 ± 1.22	0.25	3.36 ± 1.17	0.678
Video lenght(≤3 minutes)	28	59.57 ± 9.379		2.82 ± 1.02		3.50 ± 1.45		3.39 ± 1.13	
VPI (≤95)	19	53.58 ± 10.75	0.222	1.74 ± 0.8	0.131	2.11 ± 0.875	0.335	2.47 ± 1.1	0.069
VPI (>95)	31	63 ± 8.88		3.45 ± 0.62		4.42 ± 0.60		3.94 ± 0.92	

Discussion

In this study, we objectively examined the quality of the videos shared on the Youtube video platform related to the TAP block application, which is frequently used in anesthesiology and reanimation clinics. The quality of this video-sharing platform, which is often followed by doctors, is important. Many studies conducted examine the quality of the new generation video sharing platform [6,13-15]. Evaluation scoring systems such as DISCERN, JAMA, and GQS are not planned for youtube videos. However, it has been used frequently in recent studies [8].

The main goal in postoperative pain management is to keep drug doses as low as possible to reduce side effects. TAP is a relatively new regional anesthesia technique that provides analgesia to the parietal peritoneum and lower abdominal wall muscles in various abdominal surgeries and can form part of a multimodal analgesic approach [16]. The anterior abdominal wall is innervated by sensory afferent nerve branches of the lower six thoracic and upper lumbar nerves, which are the therapeutic focus of local anesthetic to provide analgesia for the abdominal surgical incision [17]. Rafi et al. [9] perhaps the most popular development after the classical application recipe is the use of ultrasound guidance to improve the accuracy of the local anesthetic in the correct plane. This method also made it possible to reduce complications and achieve more successful results [18,19].

Our study is not the first study to examine the quality of the Youtube platform. But it is the first study to examine the quality of the TAP block application in youtube videos, which should be followed visually.

Most studies have argued that the quality of videos on Youtube is poor [8,20,21]. Some studies have even concluded that videos may be more harmful than beneficial [20]. It is included in many reports that videos uploaded by health professionals or academic institutions are of higher quality than videos uploaded by individuals, and these videos may be useful for patients to watch [22]. In our study, similarly, the videos of health professionals were evaluated and quality videos were obtained. Considering that many videos are uploaded for educational purposes and not for patient information purposes, strict adherence to the appropriate guidelines will be useful in terms of improving the quality of these videos.

Since the TAP block is considered an interventional procedure, we found that the procedures performed were of high quality in showing anatomical points. However, the information before the procedure was more detailed in the videos prepared in the form of a presentation of the possible procedure sequence and post-procedure complications. The fact that high-quality videos come across as too much in this area may be due to the specificity of the topic and the clickbait excuse may not be made by extra users.

There were some limitations of our study. First of all, the videos were not watched much because the topic was very specific and aimed at health professionals. In addition, there is currently no scoring system to fully reflect the educational quality of the videos. We have included only English videos and have not included videos in other languages.

Conclusion

As a result, the quality of the TAP block videos we watched and objectively evaluated was quite good. TAP block videos on Youtube can be watched because of its contribution to practical and visual memory. But it should not be forgotten that these videos should be used as an aid, not as a source.

Conflict of Interest

all authors confirmed that there is no conflict of interest

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Research Article

Correction of posterior mitral leaflet prolapse with Fundaro annuloplasty: Can suture annuloplasty techniques be helpful for surgeon?

Posteriyor mitral liflet prolapsusunun Fundaro anüloplasti ile onarımı: Sütür anüloplasti teknikleri cerraha yardımcı olabilir mi?

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Abstract

Aim: Fundaro annuloplasty is a posterior leaflet repair technique developed for asymmetric tethering of mitral leaflets due to inferior myocardial infarction. ". In our study, we aimed to share our the operative and mid-term results of the fundaro annuloplasty technique.

Material and Methods: 30 patients who underwent Fundaro annuloplasty for type 3b mitral regurgitation were included in the study. Fundaro annuloplasty with CABG was performed in 20 patients from this patient group, the remaining 10 patients underwent combined procedures. During the flollow-ups of the patients, physical examination, electrocardiography and transthoracic echocardiography were performed.

Results: The mean follow-up period of the patients included in the study was 35.8±20.3 months (min:1 max:59). According to the TEE datas performed intraoperatively, MR was not detected in 24 (80%) patients. The mean postoperative follow-up period of the patients was 35.8±20.3 months. During the follow-up period, recurrent MR was not observed in 23 (76.7%) patients. Mortality developed in 2 (6.7%) patients in the early postoperative period. Significant improvement was observed in their functional capacities($p<0.001$). Improvements in mean left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left atrial diameter, and pulmonary artery pressure were found to be statistically significant when compared with preoperative values ($p=0.001$, $p=0.001$, $p=0.007$ and $p=0.001$, respectively).

Conclusion: Fundaro annuloplasty is an advantageous because it can be performed in shorter XCL time. Low recurrence rate after repair and positive effects on ventricular remodeling can be achieved with this technique in patient with mitral valve insufficiency due to ischemia.

Keywords: mitral valve; ischemic heart disease; fundaro annuloplasty

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Öz

Amaç: Fundaro anuloplasti, inferior miyokard enfarktüsü nedeniyle oluşan mitral yetmezlikte lifletlerin asimetrik bağlanması için geliştirilmiş bir posteriyor liflet onarım tekniğidir. Çalışmamızda fundaro anuloplasti tekniğinin operatif ve orta dönem sonuçlarımızı paylaşmayı amaçladık.

Gereç ve Yöntemler: Tip 3b mitral yetersizliği nedeniyle Fundaro anuloplasti uygulanan 30 hasta çalışmaya dahil edildi. Bu hasta grubundan 20 hastaya KABG ile birlikte Fundaro anuloplasti uygulandı, geri kalan 10 hastaya kombine işlemler uygulandı. Hastaların takiplerinde fizik muayene, elektrokardiyografi ve transtorasik ekokardiyografi yapıldı.

Bulgular: Çalışmaya alınan hastaların ortalama takip süresi 35,8±20,3 aydı (min:1 max:59). İntraoperatif yapılan TEE verilerine göre 24 (%80) hastada MY saptanmadı. Hastaların ameliyat sonrası ortalama takip süresi 35,8±20,3 aydı. İzlemde 23 (%76,7) hastada tekrarlayan MY izlenmedi. Postoperatif erken dönemde 2 (%6,7) hastada mortalite gelişti. Fonksiyonel kapasitelerinde anlamlı iyileşme gözlendi($p<0.001$). Ortalama sol ventrikül diyastol sonu çapı, sol ventrikül sistol sonu çapı, sol atriyum çapı ve pulmoner arter basıncındaki düzelmeler ameliyat öncesi değerlere göre istatistiksel olarak anlamlı bulundu (p=0,001, p=0,001, p=0,007 ve p) = 0.001, sırasıyla).

Sonuç: Fundaro anuloplasti daha kısa XCL süresinde yapılabilmesi nedeniyle avantajlıdır. İskemiye bağlı mitral kapak yetmezliği olan hastalarda bu teknik ile onarım sonrası düşük nüks oranı ve ventriküler yeniden şekillenme üzerinde olumlu etkiler elde edilebilmektedir.

Anahtar Kelimeler: mitral kapak; iskemik kalp hastalığı: fundaro anüloplasti

Introduction

Myocardial infarction due to coronary artery disease may lead to a number of mechanical complications. Mitral regurgitation is also one of them. The incidence of ischemic mitral regurgitation in patients undergoing coronary angiography after myocardial infarction (MI) varies between 10.9 and 19.4%. Ischemic mitral regurgitation (IMF) was detected in 4-5% of patients who underwent coronary artery bypass (CABG) surgery. (1-3).

This coexistence increases mortality and morbidity and the treatment of this patient group is one of the most discussed topics in today's cardiac surgery practice. Chronic IMD is a functional disorder due to postinfarct ventricular remodeling. Among the pathophysiological mechanisms, apical displacement of the posterior papillary muscle due to infarction and global ventricular dilatation are seen. As a result, tethering occurs to both leaflets.

Prosthetic ring annuloplasty is considered the gold standard technique for mitral valve repair, but it has been associated with some drawbacks. Suture annuloplasty is less expensive and may have some physiopathologic advantages Fundaro annuloplasty is a posterior leaflet repair technique developed for asymmetric tethering of mitral leaflets due to inferior myocardial infarction. The technique includes partial detachment of the posterior leaflet from the mitral annulus, annular plication, and posterior cusp plasty. It aims to eliminate the functional problem at the valvular level caused by the LV lesion. Moreover, It can restore annular geometry by bringing the anteroposterior and intercommissural distances to a near-normal ratio. On the other hand, plication to the annulus reduces the posterior annulus diameter and repositions the tension in the mitral valve a little more anteriorly. The posterior leaflet widens in the anteroposterior axis and narrows in the intercommissural axis, thus providing better coaptation of the segment adjacent to the annular plication (4).

Although there have been many studies on the results of mitral valve repair tecniques, there is no publication about the results of "Fundaro Annuloplasty". In our study, we aimed to share our the operative and mid-term results of the fundaro annuloplasty technique.

Material and Methods

30 patients who underwent Fundaro annuloplasty for type 3b mitral regurgitation at the Cardiovascular Surgery Clinic of Turkey Yüksek İhtisas Training and Research Hospital between August 2007 and August 2013 were included in the study. While Fundaro annuloplasty with CABG was performed in 20 patients from this patient group due to CAD and MR, the remaining 10 patients underwent combined procedures (ascending aorta, mitral-tricuspid-aortic valve surgeries, etc.). All surgeries were performed by the same surgeical team, datas of the patients were found from the hospital archive and preoperative demographic, clinical and operative data were accessed and recorded. The patients were followed for an average of 35.8±20.3 months.

During the flollow-ups of the patients, physical examination, electrocardiography and transthoracic echocardiography were performed. Postoperative severe mitral regurgitation, reoperation and mortality at any time were considered as the Primary Endpoint. Mortality duringt the first 30-day period after surgery was defined as early mortality and later ones defined as post-operative late mortality.

Surgical Technique

After general anesthesia, transesophageal echocardiography probe was placed in the patients for routine intraoperative evaluations. The operation was performed under CPB with bicaval cannulation following median sternotomy. Cardiac arrest were achieved with antegrade and retrograde cold blood cardioplegia routinely.

Mitral valve intervention was performed via left atriotomy at the Sondergaard plan in 27 (90%) patients and transseptal approach were preferred in 3 (10%) patients. Fixation sutures were placed on both commissures to provide a good surgical exposure. Mitral valve was examined with surgical hooks. Reactive endocardial thickening zone (candle flame appearance) due to the jet of regurgitant volume into the left atrium was tried to be determined. Posterior annular dilatation was seen. The tense portion of the posterior leaflet was separated from the mitral annulus with the help of an incision. Secondary chordas were transected to ensure posterior leaflet mobility. The separated posterior annulus part was plied in the vertical plane with individual sutures. The remaining defect on the posterior leaflet was closed with a continuous suture technique. The plicated annulus was reinforced with flexible ring in 17 (56.7%) patients, rigid ring in 6 (20%) patients, and Teflon strip in 7 (23.3%) patients. After the procedures, saline test was performed to check the coaptation and then left atrium was closed with continuous prolene sutures. Warm blood cardioplegia was given and the cross-clamp was removed. Anticoagulation was neutralized with protamine sulfate at a ratio of 1:1 and cardiopulmonary bypass was terminated. TEE was performed in patients who have weaned from CPB. While MR was not detected in 24 (80%) patients, mild MR was detected in 6 (20%) patients. Following the bleeding control, 36 French drains and one pace wire were placed and the median sternotomy was closed with 4 figure of eight wires. After the closure of the skin and subcutaneous tissues, the operation was finalized and the patients were followed up in the intensive care unit.

Statistical Analysis

Statistical analysis was performed using SPSS v 20.0 (SPSS Inc., Chicago, IL, USA) package program. Continuous variables were expressed as mean±standard deviation. Categorical variables were given as frequency percentages. Statistical differences between patients in the intervention and control groups were investigated with the t-test for continuous variables and the Mann-Whitney U test. Categorical data were evaluated with the chi-square test. A P value less than 0.05 was considered statistically significant.

Results

The mean follow-up period of the patients included in the study was 35.8±20.3 months (min:1 max:59). Demographic characteristics and preoperative echocardiographic data of these patients are presented in Table 1.

Table 1. Demographic characteristics and preoperative echocardiographic data of these patients are presented

Patient count(n)	30
Follow-up time(month)	35.8±20.3 (min:1 max:59)
Age	55.5±16.0 (min:15 max:84)
Sex(male)	16(%53.3)
NYHA classification	
I	3(%10)
II	22(%73.3)
III	3(%10)
IV	2(%6.7)2
BMI(kg/m^2)	25.2±8.2
Hypertension	12(%40)
Diabetus Mellitus	5(%16.7)
Smoker	10(%33.3)
COPD	14(%46.7)
CVA	2(%6.7)
MI	4(%13.3)
Chronic Renal Insufficiency	3(%10)
Re-operation	-
ECG	
Sinus rythm	27(%90)
Atrial Fibrillation	3(%10)
AV block-Pace	0
Mitral Insufficiency	
None	0
Mild	0
Moderate	4(%13.3)
Severe	26(%86.7)
EF(%)	46.7±11.7 (min: 28 max:65)
LVEDD(cm)	5.77±0.69
LVESD(cm)	4.37±0.69
PAP(mmHg)	43±11.8
LA diameter(cm)	4.9±1

NHYA:Newyork Heart Assosiciation, BMI: Body Mass Index, COPD:Chronic Obstructive Pulmonary Disease, CVO: Cerebrovascular Accident, MI: myocardial infarction, ECG: Electrocardiogram, EF:Ejection fraction, LVEDD: Left ventricular end-diastolic diameter, LVSDD: Left ventricular end-systolic diameter, PAP:Pulmonary artery pressure, LA:Left atrial

In addition to fundaro annuloplasty, coronary bypass surgery in 20 (66.7%) patients, aortic valve surgery in 4 (13.3%) patients, ascending aortic surgery in 1 (3.3%) patient, tricuspid valve surgery in 6 (20%) patients, atrial valve surgery in 1 (3.3%) patient septal defect repair, left ventricular aneurysm repair in 3 (10%) patients were performed. The mean cross-clamp duration was 106.7±28.7 minutes, and the cardiopulmonary bypass duration was 142.1±28.6 minutes. The mean ring size of used in the patients after Fundaro annuloplasty was 29.09±1.9. Operative datas are presented in table 2.

Table 2. Operative datas

Combined Intervention	Coronary artery bypass	20(%66.7)
	Aortic valve surgery	4(%13.3)
	Ascending aorta surgery	6(%20)
	Tricuspid valve surgery	11(%36.7)
	Atrial septal defect surgery	3(%10)
	Left atrial plication	3(%10)
Left Atrial Approach	Sondergaard Plane	27(%90)
	TSA	3(%10)
Cross-Clamp Time(min)		106.7±28.7
Cardiopulmonary Bypass Time(min)		142±28.6
Annuloplasty Type		
Flexible Ring		17(%56.7)
Rigid Ring		6(%20)
Teflon stripe		7(%23.3)
No Annuloplasty		0
Median Ring Size		29.09±1.9 (26-33)

TSA:Transseptal Approach

According to the TEE datas performed intraoperatively, MR was not detected in 24 (80%) patients, while mild MR was observed in 6 (20%) patients. Moreover, there was no need for intraoperative MVR since no patients were found to have moderate or severe MR. There was no intraoperative mortality.

In the postoperative period, 10 (33.3%) patients needed inotrope support and 1 (3.3%) needed intra-aortic balloon pump during intensive care follow-up. The patients were intubated for an average of 17.4±9.7 hours, the follow-up duration in the intensive care unit was 3.0±2.1 days, and the hospital stay was 10.2±4.3 days. The average drainage of the patients was 740±479.8 ml, and 1 (3.3%) patient underwent reoperation due to bleeding. While no neurological complication was observed in any patient in the postoperative period, ARF requiring dialysis was developed in 1 (3.3%) patient, pneumonia was seen in 1 (3.3%) patient, and GIS complication was occured in 1 (3.3%) patient.

The mean postoperative follow-up period of the patients was 35.8±20.3 months (min:1 max:59). During the follow-up period, recurrent MR was not observed in 23 (76.7%) patients, while mild MR was observed in 1 (3.3%) patient. Re-repair was performed in 1 (3.3%) patient due to severe MR and MVR was performed in 1 (3.3%) patient. Mortality developed in 2 (6.7%) patients in the early postoperative period. While the first mortality was due to respiratory failure after aspiration on the 4th postoperative day, Sepsis secondary to mediastinitis on the 25th postoperative day is the cause of mortality of the other patient. Late mortality was observed in 2 (6.7%) patients during the postoperative follow-ups. The first of the late mortality was sudden cardiac death at 12 months and the second was due to heart failure at 48 months. Endocarditis, thromboembolism and hemolysis were not observed in any of the patients during the follow-up period.

When the preoperative and postoperative variables of the patients were compared, a statistically significant improvement was observed in their functional capacities according to the NYHA classification ($p<0.001$). In addition, the mitral regurgitation degree of the patients decreased from 3.1±0.5 to 1.07±0.8, which was also statistically significant ($p<0.001$). According to the postoperative ECHO datas, the mean ejection fraction increased to 48.5±11.3. However, this change was not statistically significant ($p=0.46$). On the other hand, improvements in mean left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left atrial diameter, and pulmonary artery pressure were found to be statistically significant when compared with preoperative values ($p=0.001$, $p=0.001$, $p=0.007$ and $p=0.001$, respectively).

Discussion

Although the results of mitral valve repair are good in all etiologies of mitral regurgitation, surgical mortality in ischemic MR is higher. In addition, the long-term outcomes are less satisfactory and the recurrence rate of MR is higher after valve repair (5). In previous studies, preoperatively increased PLA (posterior leaflet angle) and ALA (anterior leaflet angle) values were found to be important in mid-term recurrence of MR in patients, and it was reported that mitral anterior tethering and posterior tethering determined by these values are independent predictors of recurrent MR(6).

Tethering is often seen in the posterior leaflet. While this causes an asymmetric and restricted leaflet movement in systole, a corresponding pseudoprolabsus is seen in the anterior leaflet. Although it varies, the posterior papillary muscle is often non-atrophied and displaced towards the apex due to segmental wall motion disorder or dyskinesia/akinesia (7-8). The reason why the repair results in type 3b mitral regurgitation are not satisfactory is due to this complex pathology and often co-existing serious diseases in these patients. However, it should not be forgotten that the experience and ability of the surgeon is an important determinant in the results of the operation.

Performing surgical techniques to restore the LV geometry, which will be done carefully and effectively to eliminate the functional IMR is important for the success of the repair. For his reason, it is necessary to narrow and fix the mitral annulus in the anteroposterior axis with annular ring. In addition, there is evidence that patients will benefit more from valve repair performed with CABG in the presence of significant myocardial viability in ischemic mitral regurgitation due to CAD. Many studies have also shown that severe ischemic MR in this disease group usually does not improve with revascularization alone (9-11).

While rigid rings are recommended for annuloplasty in ischemic MR patients, in this study group; Flexible, rigid rings or teflon felt strip are used according to the availability. It is known that flexible rings become rigid after a certain time (12).

In their study involving 482 patients Gillinov and his colleagues reported that in patients with ischemic mitral regurgitation mitral repair is more beneficial compared to MVR. At the end of the 5th year, the success rate of the repair group was 91% (13) in same study. Kang et al. İnvestigated the question of "revascularization alone or revascularization with repair in ischemic MR?" in a study. Repair and CABG were performed in 50 patients, and CABG was performed alone in 57 patients. According to their results , CABG with repair is a good option, but it was emphasized that only CABG is a better option in patients with moderate MR, especially if there are additional risk factors (advanced age, AF). They stated that it should be preferred due to positive effects in terms of LV remodeling (14).

Conclusion

In mitral valve insufficiency due to ischemia it is important to evaluate structural changes in the mitral valvular apparatus preoperatively and intraoperatively. The choice of techniques to eliminate the existing pathology in the repair is crucial. One of these techniques is the Fundaro annuloplasty technique, which has the feature of a repair technique for primary pathology, just like in IMI. In addition, this method is advantageous because it can be performed in shorter XCL time. Low recurrence rate after repair and positive effects on ventricular remodeling can be achieved with this technique.

Declaration of conflict of interest

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Research Article

Factors affecting adequate myocardial perfusion in patients with acute st-elevation myocardial infarction with successful epicardial flow

Başarılı epikardal akım sağlanan akut st elevasyonlu miyokardiyal enfarktüslü hastalarda yeterli miyokardiyal perfüzyonu etkileyen faktörler

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Abstract

Aim: The aim of this study was to evaluate and compare multifarious parameters between complete and incomplete ST-segment resolution (STR) patients groups and to identify associates of STR in patients with acute ST-segment elevation myocardial infarction (STEMI) after successful primary percutaneous coronary intervention (pPCI).

Material and Methods: 888 consecutive patients were divided into two groups according to the STR <70% and ≥70% 60-90 min after pPCI. The cardiovascular risk factors and various angiographic parameters were assessed and compared between the groups.

Results: There were 346 patients with incomplete STR and 542 patients with complete STR. In multivariable regression analysis, culprit lesion (Left Anterior Descending artery) (Odd's Ratio (OR)=1.768; p=0.048), door-to-wire crossing time (OR=0.993; p=0.033), total procedure time (OR=0.994; p=<0.001) and glycoprotein 2b/3a inhibitor use (OR=2.135; p=0.013) were found to be independent risk factors for complete STR. The Area Under Curve of door-to-wiring and total procedure time for STR prediction was 0.668, 0.831, the cut-off value was 58, 52 min, and the sensitivity and specificity were 63.9%, 70.8%, and 63.1%, 76.8%.

Conclusion: Even if the successful flow is achieved at the end of pPCI, keeping the procedure time as short as possible and using glycoprotein 2b/3a are the factors that can increase perfusion at the myocyte level.

Keywords: ST-elevation myocardial infarction, TIMI-3 flow, ST elevation resolution, electrocardiography

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Öz

Amaç: Bu çalışmanın amacı, başarılı primer perkütan koroner girişimden (pPKG) sonra akut ST segment yükselmeli miyokard enfarktüslü (STEMI) hastalarda tam ve yetersiz ST segment rezolüsyonlu (STR) hasta grupları arasında çok yönlü parametreleri değerlendirmek ve karşılaştırmak ve STR ile ilişkili ilişkileri belirlemektir.

Gereç ve Yöntemler: 888 hasta çalışmaya dahil edildi, hastalar pPKG'den 60-90. Dakikada çekilen elektrokardiyografide STR <%70 ve ≥%70 olmak üzere iki gruba ayrıldı. Kardiyovasküler risk faktörleri ve çeşitli anjiyografik parametreler değerlendirildi ve gruplar arasında karşılaştırıldı.

Bulgular: Yetersiz STR'li 346 hasta ve tam STR'li 542 hasta vardı. Çok değişkenli regresyon analizinde sorumlu lezyonun LAD olması (OR=1.768; p=0,048), kapı-tel geçiş süresi (OR=0.993; p=0,033), toplam işlem süresi (OR=0.994; p=<0,001) ve glikoprotein 2b/3a inhibitörü kullanımı (OR=2,135; p=0,013) tam STR için bağımsız risk faktörleri olarak bulundu. Kapı-tel ve toplam işlem süresinin eğri altında kalan alanı 0.668, 0.831, cut-off değeri 58, 52 dakika ve duyarlılık ve özgüllük %63,9, %70,8 ve %63,1, %76,8 olarak belirlendi.

Sonuç: pPKG sonunda başarılı akım sağlansa bile işlem süresinin mümkün olduğunca kısa tutulması ve glikoprotein 2b/3a kullanılması miyosit düzeyinde perfüzyonu artırabilen faktörler olarak bulundu.

Anahtar Kelimeler: ST elevasyonlu miyokard enfarktüsü, TIMI-3 akım, ST elevasyon rezolüsyonu, elektrokardiyografi

Introduction

Over the past years, great endeavors have been made to improve the outcome of patients with acute ST-elevation myocardial infarction (STEMI). In STEMI, primary percutaneous coronary intervention (pPCI) is the cornerstone of therapy that reduces hospital mortality and long-term mortality.1 Rapid recanalization of infarct-related artery (IRA) with pPCI is associated with better cardiac performance and lower mortality.2 The success of pPCI can be established electrocardiographically (ECG) by measuring ST-segment resolution (STR) after the procedure and angiographically by evaluating Thrombolysis in Myocardial Infarction (TIMI) flow.3 Although revascularization therapy provides complete epicardial blood flow recovery in most STEMI patients sometimes its beneficial effects are not sufficient. Because epicardial blood flow does not necessarily mean adequate perfusion at the myocyte level, STR is considered a surrogate for reperfusion of cardiac myocytes4 because it reflects the physiology of the cardiac cells.5 Complete STR is defined by a drop ≥70% of the ST-segment elevation recorded after PCI.6

In studies on STR, some patients in the incomplete STR group consisted of patients with post-PCI TIMI flow 0-2. The prognosis is affected due to this situation and worse in this group, as expected, due to more procedural complications and comorbidities.5,7-9 There was a need for re-evaluation on this subject due to reasons such as expanded medical treatment options, shortening of the time to reach pPCI, new procedural techniques, and the quality of the materials used. Additionally, considering that these studies were performed in the first-generation drug-eluting stent (DES) and bare-metal stent (BMS) era, STR predictors in patients with the successful epicardial flow at the end of the procedure arouse curiosity. Our study aimed to evaluate and compare clinical parameters between complete STR and incomplete STR patients' groups in post-PCI normal epicardial flow and to identify clinical associates and their impact on STR.

Material and Methods

Study population

A total of 888 consecutive patients with acute STEMI who underwent PPCI from December 1, 2017, to August 31, 2020, were enrolled in the study in a high-volume tertial-level hospital. The necessary patient information was collected from files from the hospital archive. The inclusion criteria have collaborated diagnosis of STEMI 10 (typical chest pain lasting for more than 20 min and ST-segment elevation of ≥2 mm in men or ≥1.5 mm in women in V2-V3 leads and ≥1 mm in at least other two contiguous leads); symptoms of less than 12 h duration and persistent ST-segment elevation; eligibility for pPCI. The exclusion criteria were thrombolytic therapy; symptom onset more than 12 h; absence or doubtable culprit lesion; culprit lesion not crossable with guidewire; history of coronary artery disease; history of previous MI; paced rhythm; left bundle branch block and post-PCI TIMI flow <3.

Dual antiplatelet therapy (300 mg acetylsalicylic acid (ASA)+ 600 mg clopidogrel/180 mg ticagrelor) was given to all the patients, and they were anticoagulated with heparin infusion following the indication.

This study aimed to compare demographic and procedure-related characteristics of patients with and without complete ST-segment resolution after performing pPCI and to identify the variables associated with incomplet ST resolution. Cardiovascular disease risk factors (age, arterial hypertension, diabetes mellitus, dyslipidemia, smoking), sex, and door-to-wiring time were assessed and compared between complete and incomplete STR groups.

Electrocardiographic evaluation

The electrocardiographic analysis followed the prevalent normative guidelines, considering complete an ST-segment resolution ≥ 70%. 11 Technically adequate 12-lead ECGs before and 60-90 min after pPCI was finished were registered using a speed of 25 mm/s and amplitude of 10 mm/mV. ST-segment resolution in ECG was assessed based on ST-segment regression percentage on 60-90th minute ECG, and 70% and above ST resolution was concluded as successful reperfusion. The elevation of the ST segment was measured at the J point in mm. The arithmetic mean of ST-segment elevation was calculated for anterior STEMI from V1-V6 leads and inferior STEMI from II, III, and aVF leads.

Angiographic evaluation

Coronary angiography was routinely performed through the femoral and radial approach using Judkins catheters (Philips DCI-SX Integris Monoplane system). pPCI was applied to the culprit's vessel in all patients. Patients who underwent pPCI were treated with direct stenting if possible; otherwise, stent implantation was done after balloon angioplasty. Angiograms were recorded at 15 frames/s. The calculated value was doubled to reach the standardized 30 frames/second. The TIMI flow grade was assessed previously at the TIMI Angiographic Core Laboratory.12 Frame counts were determined by the method described previously by Gibson et al13 Left anterior descending artery (LAD) measurements were divided by 1.7 and used as corrected TIMI frame count (TFC). TFC of those with an before the procedure TFG >0 was calculated. The GpIIb-IIIa inhibitor [tirofiban (Aggrastat) 12.5 mg/50 mL; DSM Pharmaceuticals, Greenville, North Carolina] was applied as recommended by ad-hoc guidelines according to the operator's decision based on the coronary angiography result. The total processing time was obtained by calculating the time between the first cine recording and the last recording, which is the time after the removal of the guidewire and no no-reflow detected after that. Door-wiring time was calculated as the time between the patient's admission to the emergency department and the time the wire passed through the lesion angiographically. The American College of Cardiology (ACC) and the American Heart Association (AHA) classification was used to evaluate the morphology of coronary stenotic lesions.14

The study was conducted in accordance with the protocol, the Declaration of Helsinki revised in 2013, and applicable local requirements. İnformed consent was not obnained from the patients because of retrospective nature.

Statistical analysis

Statistical analyses were performed using SPSS software for Windows 20 (IBM SPSS Inc., Chicago, IL). The distributional properties of the variables were assessed using the Shapiro–Wilk test. Student t-test was used to analyze the normally distributed variables expressed as mean ± standard deviation. Mann–Whitney U test was used for non-normally distributed variables expressed as median (interquartile range). The parameters that may be clinically related to STR were first evaluated by univariable regression analysis. Then, a multivariable regression analysis including the variables with a p-value ≤0.05 at univariate analysis was performed. A receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was calculated to assess diagnostic value. ROC curve plots the true-positive rate (sensitivity) against the false-positive rate (1- specificity) for all possible cut-off values (Youden's index). AUC and %CI for variables in the ROC analysis are indicated as 1- for easier understanding. P values 2-sided <0.05 were considered statistically significant.

Results

Eight hundred eighty-eight patients were divided into two groups according to STR ≥70% (542, 61.0%) or STR <70% (346, 39.0%). The mean age (57.1 ±12.2 vs. 60.1 ± 12.9; p =0.037), heart rate (77.5 ±16.3vs. 76.6 ± 15.8; p=0.611), loading dose of ticagrelor (66.8% vs. 67.6%; p=0.795) and Diabetes mellitus (DM) (28.0% vs. 26.6%; p = 0.757) were higher in patients STR ≥70% compared to <70%. Body-mass index (BMI), (27.3 ± 4.1 vs. 28.1 ± 4.5; p=0.02), rates of HT (232 (42.8%) vs. 178 (51.4%); p=0.067) and interventricle septum (IVS), mm (1.07 ± 0.14 vs. 1.23 ± 0.20; p= <0.001) was higher in STR <70% group. Table 1 summarizes the patients' baseline characteristics.

Table 1. Baseline characteristics of the patients.				
	All patients n = 888	STR > 70% n = 542	STR < 70% n = 346	P value
Age, mean ± SD	58.1 ± 12.5	57.1 ±12.2	60.1 ± 12.9	0.037
Gender (Male), n(%)	666 (75.0%)	400 (73.8%)	266 (76.9%)	0.465
Smoking, n (%)	514 (57.9%)	326 (60.1%)	188 (54.3%)	0.191
BMI (kg/m^2), mean ± SD	27.2 ±4.4	27.3 ± 4.1	28.1 ± 4.5	0.020
Loading P2Y12 therapy (Ticagrelor)	596 (67.1%)	362 (66.8%)	234 (67.6%)	0.795
Previous ASA exposure, n(%)	73 (8.2%)	49 (9.0%)	24 (6.9%)	0.057
WBC (109/L) , mean ± SD	7.96±2.13	8.18±2.91	7.73±1.27	0.142
Neutrophil (K/ul), median (IQR)	5.2 (3.6-7.5)	5.3 (3.7-7.3)	5.1 (3.6-7.5)	0.097
Hemoglobin (g/dL), mean ± SD	14.9 (13.4-16.1)	14.6 ± 2.0	14.6 ± 1.8	0.958
Platelet (K/ul), median (IQR)	253 (210-298)	257 (214-300)	251 (208-291)	0.466
Creatinine (mg/dL), median (IQR)	1.02 (0.91-1.18)	1.03 (0.92-1.18)	1.01 (0.90-1.19)	0.282
Sodium (mmol/L), median (IQR)	137 (136-138)	137 (135-138)	137 (135-139)	0.398
Potassium (mmol/L), median (IQR)	4.02 (3.75-4.31)	4.04 (3.80-4.29)	4.01 (3.75-4.34)	0.474
Troponin (ng/mL), median (IQR)	25.2 (6.8-75.2)	23.2 (6.5-66.3)	28.7 (7.1-93.8)	0.204
LDL (mg/dL), mean ± SD	131 ± 34.7	131.4 ± 34.9	131.7 ±33.1	0.781
HbA1c, mean ± SD	6.8 ± 1.9	6.7 ± 1.7	6.9 ± 2.1	0.147
TSH (mIU/L), mean ± SD	1.70 ±2.55	1.80 ± 3.14	1.56 ± 1.23	0.456
Glucose (mg/dL), median (IQR)	126 (103-165)	125 (103-160)	131 (101-176)	0.281
ALT (U/L), median (IQR)	40 (23-78)	43 (24-82)	37 (23-76)	0.956
Heart rate (bpm), mean ± SD	77.4 ± 16.4	77.5 ±16.3	76.6 ± 15.8	0.611
Diabetes Mellitus, n(%)	244 (27.5%)	152 (28%)	92 (26.6%)	0.757
Hypertension, n(%)	410 (46.2%)	232 (42.8%)	178 (51.4%)	0.067
COPD, n(%)	106 (11.9%)	56 (11.4%)	50 (14.4%)	0.585
LVEF (%), mean ± SD	45.4 ± 9.0	46.1 ± 8.1	44.4 ± 8.9	0.047
IVS (cm), mean ± SD	1.15 ± 0.19	1.07 ± 0.14	1.23 ± 0.20	<0.001
SBP (mmHg), median (IQR)	130 (112-149)	130 (111-147)	130 (114-150)	0.326
DBP (mmHg), median (IQR)	80 (70-90)	79.5 (71-89)	80 (70-90)	0.542
The data without normal distribution is presented as median (interquartile range-IQR). COPD: Chronic obstructive pulmonary disease ALT: Alanine Transaminase IVS: Interventricular-septum ASA: Acetylsalicylic acid				

Compared with patients with STR <70%, those with complete STR were wider stent diameter (3 (2.25-4.5) vs. 3 (2.0-4.0); p = 0.022), more use of glycoprotein 2b/3a (231 (42.6%) vs. 101 (29.2%); p = <0.001), shorter duration of the door-to-wiring time (51 (20-216) vs. 66 (16-197); p= <0.001) and total procedure time (40 (18-90) vs. 56 (29-118); p = <0.001), were less likely to have an anterior myocardial infarction (206 (38.0%) vs. 172 (49.7%); p =0.005). Initial TIMI flow grade, TIMI frame count, and final TIMI frame count did not significantly differ between the two groups (0.877, 0.732, and 0.799, respectively). There were no significant differences between the two groups in regard to the number of stents, stent length, post-dilatation, thrombus aspiration, and stent type. Angiographic parameters are shown in Table 2.

In the univariate analysis, increase in age (OR=0.983; p=0.038), BMI (OR=0.942; p=0.021), culprit lesion (LAD) (OR=1.258; p<0,001), stent diameter (OR=1.323; p=0.023), IVS diameter (OR=0.522 ; p<0,001), door-to-wire crossing time (OR=0.998; p=<0.001), total process time (OR=0.996; p=<0.001), glycoprotein 2b/3a inhibitor use (OR=1.803; p=<0.001) and LVEF (OR=1.016; p=0.048) were determined as possible risk factors for STR ≥%70. In the multivariable regression model, in which possible risk factors were included culprit lesion (LAD) (OR=1.768; p=0.048), door-to-wire crossing time (OR=0.993; p=0.033), total process time (OR=0.994; p=<0.001) and glycoprotein 2b/3a inhibitor use (OR=2.135; p=0.013) levels were found to be independent risk factors for complete STR. (-2 Log-Likelihood: 302,681 Nagelkerke R2:0.55) (Table-3)

Table 2. Angiographic characteristics of patients				
	All patients n =888	STR > 70% n = 542	STR < 70% n = 346	P value
Culprit lesion location, n(%)				
Left anterior desending	378 (42.6%)	206 (38.0%)	172 (49.7%)	0.005
Left circumflex	140 (15.9%)	88 (16.2%)	52 (15.0%)	
Right coronary artery	344 (38.7%)	236 (43.5%)	108 (31.2%)	
Diagonal	20 (2.3%)	10 (1.8%)	10 (2.9%)	
Other	6 (0.7%)	2 (0.4%)	4 (1.2%)	
Characteristics of lesion				
Type A	472 (53.1%)	313 (57.7%)	159 (45.9%)	0.003
Type B	283 (31.8%)	167 (30.8%)	116 (33.5%)	
Type C	133 (14.9%)	62 (11.4%)	71 (20.5%)	
No stent, n(%)	54 (6.1%)	40 (7.4%)	14 (4.0%)	0.189
1, n(%)	636 (71.6%)	386 (71.2%)	250 (72.3%)	
2, n(%)	168 (18.9%)	98 (18.1%)	70 (20.2%)	
3+, n(%)	30 (3.4%)	18 (3.3%)	12 (3.5%)	
Stent diamater, median (min-max)	3 (2.0-4.5)	3 (2.25-4.5)	3 (2.0-4.0)	0.022
Stent length, median (min-max)	24 (8-104)	24 (8-82)	25 (12-104)	0.065
Post-dilatation, n(%)	320 (36.0%)	194 (35.8%)	126 (36.4%)	0.850
Manual thrombus aspiration, n (%)	88 (9.9%)	58 (10.7%)	30 (8.7%)	0.323
Glycoprotein IIb/IIIa inhibitor, n (%)	332 (37.4%)	231 (42.6%)	101 (29.2%)	<0.001
Initial TIMI flow grade, n(%)				
0	564 (63.5%)	342 (63.1%)	222 (64.2%)	0.877
1	78 (8.8%)	48 (8.9%)	30 (%8.7)	
2	160 (18.0%)	106 (19.6%)	54 (15.6%)	
3	86 (9.7%)	46 (8.5%)	40 (11.6%)	
Stent type				
Paclitaxel-eluting	129 (15.5%)	74 (13.8%)	55 (18.1%)	0.062
Zotaralimus-eluting	705 (84.5%)	433 (86.2%)	272 (81.9%)	
Access site, n(%)				
Radial artery, n(%)	73 (8.2%)	46 (8.4%)	27 (7.8%)	0.168
Femoral artery, n(%)	815 (91.8%)	498 (91.6%)	317 (92.2%)	
Symptom to wire crossing time (minutes), median (IQR)	125(103-165)	121(103-160)	130(104-168)	<0.001
Door-to-wire crossing time (minutes), median (min-max)	56 (16-216)	51 (20-216)	66 (16-197)	<0.001
Total processing time (minutes), median (min-max)	48 (18-118)	40 (18-90)	56 (29-118)	<0.001
Initial TIMI frame count, median (min-max)	42 (18-96)	43 (18-90)	39 (20-96)	0.732
Final TIMI frame count, median (min-max)	26 (14-79)	26 (14-79)	26 (14-49)	0.799
The data without normal distribution is presented as median (interquartile range-IQR). TIMI = Thrombolysis in Myocardial Infarction				

Table 3. Univariate and multivariate analysis for prediction of STR				
Variables	Univariate analysis		Multivariate analysis	
	OR (95 CI%)	P value	OR (95% CI)	P value
Age	0.983 (0.961-0.998)	0.038	0.984 (0.960-1.011)	0.138
Body-Mass Index	0.942 (0.902-0.997)	0.021	0.987 (0.921-1.054)	0.728
Interventricle septum diamater	0.522 (0.022-0.854)	<0.001	0.140 (0.022-1.101)	0.062
Culprit lesion (for LAD)	1.258 (1.221-1.279)	<0.001	1.768 (1.007-3.106)	0.048
Stent diamater	1.323 (1.041-1.691)	0.023	1.363 (0.814-2.260)	0.237
Door-to-wire crossing time	0.998 (0.997-0.999)	<0.001	0.993 (0.987-0.997)	0.033
Total procedure time	0.996 (0.992-0.999)	<0.001	0.994 (0.990-0.999)	<0.001
Glikoprotein 2b/3a inhibitor use	1.803 (1.352-2.406)	<0.001	2.135 (1.170-3.894)	0.013
Left Ventricle Ejection Fraction	1.016 (1.002-1.035)	0.048	1.003 (0.975-1.042)	0.635

We used ROC analysis to examine the ability of door-to-wiring and total procedure time to discriminate STR. The AUC of door-to-wiring time for STR prediction was 0.668 (95% CI = 0.632-0.704; p < 0.001), the cut-off value was 58 min, the sensitivity and specificity were 63.9%, and 63.1%. The AUC values were 0.831 (95% CI = 0.804-0.859; p < 0.001), the sensitivity and specificity were 70.8% and 76.8% for total procedure time, and the cutoff value was 52 min. (Figure-1)

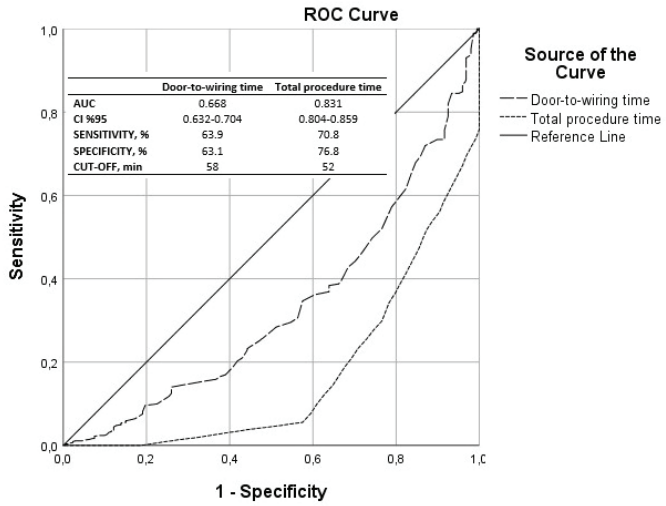

Figure 1. ROC analysis examines the door-to-wiring ability and total procedure time to discriminate STR. AUC: area under the curve, CI: confidence interval

Discussion

In this study, we tried to determine the factors affecting the ST-elevation resolution after successful revascularization. As far as we know, this is the first study on this subject. As a result of this study, we determined that short door-wiring time, short procedure time, use of glycoprotein 2b/3a in the procedure, and culprit lesion location (LAD) were predictors for STR.

The fact that the end-of-procedure flow has not been fully provided, as expected, is a more important reason than other factors because it will affect the myocardial blood supply. This study was planned because the main issue is determining the factors affecting the STR despite the successful flow. Measuring STR after pPCI is one of the most convenient methods of assessing microvascular injury. Microvascular damage can be structural due to myocardium necrosis or functional due to increased restriction of the microvascular region, edema, endothelial dysfunction, or obstruction with platelets or neutrophils. 15 Also, the PCI itself can cause microvascular obstruction with plaque debris or thrombus particles.16 The development of drugs and treatment regimens that can improve blood flow before PCI is crucial to reducing microvascular injury in STEMI patients.5 Early restorations of coronary blood flow are gained by the dissolution of clots, which can be promoted by drugs such as aspirin, other adenosine diphosphate receptor inhibitors (ADP), and heparin. Especially, new generation anti-aggregates play an active role due to more potent platelet inhibition. However, ticagrelor do not affect STR at the end of the pPCI, as in the subgroup analysis of the PLATO study.17 Probably because the onset effect of the ticagrelor is between 30 minutes and 2 hours, the procedure often ends until the effect begins. However, ticagrelor's long-term effects are likely superior to clopidogrel, especially in patients with TFG <3. Previous studies have provided evidence of the beneficial effect of GP IIb/IIIa inhibition in acute coronary syndromes.18,19 In the Platelet Receptor Inhibition for Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial, tirofiban was shown to reduce intracoronary thrombus.20 These studies demonstrate that GP IIb/IIIa inhibition is valuable in maintaining microvascular perfusion and associated with ST-segment resolution.

One of the results in the study in patients with anterior MI had lower STR compared with non. The likely mechanism is that the affected area is more extensive in patients with anterior MI. This finding is concordant with other studies.6,15

The prevalence of hypertension was a prominent finding in STR <70% of patients. Parallel to this finding, the thickness of the IVS was more remarkable. Additionally, IVS was also an independent prognostic factor for an incomplete STR. These results support the possibility that microvascular dysfunction is common in patients with hypertension and that ST-segment recovery is less measured in hypertensive patients with left ventricular hypertrophy. 5

Optical coherence tomography detected a smaller thrombus volume in the culprit lesion in patients with the acute coronary syndrome who took aspirin before their first presentation compared to those who did not use aspirin before.21 In addition to the effects of secondary prevention, antiplatelet therapy may improve coronary reperfusion and clinical outcomes.22 In our study, the rate of aspirin users before the procedure was higher in the complete STR group, but it did not reach statistical significance.

Lesion complexity is one of the most critical determinants of procedural success and survival in patients undergoing pPCI.23 In particular, the type of vessel (according to the criteria of

lesion length, calcification, tortuosity, angled segments, and major side branches to be protected) expressed as a type C lesion according to the ACC lesion classification system causes the intensive use of pre dilatation and post-dilation, the need for extra support material and the possibility of bifurcation of the procedure and prolongation of the procedure time. It is one of the most important parameters affecting adequate flow at epicardial and myocardial levels since the risk of developing no-reflow during the procedure is high in patients with vessels with this feature. In our study group, the most remarkable proportional difference between the groups was observed in patients with type C lesions.

Over the years, stent technology has come a long way. Significant advantages have been achieved with new-generation DESs. Late and very late stent micro and macro thrombosis (ST) is more common in BMS compared to first-generation DES. Also, this stent group is associated with incomplete strut reendothelialization, polymer-induced chronic inflammation, hypersensitivity reaction, stent malapposition, and accelerated neoatherosclerosis.24,25 The probability of successful myocardial blood supply at the end of the procedure increases due to more potent antiaggregant therapies, shorter transportation times to PCI centers, and increased operator experience in the new generation stents era. Stent length and multiple stent treatments may not be as related to damage to the microvascular area as before due to the factors mentioned.

Early intervention and the use of potent agents are closely associated with STR. The most critical point of the study is that the shorter duration of the PCI time provides more effective angiographic and electrocardiographic results. This data should be supplemented with symptom-balloon time. Durmaz et al. found that even if no reflow developed, a short ischemic time was significantly associated with its reversibility.26 The prolongation of the procedure may be associated with complications, complex intervention during the process, or the desire to achieve the best angiographic image. Sometimes the effort to search for the best can result in problems because of deceleration of the heparin effect due to prolonged processing time, endothelial damage and microthrombuses due to further material transport, and excessive post-dilatation. According to an interesting study on this subject, an increase in peak cardiac troponin levels was detected when balloon occlusion in the coronary arteries lasted for 30 seconds or more, and thus cardiac ischemia was detected.27. Moreover, Reidar Winter et al. showed that catheter and balloon induced ischemia using automated frame-to-frame tracking of gray-scale speckle pattern and subsequent 2D quantification of myocardial motions.28 Our findings support keeping the procedure time short in patients with acute MI unless strictly necessary. According to SINCERE database results, procedure time is one of the important parameters in terms of long-term prognosis.29

Our study has some limitations. Firstly this study was designed as a retrospective. It is a study investigating the short-term effects of the factors affecting STR and does not show long-term results. Myocardial blush grade calculation was not made. There are also possibly operator-related factors affecting STR, but they could not be categorized.

Conclusion

Even if TIMI-3 flow is achieved in patients after PCI, it is important to keep the procedure time as short as possible and increase the use of glycoprotein 2b/3a to ensure adequate perfusion at the myocardial level.

Conflict of interest

All authors declare that they do not have any conflicts of interest.

Disclosure Statement

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Araştırma Makalesi

Akut ve kronik kemik çekiç parmak hastalarının cerrahi tedavi sonuçları

Surgical treatment results of acute and chronic bone mallet finger patients

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Öz

Amaç: Biz bu çalışmada cerrahi olarak tedavi edilen kronik kemik çekiç parmak olguları ile akut kemik çekiç parmak olgularını sonuç ve komplikasyonlar açısından karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Toplam 33 kemik parça içeren 17 akut (grup 1) ve 16 kronik (grup 2) çekiç parmak hastası dahil edildi. Akut olgular grup 1, kronik olgular grup 2 olarak isimlendirildi. Yaş, cinsiyet, başvuru şekli, travma tipi gibi klinik veriler, hangi parmağın yaralandığı, başvuru zamanı, ayrılan kemik parçası miktarı, cerrahi öncesi ve sonrası ekstansiyon kaybı açısı, cerrahi tedavi yöntemi ve Crawford sınıflamasına göre derecesi hasta dosyalarından retrospektif olarak kayıt edildi.

Bulgular: Çalışmamızda sadece son başvuru tarihinde gruplar arasında anlamlı fark bulunurken, diğer tüm verilerde gruplar arasında istatistiksel olarak anlamlı bir fark bulunmadı.

Sonuç: Bu çalışma doğru tedavi seçimi ile kronik kemik çekiç vakalarında cerrahi tedavi sonuçların akut vakalar kadar iyi olabileceğini göstermektedir..

Anahtar kelimeler: Çekiç parmak, ekstansör tendon, distal falanks

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Abstract

Aim: We aimed to compare chronic bone mallet cases treated surgically with acute bone mallet cases in terms of results and complications.

Materal and Methods: In this study, 17 acute 16 chronic mallet finger patients with a total of 33 bone fragments who were operated by the same surgical team between 2011 and 2020 were included in this study. Acute cases were named as group 1, chronic cases as group 2. In acute (Group 1) and chronic cases (Group 2), all clinical data such as the age, gender of the patients, the way of admission, the types of trauma, the time of admission which finger was injured, the amount of bone fragment reserved, the pre- and post-surgical extension lag angle, the surgical treatment method, and the degree according to Crawford classification were all obtained from hospital databases obtained.

Results: In all data, there was a significant difference between the groups only in the application deadline, while no statistical difference was found between the groups in the other data.

Conclusion: The results of our study show that the results of chronic bone mallet cases can be as good as acute cases, together with the right treatment choice

Keywords: mallet finger, extensor tendon, distal phalanx

Giriş

Çekiç parmak (mallet finger) terminal ekstansör tendonun yapışma yerinden ayrılması olarak tanımlanmaktadır. Bu durum bazen sadece yumuşak doku ile sınırlı iken bazen de kemik dokuyu da içerebilmektedir. Kemik doku içeren çekiç parmaklarda (kemik mallet) ayrılan kemik doku eklem yüzeyi üçte birinden fazla ise cerrahi tedavi önerilmektedir (1-3). Bu hastaların cerrahi tedavisinde ayrılan parçanın yerine tespiti temel hedeftir. Bunun için vidalar, Kirschner telleri (K-telleri), gergi çekme telleri ve kanca plakları kullanılabilir (3-6). Bu hastalar da tedavi sonucunu etkileyen önemli faktörlerden biri de operasyon zamanlamasıdır. Kemik malletlerin kronik olarak kabul edilmesi için yaralanmadan sonra en az 4 hafta geçmesi gerekmektedir (7). Çünkü tedavi gecikmesi sonucunda ekstansiyon kısıtlılığı, (DIP) eklem dejenerasyon veya kuğu boynu deformitesi gibi durumlar ile karşılaşılmaktadır (8). Kronik olgularda kırık segmentler arası oluşan skar ve kallus dokusu anatomik redüksiyonu engeller bu da başarı şansını azaltır (9). Bu nedenle akut kemik malletlerde tedavi planlaması kolay olabilirken kronik vakalarda bu durum zorlaşabilmektedir. Literatürde akut kemik mallet olgularının sonuçlarını sunan birçok çalışma bulunmaktadır. Biz bu çalışmada kronik kemik çekiç parmak olgularında doğru cerrahi yöntem ile akut olgular gibi benzer fonksiyonel sonuçlar olabileceğini varsaydık ve cerrahi tedavi yapılan kronik kemik mallet olguları ile akut kemik mallet olgularının sonuçlarını ve komplikasyonlarını karşılaştırılmayı amaçladık.

Gereç ve Yöntemler

Bu çalışma Selçuk Üniversitesi Yerel Etik Kurulundan (2022/420) gerekli izin alındıktan sonra Helsinki Deklarasyonu ilkelerine uygun retrospektif olarak yapılmıştır. Aynı cerrahi ekip tarafından 2011 ve 2016 tarihleri arasında ameliyat edilen 17 akut (grup 1) ve 16 (grup 2) kronik toplamda 33 kemik parça içeren çekiç parmak hastası bu çalışmaya dâhil edilmiştir ve tüm olgulardan bilgilendirilmiş onam alınmıştır. Dahil edileme kriterleri akut ve kronik olgular için distal falanks tabanının en az %30'unu içeren dorsal eklem içi kırık parçası içermesi ve kronik olgular için tedavi olmakszın travmadan en az dört hafta geçmesidir.

Olguların yaşları, cinsiyetleri, başvuru şekilleri, travma şekilleri, hangi parmağın yaralandığı, başvuru zamanları, ayrılan kemik parçanın miktarı, cerrahi öncesi ve sonrası ekstansiyon, lag açısı cerrahi tedavi yöntemi ve Crawford sınıflamasına göre derecesi gibi klinik veriler hastane veri tabanından elde edildi. Çalışmaya parmakta açık yarası olan %30 dan daha az kemik parça içeren ve DIP eklemde artriti olan olgular dahil edilmedi.

Olguların ekstansiyon lag açıları gonyometre ile ölçüldü ve elde edilen verilerin değerlendirilmesi için ekstansiyon açığı, fleksiyon miktarı ve ağrı değerlendirmesi için crawford kriterleri kullanıldı (10). Ekstansiyon açığı 0 ile 10 derece arasında ise sonuç mükemmel; 10 ile 25 derece arasındaysa iyi; 25 dereceden fazla ise fakat ağrı yoksa makul; ağrılı ise zayıf olarak değerlendirildi.

Tüm olgularda radyolojik olarak kaynama gözlemlendi ve K telleri ortalama altıncı hafta çıkarıldı.

İstatistiksel Analiz

Elde edilen verilerin analizi için SPSS 15.0 (SPSS, Chicago, IL, ABD) programı kullanıldı. Sürekli değişkenlerin dağılımının normalliğini belirlemek için Shapiro-Wilk testi kullanıldı. Normal dağılan değişkenler için Student's t-testi, normal dağılım göstermeyen değişkenler için Mann-Whitney U testi

kullanıldı. Sürekli değişkenler ortalama±standart sapma veya ortanca çeyrekler arası aralık (25. ve 75. persentil) ve nominal veriler vaka sayısı ve yüzde olarak ifade edildi. Kategorik veriler, uygun olduğu şekilde Pearson Ki-kare veya Fisher'in kesin testi kullanılarak analiz edildi. Hesaplanan p değeri 0.05'ten düşük ise istatistiksel olarak anlamlı kabul edildi.

Bulgular

Cerrahi Teknik

Tüm olguların bulguları Tablo 1 ve 2 'de sunulmuştur. Grupların sosyodemografik ve klinik özelliklerinin istatistiksel verileri Tablo 3 te sunulmuştur. Grup 1 de ortalama başvuru süresi 7 gün olurken grup 2 de ortalama başvuru süresi 60 gün olarak tespit edilmiştir. Grup 1 de ortalama ayrılan kemik alanı %35 iken grup 2 de %37 olarak bulunmuştur. Çalışmamıza dahil ettiğimiz tüm olgularda ayrılan kemik fragmanlar yerlerine cerrahi olarak K telleri ile tespit edilmiştir. Ancak kronik olguların 2 tanesinde anchor sutur ile kemik tespiti yapılmıştır. Grup 1 deki hastaların 10 tanesi ekstansiyon blok (kapalı teknik) (Resim 1) 7 tanesi açık teknik ile opere edilirken grup 2 deki hastaların tamamı açık teknik (Resim 2) ile tedavi edilmiştir. Her iki grupta da benzer ilk ve son ekstansiyon açılarına ulaşılmıştır. Grup 1 in crawford sınıflamasına göre sonuçları 1 hastada 0 , 1 hastada 1 , 3 hastada 2 ve 12 hastada 3 olarak tespit edilirken , grup 2 nin crawford sınıflamasına göre sonuçları 1 hastada 1 ,2 hastada 2 ve 13 hastada 3 olarak bulunmuştur. Gruplar arasında yaş, cinsiyet, travma şekli, yaralanan parmak. ayrılan kemik oranı, tedavi şekli, ilk ve son ekstansiyon açıları, deplasman ve crawford sınıflaması verileri açısından istatistiksel anlamlı bir fark bulunmazken (p>0.05), başvuru süresi açısından anlamı fark bulunmuştur (7.0 [2.5-9.5] vs 60.0 [30.0-90.0], p<0.001).

Tablo 1: Akut olgular

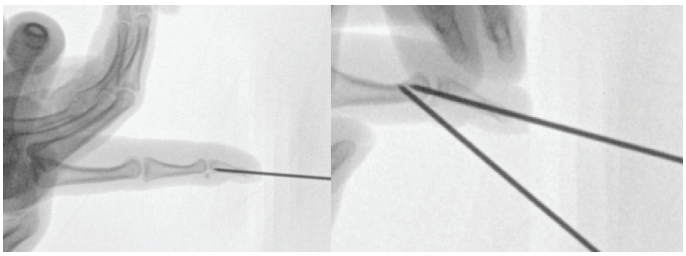
Grup 1 (Akut)	Yaş	Cinsiyet	Travma Şekli	Meslek	Par-mak	Basvuru	Ayrılan kemik oranı	Tedavi	Preop_ lag acisı	Postop lag acisı	Crowford sınıflaması	kom-plikasyon
1	23	Erkek	Top çarpma	Öğrenci	4	3	50	K teli, ext blok	45	5	Mükemmel	-
2	36	Kadın	Düşme	Ev hanımı	5	11	35	K teli, Tendon tamiri	45	5	Mükemmel	-
3	36	Erkek	Top çarpma	Tekstil işçisi	2	6	50	K teli Ten-don tamiri,	30	5	İyi	Kısmi eklem sertliği
4	27	Erkek	Düşme	Bankacı	5	4	50	K teli, ext blok	30	5	Mükemmel	-
5	39	Erkek	Sıkışma	İşçi	5	10	25	K teli, ten-don tamiri	30	5	Mükemmel	-
6	33	Erkek	Top çarpma	Bankacı	5	2	40	K teli, ext blok	15	0	Mükemmel	-
7	12	Kadın	Top çarpma	Öğrenci	3	9	35	K teli, ext blok	35	20	Zayıf	Ağrılı eklem sertliği
8	30	Erkek	Düşme	Serbest meslek	2	10	35	K teli, ext blok	45	10	Makul	Eklem sertliği
9	33	Kadın	Düşme	Müzisyen	4	8	50	K teli, ext blok	30	3	Mükemmel	-
10	37	Erkek	Top çarpma	Bankacı	4	7	30	Pull-out suture	30	3	Mükemmel	-
11	33	Erkek	Düşme	Öğretmen	5	7	20	K teli	20	3	Mükemmel	-
12	16	Erkek	Sıkışma	Öğrenci	3	6	45	K teli, tendon tamiri	30	4	Mükemmel	-
13	15	Erkek	Top çarpma	Öğrenci	3	2	30	K teli, ext blok	30	4	Mükemmel	-
14	18	Kadın	Top çarpma	Öğrenci	4	7	35	K teli, ext blok	45	5	Mükemmel	-
15	16	Erkek	Top çarpma	Öğrenci	5	1	35	K teli, ext blok	20	3	Mükemmel	-
16	27	Erkek	Sıkısma	Teknisyen	5	1	40	K teli, Tendon tamiri	20	5	İyi	-
17	30	Kadın	Sıkısma	Fizyotera-pist	3	10	50	K teli, ext blok	45	5	İyi	-

Tablo 2: kronik olgular

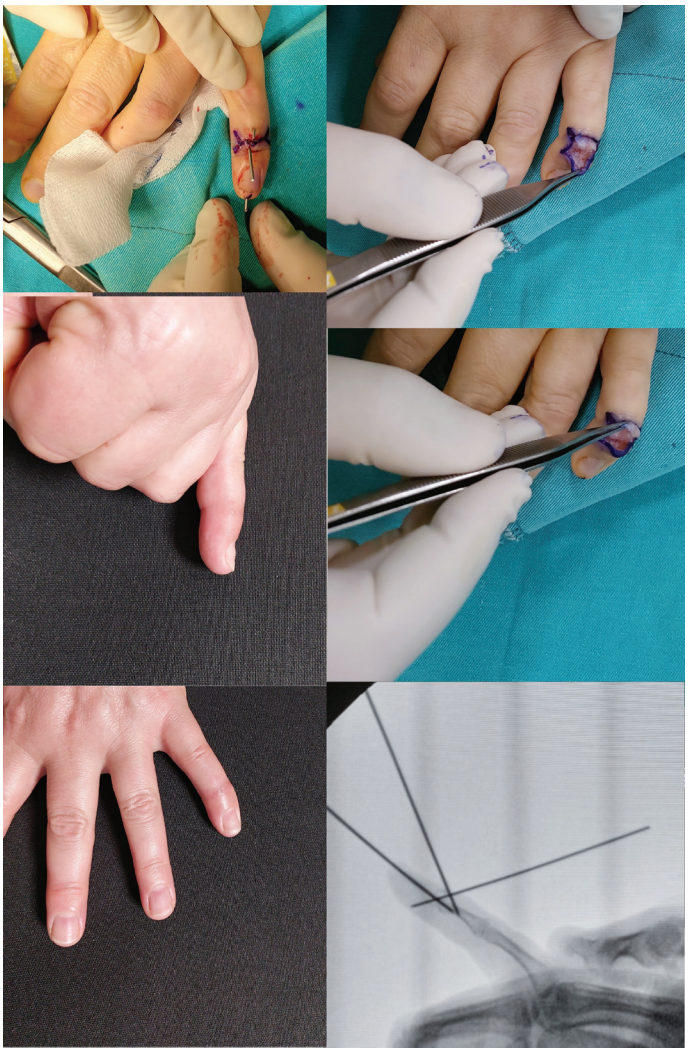
Grup 2 (Kronik)	Yaş	Cinsiyet	Travma Şekli	Meslek	Par-mak	Basvuru	Ayrılan kemik oranı	Tedavi	Preop_ lag acisi	Postop lag acisi	Crowford sınıflaması	kom-plikasyon
1	14	Erkek	Top çarpma	Ögrenci	3	30	35	K teli, açık red	20	5	Mükemmel	-
2	14	Erkek	Top çarpma	Ögrenci	3	55	40	K teli, açık red	30	3	Mükemmel	-
3	36	Kadın	Düşme	Doktor	4	35	40	K-teli sütür ankor pull out	30	5	İyi	Kısmi eklem sertliği
4	39	Kadın	Düşme	Öğretmen	5	65	50	K teli, pull out sütür	50	5	Makul	Eklem sertliği
5	35	Erkek	Top çarpma	Yönetici	4	25	40	K teli, küre-taj	30	3	Mükemmel	-
6	15	Kadın	Top çarpma	Öğrenci	2	28	35	K teli, açık red	30	4	Mükemmel	-
7	35	Erkek	Top çarpma	Öğretmen	2	17	35	K teli, açık red	35	10	İyi	Kısmi eklem sertliği
8	15	Erkek	Top çarpma	Öğrenci	3	33	25	K teli, ten-don tamiri	15	3	Mükemmel	
9	44	Erkek	Sıkışma	İşçi	5	22	30	K teli, açık red	25	3	Mükemmel	-
10	47	Erkek	Düşme	Yönetici	2	20	30	K teli, açık red	30	4	Mükemmel	-
11	25	Erkek	Düşme	Bankacı	4	31	50	Kemik ek-sizyonu, K teli, tendon tamiri	40	5	Mükemmel	-
12	42	Kadın	Top çarpma	Öğretmen	5	19	30	k teli, ten-don tamiri	35	4	Mükemmel	-
13	28	Erkek	Top çarpma	Kimyager	2	28	40	K teli, açık red	30	3	Mükemmel	-
14	14	Erkek	Top çarpma	Öğrenci	3	20	50	K teli, ankor pull out	45	5	Mükemmel	-
15	40	Erkek	Düşme	Serbes MESLEK	2	19	40	K teli, pull out	30	5	Mükemmel	-
16	14	Erkek	Sıkışma	Ögrenci	3	30	35	K teli, açık red	20	5	Mükemmel	-

Tablo 3: istatistiksel analiz

		Grup 1 (akut) (n=17)	Grup 2 (kronik) (n=16)	p
Yas		27.12+8.80	29.63+11.94	0.496
Cinsiyet	Female	5 (29.4%)	4 (25.0%)	0.776
	Male	12 (70.6%)	12 (75.0%)	
Travma	Top Çarpma	8 (47.1%)	10 (62.5%)	0.612
	Düşme	5 (29.4%)	4 (25.0%)	
	Sıkışma	4 (23.5%)	2 (12.5%)	
Parmak		-	-	-
Başvuru süresi		7.0 (2.5-9.5)	60.0 (30-90)	<0.001*
Bony yuzde		35 (32.5-50)	37.5 (31.25-40.0)	0.845
Tedavi	Kischner	10 (58.8%)—Ext Blok	7 (43.8%)—Açık redük	0.494
	Kischner + Ek	7 (41.2%)—Açık redük	9 (56.27%)—Açık redük	
İlk ekstansiyon acı		30.0(25.0-45.0)	30.0 (30.0-35.0)	0.958
Son ekstansiyon acı		5.0 (3.0-5.0)	4.5 (3.0-5.0)	0.873
Deplasman		40.0 (30.0-45.0)	40.0 (32.5-43.75)	0.901
Crawford	0	1 (5.9 %)	0 (0 %)	0.394
	1	1 (5.9 %)	1 (6.3 %)	
	2	3 (17.6 %)	2 (12.5 %)	
	3	12 (70.6 %)	13 (81.2 %)	



Resim 1.



Resim 2.

Tartışma

Bu çalışmada gruplar arasında başvuru süreleri hariç diğer değerlendirilen hiçbir parametrede fark olmadığını gördük. Bu durum doğru tedavi seçimi ile birlikte kronik kemik mallet olgularının sonuçlarının akut olgular kadar iyi olabileceğini göstermektedir. Eklem yüzeyinin %30 içeren akut olgularda minimal invaziv peruktan ekstansiyon bloklama yöntemi ile iyi sonuçlar alınacağı bildirilmiştir (11-12). Ancak kronik olgularda da buna benzer minimal invaziv yöntemler kullanılmamaktadır. Bunu temel sebebi kemik dokular arasında oluşan fibröz ve kallus dokusunun yeterli redüksiyona izin vermemesidir. Bu açıdan kronik olgularda daha çok açık cerrahi yöntemler uygulanmaktadır (13). Lee ve arkadaşlarının yaptıkları çalışmada kronik olgularda açık cerrahiye göre daha iyi sonuçlar bildirilmiştir (14-15). Açık cerrahi ile kallus dokusu daha iyi çıkarılıp eklem restorasyonu daha iyi yapılabilmektedir. (12). Çalışmamızda da kronik olguların tamamı açık cerrahi yöntem ile tedavi edilmiş olup bu anlamda literatür ile uyumludur.

Kronik hasta grubunun (grup 2) %81,3 de crawford sınıflamasına göre iyi sonuç elde edilmiştir. Ayrıca kronik grupta oluşan ekstansiyon kaybını ortalama 4.5 derece olarak bulduk. Bu bulgular literatür ile uyuşmaktadır(14). Akut grupta da hastaların %70 de crawford sınıflamasına göre iyi sonuç elde edilmiş ve ortalama ekstansiyon kaybı da 5 derece olarak bulunmuştur. Bu veriler bize cerrahi tedavileri sonrası her iki grup içinde benzer sonuçlar alındığını göstermektedir. Ayrıca gecikmiş olarak başvuran kronik olgularda akut olgular kadar iyi sonuçların alınabileceğini göstermektedir. Ancak kronik çekiç parmak olgularında tedavi protokolleri hala tartışmaldır. Kemik mallet olgularında temel amacımız eklem yüzünün tam restorasyonun sağlanması ve ekstansiyon kaybının olabildiğinde azaltılmasıdır. Birçok çalışma bize kronik olgularda açık redüksiyon ve internal fiksasyonun ile iyi sonuçlar alınabileceğini göstermiştir (14-15). Litaratürde kemik malletlerde açık cerrahi önerilmesinin temel sebebinin temas yüzeyini artırmak olduğu belirtilmektedir (14-15). Ayrıca Reddy ve Ho yaptıkları çalışmada açık redüksiyonun sadece kemik yüzeyini artırmadığı ekstansör tendonu da serbestlediğini göstermiştir (16). Buna rağmen kronik olgularda kapalı cerrahi tedavi olan ekstansiyon blok yöntemini savunan çalışmalar da mevcuttur (13). Pegol ve arkadaşları ekstansiyon blok yöntemi ile tedavi ettikleri altı kronik kemik mallet vakasında iyi sonuçlar aldıklarını bildirmişlerdir (12). Benzer sonuc Takase ve arkadaşları tarafından da bulunmuştur (13). Ancak çalışmamızda kronik olguların tamamına açık cerrahi uygulanmıştır. Konik kemik mallet olgularında açık cerrahideki parça redüksiyonun ve eklem restorasyonunun kapalı tekniğe göre daha iyi olacağını düşünmekteyiz. Gruplar arasındaki tedaviler karşılaştırıldığında kronik gruptaki hastalarımızın tamamında açık cerrahi teknik uygulanırken akut grupta hastaların yedisinde açık cerrahi uygulanmıştır. Bu sonuç bize kronik olgulardaki sonuçlarımızın akut olgular kadar iyi olmasının temel sebebinin seçilecek tedavi şekli ile ilgili olabileceğini göstermektedir.

Kemik parça içeren çekiç parmaklarda cerrahi başarıyı etkileyen en önemli parametrelerden diğer ikisi hastanın yaşı ve başvuru süresidir. Genç olgularda kallus oluşumu daha hızlı olduğundan başvuru süresi uzadıkça tedavide

başarı şansını düşmektedir (13). Bu durum genç olgular kadar olmasa da kronik olgular içinde geçerlidir (13). Çalışmamızda kronik gruptaki hastaların yaş ortalaması 29 akut gruptaki hastaların yaş ortalaması ise 27 olarak bulunmuştur. Kronik grupta crawford sınıflamasına göre sadece bir olguda makul sonucuna ulaşılmıştır. Makul sonucuna ulaşılan hastanın yaşı 39, başvuru süresi 65 gün olarak tespit edilmiştir. Akut olgularda ise crawford sınıflamasına göre sadece bir olguda zayıf sonucuna ulaşıldı. Bu olguda ki yaş 12 başvuru süresi ise 9 gün olarak belirlendi. Bu iki bulgu hastanın yaşı ve başvuru süresinin klinik sonucu etkilediğini göstermektedir.

Çalışmamızın temel kısıtlılığı örneklem sayının az olması ve retrospektif bir çalışma olmasıdır.

Sonuç olarak her ne kadar travma süresi hariç gruplar arasında diğer parametreler açısından anlamlı bir fark olmamasına rağmen uygulanan tedavi protokolleri farklıdır. Çalışmamızda kronik olgularımızın tamamına birkaç farklı açık cerrahi teknik uygulanmıştır. Buna rağmen kronik kemik parça içeren çekiç parmaklarda hangi cerrahi tekniğin uygulanması gerektiği ile ilgili birçok çalışma vardır (17-19). Sonuç olarak kronik kemik parça içeren çekiç parmak olgularında genel olarak açık cerrahi tekniği ile akut olgulardaki gibi olumlu sonuçlar elde edilir.

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Research Article

Parameters of Complete Blood Count Might Predict the Prognosis of Patients with Advanced Gastric Cancer

Tam Kan Sayımı Parametreleri ile İleri Evre Mide Kanseri Olan Hastaların Prognozunu Tahmin Edilebilir Mi?

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Abstract

Aim: Metastatic gastric cancer is a common disease with poor prognosis. In this common disease, estimating the prognosis with a simple complete blood count has attracted the attention in many studies. However, the results of the studies are incompatible with each other. The aim of the study was to evaluate the relationship between parameters of the complete blood count and disease prognosis in patients with advanced gastric cancer(AGC).

Material and Methods: Blood counts of the patients were examined before receiving any treatment at the time of diagnosis of AGC. All parameters derived from complete blood count. These were; Neutrophil lymphocyte ratio(NLR), platelet lymphocyte ratio(PLR), monocyte lymphocyte ratio(MLR), systemic immune-inflammation index(SII). The patients were divided in two subgroups according to the median values of NLR, PLR, MLR and SII.

Results: A total of 105 patients with AGC were included in the study. The median survival in the patients with low NLR group was 14.6 months compared with high NLR group was 7.9 months(p=0.008). The median survival was 12.7 months in the low PLR group versus 8.2 months in the high PLR group (p=0.019). While the median survival time was 14.6 months in the high MLR group, it was 7.9 months in the low MLR group (p=0.06).

Conclusion: Through the parameters derived from complete blood count, NLR appears to be a promising prognostic marker in patients with AGC.

Keywords: gastric cancer, inflammation, neutrophil, overall survival, neutrophil-lymphocyte ratio, complete blood count

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Öz

Amaç: Metastatik mide kanseri sık görülen ve prognozu kötü olan bir hastalıktır. Bu yaygın hastalıkta prognozun basit bir tam kan sayımı ile tahmin edilmesi birçok çalışmada dikkatleri üzerine çekmiştir. Ancak çalışmaların sonuçları birbiriyle uyumlu değildir. Bu çalışmanın amacı, ilerlemiş mide kanserli (İMK) hastalarda tam kan sayımı parametreleri ile hastalık prognozu arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: Hastaların İMK tanısı anında herhangi bir tedavi almadan önce kan sayımları incelendi. Tam kan sayımından elde edilen tüm parametreler kayıt edildi; Nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR), monosit lenfosit oranı (MLR), sistemik immün-enflamasyon indeksi (SII). Hastalar medyan NLR, PLR, MLR ve SII değerlerine göre iki alt gruba ayrıldı.

Bulgular: Çalışmaya İMK'li toplam 105 hasta dahil edildi. Düşük NLR grubundaki hastalarda medyan sağkalım 14,6 ay iken, yüksek NLR grubunda 7,9 aydı (p=0,008). Ortanca sağkalım düşük PLR grubunda 12.7 aya karşı yüksek PLR grubunda 8.2 aydı (p=0.019). Ortanca sağkalım süresi yüksek MLR grubunda 14.6 ay iken, düşük MLR grubunda 7.9 aydı (p=0.06).

Sonuç: Tam kan sayımından elde edilen parametreler aracılığıyla NLR, İMK'li hastalarda umut verici bir prognostik belirteç gibi görünmektedir.

Anahtar Kelimeler: mide kanseri, inflamasyon, nötrofil, genel sağkalım, nötrofil-lenfosit oranı, tam kan sayımı

Introduction

Gastric cancer is one of the most common types of cancer and is usually diagnosed at an advanced stage and has a poor prognosis [1]. With the increase of cancer screening, more patients are diagnosed at an early stage and a contribution to survival is provided with the advances in treatments. Despite these developments, the median survival of patients with metastatic gastric cancer is poor. Although the Tumor Node Metastasis (TNM) stage is frequently used to predict the prognosis of patients, it is observed that patients with the same TNM stage progress differently. In addition to the TNM stage, many variables such as pathophysiological classification, tumor differentiation, serosa involvement, and lymphovascular invasion have been shown to affect the prognosis of the disease [2, 3]. Although these factors have been shown to affect gastric cancer prognosis, there is no single marker that can predict survival in patients with metastatic gastric cancer. Therefore, there is a need for a simple, easily accessible and cheap prognostic marker.

In recent studies, the relationship between immunity and tumor microenvironment has been investigated, and the effects of systemic immune response on tumor development and progression have been revealed [4-6]. Therefore, it is thought that analyzing the data of the host immune system may give clues about the prognosis of cancer. There are various markers that can give information about the immune system. For example, with advances in the field of immunotherapy, immune markers related to treatment response, such as tumor mutation burden, PD-L1 level, have been identified [7]. Besides, the relationship between more easily accessible acute phase reactants such as C-reactive protein, erythrocyte sedimentation rate and cancer prognosis has been studied many times [8-10]. In addition to these markers, the Neutrophil / lymphocyte ratio (NLR), which can be detected by complete blood count, is known as a good marker of host immunity and has shown its power to predict prognosis in many types of cancer [11-13]. In addition to NLR, the platelet / lymphocyte ratio (PLR) and monocyte / lymphocyte ratio (MLR) and systemic inflammation index (SII), which can be calculated with parameters of complete blood count, in predicting the prognosis of gastric cancer have been demonstrated by various studies [14-16]. These ratios could not be used in routine practice because the results were inconsistent.

In this study, we aimed to evaluate the relationship between NLR, PLR, MLR and SII and the median overall survival (mOS) of patients with de novo metastatic gastric cancer. The secondary aim of this study is to evaluate the combined clinical use of NLR and other blood count parameters and the effect of these rates on progression-free survival.

Materials and Methods

Study design and population

After the approval of the Gazi University Faculty of Medicine

Ethics Committee, the data of the patients who applied to the medical oncology department and whose diagnosis of metastatic gastric cancer was confirmed at the time of diagnosis were retrospectively analyzed. The data of the patients were collected through oncology files and the hospital operating system.

All patients had pathologically diagnosed gastric adenocarcinoma. Patients who were followed up in the medical oncology department, received at least 1 course of chemotherapy, ≥18 years old and had complete blood count at the time of diagnosis were included in the study. The exclusion criteria of the study were defined as the presence of bone marrow involvement, active infection at the time of diagnosis, relapsed gastric cancer and additional hematological disease (eg. myelodysplatic syndrome, polistemia vera, essential thrombocytosis). Patients with insufficient file data and lost to follow up were not included in the study. 44 of these patients were not included in the study for various reasons (12 patients insufficient file data, 24 patients lost to follow up, 4 patients active infection at diagnosis, 2 patients with bone marrow involvement and 2 patients additional hematological diseases). Overall survival (OS) was determined as the time from diagnosis to the patient's final visit. Progression free survival (PFS) was calculated as the time from diagnosis to progression, death or final visit.

Data collection

Patients' demographic data, clinical characteristics, Eastern Clinical Oncology Group performance status (ECOG), pathological data, Her-2 status and data on the chemotherapy regimens they received were collected. Data of complete blood count (hemoglobin, platelet, leukocyte, neutrophil, monocyte, lymphocyte) and serum biochemistry measurements at the time of diagnosis were analyzed. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) data were collected before starting oncological treatment. Absolute neutrophil, platelet and monocyte counts were divided by absolute lymphocyte counts to calculate NLR, PLR and MLR, respectively. The systemic inflammation index was calculated by dividing the multiplication value of absolute platelet and neutrophil measurements by the absolute lymphocyte measurement (SII= Neutrophil x Platelet / Lymphocyte).

Statistical analysis

Statistical analyses were performed using SPSS software version 23. Mean (standard deviation) was used for normally distributed data and median ± min / max values were used for non-normally distributed data. Categorical data are expressed as percentages (%). Distribution analyzes were performed for NLR, PLR, MLR and SII values and cut-off values were determined according to their medians. The patients were divided into two groups according to these cut-off values. We used 2 different models for survival analysis. For univariate analysis, Kaplan-Meier analysis was performed and log-rank analysis was performed and Hazard Ratios (HR) was calculated using Cox proportional hazard regression models. Possible factors determined by univariate analyzes were evaluated by Cox regression analysis with backward selection to determine independent predictors of overall survival rate of gastric cancer. HR values determined by multivariate analysis are presented with the 95% confidence interval (95% CI). In the interpretation of all analyzes, $p < .05$ value was considered statistically significant.

Results

Between January 2009 and January 2019, a total of 149 patients with de novo metastatic gastric cancer were detected. After these patients were excluded, a total of 105 patients were included in the study. The characteristic features of the patient population are given in Table 1. he median age of the patients was 61 years (range 31-85), and the majority of the cases involved men (70%). The ECOG performance status of 70 patients was found to be 0 or 1.

When the histopathological features of the tumors were examined, it was found that the majority (59%) had poorly differentiated tumors. Tumor subtypes were analyzed and it was seen that 67 (64%) patients were diagnosed with adenocarcinoma and 37 (35%) patients with ring cell cancer. HER-2 positivity was detected in only 15% of patients. The most common site of metastasis was the peritoneum (34%). It was also found that almost half of the patients (47%) received a combination of taxane, platinum and 5-fluorouracil chemotherapy.

The median overall survival of 105 patients included in the study was calculated as 9.03 months. When the variables affecting overall survival were examined with univariate analysis, no relationship was found between age, gender, ECOG performance status and overall survival. There was no association between median overall survival and anemia (Hgb <12gr/dl) ($p = 0.29$). Similarly, no statistically significant relationship was found between thrombocytopenia (100,000/µL) and mOS ($p = 0.49$). While the median survival was 11.2 months in patients with high CEA levels, this rate is 9 months in the low group ($p= 0.46$). Patients were divided into groups according to the medians of NLR, PLR, and MLR values, and survival in these groups was evaluated. The median overall

survival was 14.5 months in the patient group with a low NLR levels and this period was calculated as 7.9 months in the group with a high NLR levels (p= 0.008). In addition to this information, in the patient group with low PLR and MLR levels, mOS was measured 12.7 months and 8.2 months, respectively. In the patient group with high PLR and MLR levels, these durations were found to be 8.2 months and 7.8 months (p = 0.019 and p = 0.006, respectively). Although there was a 3.6-month difference between low-SII and high-SII patients, it could not reach a statistically significant value (p = 0.375). Survival charts created according to these ratios are presented in Figure I. The data of univariate and multivariate analyses of factors for the prediction of mOS are presented in Table 2.

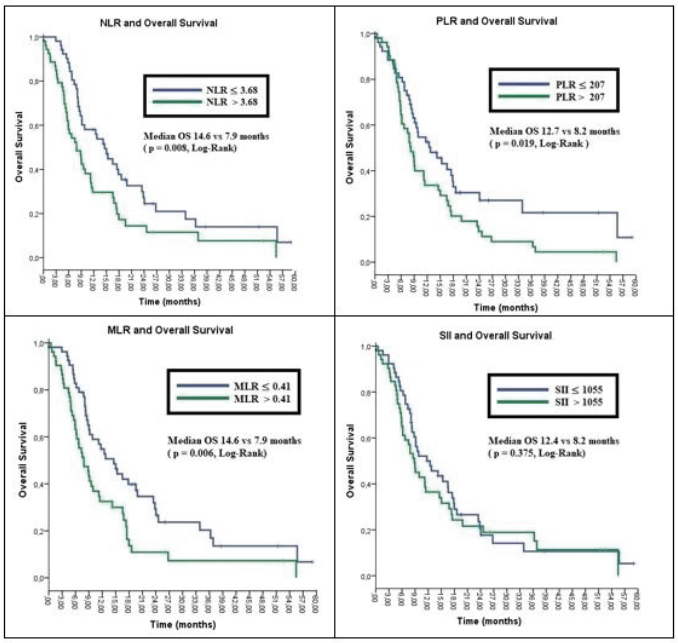

Figure I. NLR, PLR, MLR and Overall Survival

The factors affecting PFS were evaluated and it was found that age, gender and ECOG performance status at the time of diagnosis had no effect on PFS. The median PFS of patients with liver metastasis was 6.3 months, this time was measured as 5.9 months in patients without liver metastatic disease (p = 0.95). There was no effect of PLR and SII values on PFS (p = 0.83 and p = 0.75). The median progression free survival in the patients with low NLR group was 7.5 months compared with high NLR group was 5.2 months. (p = 0.0012). In low MLR group the PFS was 8.5 months compared with high MLR was 4.9 months respectively (p = 0.009). When multivariate analysis was done, it was seen that the only factor affecting PFS was MLR (p = 0.003). The data of univariate and multivariate analysis of factors affecting progression-free survival are presented in Table 3.

The effects of NLR, PLR, and MLR on overall survival were statistically significant, and the predictive value of these rates was thought to increase when they were combined. Since NLR was found to be the only variable affecting median OS in multivariate analysis, we examined the effect of combining MLR and PLR with NLR on prognosis. Survival charts are presented in Figure II.

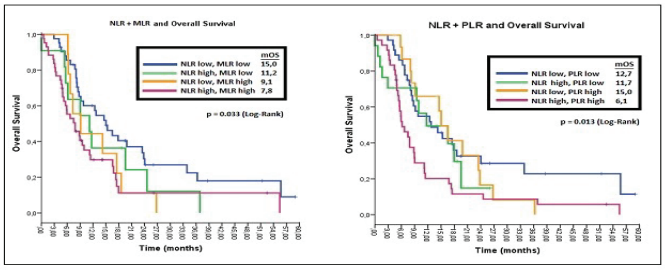

Figure II. NLR, PLR, MLR combinations and Overall Survival

Discussion

Gastric cancer is an aggressive disease with a poor prognosis, and markers are needed to predict prognosis. In this study, we showed the relationship between complete blood count parameters and the prognosis of metastatic gastric cancer. Increased NLR, PLR and MLR values were associated with shorter overall survival. On the other hand, combining scores into NLR-PLR and NLR-MLR rather than using them alone increases the predictive value of the ratios.

Studies conducted with inflammation-related scores are quite diverse and it has been found that an increase in scores such as NLR and PLR is associated with poor survival in diseases such as breast cancer, lung cancer, and colon cancer [13, 17, 18]. Additionally, studies focusing on gastric cancer revealed the effect of these immune scores on overall survival [14, 19]. In a meta-analysis conducted by Zhang et al., data of 2952 gastric cancer patients were analyzed and it was found that a lower NLR rate was associated with longer OS (HR1.83 ([95% CI], 1.62–2.07)) [20]. Unlike supporting data, the NLR score does not appear in routine practice. The most important reason for this situation may be the differences in the NLR cut-off values used in the studies. In our study, the median value for NLR was determined as 3.68 and 3.68 was used as the cut-off value. In some studies, a NLR level above 2, 2.5 or 3 was determined as the cut-off value, while there are studies that determine the cut-off value based on the ROC analysis or as we also use, the median value [21-24]. Different cut-off values make standardization difficult and limit its international use.

Infiltrated neutrophils and lymphocytes may be the underlying cause of the prognostic power of NLR and PLR. The progression of

Table I. Characteristics of the study population			
Group		Number	(%)
Age			
	< 65 years	66	(62%)
	≥ 65 years	39	(38%)
Gender			
	Female	31	(30%)
	Male	74	(70%)
ECOG performance status			
	0-1	70	(67%)
	≥ 2	35	(33%)
Differentiation status			
	Poor	61	(59%)
	Moderately	33	(31%)
	Well	11	(10%)
Her-2 Status			
	Negative	89	(85%)
	Positive	16	(15%)
Metastasis site			
	Peritoneum	36	(34%)
	Liver	29	(28%)
	Lymph Node	18	(17%)
	Bone	15	(14%)
	Others	7	(7%)
	Multiple	26	(25%)
Chemotherapy			
	5-Fluorouracil monotherapy	9	(8%)
	Platinum based doublet regimens	26	(25%)
	Combinations with anti HER-2 agents	10	(9%)
	Taxane and Platinum based triplet regimens	48	(47%)
	Others	12	(11%)
		Median	(min- max))
CEA (ng/mL)		6.7	(0.6-2100)
CA 19-9 (U/mL)		22	(0.5-10.800)
Hemoglobin (g/dL)		11.9	(5.8-17.0)
Platelet (/µL)		322000	(32000-978000)
Absolute neutrophil count (/µL)		5500	(1900-39000)
Absolute lymphocyte count (/µL)		1500	(500-3600)
Absolute monocyte count (/µL)		660	(90-2300)

Table 2. Univariate and multivariate analyses of factors for the prediction of overall survival

Characteristics		n, %	mOS (months)	Univariate analyses HR (95% CI)	p value	Multivariate analyses HR (95% CI)	p value
Age							
	<65y	66 (62%)	11.1	1.00			
	≥65y	39 (38%)	8.9	1.30 (0.83-2.02)	0.24	-	-
Gender							
	Female	31 (30%)	9.0	1.00			
	Male	74 (70%)	9.8	1.08 (0.66-1.77)	0.73	-	-
ECOG							
	0-1	70 (67%)	11.2	1.00			
	≥ 2	35 (23%)	8.9	1.18 (0.75-1.87)	0.45	-	-
Differentiation status							
	Well	11 (10%)	9.0	1.00		-	-
	Moderately	33 (31%)	12.7	1.00			
	Poor	61 (59%)	9.5	0.78 (0.55-1.12)	0.17		
Liver metastasis							
	No	76 (72%)	8.8	1.00			
	Yes	29 (28%)	12.3	0.62 (0.37-1.03)	0.06	-	-
CEA (ng/mL)							
	Low CEA	45 (43%)	9.0	1.00			
	High CEA	60 (57%)	11.2	0.83 (0.52-1.33)	0.46	-	-
CA 19-9 (U/mL)							
	Low CA 19-9	62 (59%)	9.1	1.00			
	High CA 19-9	43 (41%)	9.5	1.25 (0.73-2.00)	0.34	-	-
NLR							
	Low NLR	52 (%50)	14.6	1.00			
	High NLR	53 (%50)	7.9	1.77 (1.15-2.74)	0.008	2.14 (1.30-3.50)	0.002
PLR							
	Low PLR	53 (%50)	12.7	1.00			
	High PLR	52 (%50)	8.2	1.68 (1.08-2.61)	0.019	1.15 (0.66-1.99)	0.61
MLR							
	Low MLR	53 (%50)	14.6	1.00			
	High MLR	52 (%50)	7.9	1.81 (1.18-2.83)	0.006	1.45 (0.80-2.62)	0.21
SII							
	Low SII	53 (%50)	12.4	1.00			
	High SII	52(%50)	8.2	0.82 (0.53-1.26)	0.375	-	-

Table 3. Univariate and multivariate analyses of factors for the prediction of progression free survival

Characteristics		n, %	mOS (months)	Univariate analyses HR (95% CI)	p value	Multivariate analyses HR (95% CI)	p value
Age							
	<65y	66 (62%)	6.5	1.00			
	≥65y	39 (38%)	5.8	1.31 (0.86-1.98)	0.20	-	-
Gender							
	Female	31 (30%)	5.4	1.00			
	Male	74 (70%)	6.5	0.83 (0.54-1.28)	0.40	-	-
ECOG							
	0-1	70 (67%)	6.5	1.00			
	≥ 2	35 (23%)	5.8	1.24 (0.81-1.91)	0.30	-	-
Differentiation status							
	Well	11 (10%)	6.1	1.00		-	-
	Moderately	33 (31%)	7.9	1.00			
	Poor	61 (59%)	5.7	1.26 (0.72 -1.62)	0.51		
Liver metastasis							
	No	76 (72%)	5.9	1.00			
	Yes	29 (28%)	6.3	1.01 (0.65-1.57)	0.95	-	-
CEA (ng/mL)							
	Low CEA	45 (43%)	5.2	1.00			
	High CEA	60 (57%)	6.1	1.00 (0.65-1.53)	0.99	-	-
CA 19-9 (U/mL)							
	Low CA 19-9	62 (59%)	5.3	1.00			
	High CA 19-9	43 (41%)	5.9	1.09 (0.71-1.69)	0.67	-	-
NLR							
	Low NLR	52 (%50)	7.5	1.00			
	High NLR	53 (%50)	5.2	1.67 (1.11-2.51)	0.012	1.30 (0.80-2.11)	0.28
PLR							
	Low PLR	53 (%50)	6.7	1.00			
	High PLR	52 (%50)	5.8	1.04 (0.69-2-1.55)	0.83	-	-
MLR							
	Low MLR	53 (%50)	8.5	1.00			
	High MLR	52 (%50)	4.9	1.85 (1.22-2.78)	0.009	1.85 (1.22-2.78)	0.003
SII							
	Low SII	53 (%50)	6.7	1.00			
	High SII	52(%50)	5.9	1.06 (0.74-1.59)	0.752	-	-

cancer cells increases neutrophil flow to that area and increased neutrophils cause the release of many proinflammatory cytokines (Interleukin-6, Interleukin-10, Vascular endothelial growth factor, Tumor necrosis factor alpha) [25]. Vascular endothelial growth factor, one of these cytokines, contributes to tumor progression by increasing tumor angiogenesis and studies have also revealed the relationship of increased vascular endothelial growth factor levels with cancer cachexia [26]. In addition, increased interleukin-10 and tumor necrosis factor-alpha levels leads to a decrease in lymphocyte function and number, and suppresses T-lymphocyte-related antitumor response [27]. These pathophysiological results, resulting from changes in the levels of peripheral blood cells, explain the rationale of our idea to predict the mOS of metastatic gastric cancer through complete blood count measurements. In point of fact, in our study, a decrease in mOS was found in patients with gastric cancer with increased NLR, PLR and MLR. These scores can be thought to be a reflection of the underlying immune response and various released cytokines.

Although there are studies arguing that increased monocyte count negatively affects cancer prognosis, the underlying mechanism was not fully explained [28, 29]. However, there was evidence that the monocyte / lymphocyte ratio was more closely related to the malignant process rather than the absolute monocyte count effect alone [30]. In a retrospective study by Chen et al., it has been proven that increased MLR rate was associated with shorter survival times in gastric cancer patients receiving neoadjuvant therapy [31]. In addition, in a study investigating the factors affecting PFS duration in patients with metastatic gastric cancer, it has been revealed that MLR is sensitive in predicting PFS duration [32]. In our study, it was found that the only factor affecting PFS value independent from the other factors was MLR and these results support the results of the study conducted by Zhou et al.

In our study, unlike rates such as NLR, PLR and MLR, no relationship was found between SII and metastatic gastric cancer survival times. When the literature was reviewed, it was found that lower SII values were associated with better postoperative outcomes and longer survival in patients with gastric cancer [33]. In our study, the systemic inflammatory index not being correlated with gastric cancer survival may be associated with the cut-off value determination method or the low number of patients. It is necessary to determine a certain cut-off value for SII and to conduct additional studies with more patients.

This study has some limitations. Its retrospective design and including patients from a single center can be stated as the biggest limitation of the study. Detection of changes in neutrophil, thrombocyte and monocyte levels with control blood counts after oncological treatments may guide the evaluation of treatment response. In addition, poor differentiation, high CEA levels and liver metastasis are known to be poor prognostic factors for gastric cancer. In our study, when the survival of patients with these poor prognostic features and those who did not were examined, no statistically significant difference in survival was found. Although there was no statistically significant difference, patients with poor characteristics had numerically better survival times. The small number of patients in the groups, differences such as the patients' ECOG status and age may explain these surprising results. Therefore, prospective, multicenter studies including more patients with metastatic gastric cancer are needed.

Conclusion

In conclusion, increases in NLR, PLR and MLR levels were found to be associated with poor gastric cancer survival. The association of NLR with poor gastric cancer survival has been demonstrated, independent of other factors. Regardless of other factors and ratios, the increase in NLR level is associated with shorter gastric cancer survival. These rates are an in-direct reflection of the patient's immune system and we think that after standardization with clinical studies, oncology physicians will benefit more from these parameters in their daily practice.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Osman Sütcüoğlu], [Abdülkadir Fincan], [Bediz Kurt İnci] [Fatih Gürler] and [Ozan Yazıcı]. The first draft of the manuscript was written by [Osman Sütcüoğlu], [Ozan Yazıcı] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declerations

Part or all of the article has not been published elsewhere. It is not in the process of being evaluated in another journal at the same time.

Etthical approval

Ethical approval was waived by the local Ethics Committee of Gazi University in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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Conflict of interest

The authors declare that they have no conflict of interest.

Availability of data and material

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

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Research Article

The Effect of Surgical Treatment Option on inflammatory Response in Breast Cancers

Meme Kanserlerinde Cerrahi Tedavi Seçeneğinin İnflamatuar Yanıt Üzerine Etkisi

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Abstract

Aim: The aim of the study was to assess effect of different breast surgery techniques on the inflammatory response.

Material and Methods: The study executed between February 2013 and April 2013 in the General Surgery Clinic.The 42 patients aged between 18-70 years, who were diagnosed with breast cancer by tru-cut or incisional biopsy, were evaluated as stage I and II breast cancer according to AJCC criteria and underwent surgical treatment.In this prospectively study, descriptive statistics are given as mean±standard deviation, percentage and frequency.In comparison of groups, Kruskal-wallis test was used in comparison of three groups and Mann-Whitney-U test was used in comparison of two groups. Wilcoxon test was used for in-group comparison. The chi-square test was used to compare the count values between groups.The $p<0.05$ value at the 95% confidence interval was considered statistically significant.In correlation;Pearson correlation and Spearman correlation test were used.

Results: The total number of cases was 42. The mean age of the patients included in the study was 52.54±12.7 years old. Especially in terms of comparison of the preoperative and postoperative inflamatuvar markers;Postoperative IL-6 values were significantly higher than the preoperative IL-6 values in all three groups($p=0.001$), postoperative white blood cell count too was found to be significantly higher in all three groups ($p=0.003$, $p=0.001$, $p=0.001$).Additionally, CRP levels were found to increase significantly in all three groups after surgery compared to preoperatively . While there was no difference between the groups in terms of preoperative CRP levels, CRP levels were found to be higher in the group that underwent lumpectomy and axillary dissection in the postoperative period compared to the other groups ($p=0.004$).

Conclusion: In the surgical methods to be chosen in breast cancer, methods that can keep the inflammatory reactions to a minimum by considering the severity of the trauma and fully meet the oncological principles for the patient should be kept in mind first.

Keywords: breast cancer, surgical treatment , inflammatory response

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Öz

Amaç: Bu çalışmanın amacı, farklı meme cerrahisi tekniklerinin inflamatuar yanıt üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntemler: Çalışma Şubat 2013-Nisan 2013 tarihleri arasında Genel Cerrahi Kliniği'nde gerçekleştirildi. Tru-cut veya insizyonel biyopsi ile meme kanseri tanısı konulan 18-70 yaş arası 42 hasta AJCC kriterlerine göre evre I ve II meme kanseri olarak değerlendirilerek cerrahi tedavi uygulandı. Bu prospektif çalışmada, tanımlayıcı istatistikler ortalama±standart sapma, yüzde ve frekans olarak verilmiştir. Grupların karşılaştırılmasında üç grubun karşılaştırılmasında Kruskal-wallis testi, iki grubun karşılaştırılmasında Mann-Whitney-U testi kullanıldı. Grup içi karşılaştırmada Wilcoxon testi kullanıldı. Gruplar arasındaki sayım değerlerinin karşılaştırılmasında ki-kare testi kullanıldı. %95 güven aralığındaki $p<0,05$ değeri istatistiksel olarak anlamlı kabul edildi. Korelasyonda; Pearson korelasyonu ve Spearman korelasyon testi kullanıldı.

Bulgular: Toplam olgu sayısı 42 idi. Çalışmaya alınan hastaların yaş ortalaması 52,54±12,7 idi. Özellikle preoperatif ve postoperatif inflamatuvar belirteçlerinin karşılaştırılması açısından; Postoperatif IL-6 değerleri her üç grupta da preoperatif IL-6 değerlerinden anlamlı olarak yüksek bulundu($p=0,001$), postoperatif lökosit sayısı da her üç grupta da anlamlı olarak yüksek bulundu ($p=0,003$, $p=0,001$, $p =0.001$).Ayrıca ameliyattan sonra her üç grupta da ameliyat öncesine göre CRP düzeylerinin anlamlı olarak arttığı bulundu. Preoperatif CRP düzeyleri açısından gruplar arasında fark bulunmazken, postoperatif dönemde lumpektomi ve aksiller diseksiyon uygulanan grupta CRP düzeyleri diğer gruplara göre daha yüksek bulundu($p=0,004$).

Sonuç: Meme kanserinde seçilecek cerrahi yöntemlerde öncelikle travmanın şiddeti göz önünde bulundurularak inflamatuar reaksiyonları minimumda tutabilen ve hasta için onkolojik prensipleri tam olarak karşılayan yöntemler akılda tutulmalıdır.

Anahtar Kelimeler: meme kanseri, cerrahi tedavi, inflamatuar yanıt

Introduction

In recent years, it has been observed that there is a general trend towards less invasive approaches in the surgical treatment of cancer. For example, laparoscopic and endoscopic treatment methods are increasingly used in abdominal cancer surgery (1). Similarly, recently, the surgical treatment of breast cancer has evolved from mastectomy to breast-conserving surgery, from axilla dissection to sentinel lymph node biopsy (2). Surgical treatment of breast cancer is managed without compromising oncological principles and clinical results, but also considering cosmetic concerns, and more limited, less morbid surgical procedures are preferred. These treatments, referred to as "minimally invasive breast surgery" or "oncoplastic breast surgery", have become very popular among breast surgeons (surgical treatment of breast cancer) in recent years (3). While minimally invasive breast surgery originally referred to breast-conserving surgery and sentinel lymph node biopsy, it has recently been used to describe endoscopic breast and axillary surgery.The main point here is; It is to improve cosmetic results by using smaller incisions (4,5). In addition, for another purpose, more minimal surgery means less tissue trauma and less inflammatory response. As is known, surgical procedures are an important cause of trauma to the body. Tissue damage caused by surgery, anesthetic and analgesic drugs, hypothermia, blood loss, transfusion, pain and perioperative stress trigger hormonal and inflammatory response and cause immunosuppression (6). Postoperative immunosuppression is a well-known complication and has been extensively studied. Postoperative period especially for major surgery, there is a prominent augment in plasma concentrations of acute inflammatory cytokines (Interleukin; IL-6 and IL-8), prostaglandins (PGE2), stress hormones (such as catecholamines and corticosteroids) whereas on the other hand in cytotoxic and helper T lymphocyte functions decrease (7). These changes form the basis of the profound suppression of post-surgical cellular immunity, especially natural killer cell cytotoxicity (7,8). Immunosuppression develops hours after surgery, lasts for a few days, and increases in direct proportion to the magnitude of surgical trauma (9,10). There is a direct relationship between the extent of surgical trauma and the amount of cytokines that enter the systemic circulation (11). It is therefore natural that different surgical techniques, which cause different amounts of tissue damage, cause different degrees of trauma response. This situation has been clearly demonstrated in the literature in studies comparing laparoscopic and open cholecystectomy; It was found that laparoscopic cholecystectomy caused less elevation of IL-6 and CRP levels compared to open cholecystectomy (12), and peripheral leukocyte functions were better preserved (13).

Smaller incisions and less tissue trauma minimize surgical stress and reduce morbidity (13,14). It has been shown that changes in surgical procedures increase or decrease the probability of tumor recurrence by causing more or less immunosuppression (6). For instance, minimally invasive surgeries such as laparoscopy are known to be less immunosuppressive than standard procedures such as laparotomy. It is not clear whether a similar effect also applies to surgical treatment techniques for breast cancer. In a recent study, although surgical treatment of breast cancer was considered as a minor surgery, it was shown that it significantly affected the immune system by decreasing natural killer cell activity and HLA-DR expression, and increasing the proinflammatory response (15). In another study, it was shown that decreased perioperative natural killer activity and increased inflammatory cytokines increase cancer-related morbidity and mortality in patients with breast cancer (16). But furthermore, the differences between different surgical techniques used in the treatment of breast cancer are unknown. Therefore, the aim of the study was to assess effect of different breast surgery techniques on the inflammatory response.

Material and Methods

The study included 42 patients aged 18-70 years, who were diagnosed with breast cancer by tru-cut or incisional biopsy in the General Surgery Clinic of Ankara Oncology Hospital. The patients were recruited between February 2013 and April 2013. The evaluation were done to the patients who as stage I and II breast cancer according to AJCC criteria underwent surgical treatment. The patients were divided into 3 groups according to the surgical treatment to be applied. The study coordinator did not interfere with the surgical treatment decision, the surgical treatment decision to be applied was determined by the physician conducting the patient's treatment.In terms of exclusion criterias; The patients who over 70 years of age, concomitant systemic disease, autoimmune disorders, infection, bilateral breast cancer, concurrent or a history of other malignant diseases, receiving immunostimulant or immunosuppressive therapy for any reason, or using nonsteroidal anti-inflammatory drugs patients were excluded. The first group includes patients who underwent breast-conserving surgery and sentinel lymph node biopsy, the second group included patients who underwent axillary dissection in addition to breast-conserving surgery, and the third group included patients who underwent modified radical mastectomy. Blood sample was drawn from the patients in each group on the day before the operation and at the 24th hour after the operation, after they were allowed to rest in the supine position for 15 minutes.The serum samples obtained were kept at -20 degrees until the measurement time. IL-6 levels in the samples were evaluated with the commercially available ELISA (enzyme-linked immunosorbent assay) human IL-6 kit (Biosource, California, USA). Test samples of serum IL-6, whose standard curve showed linearity between 0-300 pg/mL, were diluted before measurement.C-reactive protein levels were determined quantitatively by turbudimetric method in a fully automatic device (Rosch Diagnostic Noduler P, Germany). Serum leukocyte count was done with laser method and automatic device (Siemens Diagnostics, Bayer Adria 2120, Germany). The results of the measurements were calculated automatically by the device. The expected leukocyte value in healthy subjects was accepted as between 4000-10000/mm3.

Statistical analysis

Statistical analyzes were performed using the SPSS 15.0 computer package program (SSPS Inc., Chicago, USA) to evaluate the findings obtained in the study. Frequency and percentage distribution were used for descriptive analyses, and the averages were given as mean-standard deviation. The Mann-Whitney-U test was used for two-group comparisons of continuous variables, and the Kruskal Wallis test for three-group comparisons. Subgroup comparisons were made with the Wilcoxon test. Chi-square test was used to compare categorical data. A p value of <0.05 was considered statistically significant in the analyses.

Results

Some clinicopathological demographic distinctives of the patients included in the study are summarized in Table 1. Among the working groups; No statistically significant difference was found in terms of age (p=0.73), pathological tumor diameter (p=0.08), estrogen receptor (p=0.82), progesterone receptor (p=0.88) and HER-2 status (p=0.14). There was no difference between groups 2 and 3 in terms of the number of lymph nodes removed, axillary involvement and the number of metastatic lymph nodes. On the other hand; In group 1 (patients who underwent sentinel lymph node biopsy), the total number of lymph nodes removed (p=0.001), axillary involvement (p=0.001) and the number of metastatic lymph nodes (p=0.002) were significantly less than the other two groups. Similarly, lymphovascular invasion (p=0.02) and extracapsular invasion rate (p=0.04) were significantly lower in patients in this group than in other

groups (group 2-3). In terms of mean white blood cell counts, there was no significant difference among these three groups in both preoperative and postoperative periods (Figure 1). When the mean preoperative and postoperative mean white blood cell counts were compared; Postoperative white blood cell count was found to be significantly higher in all three groups (p=0.003, p=0.001, p=0.001).

Preoperative and postoperative mean IL-6 values of the groups are shown in Figure 1. When the preoperative and postoperative mean IL-6 values of the patients in the groups were compared, it was found that the postoperative IL-6 values were significantly higher than the preoperative IL-6 values in all three groups (p=0.001). However, when the groups were compared in terms of both preoperative and postoperative IL-6 values, no statistically significant difference was found among the groups (p=0.21, p=0.33).In terms of the preoperative leukocyte levels of the three groups were compared, there was not statistically significancy among the groups. Additionally, for the postoperative leukocyte levels for these three groups were compared, again there wasn't any statistically significancy among the groups (Figure 2). Like other inflammation parameters, CRP levels were found to increase significantly in all three groups after surgery compared to preoperatively (Figure 3). While there was no difference between the groups in terms of preoperative CRP levels, CRP levels were found to be higher in the group that underwent lumpectomy and axillary dissection in the postoperative period compared to the other groups (p=0.004). The mean age of the patients included in the study was 52.54±12.7 in Group 1, 54.15±13.1 in Group 2 and 53.25±11.8 in Group 3. There was no statistically significant difference between the groups in terms of age. There is a statistically significant difference between preoperative IL-6 and postoperative IL-6 values in group 1, group 2 and group 3. Postoperative IL-6 values were higher in all three groups.When the preoperative IL-6 values of the three groups were compared; There was a statistically significant difference between the groups. This difference is due to group 2 with a higher preoperative IL-6 value (Mann-Whitney-U test). When the postoperative IL-6 values of the three groups were compared, no statistically significant difference was found between the groups. There was a statistically significant difference between preoperative and postoperative leukocyte values in group 1, group 2 and group 3. Postoperative leukocyte values were higher in all three groups. When the preoperative leukocyte values of the three groups were compared; No statistically significant difference was found between the groups. When the postoperative leukocyte values of the three groups were compared, no statistically significant difference was found between the groups. There was a statistically significant difference between pre-op CRP and post-op CRP values in group 1, group 2 and group 3. Postoperative CRP values were higher in all three groups. When the preoperative CRP values of the three groups were compared; No statistically significant difference was found between the groups. When the postoperative CRP values of the three groups were compared, a statistically significant difference was found between the groups. This difference is due to group 3 with higher postoperative CRP value (Mann-Whitney-U test). The Ki-67 values of the patients included in the study are given in Table 5, there was not any statistically significant difference between the three groups. When the tumor diameters of the patients in the three groups were compared, no statistically significant difference was found between the groups.When the Total Number of Lymph Nodes of the Patients Included in the Study was compared, a statistically significant difference was found between the three groups. The difference is source from group 1 with a low number of lymph nodes.When the Metastatic Lymph Node Numbers of the Patients Included in the Study were compared, a statistically significant difference was found between the three groups. The difference is due to group 1 without metastatic lymph nodes.When the three groups were compared in terms of the presence of estrogen receptors, no statistically significant difference was found between the groups. When the three groups were compared in terms of the presence of progesterone receptors, no statistically significant difference was found between the groups. When the three groups were compared in terms of the presence of HER-2, no statistically significant difference was found between the groups. When the three groups were compared in terms of pathological tumor staging, no statistically significant difference was found between the groups. When the three groups were compared in terms of axillary lymph node involvement, a statistically significant difference was found between the groups. The difference is source from group 1 without lymph node involvement.When the three groups were compared in terms of lymphovascular invasion, a statistically significant difference was found between the groups. It is group 1 that makes the difference.When the three groups were compared in terms of Extracapsular Invasion, a statistically significant difference was found between the groups. This difference sourced from 1 th group.

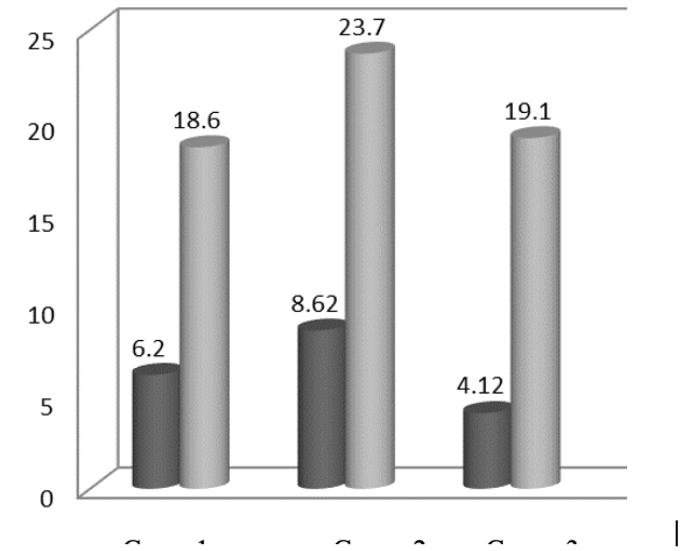

Figure 1: IL-6 Mean of the cases included in the study

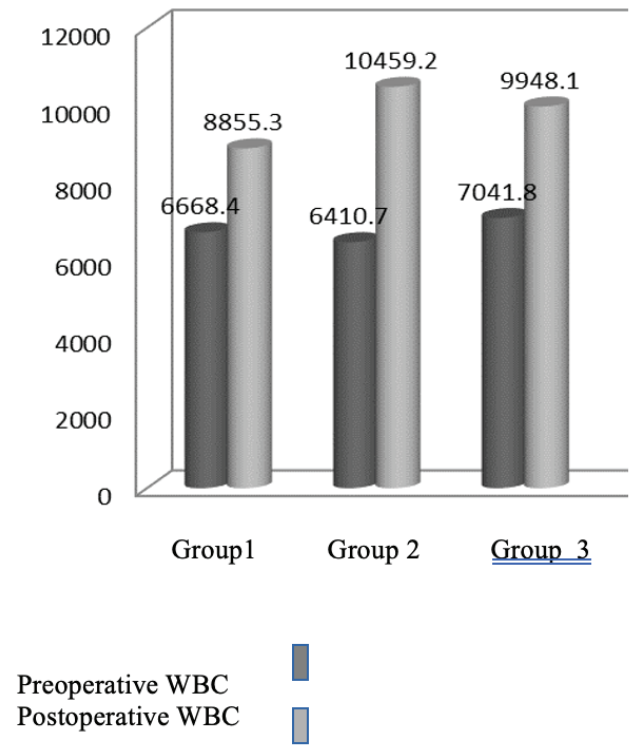

Figure 2: The mean of the white blood cells of the cases included in the study.

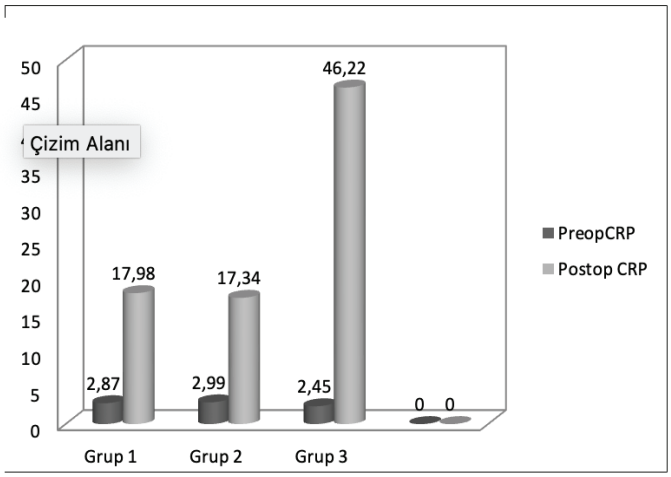

Figure 3: The mean of the CRP for cases included in the study

Table 1: The distribution age of the patients included to the study

Age	Mean± Std.Dv.	Median(Min-Max)	
Group 1	52.54±12.7	50(33-73)	*P=0.73
Group 2	54.15±13.1	52(33-74)	
Group 3	53.25±11.8	53(31-79)	

*:The test of Kruskal-Wallis
Minimum and maximum range
Std.Dv. :Standard deviation

Discussion

Surgical intervention naturally triggers the inflammatory response. This is actually the body's response to surgery-related trauma. Post-traumatic physiological orientation has always been based on the strategy of overcoming the trauma with the least damage. The euroendocrine and inflammatory response that occurs in the organism with trauma is a compensatory mechanism that develops for survival, and this response increases in direct proportion to the amount of various hormones and mediators that occur during this response, and this may show differences in response depending on the type and severity of the trauma. (17,18). Acute phase proteins that emerge in the inflammatory response are a group of proteins synthesized in the liver and whose levels change depending on infection, trauma and malignancy. These proteins include CRP, fibrinogen, C3 complement, haptoglobulin, serum amyloid A and α-1 antichymotrypsin. In post-surgical cases, CRP level is used as an indicator that can show the severity of the inflammatory response and thus the infection, and whether the response to treatment is adequate (19). The increase in CRP levels is mediated by IL-6, a proinflammatory cytokine (20). IL-6, the major regulator of the inflammatory response, is produced by

Table 2: The IL-6 mean and median values of patients included to the study

	Preoperative IL-6		Postoperative IL-6		
	Mean± Std.Dv.	**Median (Min-Max)**	**Mean± Std.Dv.**	**Median (Min-Max)**	
Group 1	6.20±9.53	2.95 (1.56-36.90)	18.6±10.8	18.6 (5.26-42.86)	**#p=0.001**
Group 2	8.62±5.11	7.62 (1.81-17.25)	23.7±19.6	18.4 (8.52-85.60)	**#p=0.001**
Group 3	4.12±3.11	2.54 (1.56-10.99)	19.1±18.1	19.1 (2.22-66.69)	**#p=0.001**
	*p=0.021		*p=0.33		

*:Kruskal-Wallis test #:Wilcoxon test

Table 3: The mean and median values of leukocytes of the patients included to the study

	Preoperative leukocyte		Postoperative leukocyte		
	Mean± Std.Dv.	Median (Min-Max)	Mean± Std.Dv.	Median (Min-Max)	
Group 1	6668.4±1892.6	7160 (4190-10280)	8855.3±3377.3	9340 (3670-15280)	**#p=0.003**
Group 2	6410.7±2041.7	6400 (3670-10170)	10459.2±3200.1	11040 (4920-16800)	**#p=0.001**
Group 3	7041.8±1811.8	7165 (4560-10440)	9948.1±2685.7	9750 (5280-15020)	**#p=0.001**
	*P=0.59		*P=0.41		

*:Kruskal-Wallis test #:Wilcoxon test

Table 4: CRP mean and median values of the patients included to the study

	Preoperative CRP		Postoperative CRP		
	Mean± Std.Dv.	**Median (Min-Max)**	**Mean± Std.Dv.**	**Median (Min-Max)**	
Group 1	2.87±2.77	1.79 (0.60-11.10)	17.98±8.65	18.29 (1.10-35.77)	**#p=0.002**
Group 2	2.99±2.49	3.10 (0.30-8.90)	17.34±14.89	13.30 (1.97-43.90)	**#p=0.001**
Group 3	2.45±2.37	1.29 (0.23-8.73)	46.22±23.84	47.14 (2.44-88.91)	**#p=0.001**
	* P=0.73		*P=0.001		

*:Kruskal-Wallis test #:Wilcoxon test

Table 5: Ki-67 mean and median values of the patients included to the study

Ki-67	**Mean± Std.Dv.**	**Median (Min-Max)**	
Group 1	21.46±15.0	30(4-40)	*P=0.37
Group 2	29.58±23.68	20(5-70)	
Group 3	32.31±24.28	38(5-80)	

*:Kruskal-Wallis test

Table 6: The mean and median tumor diameter of the patients included to the study

Tm çapı	**Mean± Std.Dv.**	**Median(Min-Max)**	
Group 1	2.22±0.58	2.10(1.50-3.0)	*P=0.08
Group 2	2.13±0.84	2.0(1.20-4.0)	
Group 3	3.23±1.67	3.10(1.0-6.70)	

*:Kruskal-Wallis test

Table 7: The mean and median values of total lymph node counts of patients included to the study

Total lymph nodes LN	**Mean± Std.Dv.**		**Median (Min-Max)**	
Group 1	2.46	1.33	2.0(1-5)	*P=0.001
Group 2	18.92	7.97	17(9-32)	
Group 3	20.10	6.45	19(12-39)	

*:Kruskal-Wallis test

Table 8: The mean and median of metastatic lymph node counts of patients included to the study

Metastatic Lymph Node Counts	**Mean± Std.Dv. SS**		**Median (Min-Max)**	
Group 1	-	-	-	*P=0.002
Group 2	5.0	10.1	1(0-31)	
Group 3	2.75	3.85	1(0-14)	

*:Kruskal-Wallis test

Table 9: The presence of estrogen receptors in patients included to the study

	(n)	**Percentage (%)**	
Group 1			
Negative	1	7.7	
Pozitive	12	92.3	
Group 2			*p=0.82
Negative	2	15.4	
Positive	11	84.6	
Group 3			
Negative	2	12.5	
Positive	14	87.5	

* :χ2 test

Table 10: The presence of progesterone receptors in patients included to the study

	(n)	**Percentage (%)**	
Group 1			
Negative	2	15.4	
Positive	11	84.6	
Group 2			*p=0.88
Negative	3	23.1	
Positive	10	76.9	
Group 3			
Negative	3	18.8	
Positive	13	81.3	

*: χ2 test

Table 11: Presence of HER-2 in patients included to the study

	(n)	Percentage (%)	
Group 1			
Negative	11	84.6	
Positive	2	15.4	
Group 2			*p=0.14
Negative	11	84.6	
Positive	2	15.4	
Gruop 3			
Negative	9	56.3	
Positive	7	43.8	

*: χ2 test

Table 12: The pathological stage distribution of the patients included to the study

	(n)	Percentage (%)	
Group 1			
pT0	1	7.7	
pT1	5	38.5	
pT2	7	53.8	
Group 2			*p=0.21
pT0	1	7.7	
pT1	6	46.2	
pT2	6	46.2	
Group 3			
pT0	6	37.5	
pT1	6	37.5	
pT2	4	25.0	

*:χ2 test

Table 13: The axillary lymph node involvement of the patients included to the study

	(n)	Percentage (%)	
Group 1			
Negative	13	100	
Positive	-	-	
Group 2			*p=0.001
Negative	5	38.5	
Positive	8	61.5	
Group 3			
Negative	6	37.5	
Positive	10	62.5	

*:χ2 test

Table 14: The lymphovascular invasion status of the patients included to the study

	(n)	Percentage (%)	
Group 1			
Negative	13	100	
Pozitive	-	-	
Group 2			*p=0.02
Negative	8	61.5	
Positive	5	38.5	
Group 3			
Negative	9	56.3	
Positive	7	43.8	

*:χ2 test

Table 15: The extracapsular invasion status of the patients included to the study with χ2 test

	(n)	Percentage (%)	
Group 1			
Negative	13	100	
Positive	-	-	
Group 2			*p=0.04
Negative	8	61.5	
Positive	5	38.5	
Group 3			
Negative	13	81.3	
Positive	3	18.7	

*:χ2 test

stimulated macrophages, monocytes, endothelial cells, and fibroblasts. It plays a central role especially in the acute phase of inflammation and tends to rise rapidly within the first few hours after surgical incision (21). It has been reported that mediators responsible for the inflammatory response, especially IL-6 and CRP, correlate with the severity and duration of trauma (21). In our study, IL-6, its induced CRP and leukocyte values were examined in order to evaluate the effects of three different surgical procedures performed for breast cancer on the inflammatory response. Lumpectomy + sentinel lymph node dissection (SLND) was performed on patients in Group 1 due to breast cancer , the patients in group 2 underwent modified radical mastectomy and for group 3; Lumpectomy + axillary lymph node dissection was performed. Post-op IL-6 levels in all three groups were higher than pre-op IL-6 values, and this difference was statistically significant ($p<0.05$). Although post-op IL-6 levels were found to be higher in patients in group 2, no statistically significant difference was found when the groups were compared with each other ($p>0.05$). However, IL-6 values in the post-op period were

found to be higher in patients in groups 2 and 3 than in patients in group 1. As mentioned before, as the severity and duration of the trauma increase, the release of proinflammatory cytokines increases in order to adapt the organism to this situation. Here, the most important points are; Along with all these general principles, it is important to apply a careful and gentle surgery, on the condition that the patient is diagnosed correctly, the stage of the disease is determined well, the most accurate choice is made according to the current surgical treatment guidelines, and the patient is informed throughout this process, and on the condition that the cancer surgery safety is the basis during the surgery. As a result; all these factors are very important in terms of alleviate this inflammatory process, which impairs its life quality. There are studies showing that the level of IL-6, the most important of these cytokines, is directly related to the duration of surgery (22). Among the surgical procedures performed, post-op IL-6 values were found to be higher in the modified radical mastectomy group with the most tissue damage and the longest operation time, and in the axillary dissection group, which is consistent with the literature. On the other hand, considering that circulating cytokines such as adipose tissue inflammation, tumor necrosis factor (TNF)-α and interleukin (IL)-6 have the potential to affect breast cancer cells systemically; Since breast tissue is a tissue rich in fat, recent studies have focused on the local effects of the inflammatory process on the adipose tissue, and the levels of these cytokines in the adipose tissue have been measured in different studies (23,24). In our study, when post-op leukocyte values were compared with pre-op leukocyte values in all three groups, post-op leukocyte values were found to be higher and this situation was statistically significant. However, when the groups were compared within themselves, no statistically significant difference was found in terms of pre-op and post-op values. Since it is the most important indicator of the microvascular inflammatory response in trauma, increased leukocyte adhesion in this region and adhesion of leukocytes to the endothelium are the main cornerstones of this inflammatory response(25). It has been shown that these events become more evident when tissues are manipulated with excessive amounts of hands and pulled with hard movements, forgetting the principle of respect for the tissue (25). As the general opinion; It is a condition that the leukocyte values are predicted to increase at first after surgery. In our study, as expected, leukocyte levels were found to be high in all three groups in thepost-op period. As is known, one of the functions of IL-6 is to stimulate the release of acute phase reactants fromhepatocytes. In our study, the increasing occur in post-op IL-6 also causes an increase to CRP. Furthemore in terms of statistically; There was found significancy different preoperative and postoperative CRP levels in all patients in each group.In addition, when post-op CRP values were compared between the groups, it was found to be higher in group 3 who underwent axillary dissection, and this was statistically significant ($p<0.05$). We can see this by adding a cut-off value. In addition, this study; It showed that the CRP values were higher in the group with the most dissection, which is consistent with the literature. HER-2 is one of the epidermal growth factor receptor family (26). When Her-2 receptors become active, they activate the signal transduction pathways in the cell, causing the cell to change and multiply. Her-2 positive breast cancer usually has high grade and proliferation rate, and hormone receptors are negative. In this group, the tumor is larger, lymph node positivity, and visceral and central nervous system metastases are more common(27). In our study, there was a strong positive correlation between Post-op IL-6 and Her-2 in group 2, and this was statistically significant ($r=0.64, p=0.02$). In other words, if Her-2 receptor was positive, IL-6 values were found to be higher. This situation causes the CRP value to be found high in Her-2 positivity with the mechanism mentioned above. This situation creates the need for dissection in our patients with positive Her-2 receptors, since axillary lymph node metastases are more common. In this regard, the inflammatory response becomes more dominant in the postoperative period. However, on the other hand; In support of this situation, no relationship was found between post-op IL-6, leukocyte and CRP values and other parameters in group 1; So it can be said very clearly that the less surgical dissection, the cause of the less the inflammatory response. Ki-67 antigen; It is a "non-histone" bimolecular complex weighing between 345 and 397 kDa. Ki-67 is a proliferation-associated nuclear antigen and is monitored throughout the cell cycle, except in the G0 phase; It is expressed in growth and synthesis phases (G1, S, G2, mitosis) (28). It is used as a marker of cell proliferation (28). Therefore, a high Ki-67 proliferation index is accepted as a negative prognostic factor. For this reason, the fact that the tumor is more likely to metastasize to lymph nodes and other organs by displaying a more aggressive behavior creates the need for axillary dissection in these patients. In support of this

information, in our study, there was a strong positive correlation between the post-op leukocyte value and Ki-67 and it was statistically significant (r=0.59 p=0.04). Similarly, there re a strong positive correlation between leukocytes and total lymph node and it is statistically significant (r=0.63 p=0.02). Extra capsular invasion, which is one of the features of the tumor, is another negative prognostic factor. This case depend on , the spread and metastasis of the tumor to the lymph node becomes more frequent as mentioned above. There is a strong positive correlation between post-op IL-6 and extra capsular invasion in the group, and this correlation is statistically significant (r=0.60 p=0.01). In case of extra capsular invasion in the tumor, the IL-6 value was found to be much higher. This indicates that the wider the surgery, the greater the inflammatory response.

Conclusion

In all surgical methods which performed for breast cancer, an inflammatory response occurs due to the severity of trauma. However, the degree of this response directly depend to the surgical procedure and duration. Of course, the characteristics of the tumor limit the surgical procedure to be performed, but in terms of reducing the mortality and morbidity that may occur in the post-operative period, it should be ensured that the oncological principles are fully implemented, but on the other hand, the applied surgery should be carefully chosen so that for the least invasive level.

Ethic

In this retrospective study, national and international ethical rules were complied with.

Conflict of Interest

No conflict of interest was declared by the authors. In addition, no financial support was received for this study.

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Araştırma Makalesi

Double-J Stentlerin Erkek Cinsel Fonksiyonu Üzerine Etkisi

The Effect of Double-J Stents on Male Sexual Function

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Öz

Amaç: Bu çalışmamızla URS/RIRS sonrası çok sık kullanılan double-J stentler'in (DJS) erektil fonksiyon üzerine etkisini araştırarak literatüre katkıda bulunmayı amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışmada, üreter ve/veya böbrek taşı nedeniyle yapılan URS/RIRS sonrası DJS uygulanan erkek hastalar yer almaktadır. Hastaların stentli iken ve stent çıkarıldıktan sonraki İİEF-5 skor değişimi ile demografik verileri, alfa blokör kullanımı, cerrahi türü, IPSS, İİEF-5, VAS skoru ve stent takılı kalma süresi univariate analiz ile değerlendirildi. p<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Dahil edilme kriterlerine uyan 75 erkek hasta istatistiksel analize dahil edildi. Alfa blokörlerden silodosin kullanan hasta grubunda İİEF-5 skor değişimi istatistiksel anlamlı yüksek saptandı (7,16 ± 7,34, p: 0,03). VKİ<25kg/m2 olan hasta grubunda, VKİ≥25 kg/m2 olan hasta grubuna göre istatistiksel anlamlı yüksek İİEF-5 skor değişimi gözlendi(p:0,04). Yaş ile İİEF-5 skor değişimi arasında <40 yaş olanlarda İİEF-5 skor değişimi ≥40 yaş olan hastalara göre istatistiksel anlamlı yüksek saptandı(p:0,006). İİEF-5 skor değişimi ile IPSS ve stent takılı kalma süresi arasında korelasyon saptanmazken(p>0,05) VAS skoru ile istatistiksel anlamlı pozitif korelasyon saptandı (r: 0,306 ve p:0,01). Stentli İİEF-5 skoru ile stent çıkarılmasından 4 hafta sonraki İİEF-5 skoru arasında istatistiksel anlamlı değişim gözlendi (15,72±6,49 ve 20,63±4,81, sırasıyla) (p<0,001).

Sonuç: DJS, erkek cinsel sağlığını geçici de olsa olumsuz etkilemektedir. Özellikle de genç, sağlıklı ve cinsel aktif popülasyonda bu etki daha belirgin olarak ön plana çıkmaktadır. DJS'nin erkek cinsel sağlığı üzerine etkilerinin daha net ortaya konulabilmesi için randomize prospektif ve daha fazla sayıda hasta ile yapılan, ayrıca hastaların ek hastalıklarıyla birlikte hormonal durumlarının da değerlendirildiği çalışmalara gereksinim olduğuna inanmaktayız.

Anahtar Kelimeler: double-j stent; iief-5; erkek cinselliği

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Abstract

Aim: In this study, we aimed to contribute to the literature by investigating the effect of double-j stent (DJS), which is frequently used after URS/RIRS, on erectile function.

Material and Methods: This retrospective study included male patients who underwent DJS after URS/RIRS for ureteral and/or renal stones. Demographic data, alpha-blocker use, type of surgery, IPSS, IIEF-5, VAS score, and the duration of stenting were evaluated by univariate analysis. p<0.05 was considered statistically significant.

Results: 75 male patients who met the inclusion criteria were included in the statistical analysis. The change in IIEF-5 score was found to be statistically significantly higher in the silodosin group among the alpha-blockers (7.16 ± 7.34, p: 0.03). A statistically significant higher IIEF-5 score change was observed in the patient group with BMI<25 kg/m2 compared to the patient group with BMI≥25 kg/m2 (p: 0.04). Between age and IIEF-5 score change, IIEF-5 score change was statistically significantly higher in patients aged <40 years than in patients aged ≥40 years (p:0.006). There was no correlation between IIEF-5 score change and IPSS and duration of stent implantation (p>0.05), while a statistically significant positive correlation was found with VAS score (r: 0.306 and p:0.01). A statistically significant change was observed between IIEF-5 score with stent and IIEF-5 score 4 weeks after stent removal (15.72±6.49 and 20.63±4.81, respectively) (p<0.001).

Conclusion: DJS has a negative, albeit temporary, effect on male sexual health. This effect is particularly pronounced in the young, healthy and sexually active population. We believe that randomized prospective studies with larger numbers of patients and evaluation of patient comorbidities and hormonal status are needed to clarify the impact of DJS on male sexual health.

Keywords: double-j stent; iief-5; male sexuality

Giriş

Ürolitiazis farklı toplumlarda %1-20, Türkiye'de ise %10-15 arasında değişen sıklıkta görülen yaygın bir antitedir[1-3]. Ürolitiazisin tedavisinde üreterorenoskopi (URS) ve retrograd intrarenal cerrahi (RIRS) gibi endoskopik girişimler sonrası, perkütan ve açık cerrahilerinin per-operatif dönemlerinde Double-J stentler (DJS) toplayıcı sistemin taş parçacıkları, pıhtı kalıntıları veya mukozal ödem sonucu obstrükte olmasını önlemek amacıyla yaygın olarak kullanılmaktadır. DJS'nin bu kadar kritik bir fonksiyonu yerine getirirken hastaların yaklaşık %80 'inde dizüri, urgency gibi alt üriner sistem semptomları (AÜSS) başta olmak üzere yaşam kalitesinde bozulma, iş performansında azalma ve cinsel fonksiyonlarda bozulma gibi birtakım olumsuz etkileri de olmaktadır[4, 5].

Cinsellik neredeyse tüm türlerde gözlenen köklü ve karmaşık bir süreçtir. Hayvanlarda cinsellik genetik, hormonal, nöronal perspektiflerden ele alınırken insanda bu faktörlere kültür ve psikolojik faktörler de eklenmektedir[6]. İnsanda cinsel arzu, uyarılma ve orgazm aşamaları benzer sıralarla kadın ve erkekte oluşsa da, fizyolojik tepkiler farklılık göstermektedir[7]. Erkek cinselliğinde uyarılma ereksiyon ile başlayıp sonrasında plato, orgazm ve rezolusyon safhalarından oluşan karmaşık nörofizyolojik, endokrin ve psikolojik süreçlerden oluşur[8]. Bu kadar karmaşık bir yapı olan cinsellik birçok faktör tarafından da doğal olarak etkilenebilmektedir.

Şimdiye kadar birçok hastalığın ve cerrahi tekniğin cinsellik üzerine etkilerini araştıran çalışmalar literatürde yaygın olarak bulunmaktadır [9-11]. Bununla birlikte, DJS'nin erkek cinsel fonksiyonları üzerine etkisini araştıran ve birbirinden farklı sonuçlar bulan literatürde kısıtlı sayıda çalışma bulunmaktadır [12, 13]. Uluslararası erektil fonksiyon indeksi-5 (İİEF-5) erkek hastaların erektil fonksiyonlarıyla ilgili beş sorudan oluşan ve uluslararası güvenilirliği gösterilmiş bir anket formudur [14]. Bu çalışmamızda İİEF-5 ekseninde DJS'nin erkek hastaların erektil fonksiyonlarına etkisini değerlendirdik. Bu çalışmamızla URS/RIRS sonrası çok sık kullanılan DJS'nin erektil fonksiyon üzerine etkisini araştırarak ve ihmal edilen bu durum hakkında farkındalık oluşturup literatüre katkıda bulunmayı amaçladık.

Gereç ve Yöntemler

Çalışmamız Helsinki Bildirgesi prensiplerine uygun olarak hazırlanmış olup 25.04.2023 tarihinde, Ankara Şehir Hastanesi Klinik Araştırmalar Etik Kurulu tarafından incelenmiş ve oy birliğiyle etik açıdan uygun görülmüştür (Etik kurul onay numarası: -E2-23-3986). Bu retrospektif çalışmada, 01.06.2022 ve 01.01.2023 tarihleri arasında üreter ve/veya böbrek taşı nedeniyle yapılan URS/RIRS sonrası DJS (4,8 F, 26 cm standart stent, poliüretandan yapılmış) uygulanan hastalar yer almaktadır. Çalışmaya dahil edilen URS prosedürleri genel anestezi altında 8/9.8 F rijit üreteroskop (Richard Wolf, Almanya), ve RIRS prosedürleri ise genel anestezi altında Karl

Storz flex X2 renoskop (Karl Storz, Almanya) ve 10 F üreter kılıfı (Plastimed Co., Türkiye) kullanılarak gerçekleştirilmiştir. Tüm hastalara ameliyat sonunda 16 F Foley üretral kateter takıldı ve bu kateterler ameliyat sonrası 1. günün sabahında çıkarıldı. Bu çalışmaya dahil edilen tüm hastalar yazılı bilgilendirilmiş onam vermiştir. Bu çalışmada cinsel olarak aktif 18 yaş üstü erkek hastalar değerlendirildi. AÜSS, hipertansiyon, diabetes mellitus, idrar yolu enfeksiyonu, nörojenik mesane disfonksiyonu, üretral darlık ve önceden ürogenital cerrahi öyküsü olan hastalar çalışma dışı bırakıldı.

Tüm hastalara ameliyat öncesi direk üriner sistem grafisi (DÜSG) ve kontrastsız taş protokollü bilgisayarlı tomografi (BT) ile görüntüleme yapılmıştır. Bazı hastalarda BT öncesinde ultrasonografi yapılmış ancak tanı kesin olmadığı için tanı BT ile desteklenmiştir. Maksimum taş boyutu BT ile ölçüldü. Hastaların post-operatif 1. gün ameliyatta yerleştirilen DJS'nin pozisyonu DÜSG ile doğrulandı. DÜSG sonrası stent pozisyonunda problem olmayan hastalar, ameliyat sonrası ilk gün taburcu edildi. Hastalara taburculuk sonrası stent çıkarılana kadar kullanılmak üzere ameliyat sonrası klinik rutin uygulaması kapsamında, alfa-blokör olarak günde bir kez oral yoldan alfuzosin 10 mg tablet (n:26), tamsulosin 0,4 mg tablet (n:12) veya silodosin 8 mg tablet (n:32) randomize sekilde reçete edildi. Ayrıca 5 hasta α-blokör kullanmak istemediği için bu hastalara α-blokör reçete edilmedi. Hastalara alerji durumları da soruldu ve böbrek fonksiyon testleri normal olanlara ameliyat sonrası bir hafta boyunca sefpodoksim 200 mg tablet 2x1 ve ağrı için gerektiğinde kullanılmak üzere diklofenak 25 mg tablet reçete edildi. Rutin klinik uygulamamızda, ek bir sorun ortaya çıkmazsa DJS'nin ameliyattan iki ile dört hafta sonra çıkarılması önerilmektedir. Hastalar DJS'in çıkarılması için geldiklerinde hastalara reçete edilen ilaçları düzenli kullanıp kullanmadıkları, ilaçlarını alırken herhangi bir yan etki görülüp görülmediği ve görülmüşse bu yan etkilerin neler olduğu sorulmuştur. Tüm hastalara DJS çıkarılmadan önce rezidüel taş parçalarını ekarte etmek için DÜSG çekildi ve problem olmayan hastalarda DJS aynı gün lokal anestezi altında 8/9.8F rijit üreteroskop (Richard Wolf, Almanya) ile çıkarıldı.

Tüm hastalardan stent çıkarılmadan bir gün önce (yani stent takılı iken) Türkçe validasyonu yapılmış İİEF-5 [15], Uluslararası Prostat Semptom Skoru (IPSS) [16] ve Vizüel Analog Skala'ya (VAS) göre ağrı skoru ve DJS çıkarıldıktan bir ay sonraki (yani stentsiz) kontrollerinde İİEF-5 formunu doldurmaları istendi. Hastaların demografik verileri, taş boyutu, stent kalma süresi, operasyon türü ve tarafı, kullandığı alfa blokör (alfuzosin, silodosin ve tamsulosin) verileri kaydedildi. Yetişkinler için Dünya Sağlık Örgütü'ne (WHO) göre fazla kilolu kabul edilen vücut kitle indeksi (VKİ) ≥25kg/m2 sınırı baz alınarak, hastalar VKİ<25 kg/m2 ve VKİ≥25kg/m2 olarak kategorize edildi[17]. Ayrıca, hastalar yaşına göre <40 yaş ve ≥40 yaş olarak kategorize edildi. Hastaların stentli iken ve stent çıkarıldıktan sonraki İİEF-5 skor değişimi ile demografik verileri, alfa blokör kullanımı, cerrahi türü, IPSS, İİEF-5, VAS skoru ve stent takılı kalma süresi univariate analiz ile değerlendirildi.

İstatistiksel Analiz

Araştırma verilerinin istatistiksel analizi için Statistical Package for Social Sciences (SPSS), sürüm 22.0 (SPSS Inc. Chicago, ABD) bilgisayar paket programı kullanıldı. Verilerin dağılımı Kolmogorov-Smirnov testi ile test edildi. Tanımlayıcı istatistikler bölümünde kategorik değişkenler sayı, yüzde olarak sunuldu. Parametrik olmayan veriler ortalama± SS olarak rapor edildi. Normallik analizinin bir sonucu olarak gruplar arasında karşılaştırmalı analiz için Mann-Whitney U ve Kruskal-Wallis Testi kullanıldı. Bağımsız değişkenler ile İİEF-5 değişimi arasındaki ilişki, Spearman's korelasyon yöntemi kullanılarak değerlendirildi. İİEF-5 skorunun stentli ve stent çıkarıldıktan sonraki karşılaştırılmasında Wilcoxon testi kullanıldı. $p<0.05$ istatistiksel olarak anlamlı kabul edildi

Bulgular

Dahil edilme kriterlerine uyan 75 erkek hasta istatistiksel analize dahil edildi. Hastaların demografik özellikleri ve verileri Tablo 1'de gösterilmiştir. Hastaların ortalama yaşı 42,31 ±11,33 yıl ve ortalama VKİ 28,32 ± 3,5 kg/m2 olarak bulundu. Hastaların ortalama IPSS skoru 9,96 ± 6,83 ve ortalama VAS skoru 4,55±2,54'tü. Hastalardan 26(%34,7)'si alfuzosin, 32(%42,7)'si silodosin, 12(%16)'sı tamsulosin kullanırken 5(%6,7)'si alfa blokör kullanmıyordu. Alfa blokör kullanan hastalardan sadece silodosin kullanan grupta 8(%25) hastada retrograd ejakülasyon yan etkisi gözlenirken diğer ilaçları kullananlarda herhangi bir yan etki bildirilmedi. Hastaların tamamı reçete edilen ilaçları tedaviyi yarıda kesmeden düzenli kullandıklarını belirtti.

İİEF-5 skor değişimi ile hastaların demografik ve klinik verileri arasındaki ilişki Tablo 2'de gösterilmiştir. Eğitim durumu ve cerrahi tipi ile İİEF-5 skor değişimi arasında istatistiksel anlamlı ilişki saptanmadı(p>0,05). Alfa blokörlerden silodosin kullanan hasta grubunda İİEF-5 skor değişimi istatistiksel anlamlı yüksek saptandı (7,16 ± 7,34, p: 0,03). VKİ<25kg/m2 olan hasta grubunda, VKİ≥25 kg/m2 olan hasta grubuna göre istatistiksel anlamlı yüksek İİEF-5 skor değişimi gözlendi(p:0,04). Yaş ile İİEF-5 skor değişimi arasında <40 yaş olanlarda İİEF-5 skor değişimi ≥40 yaş olan hastalara göre istatistiksel anlamlı yüksek saptandı(p:0,006).

Tablo 1: Hastaların Demografik ve Klinik Sonuçları	
	Ortalama± SS
Yaş, yıl	42,31 ± 11,33
<40, n(%)	39(52)
≥40, n(%)	36(48)
VKİ, kg/m2	28,32 ± 3,5
<25, n(%)	17(22,7)
≥25, n(%)	58(77,3)
Taş boyutu, mm	9,93 ± 5,31
Taraf(sağ/sol)	35/40
Eğitim durumu, n(%)	
İlk-ortaöğretim	24(32)
Lise-ön lisans	27(36)
Üniversite mezunu	24(32)
Stentli IIEF-5 skoru	15,72 ± 6,49
Stentsiz IIEF-5 skoru	20,63 ± 4,81
IPSS skoru	9,96 ± 6,83
VAS skoru	4,55 ± 2,54
URS/RIRS	57/18
Stent süresi, gün	24,13 ± 8,49
Alfa blokör, n(%)	
alfuzosin	26(34,7)
silodosin	32(42,7)
tamsulosin	12(16)
kullanmayan	5(6,7)
VKİ; vücut kitle indeksi, IIEF; international index of erectile function, IPSS; international prostate symptom score, VAS; visual analogue score; URS; ureterorenoskopi; RIRS; retrograd intrarenal cerrahi	

Tablo 2: IIEF-5 Skor Değişimi ile Demografik ve Klinik Verilerin Karşılaştırılması		
	IIEF-5 skor değişimi	p
Alfa blokör, n(%)		0,03
kullanmayan	4 ± 3,61	
alfuzosin	3,92 ± 4,76	
silodosin	7,16 ± 7,34	
tamsulosin	1,17 ± 2,37	
Eğitim durumu, n(%)		0,74
İlk-ortaöğretim	3,36 ± 5,61	
Lise-ön lisans	5,12 ± 5,41	
Üniversite mezunu	6,17 ± 7,24	
Cerrahi tipi		0,85
RIRS	6 ± 7,79	
URS	4,6 ± 5,62	
VKİ, kg/m2		0,04
<25	7,08 ± 5,16	
≥25	4,43 ± 6,27	
Yaş, yıl		0,006
<40	6,66 ± 6,3	
≥40	3,22 ± 5,55	
VKİ; vücut kitle indeksi, IIEF; international index of erectile function, IPSS; international prostate symptom score, VAS; visual analogue score; URS; ureterorenoskopi; RIRS; retrograd intrarenal cerrahi		

IPSS, VAS skoru ve stent takılı kalma süresi ile İİEF-5 skor değişimi arasında Spearman korelasyon analizi Tablo 3'te sunulmuştur. İİEF-5 skor değişimi ile IPSS ve stent takılı kalma süresi arasında korelasyon saptanmazken(p>0,05) VAS skoru ile istatistiksel anlamlı pozitif korelasyon saptandı (r: 0,306 ve p:0,01). Stentli İİEF-5 skoru ile stent çıkarılmasından 4 hafta sonraki İİEF-5 skoru arasında istatistiksel anlamlı değişim gözlendi ve Tablo 4'te sunuldu (15,72±6,49 ve 20,63±4,81, sırasıyla) (p<0,001).

Tablo 3: IIEF-5 Skor Değişimi ile IPSS ve VAS Skorunun Spearman Korelasyon Analizi		
	IIEF-5 skor değişimi	
	r	p
IPSS	0,096	0,42
VAS skor	0,306	0,01
Stent süresi, gün	-0,220	0,08
IIEF; international index of erectile function, IPSS; international prostate symptom score, VAS; visual analogue score		

Tablo 4: Stentli ve Stentsiz IIEF-5 Skorunun Değişim Analizi			
	Stentli	Stentsiz	p
IIEF-5 skoru	15,72 ± 6,49	20,63 ± 4,81	<0,001
IIEF; international index of erectile function			

Tartışma

Cinsel sağlık genel sağlığın ayrılmaz bir parçası ve tamamlayıcısıdır. Bunun yanında kaliteli bir cinsel yaşamın hastaların fizyolojik ve psikolojik durumu üzerine de olumlu etkileri olacağını gösteren çalışmalar da mevcuttur[18, 19]. Bu perspektiften birçok hastalığın yönetiminde uygulanan tedavinin hastaların cinsel fonksiyonları üzerine olan etkisi göz önünde bulundurularak bütüncül bir yaklaşım sergilenmelidir. Double-J stentler ürolojide sıkça kullanılmalarına rağmen hastalarda urgency gibi işeme semptomları, dizüri, hematuri ve yan ağrısı gibi şikayetlere neden olarak morbidite oluşturmaktadır[5]. Bunun yanında DJS'nin birçok çalışmada hastaların cinsel fonksiyonları üzerine de olumsuz etkisinin olduğu gösterilmiştir[20, 21]. Aggarwal ve ark. yaptıkları prospektif çalışmada stentli dönemde cinsel fonksiyonların stentsiz döneme göre azaldığını göstermişlerdir. Çalışmamızda hastaların stent çıkarıldıktan sonraki İİEF-5 skorunun literatürle uyumlu olarak, stentli dönemdeki İİEF-5 skoruna göre istatistiki anlamlı olacak şekilde daha yüksek olduğunu tespit ettik. Arora ve ark.'nın yaptığı randomize prospektif çalışmada da DJS çıkarıldıktan sonraki dönemde İİEF-5 skorlarının stentli döneme göre yükseldiği gösterilmiştir. Aynı çalışmada stent çıkarıldıktan yaklaşık 1 ay sonra İİEF-5 skorlarının operasyon öncesi bazal düzeylerine döndüğü gösterilmiştir[21]. Çalışmamızda hastaların

operasyon öncesi İİEF-5 değerlerine bakılmamış olmasından dolayı, bulgularımız Arora ve ark.'nın yaptığı İİEF-5 değerleri bazal seviyesine dönmüştür çıkarımını destekleyememektedir.

DJS'nin AÜSS benzeri şikayetler oluşturduğu bilinmektedir. Hatta bazı araştırmacılar DJS sonrası görülen cinsel işlev bozukluğunu AÜSS'ye bağlamışlar, bir diğer grup araştırmacı bu sava karşı çıkarak AÜSS geçse bile cinsel işlev bozukluğunun devam ettiğini göstererek bu iki durumun birbirinden bağımsız olduğunu öne sürmüşlerdir[12, 22]. DJS ilişkili AÜSS benzeri semptomların tedavisinde α-blokörler, anti-muskarinikler, beta agonistler ve fosfodiesteraz-5 inhibitörleri (PDE-5inh) gibi birçok ilaç kullanılmaktadır[4, 20]. Çalışmamızda DJS ilişkili semptomların tedavisinde silodosin kullanan grupta İİEF-5 değişimi istatistiki anlamlı olacak şekilde alfuzosin, tamsulosin kullanan ve α-blokör kullanmayan gruplara göre daha yüksek bulunmuştur. Bu sonuçta silodosin grubunda, 8 (%25) hastada görülüp diğer gruplarda gözlenmeyen retrograd ejakulasyonun önemli bir etken olabileceğini düşünmekteyiz. Aggarwal ve ark. yaptığı tamsulosin ile tadalafilin DJS ilişkili semptomlardaki etkilerini karşılaştırdıkları randomize prospektif çalışmalarında tadalafilin DJS ilişkili AÜSS'de tamsulosin kadar etkili olduğunu, ayrıca seksüel fonksiyonların tedavisinde tamsulosinden daha etkili olduğunu göstermişlerdir[20].

Eryıldırım ve ark. ile Bolat ve ark'nın çalışmamıza benzer şekilde URS/RIRS sonrası hastaların cinsel fonksiyonlarını değerlendirdikleri iki ayrı prospektif çalışmada, hastaları DJS takılan ve DJS takılmayan olmak üzere iki gruba ayırmışlar; DJS takılan grubun takılmayan gruba göre cinsel olarak daha olumsuz etkilendiğini tespit etmişlerdir[12, 23]. Bu çalışmalar da göstermektedir ki üretral yoldan yapılan bu iki cerrahinin kendisinin değil DJS'nin erektil fonksiyon üzerine olumsuz etkisi olmaktadır. DJS'in cinsellik üzerine olumsuz etkileri olsada, DJS takılı kalma süresi ile İİEF-5 skorları arasında çalışmamızda bir korelasyon saptanamamıştır. Bizim sonucumuzdan farklı olarak Sighinolfi ve ark.'nın yaptığı çalışmada ise stentli kalma süresi uzadıkça İİEF-5 skorunun azalarak olumsuz etkilendiğini göstermişlerdir. Yine aynı çalışmada DJS takılı iken AÜSS'nin önemli bir göstergesi olan IPSS skorunun da stentli kalınan süre uzadıkça yükseldiğini ve İİEF-5 skorunu olumsuz yönde etkilediğini belirtmişlerdir[24]. Bizim çalışmamızda ise Sighinolfi ve ark.dan farklı olarak IPSS ile İİEF-5 değişimi arasında bir korelasyon bulunamamıştır. Bu sonucun ortaya çıkmasında çalışmamızda hastaların IPSS değerlerinin stentin takılı olduğu dönemde elde edilmiş olmasının rolü olabilir.

Erkeklerde cinsel işlevlerin yaşla ve obezite ile olumsuz etkilendiği bilinmektedir[25]. VKİ ile İİEF-5 değişimi, DJS ile erkek cinsel fonksiyonlarının değerlendirildiği diğer çalışmalarda ele alınmamış ancak çalışmamızda İİEF-5 değişimi, fazla kilolu gruba göre, VKİ 25'in altında olan grupta istatistiki anlamlı olacak şekilde yüksek tespit edilmiştir. Benzer şekilde 40 yaş altı grupta, 40 yaş üstü gruba göre stentli dönem ile stent çıkarılmasını takip eden dönem arasında istatistiki anlamlı İİEF-5 değişimi tespit edilmiştir. Bu iki bulgu da göstermektedir ki DJS cinsel fonksiyonlarının daha iyi olacağını düşündüğümüz genç, fit erkeklerde yaşlı veya fazla kilolu erkeklere göre cinsel fonksiyonları daha olumsuz etkilemektedir. Bu sonuçta ikinci grubun zaten cinsel işlevlerinin zeminde görece daha bozuk olması yatabileceği gibi özellikle VKİ 25 üstü olan grupta DJS üzerine binen mekanik intraabdominal yükün daha fazla olmasından kaynaklanabileceği de akılda tutulmalıdır. Mosharafa ve ark. yaptıkları prospektif çalışmada, hastaların stentli dönem ile stent çıkarıldıktan sonraki dönemlerinde cinsel fonksiyonlar açısından anlamlı bir farklılık bulamamışlardır. Literatürün genel eğilimine ters olan bu sonucun ortaya çıkmasında, hasta popülasyonun görece yaşlı olmasından ve hastaların zaten %40'ında pre-operatif dönemde de erektil disfonksiyon olmasından kaynaklanabileceği düşünülmektedir.

Arora ve ark. çalışmalarında hastaların %61'inde ağrılı ereksiyon ve ejakulasyon tespit etmişlerdir. Bunun da hastaların cinsel ilişkiye girmeden kaçınma, artmış anksiyete ve azalmış İİEF-5 skoru anlamına gelebileceğini belirtmişlerdir[21]. Çalışmamızda VAS skoru ile İİEF-5 değişimi arasında istatistiki anlamlı korelasyon olduğunu tespit ettik. Buradan hareketle DJS takılı iken ağrı şiddeti ne kadar fazla ise hastaların cinsel fonksiyonlarının o derece olumsuz etkilenebileceğini düşünmekteyiz.

Çalışmamızın retrospektif olması, hastaların cinsel ilişki esnasında hissettikleri ağrının ayrıca sorgulanmamış olması, hastaların erektil fonksiyonlarını etkileyebilecek hormonal durumlarının değerlendirilmemiş olması, çalışmada sadece tek boyut ve materyalden yapılmış DJS kullanılmış olması, pre-operatif dönemde hastaların İİEF-5 değerlendirilmesinin yapılmamış olması gibi kısıtlılıkları bulunmaktadır.

Sonuç

Bu çalışmamız da göstermiştir ki DJS, erkek cinsel sağlığını geçici de olsa olumsuz etkilemektedir. Özellikle de genç, sağlıklı ve cinsel aktif popülasyonda bu etki daha belirgin olarak ön plana çıkmaktadır. Ameliyat öncesinde hastaların cinsellik konusunda bilgilendirilerek anksiyetelerinin

azaltılması ve post-operatif dönemde DJS ilişkili AÜSS ve ereksiyon problemlerinde etkinliği gösterilmiş PDE5 inhibitörü gibi ilaçların tedavi seçeneği olarak akılda bulundurulmasının faydalı olacağını düşünmekteyiz. DJS'nin erkek cinsel sağlığı üzerine etkilerinin daha net ortaya konulabilmesi için randomize prospektif ve daha fazla sayıda hasta ile yapılan, ayrıca hastaların ek hastalıklarıyla birlikte hormonal durumlarının da değerlendirildiği çalışmalara gereksinim olduğuna inanmaktayız.

Maddi destek ve çıkar ilişkisi

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

Yazarların katkıları

MEŞ: protokol/proje geliştirme, veri toplama, veri analizi ve metin yazma/düzenleme. MK: protokol/proje geliştirme, istatistiksel analiz ve taslak yazımı. EÖ: protokol/proje geliştirme, metin yazma/düzenleme. MEP: veri toplama, veri analizi ve metin yazma/düzenleme. MY: protokol/proje geliştirme, taslak yazımı. Tüm yazarlar sonuçları tartıştı ve makale yazımı hakkında yorum yaptı.

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Research Article

Assessment of serum cyanocobalamin level and importance in patients with hematological malignancies

Hematolojik malignitesi olan hastalarda serum siyanokobalamin düzeyi ve öneminin değerlendirilmesi

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ABSTRACT

Aim: In our study, we planned to investigate the effect of serum cyanocobalamin (Vitamin B12) levels at the time of diagnosis in patients with various hematological malignancies.

Material and Methods: Two hundred and one patients between 18-75 years old diagnosed with various hematological malignancies and 30 healthy controls applying to outpatient and inpatient clinics of Hematology Department in Necmettin Erbakan University Meram Faculty of Medicine between 2010-2014 years were included in the study. Demographic and clinical data and laboratory findings of the patients included in the study were recorded retrospectively.

Results: A total of 231 patients, 132 men (57.1%) and 99 women (42.9%), were included in our study, of which 201 were patients and 30 were healthy controls. The mean serum vitamin B12 concentration of all patients was found as 344.9 ± 279.0 pg/mL. When vitamin B12 levels were analyzed according to diagnostic groups, it was found to be highest in CML (596.0 ± 428.3 pg / mL) and ALL (524.5 ± 442.6 pg / mL) patients and lowest in AML patients (240.9 ± 178, 0 pg / mL); the difference was statistically significant (p <0.001). Vitamin B12 levels of diagnostic groups were found to have no significant effect on survival.

Conclusion: Cyanocobalamin levels were found to be high in patients with hematological malignancies, especially in CML patients. A high level of cyanocobalamin may be helpful in prediction of CML, however prospective studies are required to support this finding.

Keywords: cyanocobalamin, CML, ALL,AML, Vitamin B12

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ÖZ

Amaç: Çalışmamızda farklı hematolojik maligniteleri olan hasta gruplarında tanı anındaki serum siyanokobalamin (Vitamin B12) düzeylerinin tanıları ön görmede etkisini araştırmayı planladık..

Gereç ve Yöntemler: Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hematoloji poliklinik ve kliniğine 2010-2014 yılları arasında başvurmuş olan 18-75 yaş arası hematolojik malignite tanısı almış olan 201 hasta ve 30 sağlıklı kontrol grubu çalışma kapsamına alındı. Çalışma kapsamına dahil edilen hastaların demografik, klinik ve laboratuar verileri retrospektif olarak kayıt altına alınmıştır.

Bulgular: Çalışmamıza 132'si erkek (%57,1) ve 99'u kadın (%42,9) olmak üzere toplam 201 hasta ve 30 sağlıklı kontrol grubu olmak üzere 231 kişi dahil edildi. Tüm hastaların ortalama serum Vitamin B12 konsantrasyonu 344,9±279,0 pg/mL olarak gözlendi. Tanı gruplarına göre Vitamin B12 düzeylerinin değerlendirmesinde ise; KML (596,0±428,3 pg/mL) ve ALL (524,5±442,6 pg/mL) hastalarında en yüksek, AML (240,9±178,0 pg/mL) hastalarında ise en düşük olduğu ve bu farklılığın istatistiksel olarak anlamlı olduğu gözlendi ($p<0,001$). Hastalık gruplarının Vitamin B12 düzeylerinin sağ kalım üzerine anlamlı fark saptanmamıştır.

Sonuç: Hematolojik malignitesi olan hastalarda ve özellikle KML hastalarında siyanokobalamin düzeyi yüksek bulunmuştur. KML hastalığının tanısı için yüksek siyanokobalamin düzeyi hastalığı ön görmede yardımcı olabilir ancak bunun prospektif çalışmalarla deseklenmesi gerekmektedir.

Anahtar Kelimeler: siyanokobalamin, KML, ALL,AML, Vitamin B12

Introduction

The historical process of cyanocobalamin goes back to the first studies in dogs with anemia in 1925 [1]. It has been reported in the literature that vitamin B12 may be associated with malignancies in people with high levels of vitamin B12 analyzed for any reason [2, 3]. Furthermore, there are studies reporting an increase in serum cobalamin levels in patients with liver cancer, some solid tumors, and various hematological malignancies [4-9]. There is no study evaluating serum cyanocobalamin levels in hematological malignancies in our country. In this study, we wanted to evaluate the importance of serum cyanocobalamin level analysis at the time of diagnosis in patients with various hematological malignancies.

Material and Methods

Two hundred and one patients between 18-75 years old applying to outpatient and inpatient clinics of Hematology Department in Necmettin Erbakan University Meram Faculty of Medicine between 2010-2014 years and diagnosed with various hematological malignancies including Acute Lymphoblastic Leukemia (ALL), Acute Myeloblastic Leukemia (AML), Chronic Lymphocytic Leukemia (CLL), Chronic Myelocytic Leukemia (KML), Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), Multiple Myeloma (MM), Myelodysplastic Syndrome (MDS) and Polycythemia Vera (PV), were included in this study. The data of the newly diagnosed patients with above-mentioned diagnosis groups were investigated via retrospective screening of hospital automation system and, the patients whose vitamin B12 levels were analyzed at the time of diagnosis were included in the study. Patients using cyanocobalamin preparations in the recent year or diagnosed with a disease leading to malabsorption defect (gastrectomy, inflammatory bowel disease, etc.) or having vegetarian diet habits were excluded from the study. Thirty healthy individuals with no known chronic disease or anemia or neurological complaints were included in the study as the control group. The normal range for serum cyanocobalamin level was accepted as 126.5-505 pg/mL considering the reference range used by the laboratory of our hospital.

Statistical Analysis

The numerical data of the study were shown as mean values and standard deviations. Categorical data were summarized as percentages. Numerical data comparisons between genders were performed with Mann-Whitney U test, and comparisons between diagnostic groups were performed with Kruskal-Wallis test. Mann-Whitney U test was used for pairwise comparisons in post hoc analysis in case of difference as the result of Kruskal-Wallis analysis and, Bonferroni correction was performed for significance assessment. All statistical analyzes of the study were performed bidirectionally with the assumptions of 5% Type-I error and 80% study power. SPSS 21 (IBM Inc, USA) software was used for the analyses.

Compliance with Ethical Standards:All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for this cross-sectional study was granted by Necmettin Erbakan University Faculty of Medicine Ethics Committee This study was produced from the internal medicine thesis of Dr. Esra Zeynelgil.

Results

A hundred and thirty-two men (57.1%) and 99 women (42.9%) were included in our study, of which 201 were patients and 30 were healthy controls. The serum vitamin B12 levels at the time of diagnosis and numerical and demographic data of the patients are shown in the table (Table-1). Vitamin B12 levels were found as 596.0 pg/mL (± 428.3) in CML patients, 240.9 pg/mL (± 178.0) in AML patients, 280.8 pg/mL (± 262.9) in CLL patients, 216 pg/mL (± 164.3) in MDS patients.

Table-1. Demographic features and B12 levels of patients

	ALL (n:13)	AML (n:26)	HL (n:20)	KLL (n:30)	KML (n:20)	MDS (n:16)	MM (n:16)	NHL (n:43)	PV (n:17	Kontrol (n:30
Age Mean	52,1±11,5	53,5±19,5	52,1±14,5	62,2±8,8	62,2±11,2	67±11,1	67±1,1	57,1±16	52,2±14,9	40,3±14,5
Gender										
Male	8 (%62)	15 (%58)	9 (%45)	24 (%80)	8 (%40)	9 (%57)	9 (%57)	25 (%59)	15 (%89)	10 (%34)
Female	5 (%38)	11 (%42)	11 (%55)	6 (%20)	12 (%60)	7 (%43)	7 (%43)	18 (%41)	2 (%11)	20 (%66)
B12 range (pg/mL)	524,5±442,6	240,9±178,0	338,1±196,0	280,8±262,9	596,0±428,3	216±164,3	295,1±138,9	370,3±332,2	331,7±167,2	324,4±107,1
Final Situation										
Alive	3 (%23)	15 (%58)	17 (%85)	21(%70)	12 (%60)	13 (%82)	13 (%82)	26 (%60)	17 (%100)	30 (%100)
Ex	10(%77)	11 (%42)	3 (%15)	9 (%30)	8 (%40)	3 (%18)	3 (%18)	17 (%40)	0 (%0)	0 (%0)

The results of statistical analyses revealed that vitamin B12 levels showed a significant difference between diagnostic groups ($p < 0.001$). Post-hoc analysis results performed for determination of factors causing the difference revealed that vitamin B12 levels were highest in the CML and ALL groups followed by the PV and healthy control groups and, the levels were similar in the other diagnostic groups but lower than those groups. The p values obtained by comparing B12 median levels of the disease groups with the control group are presented in Table-2. It may be stated that there is a statistically significant difference between B12 levels of the control group and the diagnostic groups including AML, CLL, CML and MDS diseases.

Table-2. Comparison of the disease groups with the B12 medians and the median of the control group

No	Hastalık Grupları	Kontrol ile Karşılaştırma Sonucu p Değeri
1	ALL	0.552
2	AML	0.009
3	HL	0.394
4	KLL	0.006
5	KML	0.013
6	MDS	0.002
7	MM	0.460
8	NHL	0.166
9	PV	0.698

Discussion

Vitamin B12 is a water-soluble vitamin involved in lipid, carbohydrate and protein metabolisms [10]. Vitamin B12 has a wide reference range in the literature varying between 200-700 pg/mL, but a specified reference range has not been reported in studies. Diagnostic sensitivity and specificity of plasma cobalamin levels below 400 pg/mL is limited [11]. Therefore, B12 deficiency cannot be excluded at levels below 400 pg/mL and signs and symptoms of deficiency may be detected even in normal reference range [12]. In our study, the reference range accepted by the laboratory of our hospital, 126.5-505 pg/mL, was determined as the lower and upper limits for vitamin B12.

High serum levels of B12 were shown to be likely associated with kidney failure, carcinoma, hematological malignancies such as acute and chronic leukemias, polycythemia vera, hypereosinophilic syndrome, cirrhosis, hepatitis, hepatocellular carcinoma and metastatic liver tumors in studies conducted on clinical reflections of changes in vitamin B12 levels [13-17].

According to our results, vitamin B12 levels were in the normal range in 69.2% of patients with hematological malignancies, while 11.9% were below and 18.9% were above normal limits. The main reason of significantly lower vitamin B12 levels in patients with AML, CLL and MDS compared to the control group is the physiological role of vitamin B12 in DNA methylation and increased consumption in these patient groups. The highest vitamin B12 level was determined in CML patients. It was reported in some studies that the reference range of vitamin B12 might increase up to ten times in CML patients [18, 19]. Possible cause of this situation is the increase in leukocyte-induced haptocorrin production due to increasing number of leukocytes.

In the literature, high serum vitamin B12 levels were reported to result from various mechanisms. Elevation of serum plasma transcobalamin I/III, also called as haptocorrin, which is a carrier protein synthesized by myeloid cells, hepatic cells and other cell types in the body, may be due to increased hepatic cytolysis, decreased vitamin B12 clearance in the liver, accumulation in peripheral tissues as a result of decreased production of transcobalamin II in the liver or secondary effects resulting from therapeutic applications [20]. Besides these, circulating cobalamin-binding proteins and antibodies have also been reported to cause high plasma cobalamin levels [21, 22]. In a study conducted by Chiche et al., serum vitamin B12 levels exceeding 1275 pg/mL were reported to have a strong and statistically significant relationship with hematological malignancies and, a detailed etiology analysis was recommended especially in patients with elevated serum vitamin B12 [3].

Conclusion

In conclusion, it was determined that the serum vitamin B12 level at the time of diagnosis may be beneficial in patients likely to be diagnosed with CML. Useful results may be obtained by studies with larger patient population in other hematological malignancy groups.

Declaration of conflict of interest

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Research Article

Real-life data of pazopanib usage in soft tissue sarcoma

Yumuşak doku sarkomunda pazopanib kullaniminin gerçek yaşam verisi

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Abstract

Aim: Soft tissue sarcomas are heterogeneous group of malignancies consisting of more than 50 subtypes. Although it is rare, it is usually resistant to chemotherapy and has a poor prognosis. In this study, we planned to investigate the efficacy, tolerability and side-effect profile of pazopanib in metastatic soft tissue sarcomas.

Material and Methods: Our study was a single-center retrospective study and included metastatic patients over the age of 18 who were treated with pazopanib. Data of 37 patients were obtained in retrospective medical records. In patients using pazopanib; tumor location, histological subtype, tumor grade, disease stage, the line at which pazopanib was used, efficacy, tolerability, and side-effect profile of pazopanib were examined.

Results: The mean age of the patients at the time of diagnosis was 49 years. Pleomorphic sarcoma was the most common subtype. The progression-free survival (PFS) of patients after first-line therapy was 18 weeks. The median overall survival (OS) of the patients was 20 months. The median PFS with pazopanip was 18 weeks. Any degree of thrombocytopenia was observed in 4 (10.8%) patients using pazopanib, any degree of anemia was observed in 18 (48.6%) patients, and any degree of neutropenia was observed in 7 (18.9%) patients. Hypothyroidism was observed in 5 (13.5%) patients using pazopanib, and hepatic dysfunction of any degree was observed in 10 (27%) patients.

Conclusion: The use of pazopanib in soft tissue sarcoma was found to be effective in terms of both PFS and OS. Side effects were tolerable and treatable. In our study, PFS of 32 weeks was obtained in patients with hypothyroidism and 16 weeks in patients without. In this respect, the development of hypothyroidism may be a predictive parameter for response.

Keywords: sarcoma, pazopanib, hypothyroidism, side effect

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Öz

Amaç: Yumuşak doku sarkomu 50'den fazla alt sınıftan oluşan heterojen bir malignite grubudur. Nadir görülmekle birlikte genellikle kemoterapiye dirençli olup, prognozu kötüdür. Çalışmamızda metastatik yumuşak doku sarkomlarında pazopanib kullanımının etkinliği, tolerabilitesi ve yan etki profilini araştırmayı planladık.

Gereç ve Yöntemler: Çalışmamız tek merkezli retrospektif bir çalışma olup, metastatik olan ve pazopanib alan 18 yaş üstü hastalar dahil edildi. Geriye yönelik dosya taramasında toplam 37 hastanın verisine ulaşıldı. Pazopanib kullanan hastalarda; tümörün yerleşim yeri, histolojik alt tipi, tümör derecesi, hastalığın evresi, pazopanibin hangi basamakta başlandığı, pazopanibin etkinliği, tolerabilitesi ve yan etki profili incelendi.

Bulgular: Hastaların tanı sırasında ortalama yaşı 49 idi. Pleomorfik sarkom en sık görülen alt tip idi. Birinci basamak tedavi sonrası hastaların progresyonsuz sağ kalımı (PFS) 18 hafta idi. Hastaların genel sağ kalımı (OS) 20 ay bulundu. Pazopanib ile ortanca PFS 18 hafta olarak saptandı. Pazopanib kullanan hastaların 4'ünde (%10,8) hastada herhangi bir derecede trombositopeni, 18 (%48,6) hastada herhangi bir derecede anemi ve 7 (%18,9) hastada herhangi bir derecede nötropeni gözlendi. Pazopanib kullanan 5 (%13,5) hastada hipotiroidi, 10 (%27) hastada herhangi bir derecede karaciğer fonksiyon bozukluğu gözlendi.

Sonuç: Yumuşak doku sarkomunda pazopanib kullanımı hem PFS hem OS açısından etkin bulundu. Yan etkiler tolere edilebilir ve tedavi edilebilir yan etkilerdi. Çalışmamızda hipotiroidi gelişen hastalarda 32 hafta, gelişmeyelerde ise 16 haftalık bir PFS elde edildi. Bu açıdan hipotiroidi gelişim yanıt için bir prediktif parametre olabilir.

Anahtar kelimeler: sarkom, pazopanib, hipotiroidi, yan etki

Introduction

Sarcomas are a group of heterogeneous, malignant tumors originating from mesenchyme and constitute approximately 1% of adult malignancies (1,2). Around 80% of sarcomas originate from soft tissue while the remaining originate from the bone (1). The most common types of sarcoma include liposarcoma, leiomyosarcoma, undifferentiated pleomorphic sarcoma, gastrointestinal stromal tumors and synovial sarcoma (3,4). Histological grade has prognostic importance in sarcomas; histological grading is performed according to differentiation, mitotic activity and necrosis rate of the tumor (5,6). In sarcoma cases with local disease at diagnosis, primary treatment is R0 resection which provides a safe surgical limit (7). Post-surgery radiotherapy (RT) and adjuvant - neoadjuvant chemotherapy may be added to the treatment depending on the tumor characteristics, tumor size and grade (8). Anthracycline-based chemotherapy is recommended as first-line therapy in patients with metastatic disease (9). Pazopanib, a multityrosine kinase inhibitor, is used in non-liposarcoma soft tissue sarcomas progressing after chemotherapy.

Pazopanib is a multityrosine kinase inhibitor which inhibits vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, VEGFR-3, platelet-derived growth factor (PDGFR) -α -β, fibroblast growth factor receptor (FGF)-1, FGF-3 and KIT (10). In pre-clinical studies, pazopanib was demonstrated to reduce angiogenesis and growth by inhibiting these growth factors (11). The method of administration and standard dose of pazopanib is 800 mg/day via oral route. In a study comparing pazopanib with placebo, it was observed that pazopanib was superior with a progression-free survival (PFS) of 4.6 months compared to 1.6 months with placebo (12). The most common side effects associated with pazopanib are predisposition to thrombosis, hypertension, bleeding, proteinuria, hypothyroidism, hepatotoxicity, cardiac toxicity, depigmentation and gastrointestinal irritation (13). Since pazopanib is eliminated through hepatic metabolism by CYP3A4, medicinal products that induce and inhibit CYP3A4 should be avoided.

In our study, we planned to investigate the efficacy, tolerability and side-effect profile of pazopanib use in non-liposarcoma soft tissue sarcomas. In patients using pazopanib; The location of the tumor, histological subtype, tumor grade, disease stage, the series in which pazopanib was used, the efficacy, tolerability and side-effect profile of pazopanib were examined.

In this study, the use of pazopanib in soft tissue sarcoma was found to be effective in terms of both PFS and OS. Side effects were tolerable and treatable. In the study, PFS of 32 weeks was obtained in patients with hypothyroidism and 16 weeks in patients without hypothyroidism. In this respect, the development of hypothyroidism may be a predictive parameter for response.

Material and Methods

It is a retrospective, single-center study including patients with metastatic soft tissue sarcoma who started to receive pazopanib in Dicle University Faculty of Medicine, Medical Oncology Outpatient Clinic between February 2015 and October 2018. The data of 37 patients were obtained by retrospective chart review in the study. The patients with non-liposarcoma soft tissue sarcoma between the ages 18-85 who were treated with pazopanib were included in this study. Patients with a subtype of liposarcoma, patients with secondary malignancies, and patients younger than 18 years and older than 85 years were excluded from the study. In patients diagnosed with non-liposarcoma soft tissue sarcoma who are receiving pazopanib; tumor localization, histological subtype, tumor grade, disease stage, treatment line in which pazopanib was used, the efficacy, tolerability and side effect profiles of pazopanib were investigated. Patients started to receive treatment at a standard dose of 800 mg/day. In cases where a side effect was developed, the dose was reduced to 200-400 mg/day. Tumor sizes were investigated using systemic imaging methods performed every three months in order to evaluate the efficacy of pazopanib. Response status was evaluated according to RECIST 1.1, and progression-free survival (PFS) and overall survival (OS) were calculated. The time from the starting date of pazopanib to the date of disease progression or death from any cause was calculated as PFS while the time from the starting date of pazopanib to death from any cause was calculated as OS. This study was granted ethical approval by Non-Interventional Clinical Trials Ethics Committee of Gazi Yasargil Training and Research Hospital (date and number of decision: 04.07.2019-324) and carried out in accordance with the principles of Declaration of Helsinki.

Statistical Analysis

Kaplan-Meier test was used to estimate the progression-free survival (PFS) and overall survival (OS) of pazopanib, and the variables were compared using the log-rank test. Descriptive statistics for variables were presented as mean, standard deviation, and minimum and maximum values. Categorical variables were expressed as numbers and percentages. Chi-square test was performed for categorical variables to find differences between groups. For numerical data, mean data were used for normally distributed values and median data were used for non-normally distributed values, while in independent data sets with non-normally-distributed numerical values, Mann-Whitney U test was used for the difference between two groups and Kruskall-Wallis test was used if there are more than two groups. For numerical data with normal distribution, Student T test was performed if there are two groups and ANOVA test was performed if there are more than two groups in independent data sets. Statistical significance level was set to 5% in the calculations. SPSS (IBM, version 18.0, USA) statistical software package was used for the analysis of our study.

Results

The mean age of the patients included in our study was 49.3 years (18.8 - 80.2) at diagnosis. Among all patients, 24 were female and 13 were male. The most frequently observed subtypes were pleomorphic sarcoma 35.1% (13/37) and leiomyosarcoma 32.4% (12/37). When the cases were evaluated in terms of grade, 37.8% (14/37) of the patients had grade 4, 29.7% (11/37) of the patients had grade 3 and 21.6% (8/37) of the patients had grade 2 disease. At diagnosis, the disease stage was determined as stage 4 in 45.9% (17/37) and stage 3 in 35.1% (13/37) of the patients. General characteristics of the patients were shown in Table 1. A total of 3 patients (8.1%) received neoadjuvant chemotherapy and 10 patients (27.2%) received adjuvant chemotherapy. In the first-line therapy of metastatic stage disease, 16 patients received IMA (ifosfamide + mesna + adriamycin), 11 patients received docetaxel + gemcitabine and 6 patients received pazopanib. The median progression-free survival (PFS) of the patients receiving first-line therapy was 18 weeks (14-21 weeks) (figure 1 A) while the PFS was 19 weeks (figure 1 B) for 28 patients receiving second-line therapy. Overall survival (OS) of the patients was calculated to be 20 months (4.3-25.6 months) (figure 1 C). The med ian duration of pazopanib treatment was 16.7 weeks (1 -164.2 weeks).

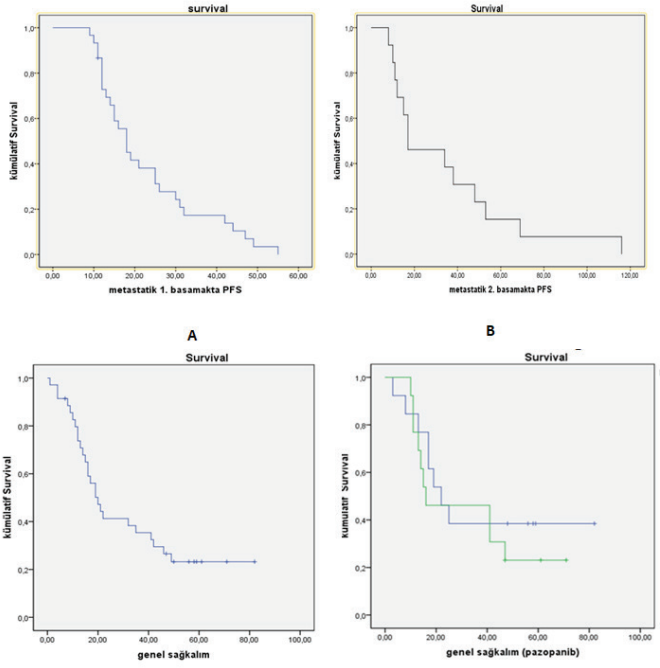

Figure 1: Overall survival and progression-free survival values of the patients

A: Progression-free survival for 1st-line therapy in patients with metastatic disease

B: Progression-free survival for 2nd-line therapy in patients with metastatic disease

C: Overall survival of all patients

D: Comparison of overall survival for pazopanib given as 2rd vs. 3rd-line of therapy

Table 1: Patient characteristics

Patient characteristics (n:37)		
	Number (n)	Percentage (%)
Gender		
Female	24	64.9
Male	13	35.1
Histological subtypes		
Pleomorphic sarcoma	13	35.1
Leiomyosarcoma	12	32.4
Fibrosarcoma	4	10.8
Synovial sarcoma	3	8.1
Other types	5	13.5
Primary tumor location		
Extremities	15	40.5
Head and neck	1	2.7
Abdomen	15	40.5
Thorax	6	16.2
Grade		
Grade 2	8	21.6
Grade 3	11	29.7
Grade 4	14	37.8
Unknown	4	10.8
Stage at diagnosis		
Stage 2	7	18.9
Stage 3	13	35.1
Stage 4	17	45.9
Line of treatment in which pazopanib was given		
1st line	1	2.7
2nd line	18	48.6
3rd line	14	37.8
4th line	4	10.8
Response to pazopanib		
Partial regression	7	18.9
Stable disease	7	18.9
Progression	19	51.4
Not evaluable	4	10.8
Dose reduction		
No	32	86.5
Yes	5	13.5

Among all patients receiving pazopanib, 18 (48.6%) had stage 2 disease, 14 (37.8%) had stage 3 disease and 4 (10.8%) had stage 4 disease at diagnosis. The median PFS was detected to be 18 weeks with pazopanib. According to tumor grade, PFS was 17 weeks in grade 2 tumors, 19 weeks in grade 3 tumors, 13 weeks in grade 4 tumors and there was no statistical difference between the groups in patients with pazopanib administered(p>0.05) . The PFS was 32 weeks in patients who developed hypothyroidism and 16 weeks in patients who did not develop hypothyroidism. The treatment of pazopanib either in second or third-line therapy did not make difference to overall survival (figure 1D). The median OS was 22 months in patients receiving pazopanib who had stage 2 disease at time of diagnosis while it was 16 months in patients with stage 3 disease (p>0.05) at time of diagnosis. Likewise, the median PFS was 19 weeks in patients receiving pazopanib who had stage 2 disease at diagnosis and then had metastasis while it was 12 weeks in patients with stage 3 disease (p>0.05). During pazopanib use, a total of 22 (59.4%) patients had a history of proton pump inhibitor (PPI) use, 14 (37.8%) patients did not have a history of PPI use. While using pazopanib, any degree of thrombocytopenia was observed in 4 (10.8%) patients, any level of anemia was observed in 18 (48.6%) patients and any level of neutropenia was observed in 7 (18.9%) patients. Hypothyroidism was developed in 5 (13.5%) patients while using pazopanib. Any degree of hepatic dysfunction was observed in 10 (27%) patients, increased bilirubin levels in 11 (29.7%) patients and increased creatinine levels in 5 (13.5%) patients.

Pazopanib dose was reduced in 4 patients as part of our study. Pazopanib dose was reduced in two patients due to cardiac failure, one patient due to hypertension and one patient due to diarrhea.

Discussion

In phase 3 PALETTE study pazopanib was compared with placebo,while PFS was 1.6 months in the placebo arm it was 4.6 months in the pazopanib arm (12). In another study PFS was 3 months in patients who received pazopanib (14). In our study, the PFS was calculated to be 18 weeks and found to be consistent with the literature. It is known from previous studies that patients who developed hypothyroidism due to pazopanip usage had better treatment responses than who did not develop hypothyroidism(15). In our study, PFS was 32 weeks in patients who developed hypothyroidism and 16 weeks in those who did not develop hypothyroidism and there was a significant numerical superiority. In a study performed by Mannavola et al (16), it was detected that the inhibition of iodine intake was associated with the etiology of hypothyroidism induced by tyrosine kinase inhibitors and the mechanism of tyrosine kinase inhibitors to develop hypothyroidism is not entirely known (17). We think that it may be used in the future as a predictive parameter for pazopanib response in patients who develop hypothyroidism compared to those who do not.

The most common side effects were fatigue (65%), diarrhea (58%), nausea (54%), weight loss (48%) and hypertension (41%) in PALETTE study while the most common side effects were anemia (48.6%), hepatic dysfunction (29.7%) and neutropenia (18.9%) in our study. Abnormal hepatic function test is a common side effect observed with pazopanib use (18). In our study, any degree of hepatic dysfunction was observed in 11 patients (29.7%), which is consistent with the literature.

Since impaired hepatic function test is a common side effect, routine hepatic function tests and follow-ups should be performed in patients while using pazopanib.

Since clinical studies were conducted in selected patient groups, the results obtained here should be supported by real-life data. Our study had some limitations such as being single-center, retrospective design, and small number of patients. Due to the small number of patients, subgroup analyzes could not be performed sufficiently. Another limitation of the study is that it was not randomized due to the retrospective nature of the study and the small number of patients. The efficacy and safety of pazopanib should be evaluated as part of multicenter, prospective studies.

Conclusion

Soft tissue sarcomas are a heterogeneous group of malignancies and treatment options are limited. In our single-center, observational study investigating the efficacy of pazopanib in soft tissue sarcomas, pazopanib was found to be effective. In our study, pazopanib showed similar features with other clinical studies in terms of efficacy and side-effect profile. No life-threatening side effects were observed with the use of pazopanib. Side effects associated with pazopanib were acceptable and manageable compared to standard chemotherapies. The development of hypothyroidism associated with pazopanib use may be a predictive marker for response.

Ethics approval

This study was granted ethical approval by Non-Interventional Clinical Trials Ethics Committee of Gazi Yasargil Training and Research Hospital (date and number of decision: 04.07.2019-324) and carried out in accordance with the principles of Declaration of Helsinki.

Conflict of interests

Authors have declared no conflict of interest for this article.

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The authors declared that they received no financial support for this study.

Authors' contributions

O. K. and Y.S. in concept and design, S. İ. and H. Y. in collecting and processing data, M.Ü. in literature screening.

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Research Article

Acil servise başvuran Covid-19 hastalarında mukosiliyer klirensin incelenmesi

Evaluation of Mucociliary Clearance in COVID-19 Patients Presenting to the Emergency Department

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Öz

Amaç: Solunum yolu epitelinde yer alan mukosiliyer tabaka, solunum yollarındaki ilk koruma mekanizması olarak görev yapmaktadır. Şiddetli akut solunum sendromu koronavirus-2 de (SARS-Cov-2), diğer bazı solunum yolu virüsleri gibi siliyer hücrelere yapışmakta ve mukosilier aktiviteyi etkilemektedir. Sakkarin testi ile mukosilier klirensin ölçülmesi mümkündür. Çalışmamızda acil servise başvuran hastalarda SARS-CoV 2 ye bağlı olarak gelişen Korona virus hastalığı-2019 (COVID-19) enfeksiyonunda erken dönemde mukosiliyer klirensin etkisini değerlendirmeyi amaçladık

Gereç ve Yöntemler: Acil servise başvuran ve son 48 saat içerisinde COVID-19 düşündüren yakınmaları olan ve Polimeraz zincir reaksiyonu (PCR) testi çalışılan 84 kişilik hasta grubunda mukosilier klirens zamanı (MCT), sakkarin testi ile ölçülerek sağlıklı gönüllülerde yapılan ölçüm ile karşılaştırılmıştır.

Sonuçlar: PCR pozitif olarak tespit edilen katılmcılarda ortalama MCT 14.58 dakika olarak, sağlıklı gönüllülerde ise ortalama MCT 13,72 dakika olarak ölçüldü. İki grup arasında istatistiksel açıdan fark saptanmadı (p=0,657).

Tartışma: COVID-19 etkeni olan SARS-CoV-2'nin solunum yolu epiteli hasarı yaptığı ve solunum yollarında hastalık oluşturduğu bilinmektedir. Erken dönemde yapılan PCR testlerinde üst solunum yolu mukozasında tespit edilmekle beraber, erken dönemde MCT üzerine etkisi bulunmamaktadır.

Anahtar Kelimeler: COVID-19; Mukosiliyer klirens; sakkarin testi

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Abstract

Aim: The mucociliary layer in the respiratory epithelium acts as the first protective mechanism in the respiratory tract. Severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2) also adheres to ciliary cells and affects mucociliary activity, like some other respiratory viruses. It is possible to measure mucociliary clearance with the saccharine test. In our study, we aimed to evaluate the effect of mucociliary clearance in the early period of Corona virus disease-2019 (COVID-19) infection due to SARS-CoV 2 in patients admitted to the emergency department.

Material and Methods: Mucociliary clearance time (MCT) was measured with the saccharin test and compared with the measurement made in healthy volunteers in a group of 84 patients who applied to the emergency department and had symptoms suggestive of COVID-19 in the last 48 hours and whose Polymerase chain reaction (PCR) test was studied.

Results: Mean MCT was measured as 14.58 minutes in PCR positive participants and 13.72 minutes in healthy volunteers. There was no statistical difference between the two groups (p=0.657).

Conclusion: It is known that SARS-CoV-2, which is the cause of COVID-19, causes respiratory tract epithelial damage and causes diseases in the respiratory tract. Although it is detected in the upper respiratory tract mucosa in early PCR tests, it is thought to have no effect on MCT in the early period.

Keywords: COVID-19; Mucociliary clearance; saccharine test

Giriş

2019 yılı sonunda Çin'in Wuhan eyaletinde görülen ve hızla yayılarak bir pandemiye yol açan, Koronavirüs ailesinden SARS-Cov-2 nin sebep olduğu COVID-19 ciddi bir hastalık tablosuna yol açmaktadır (1). Hastalığa neden olan bu ajanın siliyer kayıp ve pulmoner epitel hasarına neden olduğu bilinmektedir (2).

Mukosiliyer sistem mukus ve siliadan oluşan iki birimden oluşmaktadır ve iki yapının ortak etkisi olan mukosilier klirens, bir savunma mekanizması olarak bazı solunum sistemi hastalıklarının patofizyolojisinde önemli bir yer tutmaktadır. Solunum yolu epitelinde yer alan mukosiliyer tabaka, solunan havadaki partikülleri uzaklaştırmakta ve solunum yolundaki viral enfeksiyonlara karşı ilk koruma mekanizması olarak görev yapmaktadır. Koronavirüslerde, diğer bazı solunum yolu virüsleri gibi siliyer hücrelere yapışmakta ve mukosilier aktiviteyi etkilemektedir (3, 4).

Havayollarında mukosilier taşımayı incelemek için radyoaerosoller kulanılabilir ancak dünya genelinde sınırlı merkezde bu inceleme yapılabilmektedir (5). Bunun yanında mukosilier klirens (MCC) çalışmalarında basit uygulanabilen, noninvaziv, düşük maliyetli bir test olarak Sakkarin testi yaygın olarak kullanılmaktadır (6, 7).

Çalışmamızda acil servise başvuran hastalarda SARS-CoV 2 ye bağlı olarak gelişen COVID-19 enfeksiyonu gelişiminde üst ve alt solunum yolu bağışıklığında kritik bir rolü bulunan mukosiliyer klirensin etkisini değerlendirmeyi amaçladık

Gereç ve Yöntemler

Acil servise ayaktan başvuran ve son 48 saat içerisinde COVID-19 düşündüren yakınmaları olan ve PCR testi çalışılan 84 kişilik hasta grubunda (Grup 1) mukosilier klirens zamanı (MCT), sakkarin testi ile ölçülerek sağlıklı gönüllülerde (Grup 2) yapılan ölçüm ile karşılaştırılmıştır. Çalışma prospektif olarak planlanmıştır. Bu çalışma Sağlık Bilimleri Üniversitesi Dr.Abdurrahman Yurtaslan Ankara Onkoloji Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu tarafından 2020-09/787 Karar No ile onaylanmış ve Helsinki İlkeler Deklerasyonuna uygun şekilde gerçekleştirilmiştir.

Çalışmaya 18-65 yaş arası hasta ve gönüllüler dahil edilmiştir. 18 yaş altı ve 65 yas üstü grup, son 6 ay içerisinde yüz ve burun cerrahisi geçirenler, sigara kullananlar, yapısal ya da edinsel yüz anomalisi/deformitesi olan hastalar ile tat ve koku duyusunu kaybetmiş hasta ve gönüllüler çalışmaya dahil edilmemiştir. Çalışmaya katılanlarda hastalık öyküsü (Kronik Obstrüktif Akciğer Hastalığı, Diabetes Mellitus, Sinüzit), Sakkarin Allerjisi öyküsü sorgulanmış ve bu gruplar çalışmaya dahil edilmemiştir. Çalışmaya katılan tüm gruplara PCR testi uygulanmıştır.

Çalışmaya katılan hastaların hiçbirinde yoğun bakım gerektirecek bir hastalık seyri gözlemlenmemiştir. Sakkarin testi gerçekleştirildiği sırada hastanın genel durumunun iyi olması ve şiddetli dispne şikayetinin olmaması testin efektif bir şekilde yapılabilmesi ve sonucunun güvenilir olabilmesi için önem arz etmektedir.

Sakkarin testi

Hastanın burnundaki sekresyonları temizlemesi istenerek 5 miligramlık sakkarin tablet port koton yardımıyla, nazal kavitelerden birinde inferior concha medial yüzüne yerleştirilir. Uygulamadan sonra ilk tat hissi oluşana kadar geçen süre bir kronometre yardımı ile ölçülerek bu süre MCT olarak not edilir. Bu süre içerisinde hasta oturur pozisyonda olmalıdır. Hastanın oral alımı kısıtlanır ve konuşmaması, öksürmemesi, hapşırmaması ve burnunu sümkürmemesi istenir. 0-20 dakika arası ölçülen değerler normal MCT olarak değerlendirilmiştir. 20 dakikadan fazla süreler uzamış klirens ve 60 dakikadan fazla süren ölçümler hatalı test olarak değerlendirilmiştir.

Sakkarin testi hasta ya da gönüllü, Kulak Burun Boğaz (KBB) uzmanı tarafından muayene edildikten sonra aynı hekim tarafından uygulanmıştır.

İstatistiksel analiz

İstatistiksel analizler IBM SPSS sürüm 20 yazılımı kullanılarak yapılamıştır. Değişkenlerin normal dağılıma uygunluğu görsel (Histogram ve Olasılık Grafikleri) ve analitik yöntemler (Kolmogorov – Smirnov / Shapiro – Wilk Testleri) kullanılarak incelenmiştir. Tanımlayıcı istatistikler normal dağılan değişkenler için ortalama ± standart sapma verilerek yapılamış, normal dağılım göstermeyen değişkenler için tanımlayıcı istatistikler ortanca ve çeyrekler arası aralık kullanılarak verilmiştir. Bağımsız gruplar arası değerlendirmelerde, verilerin normal dağılım özelliğine göre Mann Whitney U veya T testi kullanılmış, çoklu gruplarda karşılaştırma için Kruskal Wallis testi uygulanmıştır.

Sonuçlar

Toplam 168 kişinin dahil edildiği çalışmada katılımcıların %44'ü kadın (n=74) ve %56'sı (n=94) Erkektir. Kadınlar ve erkekler arasında MCT açısından fark gözlenmemiştir.

MCT değerlendirilmesinde Grup 1'de (Sağlıklı) ortalama MCT 14,58 dakika olarak (n=84), Grup 2'de (PCR pozitif) ise ortalama MCT 13,72 dakika olarak (n=84) ölçülmüş (Tablo 1), iki grup arasında istatistiksel açıdan fark saptanmamıştır (p=0,657).

Tablo 1. Mukosiliyer Klirens Zamanı

PCR	Ortalama	Standart Hata	Orta değer	25. Persentil	75. Persentil	Minimum	Maksimum	P değeri
Pozitif	14,58	1,05	11,5	8	22	5	25	0,657
Negatif	13,72	0,771	12,5	8,5	18	4	27	

Tartışma

Mukosiliyer klirens, burundan başlayarak solunum mukozasını solunan partiküller ve mikroorganizmaları orofarinkse doğru tek yönlü mukus akışı üreterek korumakta ve solunum sisteminin savunmasında çok önemli bir rol oynamaktadır. Sakkarin geçiş süresi, nazal MCT'nin değerlendirilmesi için yaygın olarak kullanılmaktadır. Bu amaçla sakkarin metodu ile nasal mukoklirens zamanının ölçülmesi ucuz, güvenilir ve hızlı sonuç alabileceğimiz bir test yöntemidir (8). Acil servise başvuran hastalarda SARS-CoV 2 ye bağlı olarak gelişen Korona virus hastalığı-2019 (COVID-19) enfeksiyonunda mukosiliyer klirensin değerlendirilmesinin, etiyoloji, tedavi ve prognoz açısından erken dönemde fayda sağlayacak bir değerlendirme yöntemi olduğu düşünülmektedir.

Yapılan çalışmalarda sigara içenlerde (9, 10, 11), kömür madeni işçilerinde (12), Silikozis hastalarında (13), OSAS Hastalarında (14), allerjik rinitte (15) mukosilier klirensin uzadığı görülmüştür. Sigara kullanımının MCC üzerine etkisi olduğu düşünüldüğü için çalışmamıza sigara içenler dahil edilmemiştir.

MCC zamanının bazı faktörlerden etkilenmekle birlikte bu zamanın normal popülasyonda da değişkenlik gösterdiği bilinmektedir. Yapılan bir çalışmada 249 sağlıklı ve sigara içmeyen kişide MCT ortalama 16 (12-20) dakika olarak ölçülmüştür (16). Aktif ve pasif smokerlar ile sağlıklı gönüllülerin incelendiği bir çalışmada smokerlarda MCT'nin uzadığı tespit edilmiş ve sigara içmeyen sağlıklı grupta ortalama MCT 6,4 ± 1.55 dakika olarak ölçülmüştür (17). Radyonüklid ile MCC zamanının ölçüldüğü ve 43 kişinin katıldığı bir çalışmada ise 22 sağlıklı gönüllünün nasal geçiş zamanı ortalama 6,2 ± 1.2 mm/dak, kadınlarda ise ortalama 4,3 ± 1.4 mm/dakika olarak ölçülmüştür (18). Kadın ve erkek sigara içenler ile içmeyen sağlıklı gönüllülerin karşılaştırıldığı bir başka çalışmada ise gruplar arasında anlamlı bir fark saptanmamış ve ortalama MCT 7-10,8 dakika arasında ölçülmüştür (19). Bizim çalışmamızda MCT sağlıklı gönüllülerde ortalama 13,72 dakika olarak ölçülmüştür.

SARS-CoV-2 enfeksiyonunun epitel bariyer işlevini geçişi olarak etkilediği ve mukosilier transportu bozduğu bildirilmiştir (20). Öztürk ve arkadaşlarının yaptığı bir çalışmada, COVID-19 testi pozitif çıkan hastalara 10. ve 20. günler arasında yapılan sakkarin testinde mukosilier aktivitenin negatif olarak etkilendiği ve mukosilier klirens zamanının uzadığı

görülmüştür (21). Kahraman ve arkadaşlarının yaptığı bir çalışmada da nazal semptomları olmayan COVID-19 hastalarında mukosilier klirens zamanının uzadığı bildirilmiştir (22). Uğurlu ve arkadaşları tarafından yapılan bir çalışmada ise COVID-19 tanılı hastalarına semptomların başlamasından sonra ortalama 5. Günde sakkarin testi uygulanması sonucunda nasal mukoklirens zamanında bir etkilenme olmadığını tespit etmişlerdir (23). Koparal ve arkadaşları da COVID-19 hastalarında mukosilier klirens zamanının uzadığını bildirmişlerdir (24). Çeçen ve arkadaşlarının yaptığı çalışmada da ise COVID-19 hastalarında mukosilier klirens zamanında bir uzama tespit edilmemiştir (25). Bizim çalışmamızda da benzer şekilde COVID-19 hastaları ile sağlıklı gönüllüler arasında ölçülen MCT arasında anlamlı fark saptanmamıştır. Biz, çalışmamızda son 48 saattir şikayetleri ve PCR testi pozitif olan hastaları değerlendirdik ve erken dönemde SARS-CoV-2 enfeksiyonunun MCT üzerine etkisi olmadığını saptadık.

Çalışma yapılan hasta grubunun ayaktan başvuran ve hafif-orta şiddette hastalık ile seyreden hasta grubu olması, yoğun bakım ya da servis yatışı yapılan hasta grubu ile arasında MCT farklılığının değerlendirilememesi çalışmanın kısıtlılıklarından birisi olmuştur.

Sonuç

COVID-19 etkeni olan SARS-CoV-2'nin solunum yolu epiteli hasarı yaptığı ve solunum yollarında hastalık oluşturduğu bilinmektedir. Erken dönemde yapılan PCR testlerinde üst solunum yolu mukozasında tespit edilmekle beraber, hafif-orta şiddetli enfeksiyon geçirenlerde, erken dönemde MCT üzerine etkisi bulunmadığı düşünülmektedir.

Çıkar Çatışması

Yazarlar arasında çıkar çatışması tarif eden herhangi bir kişi bulunmamaktadır. Tüm yazarlar çalışmanın tasarımında, verilerin toplanmasında ve analizinde katkıda bulunmuşlardır. Tüm yazarlar verileri ve sonuçları onaylamaktadır.

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Araştırma Makalesi

Acil serviste idrar yolu enfeksiyonu için başlanan ampirik antibiyotik ile kültür antibiyogram duyarlılığının karşılaştırılması

Comparison of empiricular antibiotic and culture antibıogram sensitivity for urinary trut infection in emergency department

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Öz

Amaç: Üriner sistem enfeksiyonları (ÜSE) hem ayaktan hem de yatarak tedavi edilen en yaygın enfeksiyonlardan biridir. Tedavide antibiyotik kullanımı yanı sıra antibiyotiklere direnç gelişimi de git gide artmaktadır. Çalışmamızda, acil serviste ayaktan tedavi edilen ÜSE olgularına reçete edilen antibiyotik ile kültür antibiyogramındaki direnç/duyarlılık düzeylerini karşılaştırmayı ve literatüre katkı sağlamayı amaçladık.

Gereç ve Yöntemler: Çalışmamız, retrospektif ve tek merkezli bir çalışmadır. Çalışma, dahil edilme kriterlerini karşılayan 1503 hasta ile yapıldı. Olguların demografik, laboratuvar ve klinik verileri daha önceden oluşturulmuş çalışma formuna kaydedildi. İstatistiksel anlamlılık düzeyi için $p<0.05$ kabul edildi.

Bulgular: Olguların %70,5'i kadın ve yaş ortalaması 55,83±23,36 yıldı. Olguların %12,2'sinde idrar kültürlerinde üreme olmazken; %3,2'sinde ise bulaş nedeniyle etken tespit edilemedi. Çalışmamızda olgulara başlanan antibiyotiklerin %2,8'ine karşı bakterilerin dirençli olduğu görüldü. Bakterilerden en yüksek antibiyotik direnç oranına E. Coli'nin sahip olduğu; Enterobacter spp. ve Klebsiella spp.'nin E. Coli'yi takip ettiğini gördük. Antibiyotiklerden en fazla sefuroksime direnç olduğu görülürken; bunu sefotaksim ve sefiksim takip etmektedir. E.Coli'nin en fazla sefuroksime; Enterebacter spp.'nin en fazla sefotaksime; Klebsiella spp.'nin en fazla sefuroksime; KNS'nin en fazla sefiksime; Pseudomonas spp'nin en fazla sefotaksime; Proteus spp'nin en fazla sefdinire; Staphylococcus Aureus'un en fazla sefiksime ve TMP-SXT'ye; Streptococcus Agalactia'nın en fazla sefuroksime direnç olduğu görüldü. Hem gebe hastalarda hem de diyabetik hastalarında direnç düzeylerinin anlamlı yüksek olduğu (sırasıyla $p=0.044$ ve $p=0.009$) görüldü.

Sonuç: ÜSE olgularında antibiyotik direnç düzeyinin çalışmamızda %20'nin üzerinde olduğu; yapılacak eğitimle ve antibiyotik seçimlerinin, yıllık yapılacak olan antibiyotik direnç raporlarına göre seçilmesiyle direnç oranının düşürülebileceğini düşünmekteyiz.

Anahtar Kelimeler: Ampirik Tedavi, Antibiyotik Direnci, Antibiyogram, Üriner Sistem Enfeksiyonları

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Abstract

Aim: Urinary tract infections (UTI) are one of the most common infections, both outpatient and inpatient. In addition to the use of antibiotics in treatment, the development of resistance to antibiotics is gradually increasing. In our study, we aimed to compare the resistance/sensitivity levels of the antibiotic prescribed to UTI cases treated in the emergency department with the culture antibiogram and to contribute to the literature.

Material and Methods: Our study is a retrospective and single-center study. The study was conducted with 1503 patients who met the inclusion criteria. Demographic, laboratory and clinical data of the cases were recorded in the previously created study form. For statistical significance level, $p<0.05$ was accepted.

Results: 70.5% of the cases were female and the mean age was 55.83±23.36 years. In our study, bacteria were found to be resistant to 20.8% of the antibiotics administered to the cases. E. Coli has the highest antibiotic resistance rate among bacteria; Enterobacter spp. and Klebsiella spp. followed by E. Coli. Among the antibiotics, it was observed that the resistance to cefuroxime was the most; this is followed by cefotaxime and cefixime. E. Coli is most resistant to cefuroxime; Enterebacter spp. is most resistant to cefotaxime; Klebsiella spp. is most resistant to cefuroxime; CNS is most resistant to cefixime; Pseudomonas spp. is most resistant to cefotaxime; Proteus spp. is most resistant to cefdinir; Staphylococcus Aureus is most resistant to cefixime and TMP-SXT; It was observed that Streptococcus Agalactia was most resistant to cefuroxime. It was observed that the resistance levels were significantly higher in both pregnant patients and diabetic patients ($p=0.044$ and $p=0.009$, respectively).

Conclusion: The antibiotic resistance level in UTI cases was above 20% in our study; we think that the resistance rate can be reduced by training and choosing antibiotics according to the annual antibiotic resistance reports.

Keywords: Empirical Treatment, Antibiotic Resistance, Antibiogram, Urinary Tract Infections

Giriş

Üriner sistem enfeksiyonu (ÜSE), dünya çapında hem ayaktan hem de yatarak tedavi edilen en yaygın hastalıklardan biridir ve yılda yaklaşık 150 milyon kişi bu hastalıktan mustarip olmaktadır (1). Amerika Birleşik Devletleri'nde yıllık yaklaşık 8 milyon poliklinik başvurusu mevcuttur (1,2). Hastalık Kontrol ve Önleme Merkezi verilerine göre her yıl 13 bin hastada ÜSE nedeniyle mortalite görülmektedir (3). Kadınlar, erkeklerden 6 kat fazla risk altındadır. Kadınların %50'si yaşamları boyunca ÜSE ile karşılaşır; %30'unda nüks olur ve %20'si tekrarlayan ÜSE atakları yaşayacaklardır (4-6).

Üriner sistem enfeksiyonun yaygınlığı nedeniyle, insanlar geçmişten beri tedavi arayışına girmişlerdir. Günümüzde yazılan antibiyotiklerin %15'i ÜSE için reçete edilmektedir. 1953'te nitrofuratoinin, sonrasında amoksisilin ve tirmetroprim/sülfametoksazol (TMP-SMZ)'ün keşfinden sonra uzun süre bu ajanlar ÜSE tedavisi için kullanılmış ve maalesef bu etkenlere karşı direnç gelişmiştir (7). ÜSE için küresel antibiyotik kullanımı hem ayaktan hem de yatarak tedavi edilen hastalarda dirençli bakterilere neden olmuştur (8,9). ÜSE'ye neden olan birçok bakteri mevcuttur, fakat bunlar için Escherichia Coli (E. Coli), Klebsiella spp., Enterococcus spp. ve Stapylococcus saprophtyicus en yaygın olanlarıdır (2). Bu bakterilerin direnç geliştirme yeteneklerinin olması nedeniyle birçok antibiyotiğin bu bakterileri yok etme yeteneği azalmıştır (3).

Antibiyotik direncini azaltmak için yapılması gerekenlerden biri, doğru bir şekilde tanı koymakken; bir diğeri ise, doğru antibiyotik reçete etmektir. Doğru tanı ne kadar idrar kültür sonuçları ile olsa da maliyet ve zaman kaybı nedeniyle klasik ÜSE semptomlarına göre tedavi yapılmaktadır. Bu durum da bakterilerin fazla direnç geliştirmesine neden olabilmektedir. Bu durumdan kaynaklı hem ÜSE sonrası oluşan septisemi hem de antibiyotik kullanımından kaynaklı ortaya çıkan Clostridium Difficile koliti nedeniyle mortalite artmaktadır (3,10).

Çalışmamızda, acil servise başvuran ve ÜSE tanısı konulan hastalarda başlanan antibiyotik tedavisinin, idrar kültür antibiyogramındaki direnç durumunu karşılaştırmak; elde edilen veriler ile literatüre katkı sağlamak amaçlandı.

Gereç ve Yöntemler

Çalışma Planı ve Hasta Popülasyonu

Çalışma 1 Ocak 2019 ile 1 Ocak 2020 arasında ÜSE bulguları ile başvuran hastalar ile retrospektif ve tek merkezli olarak yapıldı.

Çalışma, 3. basamak eğitim ve araştırma hastanesinde yapıldı. Çalışmaya, ÜSE tanısı alan ve idrar kültürü istenmiş olan erişkin hastalar dahil edildi. Bu hastalar içinden; 18 yaşın altı, üriner sistem enfeksiyonu dışında tanı almış, değerlendirmeden 1 hafta öncesinde antibiyotik kullanım öyküsü olan, son 1 ay içinde hastane yatış öyküsü olan, kronik üriner sistem en-

feksiyon öyküsü olan, idrar kültürü istenmemiş, kronik üriner kataterizasyon öyküsü olan ya da tak çıkar sonda kullanan, nefrostomisi olan, bening prostat hipertrofisi olan ya da üriner sistem tıkayıcı kitle öyküsü olan ve immün sistem baskılanmış hastalar çalışma dışı bırakıldı. Medikal geçmişleri bilinmeyen ya da öğrenilemeyen hastalar da çalışmaya alınmadı.

Veri Toplama

Acil servise ÜSE bulguları ile başvuran hastaların acil tıp hekimleri tarafından değerlendirmesi yapıldı, tam idrar analizi ve kan tetkikleri istendi.

Acil serviste semptomlara bağlı olarak ÜSE tanısı konuldu ve tetkik istendi. ÜSE tanısı için akut sistit, prostatit ve üretrit gibi durumlarda dizüri ve sık idrara gitme şikayetleri; pyelonefrit durumunda ise ateş, yan ağrısı, kostovertebral açı hassasiyeti, inkontinans, kötü kokulu idrar, suprapubik ağrı ve hematüri şikayetleri esas alındı (11).

Tüm olguların demografik (yaş, cinsiyet, DM ve gebelik öyküleri) ve laboratuvar verileri (Tam idrar analizi (TİT) sonuçları, kültür antibiyogram sonuçları ve patojen analiz sonuçları) daha önceden oluşturulmuş çalışma formuna kaydedildi. Olgulara verilen ilaçlar, hastane otomasyon sisteminden, hastaların reçete kayıtlarından ve hasta dosyalarından öğrenildi. Yine olguların idrar kültürü antibiyogram sonuçları hastane otomasyon sisteminden öğrenildi.

Kültürden izole edilen bakteriler öncelikle gram boyama ile değerlendirildi. Daha sonrasında katalaz, oksidaz, karbonhidrat ve sitrat kullanımı özelliklerine göre tanımlandı; geri kalanlarda triptofanaz aktivitesi ve üreaz aktivitesine göre konvansiyonel yöntemler ile tanımlandı. Bazı bakterilerin tanımlanmasında ve antibiyotik duyarlılık testleri için VITEK 2 Compact (bioMérieux-Fransa) sistemi kullanılarak yapıldı. Yine antibiyotik duyarlılık tespiti için Avrupa Antimikrobiyal Duyarlılık Testi Komitesi (EUCAST) önerilerine göre analizler ve tanımlamalar yapıldı (12).

Hasta tarama işlemleri bittikten sonra veriler dijital ortama aktarıldı ve istatistiksel analiz yapıldı.

İstatistiksel Analiz

SPSS 26.0 for Windows® istatistik programı (IBM Inc. Chicago, IL, USA) kullanılarak yapıldı. Tanımlayıcı verilerin sunumunda sayı, yüzde, ortalama, standart sapma, ortanca, minimum, maksimum kullanıldı. Verilerin normal dağılıma uygunluğu Kolmogorov-Smirnov Testi ile değerlendirildi. Kategorik verilerin karşılaştırılmasında Pearson ki-kare testi ve Fisher's Exact testi kullanıldı.

Sonuçlar için %95 güven aralığı ve $p<0.05$ anlamlılık düzeyi kabul edildi.

Bulgular

Çalışmamızdaki 1503 hastanın %70,5'i kadın ve yaş ortalaması 55,83±23,36 yıldı. Olguların %41,8'i 65 yaş üstü hastalardı. Çalışmamızda olgulardan alınan TİT sonuçları incelendi ve %48,6'sında nitrit pozitif iken; %44,0'ında bakteri pozitifliği mevcuttu. Olguların yapılan idrar kültür sonuçlarında %88,8'inde üreme olurken; %3,2'sinde bulaş tespit edildi. Etkenler içinde %39,1 oranı ile E. Coli en sık etken, %17,6 ile Enterobacter spp. en sık 2. etken ve %14,2 ile Klebsiella spp. en sık 3. etken olarak tespit edildi. Olgulara ise %28,5 oranı ile en sık siprofloksasin reçete edilirken; %0,3 oranı ile en az azitromisin reçete edildiği görüldü. Olgulara reçete edilen antibiyotiklere, üreme olmayan ve bulaş vakaları çıkarıldığında; %20,8'ine direnç olduğu görüldü. Olguların %3,8'inde gebelik ve %16,2'sinde DM olduğu tespit edildi (Tablo 1).

Yaş grupları ile direnç durumu arasında istatistiksel anlamlı ilişki saptanmadı (p=0.180).

Patojenlerin reçete edilen antibiyotik tedavisine göre duyarlılık ve direnç durumlarına bakıldığında; en yüksek direncin E. Coli'de olduğu; sonrasında E. Coli'yi, Enterobacter spp. ve Klebsiella spp.'nin takip ettiği görüldü. Bu fark istatistiksel anlamlı bulundu (Tablo 2).

Reçete edilen ajanlara karşı direnç durumu incelendiğinde ise; en fazla direncin azitromisinde olduğu görülürken; olgu sayısına göre değerlendirdiğimizde en yüksek direncin sefuroksim'e karşı olduğu görüldü. Sefuroksim'i, direnç oranına göre en sık ikinci sefotaksim ve üçüncü sefiksim takip etmektedir (Tablo 2).

Olguların gebelik durumlarına ve DM öyküsü varlığına göre direnç düzeyleri incelendiğinde hem gebe hastalarda hem de diyabetik hastalarında direnç düzeylerinin anlamlı yüksek olduğu görüldü (Tablo 2).

Olgularda tespit edilen etken patojenlerin reçete edilen etken maddelere göre direnç düzeyleri incelendi. E. Coli'nin en yüksek oranda sefuroksime dirençli olduğu görüldü. Enterebacter spp.'de ise en yüksek direncin sefotaksime olduğu; Klebsiella spp.'de en yüksek direncin sefuroksime; KNS (Koagülaz Negatif Stafilokoklar)'de en yüksek direncin sefiksime; Pseudomonas spp.'de en yüksek direncin sefotaksime olduğu; Proteus spp.'de en yüksek direncin sefdinire; Staphylococcus Aureus'ta en yüksek direncin sefiksim ve TMP-SXT'ye; Streptococcus Agalactia'da en yüksek direncin sefuroksime olduğu görüldü. Morganella Morganii ve Acinetobacter Baumannie'ye karşı ise direnç gelişmediği tespit edildi (Tablo 3).

Tablo 1 Olguların demografik, laboratuvar ve klinik verilerinin değerlendirilmesi		
Parametre		**n (%) / Ortalama±SD**
Yaş (yıl)		55,83±23,36
Yaş Grup	18-65 yaş	875 (58,2)
	>65 yaş	628 (41,8)
Cinsiyet	Kadın	1052 (70,0)
	Erkek	451 (30,0)
TİT Nitrit Varlığı	Negatif	772 (51,4)
	Pozitif	731 (48,6)
TİT Bakteri Varlığı	Negatif	842 (56,0)
	Pozitif	661 (44,0)
Etken	E. Coli	588 (39,1)
	Enterobacter Spp.	265 (17,6)
	Klebsiella Spp.	213 (14,2)
	KNS	77 (5,1)
	Organella Morganii	8 (0,5)
	Pseudomonas Spp.	40 (2,7)
	Proteus Spp.	28 (1,9)
	Staphylococcus Aureus	24 (1,6)
	Streptococcus Agalactia	40 (2,7)
	Acinebacter Baumannii	3 (0,2)
	Multiple Üreme-Bulaş	48 (3,2)
	Üreme yok	169 (11,2)
Reçete Edilen Antibiyotik Etken Madde	Amoksisilin	8 (0,5)
	Seftirakson	9 (0,6)
	Sefuroksim	167 (11,1)
	TMP-SXT	245 (16,3)
	Azitromisin	4 (0,3)
	Siprofloksasin	428 (28,5)
	Sefaklor	237 (15,8)
	Sefotaksim	78 (5,2)
	Fosfomisin	61 (4,1)
	Nitrofurantoin	60 (4,0)
	Sefdinir	24 (1,6)
	Sefiksim	182 (12,1)
Antibiyogram Durumu	Duyarlı	1018 (67,7)
	Dirençli	268 (17,8)
	Bulaş	48 (3,2)
	Üreme yok	169 (11,2)
Gebelik Durumu	Var	57 (3,8)
	Yok	991 (66,2)
DM Durumu	Var	243 (16,2)
	Yok	1260 (83,8)
SD: Standart Deviasyon; TİT: Tam idrar Analizi; KNS: Koagülaz Negatif Stafilokoklar; TMP-SXT: Trimetoprim/sulfametoksazol		

Tablo 2 Etken patojen, reçete edilen etken maddelere ve özgeçmişlerine göre direnç düzeylerinin incelenmesi

Etken Patojen	Duyarlı		Dirençli		p
	n	%	n	%	
E. Coli	455	77,4	133	22,6	<0.001
Enterobacter Spp.	207	78,1	58	21,9	
Klebsiella Spp.	170	79,8	43	20,2	
KNS	62	80,5	15	19,5	
Pseudomonas Spp.	35	87,5	5	12,5	
Streptococcus Agalactia	35	87,5	5	12,5	
Proteus Spp.	22	78,6	6	21,4	
Staphylococcus Aureus	21	87,5	3	12,5	
Morganella Morganii	8	100,0	0	0,0	
Acinebacter Baumannii	3	100,0	0	0,0	
Reçete Edilen Etken Madde					
Siprofloksasin	301	82,9	62	17,1	<0.001
Sefaklor	197	93,8	13	6,2	
TMP-SXT	152	70,7	63	29,3	
Sefiksim	112	70,4	47	29,6	
Sefuroksim	89	64,0	50	36,0	
Sefotaksim	45	67,2	22	32,8	
Nitrofurantoin	54	100,0	0	0,0	
Fosfomisin	39	86,7	6	13,3	
Sefdinir	19	95,0	1	5,0	
Amoksisilin	4	66,7	2	33,3	
Seftirakson	5	83,3	1	16,7	
Azitromisin	1	50,0	1	50,0	
Gebelik					
Var	32	69,6	14	30,4	0.044
Yok	677	78,1	190	21,9	
DM Varlığı					
Var	156	72,6	59	27,4	0.009
Yok	862	80,5	209	19,5	

KNS: Koagülaz Negatif Stafilokoklar; TMP-SXT: Trimetoprim/sulfametoksazol; DM: Diabetes Mellitus

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Tablo 3 Etken patojenlerin reçete edilen etken maddelere göre direnç durumlarının belirlenmesi

Etken	E. Coli Diren-çli/Duyarlı (Direnç yüzdesi)	Enterobacter Spp. Dirençli/ Duyarlı (Direnç yüzdesi)	Klebsiella Spp. Dirençli/ Duyarlı (Direnç yüzdesi)	KNS Diren-çli/Duyarlı (Direnç yüzdesi)	Organella Morgannii Dirençli/ Duyarlı (Direnç yüzdesi)	Pseudomo-nas Spp. Diren-çli/Duyarlı (Direnç yüzdesi)	Proteus Spp. Dirençli/ Duyarlı (Direnç yüzdesi)	Staphylococcus Aureus Dirençli/ Duyarlı (Direnç yüzdesi)	Streptococ-cus Agalactia Dirençli/ Duyarlı (Direnç yüzdesi)	Acinetobacter Baumannie Dirençli/ Duyarlı (Direnç yüzdesi)
Siprofloksasin	34/133 (20,3)	13/62 (17,3)	9/50 (15,3)	3/18 (14,3)	0/2 (0,0)	1/9 (10,0)	0/8 (0,0)	1/9 (10,0)	1/9 (10,0)	0/1 (0,0)
Sefaklor	7/89 (7,2)	2/37 (5,1)	3/31 (8,8)	0/13 (0,0)	0/1 (0,0)	0/7 (0,0)	1/5 (16,6)	0/2 (0,0)	0/11 (0,0)	0/1 (0,0)
TMP-SXT	31/68 (31,3)	11/29 (27,5)	9/24 (27,3)	4/8 (33,3)	0/1 (0,0)	1/7 (12,5)	¾ (42,9)	½ (33,3)	3/8 (27,3)	0/1 (0,0)
Sefiksim	24/52 (27,9)	10/23 (30,3)	7/18 (28,0)	4/5 (44,4)	0/2 (0,0)	0/4 (0,0)	½ (33,3)	½ (33,3)	0/4 (0,0)	0/0 (0,0)
Sefuroksim	22/37 (37,3)	12/25 (32,4)	10/14 (41,7)	3/7 (30,0)	0/0 (0,0)	2/2 (50,0)	0/1 (0,0)	0/1 (0,0)	½ (33,3)	0/0 (0,0)
Sefotaksim	12/21 (36,4)	5/10 (33,3)	3/6 (33,3)	1/5 (16,7)	0/0 (0,0)	1/1 (50,0)	0/0 (0,0)	0/2 (0,0)	0/1 (0,0)	0/0 (0,0)
Nitrofurantoin	0/29 (0,0)	0/6 (0,0)	0/11 (0,0)	0/3 (0,0)	0/2 (0,0)	0/1 (0,0)	0/0 (0,0)	0/1 (0,0)	0/0 (0,0)	0/0 (0,0)
Fosfomisin	3/18 (14,3)	2/7 (22,2)	1/9 (10,0)	0/1 (0,0)	0/0 (0,0)	0/2 (0,0)	0/1 (0,0)	0/2 (0,0)	0/0 (0,0)	0/0 (0,0)
Sefdinir	0/5 (0,0)	0/3 (0,0)	0/6 (0,0)	0/2 (0,0)	0/0 (0,0)	0/0 (0,0)	1/1 (50,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)
Amoksisilin	0/1 (0,0)	2/3 (40,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)
Seftirakson	0/2 (0,0)	1/1 (50,0)	1/1 (50,0)	0/0 (0,0)	0/0 (0,0)	0/1 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)
Azitromisin	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)	0/0 (0,0)

KNS: Koagülaz Negatif Stafilokoklar; TMP-SXT: Trimetoprim/sulfametoksazol;

Tartışma

Üriner sistem enfeksiyonları, en fazla acil servis ziyaretine neden olan ve klinisyenler tarafından en fazla antibiyotik reçete edilen enfeksiyonlardan biridir (13,14). Bu durum hem çeşitli etken patojenlerin virülans kodlayarak antimikrobiyal direnç gelişimine neden olur hem de çok yüksek düzeyde sağlık bakım maliyetine neden olmaktadır. ÜSE'lerdeki nüks oranlar her antibiyotiğin etkin bir tedavi olmadığını göstermektedir. Bu nedenle; son dönemde ÜSE hastalarında artan antibiyotik direnci nedeniyle bu enfeksiyonların önemi daha da artmıştır (13). İdrar yolu enfeksiyonlarında altın standart tanı testi idrar kültürüdür (15). Fakat idrar kültüründe etken patojenin belirlenmesi ve antibiyogram süreci 2 gün sürmekte ve bu nedenle çoğu klinikte ampirik tedavi başlanmaktadır. Bu bağlamda, ampirik tedavide seçilecek antibiyotiğin doğru seçilmesi gerekir. Bunun için de bölgenin ya da sağlık merkezinin en sık etkenleri ve etkenlerin antibiyotik dirençlerinin izlenmesi ve iyi analiz edilmesi gerekmektedir (16).

Tüm yaş gruplarında, toplum kökenli ÜSE'lerde etken sıklıkla gram negatif bakteriler olup; bunlar içinde de en sık E. Coli (%50-90)'dir. Bu sıralamayı Klebsiealla pneumoniae, Staphylococcus Saprophyticus, Enterococcus spp, Proteus spp ve Stapylococcus Aureus takip etmektedir (17,18). 2016-2019 yılları arasında Balıkesir Devlet Hastanesi'nde yapılan analizde; ÜSE'de en sık etken patojenin E. Coli; ikinci sıklıkta ise Klebsiella spp. olduğu tespit edilmiştir (19). Keskin ve arkadaşlarının yaptıkları çalışmada; %73 oranında E. Coli ve %19 oranında Klebsiella spp. Etken olarak tespit etmiştir (20). Çalışmamız sonuçlarında ise; ÜSE olgularının %39,1'inde E. Coli, %17,6'sında Enterobacter spp. ve %14,2'sinde Klebsiella spp. saptandı. Çalışmamızda E. Coli oranının literatürden düşük çıkmasının nedeni olarak ayaktan tüm ÜSE olgularına kültür istenmemiş olmasından kaynaklı olabileceğini düşünmekteyiz.

Ampirik tedavide ilk seçenek olarak sıklıkla oral antibiyotikler tercih edilmektedir. Gupta ve arkadaşlarının yaptığı çalışmada; ayaktan ÜSE olgularına en sık reçete edilen antibiyotik tercihinin sırasıyla TMP-SXT, siprofloksasin, nitrofurantoin, fosfomisin ve beta-laktam grubu antibiyotik olduğunu bildirmiştir (21). Drapkin ve arkadaşlarının yaptıkları çalışmada; E. Coli suşlarının TMP-SXT'ye (%77), nitrofurantoine (%99), siprofloksasine (%84) ve levofloksasine (%85) duyarlı olduğunu tespit etmişlerdir (22). Budak ve arkadaşlarının 2015 yılında yaptıkları çalışmalarda; E. Coli'nin %40,1 oranında ampisiline, %20,3 oranında sefuroksime, %31,4 oranında TMP-SXT'ye ve %36,5 oranında siprofloksasin'e dirençli olduğu bildirilmiştir (16). Duran ve arkadaşlarının 2020'de yaptıkları çalışmada ise; E. Coli suşlarının ampisiline %64, seftriaksona %38,5, amoksisiline %42,3, TMP-SXT'ye %42,6 ve siprofloksasine %42,9 oranında dirençli olduğu bildirilmiştir. Çalışmamız sonuçlarında ise; E. Coli suşunun sefuroksime %37,3, sefotaksime %36,4, TMP-SXT'ye %31,3, sefiksime %27,9 ve siprofloksasine %20,3 oranında direnç geliştirdiği görüldü. Çalışmamız verileri literatürü destekler nitelikte olup; bakteri dirençlerinin hızla arttığı günümüzde ampirik tedaviler konusunda konsensusların sağlanması gerektiğini düşünüyoruz.

Çalışmamızda en sık 2. patojen Enterobacter spp. olarak bulundu. Enterobacter spp. patojenlerinin %40 oranında amoksisiline; %33,3 oranında sefotaksime, %32,4 oranında sefuroksim ve %27,5 oranında TMP-STX'e direnç geliştirdiği görüldü. Keskin ve arkadaşlarının yaptıkları çalışmada; Enterobacter spp.'nin ampisiline %69, sefuroksime %38, sefiksime %36, amoklavine %33, TMP-SXT'ye %34 ve siprofloksasine %23 oranında direnç geliştirdiğini tespit etmişlerdir. Çalışmamız Keskin ve arkadaşlarının yaptıkları çalışma sonuçlarını destekler niteliktedir.

Çalışmamızda, Staphylococcus aureus'un antibiyotik direnci KNS'den düşük olup, Pseudomonas spp. ve Streptococcus Agalactia ile benzer orandadır. Staphylococcus Aureus en yüksek oranda Sefiksim ve TMP-SXT'ye (Sırasıyla %33,3 ve %33,3) direnç göstermektedir. Keskin ve arkadaşlarının yaptıkları çalışmada Staphylococcus Aureus'un en duyarlı olduğu antibiyotiğin TMP-SXT olduğunu; Metisiline ise en fazla direnç geliştirdiğini bildirmiştir (20). Çalgın ve arkadaşlarının ise; Staphylococcus Aureus'un en fazla penisiline (%90) direnç gösterdiğini; en çok ise TMP-SXT'ye duyarlı olduğunu bildirmiştir (15). Çalışmamız, Keskin ve arkadaşları ile Çalgın ve arkadaşlarının yaptığı çalışma sonuçlarından farklı bulundu. Bu farklılığın hastaların daha öncesinde kullandıkları antibiyotiği ne kadar sıklıkta kullandığı konusunda bilgi sahibi olunmaması ve bu kullanıma bağlı direnç ve duyarlılık durumunun değişkenlik göstereceğini düşünmekteyiz.

Çalışmamızda diğer gram negatif bakterilerin üremeleri de görülmektedir. Pseudomonas spp., Proteus spp., A. baumannii ve KNS bunlar içinde yer alanlardır. KNS'de direnç oranı %19,5 iken; Proteus spp. %21,4; Pseudomonas spp. %12,5 ve A. baumannii'de ise direnç tespit edilmemiştir. Demir Çuha ve arkadaşlarının yaptıkları çalışmada; A. baumannii'de antibiyotik direncinin %60'larda olduğu; Pseudomonas spp.'de ise aminoglokozid, karbapenem, piperasilin/tazobactam ve antispöodomonal sefalosporinlere direncin %20'nin altında olduğu ve siprofloksasine %25 dirençli olduğu bildirilmiştir (23).

Yine Keskin ve arkadaşlarının yaptıkları çalışmada, Demir Çuha ve arkadaşlarının yaptıkları çalışmaya benzer oranda gram negatif bakterilerin antibiyotik direnci tespit etmişlerdir (20). Çalışmamızda belirtilen bakteri gruplarına direncin literatürden düşük oranda olmasının nedeni olarak, belirtilen bakteri gruplarının hastane kaynaklı enfeksiyonlarda rol oynadığını ve çalışmamızın ayaktan hastalarla yapılmasından kaynaklı düşük olduğunu düşünmeketyiz.

Çalışmamızda gebe hastalarda ve diyabetik hastalarda tespit edilen etken patojenlerin reçete edilen antibiyotiklere dirençlerinin anlamlı yüksek olduğu görüldü. Nicolle ve arkadaşlarının yaptıkları çalışmada; risk faktörü olan olgularda ÜSE gelişim riskini artırdığını belirtmektedir. Özellikle diyabetik hastalarda idrardaki glukozun bakteri kolonizasyonu için risk oluşturduğunu bildirmektedir (24). Bunun yanı sıra; Muanda ve arkadaşlarının yaptıkları çalışmada; ÜSE'si bulunan gebe hastalarda gereksiz antibiyotik kullanımın hem antibiyotik direncini arttırdığını hem de antibiyotik direnci gelişen bakteriler kaynaklı abortusların ve erken doğumların olduğunu bildirmişlerdir (25). Bu nedenle özellikli hasta grubu olan gebe ve diyabetik hastalarda antibiyotik seçiminde dikkatli olmak gerektiği gibi bu durumun abortus ve erken doğum gibi komplikasyonlara da neden olduğu unutulmamalıdır.

Kısıtlılıklar

Çalışmamızda birkaç kısıtlılık mevcuttur. Bu kısıtlılıklardan ilki; çalışmamızın retrospektif olması ve her ne kadar verilerin eksik olmadığı kontrol edilmiş olsa da retrospektif yapılan veri taramasında olabilecek kabul edilebilir düzeyde kayıplar mevcuttur. İkincisi; kültürden etken patojen üremesi olmayan olgularda iatrojenik etkilerden dolayı olup olmadığı ya da olguların antibiyotik öykülerinde hatalar olup olmadığı bilinmemektedir. Üçüncü kısıtlılığımız ise; bazı olgularda bulaş olduğu görülmektedir ve net bir etken patojen saptanmamıştır. Fakat çalışmamız kısıtlılıklarının çalışma verilerini değiştirecek düzeyde olmadığını düşünmekteyiz.

Sonuç

Çalışmamızda hastanemizde ÜSE olgularına reçete edilen antibiyotiklerde direnç %20'nin üzerine çıktığını görüldü. Bu direnç oranlarının, her yıl yapılacak eğitimlerle, antibiyotik direnç raporlarının antibiyotik reçete edilirken göz önünde bulundurulmasıyla ve gereksiz antibiyotik kullanımının azaltılması ile düşürülebileceğini düşünmekteyiz. Bu sayede hem varolan antibiyotiklerin daha uzun süre kullanımına hem de yüksek sağlık maliyetlerini düşürülmesine fayda sağlayacağını düşünmekteyiz. Bunun yanı sıra; özellikle gebe ve diyabetik hastalarda kültür antibiyogram sonucuna göre antibiyoterapi başlanmasının faydalı olacağını düşünmekteyiz.

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Research Article

Tracheostomy experiences in chronic respiratory failure after congenital heart surgery

Konjenital kalp cerrahisi sonrasi gelişen kronik solunum yetmezliğinde trakeostomi deneyimlerimiz

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Abstract

Aim: A small number of children with repaired congenital heart defects may require a tracheostomy for ongoing ventilatory support. Congenital airway anomalies, laryngomalacia, postoperative airway complications and genetic syndromes associated with airway and facial anomalies, such as DiGeorge Syndrome (22q11 deletion), can be counted among the reasons why patients are unable to be weaned from the ventilator. In this study, we aimed to define the outcomes of patients who required a tracheostomy due to chronic respiratory failure after congenital heart surgery, and the existing risk factors for in-hospital and post-discharge mortality.

Material and Methods: The files of 1382 patients who underwent surgery due to congenital heart disease in the Pediatric Cardiovascular Surgery Clinic in Ankara Bilkent City Hospital, between February 2019 and February 2023, were retrospectively scanned. Patients' age, gender, body weight, cardiac diagnosis, surgical intervention, length of stay in the intensive care unit, number of extubation attempts, total length of stay on the ventilator, need for ventilator at discharge, rates of weaning from tracheostomy and time of weaning from tracheostomy and mortality rates, were obtained from patient files and hospital database.

Results: Tracheostomy was performed in 15 of 1382 patients who underwent surgery during the four year study period. Mean (SD) duration of ventilation prior to tracheostomy was 35 days (IQR= 19 – 47). The median follow up time in patients was 224 days (IQR=116-538). Three patients were decannulated and six had died. Causes of death in six patients included sepsis (2), cardiac instability (1), neurological complications (2) and pulmonary haemorraghia (1).

The median time to discharge after tracheostomy in patients was 51 days (IQR= 33.50 – 147). Eight patients (53.3%) were discharged on home ventilation. One patient (6.6%) were decannulated during the hospital stay before discharge. Causes of deaths were often multifactorial for children who died during their initial hospital stay. Mortality was seen in six patients, a rate of 40%.

Conclusion: The need for tracheostomy after cardiac surgery plays an important role in early and late mortality in children. Ventilator-dependent chronic respiratory failure is the most common cause of childhood tracheostomies. We believe that determining the optimal timing for tracheostomy in the pediatric population will be effective in reducing prolonged ventilation and tracheostomy-related morbidities.

Keywords: congenital heart diseases; tracheostomy; chronic respiratory failure; cardiac surgery

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ÖZ

Amaç: Konjenital kalp cerrahisi geçiren çoğu hasta cerrahi sonrasında ekstübasyonu tolere etmektedir, fakat bazı hastalarda entübasyon süresi uzamakta, ventilatörden ayrılma zorlaşmaktadır. Hastaların ventilatörden ayrılamama sebepleri arasında konjenital hava yolu anomalileri, laringomalazi, postoperatif havayolu komplikasyonları, DiGeorge Sendromu (22q11 delesyonu) gibi havayolu ve yüz anomalileri ile ilişkili genetik sendromlar sayılabilir. Bu çalışmanın ile konjenital kalp cerrahisi sonrası kronik solunum yetmezliği sebebiyle trekeostomi ihtiyacı duyulan hastaların sonuçlarını, hastane içi ve taburculuk sonrası mortalitede mevcut risk faktörlerini tanımlamayı amaçladık.

Gereç ve Yöntemler: Ankara Bilkent Şehir Hastanesi Çocuk Kalp ve Damar Cerrahisi Kliniğinde Şubat 2019-Şubat 2023 tarihleri arasında KKH nedeniyle ameliyat edilen 1382 hastanın dosyaları retrospektif olarak tarandı. Hastaların yaşı, cinsiyeti, vücut ağırlığı, kardiyak tanı, cerrahi girişim, yoğun bakımda kalış süresi, ekstübasyon girişimi sayısı, ventilatörde toplam kalış süresi, taburculukta ventilatör ihtiyacı, trakeostomiden ayrılma oranları ve süresi trakeostomiden ayrılma ve mortalite oranları, hasta dosyalarından ve hastane veri tabanından elde edildi.

Sonuç: Dört yıllık çalışma döneminde ameliyat edilen 1382 hastanın 15'ine trakeostomi uygulandı. Trakeostomi öncesi ortalama (SD) ventilasyon süresi 35 gündü (IQR= 19 – 47). Hastalarda ortanca takip süresi 224 gündü (IQR=116-538). Üç hasta dekanüle edildi ve altı hasta öldü. Altı hastada ölüm nedenleri arasında sepsis (2), kardiyak instabilite (1), nörolojik komplikasyonlar (2) ve pulmoner hemoraji (1) vardı.

Hastalarda trakeostomi sonrası medyan taburcu olma süresi 51 gündü (IQR= 33.50 – 147).

Sekiz hasta (%53.3) ev tipi ventilatör ile taburcu edildi. Bir hasta (% 6.6) hastane yatışı sırasında taburculuk öncesi trakeostomiden ayrıldı. Hastanede ilk kalışları sırasında ölen çocuklar için ölüm nedenleri genellikle çok faktörlüydü. Altı hastada (%40) mortalite görüldü.

Tartışma: Çocuklarda kalp cerrahisi sonrası trakeostomi ihtiyacı erken ve geç mortalitede önemli rol oynamaktadır. Ventilatöre bağlı kronik solunum yetmezliği, çocukluk çağı trakeostomilerinin en yaygın nedenidir. Pediatrik popülasyonda trakeostomi için en uygun zamanlamanın belirlenmesinin uzamış ventilasyonu ve trakeostomiye bağlı morbiditeleri azaltmada etkili olacağına inanıyoruz.

Anahtar Kelimeler: konjenital kalp hastalıkları; trakeostomi; kronik solunum yetmezliği; kardiyak cerrahi

Introduction

Most patients undergoing congenital heart surgery tolerate extubation after surgery, but in some patients the intubation time is prolonged and weaning from the ventilator becomes difficult.[1] Approximately 10% of patients are still intubated at the end of the first week after congenital heart surgery.[2] Although most of these patients are extubated during their follow-up, a small group of patients undergo tracheostomy and are discharged with a home ventilator. Congenital airway anomalies, laryngomalacia, postoperative airway complications and genetic syndromes associated with airway and facial anomalies, such as DiGeorge Syndrome (22q11 deletion), can be counted among the reasons why patients are unable to be weaned from the ventilator.[3] Airway problems after cardiac surgery in infants prolong mechanical ventilator times and intensive care unit stays. In addition, the risk of surgical complications is higher in patients who require repetitive repair for reasons such as single ventricle surgery, and for whom respiratory complications are more common. Among these are diaphragm paralysis and vocal cord paralysis due to recurrent laryngeal nerve damage seen during complex aortic arch repairs.[1] In the adult population, tracheostomy is opened earlier in prolonged intubation, but there are no criteria and routine practices for these in the pediatric population.[4] Pediatric patients thus constitute the high-risk patient group for tracheostomy and children face more complications due to smaller airways.[5]

While the presence of congenital heart disease (CHD) and/or congenital heart surgery in children is a risk factor on its own, tracheostomy after cardiac surgery carries a five-fold higher risk of death compared to other tracheostomy cases.[6] In this study, we aimed to define the outcomes of patients who required a tracheostomy due to chronic respiratory failure after congenital heart surgery, and the existing risk factors for in-hospital and post-discharge mortality.

Material and Methods

In our study, the files of 1382 patients who underwent surgery due to CHD in the Pediatric Cardiovascular Surgery Clinic in Ankara Bilkent City Hospital, between February 2019 and February 2023, were retrospectively scanned. Patients who were younger than eighteen years of age at the time of the surgery

and who underwent a tracheostomy due to prolonged intubation in the intensive care unit, were included in the study. Patients who were older than eighteen years of age at the time of the operation, who underwent an emergency tracheostomy and who underwent tracheostomy for any reason before the surgery, were excluded in the study.

Patients' age, gender, body weight, cardiac diagnosis, surgical intervention, length of stay in the intensive care unit, number of extubation attempts, total length of stay on the ventilator, need for ventilator at discharge, rates of weaning from tracheostomy and time of weaning from the tracheostomy as well as mortality rates, were obtained from patient files and hospital database. When evaluating the diagnosis of the patient, if patient had more than one cardiac anomaly, the hemodynamically prominent disease was accepted as the primary disease.

Genetic diseases such as Down and DiGeorge Syndrome were recorded. Comorbidities of the patients (prematurity, prolonged intubation in the neonatal period, previous surgical operations such as tracheoesophageal fistula repair, congenital diaphragmatic hernia repair), were also evaluated.

Patients undergoing cardiac surgery in our center are followed up by pediatric cardiovascular surgeons in the pediatric cardiovascular surgery intensive care unit, and opinions are obtained from pediatric cardiologists, pediatric intensive care specialists and neonatologists when necessary.

Extubation is attempted in all patients in the early postoperative period. In the phase of weaning from the ventilator, blood gas sampling and saturation values suitable for the patient's cardiac pathology and surgery are taken as a basis.

At least five extubation attempts are made before tracheostomy in patients with extubation failure. Bronchoscopy, neurological imaging, echocardiogram, cardiac catheterization and fluoroscopy imaging of diaphragm movements are performed within indications in extubation failure.

Tracheostomy indications

With prolonged intubation and repeated extubation failure was determined as follows:

- Tracheobronchomalacia
- Tracheal or subglottic stenosis
- Bilateral vocal cord paralysis
- Upper respiratory tract problems, such as cleft palate
- Diaphragm paralysis
- Suboptimal hemodynamic status (moderate/severe systemic ventricular failure, severe AV valve failure, severe hypoxia, hemodynamically significant residual disease)

Tracheostomy opening is performed in our hospital by otolaryngology, anesthesia or paediatric cardiovascular surgery, depending on availability.

Statistical analysis used descriptive statistics (SPSS.25. SPSS Inc., Chicago, IL, USA) including mean, standard deviation (SD), median and range, number and percent, as appropriate.

Results

Tracheostomy was performed in 15 of 1382 patients who underwent surgery during the four-year study period. The demographic characteristics of the patients are summarized in Table-1.

Table-1: Demographic characteristics of patients (AVSD: Atrioventricular Septal Defect, VSD: Ventricular Septal Defect, ASD: Atrial Septal Defect)

	n=15 n%
Male Gender	10 (66.6%)
Primary cardiac disease	
Unbalanced AVSD	3 (20%)
Tetralogy of Fallot	2 (13.3%)
Tetralogy of Fallot + Ebstein Anomaly	1 (6.6%)
VSD + Pulmonary Atresia	3 (20%)
Aortic Insufficiency + Ascending Aorta An Aneurysm	1 (6.7%)
Aortic Stenosis	1 (6.7%)
Pulmonary Banding + VSD	1 (6.7%)
Residual ASD + Ellis Van Crevald Syndrome	1 (6.7%)
Transposition of Great Arteries	1 (6.7%)
Double Inlet Left Ventricle	1 (6.7%)

Seven of the patients had previously undergone cardiac surgery. Blalock Taussig(BT) shunt was performed in four of these patients, pulmonary artery banding was performed in one patient, aortic stenosis was repaired in one patient, and atrial septal defect repair was performed in one patient.

Two of the three patients who underwent BT shunt in the neonatal period had tracheomalacia due to prolonged intubation in the neonatal period. Our patient with subglottic stenosis underwent a BT shunt operation at the age of four months due to Ebstein Anomaly + Fallot Tetralogy and was intubated for a long time.

Extracorporeal membrane oxygenator (ECMO) was inserted in 5 of 15 patients who underwent tracheostomy in the postoperative period, and all of them were successfully weaned from ECMO.

Diaphragm plication due to left diaphragmatic paralysis was performed in three patients. Tracheostomy was performed in patients who could not be extubated despite a diaphragmatic plication. Primary patology of these patients were, tetralogy of Fallot, unbalanced complete atrioventricular septal defect and tricuspid atresia.

Cardiovascular instability and neurological events were the most common indications for tracheostomy accounting for 53.4% of patients. Although cardiac instability is a broad definition, we evaluated the increased need for inotropes, resistant hypotension, documented ventricular dysfunction, and hemodynamically significant residual defects in this context. The reasons for opening a tracheostomy are summarized in Table-2.

Table-2: Reasons for tracheostomy

	n=15 n%
Tracheomalasia	2 (13.3%)
Cardiac Instability	4 (26.7%)
Subglottic stenosis	3 (20%)
Neurological Events	4 (26.7%)
Laryngomalacia	1 (6.7%)
Pulmonary Hemorrhage	1 (6.7%)

Mean (SD) duration of ventilation prior to tracheostomy was 35 days (IQR= 19 – 47). Pressure supported-synchronized intermittent mandatory ventilation was the commonest mode of ventilation in all patients.

The median time elapsed until mortality develops after tracheostomy in patients was eight days (IQR= 3.75 – 21.75).

The median (range) age at the time of the tracheostomy was fifteen months (IQR= 11–30). The median weight of the patients, in grams, at the time of operation was 9500 (IQR= 6000 – 12000).

The median CPB time (minutes) of the patients was 123 (IQR= 80 – 178) and The median cross-clamp time (minutes) of the patients was 65 (IQR= 45 – 120).

The median follow up time in patients was 224 days (IQR=116-538). 3 patients were decannulated and 6 had died. Causes of death in 6 patients included sepsis (2), cardiac instability (1), neurological complications (2), pulmonary haemorraghia (1).

The median time to discharge after tracheostomy in patients was 51 days (IQR= 33.50 – 147).

Eight (53.3%) patients were discharged home on home ventilation.

Causes of death are listed in Table-3. Causes of deaths were often multifactorial for children who died during their initial hospital stay. Mortality was seen in six patients and the mortality rate was 40%.

Table-3: Causes of deaths.

	n=6
Hearth failure	1
Neurological events	2
Possible/confirmed sepsis	2
Pulmonary haemorraghia	1

At the time of follow up three patients had been decannulated. One of these patients was decannulated after fifteen months and the other one was decannulated twelve months after the tracheostomy, whereas the last patient was decannulated three months after the tracheostomy. Of the six surviving patients that were discharged from the hospital on a ventilator, only four still required positive pressure ventilation.

Discussion

The indications and outcomes of tracheostomies in children with CHD have been described in previous studies.[7] Cardiac insufficiency, tracheobronchomalacia, diaphragmatic palsy and new central nervous system events, are the commonest reasons described in prolonged ventilation. Children with more complex CHD lesions, single ventricle physiology or greater risk adjustment for congenital heart surgery scores, had higher mortality and less weaning off ventilation.[8] A tracheostomy is required in a small percentage of patients undergoing surgery for CHD.[7] This rate was found to be 1.09% in our study and is similar to the literature.[9]

With studies conducted in a single center such as ours, both the experience of the center and the number of patients is critical in determining the conditions that require a tracheostomy after congenital heart surgery and the factors affecting this process. There are no guidelines regarding timing of tracheostomy after congenital heart surgery. The general approach, if a patient cannot be extubated, should first be to identify the potential causes of this condition. For example, it would be appropriate to detect and repair the paralyzed diaphragm with a fluoroscopy, to detect subglottic stenosis, vocal cord paralysis or tracheomalacia by bronchoscopy and to perform treatment for it, and then to try extubation again. Although there are three extubation attempts before tracheostomy on average in the literature, we decided to attempt the tracheostomy after a minimum of five extubation attempts in our clinics. The exception to this situation is patients whose neurological status was poor on cranial imaging.

The median duration from cardiac surgery to tracheostomy of 35 days (IQR= 19 – 47) is slightly longer than the 30 days duration published previously.[9] These durations are significantly longer than the standard practice of tracheostomy occurring within 1 to 3 weeks in adult patients. This is supported by data demonstrating longer ICU stay, higher ICU mortality and higher rate of failure to wean from mechanical ventilation, in adults undergoing tracheostomy after greater than 21 days on intubation.[4] Although early tracheostomy in adults has better outcomes, such information is not available for the pediatric population.

Single ventricle patients constitute the group with the worst tracheostomy results in the pediatric population.[1] In our study, six of fifteen patients underwent single ventricular surgery. Four of these patients died after tracheostomy. All three patients on whom we performed tracheostomy weaning were patients who underwent double ventricular repair. If high-risk patients with single ventricle require tracheostomy and long-term mechanical ventilation, parents should be informed about the poor prognosis for this patient population. Our clinical and literature experience shows that tracheostomy weaning is more difficult in patients with single ventricular physiology.[7] Our mortality rate of approximately 40% was similar to the literature but our follow-up duration was shorter.[1,2] Among the reasons for the relatively high mortality in our study, we found that since we are a newly established clinic, the number of our patients was low and our follow-up period was short. In addition, tracheostomy weaning could be performed in a small proportion of our patients (20%). This seems to indicate that some airway problems, respiratory and cardiac failure may improve over time with growth and cardiac recovery.

One of the most important limitations of our retrospective study is the lack of sufficient resources in the literature regarding the indications and timing of tracheostomy in children. In addition, since our study was a single-center study, the results may vary in different centers and may not be valid for all centers.

Conclusion

The need for tracheostomy after cardiac surgery has an important role in early and late mortality in children. Ventilator-dependent chronic respiratory failure is the most common cause of childhood tracheostomies. The timing of tracheostomy in prolonged ventilation in patients undergoing surgery for congenital heart disease is uncertain. Similar studies in the pediatric population with congenital heart disease will improve clinical outcomes. We believe that determining the optimal timing for a tracheostomy in the pediatric population will be effective in reducing prolonged ventilation and tracheostomy-related morbidities.

Ethical Approval: Ankara Bilkent City Hospital Clinical Researches Ethics Committee, (No: E2-23-3576, Date: 01/03/2023) 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.

Conflict Of Interest

The authors declare no conflict of interest.

Disclosure

None.

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Authors' Contributions

BST: Acquisition, analysis.

AA: Drafting of the work, revising, final approval.

MY: Drafting of the work, analysis.

ANE: Analysis

CLB: Final approval

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Research Article

Carotid body enlargement in patients with hypertension and comorbid diseases: a CT angiographic study

Karotid Cisim Boyutlarının Hipertansiyon ve Komorbid Hastalıklarla İlişkisi: BT Anjiyografik Çalışma

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Abstract

Aim: To determine the carotid body (CB) size and its relationship with hypertension, other sympathetically mediated disorders and smoking.

Materials and Methods: Neck CT angiographies of 180 patients performed in our clinic in the previous year were included in the study. The patients' histories were assessed for hypertension (HT), congestive heart failure (CHF), diabetes mellitus (DM), chronic obstructive pulmonary disease and smoking. The study groups were smokers without any chronic condition (S group, n=21), patients with HT alone (HT group, n=26), patients that had at least two chronic disorders (CD+S group, n=78) and the controls (n=33). The widest axial diameter of the CB was measured on axial sections.

Results: CB diameter could be measured in 158 patients. The CB diameter was significantly greater in HT (2.77±3.28 mm, p=0.02) and CD+S (2.76±3.38 mm, p<0.01) groups compared to the controls (2.22±3.41 mm). There was no significant difference between the S group (2.47±3.44 mm) and the control group (p=0.123). Repeated measurements showed a high intra-observer correlation for both sides.

Conclusion: HT causes a significant increase in CB size. CB size also increases significantly in individuals with the combination of sympathetically mediated disorders, including HT, CHF, and DM. CTA may provide a better understanding of the relationship between CB and sympathetically mediated diseases and guide further studies as well as therapies targeting CB.

Keywords: computed tomography angiography; carotid body; hypertension.

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Öz

Amaç: Karotid cisim (KC) boyutlarının hipertansiyon, sempatik sistem hiperaktivasyonunun görüldüğü diğer hastalıklar ve sigara ile ilişkisinin araştırılması.

Gereç ve Yöntemler: Son bir yıl içerisinde kliniğimizde boyun bilgisayarlı tomografi (BT) anjiyografi tetkiki yapılmış olan hastalar çalışmaya dahil edildi. Hastaların klinik öykülerinden hipertansiyon, konjestif kalp yetmezliği (KKY), diyabetes mellitus (DM), kronik obstrüktif akciğer hastalığı ve sigara içiciliği durumları kaydedildi. Hastalar yalnız sigara içen ve hiç komorbid hastalığı olmayan (Grup S, n=21), yalnızca hipertansiyonu olan (Grup HT, n=26), en az 2 komorbid hastalığa sahip olan (Grup KH, n=78) hastalar ve kontrol grubu (n=33) olmak üzere 4 gruba ayrıldı. BT anjiografi kesitlerinde KC'nin aksiyal planda en uzun aksı ölçüldü.

Bulgular: KC boyutu 158 hastada ölçülebildi. KC boyutu, grup HT'de (2,77±3.28 mm, p=0,02) ve grup KH'de (2,77±3,28 mm, p=0,02) kontrol grubu (2,22±3,41 mm) ile karşılaştırıldığında anlamlı olarak daha fazlaydı. Grup S (2,47±3,44 mm) ile kontrol grubu arasında anlamlı farklılık saptanmadı (p=0,123). Tekrarlanan ölçümlerde her iki taraf için yüksek gözlemci içi uyum saptandı (ICC=0,91/0,94).

Sonuçlar: Hipertansiyonu olan hastalarda KC boyutu artmaktadır. Ayrıca KC boyutu hipertansiyon, KKY ve DM gibi sempatik hiperaktivasyonun görüldüğü diğer hastalıklarda da anlamlı olarak artış göstermektedir. BT anjiyografi, KC ile sempatik hiperaktivasyonun görüldüğü hastalıklar arasındaki ilişkinin daha iyi anlaşılmasının yanında bu alandaki çalışmalarda ve tedavi seçeneklerinde yol gösterici olabilir.

Anahtar kelimeler: bilgiayarlı tomografi anjiyografi; karotid cisim; hipertansiyon

Introduction

Carotid body (CB) is the dominant peripheral chemoreceptor organ of the human body and initiates a protective chemoreceptor reflex through its sensitivity to changes in carbon dioxide, pH, potassium, and glucose in the blood (1). It has been supposed to play a role in the autonomic nervous system dysregulation and sympathetic hyperactivity, and the latter is supposed to be partially responsible for the pathogenesis of hypertension (HT), congestive heart failure (CHF), and diabetes mellitus (DM) (2-7). It has been suggested that resection of CB and blockade of P2X3 receptors in CB can be used in the treatment of hypertension (8,9).

Computed tomographic angiography (CTA) and ultrasonography studies have shown that CB can be visualized on routine examinations and that increased CB size is associated with HT, CHF, and DM (10-13). However, to the best of our knowledge, the isolated effect of smoking on CB size has never been demonstrated in detail. Therefore, this study aimed to determine the CB dimensions and its correlations with smoking, HT, and other disorders associated with sympathetic hyperactivity.

Material and Methods

Our hospital's electronic patient recording system was used to extract the data of the patients who had neck CTA. The patients diagnosed with HT, DM, CHF, and/or chronic obstructive pulmonary disease (COPD) for at least three years were included in the study. Smoking status and the demographic characteristics of the patients were also recorded from the hospital's electronic patient recording system. The local ethics committee has approved the study protocol of this retrospective study and written informed consent was obtainede from all patients.

The neck CTA scans performed in our institution in the previous year before starting the study were analyzed retrospectively, and a total of 180 patients who underwent neck CTA were found. Five patients with inadequate arterial phase, 12 patients with motion artifacts were excluded, and 163 patients' CTA scans were examined. After examination, the patients with CB borders were indistinguishable from the adjacent vascular structures on both sides, and the patients with carotid stents were also excluded to avoid measurement errors.

CB could not be visualized on the right side in 8 (4.9%) and on the left side in 11 (6.7%) patients. CB could not be distinguished on either side in 2 (1.2%) patients. The visualization rate was 93.8% on the left (153 of 163 patients) and 92% on the right (150 of 163 patients). Unilaterally visualized and measured CBs were included in the statistical analysis. The total number of patients included in the study was 158.

The criteria for exclusion and the numbers and rates of the included and excluded patients are presented in the flowchart of patient selection (Figure 1).

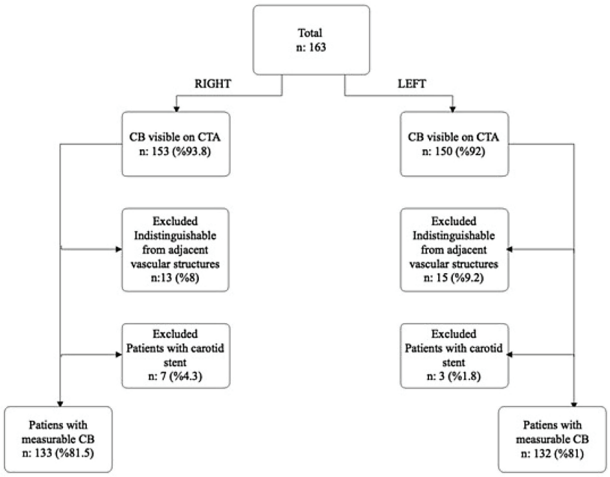

Figure 1. The flowchart of patient selection.

Study groups

The control group consisted of non-smokers without any of the chronic disorders investigated (n=33).

The study group was divided into three subgroups as:

1. Smokers only (S group) (n=21),

2. The patients with hypertension alone (HT group) (n=26),

3. The patients with at least two chronic disorders or the smokers with one chronic disorder (CD+S group) (n=78). This group included 71 patients with hypertension, 33 with diabetes mellitus (DM), 13 with chronic heart failure (CHF), and 13 with chronic obstructive pulmonary disease (COPD). In this group, 52 individuals were smokers.

Imaging protocol

The CTA scans were obtained with a 64 multi-row detector CT system (Aquilion 64, Toshiba Medical Systems, 2011, Japan). The CT protocol parameters were as follows: Tube voltage: 120 kV, tube current: 300 mA, rotation time: 0.5 sec, pitch: 0.6, axial section thickness: 0.5 mm, reconstruction interval: 0.4 mm. The scans were performed between the inferior border of the aortic arch and the superior border of the frontal sinus. The bolus tracking method was used for contrast delay, and the imaging was started when the aortic density was 120 Hounsfield units (HU). 100 ml non-ionic, iodinated contrast agent (350 mg/ml iodine concentration) and then 30 ml saline were administered intravenously from the antecubital vein through an 18-20 G catheter at a rate of 5 ml/sec, using an automatic pump (Ulrich Medizin technical version, 2004, Germany).

Image Analysis

The obtained CTA images were examined on axial, sagittal, coronal or oblique plans in the work-station using Aquarius iNtuition® software (ver. 4.4.11.82.6784, California, USA). To obtain a standard view, 200% magnification was used at a window width of 700 and a window level of 200. The usual CB localization, the infero-medial aspect of the carotid bifurcation, was examined to identify CB. In the aforementioned localization and on the axial sections, the ovoid structure, which was highly enhanced in the arterial phase, was considered CB (Figure 2). Axial, coronal, sagittal, coronal oblique and sagittal oblique images were examined in terms of the location, size, and borders of CB (Figures 3, 4).

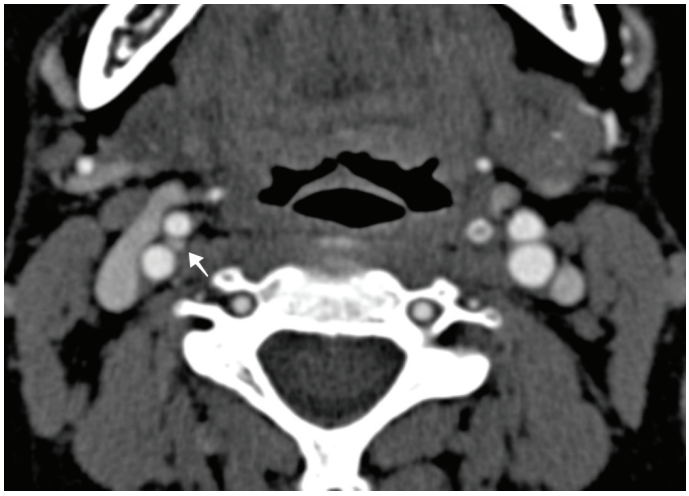

Figure 2. Axial CT image. Normal CB (arrow) in the right carotid bifurcation.

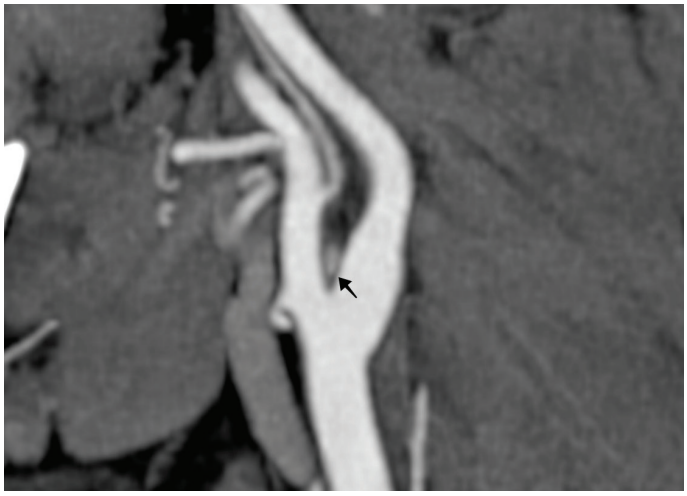

Figure 3: Sagittal MIP image. Normal CB (arrow) in the right carotid bifurcation.

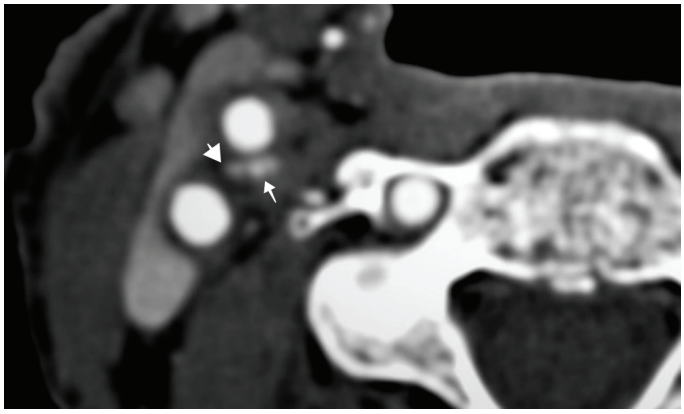

Figure 4. Axial CT image. CB in the right carotid bifurcation (arrow) and a branch of external carotid artery adjacent to CB (arrowhead).

The images with motion artifacts or with an inadequate arterial phase, the patients with CB tumors, tubular structures suggestive of vessels showing continuity in the consecutive sections, and the CB-like structures which were not located in the typical site were excluded. To avoid measurement errors, the CBs were excluded if their borders could not be clearly distinguished from the neighboring vessels (Figure 5). The sides on which patients had carotid stents were excluded since the borders of CB could not be distinguished clearly due to streak artifacts.

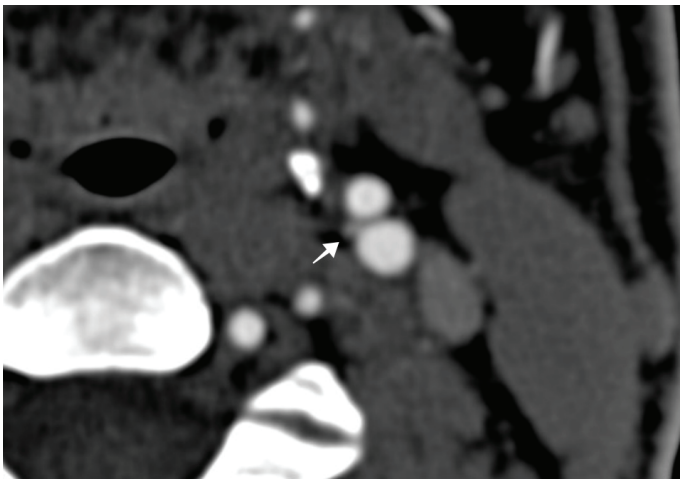

Figure 5. Axial CT image. CB in the left carotid bifurcation with indistinguishable borders from internal and external carotid arteries (arrow).

Since no standard technique has yet been determined to measure the CB size, and coronal, sagittal, and oblique sections have spatial resolution limitations, the CB diameters were measured only on axial sections. The measurements were performed by a single radiologist with 5-year experience and blinded to patient data. On axial sections where CB was seen the largest on both sides, the longest axis of CB was measured (Figure 6).

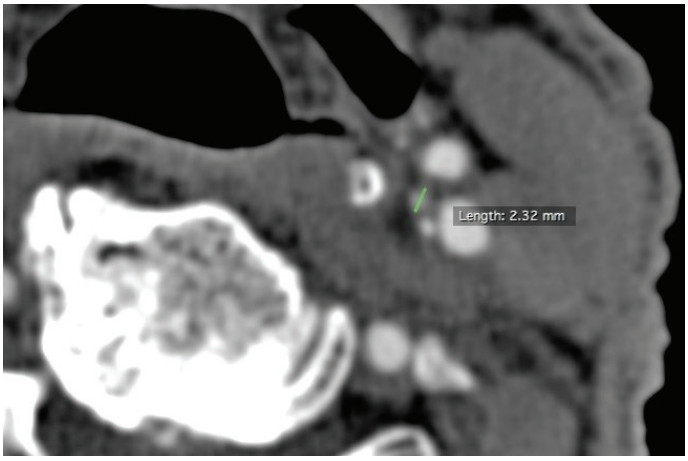

Figure 6. Measurement of CB's longest diameter on axial CT image.

Thirty patients were selected randomly without any distinction among the study groups, and the measurements were repeated independently of the initial measurements to test intra-observer agreement.

Statistical analysis

The data were analyzed using SPSS v.15.0 (SPSS Inc., Chicago, USA) package program. The descriptive statistics were presented as mean and standard deviation for the variables with normal distributions and median and minimum-maximum values without normal distribution. The numbers and percentages were presented for nominal variables. Two-group comparisons of the means were analyzed with Student's t-test, and two-group comparisons of the medians were analyzed with the Mann-Whitney U test. Kruskal Wallis test was used to analyze the difference of medians when the number of groups was more than two. Bonferroni correction was performed to determine the group causing the difference. Nominal variables were analyzed with Pearson Chi-Square or Fisher exact tests. Generalized Estimating Equations (GEE) analysis was used to test whether the right and left CB measurements affected the study group, age, or gender factors. The Wilcoxon test compared right and left CB measurements on the axial plane since the group distributions were not normal. Intraclass Correlation Coefficient (ICC) was used to analyze the intra-observer agreement. P <0.05 was considered as statistically significant.

Results

The ages of the control and S groups were similar (p=0.129); however, the mean ages of the HT and CD+S groups were significantly higher than the control group (p=0.001 for both). The gender distribution was homogenous in the control and HT groups (p=0.218 and p=0.175, respectively); however, it was heterogeneous in the S group and the CD+S group (p=0.004 and p=0.015, respectively). The male/female ratio was higher in the S group and the CD+S group. The demographic data of the study groups are summarized in Table 1.

Table 1. Demographic characteristics of the study groups.

	Gender					
	Female	Male	Total (n)	Age (years) Median (min-max)	p for age	p for gender
Control	19 (58%)	14 (42%)	33	49 (18-88)	-	0.218
S	6 (%29%)	15 (71%)	21	48 (21-68)	0.129	0.004§
HT	18 (69%)	8 (31%)	26	65 (50-67)	0.001*	0.175
CD+S	31 (40%)	47 (60%)	78	63 (25-88)	0.001*	0.015§
Total (n)	74 (47%)	84 (53%)	158			

S: Smoking group, HT: Hypertension group, CD+S: Chronic disorder + smoking group. * The median ages of HT and CD+S groups are greater than the S group and the control group. § The gender distribution is not homogenous in S group and CD+S group.

The mean diameters of CB were 2.62 ±0.7 mm and 2.62 ±0.76 mm on the right and left sides, respectively, without any statistically significant difference between them (p=0.167). The CB diameter was not significantly correlated with age (Pearson's r=0.218; p=0.078) or gender (p=0.289).

Considering age and gender, the right and left CB diameters were analyzed altogether and compared with GEE analysis. There was no significant difference between the control group and the S group for CB diameters (p=0.123), however HT group (p=0.020) and CD+S group (p= 0.001) had greater CB diameters compared to the control group (Table 2).

Table 2. Comparison of CB diameters among the study groups.

Groups	Mean	Standard Deviation	95% Wald Confidence interval		P
			Lower	Upper	
Control	2.22	3.41	-4.47	8.92	-
S Group	2.47	3.44	-4.28	9.23	0.123
HT Group	2.77	3.28	-3.68	9.2	0.020*
CD+S Group	2.76	3.38	-3.86	9.4	0.001*

*p<0.05
S: Smoking group, HT: Hypertension group, CD+S: Chronic disorder + smoking group.

Thirty patients were randomly selected without taking the study groups into consideration, and the observer performed two measurements at different times to evaluate intra-observer repeatability and agreement. Intraclass Correlation Coefficient (ICC) was found as 0.91 on the right and 0.94 on the left side, which indicated a strongly high intra-observer agreement.

Discussion

In this study, we found that smokers without any comorbid disease did not have a higher CB diameter compared to the controls. A greater CB diameter was determined in patients with HT alone and those with at least two sympathetically mediated chronic conditions compared to the controls.

The small size of CB and the difficulty of its dissection have made studies on CB difficult. Until recently, our knowledge about CB was limited to animal experiments and postmortem studies, but it is now possible to visualize CB in vivo by means of different imaging modalities (10-13). Normal CB has a high vascularity and this feature allows its detection on CTA images. Nguyen et al. were the first authors who demonstrated normal CB on routine neck CTA studies in 2011 (10). In our study, CB was seen on the right in 93.8% of the patients who underwent CTA, and on the left in 92%, which was higher than the rates reported in the literature (10-12). This result may be explained by thinner section thickness, 0.5 mm, we used in the axial reconstructions; the cross-section thickness of 1 mm was used in the aforementioned studies.

The normal-sized CB should be differentiated from nerve sheath or CB tumors; therefore the normal radiological limits of CB diameters should be determined. CB tumors can be easily identified in cross-sectional imaging modalities since they reveal typical findings when they are bigger than certain diameters. However, the absence of typical imaging findings in tumors smaller than 10 mm in diameter makes the differential diagnosis difficult in lesions located in this region (14). In our study, the maximum CB diameter was 3.5 mm in patients with no comorbid disorders and 6.8 mm in patients with a sympathetically mediated comorbid disease. In light of this data, a highly contrast-enhanced structure measured less than 7 mm in its maximum diameter on transverse plain should be considered normal CB, provided that they are in their typical localization.

The relationship between CB hypertrophy and the disorders with sympathetic hyperactivity, including HT, CHF, and DM, has been demonstrated in several studies (11,12,15). Cramer et al. showed that the patients with at least one of HT, CHF, or DM had a 20-25% increase in CB size compared to the control group (11). Nair et al. found a significant increase in CB diameter in patients with HT and CHF compared to the control group (12). In addition to these studies, greater CB diameters were found in the patients with HT alone (16). Similarly, we found a significantly greater CB diameter in patients with HT alone, and in patients with more than one sympathetically mediated disease.

It has been known that high altitude and chronic hypoxia-related states play a role in the etiology of CB tumors (17,18). It may be assumed that chronic hypoxia may affect the CB size, and cause hypertrophy. Smoking may cause chronic hypoxia, and thus may cause an increase in the size of CB. Although Nguyen et al. reported that smoking was not correlated with CB hypertrophy, they did not provide statistical data, and to the best of our knowledge, no studies in the literature have investigated the isolated effect of smoking on CB diameters on CTA in detail after excluding other conditions with sympathetic hyperactivity (10). In our study, we found that smokers without any sympathetically mediated disorders did not have increased CB diameters (p=0.123). This may be explained by the absence of chronic hypoxemia in smokers without chronic lung disease.

After CB's role in disorders with sympathetic hyperactivity has been revealed, treatment options targeting CB have come to the agenda. In preclinical experiments, CB denervation in rats with spontaneous HT has been shown to cause a decrease in systemic blood pressure (2,19). Recently, human studies of CB resection in the treatment of essential HT and CHF reported promising results (20-24). We think that the evaluation of CB location and size with CTA may be useful for the research and development of treatment options targeting CB.

Our study has some limitations. First, when evaluating CB hypertrophy, volume measurement would give better results due to the irregular and asymmetrical shape of the organ. However, the volume measurements made on the workstations on CTA images do not provide reliable results due to the small size of CB. In our study, the longest axial diameter was measured to evaluate the CB dimensions, and the single-axis measurement was insufficient to measure the volume of this organ. Also, although we found statistically significantly different CB sizes in our study groups, the difference was approximately 0.5 mm due to the small size of CB. There were overlaps in the CB diameters among the study groups. This makes a determination of a definitive cut-off value difficult when evaluating the increase in CB diameters. Second, although we planned to investigate the relationship of CB diameters with DM, CHF, and COPD separately at the beginning of our study, we could not do this due to the small number of patients with the aforementioned disorders; therefore, we included all those disorders into CD+S group. The retrospective nature of our study did not let us consider the severity of these conditions, whether the patients were on treatment or not, as well as the determination of the duration of the disorders and hence their correlations with CB size.

Conclusion

It is possible to visualize normal CB on CTA in the majority of cases. Smoking, in absence of any sympathetically mediated disorder, does not cause a significant increase in CB size. In hypertensive individuals, there is a greater CB size, independent of other sympathetically mediated disorders. CB size also increases significantly in individuals with combination of disorders related to sympathetic hyperactivity such as HT, CHF, and DM. CTA may provide a better understanding of the relationship between CB and sympathetically mediated disorders and guide further studies as well as therapies targeting CB.

Declerations

Ethical approval

Our retrospective study has been approved by the local ethics committee (E-15-590).

Competing interest

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

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Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article.

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Research Article

Assessment of cervical cancer screening and human papillomavirus awareness among female nurses

Kadın hemşireler arasında serviks kanseri taraması ve human papillomavirus farkındalığının değerlendirilmesi

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Abstract

Aim: The purpose of this article is to investigate the level of cervical cancer screening and human papillomavirus (HPV) awareness among female nurses and potential factors that influence their knowledge and practices.

Material and Methods: A cross-sectional survey comprising of a self-administered questionnaire in four parts was distributed to nurses employed in two hospitals located in Turkey. The questionnaire included 27 items focused on topics including HPV transmission, vaccination, and prevention methods, cervical cancer risk factors, and symptoms. A total of 260 nurses participated in the study, and descriptive statistics were reported, including mean and standard deviation for continuous variables and frequency and percentage for categorical variables.

Results: The results showed that 35.4% of participants had reservations about undergoing a gynecological examination, and 64.6% had not undergone a smear test within the last five years. Moreover, 75.4% had not undergone an HPV test within the last five years. With increasing age, awareness of HPV, frequency of undergoing smear and HPV tests increased, and this difference was found to be statistically significant. No statistical relationship was found between hospital type and knowledge about HPV vaccination, while married nurses had more knowledge about the vaccine and underwent smear and HPV tests more frequently than single nurses.

Conclusion: The findings from this study may help improve cervical cancer prevention and screening programs, enhance HPV awareness, and promote better health outcomes for women.

Key words: Cervical cancer, human papilomavirus, awareness, nurse

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Öz

Amaç: Bu makalenin amacı, kadın hemşireler arasında serviks kanseri tarama ve insan papilloma virüsü (HPV) farkındalık düzeyini ve bilgi ve uygulamalarını etkileyen olası faktörleri araştırmaktır.

Gereç ve Yöntemler: Türkiye'deki iki hastanede çalışan hemşirelere, dört bölümden oluşan bir anket formunu elektronik ortamda yanıtlamaları istenerek kesitsel bir araştırma yapılmıştır. Anket, HPV bulaşma, aşılanma ve önleme yöntemleri, serviks kanseri risk faktörleri ve semptomları gibi konulara odaklanan 27 sorudan oluşmaktadır. Toplam 260 hemşire çalışmaya katılmış ve sürekli değişkenler için ortalama ve standart sapma, kategorik değişkenler için ise frekans ve yüzde gibi betimsel istatistikler rapor edilmiştir.

Bulgular: Katılımcıların %35.4'ünün jinekolojik muayene yapılması konusunda tereddütleri olduğunu ve %64.6'sının son beş yıl içinde smear testi yaptırmadığını göstermiştir. Ayrıca, %75.4'ünün son beş yıl içinde HPV testi yaptırmadığı saptanmıştır. Yaşın ilerlemesiyle birlikte, HPV farkındalığı, smear ve HPV testleri sıklığı artmakta ve bu farkın istatistiksel olarak anlamlı olduğu bulunmuştur. Hastane tipi ile HPV aşısı hakkındaki bilgi arasında istatistiksel bir ilişki bulunmamışken, evli olan hemşireler aşı hakkında daha fazla bilgi sahibi olmuş ve bekâr hemşirelere göre daha sık smear ve HPV testi yaptırmışlardır.

Sonuç: Bu çalışmanın bulguları, serviks kanseri önleme ve tarama programlarını geliştirmeye, HPV farkındalığını artırmaya ve kadınlar için daha iyi sağlık sonuçlarını teşvik etmeye yardımcı olabilir.

Anahtar kelimeler: Serviks kanseri, human papillomavirüs, farkındalık, hemşire

Introduction

Cervical cancer (CC) is the most common gynecologic cancer, with 604,000 women diagnosed and 341,000 deaths in 2020 [1]. Human Papilloma Virus (HPV) is present in 99.7% of cases and is used for cervical cancer screening (CCS) [2]. In developed countries where screening programs, HPV testing, and vaccination are routinely implemented, the incidence and mortality of CC are low [3]. It is predicted that reaching 70% vaccination worldwide could prevent 178,000 CC deaths [4]. Risk factors for CC include early sexual activity, early childbirth, multiple sexual partners, high-risk sexual partners, immunosuppression [5], oral contraceptive use, low socioeconomic level, and smoking [6]. CC may not show symptoms in its early stages, with irregular and excessive bleeding and postcoital bleeding being the most common symptoms [7]. Cervical cytology is a diagnostic and screening method for CC, but in some countries, the screening test is HPV testing, followed by cervical cytology for positive cases [8].

Prevention and early detection of CC are possible through awareness of CC risk factors, HPV, and screening methods [9]. Early detection through regular CCS and awareness of HPV is crucial in preventing and reducing the burden of this disease. As frontline healthcare providers, female nurses play a vital role in educating and promoting CCS and HPV awareness among women in their communities [10]. Therefore, it is essential to investigate the level of CCS and HPV awareness among female nurses and identify potential factors influencing their knowledge and practices. The findings from this study may help improve CC prevention and screening programs, enhance HPV awareness, and promote better health outcomes for women.

Material and Method

The present study was designed as a cross-sectional survey utilizing a questionnaire-based approach.The study instrument was built using a culturally modified version of the University College London's Health Behaviour Research Center's CC Awareness Measure questionnaire. Using Google Forms to transfer survey questions is a simple and effective way to streamline the data collection process. The Google Forms helped to get the data needed to make informed decisions. Participants were requested to answer survey questions created using Google Forms by sending them via WhatsApp link.

A cross-sectional survey comprising of a self-administered questionnaire in four parts and 27 items focused on topics including HPV transmission, vaccination, and prevention methods, CC risk factors, and symptoms, was distributed to nurses employed in two hospitals located in Turkey.

Informed consent forms were obtained from the participants.

Suleyman Demirel University Ethics Committee approval was obtained on 20.09.2022 with approval number 18/241.

Statistical analysis

The statistical data were transferred to IBM SPSS.26 (IBM Inc, Chicago, IL, USA) for analysis. Prior to conducting statistical analyses, parameters were checked to ensure that there were no data input errors and that they fell within expected ranges. Descriptive statistics including mean and standard deviation for continuous variables and frequency (n) and percentage (%) for categorical variables were reported. The relationship between categorical variables was assessed using the Chi-square test. Differences between means of independent groups were examined using ANOVA for normally distributed variables and Kruskal Wallis test for non-normally distributed variables. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 260 nurses were included in our study, with a mean age of 30.8 ± 8.6 (range 18-59) years. Of the participants, 154 (79.5%) were married and 106 (20.5%) were single. Demographic characteristics of the participants are summarized in Table 1.

Table 1. Socio-demographic characteristics of the participants.

	n	%
Institution		
Public	164	63,1
Private	96	36,9
Marital Status		
Single	106	40,8
Married	154	59,2
Education		
High School	96	36,9
University	164	63,1
Child Status		
Exist	124	47,7
Not exist	136	52,3
Chronic disease		
Exist	44	16,9
Not exist	216	83,1
Relatives with cancer		
Exist	112	43,1
Not exist	148	56,9
Friends with cancer		
Exist	92	35,4
Not exist	168	64,6
	n	%
Institution		
Public	164	63,1
Private	96	36,9
Marital Status		
Single	106	40,8
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Education		
High School	96	36,9
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Child Status		
Exist	124	47,7
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Chronic disease		
Exist	44	16,9
Not exist	216	83,1
Relatives with cancer		
Exist	112	43,1
Not exist	148	56,9
Friends with cancer		
Exist	92	35,4
Not exist	168	64,6

The answers given by the participants to the survey questions are shown in tables 2, 3, 4, and 5.

Table 2. Responses given for diseases caused by HPV.

	n	%
"Does HPV cause genital warts?"		
Yes	192	73,8
No	12	4,6
I have no idea	56	21,5
"Does HPV cause CC?"		
Yes	180	69,2
No	16	6,2
I have no idea	64	24,6
"Does HPV causes oral and throat cancer? "		
Yes	88	33,8
No	76	29,2
I have no idea	96	36,9

Table 3. Responses to questions about HPV transmission, vaccination, and prevention methods.

	n	%
"Can HPV be sexually transmitted?"		
Yes	200	76,9
No	20	7,7
I have no idea	40	15,4
"Can the risk of HPV sexual transmission be reduced by condom use?"		
Yes	156	60,0
No	40	15,4
I have no idea	64	24,6
"Do you know anything about the HPV vaccine?"		
Yes	160	61,5
No	76	29,2
"Can HPV infection be prevented by vaccination?"		
Yes	144	55,4
No	24	9,2
I have no idea	92	35,4
"Is HPV vaccine routinely administered in Turkey?"		
Yes	20	7,7
No	152	58,5
I have no idea	88	33,8
"Have you been vaccinated against HPV?"		
Evet	28	10,8
Hayır	232	89,2
"Is there a CC and HPV screening program in Turkey?"		
Yes	132	50,8
No	44	16,9
I have no idea	84	32,3

Table 4. Responses to CC risk factors

	n	%
"Does HPV infection increase the risk of CC?"		
Yes	176	67,7
No	12	4,6
I have no idea	72	27,7
"Does smoking increase the risk of CC?"		
Yes	172	66,2
No	16	6,2
I have no idea	72	27,7
" Does suppression of the immune system increase the risk of CC?"		
Yes	176	67,7
No	12	4,6
I have no idea	72	27,7
"Does taking oral contraceptives for more than 5 years increase the risk of CC? "		
Yes	92	35,4
No	52	20,0
I have no idea	116	44,6
"Does having multiple sexual partners increase the risk of CC?"		
Yes	216	83,1
No	4	1,5
I have no idea	40	15,4
"Does starting sexual intercourse under 20 years old increase the risk of CC?"		
Yes	116	44,6
No	32	12,3
I have no idea	112	43,1

When we asked if they had any reservations about undergoing a gynecological examination, 92 (35.4%) stated that they had reservations, while 168 (64.6%) stated that they did not have reservations. When we asked those who were hesitant to undergo a gynecological examination about the reason, 26.2% stated that they experienced pain during the examination, 24.6% stated that they felt embarrassed, and 10.8% cited work-related busyness as the reason. When we asked if they had undergone a smear test within the last 5 years, 64.6% stated that they had not, while 35.4% stated that they had undergone the test.

When we asked if they had undergone an HPV test within the last 5 years, 75.4% stated that they had not, while 24.6% stated that they had undergone the test. With increasing age, awareness of HPV, frequency of undergoing smear and HPV tests increased, and this difference was found to be statistically significant.

When compared with questions about knowledge of HPV vaccination, whether they had received the HPV vaccine, whether they had undergone a smear test within the last 5 years, and whether they had undergone an HPV test within the last 5 years, nurses in public hospitals were found to have more knowledge about the vaccine and to undergo smear and HPV tests more frequently than those in private hospitals. No statistical relationship was found between the given values ($p>0.05$).

Table 5. Participants' responses to questions about symptoms of CC.

	n	%
"Can intermenstrual bleeding be one of the symptoms of CC?"		
Yes	160	61,5
No	20	7,7
I have no idea	80	30,8
"Can persistent low back pain be one of the symptoms of CC?"		
Yes	136	52,3
No	44	16,9
I have no idea	80	30,8
"Can persistent vaginal discharge be one of the symptoms of CC?"		
Yes	188	72,3
No	16	6,2
I have no idea	56	21,5
"Can painful sexual intercourse be one of the symptoms of CC?"		
Yes	156	60,0
No	16	6,2
I have no idea	88	33,8
"Can prolonged or heavy menstrual bleeding be a symptom of CC?"		
Yes	140	53,8
No	36	13,8
I have no idea	84	32,3
"Can persistent diarrhea be one of the symptoms of CC?"		
Yes	32	12,3
No	84	32,3
I have no idea	144	55,4
Can vaginal postmenopausal bleeding be one of the symptoms of CC?		
Yes	148	56,9
No	12	4,6
I have no idea	100	38,5
"Can persistent pelvic pain be one of the symptoms of CC?"		
Yes	156	60
No	16	6,2
I have no idea	88	33,8
"Can bleeding during sexual intercourse be one of the symptoms of CC?"		
Yes	140	53,8
No	16	6,2
I have no idea	104	40,0
"Can blood in the urine or stool be one of the symptoms of CC?"		
Yes	24	9,2
No	68	26,2
I have no idea	168	64,6
"Could involuntary weight loss be one of the symptoms of CC?"		
Yes	136	52,3
No	24	9,2
I have no idea	100	38,5

When compared with questions about knowledge of HPV vaccination, whether they had received the HPV vaccine, whether they had undergone a smear test within the last 5 years, and whether they had undergone an HPV test within the last 5 years, it was found that married nurses had more knowledge about the vaccine and underwent smear and HPV tests more frequently than single nurses. No statistical relationship was found between marital status and knowledge about HPV vaccination ($p>0.05$). However, a statistical relationship was found between marital status and whether they had received the HPV vaccine, undergone a smear test within the last 5 years, and undergone an HPV test within the last 5 years ($p<0.05$).

Discussion

The results of this study suggest that there is a need for increased awareness of CC and HPV among nurses. While the majority of nurses surveyed were aware of CC and HPV, a significant proportion reported a lack of knowledge and confidence in their ability to educate patients on the topic. This is particularly concerning, given the important role that nurses play in providing patient education and promoting preventative health behaviors.

In a study conducted in Cameroon to evaluate the level of CC awareness among healthcare workers. While the majority of the participants were aware of the significance of CC as a public health issue, as well as the associated risk factors and diagnostic methods, the level of awareness among nurses and midwives was comparatively lower [11].

A study on the knowledge of CC and screening practices among nurses in Tanzania revealed that less than half of the nurses were aware of CC. Moreover, the majority of nurses were unaware of the recommended screening intervals, and only a few were aware of the HPV vaccine. Additionally, 84.6% of the participants had never undergone a Pap smear examination. However, in this study, 61.5% of the nurses were aware of the HPV vaccine, and 10.8% had been vaccinated. In our study, 35.4% of the participants had undergone a Pap smear examination [12]. This difference may be due to the higher level of education of nurses in Turkey.

In a study conducted in Turkey on the awareness of CC and HPV infection and attitudes towards the HPV vaccine among women, it was found that women were fearful of being diagnosed with CC and HPV infection, despite having inadequate knowledge on the subject matter. The participants had limited knowledge on the HPV vaccine, lacked knowledge on where to acquire it, and had insufficient knowledge on its potential benefits and harmful effects [13].

One possible explanation for these findings is a lack of formal education and training on CC and HPV during nursing programs. It is possible that many nurses have not received adequate education on these topics and therefore may not feel confident in their ability to provide accurate and comprehensive patient education.

Moving forward, it is important to consider strategies for improving awareness and education among nurses, such as incorporating comprehensive CC and HPV education into nursing curricula, providing ongoing professional development opportunities, and promoting interdisciplinary collaboration between nurses and other healthcare providers. By increasing awareness and knowledge of CC and HPV among nurses, we can improve patient education and ultimately contribute to the prevention and early detection of CC.

The findings of this study highlight the need for increased awareness and education on CC and HPV among healthcare workers, particularly nurses. While many nurses are aware of the importance of CC and HPV, a significant proportion lack knowledge and confidence in educating patients on the topic. The findings also suggest that there may be a need for more comprehensive education on CC and HPV during nursing programs. Strategies such as incorporating education on CC and HPV into nursing curricula, providing ongoing professional development opportunities, and promoting interdisciplinary collaboration between healthcare providers could be useful in improving awareness and knowledge among nurses. Ultimately, improving awareness and knowledge among healthcare workers can contribute to the prevention and early detection of CC, which is essential for reducing its burden on society.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

Suleyman Demirel University Ethics Committee approval was obtained on 20.09.2022 with approval number 18/241.

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Araştırma Makalesi

Kendine zarar verme davranışı olan ergenlerde aile işlevlerinin, ebeveyn ve arkadaşlara bağlanmanın, karar verme stillerinin ve problem çözme becerilerinin değerlendirilmesi

Evaluation of family functioning, attachment to parents and friends, decision-making styles and problem solving skills in adolescents with non suisidal self-injury behavior

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Öz

Amaç: Kendine zarar verme davranışı, intihar amacı olmaksızın kişinin kendi bedenine yönelik zarar verici davranışta bulunmasıdır. Yapılan çalışmalarda birçok psikiyatrik bozuklukla beraber olabildiği gösterilmiştir. Ayrıca kendine zarar verme davranışının etiyolojisinde kişiler arası etkileşim (aile ve arkadaşlara bağlanma), akran zorbalığı, istismar öyküsü gibi birçok etkenin yer aldığı bilinmektedir. Kendine zarar verme davranışı olan ergenlerin klinik uygulamalarda problem çözme ve karar verme becerilerinde güçlükler yaşadıkları görülmekle birlikte bu alanda yazında oldukça az araştırma olduğu dikkati çekmektedir. Çalışmamızda kendine zarar verme davranışı nedeniyle polikliniğe başvuran ergenlerin karar verme stillerini, problem çözme becerilerini, arkadaş ve ebeveyne bağlanmalarını, aile özellikleri ve işlevselliklerini sağlıklı ergenlerle karşılaştırarak incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmamıza Manisa Ruh Sağlığı ve Hastalıkları Hastanesine başvuran, kendine zarar verme davranışı olan, 10-17 yaş aralığında bulunan 46 olgu ve 33 sağlıklı kontrol alınmıştır. Olgu ve kontrol grubundaki her ergene sosyodemografik veri formu, aile değerlendirme ölçeği, ebeveyn ve arkadaşlara bağlanma envanteri, ergenlerde karar verme ölçeği ve problem çözme envanteri uygulanmıştır.

Bulgular: Gruplar sosyodemografik veriler açısından karşılaştırıldığında olgu grubunda anne baba boşanmasının daha sık ve ailenin aylık gelirinin daha düşük olduğu sonucuna varılmıştır. Kendine zarar veren grupta sigara kullanımı ve intihar

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girişimi istatistiksel olarak anlamlı derecede yüksek bulunmuştur. Kendine zarar veren ergenlerde aile değerlendirme ölçeğinin gereken ilgiyi gösterme ve genel işlevler alt boyutunda kontrol grubuna göre anlamlı derecede olumsuzluk saptanmıştır. Ergenlerde karar verme ölçeği değerlendirildiğinde karar vermede öz saygı bölümü kendine zarar veren grupta anlamlı derecede düşük bulunmuştur. Aynı ölçeğin panik kısmı hasta grubunda anlamlı derecede yüksek bulunmuştur. Kendine zarar veren grupta bağlanma envanterinin ebeveyn alt ölçeği anlamlı derecede düşük bulunmuştur. Problem çözme envanteri değerlendirildiğinde kendine zarar veren grupta anlamlı derecede yüksek puan aldığı saptanmıştır.

Sonuçlar: Kendine zarar veren çocuk ve gençlerde aile ile olan ilişkide, karar verme süreçlerinde, aile bağlanması ve problem çözmede yazınla uyumlu şekilde sorunlar mevcuttur. Kendine zarar veren çocuk ve gençlerin bu alanlarda desteklenmesi tedavinin bir parçası olmalıdır.

Anahtar Kelimeler: Kendine zarar verme, ergen, karar verme, problem çözme, aile işlevselliği, ebeveyne bağlanma

Abstract

Aim: Non-suisidal self injury is an act that involves self-harm without a thought about suisid. Non- suisidal self injury may be associated with many psychiatric disorders. It is known that many factors such as interpersonal interaction (attachment to family and friends), peer bullying, and a history of abuse are involved in the etiology of self-harming behavior. In our study, we aimed to examine the decision-making styles, problem-solving skills, attachment to friends and parents, family characteristics and functionality of adolescents who have non-suisidal self-injury and applied to the outpatient clinic.

Materıal and Methods: Fourty six patients aged between 10 and 17 years and 33 healthy controls were included in our study who applied to Manisa Mental Health Hospital. Sociodemographic data form, Family Assesment Device, Inventory of Parent and Peer Attachment, Adolescent Decısıon Makıng Questıonnaıre and Problem Solving Inventory were applied to the patient and control groups.

Results: When the groups were compared in terms of sociodemographic data, it was concluded that the parental divorce was more frequent and the monthly income of the family was lower in the case group. Simoking and suicide attempt was significantly higher in non-suisidal self injury group. In the subscales of the Family Assesment Device showing the required attention and general functioning were found significantly lower in the non-suisidal self injury group. Self-esteem subsscale in decision making was found to be significantly lower, the panic part of the same questıonnaıre was significantly higher and the family subscale of the attachment inventory was significantly lower in the case group. When Problem Solving Inventory was evaluated, it was found that the non-suisidal self injury group had significantly higher scores.

Conclusıon: In children and adolescents with non-suisidal self injury, there are problems in relation to family, decision-making processes, family attachment and problem solving in accordance with literature. Supporting children and young people in these areas should be part of the treatment.

Keywords: Non suisidal self injury, adolescent, desicion making, problem solving, family functioning, attachment to parent

Giriş

Kendine zarar verme davranışı (KZVD), intihar amacı olmaksızın kişinin kendi bedenine yönelik zarar verici davranışta bulunmasıdır [1]. Yapılan en geniş kapsamlı meta analiz çalışmalarından birinde 18 yaş altında kendine zarar verme sıklığı yüzde 17,2 olarak bulunmuştur [2]. KZVD'nin genellikle 10-24 yaş arasında başladığı ve ortalama başlangıç yaşının 13-14 olduğu bildirilmektedir [3]. Geçmişte yaşanmış fiziksel, duygusal ve cinsel istismarın, nörobiyolojik ve genetik faktörlerin, olumsuz kendilik algısı, olumsuz duygulanım, impulsivite, düşük stres toleransı ve disosiyatif yaşantılar gibi kişisel psikolojik etkenlerin KZVD'nin ortaya çıkmasında etken olduğu bildirilmektedir [3]. KZVD'nin ortaya çıkmasında kişiler arası etkileşim (aile ve arkadaşlara bağlanma), akran zorbalığı, istismar öyküsü gibi birçok etken neden olabilir [4]. Aile içi çatışmaların KZVD için risk faktörü olduğu, aile içi bağların sağlamlığının ve aile bütünlüğünün olmasının ise koruyucu faktörlerden biri olduğu bildirilmektedir [5]. Güvenli bağlanma biçimine sahip ergenler aile ve arkadaşlarıyla daha fazla uyumlu, kendilerine ve başkalarına daha çok güvenen ve daha az sosyal problemler

yaşamaktadırlar. Güvensiz modellere sahip olan ergenler daha az uyuma sahiptir ve kendi duygularını düzenlemede ve stresle başa çıkmada sorunlar yaşayabilirler [6]. Literatürde güvensiz bağlanma ile KZVD arasındaki ilişki ile ilgili net veriler olmamakla birlikte, bağlanma kaygısı ve bağlanma kaçınmasının ikisinin de KZVD'yi etkilediğini ve her ikisinin de duygu düzenlenmesindeki zorluklarla ve problemlerle baş etme becerileri ile ilişkili olduğu bulunmuştur [7]. Literatürde intihar girişiminde bulunan ergenlerin zayıf problem çözme becerilerine sahip oldukları ve probleme odaklanma konusunda güçlük çektikleri, alternatiflerin genellenmesi, karar verme becerileri ve bulunan çözümlerin uygulanması konusunda da sağlıklı ergenlerden daha fazla güçlükler yaşadıkları belirtilmektedir [8,9]. KZVD'si olan ergenlerin de klinik uygulamalarda problem çözme ve karar verme becerilerinde güçlükler yaşadıkları görülmekle birlikte bu alanda yazında oldukça az araştırma olduğu dikkati çekmektedir. Kendine zarar veren çocuk ve gençlerin bu alanlarda desteklenmesi tedavinin bir parçası olmalıdır. Tüm bu bilgiler ışığında KZVD'nin ortaya çıkmasında ergenlere ve aileye ait birçok özellik risk faktörü olarak bildirilmektedir. Olumsuz ebeveyn tutumlarına sahip anneleri olan, problem çözme ve sağlıklı karar vermede güçlükleri olan ergenlerin KZVD gösterdikleri hipotezi kurularak çalışmamızda KZVD nedeniyle polikliniğe başvuran ergenlerin karar verme ve problem çözme becerilerini, arkadaş ve ebeveyne bağlanmalarını, aile özellikleri ve işlevselliklerini sağlıklı ergenlerle karşılaştırarak incelemeyi amaçladık. Bilebildiğimiz kadarıyla yazında ergenlerde bağlanma özelliklerinin, problem çözme ve karar verme becerilerinin, aile işlevselliğinin KZVD ile olan ilişkisinin aynı örneklemde incelendiği bir başka araştırma bulunmamaktadır.

Gereç ve Yöntemler

Çalışmamıza olgu grubu olarak çocuk ve ergen ruh sağlığı ve hastalıkları polikliniğine başvuran en az bir yıl içerisinde bir kez kendine zarar verme davranışı olan yaşları 10-17 yaş arasında değişen 46 ergen alınmıştır. Kontrol grubu olarak yaş ve cinsiyet açısından eşleştirilmiş 33 sağlıklı ergen ile görüşülmüştür. Hem olgu hem de kontrol grubu için en az bir ebeveynin ulaşılabiliyor olması göz önüne alınmıştır. Şizofreni ve psikotik bozukluk, bipolar ve ilişkili bozukluklar, alkol ve madde kullanım bozukluğu, otistik spektrum bozukluğu, mental retardasyon gibi klinik tanıları olan ergenler çalışmaya dahil edilmemiştir. Çalışmaya katılmayı kabul eden ve çalışma kriterlerine uyan ergenlerden ve ebeveynlerinden yazılı onam alınmıştır. Çalışmaya başlanmadan önce Celal Bayar Üniversitesi Girişimsel olmayan Araştırmalar Etik Kurulundan 27.07.2017 tarih ve 20.478.486-53 numaralı etik onam alınmıştır.

Her ergen ve ailesi ile görüşülerek yarı yapılandırılmış bir görüşme olan Okul Çağı Çocukları İçin Duygulanım Bozuklukları ve Şizofreni Görüşme Çizelgesi-Şimdi ve Yaşam boyu Şekli Türkçe uyarlaması (Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version, K-SADS-PL) uygulanmıştır. Bu uygulama ile diğer psikiyatrik hastalıklar dışlanmıştır. Araştırmacı tarafından sosyodemografik veri formu doldurulmuştur. Ayrıca olgu ve kontrol grubundaki her ergene aile değerlendirme ölçeği, ebeveyn ve arkadaşlara bağlanma envanteri, ergenlerde karar verme ölçeği ve problem çözme envanteri uygulanmıştır.

Veri Toplama Araçları

Sosyodemografik Veri Formu;

Ergenin yaşı, cinsiyeti, aile yapısı, aile ile ilgili özellikleri, sosyoekonomik düzeyi hakkında bilgileri içeren literatür temel alınarak araştırmacılar tarafından hazırlanmış bir formdur.

Aile Deðerlendirme Ölçeği (ADÖ);

Aile Değerlendirme Ölçeği ABD'de Aile Araştırma Programı çerçevesinde geliştirilen ve aile işlevlerini çeşitli boyutlarda ölçmek için kullanılan 60 maddelik bir ölçektir. Problem çözme, iletişim, roller, duygusal tepki verme, gereken ilgiliyi gösterme, davranış kontrolü ve genel fonksiyonlar adı altında yedi alt ölçekten oluşmaktadır. Ölçek "aynen katılıyorum" cevabı için bir puan ile "hiç katılmıyorum" cevabı için dört puan arasında değişen şekilde puanlanmaktadır. On iki yaş üzeri her aile bireyine uygulanabilmektedir. Ölçeğin alt ölçek puanları iki veya üstü olduğu durumlarda o aile işlevinin sorunlu olduğu düşünülmektedir. Ölçeğin Türkçe'ye uyarlaması Bulut ve ark. Tarafından yapılmıştır [10].

Ebeveyn ve Arkadaşlara Bağlanma Envanteri (EABÖ):

Armsden ve Greenberg tarafından geliştirilmiş olan Ebeveyn ve Arkadaşlara Bağlanma Ölçeği'nin Raja ve arkadaşları tarafından hazırlanan 12 maddelik kısa formudur. Ölçek Türkçe'ye Günaydın ve arkadaşları tarafından uyarlanmıştır. Ölçekteki her madde 1-7 arasında puanlanmaktadır (1=asla, 7=daima). Toplamda ölçekten elde edilen puanın yüksekliği güvenli bağlanmaya işaret etmektedir. Bu ölçekte bağlanma puanı anne, baba ve arkadaş için ayrı ayrı hesaplanabilmektedir [11,12].

Ergenlerde Karar Verme Ölçeği

Mann, Harmoni ve Power (1989) tarafından karar vermede öz-saygı ve başa çıkma stillerini belirlemek amacıyla geliştirilmiştir. Ölçek iki bölümden ve 5 alt ölçekten oluşmaktadır. Bunlar; Karar Vermede Öz-saygı (Decisional Self Esteem) ve Karar Vermede Başa Çıkma Stilleri (Decisional Coping Patterns)'dir. Ölçeğin

Karar Vermede Öz-saygı bölümü karar verme durumunda bireyin öz-saygı düzeyini ölçmeyi amaçlamaktadır. Bu bölüm için ölçekte altı madde yer almaktadır. Karar vermede öz-saygı bölümünden alınabilecek en yüksek puan 18, en düşük puan 0'dır. Puan yüksekliği karar vermede öz-saygının yüksekliğine işaret ederken, düşük puan karar vermede öz-saygı düzeyinin düşük olduğunu göstermektedir [13].

Ölçeğin ikinci bölümü karar vermede başa çıkma stillerinden oluşmaktadır. Karar vermede başa çıkma stilleri ihtiyatlı-seçicilik (vigilance), panik (panic), sorumluluktan kaçma (Cop-Out) ve umursamazlık (complacency) alt ölçeklerinden oluşmaktadır. Bu alt ölçeklerin her birini değerlendiren altı madde vardır. Her bir alt ölçekten alınabilecek en yüksek puan 18 en düşük puan 0'dır. Puan yüksekliği ilgili karar stilinin kullanıldığına işaret etmektedir.

Çolakkadıoğlu ve Güçray (2007), "Ergenlerde Karar Verme Ölçeği'nin (EKVÖ) Türkçe'ye uyarlama, geçerlik ve güvenirlik çalışmalarını yapmışlardır [14].

Problem Çözme Envanteri

Problem çözme envanteri bireyin problem çözmede kendisine güvenini, bireysel kontrol duygusunu ve yaklaşım biçimini değerlendirmeyi amaçlamaktadır. Üniversite öğrencilerinin problem çözme becerilerini nasıl algıladıklarını belirlemek için, Heppner ve Petersen tarafından geliştirilen Problem Çözme Envanteri 35 maddeden oluşmaktadır [15]. Likert tipi bir ölçektir ve maddeleri 1-6 arasında puanlanmaktadır. Ölçekten alınabilecek en düşük puan 32, en yüksek puan ise 192'dir. Ölçekten alınan puanların yüksekliği ise bireylerin kendilerini problem çözme becerileri konusunda yetersiz olarak algıladıklarını göstermektedir. Bu çalışmada Şahin, Şahin ve Heppner (1993) tarafından Türkiye'ye uyarlanmış olan ölçek kullanılmış, toplam puan değerlendirmeye alınmıştır [16].

İstatiksel Analiz

İstatistiksel analiz için SPSS 20 kullanılmıştır. Verilerin değerlendirmesinde tanımlayıcı istatistikler (ortalama, standart sapma, minumum, maximum, yüzde) ve değişkenlerin karşılaştırılmasında Kategorik veriler için ki kare, parametrik varsayımı yerine getiren gruplarda Indepentent T testi, parametrik varsayımları yerine getiremeyen gruplarda Mann-Whitney U testi kullanılarak değerlendirilmiştir. $p<0,05$ istatistiksel olarak anlamlı kabul edilmiştir.

Bulgular

Çalışmada olgu grubu 46, sağlıklı kontrol grubu 33 ergenden oluşmuştur. Gruplar arası karşılaştırmalarda olgu grubunun yaş ortalaması 14,8±2,7, kontrol grubunun yaş ortalaması 15,15±1,6 olarak saptanmıştır. Cinsiyet açısından olgu grubunun %80,4'ünü (n=37), kontrol grubunun %72,7'sini (n=24) kız cinsiyet oluşturmaktadır. Gruplar arasında yaş ve cinsiyet açısından anlamlı farklılık bulunmamıştır (p>,05).

Olgu ve kontrol grubu sosyodemografik veriler açısından karşılaştırıldığında ders başarısı (iyi, orta, kötü) ve kardeş sayısı açısından gruplar arasında istatistiksel olarak anlamlı düzeyde fark bulunmamıştır.

Olgu grubunun %30,4'ü (n=14) orta, %69,6'ü (n=32) düşük; kontrol grubunun %9,1'i (n=3) yüksek, %66,6'sı (n=22) orta, %24,2'si (n=8) düşük aylık gelire sahip olduğunu belirtmiştir. Olgu ve kontrol grubu aylık gelir düzeyi açısından karşılaştırıldığında olgu grubunun aylık gelir düzeyinin anlamlı olarak daha düşük olduğu görülmüştür ($x2=17,67$, $p=0,001$).

Olgu ve kontrol grubu aile özellikleri açısından karşılaştırıldığında aile yapısı açısından (çekirdek, geniş) iki grup arasında anlamlı bir fark saptanmazken; anne ve babanın boşanmış olma durumunun olgu grubunda anlamlı olarak daha fazla olduğu görülmüştür ($x2=8,39$, $p=0,047$). Olgu grubundaki ergenlerin % 45,6'sının (n=21); kontrol grubundaki ergenlerin ise %18,2'sinin (n=6) ailelerinde ruhsal hastalık tanısı ile takipli birey bulunduğu ve her iki grup arasında bu açıdan istatistiksel anlamlı bir fark olduğu anlaşılmıştır ($x2=6,44$, $p=0,01$).

Ergenler sigara, alkol ve uyuşturucu madde kullanımları açısından sorgulanmıştır. Olgu grubunda ayda birkaç kez den fazla sigara kullananlar %50 (n=23) iken; kontrol grubunda %78,7 (n=26) olarak hesaplanmıştır. Olgu ve kontrol grubundaki ergenler arasında alkol ve uyuşturucu madde kullanımı açısından anlamlı bir farklılık yokken; sigara kullanımı olgu grubunda kontrol grubuna göre anlamlı oranda artmış bulunmuştur ($x2=6,76$, $p=0,009$).

Olgu ve kontrol grubu intihar girişimlerinin varlığı açısından karşılaştırılmıştır. Kontrol grubundaki hiçbir ergenin daha önce intihar girişiminde bulunmadığı; olgu grubundaki ergenlerin ise %60,9'unun (n=28) daha önce intihar girişiminde bulunduğu görülmüştür. İki grup arasındaki fark istatistiksel olarak anlamlıdır ($x2=32,87$, $p=0,000$).

Aile işlevselliğini değerlendirmek için kullanılan ADÖ alt ölçek puanlarına bakıldığında; olgu grubundaki ergenlerin kontrol grubuna göre "davranış kontrolü" alt ölçeği dışında diğer tüm alt ölçek puanlarında daha yüksek olduğu bulunmuştur. Ancak istatistiksel anlamlılığın sadece "gereken ilgiyi gösterme" ve "genel işlevler" alt ölçek puanları arasında olduğu; "iletişim" alt ölçek puanının ise istatistiksel anlamda sınırda olduğu saptanmıştır (Tablo 1).

Tablo 1: Olgu ve kontrol grubundaki ergenlerin Aile Değerlendirme Ölçeği alt ölçek puanlarının karşılaştırılması

	Olgu grubu (n=46)			Kontrol grubu (n=33)			P
	Ort	Median	Min-max	Ort	Median	Min-max	
Gereken ilgiyi gösterme	2,54	2,57	1,71-3,29	2,36	2,42	1,71-3,00	0,016**
Davranış kontrolü	2,17	2,22	1,11-3,00	2,27	2,44	1,33-2,78	0,13*
İletişim	2,51	2,61	1,11-3,78	2,24	2,22	1,11-3,22	0,055**
Genel işlevler	2,40	2,37	1,00-4,00	2,04	2,16	1,00-3,00	0,018**
Problem çözme	2,41	2,33	1,00-4,00	2,27	2,50	1,00-3,17	0,74*
Roller	2,42	2,40	1,36-3,27	2,25	2,36	1,27-2,91	0,056**
Duygusal tepki verebilme	2,47	2,41	1,00-4,00	2,26	2,50	1,00-3,17	0,31*

*Mann-Whitney U Testi, **Student T testi

Ergenlerin doldurduğu Ebeveyn ve Arkadaşlara Bağlanma Envanteri puanları karşılaştırıldığında; olgu grubundaki ergenlerin ebeveyne bağlanmayı gösteren puanlarının kontrol grubundaki ergenlere göre daha düşük olduğu ve bu düşüklüğün istatistiksel olarak anlamlı olduğu bulunmuştur (t=3,46, p=0,01).

Ergenlerde Karar Verme Ölçeği'nin "karar vermede özsaygı" ve "ihtiyatlı seçicilik" alt ölçek puanları kontrol grubunda olgu grubuna göre daha yüksek saptanırken; istatistiksel anlamlı fark sadece "karar vermede özsaygı" ölçeğinin puanlarındaydı (z= 3,40, p=0,001). Aynı ölçeğin "panik", "sorumluluktan kaçma" ve "umursamazlık" alt ölçek puanları ise olgu grubunda kontrol grubuna göre yüksek bulunmuştur (Tablo 2). Ancak bu üç alt ölçekten sadece "panik" alt ölçeği puanlarının yüksekliği olgu grubunda kontrol grubuna göre istatistiksel olarak anlamlıydı (t=3,64, p=0,000).

Tablo 2: Olgu ve kontrol grubundaki ergenlerin Ergenlerde Karar Verme Ölçeği alt ölçek puanlarının karşılaştırılması

	Olgu grubu (n=46)			Kontrol grubu (n=33)			P
	Ort	Median	Min-max	Ort	Median	Min-max	
Karar vermede özsaygı	1,35	1,33	0,17-2,83	1,89	1,83	0,83-3,00	0,001*
İhtiyatlı seçicilik	1,76	1,66	0,50-3,00	1,86	1,83	1,00-3,00	0,46**
Panik	1,75	1,75	0,00-3,00	1.13	1,00	0,00-2,17	0,000**
Sorumluluktan kaçma	1,22	1,16	0,00-2,83	0,87	0,83	0,00-1,67	0,058*
Umursamazlık	1,05	0,83	0,00-3,00	0,81	0,83	0,00-1,67	0,38*

*Mann-Whitney U Testi, **Student T testi

Problem Çözme Envanteri'nin toplam puanı olgu ve kontrol grubu için karşılaştırıldığında; olgu grubunda toplam puanın istatistiksel olarak anlamlı yüksek olduğu saptanmıştır (z=2,63, p= 0,008).

Tartışma

Kendine zarar verme davranışı olan ve olmayan ergenlerin ailesel özelliklerinin ve ergenin karar vermesinin, problem çözmesinin, aile ve arkadaşa bağlanmasının değerlendirildiği bu çalışmada; ailenin aylık gelir düzeyi, aile işlevselliği, anne ve babanın boşanmış olması ve ailede ruhsal bozukluk varlığı alanlarında farklılık gösteren bulgulara ulaşılmıştır. Bununla birlikte kendine zarar veren ergenlerde sigara kullanımı ve intihar girişiminin fazla olduğu gösterilmiştir. Kendine zarar veren ergenlerde ebeveyne bağlanmanın düşük olması, karar verme ve problem çözme süreçlerinde sorunlar yaşadıkları da ulaşılan bulgular arasındadır.

Çalışmamızda kendine zarar veren ergenlerde ailenin aylık gelir düzeyi daha düşük bulunmuştur. Yazında da birçok çalışmada kendine zarar verme davranışı ve ekonomik düzey arasında yakından bir ilişki olduğu gösterilmiştir. Kendine zarar verme davranışının düşük ekonomik düzeyde özellikle kız ergenlerde daha sık görüldüğü bildirilmiştir [17]. Ekonomik düzeyin düşmesi ile ortaya çıkan sorunlar ergenlerin baş etmesi gereken stresi artırarak kendine zarar verme davranışında artışa sebep olabilir [18]. Çalışmamızdaki bulgular yazındaki sonuçlarla uyumludur.

Bazı çalışmalarda aile yapısı ve özelliklerinin kendine zarar verme davranışı üzerinde etkili olmadığı gösterilmesine karşın; birçok çalışmada parçalanmış yapıda olan, göç eden, aile içi şiddetin var olduğu ve ebeveynler arası evlilik sorunlarının olduğu ailelerde ergenlerin daha sıklıkla kendine zarar

verdikleri gösterilmiştir [19]. Çalışmamızda da yazın bilgisi ile uyumlu şekilde kendine zarar veren ergenlerde vermeyenlere göre anne ve babanın boşanmış olma durumunun daha fazla olduğu saptanmıştır.

Aile işlevselliğini doğrudan etkileyen ebeveynin psikiyatrik bozukluğu ile, KZVD arasındaki ilişkiyi inceleyen çalışmalar gözden geçirildiğinde yapılan bir tez araştırmasında kendine zarar verme davranışı olan ergenlerin ailelerinde sağlıklı ergenlere göre anlamlı olarak daha fazla psikiyatrik bozukluğa sahip birey saptandığı görülmüştür [20]. Bebekliğin erken dönemlerinden itibaren bakım verenlerin çocukla kurduğu ilişki ve verdiği duygusal tepkilerin çocuğun duygu düzenleme işlevlerini belirlediği bilinmektedir. Bu bilgi ışığında bakıldığında; anne veya babanın psikiyatrik bozukluğunun bulunması, çocuk ve ergenin duygu düzenleme yeteneklerinin gelişimini bozabilir [21].

Çalışmamızın sonuçlarına göre; sigara kullanımı kendine zarar veren ergenlerde sağlıklı kontrollere göre fazla bulunmuştur. Yazında sigara kullanımının kendine zarar verme riskini özellikle kız ergenlerde 2-3 kat arttırdığının gösterildiği bir çalışma mevcuttur. Bununla birlikte yapılan diğer çalışmalarda kendine zarar veren ergenlerde sigara kullanımı %36 saptanırken, sağlıklı ergenlerde bu oran %5 saptanmıştır [22]. Ülkemizde yapılan çalışmalarda da sigara kullanımının kendine zarar verme riskini 9 kat arttırdığı gösterilmiştir [19]. Tüm bu çalışmalarla paralel olarak çalışmamızda da benzer bir sonuca ulaşılmıştır. Toplumumuzda diğer toplumlara göre sigara kullanan ergenlerde KZVD riskinin artmış olduğu ve kendine zarar veren ergenlerde yüksek sigara kullanım oranlarının başka sorunların da varlığına işaret ediyor olabileceği düşünülebilir.

Kendine zarar verme ve intihar girişimi arasındaki karmaşık ilişki yapılan çalışmalarla anlaşılmaya çalışılmaktadır. Bazı çalışmalarda intihar düşüncesine sahip olma kendine zarar verme davranışı için bir risk faktörü olarak gösterilirken; KZVD olan ergenlerin intihar girişimi için risk altında olduğu da söylenmektedir [23]. Tekrarlayan kendine zarar verme davranışı ile ilgili hipotezde, tekrarlayıcı şekilde kendine zarar veren kişinin bir süre sonra buna alıştığı ve ağrı duyusunun azaldığı düşünülmektedir. Böylelikle intihar girişimi için cesaretinin arttığı, kendine zarar verme davranışının bu şekilde bir mekanizma ile intihar için bir öncül davranış olabileceği öne sürülmektedir [24]. Yazında kendine zarar veren kişilerin %50-75'inin daha sonraki bir zamanda intihar girişiminde bulunabilecekleri bildirilmektedir [24]. Çalışmamızda da tüm bu bilgileri destekleyecek şekilde kendine zarar veren ergenlerde sağlıklı kontrollere göre intihar girişiminde bulunma daha sık saptanmıştır.

Yazındaki birçok çalışma ailesinden ayrı olan veya çocukluk döneminde ailesinden ayrı kalan ergenlerin KZVD açısından daha riskli grupta olduğunu göstermiştir. Olumsuz aile ilişkilerinin, duygusal ihmalin ergenin aileden yardım istemesinin önüne geçtiği ve bu sebepten dolayı baş edemediği duygu ve düşünceleri olduğu zaman kendine zarar vermeyi seçebildiklerine dair çalışmalar mevcuttur [25]. Çalışmamızda da yazındaki çalışmalara benzer şekilde kendine zarar veren ergenlerde aile üyelerinin birbirine gösterdiği ilgi, sevgi ve bakımının sağlıklı ergenlere göre daha az olduğu saptanmıştır. Bununla birlikte Aile Değerlendirme Ölçeği'nin aile işlevselliğini gösteren altı alt boyutunu kapsayan "genel işlevler" alt ölçeği puanlarının kendine zarar veren ergenlerde sağlıklı kontrollere göre anlamlı olarak daha yüksek saptanmasının nedeni kendine zarar veren ergenlerin Aile Değerlendirme Ölçeği'nin çoğu alt ölçeğinden daha yüksek puanlar alması ile ilişkili olabilir. Bu da olgu grubundaki ergenlerin istatistiksel anlamlılık olmasa da aslında aile içinde birden fazla işlev alanında problem yaşadığını göstermektedir.

Çalışmamızda kendine zarar veren ergenlerin ebeveynlerine bağlanmalarının sağlıklı ergenlere göre daha düşük olduğu bulunmuştur. Yapılan çalışmalarda ailesel bağların daha iyi olduğu ailelerde yetişen ergenlerin daha az sıklıkla psikopatoloji gösterdiği üzerinde durulmuştur [26]. Benzer şekilde aile içi bağların sağlam olmasının ve aile bütünlüğünün KZVD için koruyucu bir faktör olduğunu gösteren çalışmalar da mevcuttur [27]. Zayıf aile bağları ile KZVD arasındaki güçlü ilişki çalışmalarda tekrarlayan bulgulardandır. Tüm bu bilgiler ışığında çalışmamızdaki bulgu yazındaki bilgilere paralellik göstermektedir.

Çalışmamız verileri değerlendirildiğinde kendine zarar veren ergenlerde karar vermede öz saygının sağlıklı ergenlere göre düşük olduğu görülmüştür. Bununla birlikte kendine zarar veren ergenlerin karar vermede başa çıkma stillerinden panik stilini kullanmaları onların sağlıklı ergenlere göre karar vermesi gereken durumlarda yeterli zamanı yoksa kendisini stresten ve çatışmadan kurtarmaya yönelik kararlar verdiğini göstermiştir.

Karar vermede öz saygı kişilerin kendilerine güven duymalarını, düşüncelerini rahatça ifade edebilmelerini, karar verirken başkalarından bağımsız olabilmelerini ve istediklerini yapabilmekte kendilerini özgür hissetmelerini kapsar [28]. Yazında yapılan çalışmalarda kendine zarar veren ergenlerin benlik saygısının daha düşük olduğu; benlik saygısındaki düşüklük arttıkça daha fazla oranla kendine zarar verme davranışı olan arkadaş seçtikleri gösterilmiştir [29]. Yine yapılan bir tez çalışmasında benzer şekilde kendine zarar veren

ergenlerin benlik saygıları sağlıklı ergen grubuna göre anlamlı olarak daha düşük saptanmıştır [30]. Benlik saygıları düşük olan ergenlerin karar verirken de başkalarından bağımsız olmakta zorlanabilecekleri düşünülebilir.

Yazında kendine zarar veren ergenlerdeki karar verme stilleri üzerine yapılan çalışmalar sınırlıdır. Kendine zarar veren ve vermeyen ergenlerin karar verme yeteneklerinin ölçüldüğü bir çalışmada iki grup arasında anlamlı fark bulunmamıştır [31]. Ancak yapılan başka bir çalışmada kendine zarar veren ergenlerin grubu kendine zarar verme davranışı halen devam edenler ve kendine zarar verme davranışı öyküsü bulunanlar şeklinde ayrıldığında; halen kendine zarar verme davranışı olanlarda kısa vadeli, yüksek ödüllü sonuçları olan kararlara daha fazla yönlendikleri ve uzun vadeli cezalardan kaçmak için stratejiye daha az uyum sağlamaları ile kendini gösteren zayıf karar verme becerileri sergiledikleri görülmüştür [32]. Karar verme yeteneğinin kendine zarar verme epizotlarının yeniliği ile doğrudan bir ilişkisi olduğu bu çalışmada söylenmiştir. Bizim çalışmamızda da kendine zarar verme davranışı devam eden ergenlerin çalışmaya dahil edildiği göz önüne alındığında ergenlerin kendini stresten kurtarmaya yönelik kısa süreli kararlar vermesinin yazınla uyumlu olduğu düşünülmüştür Bununla birlikte prefrontal korteks ergenlik döneminde gelişimini sürdürmektedir [33]. Zayıf ve yüksek riskli karar verme prefrontal korteks yetersizliğine bağlı düşünülebilir. Geçmişte kendine zarar verme öyküsü olan ergenlerin karar verme becerilerinin sağlıklı ergenlere benzer olması bu becerinin gelişim aşamasında değişebildiğini ve prefrontal korteksin gelişmesi ile hem kendine zarar verme davranışının hem de karar verme becerilerinin geliştiği söylenebilir [32].

Karar verme becerileri aynı zamanda problem çözme becerilerinin bir komponentidir. Bu yüzden çalışmamızda kendine zarar veren ergenlerde problem çözme becerileri değerlendirilmiş ve kendine zarar veren ergenlerde sağlıklı ergenlere göre problem çözme becerinin daha kötü olduğu saptanmıştır. Yazındaki çalışmalarda kendine zarar veren ergenlerin problem çözmede başa çıkma becerilerini kendine zarar vermeyenlere göre daha az kullandıkları gösterilmiştir [34]. Çalışmamızdaki veriler yazın ile uyumlu olmakla birlikte daha önceki çalışmalarda kendine zarar veren ergenlerdeki karar verme ve problem çözme becerilerinin daha az ele alındığı görülmüştür. Suisid düşüncesi veya girişimi olan ergenlerde daha çok araştırılmış bu becerilerin çalışmamızda kendine zarar veren ergenlerde araştırılmış olması çalışmamızın yazına önemli katkılarındandır.

Çalışmamızın bazı kısıtlılıkları da bulunmaktadır. Seçilen örneklem sadece kliniğe başvuran ergenlerden oluştuğundan kliniğe başvurmayan ergenler temsil edilememiştir. Kliniğe başvurmayan ama kendine zarar verme davranışı olan ergenlerin aileye ilişkin özellikleri, arkadaşlara ve ebeveyne bağlanma özellikleri, karar verme ve problem çözme becerileri farklılık gösteriyor olabilir. Çalışmamızda yapılan değerlendirmeler ergenlerin doldurması istenen formlar ile yapılmıştır aile işlevselliğini değerlendirirken ebeveynlerden de bilgi alınmamış olması çalışmamızın kısıtlılıklarından sayılabilir. Ebeveynlerin de değerlendirildiği, karar verme ve problem çözme becerilerini değiştirebilecek değişkenlerin ele alındığı, bu süreçlerin form dışında bazı testlerle ölçüldüğü, toplum tabanlı yeni çalışmalar planlanabilir.

Sonuç

Kendine zarar verme davranışının ergenlik döneminde sıklıkla karşılaşılabilen bir sağlık sorunu olduğu bilinmektedir. Çalışmamızda kendine zarar veren ergenlerin aile özelliklerinin, arkadaş ve ebeveyne bağlanmalarının, karar verme ve problem çözme becerilerinin araştırılması planlanmıştır. Yazındaki verilerle birlikte bu çalışmamızın sonuçları kendine zarar verme davranışının değerlendirilmesi ve tedavi başarısının arttırılması için aile işlevselliğinin, ebeveyne bağlanmanın, karar verme ve problem çözme becerilerinin dikkatle ele alınmasının, tedavi planı oluştururken bu alanlarda mevcut eksikliklerin göz önünde bulundurulmasının, gerekiyorsa eksikliği saptanan bu alanın tedavide odak noktası alınmasının ve gerekli müdahalelerin yapılmasının önemli olduğunu göstermektedir.

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Research Article

Evaluation of analytical performance of tests worked on the same brand devices with six sigma metrics

Aynı marka cihazlarda çalışılan testlerin six sigma metrikleri ile analitik performansının değerlendirilmesi

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ABSTRACT

Aim: The aim of this study is that evaluate the analytical performance with six sigma metrics between the same brand devices actively working in the laboratory and answer the question of which tests will be performed on these devices according to the laboratory test working rates.

Material and Methods: In the research, all tests were studied on Abbott brand, Architeck c8000, and Architeck ci4000 model devices for 6 months. Glucose (Glc), blood urea nitrogen (BUN), creatinine (CREA), aspartate aminotransferase (AST), total cholesterol (CHOL), triglycerides (Tg), sodium (Na), potassium (K), chlorine (Cl) parameters were evaluated in the sigma values were calculated according to the performance approach. The comparisons were drew between these two devices. Total allowable error (TEa) is derived from the Clinical Laboratories Improvement Amendments (CLIA) guidelines.

Results: In the comparative follow-up performed for 6 months, the determination of the parameters to be worked on which device on monthly basis varied. Since the sigma values of the glucose, urea and creatinine tests, which are the most studied in our laboratory, are lower in the Architeck ci4000 device than the Architeck c8000 device. It was decided to run these tests only on the Architeck c8000 device. All metrics have been obtained until October 2019. An increase in the sigma value was detected with the start of working of electrolytes on a single device six months later.

Conclusıon: Six sigma metrics should be used monthly to monitor tests with particularly low biological variation to evaluate the method performance of same-brand devices which is used for thousands of tests.

Keywords: six sigma, Architeck ci4000, Architeck c8000, Westgard

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Öz

Amaç: Altı sigma ile analitik testlerin istenilen kalitede olup olmadığı ve kalitenin sayısal değeri görülebilir. Laboratuvarlara sunulan testlerin yöntem kalitesini değerlendirmek, cihazlar arasında yöntem performansını karşılaştırmak, kalite kontrol prosedürlerini yeniden gözden geçirmek konusunda altı sigma metriklerinden faydalanılmaktadır.

Gereç ve Yöntemler: Bu çalışmanın amacı; laboratuvarda aktif çalışılan aynı marka cihazlar arasındaki altı sigma metrikleri ile analitik performansın değerlendirilmesi ve laboratuvar test çalışma hızına göre bu cihazlarda hangi testlerin çalışılıp çalışılmayacağı sorusuna yanıt bulmaktır. Yapılan araştırmada bütün testler ABBOTT marka Architeck c 8000 ve Architeck ci 4000 cihazlarında 6 ay süre ile çalışılmıştır. Glukoz (Glc), üre (BUN), kreatinin (CREA), aspartat aminotransferaz (AST), total kolesterol (CHOL), trigliseritler (Tg), Sodyum (Na), potasyum (K), klor (Cl) parametreleri değerlendirilmiş testlerin sigma değerleri performans yaklaşımına göre hesaplanmış ve cihazlar arasında karşılaştırma yapılmıştır. Toplam kabul edilebilir hata (TEa), Klinik Laboratuvarları İyileştirme Yasası (CLIA) klavuzlarından alınmıştır. Bias, yeterlilik test verilerine göre belirlenmiştir. Biyokimyasal analitler için varyasyon katsayısı (CV) laboratuvarımızın IQC kayıtlarından elde edilmiştir. Sigma metrikleri (SM) = (TEa-%Bias)/ %CV formülüne göre hesaplanmıştır

Bulgular: 6 ay boyunca yapılan karşılaştırılmalı takipte ay bazında hangi cihazda çalışılması gereken parametrelerin belirlenmesi değişkenlik göstermiştir. Laboratuvarımızda en fazla çalışılan glucose, urea ve creatinine testlerinin Architeck ci 4000 cihazında sigma değerleri Architeck c8000 cihazından daha düşük olduğu için bu testlerin sadece c8000 cihazında çalışılmasına karar verildi. Elde edilen metriklere göre, 2019 Ekim ayından itibaren başlattığımız çalışmada altı ay sonra elektrolitlerin tek cihazda çalışılmaya başlanması ile sigma değerinde artış tespit edildi.

Sonuç: Altı sigma metrikleri, binlerce test yapılan aynı marka cihazların yöntem performansını değerlendirmede aylık olarak özellikle düşük biyolojik varyasyona sahip testleri takip etmek için kullanılmalıdır.

Anahtar Kelimler: altı sigma, Architeck ci4000, Architeck c8000, Westgard

Introduction

Advances in medicine and health technology, increasing patient expectations, facilitating access to health services, aging of the world population, increasing chronic diseases have accelerated health expenditures and costs in the world. This situation has challenging as an important issue for both governments and health institutions [1]. In today's competitive environment, it is indispensable to develop strategies on issues such as production, quality, customer and user satisfaction, and cost advantage in health sector as well as other institutions. In this context, it is aimed to improve institutional practices by using various techniques that are considered as post-modern [2]. Considering that 75-80% of individuals who apply to the hospital have tests in clinical laboratories, keeping the quality of the total laboratory process under control becomes a necessity in terms of institutional and national health services.

Six sigma is a strong, systematic, disciplined, problem-solving, well-organized organization designed to eliminate the source of errors identified by customers as defects and mistakes, to eliminate unnecessary activities in processes to reduce deviations, and to structure in a way that corresponds to 3.4 errors per million in statistically supported organizational effectiveness and development. It is a proactive, ongoing process improvement strategy. However, Six Sigma accepts 3.4 defect scans per million, 7 Sigma, which has come to the fore in recent years, targets 0.019 defects per million [3].

The total test process in clinical laboratories consists of 3 phases: preanalytical, analytical and post analytic. According to the studies, the estimated error rates for the phases of the total test process vary between 30-75% in the preanalytical phase, 4- 30% in the analytical phase, and 9-55% in the postanalytical phase [4]. In recent years, with the significant efforts of both laboratories and manufacturers of laboratory equipment and reagents, errors in the analytical phase of the total testing process have decreased significantly [5]. Quality standardization must begin with analytical quality in a laboratory because analytical quality is the quality characteristic required for all laboratory testing. Analytical quality is not a stand-alone quality requirement, but the other quality parameters do not matter unless analytical quality is ensured. Laboratories must be able to provide accurate test results before other quality requirements [6]. The analytical

process defines the test methods, analyzers used, internal and external quality control and calibrations which come to the fore moreover makes control of variables is more possible [7].

Six sigma uses a stepwise process called DMAIC, this abbreviation means: Define, Measure, Analyze, Improve and Control. These stages allow improving the quality of any process at the project level or throughout the organization [8]. It is valuable the strong impact on the healthcare sector, including the large number of case studies published, which are focused on hospitals and improving medical procedures [9,10]. In healthcare, it is vital to use quality management systems as six sigma for ensuring efficiency because the commission of errors may seriously cause costs of patients' life. Six Sigma method; It is a quality management tool that is based on statistical calculations, focused on process variables, and provides information about process performance. The key indicator is the process sigma level. According to, six sigma method, process performance is evaluated according to the poor-quality costs determined from the process sigma levels, and it is aimed to reduce these poor-quality costs in improvement [11]. The evaluation of the pre- and post-analysis processes together with the analysis process with the six sigma method also provides a holistic view to the process.

By means of the six sigma method, it is possible to determine the possibility of an false result in a system that is thought to be under control. Considering that tests with low sigma values show poor analytical performance, they should be followed more closely and if they do not show improvement, the need for a detailed evaluation of the analytical method will arise and perhaps a decision to change the method will be carried on. Another benefit of using Sigma values is that, it gives the opportunity to tweak control applications [12]. For example, once-daily follow-up with two levels of internal quality control (IQC) and the 1_{3S} Westgard rule is recommended for tests with a sigma value ≥6. If the Sigma value is 4-6, daily two-level control and the Westgard multiple rule of 1_{3S}, 2_{2S}, R_{4S} are applied. If the Sigma value is 3-3.99, two-level control and the 1_{3S}, 2_{2S}, R_{4S}, 4_{1S} Westgard multiple rule apply twice a day. If the sigma value is less than 3, root cause analysis should be performed and method performance should be improved before it enters routine use. In this way, it is thought that the loss of time that causes delays in both cost and results can be reduced by reducing false IQC rejections [13]. The IQC rules recommended to be applied according to sigma values by Westgard are shown in Table 1. Sigma Value Performance Definition IQC Rules.

Table 1. Recommended IQC rules according to Sigma values

igma Value	Performance Definition	IQC Rules
<3	Unsatisfactory - Method performance needs improvement	1_{3S} / 2_{2S} / R_{4S} / 4_{1S}; 2 times per a day, 3 level
3-3.99	Sufficient performance More often inspection	1_{3S} / 2_{2S} / R_{4S} / 4_{1S}; 2 times per a day, 2 level
4-6	Good/acceptable performance	1_{3S} / 2_{2S} / R_{4S}; 1 time per day, 2 level
≥6	Excellent performance	1_{3S} ;1 time per day, 2 level

The process based on this study is the clinical laboratory analytical process. Expectations from this process are to obtain accurate and reliable test results. To achieve this aim, bias values, which are the accuracy criteria, were obtained from the repeatability criterion coefficient of variation (CV) and external quality control evaluation programs, which are constantly applied in IQC programs, and these values were used in the calculation of process sigma level.

The aim of these quality control processes is to reach the quality targets determined by the authorities. These quality objectives are most commonly referred to as Allowable Total Error (TEa). The total allowable error may be determined based on the clinical significance and clinical experience of the analyte, the biological variability of the analyte, the analytical competence achieved, or the level of analytical errors. Errors that do not negate the clinical usefulness of the test may fall into the allowable total error. The laboratory can document the analytical quality by comparing its Total Analytic Error (TAH) with the allowable total error limit. For patient safety, the total analytical error should not exceed the total allowable error limit. Total analytical error (TAH) is the sum of Random Error and Systematic Error reflected in a test result. Biological variation (BV) describes the variation observed in the concentration or activity of different components in an individual, reflecting regulation by homeostatic processes in the body. High-quality BV data have been produced in recent years by the European Working Group on Biological Variation (EuBIVAS). Total acceptable error limits determined according to biological variation are lower.

In this study we evaluated the analytical performance with six sigma metrics between the same brand devices actively working in the laboratory and answer the question of which tests will be performed on these devices according to the laboratory test working rates.

Material and Methods

In this study, we inspected the performance of biochemical analytes on same brand devices as calculating six sigma metrics. The research and data collection process has been retained during 6 months in Istanbul Atlas University Medicine Hospital Clinical Laboratory. The tests of sigma metrics were calculated as a performance approach and the comparison was interpreted between same brand devices. Glucose (Glc), urea, creatinine (CREA), aspartate aminotransferase (AST), total cholesterol (CHOL), triglyceride (Tg), sodium (Na), potassium (K), clor (Cl) parameters were evaluated and all test were carried on Abbott brand, Architeck c8000, and Architeck ci4000 model devices during 6 months. Total allowable error (TEa) is derived from the Clinical Laboratories Improvement Act (CLIA) guidelines. Bias was determined based on proficiency test data. The coefficient of variation for biochemical analytes was obtained from the IQC records of our laboratory.

Sigma metrics (SM) were calculated according to the formula (SM) = (TEa-% Bias) / %CV. The parameters were sorted into 6 categories conceiving world-class performance (SM = 6 or more), excellent performance (SM = 5-6), good performance (SM = 4-5), marginal performance (SM = 3-4), poor performance (SM = 2-3) and unacceptable performance (SM is less than 2) [14]. After exclusion of IQC and outlier data each parameter CV value was determined. The external quality control data were used for each deviation of parameters. The internal QC data was removed from October 2019 and March 2020 analysis records. Quality inspection was done before each analytical process. Internal quality control data (the same lot for each laboratory and level 1 QC value was determined by manufacturers) were used to determine each parameter CV after the exclusion of outliers (QC observations that contravene 13S rule). Different control levels were studied for each month. The calculation of CV% for two levels, were converted in to only one %CV value by using equation below and one sigma metric was calculated.

Total % CV = √(Level 1)2+(level 2)2

The external control assurance (EQA) data was used for the determination of each analyte's deviation. The six-month EQA sample results are included in the study. EQA data were obtained by the average of the group which is used the same device and the same method. An external quality control program consisting of twelve-month samples was followed in each cycle. The manufacturer simultaneously provided the total number of samples for the entire cycle.

Results

Table 2 shows the performance characteristics of the parameters from Istanbul Atlas University Medicine Hospital; Sigma metrics were calculated considering the total allowable errors from the several sources as shown. Among the parameters tested on the ci4000 device in October 2019, cholesterol had the highest sigma (8.2), while urea had the lowest sigma value (2.3). Among the parameters tested on the Architeck c8000 device, AST had the highest sigma (9.7), while sodium had the lowest sigma value (2.5). In addition, since the sigma values of the glucose, urea and creatinine tests, which are the most studied in our laboratory, are lower in the Architeck ci4000 device than the Architeck c8000 device, therefore it was decided to run these tests only on the c8000 device.

As shown in Table 3, among the parameters tested on the ci4000 device in November 2019, AST had the highest sigma (6.2), while sodium had the lowest sigma value (2). Among the parameters tested on the c8000 device, AST had the highest sigma (8), while sodium had the lowest sigma value (1.9). In addition, it was observed that the sigma metric values of glucose and creatinine tests increased in the c8000 device.

As seen in Table 4, AST had the highest sigma (7.3), while sodium had the lowest sigma (2) value among the parameters tested on the ci4000 device in December 2019. Among the parameters tested on the c8000 device, AST had the highest sigma (9.7), while sodium had the lowest sigma (1.6). In addition, it was observed that the sigma metric values of glucose and creatinine tests increased in the c8000 device.

As shown in Table 4, among the parameters tested on the ci4000 device in January 2020, cholesterol had the highest sigma (7.2) while sodium had the lowest sigma value (2). Among the parameters tested on the c8000 device, AST had the highest sigma (8.1), while sodium had the lowest sigma value (3.3). In addition, it was observed that the sigma metric values of glucose, urea and creatinine tests increased in the c8000 device.

As shown in Table 6, among the parameters tested on the ci4000 device in February 2020, AST had the highest sigma (7.3), while sodium had the lowest sigma value (1.7). Among the parameters tested on the c8000 device, AST had the highest sigma (11,6) while glucose had the lowest sigma (3.8) after sodium. In addition, it was decided not to run the sodium, potassium and clor tests on the c8000 device.

As seen in Table 7, among the parameters tested on the ci4000 device in March 2020, AST (7.2) and Potassium (>6) had the highest sigma, while sodium had the lowest sigma value (3.8). Among the parameters tested on the c8000 device, urea had the highest sigma (11.8) while glucose had the lowest sigma value (4.1). It was decided not to run cholesterol and triglycerides tests on the ci4000 device. Discussion and

Table 2: Parameters tested on the ci4000 and c8000 device in October 2019

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8	1.7	1.6	3.7	1.4	1.1	4.9
Urea	CLIA 2019	9	3.2	1.6	2.3	2.1	1.4	3.6
Creatinine	CLIA 2019	10	2.9	1.7	2.8	1.9	0.09	5.2
Cholesterol	CLIA 2019	10	1	1.8	>6	0.9	2.1	>6
Triglycerides	CLIA 2019	15	1.9	4.1	5.7	2.2	3.9	5
AST	CLIA 2019	15	1.8	1.8	>6	1.4	1.4	>6
Sodium	CLIA 2019	4	1	0.5	3.5	0.8	1	3.75
Potassium	BV	5.6	1.5	1.4	2.8	1.2	1.1	3.7
Clor	CLIA 2019	5	1.2	0.5	3.7	1	1.3	3.7

TEa – Total Allowable Error, CV - Coefficient Of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Table 3: Parameters tested on the ci4000 and c8000 device in November 2019.

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8				1.6	1	4.3
Urea	CLIA 2019	9				2.9	1.3	2.6
Creatinine	CLIA 2019	10				2.3	0.05	4.3
Cholesterol	CLIA 2019	10	1.2	1.6	>6	1.4	1.8	5.8
Triglycerides	CLIA 2019	15	3.4	2.9	3.5	2.8	3.4	4.1
AST	CLIA 2019	15	2.1	1.8	>6	1.7	1.4	>6
Sodium	CLIA 2019	4	1.2	0.6	2.8	1.1	0.9	2.8
Potassium	BV	5.6	1.7	1.1	2.6	1.3	0.9	3.6
Clor	CLIA 2019	5	1.2	0.6	3.6	1.1	1.2	3.4

TEa – Total Allowable Error, CV - Coefficient of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Table 4: Parameters tested on the ci4000 and c8000 device in December 2019.

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8				1.6	0.9	4.4
Urea	CLIA 2019	9				3.1	1.5	2.4
Creatinine	CLIA 2019	10				2	0.09	4.9
Cholesterol	CLIA 2019	10	1.4	1.4	>6	1	1.8	>6
Triglycerides	CLIA 2019	15	3.4	2.7	3.6	2.7	3	4.4
AST	CLIA 2019	15	1.8	1.8	>6	1.4	1.4	>6
Sodium	CLIA 2019	4	1.3	0.4	2.7	1.3	0.8	2.4
Potassium	BV	5.6	1.4	1	3.2	1.4	0.8	3.4
Clor	CLIA 2019	5	1.3	0.5	3.4	1.5	1.1	2.6

TEa – Total Allowable Error, CV - Coefficient of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Table 5: Parameters tested on the ci4000 and c8000 device in January 2019.

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8				1.4	0.5	5.3
Urea	CLIA 2019	9				1.9	0.5	4.4
Creatinine	CLIA 2019	10				2	0.08	4.9
Cholesterol	CLIA 2019	10	1.2	1.3	>6	1.1	1.3	>6
Triglycerides	CLIA 2019	15	2.2	2.8	5.5	1.7	2.8	>6
AST	CLIA 2019	15	2.1	1.4	>6	1.7	1.2	>6
Sodium	CLIA 2019	4	1.2	0.5	3.1	1	0.7	3.3
Potassium	BV	5.6	1.6	1	2.8	1.4	0.8	3.4
Clor	CLIA 2019	5	1	0.5	4.5	1.3	1.1	3

TEa – Total Allowable Error, CV - Coefficient of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Table 6: Parameters tested on the ci4000 and c8000 device in February, 2019.

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8				1.9	0.6	3.8
Urea	CLIA 2019	9				1.7	0.9	4.7
Creatinine	CLIA 2019	10				1.6	0.2	>6
Cholesterol	CLIA 2019	10	1.4	1.3	>6	1	1.7	>6
Triglycerides	CLIA 2019	15	2	2.9	6	1.7	3	>6
AST	CLIA 2019	15	1.9	1	>6	1.2	1	>6
Sodium	CLIA 2019	4	1.4	0.5	2.5			
Potassium	BV	5.6	1.6	0.8	3			
Clor	CLIA 2019	5	1.3	0.5	3.4			

TEa – Total Allowable Error, CV - Coefficient of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Table 7: Parameters tested on the ci4000 and c8000 device in March, 2019.

Parameters	TEa source	TEa	ci4000 %CV	ci4000 %BİAS	ci4000 sigma metrics	c8000 %CV	c8000 %BİAS	c8000 sigma metrics
Glucose	CLIA 2019	8				1.9	0.1	4.1
Urea	CLIA 2019	9				0.7	0.7	>6
Creatinine	CLIA 2019	10				2.1	0.01	4.7
Cholesterol	CLIA 2019	10				1.4	0.9	>6
Triglycerides	CLIA 2019	15				1.5	2.8	>6
AST	CLIA 2019	15	1.9	1.2	>6	1.5	1.3	>6
Sodium	CLIA 2019	4	1	0.2	3.8			
Potassium	BV	5.61	0.05	0.3	>6			
Clor	CLIA 2019	5	1	0.07	4.9			

TEa – Total Allowable Error, CV - Coefficient Of Variation, BİAS – deviation, BV –Biological Variation, CLIA – Clinical Laboratory Improvement Amendments 2019, AST- Aspartate Aminotransferase.

Conclusion

The analytical process is a process in which test methods, analyzers used, internal and external quality control and calibrations come to the fore and control of variables is more possible. 26 Six sigma methodology to prove their performance emerges as an effective tool [15]. In order to provide a holistic view of the process, pre- and post-analysis processes should be evaluated together with the analysis process. While selecting the tests to be evaluated, IQC data were collected for 6 months by selecting 9 frequently requested parameters. The reason for choosing these tests is that they are frequently requested tests in our laboratory, while the patient evaluates according to the test results, more patient results are obtained. Analytical process sigma levels are calculated separately for each test. Configuring the laboratory information system is important in reducing this workload due to the processes that increase the workload, such as taking the daily EQC data used in this calculation from laboratory information system and transferring them to Microsoft Excel [16].

Researches show that the majority of laboratory errors occur in preanalytical and postanalytic processes. Miller and Sandberg suggested that the total allowable error (TEa), expressed depending on the analysis, for each analyte, the optimum clinical decision should be determined to make a clinical decision based on it [17]. Some analyte changes will affect clinical decisions when relatively large (up to 50% for alanine aminotransferase and lipase activities). However, for some analytes, a relatively minor change will affect clinical judgment, such as electrolytes [18].

Gami et al. explored how the variable outputs of different parameters differs. A high biological variation parameters such as triglyceride measured by any device will give an acceptable sigma value. Electrolytes with low biological variation, such as sodium and potassium, will give a low sigma value [18,19]. Korkmaz indicated that the reason for the poor performance was examined using QGI for analytes with sigma <3 according to CLIA, which was evaluated as poor performance. According to the result, necessary corrective and preventive actions were initiated [20].

The same observation was obtained in our results. However, as of November 2019, an increase in the sigma value has been

detected, with the electrolyte starting to work in a single device. This can be used routinely in laboratories, especially to follow tests with low biological variation.

Tufail et al. investigated how effect the differantiation of the biodiversity on several parameters. A high biological variation parameter such as triglyceride measured by any device will give an acceptable sigma value. Electrolytes with low biological variation, such as sodium and potassium, will give a low sigma value.(18) The same observation was obtained in our results. However, until November 2019, an increase in the sigma value has been detected, with the electrolyte starting to work in a single device. This can be used routinely in laboratories, especially to follow tests with low biological variation. Medina et all (2019), evaluated total of twenty (28) tests on two Abbott Architect c8000 chemistry analyzers from September 2014 to July 2019 using results of quality control mean, coefficient of variation, bias and total allowable error to compute for the six sigma value. They included both level one and level two third party quality controls in the evaluation and they used six sigma metrics allowed the laboratory to evaluate the performance of the chemistry tests objectively. The results indicated that >6.0 sigma signifies world class performance and entail application of fewer Westgard rules with fewer number of runs while those that are <3.0 need method improvement or more stringent quality control measures. The findings show that usage this monitoring and performance evaluation should definitely effect quality improvement.

In our study, the comparative follow-up performed for 6 months, the determination of the parameters to be worked on which device on monthly basis varied. Since the sigma values of the glucose, urea and creatinine tests, which are the most studied in our laboratory, are lower in the Architeck ci4000 device than the Architeck c8000 device. Since 5th month, the sigma values for sodium, potassium and clor were increased from 2.5 to 3.8 for sodium; from 3 to 6 for clor and from 3.4 to 4.9 for potassium so we have reduced all measurements in single device. Meanwhile, the calibration frequency has been increased. The frequency of calibration performed 3 times a day was increased to 4. Six sigma metrics should be used monthly to monitor tests with particularly low biological variation to evaluate the method performance of same-brand devices which is used for thousands of tests. It was decided to run these tests only on the Architeck c8000 device. All metrics have been obtained until October 2019. An increase in the sigma value was detected with the start of working of electrolytes on a single device six months later.

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Research Article

Surgical management of basilar ınvagination: comparison of clinical and radiographic outcomes utilizing differing surgical approaches

Baziler invajinasyonun cerrahi tedavisi: farklı cerrahi yaklaşımların klinik ve radyografik sonuçların karşılaştırılması

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ABSTRACT

Aim: Previous studies have outlined various surgical approaches to treatment of basilar invagination, but none have compared multiple different treatment options using objective clinical and radiological criteria.

Material and Methods: We retrospectively reviewed the records of 30 patients with basilar invagination treated by five different surgical approaches. The surgical outcomes were evaluated and compared using objective clinical (Ranawat score) and radiological parameters (Chamberlain distance, atlantodental interval, and craniovertebral angle).

Results: Our results show a statistically significant improvement in the Ranawat score for patients undergoing 1) anterior decompression with posterior stabilization, 2) posterior decompression with posterior stabilization, and 3) the Goel procedure (posterior decompression, posterior reduction, cage distraction, and posterior stabilization). Of these, the Goel procedure produced the most significant improvement in functional and radiographic outcomes. Neither group without posterior stabilization (posterior decompression alone or endoscopic transnasal odontoidectomy alone) had a significant improvement in Ranawat score or radiographic outcomes.

Conclusion: For surgical management of basilar invagination, a combination of posterior decompression, posterior reduction, cage distraction, and posterior stabilization yielded the best clinical and radiological outcome. There is a risk of craniocervical instability and kyphosis and recurrence of stenosis in patients treated surgically without posterior stabilization. Therefore, when deciding on bacillary invagination surgery without posterior stabilization, it should be carefully considered.

Keywords: Basilar invagination, surgical treatment, craniocervical junction, Goel procedure, spine surgery

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Öz

Amaç: Baziler invajinasyonun cerrahi tedavisine yönelik çeşitli yaklaşımların ana hatları literatürdeki birçok çalışmada araştırılmış ancak hiçbiri objektif klinik ve radyolojik kriterler kullanarak farklı tedavi seçeneklerini karşılaştırmamıştır. Çalışmamızda farklı cerrahi girişimle opera edilen baziller invaginasyonu olan hastaların objektif klinik ve radyolojik parametreler kullanılarak karşılaştırılması amaçlandı.

Gereç ve Yöntemler: 2000-2014 yılları arasında baziler invajinasyon nedeniyle opere edilen hastalar retrospektif olarak incelendi. Sekonder baziler invajinasyon kriterlerini karşılayan romatoid artritin neden olduğu atlantoaksiyal subluksasyonu olan iki olgu da çalışmaya dahil edildi. Çalışmaya beş farklı cerrahi yaklaşımla tedavi edilen baziler invajinasyonlu toplam 30 hasta dahil edildi. Cerrahi sonuçlar objektif klinik (Ranawat skoru) ve radyolojik parametreler (Chamberlain mesafesi, atlantodental interval ve kraniovertebral açı) kullanılarak değerlendirildi ve karşılaştırıldı.

Bulgular: Çalışmamızda posterior stabilizasyonlu anterior dekompresyon, posterior stabilizasyonlu posterior dekompresyon ve Goel prosedürü (posterior dekompresyon, posterior redüksiyon, kafes distraksiyonu ve posterior stabilizasyon) uygulanan hastalarda Ranawat skorunda istatistiksel olarak anlamlı bir iyileşme olduğu saptandı. Bunlardan Goel prosedürü fonksiyonel ve radyografik surveyde en iyi sonuçları gösterdi. Posterior stabilizasyonu uygulanmayan hiçbir grupta (tek başına posterior dekompresyon veya yalnızca endoskopik transnazal odontoidektomi), Ranawat skorunda veya radyografik sonuçlarda anlamlı bir iyileşme olmadı. Anterior dekompresyon ve posterior stabilizasyonun birlikte uygulandığı cerrahi prosedürlerde de başarı oranı yüksek idi.

Sonuç: Baziler invajinasyonun cerrahi tedavisinde posterior dekompresyon, posterior redüksiyon, kafes distraksiyonu ve posterior stabilizasyonun birlikte yapıldığı cerrahi uygulamalar en iyi klinik ve radyolojik sonucu verdi. Posterior stabilizasyonsuz cerrahi tedavi edilen hastalarda, kranioservikal instabilite ve kifoz gelişimi tekrar darlık oluşumu riskleri vardır. Bu nedenle posterior stabilizasyonsuz basiler invaginasyon ameliyatı kararı alınırken titizlikle düşünülmeli bu durumlar göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Basiller invajinasyon, cerrahi tedavi, kranioservikal bileşke, Goel prosedürü, omurga cerrahisi

Introduction

Basilar invagination is an acquired or congenital anomaly of the craniocervical junction in which the odontoid projects through the foramen magnum [1]. The acquired form of basilar invagination, often referred to as basilar impression, typically results from trauma, tumor, infection, or metabolic bone disease [2,3,4]. The congenital form is often associated with other abnormalities of the craniocervical junction, such as platybasia, hypoplasia of the clivus and condyles, and atlas assimilation [5]. Regardless of the cause, the potential neurological complications often necessitate surgical intervention [6].

Surgical treatment aims to decompress neurovascular structures based on correcting and stabilizing the craniocervical junction. Anterior compression of the cervicomedullary junction by the odontoid may lead to odontoid resection, typically performed by either transpharyngeal method (via a transnasal, transmandibular, or transmaxillary approach) or retropharyngeal method (via far-lateral transatlas or far-lateral transcondylar approaches) [6-11] Both approaches can also be performed endoscopically under image guidance [12,13]. Posterior compression may require resection of the posterior elements of the craniocervical junction via midline approach. It is possible to use occipitocervical systems and C1-C2 screw systems for posterior stabilization (PS), as well as C0–C2 implant systems for patients with co-existing atlas assimilation [14,15]. Anterior grafting and stabilization methods are also available for anterior stabilization after anterior decompression (AD). However, PS is most commonly applied and is the recommended approach after AD [16-24].

Various studies have outlined the surgical treatment of basilar invagination, but no study has compared the results of different treatment options by using objective clinical and radiological criteria [14,16,21,24]. This study investigated the clinical and radiological features of patients with basilar invagination treated surgically via five different surgical approaches.

Material and Methods

Study Design

This an IRB approved retrospective study including the patients with basilar invagination who had undergone surgery between 2000 and 2014.

Chart Review

Chart review included review of medical history, physical examination findings, intensive care records, follow-up records, periodic observation notes, operation reports, re-hospitalization records, and radiologic records. The following information was recorded: age, gender, signs and symptoms (including presenting complaints), history, preoperative examination findings, operation performed, discharge examination findings, and details of any complications, morbidity, mortality, or reoperations. The Ranawat Scale[5] was used to standardize the preoperative and postoperative functional status assessments.

Patients were classified into five groups based on surgical approach. Group 1 included patients who underwent posterior decompression (PD), alone. Group 2 patients underwent PD, posterior reduction (PR) and PS. Group 3 patients underwent PD, PR, cage distraction, and PS (Goel procedure). Group 4 patients underwent AD and PS. Group 5 patients underwent endoscopic transnasal odontoidectomy (ETNO).

Radiological examination included the measurements described for cranio-cervical junctional anomalies (Figure 1). The Chamberlain distance was defined as the vertical height of the portion of the odontoid projecting above the Chamberlain line (a line connecting the posterior hard palate with the opisthion on a sagittal view of the craniocervical junction). The atlantodental interval is traditionally defined as the anterior-posterior width of the anterior atlantoaxial joint but was measured in an atlanto-clival direction in most patients due to high atlas assimilation ratios. The craniovertebral angle was measured in the sagittal projection as the angle between a line perpendicular to the posterior cortex of the odontoid and a line perpendicular to the posterior margin of the clivus. Measurements assessing degree of correction of the craniocervical junction (i.e., the Chamberlain distance, atlantodental interval, and craniovertebral angle) were repeated on postoperative images and recorded as the objective indicators of correction of the craniocervical junction and decompression of the foramen magnum. Brain stem decompression was observed in cases subject to AD as a hyper-intense line of cerebrospinal fluid in front of the brain stem in the sagittal plane on T2-weighted MRI, as well as by clinical observation. These subjective parameters were not included in the statistical analyses.

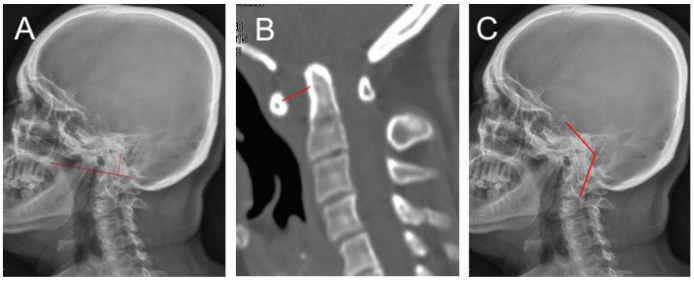

Figure 1. A: The Chamberlain distance measured as the vertical height of the portion of the odontoid projecting above the Chamberlain line (a line connecting the posterior hard palate with the opisthion on a sagittal view). **B:** Anterior atlantodental interval defined as the anterior-posterior width of the anterior atlantoaxial joint. **C:** The craniovertebral angle was measured as the angle between a line perpendicular to the posterior cortex of the odontoid and a line perpendicular to the posterior margin of the clivus.

Statistical Analysis

Data were analyzed by Wilcoxon signed ranks or paired t-tests, as appropriate. Statistical significance was set at $p < 0.05$.

Results

Demographic and clinical characteristics are included in Table 1. The mean follow-up period was 5.6±3.7 months (range 3-11 months). Two cases with atlantoaxial subluxation caused by rheumatoid arthritis meeting the criteria for secondary basilar invagination were also included. A total of 30 patients were included in the study.

An equal number of male and female patients were included with an average age of 37.8±12.2 years (range 18–63 years). The most frequent presenting complaints were paresis and paresthesia. Six patients presented with existing symptoms that deteriorated after minor trauma.

Multiple co-existing abnormalities were identified (Table 2; Figure 2). The most frequent associated finding was atlas assimilation (72.6%). Chiari malformation was present in 52.8% of cases, including seven of the eight patients presenting with cerebellar findings. Chiari malformation was also present in all patients with hydrocephalus or syringomyelia.

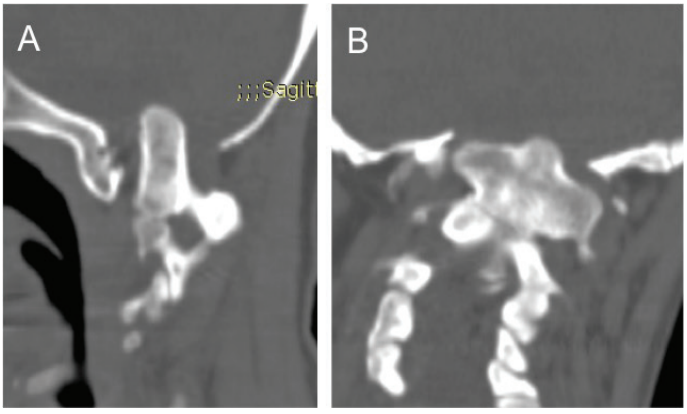

Figure 2. A: A representative case of abnormal fusion of the atlas on the axis, which gives the appearance of two bilateral pedicles on C2. The very fine structure of the real pedicle is seen below. **B**: A representative case of odontoid hypoplasia, condyle hypoplasia, atlas assimilation, Klippel–Feil anomaly, and scoliosis.

Table 1. Summary of Patient Demographics, Treatments, and Radiological and Clinical Analyses.

Case Number	Age	Gender	Operation	Ranawat Scores		Atlantodental Interval (mm)		Chamberlain Distance (mm)		Craniovertebral Angle (degrees)	
				Pre-Operative	Post-Operative	Pre-Operative	Post-Operative	Pre-Operative	Post-Operative	Pre-Operative	Post-Operative
1	44	M	AD + PS	3A	3A	–	–	10	–	140	–
2	37	F	AD + PS	3A	3A	–	–	6	–	140	–
3	34	M	ETNO	2	2	–	–	6	–	148	–
4	63	F	Goel Procedure	3B	3A	10	0	11	0	150	150
5	45	F	Goel Procedure	3B	3A	8	0	16	6	114	138
6	49	M	Goel Procedure	3B	3A	7	5	6	6	142	149
7	41	M	Goel Procedure	2	2	6	0	17	8	130	125
8	25	F	Goel Procedure	3A	3A	7	7	13	3	112	117
9	44	F	PD + PS	2	2	3	2	7	7	135	–
10	35	M	PD	2	3A	6	8	12	10	119	142
11	40	F	Goel Procedure	3A	2	11	5	15	5	120	150
12	18	M	AD + PS	3B	3A	–	–	10	–	100	–
13	30	F	AD + PS	2	2	–	–	14	–	105	–
14	44	F	PD + PS	3A	2	9	4	5	3	143	150
15	18	M	PD + PS	3A	2	1	1	2	2	111	126
16	32	F	AD + PS	3B	3A	–	–	24	–	110	–
17	46	M	PD + PS	3B	3B	1	1	9	7	112	112
18	18	M	PD	3A	3A	8	5	9	9	116	130
19	33	F	PD + PS	3A	2	1	1	3	3	145	150
20	49	M	PD + PS	3A	2	0	0	17	17	129	129
21	18	M	AD + PS	3A	3A	–	–	5	–	122	–
22	33	M	AD + PS	3B	3A	–	–	15	–	127	–
23	62	F	PD + PS	2	2	0	0	20	17	110	110
24	45	M	Goel Procedure	3A	2	9	4	11	6	114	129
25	27	F	PD + PS	3B	3A	5	2	5	5	145	151
26	34	F	Goel Procedure	3A	2	9	0	0	0	122	141
27	47	F	Goel Procedure	1	1	12	0	3	0	135	151
28	45	M	ETNO	2	2	–	–	8	–	157	–
29	37	F	PD	2	2	0	0	12	12	116	116
30	25	M	AD + PS	3A	2	–	–	10	–	127	–

* AD = anterior decompression; ETNO = endoscopic transnasal odontoidectomy; PD = posterior decompression; PS = posterior stabilization

** Some patients lacked pre-operative or post-operative measurements due to prior surgeries or procedure performed limiting assessment

Table 2. Anomalies associated with basilar invagination

	Number (n = 30)	%
Chiari malformation	16	52.8
Syringomyelia	9	29.7
Hydrocephalus	4	13.2
C1 assimilation	22	72.6
Klippel–Feil Syndrome	4	13.2
Clival agenesis	3	9.9
Condylar hypoplasia	6	19.8
Dens hypoplasia	2	6.6
Os odontoideum	2	6.6
Rheumatoid arthritis	2	6.6

The distribution of surgical procedures (Table 3) included three (10.0%) patients in Group 1 (PD alone), eight (26.7%) in Group 2 (PD + PR + PS), nine (30.0%) in Group 3 (Goel procedure), eight (26.7%) in Group 4 (AD + PS), and two (6.7%) in Group 5 (ETNO).

Group 1

For patients undergoing PD alone, there was a slight worsening in functional outcome (Ranawat score of 1.33 ± 0.577 pre-operatively to 1.67 ± 0.577 postoperatively); however, this was not statistically significant ($p = 0.317$). There was also an increase in the atlantodental interval postoperatively by 2.5 mm, not statistically significant ($p = 0.18$). No significant change was present in the pre-operative and post-operative craniovertebral angle ($p > 0.15$). Notably, Case 10 had progressive anterior compression and progressed to quadriparesis during the first year after PD.

Group 2

Group 2 patients had a statistically significant improvement in functional outcome with a decrease in Ranawat score from 2.00 ± 0.756 pre-operatively to 1.38 ± 0.741 post- operatively ($p = 0.025$). Case 17 had presented with neurological worsening after undergoing PD elsewhere, but experienced no further progression of symptoms after subsequent PR and PS.

There was 38.1% decrease in the atlantodental interval post-operatively ($p=0.18$). No significant change in the Chamberlain distance was present; however, there was a trend towards an increase in the craniovertebral angle by an average of 5.5 degrees post-operatively ($p=0.059$).

Group 3

The most significant functional improvement was found in the patients undergoing the Goel procedure with an average reduction of 62% in Ranawat score ($p = 0.014$). One case in Group 3 (Case 11) also presented with neurological worsening after undergoing PD elsewhere.

In this group, a cage was placed in the atlantoaxial joint between the condyle and axis in patients with atlas assimilation. This provided direct support at the point where distraction was needed. As such, the greatest improvement in craniocervical alignment was seen in Group 3 with a 73.4% decrease in the atlandodental interval ($p = 0.012$). Group 3 patients were the only group with a statistically significant decrease in the Chamberlain distance (average decrease of 6.8 mm; $p = 0.011$) and increased craniovertebral angle (average increase of 12.3 degrees; $p=0.012$).

Table 3. Relationship between surgical treatment and clinical and radiographic outcomes.

Surgical Treatment	No. Patients (n = 30)	Ranawat Scores			Atlantodental Interval (mm)			Chamberlain Distance (mm)			Craniovertebral Angle (degrees)		
		Pre-Operative	Post-Operative	p	Pre-Operative	Post-Operative	p	Pre-Operative	Post-Operative	p	Pre-Operative	Post-Operative	p
PD	3	1.33 ± 0.577	1.67 ± 0.577	0.317	5.500 ± 0.707	8.000 ± 0.00	0.18	-	-	-	117.500 ± 2.121	136.000 ± 8.485	0.152
PD + PR + PS	8	2.00 ± 0.756	1.38 ± 0.741	0.025	2.625 ± 3.159	1.625 ± 1.598	0.18	8.500 ± 6.590	4.000 ± 1.414	0.317	130.500 ± 16.610	136.000 ± 16.982	0.059
Goel	9	2.00 ± 1.00	1.38 ± 0.744	0.014	8.778 ± 1.986	2.333 ± 2.872	0.012	10.555 ± 5.387	3.777 ± 3.113	0.011	126.555 ± 13.519	138.888 ± 12.604	0.012
AD + PS	8	2.25 ± 0.707	1.75 ± 0.463	0.046	-	-	-	-	-	-	-	-	-
ETNO	2	1.00 ± 0.00	1.00 ± 0.00	1	-	-	-	-	-	-	-	-	-

Representative examples of two cases are presented in Figures 3 and 4. Figure 3 shows the results for a patient with basilar invagination presenting with acute quadriparesis. We performed PD, reduction, and condylar–C2 joint distraction (with a cage to the right and an autograft bone to the left) to achieve posterior fusion and occipito-cervical stabilization. As shown in the postoperative images, full reduction of the odontoid was achieved with an increase in the craniovertebral angle and decompression at the level of the foramen magnum. Figure 4 shows a representative case of secondary basilar invagination caused by rheumatoid arthritis. In this case, posterior approach with atlantoaxial joint cage distraction, odontoid reduction, and stabilization with bilateral C2 laminar screw and rod system to the lateral mass of the atlas was performed. This led to full vertical and horizontal reduction of the odontoid and effective decompression of the brain stem.

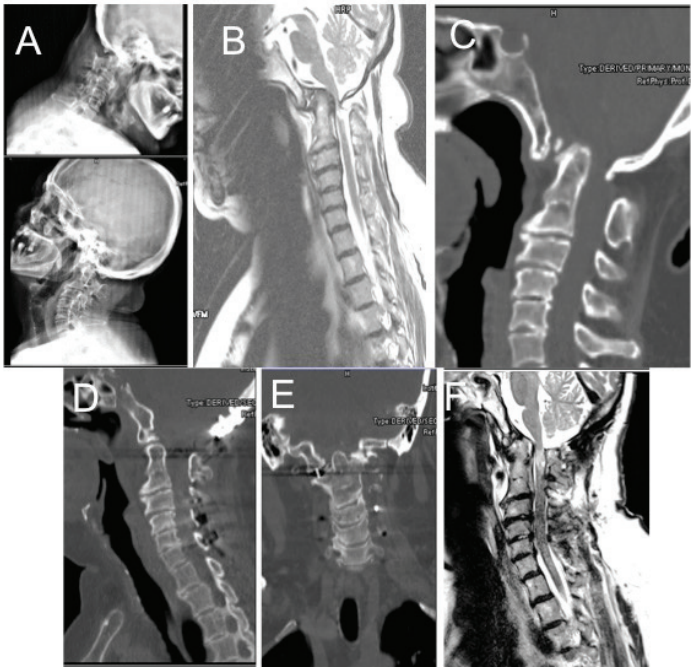

Figure 3. Pre-operative flexion–extension radiographs **(A)**, sagittal T2-weighted MRI **(B)**, and sagittal CT **(C)** show atlas assimilation with basilar invagnation resulting in severe stenosis of the foramen magnum and severe compression of the cervicomedullary junction. Post-operative sagittal **(D)** and coronal **(E)** CT images and T2-weighted MRI **(F)** show marked improvement in alignment at the craniocervical junction with resolution of stenosis at the foramen magnum and reduction in compression on the cervicomedullary junction after Goel procedure.

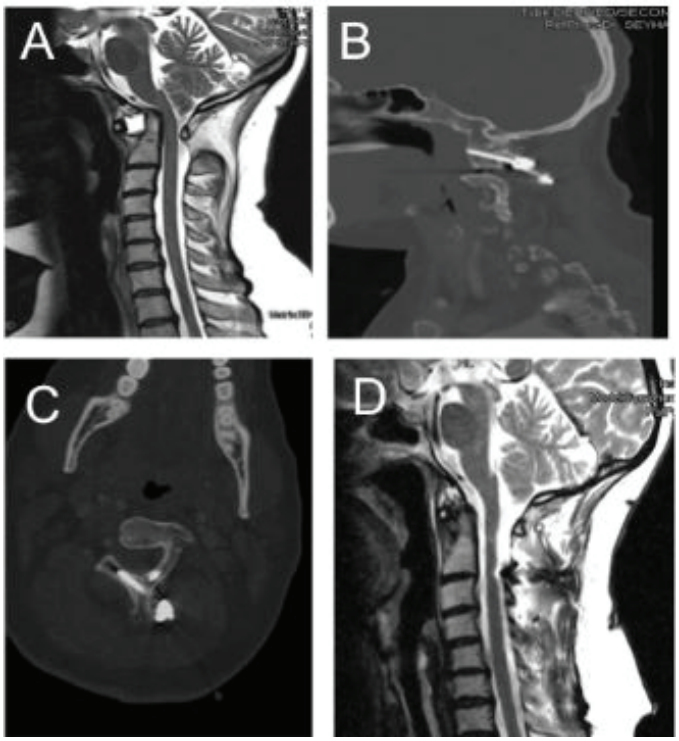

Figure 4. Pre-operative T2-weighted sagittal MRI **(A)** shows substantial widening of the anterior atlantoaxial joint and basilar invagination producing stenosis of the foramen magnum and mass effect on the cervicomedullary junction. Post-operative sagittal **(B)** and axial **(C)** CT and sagittal T2-weighted MRI **(D)** after Goel procedure show marked reduction in the atlantodental interval and reducing in basilar invagination. Compression on the cervicomedullary junction has been resolved.

Some noteworthy events in Group 3 include a died (Case 4) two months after index surgery from central nervous system infection and hydrocephalus despite the treatment with external ventricular drainage and antibiotic therapy. A complication of vertebral artery rupture due to the close relationship with atlantoaxial joint was seen in the opertaion in two patients. The arteries were repaired by primary suture in both patients,

and the lumen was preserved as confirmed by postoperative CT angiography. There was no postoperative vertebro-basilar ischemia and no related morbidity. Vertebral artery damage due to screw malposition was not observed in any patient, and there was no early surgical mortality in any of the included patients.

Group 4

The Group 4 patients also showed a slight improvement in functional outcome (average decrease in Ranawat score of 0.5; p = 0.046). There were no notable complications in patients undergoing AD + PS.

Group 5

The ETNO approach was performed in two patients who required AD. There was no significant change in Ranawat score; however, the small sample size limits interpretation. One patient recovered without complication after we achieved sufficient decompression and was discharged after only a brief period of hospitalization. In the second patient, the operation was finalized without sufficient decompression because the hard palate did not permit caudal shifting, as well as a difference between the imaging depth and that observed surgically. There was no surgical complication; however, the patient will undergo repeat surgery in the future.

Discussion

The basic principle of surgical treatment of basilar invagination is to eliminate compression and reduce the stenosis at the level of the foramen magnum. Algorithms dictate that the decompression should be performed based on where the compression is [5, 25,26] . It was found that posterior decompression alone without fusion led to a progression of brain stem compression[25]. However, anterior approaches were technically difficult even in the absence of anatomical irregularities and had serious approach-related complications.[26]

Anterior decompression alone may lead to postoperative instability requiring fixation, therefore, supporting the need for fusion.[27] Dickman, et al.reported that instability developed in over 40% of cases with anterior approaches alone [28,29].

In addition, Goel, et al. reported that various patients with basilar invagination advanced clinically and radiologically during follow up after trans-oral decompression without stabilization [6] .Based on surgical experience and biomechanical studies of AD, it was predicted that instability could be prevented after decompression by protecting the anterior arch of the atlas, the alar ligament, and the transverse ligament when there was no preoperative instability. However, many authors suggested the use of PS since the basilar invagination was already unstable, the percentage of accompanying atlas assimilation was high, and the ability to protect these ligaments during the decompressive surgery was limited [16,22,23,25] There was significant improvement in functional outcome only in patient groups with PS in this study as well.

Our results suggested that the Goel procedure was the most successful method to improve functional status and radiographic alignment compared to the other procedures. Changes in functional status were presumably linked to these radiographic endpoints as the decrease in the Chamberlain distance and atlantodental interval and an increase in the craniocervical angle are all factors that effectively decreased brain stem compression and increased the effective foramen magnum diameter [2,30]. There was no patient with Goel procedure had insufficient decompression and requirement of AD. The average vertical reduction of the odontoid was greater than 5 mm, despite only using distraction cages that were 5 mm thick. Therefore, the Goel method was reported as an effective single-stage procedure, providing both stabilization and AD [31,32].

It is important for the surgeon to be aware of potential complications that may occur from the Goel procedure. In our study, vertebral artery injuries occurred during dissection of the atlantooccipital joint (condylar–C2 joint in atlas assimilation) in two patients as a posterior approach related complicaiton. The risk of this complicaiton is high in this region where the vertebral artery leaves the foramen, encircles the joint, and enters the dura. Before surgery, it is beneficial to know if the fixation point of the atlanto-occipital membrane that covers this trough is ossified and if there is any inherited anatomic variation (e.g., arcuate foramen, ponticulus posticus, or Kimmerle's anomaly) where the vertebral artery and C1 spinal nerve pass through. It has been suggested that such variations can be present in 1.2%–37% of cases [33,34].

Various methods are used to correct the abnormal craniocervical junction and reduce compression including traction, intraoperative distraction, extension, and compression. This is done through horizontal and vertical odontoid reduction, but also through distraction that may be applied by intraoperative maneuvers to the head, surgical manipulations to the lateral atlantoaxial junction, or through a cage placed in the junction gap. PS is added when decompression is applied via reduction [27,35,36,37].

Patel et al. assessed the results of posterior occipito-cervical decompression and fusion operated with intra-operative traction/manipulation and instrumented reduction in

cases with BI and intra-operative traction/manipulation, instrumented reduction and posterior occipito-cervical fusion resulted in good correction of radiology, functional performance and clinical neurology as well as excellent fusion rates without adverse effects of trans-oral surgery [38].

Preoperative traction applied for odontoid reduction might be beneficial [39].. In the present series, traction was applied for five days to a patient who presented with severe quadriparesis and resulted in neurological improvement. The patient was operated using the Goel procedure under continued traction, and we were able to achieve full odontoid reduction and brain stem decompression. Another option that is infrequently discussed is AD after PS. We showed that this was possible in a patient who had undergone posterior stabilization at a different center and presented to us after a lack of any clinical improvement. Effective AD was then applied using transnasal endoscopy, which resolved the residual anterior compression.

For PS in our series of patients, C2 fixation was most frequently used when stabilization was applied. Occipitocervical systems for PS are challenging and may predispose to complications such as CSF leak and infection. C1–C2 screw and rod systems and condylar–C2 screw and rod systems may be preferred in the presence of atlas assimilation [25,39-41]. Additionally, C2 pedicle placement is unfavorable when there is a thin pedicle or a high vertebral artery[29] . The laminar screw method defined by Wright is biomechanically sufficient and reduces the risk of neurovascular injury [42,43]. In our patients, there were no cases of channel or vertebral artery penetration nor mechanical complications.

In addition to the standard Goel procedure, other options are available. For example, the transoral atlantoaxial reduction plaque system has promising results by combining AD with PS and fusion in a single-stage procedure [44]. The transoral transpharyngeal path was selected for eight patients who underwent AD, and another two patients were operated via the endoscopic transnasal path. Far-lateral craniocervical approaches have advantages for AD, including the provision of a sterile surgical area and the ability to offer stabilization during the same session[9,10,11,45]. Notably, the endoscopic transnasal and transoral approaches may be superior to classical transoral surgery in terms of outcomes, although the importance of accurate navigation is paramount for these procedures. Caudal shifting and odontoid resection may not be possible for a patient undergoing ETNO because the hard palate may cause an obstruction [10,46]. Endoscopic transcervical odontoidectomy via a retropharyngeal approach gives anterior access to the junction and ensures a sterile surgical area [12].

This our study soughtassesses the outcomes associated with commonly performed employed surgical methods infor the treatment ofin basilar invagination. There wasWe found a significant improvement in functional outcomes associated with: 1) PD + PR + PS, 2) Goels procedure, and 3) AD + PS. Although the sample size was limited small, no significant functional improvement in function was obtained seen by with PD alone nor ETNO. The greatest combination of improvement in function and craniocervical alignment was achieved by seen with the Goel procedure. The literature on publications regarding basilar invagination has been focused on clinical findings or assessment of new technological developments. Some descriptive studies have also been performed, as have those proposing treatment algorithms [25,39-41]. In this study, we were able to compare outcomes amongbetween several common surgical techniques as these naturally evolved in our practice over time.

On rare occasions, PD alone may be the only appropriate treatment option for patients with basilar invagination [21,22,47]. PD may be best suited for patients with no anterior compression, having a normal or near-normal atlantodental interval, no dislocation during flexion-extension examinations [19,47]. PD alone was used for only three patients in our case series; however, two additional patients in our series had received PD alone at a prior institution before presenting with neurological decline necessitating further surgery. Of the three patients in which we performed PD alone, one presented with progressive worsening after surgery and was confirmed to have an increase in anterior compression, craniovertebral angle, and atlantodental interval. In the other two patients, no significant clinical change occurred after surgery.

Conclusion

In the treatment of basilar invagination, a combination of posterior decompression, reduction, cage distraction, and stabilization yielded the best clinical and radiological outcomes. Although the sample size was small, PD alone and ETNO failed to show a significant change in functional or radiographic improvement. Our findings suggest posterior stabilization should be considered in the treatment of basilar invagination, where possible.

Highlights

- This study assesses functional and radiographic outcomes of multiple surgical approaches for treatment of basilar invagination

- Choosing an appropriate pre-operative surgical approach is critical for maximizing outcome
- Patients with posterior stabilization had the best functional outcome with the Goel procedure slightly outperforming other approaches

Conflict of Interest Statemen

The authors have no conflicts of interest to declare.

Conflict-of-interest disclosure

The authors declare no competing financial interests and no sources of funding and support, including any for equipment and medications.

Ethics Committee Approval

This study is retrospective observational research. No human/animal participant is available, so no ethics approve is mandatory. All study is done under Helsinki declarations.

Author Contributions

All 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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Research Article

Investigation the impact of liraglutide on the thyroid function tests

Liraglutidin tiroid fonksiyon testleri üzerine etkisinin araştırılması

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Abstract

Aim: Liraglutide is a once-daily glucagon-like peptide-1 receptor agonist (GLP-1 RA) which is an incretin hormone secreted from intestinal L cells in response to nutritional intake and stimulates glucose-dependent insulin secretion, decreases hepatic glucagon secretion, slows gastric emptying, provides a feeling of satiety and is the first GLP-1 RA to be indicated for weight loss treatment for obesity. The impact of liraglutide on thyroid function tests is unknown and to the best of our knowledge, there are no studies on this regard. Our aim is to compare thyroid function tests, other biochemical and hemogram parameters before and 6 months after liraglutide treatment.

Material and Methods: The patients, 18-65 years old, who used liraglutide for at least 6 months due to obesity treatment between January 2021 and January 2023 in Burdur State Hospital were included.

Results: There were 51 patients (39 female, 12 male) using liraglutide without thyroid disease during the study period. Twelve patients discontinued liraglutide use before the 6th month of treatment was completed. Weight, body mass index (BMI), fasting plasma glucose (FPG), hemoglobin A1C (HbA1c), low-density lipoprotein (LDL), triglyceride and thyroid-stimulating hormone (TSH) values were significantly lower at the 6th month of treatment. Free thyroxine (FT4) and free triiodothyronine (FT3) values were similar and there was no difference other biochemical and hemogram parameters between before and 6 months after treatment

Conclusion: After 6 months of liraglutide treatment, we found a significant decrease in TSH values and improvement in metabolic parameters, but no change in thyroid hormone levels.

Keywords: thyroid; liraglutide; obesity; thyroid-stimulating hormone (TSH)

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Öz

Amaç: Liraglutid, gıda alımına yanıt olarak intestinal L hücrelerinden salgılanan bir inkretin hormon olan glukagon benzeri peptid-1 reseptör agonistidir (GLP-1 RA). Glukoz bağımlı insülin sekresyonunu uyarır ve hepatik glukagon sekresyonunu azaltır. Ayrıca, mide boşalmasını yavaşlatır ve tokluk hissi sağlar. Obezite tedavisinde kilo verme amaçlı kullanılan ilk GLP-1 RA'dir. Liraglutidin tiroid fonksiyon testlerine etkisi bilinmemektedir ve bilgimiz dahilinde bu konuda herhangi bir çalışma bulunmamaktadır. Amacımız, liraglutid tedavisi öncesi ve tedaviden 6 ay sonrasındaki tiroid fonksiyon testlerini, diğer biyokimyasal ve hemogram parametrelerini karşılaştırmaktır.

Gereç ve Yöntemler: Burdur Devlet Hastanesi'nde Ocak 2021-Ocak 2023 tarihleri arasında obezite tedavisi nedeniyle en az 6 aydır liraglutide kullanan 18-65 yaş arası hastalar çalışmaya alındı.

Bulgular: Çalışma süresince tiroid hastalığı olmayan ve liraglutid kullanan 51 hasta (39 kadın, 12 erkek) vardı. 12 hasta, tedavinin 6. ayı tamamlanmadan liraglutid kullanımını bıraktı. Kilo, vücut kitle indeksi, açlık serum glukozu, hemoglobin A1C (HbA1c), düşük yoğunluklu lipoprotein (LDL), trigliserit ve tiroid uyarıcı hormon (TSH) değerleri tedavinin 6. ayında anlamlı olarak düşüktü. Serbest tiroksin (sT4) ve serbest triiyodotironin (sT3) değerleri benzerdi. Diğer biyokimyasal ve hemogram parametrelerinde tedavi öncesi ve tedaviden 6 ay sonrasında fark yoktu.

Sonuç: Liraglutid tedavisinin 6.ayında, TSH değerlerinde anlamlı azalma ve metabolik parametrelerde düzelme saptadık, ancak tiroid hormon düzeylerinde farklılık yoktu.

Anahtar Kelimeler: tiroid; liraglutid; obezite; tiroid uyarıcı hormon (TSH)

Introduction

Glucagon-like peptide 1 (GLP-1) is an incretin hormone secreted from intestinal L cells in response to nutritional intake and has effects in multiple target organs. GLP-1 stimulates glucose-dependent insulin secretion, decreases hepatic glucagon secretion, slows gastric emptying, provides a feeling of satiety, and limits calorie intake [1].

Endogenous GLP-1 is rapidly degraded by the dipeptidyl-peptidase 4 (DPP-4) enzyme and therefore has a short-term effect. GLP receptor agonists (GLP-1 RAs) have a longer effect as they are resistant to degradation by this enzyme. They stimulate regeneration and proliferation in pancreatic B cells and protect against damage, and provide better glycemic control and weight loss [2]. GLP-1 receptors are not limited to the pancreas, but are present in many human tissues such as stomach, intestines, kidney, lung, thyroid, skin, immune cells, and hypothalamus [3,4]. The most common side effects of GLP-1 RA treatment are related to the gastrointestinal system, such as diarrhea, nausea, vomiting, and abdominal pain [5]. This condition is often self-limiting in most patients and is rarer than 5% in clinical trials. The side effects are usually associated with high doses and decrease with slow dose titration [6].

Obesity is a metabolic disease with an increasing prevalence all over the world and is associated with an increased risk of developing type 2 diabetes mellitus (DM), hypertension (HT), and cardiovascular disease [7]. Liraglutide is a once-daily GLP-1 RA with an extended half-life, approximately 13.1 hours, similar to native GLP-1 with 97% homology [8]. Liraglutide provides weight loss by multiple mechanisms, which slows down gastrointestinal motility, prolongs the absorption time of nutrients, inhibits appetite and creates a feeling of satiety, increases the resting metabolic rate, and decreases the plasma free fatty acid level [9], and also provides cardioprotective and renoprotective effects with its pleiotropic features [10]. Liraglutide is the first GLP-1 RA to be indicated for weight loss treatment for obesity independent of type 2 DM, at a dose of 3.0 mg/day. It is recommended if the body mass index (BMI) is 30 kg/m2 and above or 27 kg/m2 with at least one comorbidity such as DM, HT, and dyslipidemia [11].

GLP-1 receptors are usually expressed in parafollicular C-cells within the thyroid gland [12]. In animal studies, liraglutide has been shown to increase calcitonin levels, a C-cell marker, and may cause hyperplasia and cancer in C-cells at higher doses [13]. Although there are few studies on the effects of exenatide, one of the GLP-1 RAs, on the thyroid gland, there are limited data on this issue for GLP-1 RAs in general. The impact of liraglutide on thyroid function tests is unknown and to the best of our knowledge, there are no studies on this regard in the literature.

Our aim in the present study is to compare thyroid function tests, other biochemical and hemogram parameters before and 6 months after liraglutide treatment and to evaluate possible differences.

Material and Methods

The present study, single-center and retrospective study, was approved by the ethics committee of the Faculty of Medicine of Suleyman Demirel University (Date: 6th March 2023, Approval number: 2023/46) and was carried out in accordance with the Helsinki declaration. The patients, between 18-65 years old, who used liraglutide for at least 6 months due to obesity treatment between January 2021 and January 2023 in Burdur State Hospital were included in the study. Obesity was defined as BMI of 30 kg/m2 and above [11].

Exclusion criteria were any thyroid and pituitary disease and drug use affecting the hypothalamo-pituitary-thyroid axis, history of thyroid surgery, history of radiotherapy to the neck, thyroid antibody positivity, pregnancy, breastfeeding, liver and kidney failure, history of malignancy, and use of liraglutide for less than 6 months.

All participants were followed with a standard hypocaloric diet, exercise program, and on a liraglutide treatment plan, starting with 0.6 mg/day and gradually reaching the target dose of 3 mg/day with weekly dose increases of 0.6 mg.

The age, gender and chronic diseases of the patients were recorded, and height, weight, BMI, fasting plasma glucose (FPG), hemoglobin A1C (HbA1c), lipid values, liver and kidney function tests, hemogram parameters and thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3) values before and 6 months after liraglutide treatment were evaluated. Thyroid function tests were measured by the electrochemiluminescence immunoassay (ECLIA) methods (Cobas; Roche Diagnostics, Mannheim, Germany). HbA1c values were measured by high-performance liquid chromatography (HPLC) method. The reference ranges of the thyroid function tests were as follows; TSH values were 0.27-4.20 µU/mL, FT4 values were 0.93-1.97 ng/dL, FT3 values were 2-4.4 pg/mL.

Statistical analysis

Data were analyzed with the IBM SPSS program version 22. The Shapiro–Wilk test was used for data distribution. Normally and non-normally distributed data were shown as mean ± standard deviation and median (quartile 25%-quartile 75%), respectively. For comparison of data before and after 6 months of treatment, paired samples t-test or the Wilcoxon test were used for normally and non-normally distrubution data, respectively. For the correlation analysis, the Pearson or Spearman analysis was used according to the data distribution. P values <0.05 were considered statistically significant.

Results

There were 51 patients (39 female, 12 male) using liraglutide without thyroid disease during the study period. Twelve patients discontinued liraglutide use before the 6th month of treatment was completed. The reasons for discontinuation were nausea (2 patients), abdominal pain (1 patient), constipation (1 patient) and financial conditions (8 patients).

Of the remaining 39 patients, 31 (79.5%) were female and 8 (20.5%) were male, with a mean age of 43.8 ± 13.5 years (range: 19-65 years). Four patients had type 2 DM, 8 patients had HT and 3 patients had coronary artery disease. Metabolic and laboratory parameters before and 6 months after treatment were compared. Weight (97 ± 16 kg vs 88 ± 14 kg, p= 0.001), BMI (38.2 ± 4.8 kg/m2 vs 34.2 ± 4.4 kg/m2, p= 0.001), FPG (102 ± 16 mg/dL vs 92 ± 12 mg/dL, p= 0.001), HbA1c [5.9 (5.3-6.4) % vs 5.4 (5-5.7) %, p= 0.001], LDL (114 ± 29 mg/dL vs 102 ± 30 mg/dL, p= 0.02), triglyceride [151 (106-220) mg/dL vs 115 (98-136) mg/dL, p= 0.001] and TSH values (2.6 ± 1 µU/mL vs 2 ± 0.8 µU/mL, p= 0.02) were significantly lower at the 6th month of treatment. FT4 (1.3 ± 0.2 ng/dL vs 1.3 ± 0.3 ng/dL, p= 0.56) and FT3 (3.2 ± 0.7 pg/mL vs 3.1 ± 0.4 pg/mL, p= 0.44) values were similar and there was no difference other biochemical and hemogram parameters between before and 6 months after treatment. The comparisons of metabolic and biochemical parameters were shown in Tables 1 and 2. The graphs of thyroid function tests was shown in Figure 1.

No significant correlation was found in the correlation analyzes of thyroid function tests and other parameters.

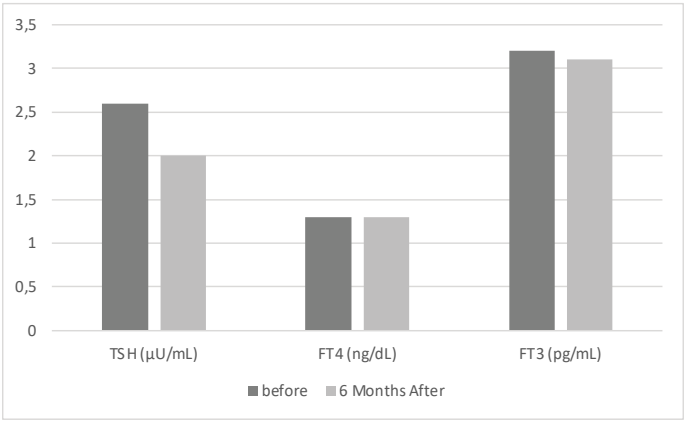

Figure 1. The graphs of thyroid function tests between before and 6 months after liraglutide

TSH: thyroid-stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine

Table 1. The comparison of metabolic parameters between before and 6 months after liraglutide

Variables Reference Range	Before	6 Months After	P value
Weight (kg)	97 ± 16	88 ± 14	0.001
BMI (kg/m2)	38.2 ± 4.8	34.2 ± 4.4	0.001
FPG (70-110 mg/dL)	102 ± 16	92 ± 12	0.001
Hb1Ac (< 5.7%)	5.9 (5.3-6.4)	5.4 (5-5.7)	0.001
LDL (< 130 mg/dL)	114 ± 29	102 ± 30	0.02
HDL (> 40 mg/dL)	49 ± 12	51 ± 14	0.12
Triglyceride (< 150 mg/dL)	151 (106-220)	115 (98-136)	0.001

BMI: Body mass index, FPG: Fasting plasma glucose, Hb1Ac: Hemoglobin A1C, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

Table 2. The comparison of biochemical parameters between before and 6 months after liraglutide

Variables Reference Range	Before	6 Months After	P value
TSH (0.27-4.20 µU/mL)	2.6 ± 1	2 ± 0.8	0.02
FT4 (0.93-1.97 ng/dL)	1.3 ± 0.2	1.3 ± 0.3	0.56
FT3 (2-4.4 pg/mL)	3.2 ± 0.7	3.1 ± 0.4	0.44
Creatinine (0.5-1 mg/dL)	0.7 (0.6-0.8)	0.7 (0.6-0.9)	0.45
ALT (0-55 mg/dL)	22 (17-34)	20 (16-28)	0.13
AST (5-34 mg/dL)	18 (16-23)	14 (11-20)	0.07
WBC (4-10.5x103/µL)	8 (6.6-9.6)	7.7 (6.4-9.4)	0.37
Neutrophil (2-7x103/µL)	4.9 ± 1.4	5 ± 1.8	0.84
Lymphocyte (0.6-3x103/µL)	2.6 (2-3.1)	2.4 (2-3.4)	0.27
Hemoglobin (12-16 g/dL)	14 ± 1.5	14 ± 1.1	0.77
Platelet (140-424x103/µL)	277 ± 76	266 ± 83	0.17

TSH: thyroid-stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine, ALT: Alanine transaminase, AST: Alanine transaminase, WBC: White blood cells

Discussion

In the present study, according to our knowledge for first time in the literature, significant decrease in TSH values was detected 6 months after liraglutide treatment in obese patients without thyroid disease, but there was no change in thyroid hormone values, and as expected, improvement in metabolic parameters was detected.

The presence of GLP-1 receptors has been demonstrated in many cells and systems in the body, and therefore, GLP-1 RAs may have potentially different and unexpected effects in organs other than the pancreas. It is known that long-term use of GLP-1 RAs may cause hyperplasia in thyroid C-cells and possible medullary thyroid cancer (4). In addition, increased GLP-1 receptor expression has been shown in follicular cell-derived hyperplasic and neoplasic conditions [14]. The patients receiving exenatide and oral antidiabetic drug treatment were evaluated retrospectively, and thyroid cancer was found to be 4.7 times higher in the exenatide group [15]. The current data on the relationship between the use of GLP-1 RAs and thyroid cancers are limited and contradictory.

In rodent studies, which were performed using higher doses of liraglutide than in humans, liraglutide was shown to lead C-cell hyperplasia and neoplasia. The possible hypothesis on this issue is the uncontrolled stimulation of C-cells by liraglutide via GLP-1 receptors [13]. The United States food and drug administration (FDA) has placed a medullary thyroid cancer warning for liraglutide [16]. However, this relationship has not been clearly demonstrated in human studies and remains unclear.

Almost all studies on the effects of GLP-1 RA treatment on the thyroid gland are only related to exenatide. Sencar et al. evaluated thyroid function tests and thyroid gland volumes before and 6 months after exenatide treatment in 46 patients with type 2 DM. They found a significant decrease in TSH values, but FT4, FT3 values, and gland volumes were similar [17]. In a similar study design, Koseoglu et al. compared 39 patients with type 2 DM before and 6 months after exenatide treatment. They revealed a significant decrease in TSH values and gland volumes, and there was no change in FT4 and FT3 values. They thought that this decrease in thyroid gland volume was a reflection of the decrease in TSH values. However, they could not reveal a clear mechanism relationship [18]. The study with the largest sample and follow-up period on this regard was revealed by Tee et al. that 112 patients with type 2 DM were prospectively evaluated before and 12 months after exenatide treatment. Like other studies, they found a significant decrease in TSH values and no change in FT4 and FT3 values [19]. In our study, we demonstrated a significant decrease in TSH values at the 6th month of liraglutide treatment and it was the first time in the literature as a GLP-1 RA different from exenatide. Since our present study was retrospective, we could not evaluate thyroid gland volume. There was no change in thyroid hormone levels, similar to exenatide studies. The common result of these

studies, the decrease in TSH values, may be a class effect of GLP-1 RAs. In addition, Koseoglu et al. also revealed a decrease in thyroid gland volume [18]. However, gland volume may also be affected by factors such as age, gender, presence of accompanying nodules, operator dependency [20]. The fact that this issue is inconsistent between the two studies may suggest that there will not be a clear result.

While all participants in the exenatide studies were diabetic and most were on metformin, only 4 (10%) patients in our study had DM. There are studies on the effects of metformin treatment on TSH values. There are studies showing that a decrease in TSH values without a change in thyroid hormone values with metformin treatment and that this situation is independent of the decrease in BMI [21,22]. Although this issue is not clear in the literature, the use of metformin in exenatide studies may also contribute to the decrease in TSH values. However, in our study, the rate of metformin use was very low compared to exenatide studies.

Several theories have been considered as the reason for the decrease in TSH values with GLP-1 RA treatment, especially with regard to exenatide. GLP-1 receptors have also been demonstrated in pituitary tissue and these receptors on pituitary TSH-producing cells in rodents were shown to bind to GLP-1 RAs with high affinity. GLP RAs may lead a decrease in TSH values with an effect at the pituitary level [23]. It has also been suggested that GLP-1 RAs may increase TSH sensitivity to thyroid cells [17]. Another possible mechanism is that GLP-1 RA-related weight loss may affects TSH values [19].

Data on the effects of weight loss on TSH value are contradictory in the literature [24]. There are some studies showing that a significant decrease in BMI values after bariatric surgery performed on obese patients has no effect on TSH values [25]. On the contrary, there are some studies showing that there is an increase in TSH values with weight gain [26] and a decrease in TSH values with weight loss [27]. On the other hand, Sencar et al. and Koseoglu et al. did not find a relationship between TSH values and the decrease in BMI [17,18]. In the study of Tee et al. with more patient participation and longer follow-up period, an independent nonlinear relationship was found between weight loss and decrease in TSH values, and there was no significant change in TSH values in patients without weight loss. They thought that the main reason for the decrease in TSH values was weight loss and that this was due to the change in the sensitivity of the hypothalamus and/or pituitary to thyroid hormones [19].

Liraglutide is an effective treatment in obesity management with its multiple action mechanisms [5]. We found significant improvements in metabolic parameters such as weight, BMI, FPG, HbA1c, LDL, and triglyceride values at 6 months of treatment. 7% and 16% of patients could not complete the 6th month due to gastrointestinal system complaints and treatment cost, respectively. As can be seen, the most important parameter limiting the use of liraglutide is financial conditions.

Our study has some limitations. The number of participants and the follow-up period of the study were relatively small and short. Prospective multicenter studies with longer follow-up periods and follow-up processes after treatment discontinuation may be more enlightening in this regard. Our study may reveal the decrease in TSH values with liraglutide use, but it is lack in terms of establishing any causality between these two conditions.

Conclusion

We evaluated for the first time in the literature, as there were similar studies with exenatide, the effects of liraglutide treatment, which is used for weight loss, on thyroid gland functions before and 6 months after treatment, and we found a significant decrease in TSH values, but no change in thyroid hormone levels. In addition, we found improvement in metabolic parameters such as weight, BMI, serum glucose, HbA1c values, and lipid profile, except HDL. It should be kept in mind that there may be a decrease in TSH values in patients using liraglutide. There is a need for further studies with larger samples, longer follow-up, and a causal relationship to this regard.

Conflict of interest

There is no conflict of interest in this study. There is no financial support for this study.

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Araştırma Makalesi

Yeni Bir Kalp Cerrahi Merkezi: Konya Şehir Hastanesinde Açık Kalp Cerrahisi Deneyimlerimiz

A New Heart Surgery Center: Our Open Heart Surgery Experience at Konya City Hospital

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Öz

Amaç: Bu çalışmanın amacı, yeni bir merkez olan Konya Şehir Hastanesi'nde 2020 yılından bu yana gerçekleştirilen açık kalp cerrahisi tecrübelerinin değerlendirilmesidir.

Gereç ve Yöntemler: Konya Şehir Hastanesi Kalp ve Damar Cerrahisi Kliniği'nde Ağustos 2020 ile Mayıs 2022 tarihleri arasında gerçekleştirilen toplam 232 açık kalp ameliyatı retrospektif olarak değerlendirilmiştir. Tüm vakalarda median sternotomi ile operasyon gerçekleştirilmiştir. Hastaların kayıtlarına hastane sisteminden ulaşılmıştır.

Bulgular: Çalışmaya dahil edilen hastaların yaş ortalaması 60,79±10,4 yıl olarak belirlenmiştir. Hastaların preoperatif risk skorlamasında EuroSCORE II sistemi kullanılmış ve 78 hastada düşük risk, 64 hastada orta risk ve 90 hastada yüksek risk saptanmıştır. Açık kalp cerrahisi operasyonları içinde en sık yapılan işlem koroner arter baypas operasyonudur (n=190, %81,89). Postoperatif dönemde en sık görülen komplikasyon atrial fibrilasyon (n=34, %14,65) olup kanama nedeniyle 16 (%6,89) hasta revizyona alınmıştır. On bir (%4,74) hastada ise postoperatif erken dönemde mortalite saptanmıştır.

Sonuçlar: Yeni kurulan bir merkez olmakla birlikte bu çalışmada gerek vaka sayısı ve çeşitliliği gerekse düşük mortalite ve morbidite oranları ile kliniğimizde yapılmış olan açık kalp ameliyatlarının sonuçlarının literatür ile uyumlu olduğu gösterilmiştir.

Anahtar Kelimeler: Açık kalp cerrahisi, yeni merkez, mortalite, komplikasyon

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Abstract

Aim: The aim of this study was to evaluate the experience of open heart surgery performed in Konya City Hospital, a new center, since 2020.

Material and Methods: A total of 232 open heart surgeries performed in the Cardiovascular Surgery Clinic of Konya City Hospital between August 2020 and May 2022 were retrospectively evaluated. The operation was performed through median sternotomy in all cases. The records of the patients were accessed from the hospital system.

Results: The mean age of the patients included in the study was 60.79±10.4 years. EuroSCORE II system was used for preoperative risk scoring of the patients and low risk was found in 78 patients, intermediate risk in 64 patients and high risk in 90 patients. Coronary artery bypass surgery was the most common open heart surgery procedure (n=190, 81.89%). The most common postoperative complication was atrial fibrillation (n=34, 14.65%) and 16 (6.89%) patients were revised due to bleeding. Eleven (4.74%) patients had early postoperative mortality.

Conclusions: Although we are a newly established center, this study shows that the results of open heart surgeries performed in our clinic are consistent with the literature with the number and variety of cases and low mortality and morbidity rates.

Keywords: Open heart surgery, new center, complication, mortality

Giriş

Kalp cerrahisi, 20. yüzyılın başlarında hayvan ve insan deneyleri ile sınırlı iken, 20. yüzyılın ikinci yarısından itibaren rutin uygulama alanına girmeye başlamıştır. Mayıs 1953`te Dr. John Gibbon, atriyal septal defekti olan 18 yaşındaki bir kadında ekstrakorporeal devre kullanarak ilk başarılı açık kalp ameliyatını gerçekleştirdi ve bu önemli bir milat oldu. Takip eden yıllarda teknolojinin de katkısı ile açık kalp cerrahisi hızla ilerlemiş ve artık günümüzde kalp transplantasyonu dahil oldukça geniş bir yelpazede cerrahi prosedürler yapılır hale gelmiştir [1].

Ülkemizde, kalp cerrahisinin serüveni dünyadaki gelişmelerle eş zamanlı olarak ilerlemiştir. İlk başarılı açık kalp ameliyatı 1960 yılında Hacettepe Üniversitesi Tıp Fakültesi'nde Dr. Mehmet Tekdoğan tarafından gerçekleştirilmiştir. 1962 yılı itibariyle ise Dr. Aydın Aytaç önderliğinde Hacettepe Üniversitesi'nde seri halinde açık kalp ameliyatlarına başlanmıştır [2]. Kalp cerrahisi ilk başladığı zamanlarda sadece büyük merkezlerde yapılırken, günümüzde ise tüm yurtta gerçekleştirilmektedir. Bu kapsamda Konya Şehir Hastanesi, 2020 yılından beri bünyesinde kalp ve damar cerrahisi bölümü hizmeti sunmaktadır. Biz bu çalışmada Konya Şehir Hastanesi'nde yapılan açık kalp cerrahisi tecrübelerimizi değerlendirmeyi amaçladık.

Gereç ve Yöntemler

Konya Şehir Hastanesi Kalp ve Damar Cerrahisi Kliniği'nde, Ağustos 2020 ile Mayıs 2022 tarihleri arasında gerçekleştirilen toplam 232 açık kalp ameliyatı retrospektif olarak değerlendirildi. Hastaların dosyalarına hastane kayıt sistemi incelenerek ulaşıldı.

Çalışmaya Konya Karatay Üniversitesi Yerel Etik Kurulu'ndan 29.11.2019/317 sayılı izin alındıktan sonra başlandı. Çalışma Helsinki Deklarasyonu ilkelerine uygun olarak yapılmıştır.

Operasyon öncesi tüm hastalara fizik muayene ve rutin kan testleri, ekokardiyografi (EKO), elektrokardiyografi, karotis arter doppler ultrasonografi, göğüs radyografi ve solunum fonksiyon testleri yapıldı. Hastaların hikayesi, muayenesi, tahlilleri ve tetkikleri doğrultusunda ilgili branşlardan konsültasyonlar istenerek önerileri alındı. Kapak ameliyatı yapılacak hastalara preoperatif dönemde diş muayenesi yapıldı. Tüm hastaların preoperatif mortalite riski European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) skorlama sistemi ile değerlendirildi. Kapak operasyonu geçirecek hastalarda preoperatif koroner anjiyografi planlanması şu kriterlere göre yapıldı: anjina varlığı, sol ventrikül sistolik fonksiyon bozukluğu, objektif iskemi kanıtı, koroner arter hastalığı öyküsü veya koroner risk faktörlerinin olması (40 yaş üstü erkekler ve postmenopozal kadınlar dahil).

Tüm vakalarda median sternotomi ile operasyon gerçekleştirildi. Koroner arter baypas greft (KABG) cerrahisi yapılan 18 hastaya atan kalpte işlem yapılırken diğer hastalara aortokaval kanülasyon tekniği ile kardiyopulmoner baypas (KPB) uygulandı. Bu hastalarda asenden aortadan arteriyel kanülasyon ve sağ atriumdan two-stage venöz kanülasyon yapıldı. Sağ atriotomi ile gerçekleştirilen operasyonlarda bikaval venöz kanülasyon uygulandı. Aort diseksiyonu ve anevrizması olgularında ise vakanın durumuna göre aort, aksiller arter, femoral arter, femoral ven ve sağ atriyum kanülasyonları ile KPB sağlandı.

Diastolik arrest rutin olarak antegrad soğuk kan kardiyopleji ve topikal hipotermi ile sağlandıktan sonra 20 dakika aralıklarla ile kardiyopleji tekrar verildi. Aort klempi kaldırılmadan önce sıcak kan kardiyoplejisi verildi. Özellikle düşük ejeksiyon fraksiyonu (EF) olan, çoklu prosedür içeren ve aort diseksiyonu operasyonlarında Custodiol® HTK veya Del Nido kardiyoplejisi tercih edildi. Operasyonlar orta derecede hipotermi (30°C-33°C) altında tamamlandı. Aort diseksiyonu vakalarında distal anastomoz için kısa süreliğine (17-23 dk) derin hipotermik total sikrulatuvar arrest uygulandı. KABG operasyonu için greft olarak sol internal mammarian arter (LIMA), sağ internal mammarian arter (RIMA), radial arter, safen ven ve nadir olarak da sefalik ven kullanıldı. Genel olarak proksimal anastomozlar side klemp eşliğinde yapılırken aortu yaygın kalsifik olan 12 (%5,17) hastada ise tek klemp tekniği kullanıldı. Distal anastomozlar 7-0 polipropilen, proksimal anastomozlar ise 6-0 polipropilen sütür kullanılarak yapıldı. Mitral kapak replasmanı (MVR) yapılan tüm hastalarda transseptal yaklaşım tercih edildi. Aort kapak replasmanı (AVR) uygulanan 1 olguda Manougian yöntemi ile aort kökü genişletildi.

Tüm hastalar operasyon sonrası entübe olarak kalp ve damar cerrahisi yoğun bakım ünitesine alındı. Yoğun bakımdaki hastalar genel durumu ve hemodinamisi stabil hale geldikten sonra drenleri ve sondaları alınarak servis takibine alındı. Koroner arter hastalığı ile beraber kronik periferik arter hastalığı tespit edilen 4 (%1,72) hastaya açık kalp cerrahisinden ortalama 4-6 hafta sonraki bir süreçte periferik vasküler girişim uygulandı. Önemli karotis arter hastalığı tespit edilen 6 (%2,58) hastaya, açık kalp cerrahisi yapılmadan yaklaşık 1 hafta önce lezyonun lokalizasyonuna göre karotis endarterektomi veya stent işlemi yapıldı.

Akut böbrek hasarı, perioperatif dönemde yaygın olarak kullanılan diüretiklerin etkisi göz önüne alındığında Kidney Disease: Improving Global Outcomes (KDIGO) kriterlerinin basit bir modifikasyonu kullanılarak tanımlandı [3]. Akut böbrek hasarı, hastanın taburcu olmadan önceki en yüksek postoperatif kreatinin düzeyi ile açık kalp ameliyatından önceki son serum kreatinin düzeyine dayanarak tanımlandı. Buna göre akut böbrek hasarı, kreatinin seviyesinde 48 saat içinde > 0.3 mg/dL veya 7 gün içinde başlangıç değerinin > 1.5 katı artışla karakterize edildi.

İstatiksel analiz

İstatistiksel analizler IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA) yazılımı kullanılarak gerçekleştirilmiştir. Nominal değişkenler sayı ve yüzde olarak ifade edilmiştir. Sürekli değişkenlerin dağılımı Kolmogorov-Smirnov testi ile değerlendirilmiştir. Sürekli değişkenlerden normal dağılım gösterenler ortalama ± standart sapma olarak ifade edilmiştir.

Bulgular

Araştırmamızda, açık kalp cerrahisi uygulanan toplam 232 hasta değerlendirildi. Bunların 56'sı (%24,14) kadın, 176'sı (%75,86) erkekti. Hastaların yaş ortalaması 60,79±10,4 yıl olarak belirlendi. Hastaların preoperatif dönemdeki ek hastalıkları ve risk faktörleri incelendiğinde, en sık tespit edilenler sırasıyla hipertansiyon 159 (%68,53), sigara içimi 156 (%67,24), diyabetes mellitus (DM) 115 (%49,56), hiperlipidemi 70 (%30,17) ve kronik obstrüktif akciğer hastalığı (KOAH) 52 (%22,41) olduğu görüldü.

Tüm hastaların preoperatif risk skorlamasında EuroSCORE II sistemi kullanıldı. Buna göre, 78 (%33,62) hastada düşük risk (0-3 puan), 64 (%27,58) hastada orta risk (4-6 puan) ve 90 (%38,79) hastada yüksek risk (7 ve yukarı puan) saptandı.

Açık kalp cerrahisi uygulanan hastaların ortalama EF %51,45±8,01 olarak hesaplandı. Hastalara ait preoperatif ek hastalıklar ve risk faktörlerinin özetlendiği veriler Tablo 1'de gösterilmiştir.

Tablo 1. Preoperatif hasta verileri

Özellik	Ortalama	Standart sapma	Sayı (n=232)	Yüzde (%)
Yaş (yıl)	60,79	10,4		
Kadın/Erkek			56/176	24/76
Sigara			156	67,24
HT			159	68,53
DM			115	49,56
KOAH			52	22,41
KBY			17	7,32
PAH			23	9,91
HL			70	30,17
EF (%)	51,45	8,01		
EUROSCORE II				
Düşük risk (0-3)			78	33,62
Orta risk (4-6)			64	27,58
Yüksek risk (≥7)			90	38,79

Kısaltmalar: HT: hipertansiyon; DM: diabetes mellitus; KOAH: kronik obstrüktif akciğer hastalığı; PAH: periferik arter hastalığı; EF: ejeksiyon fraksiyonu; HL: hiperlipidemi; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II

Açık kalp cerrahisi operasyonları içinde en sık yapılan işlem, 190 (%81,89) hastada gerçekleştirilen KABG operasyonuydu. Bu işlemlerden 18'i (%9,47) çalışan kalpte yapıldı. İzole kalp kapak ameliyatları ise toplam 17 (%7,32) hastaya uygulandı. Aort kapak replasmanı (AVR) 7 (%3,01), mitral kapak replasmanı (MVR) 5 (%2,15), AVR+MVR 3 (%1,29) ve MVR ile birlikte triküspit anuloplasti (TA) 2 (%0,86) hastada gerçekleştirilmiştir. Aort cerrahisi toplam 15 hastaya uygulandı. Dört (%1,72) hastaya acil

şartlarda aort diseksiyonu teşhisi kondu ve Bentall prosedürü uygulandı. Dokuz (%3,87) hastaya ise elektif şartlarda asendan aort anevrizma tanısı ile supra koroner aort replasmanı yapıldı. Asendan, arcus ve desendan aort anevrizma tanısı konulan 2 (%0,86) hastaya ise hibrit aortik ark debranching+TEVAR operasyonu uygulandı. Ayrıca 3 (%1,29) hastaya atrial septal defekt onarımı ve 2 (%0,86) hastaya ise miksoma eksizyonu gerçekleştirildi. Ameliyatların dağılımı Tablo 2'de verilmiştir.

Tablo 2. Gerçekleştirilen operasyon tipleri

Ameliyat Tipi	Sayı (n=232)	Yüzde (%)
KABG	190	81,89
Atan kalpte	18	9,47
KPB ile	172	90,53
AVR	7	3,01
MVR	5	2,15
AVR+MVR	3	1,29
KABG+AVR	3	1,29
KABG+MVR	2	0,86
MVR+TA	2	0,86
ASD	3	1,29
Bentall operasyonu	4	1,72
AAR	9	3,87
AAD+TEVAR	2	0,86
Miksoma eksizyonu	2	0,86

Kısaltmalar: KABG: Koroner arter baypas greftleme; MVR: Mitral kapak replasmanı; AVR: Aort kapak replasmanı; ASD: Atrial septal defekt; AAR: Asendan aort replasmanı; AAD:Aortik ark debranching; TA:Trikuspit anüloplasti; TEVAR: Torasik endovasküler aort onarımı

Kardiyopulmoner bypass altında yapılan operasyonlarda ortalama kross klemp süresi 67,72±36,06 dakika ve kardiyopulmoner baypas süresi ise 110,37±54,81 dakikaydı. Koroner arter baypas yapılan hastalarda revaskülarize edilen distal anastomoz sayısı ortalama 2,93±1,13 idi. En çok çıkarılan arteriel greft LIMA (%93,1) iken venöz greft ise büyük safen ven (%85,77) idi. Hastalar entübe olarak yoğun bakıma alındı ve ortalama 7,21±2,82 saatte ekstubasyon gerçekleştirildi. Ortalama yoğun bakım (YBÜ) kalış süresi 3,01±2,38 gün, ortalama hastane kalış süreleri ise ortalama 7,54±2,71 gün idi. Hastalara ait intraoperatif ve postoperatif veriler Tablo 3'de gösterilmiştir.

Hastalarda ortaya çıkan postoperatif komplikasyonlar, mortalite oranları Tablo 4'te gösterilmiştir. Açık kalp cerrahisi geçiren hastalar içinde postoperatif erken dönemde yoğun bakım ünitesinde takip edilen 16 (%6,89) hasta kanama nedeniyle revizyona alındı. Operasyon sonrası taburculuğa kadar olan sürede 34 (%14,65) hastada yeni atrial fibrilasyon (AF) gelişti. Olgularımızın 25'i (%10,77) medikal tedavi ve 5'i (%2,15) kardiyoversiyon ile sinüs ritmine dönmüştür. Dört (%1,72) hasta ise düşük ventrikül hızlı AF ile tedavi edilerek taburcu edilmiştir. Toplamda, 22 (%9,48) hastada postoperatif düşük kardiyak debi gelişti. Bu hastalardan 19'una (%8,18) intra-aortik balon pompası (IABP), 3'üne (%1,29) ise ekstrakorporal membran oksijenizasyonu (ECMO) uygulandı. 5 (%2,15) hastada serebrovasküler olay (SVO) görüldü. Bu hastaların 3'ünde (%1,29) major SVO vardı. On beş (%6,4) hastada akut böbrek hasarı (ABH) gelişti. Hemodiyaliz gereksinimi olmadan bu hastaların 13'ü medikal tedavi sonrasında düzeldi. Fakat 2 (%0,86) hastada akut böbrek yetmezliği (ABY) gelişti ve tüm tedavilere rağmen hastalar kaybedildi. Beş (%2,15) hastada safen ven kesi yerinde, 3 (%1,29) hastada sternal cilt insizyon yerinde enfeksiyon gelişti.

Tablo 3: İntraoperatif ve postoperatif veriler

Özellik	Ortalama	Standart sapma	Sayı	Yüzde (%)
KPB (dakika)	110,37	54,81		
KKS (dakika)	67,72	36,06		
IABP			19	8,18
ECMO			3	1,29
Yoğun bakım kalış süresi (gün)	3,01	2,38		
Entübasyon süresi (saat)	7,21	2,82		
Hastanede kalış süresi (gün)	7,54	2,71		
Distal anastomoz sayısı	2,93	1,13		
Kullanılan greftler				
LIMA			216	93,10
RIMA			16	6,89
Radial arter			10	4,31
Safen ven			199	85,77

KKS: kros klemp süresi; KPB: kardiyo pulmoner baypas; IABP: intraaortik balon pompası; ECMO: Ekstrakorporeal membran oksijenizasyonu; LIMA: sol internal mammaryan arter; RIMA: sağ internal mammaryan arter

Tablo 4: Postoperatif morbidite ve mortalite

Özellik	Sayı (n=232)	Yüzde (%)
Komplikasyonlar	102	43,96
Atrial fibrilasyon	34	14,65
Kanama (revizyona giden)	16	6,89
Düşük kardiyak debi	22	9,48
Serebrovasküler olay	5	2,15
Akut böbrek hasarı	15	6,4
Akut böbrek yetmezliği	2	0,86
Safen ven kesi enfeksiyonu	5	2,15
Sternum kesi enfeksiyonu	3	1,29
Mortalite nedenleri	11	4,74
Düşük kardiyak debi	5	2,15
Serebrovasküler olay	3	1,29
Böbrek yetmezliği	2	0,86
Enfeksiyon	1	0,43
EuroSCORE II'ye göre mortalite		
Düşük risk	1	0,43
Orta risk	3	1,29
Yüksek risk	7	3,01

Postoperatif hastane-içi mortalitemiz 11 (%4,74) idi. Mortalite gelişen hastaların EuroSCORE II skorlamasına göre sınıflaması yapıldığında, 1 (%0,43) hasta düşük riskli, 3 (%1,29) hasta orta riskli ve 7 (%3,01) hasta yüksek riskli olarak sınıflandırıldı. En sık mortalite sebebi akut miyokard enfarktüsü nedeniyle acil operasyona alınan 5 (%2,15) olguda karşılaştığımız postoperatif düşük kardiyak debi nedeniyle gelişen multiorgan yetmezliği idi. Diğer mortalite sebepleri ise sırasıyla serebrovasküler olay 3 (%1,29), böbrek yetmezliği 2 (%0,86) ve enfeksiyon 1 (%0,43) idi.

Tartışma

Kalp cerrahisi dünyada ilk defa 1938 yılında Gross'un başarılı PDA ligasyonu ile başladı [4]. Bu çığır açan operasyonun hemen ardından alanında ilk defa gerçekleştirilen ameliyatlar birbirini izledi. Özellikle de Gibbon tarafından 1953 yılında ASD vakasında kalp-akciğer makinasının kullanılması ile kalp cerrahisi çok önemli bir atılım yaptı [5].

Kalp cerrahisi açısından 20. yüzyılın ikinci yarısı hem dünyada hem de ülkemizde yeniliklerin yaşandığı bir dönem olmuştur. Kalp cerrahisindeki bu hızlı gelişmeler ülkemizde de yakından takip edilmiş ve eşzamanlı olarak operasyonlar gerçekleştirilmiştir. Dr. Mehmet Tekdoğan Türkiye'de ekstrakorporeal dolaşım ile ilk açık kalp ameliyatını Hacettepe Üniversitesi Tıp Fakültesi'nde gerçekleştirilmiştir [6]. Takip eden yıllarda Türkiye'de açık kalp cerrahisinin uluslararası standartlara gelmesinde Dr. Yüksel Bozer, Dr. Aydın Aytaç, Dr. Siyami Ersek ve Dr. Kemal Beyazıt önemli rol oynamıştır [6]. Kalp cerrahisi bir zamanlar sadece büyük şehirlerde lokalize olarak yapılıyor iken artık günümüzde giderek yaygınlaşmış ve ülkemizin birçok şehrindeki kamu ve özel hastanelerdeki kalp merkezleri, alanında dünya standartlarında hizmet veren ve oldukça başarılı sonuçlar alınan nitelikli klinikler haline dönüşmüştür. Bu merkezlerden biri olan Konya Şehir Hastanemiz 2020 yılı itibari ile hizmet vermeye başlamıştır. Sunulan bu çalışmada amacımız kalp ve damar cerrahisi bölümü olarak hastanemizde yapılan açık kalp cerrahisi sonuçlarımızı paylaşmak ve güncel literatür bilgisi ışığında değerlendirmektir.

Yapılan araştırmalar, ülkemizdeki kalp cerrahisi merkezlerinde 2009 yılında toplam 66105 açık kalp ameliyatı yapıldığını ve bu ameliyatların %72,95'inin KABG ameliyatlarından oluştuğunu göstermektedir [7]. Bizim kliniğimizde yapılan ameliyatlara bakıldığında ise %81,89 oran ile izole KABG operasyonları literatürle uyumlu olarak en sık yapılan işlem olarak görülmüştür. Kliniğimizde uygulanan kapak operasyonlarının oranı %7,32 iken, diğer kardiyak hastalıklar nedeniyle uygulanan operasyonlar %19,73 oranında idi.

KABG operasyonu yapılan 18 olguda atan kalpte KABG cerrahisi tercih edilmiştir. Bu tercihin en önemli sebepleri arasında hastaların ileri yaşta olması, DM, KOAH, kronik böbrek yetmezliği gibi ek komorbit hastalıklarının da varlığı yer almaktadır. Bu nedenle, bu hasta grubunda KPB kullanımından doğacak olası yüksek risklerin önlenmesi hedeflenmiştir. Diğer hastalarda ise KPB kullanılarak revaskülarizasyon yapılmıştır.

KABG operasyonu yapılan hastalarımızda, safen ven ve LIMA öncelikli greftler olarak tercih edilmiştir. Literatürde yapılan çalışmalar, koroner bypass cerrahisi sırasında kullanılan farklı greft tiplerinin uzun dönem sağ kalım oranları üzerinde önemli etkileri olduğunu göstermektedir [8]. LIMA'nın, diğer greft türleriyle karşılaştırıldığında daha yüksek sağ kalım oranlarına sahip olduğu ve daha az komplikasyon riski taşıdığı belirtilmektedir. Ayrıca, LIMA'nın uzun dönemde greft tıkanıklığı ve restenoz risklerinin azaltılmasında etkili olduğu da bilinmektedir [8]. Biz de KABG vakalarımızda greft tercihlerimizi literatürle uyumlu olarak yapmış ve özellikle LIMA'yı tercih etmiş bulunmaktayız.

Açık kalp cerrahisinde ameliyat sonrası görülen mortalite ve morbidite günümüzde halen önemli bir sorun olarak karşımıza çıkmaktadır. Yapılan çalışmalar postoperatif dönemde gelişen böbrek fonksiyon bozukluğu, düşük kardiyak debi, pulmoner komplikasyonlar ve enfeksiyonun mortalite ile ilişkili olduğunu göstermiştir [9]. Bu çalışmalara paralel olarak, bizim çalışmamızda da özellikle acil operasyona alınan hastalarda gelişen postoperatif düşük debi, SVO, ABY ve enfeksiyon erken dönem mortalite ile ilişkili bulunmuştur. Kalp cerrahisinde preoperatif mortalite tahmininde yaygın olarak kullanılan risk skorlaması sistemlerinden biri olan EuroSCORE II'yi hastalarımızı değerlendirmek için kullandık. Buna göre, mortalite gelişen hastaların EuroSCORE II değerleri incelenecek olursa 1 hasta düşük (%0,43), 3 hasta orta (%1,29) ve 7 (%3,01) hasta yüksek riskliydi. Literatürle uyumlu olarak, EuroSCORE II risk sınıfı arttıkça bizim hasta grubumuzda da mortalitenin artmış olduğu gösterilmiş oldu [10-12]. Genel olarak bakıldığında, farklı etkenlerden dolayı 11 (%4,74) hasta postoperatif dönemde mortal seyretmiştir. Mortalite oranımız literatür bilgisiyle uyumlu çıkmıştır [13].

Postoperatif AF (POAF), açık kalp cerrahisi sonrasında sıklıkla ortaya çıkan bir aritmi türüdür ve klinik pratiğimizde sıkça karşılaştığımız bir komplikasyondur. POAF, açık kalp cerrahisi sonrasında %30 ile %50 arasında görülebilir [14]. Ancak, çalışmamızda POAF görülme oranı %14,65 olarak belirlenmiş ve 34 hastamızda yeni başlangıçlı AF tespit edilmiştir. Olgularımızın 25'i (%10,77) medikal tedavi ve 5'i (%2,15) kardiyoversiyon ile sinüs ritmine dönmüştür. Dört

(%1,72) hasta ise düşük ventrikül hızlı AF ile medikal tedavi altında taburcu edilmiştir. Hastalarımızın hiçbirinde POAF'a bağlı nörolojik komplikasyon gelişmemiştir. POAF, hastaların morbidite ve mortalite risklerini arttırabilir [14]. Bu nedenle, antikoagülan tedavi, beta-blokerler, kalsiyum kanal blokerleri, digoksin ve amiodaron gibi ilaçlar kullanılabileceği gibi bazı durumlarda kardiyoversiyon da bir seçenek olabilir [15]. Biz de öncelikli olarak medikal kardiyoversiyonu tercih etmekle birlikte diğer tedavi seçeneklerini de uygun hastalarda kullanarak, erken tanı ve tedavi ile POAF'ın ciddi komplikasyonlarını önlemeyi başardık.

Kardiyak cerrahi sonrası ortaya çıkan komplikasyonlardan bir diğeri ise serebrovasküler olaylardır. Postoperatif nörolojik bozuklukların büyük bir kısmı sekelsiz olarak iyileşirken, literatürde %1'den biraz daha fazlasında majör SVO oluştuğu belirtilmektedir [16]. Benzer şekilde, bizim çalışmamızda da bu oran gözlemlenmiştir ve 5 (%2,15) hastamızda geçici nörolojik defisit gelişmiştir. İki (%0,86) SVO hastasında tedavi ile düzelme görülmüştür. Ancak 3 (%1,29) vakada majör nörolojik defisit geliştiği ve hastaların uzamış yoğun bakım sürecinde yaşamını yitirdiği tespit edilmiştir.

Açık kalp cerrahisi sonrasında nadir görülen fakat ölümcül sonuçlara yol açabilen bir diğer komplikasyon ise mediastinittir. Literatürde medistinitin %1-3 oranında görüldüğü belirtilmektedir [17]. Bizim çalışmamızda ise erken dönemde mediastinite rastlanmamıştır. Bununla birlikte, safen ven veya sternal cilt insizyon yerinde enfeksiyon gelişen 8 hastamız bulunmaktadır. Bu hastaların uygun antibiyotik ve pansuman tedavisi ile tamamen iyileştikleri gözlenmiştir. Antibiyotik tedavisi altındaki enfekte safen ven insizyonu olan 3 hastamıza lokalize yara debridmanı uygulanmış ve primer sütür ile kapatılmıştır.

Açık kalp cerrahisi sonrası gelişen düşük kardiyak debi, ciddi komplikasyonlara neden olabilen bir durumdur. Bu durum, özellikle kalp yetmezliği olan hastalarda daha sık görülmektedir. Düşük kardiyak debi, kalbin yeterli kan pompalamasını engelleyerek dokuların oksijen ihtiyacını karşılamada başarısız olmasına neden olur. Bu durumun tedavisi için çeşitli yöntemler kullanılabilir. İntravenöz inotropik destekler ve mekanik kardiyak destek cihazları, düşük kardiyak debili hastalarda kullanılan yaygın tedavi yöntemleridir [18]. Bu yöntemler, kalbin kontraksiyon gücünü arttırarak kan dolaşımını iyileştirir ve dokuların oksijen ihtiyacını karşılamalarına yardımcı olur. Bizim çalışmamızda, açık kalp cerrahisi sonrası 22 hastada düşük kardiyak debi gelişti. Bu hastaların 19'una IABP uygulandı ve 3 hastaya ECMO takıldı. Bu hastalar arasında takip sürecinde maalesef 5 hasta multiorgan yetmezliği nedeniyle kaybedildi. IABP ve ECMO gibi tedaviler düşük kardiyak debisi olan hastalarda kullanılabilecek etkili tedavi yöntemleri olmakla birlikte bu tedavilerin kullanımı kanama ve enfeksiyon gibi bazı riskler taşıyabilir. Dolayısı ile doğru hasta seçimi ve zamanlama tedavi yönetimi açısından önemlidir.

Çalışmamızda post operatif erken dönemde, 15 hastada (%6,4) ABH geliştiği görüldü. Bu hastaların 13'ü medikal tedavi sonrasında hemodiyaliz gereksinimi olmadan iyileşti, ancak 2 hasta ABY'ne ilerledi ve hemodiyaliz dahil tüm tedavilere rağmen takip sürecinde kaybedildi. Yapılan çalışmalar açık kalp cerrahisi sonrası gelişen ABH'nın hala önemli bir sorun olduğunu göstermektedir. ABH'nın sıklığı hem hastanede yatış süresini hem de morbidite ve mortalite oranlarını arttırmaktadır. Son zamanlarda yapılan çalışmalar, ABH' nın özellikle kalp cerrahisi sonrası dönemde görülme sıklığının yüksek olduğunu vurgulamaktadır [19]. Bizim çalışmamızda ortaya konulan ABH sıklığı önceki çalışmalarla uyumludur.

Çalışmamızın en önemli kısıtlılığı retrospektif olarak planlanmış olmasıdır. Bu durum, yanlılığa yol açma potansiyeli taşımakta ve nedensellik ilişkilerinin kurulmasını sınırlayabilmektedir. Ayrıca, çalışma tek bir kurumda gerçekleştirilmiş ve örneklem büyüklüğü biraz küçüktür, bu da elde edilen sonuçların genel geçerliliklerini etkileyebilir. Çalışmamız postoperatif erken dönem komplikasyonları hakkında bilgi sunmakla birlikte, bir diğer kısıtlama da uzun vadeli hasta takip verilerinin eksikliğidir.

Sonuç olarak, Konya Şehir Hastanesi Kalp ve Damar Cerrahisi Kliniği, yeni bir merkez olarak 2020 yılında hizmete açıldı. Cerrahi ekibimizin büyük kısmının daha önce yıllardır açık kalp cerrahisi yapılan köklü bir kurumdan gelmesi sayesinde, yeni hastanemizde hızlı bir uyum sağlandı ve çalışmamızda ortaya konulan başarılı sonuçlar elde edildi. Merkezimiz kısa süre içerisinde İç Anadolu Bölgesi'nde vaka sayısı ve çeşitliği konusunda lider pozisyona geçerek birçok çevre ilden hasta kabulü yapar hale gelmiştir. 2022 yılı itibariyle ise eğitim kliniği vasfı kazanmış olup hastalara verilen hizmetin yanında aynı zamanda uzmanlık eğitimi de vermektedir. Hedefimiz, güncel tıp araştırmaları ve teknolojik gelişmeler doğrultusunda bölge insanına yenilikçi ve kaliteli sağlık hizmetleri sunarak sağlık alanında öncü bir merkez olmaktır.

Maddi Destek ve Çıkar İlişkisi

Herhangi bir maddi destek alınmamıştır. Yazarlar arasında çıkar çatışması yoktur.

Bilimsel Sorumluluk Beyanı

1.Deneylerin konsept ve dizaynlarının oluşturulması veya verilerin toplanması: MCÇ, MD, İSY

2. Verilerin analizi ya da ifade edilmesi: MCÇ, ANB, HD

3. Makalenin taslağının hazırlanması veya bilimsel içeriğinin gözden geçirilmesi: MCÇ, EB, HG, YG

4. Makalenin basılmaya hazır son halinin onaylanması: MCÇ, KD

Kaynaklar

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Research Article

Does intra-procedural enlightenment change the level of anxiety and pain in scheduled breast ultrasonography?

Randevulu meme ultrasonları esnasında bilgilendirme yapılmasının hasta kaygısı ve meme ağrısı üzerine etkisi var mıdır?

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Abstract

Aim: Scheduled breast ultrasounds are stressful procedures for women. We aimed to study the effect of informing patients during breast ultrasound and investigate associated anxiety and pain alterations.

Material and Methods: After approval of the state hospital ethics committee and informed consent, women scheduled for breast ultrasound between November 2022 and March 2023 were prospectively enrolled in this randomized controlled study. Patients were either informed during the ultrasound about the procedure itself or not. The participants completed State-Trait Anxiety Inventory for measuring anxiety and visual analog scale for pain scores, immediately before and after the examination. Demographic data, anxiety and pain scores were statistically evaluated by using chi-square test, independent samples t-test and Mann-Whitney U test. The alteration of anxiety and pain scores considering enlightenment were compared with paired samples t-test and Wilcoxon test.

Results: Among 143 patients, preprocedural anxiety was lower in oncological follow-ups and higher in positive clinical breast examination, breast self-examination and mammography subgroups. Trait and preprocedural state anxiety scores were similar between the two groups regarding enlightenment. Anxiety and pain reduction was observed after ultrasound and both were statistically significant in the informed group ($p<0.001$ and $p=0.03$, respectively).

Conclusion: Informing the patients during breast ultrasound reduces anxiety levels and pain perception.

Keywords: Anxiety; stress; breast ultrasound; pain; enlightenment.

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Öz

Amaç: Randevulu meme ultrasonları kadınlar için oldukça stresli işlemlerdir. Bu çalışma ile ultrason esnasında hastaları bilgilendirmenin, işlem ilişkili kaygı ve meme ağrısı üzerindeki etkilerini araştırmayı hedefledik.

Gereç ve Yöntemler: Şehir hastanesi etik kurulu onayı ve hasta onamı alınmasını takiben Kasım 2022 ve Mart 2023 tarihleri arasında randevulandırılmış meme ultrasonu olan hastalar prospektif olarak değerlendirildi. Hastalar bilgilendirme yapılıp yapılmamasına göre randomize-kontrollü olarak iki gruba ayrıldı. Çalışmaya katılan hastalar kaygı ölçümü için "Durumluk-Sürekli Kaygı Ölçeği" formunu, ağrı skorları için de "Görsel Analog Ölçeği" formunu hem ultrasondan önce hem de ultrason bitiminde doldurdu. Demografik veriler, kaygı ve ağrı skorları istatistiksel olarak Ki-kare testi, bağımsız örneklem t-testi ve Mann-Whitney U testi ile analiz edildi. Hasta bilgilendirmesine göre yapılan kaygı ve ağrı skorları değişimi, eşleştirilmiş örneklem t-testi ve Wilcoxon testi ile değerlendirildi.

Bulgular: 143 hastada işlem öncesi kaygı, onkolojik takip hastalarında daha düşük olup fizik muayene bulgusu olan, öz muayene yapan ve aynı gün mamografi çekimi bulunan hastalarda ise anlamlı olarak daha yüksek saptandı. Sürekli ve işlem öncesi durumluk kaygı skorları hasta bilgilendirmeye göre iki grup arasında benzer bulundu. Ultrason sonrası genel kaygı ve ağrı skorlarında azalma dikkati çekmiş olup hastaların bilgilendirildiği grupta bu düşüş anlamlı bulundu (sırasıyla $p<0.001$ ve $p=0.03$).

Sonuç: Meme ultrasonu çekimi esnasında hastaları bilgilendirme, kaygı seviyeleri ve meme ağrısını azaltmaktadır.

Anahtar kelimeler: Kaygı; stres; meme ultrasonu; ağrı; bilgilendirme.

Introduction

There has been an increasing need for radiological imaging in recent decades. Screening programmes, diagnostic purposes and follow-up patients, either oncological or non-oncological, compose the pool of radiological examinations (1). Breast imaging is one of the main topics that attracts attention, especially of women.

Anxiety is a common problem for people having or waiting for a scheduled radiological examination. It is generally related to the possible results of health impairment (2). According to National Cancer Institute, approximately one in every eight women will be diagnosed with breast cancer in her lifetime and the death rate is 19.6 per 100.000 women every year (3). Therefore, patients that undergo breast ultrasonography (US) cannot avoid the thought of cancer possibility and experience a personal variable degree of anxiety regarding this high emotional status from the time the examination was scheduled (4). The burden of stress reflects during the ultrasound procedure, where the patient is uncomfortable and asks questions about the imaging as the radiologist performs.

Pain is one of the breast symptoms that precipitate anxiety. According to previous studies, about 10-30% of women present with breast pain in their lifetime (5). Even though breast cancer related breast pain comprises very few amount of the cases and researchers show that other symptoms, such as breast mass, nipple discharge etc, are mainly involved in malignancy diagnosis, breast pain is still one of the primary reasons for hospital referrals (6, 7).

We aimed with this study to investigate if informing the patients for breast US about the procedure itself and patient related imaging results, either during or at the end of the examination, would influence the level of anxiety and breast pain.

Material and Methods

From November 2022 to March 2023 patients (age>18 years) waiting to undergo breast US in the radiology department of one institution were invited to participate in this prospective study, after obtaining the approval of the state hospital ethics committee (decision number: 2022-10/2127). The study was conducted according to the Declaration of Helsinki. All patients were informed for the implementation of the psychological test that they will be submitted and written consent was provided. Exclusion criteria were the use of anxiolytic medication on the same day prior to the US procedure, illiteracy and reading disorders.

In the waiting hall of the radiology department, the participants were welcomed with an US technician first. They were informed about the study individually and then randomized into two groups. Group 1 was labelled for enlightenment, where patients were provided with the information of the US procedure itself and the results of a kind that the patient would understand. Before the procedure, the ultrasound technician gave the participant an enlightenment form where it is explained what breast US is, why to do this imaging, that the technique does not involve ionized radiation, what can go wrong during the session, how long will it take and when the

results can be achieved. After this interaction, the participants were asked to fill in the "trait" part of Spielberger State-Trait Anxiety Inventory (STAI) form, a sheet of demographic data and a visual analog scale (VAS) form to score pain, if the patient has breast pain. Finally, the patient was introduced to the radiologist for breast examination. She was told that the results of the US could be discussed at the end of the session. If the patient had findings of BI-RADS 3 or less, she was explained in detail by the radiologist what the findings meant and that she should not worry about the results since it would not need any further investigation. Also if called for a follow up, she was explained why and what future possibilities are likely to happen. If the participant had results of BI-RADS 4 or 5, she was explained that a suspicious finding was detected which would need histopathological confirmation before discussing anything about cancer and that benign possibilities are still in consideration. The enlightenment was provided by the same doctor and US technician for each patient. The total procedure of both enlightenment and breast US ranged from 20 minutes to 35 minutes. Group 2 was referred as the control group, where no specific information about the US procedure was provided. If the case did not need biopsy evaluation (BI-RADS 3 or less), the patient was told to see her clinician for the results. But if the BI-RADS score was 4 or higher, the patient was told that there is a problem that needs to be discussed with her doctor and was referred for an urgent appointment with the clinician. The participants were asked to fill in the STAI and VAS forms before the US, similarly as in Group 1. Immediately after the procedure, patients were asked to complete the "state" anxiety part of the STAI, together with a second VAS form for evaluating breast pain again.

STAI is a validated, 40-item questionnaire on a self-report basis that is used to evaluate anxiety in two subscales, consisting of 20 items each (8). Trait anxiety refers to individual's behavioral attitude and how they feel for anxiety in general. State anxiety is a temporary emotional condition under particular circumstance of a perceived event. Each question is scored on a scale from 1 to 4. Final evaluation of each inventory range from 20 to 80, where higher scores correlate with elevated levels of anxiety. VAS is a self-reported Likert-type scale where responses are scored from 0 (no pain) to 10 (unbearable pain). We evaluated breast pain using this scale at the beginning of the breast ultrasound and right after the procedure ended.

Data analysis was performed through the statistical software (SPSS, v. 20.0, IBM Company, Chicago, IL). The Kolmogorov-Smirnov test was used to check for data normality. Categorical variables were expressed as number (n) and percentage (%), while continuous variables were reported as mean, standard deviation (SD), or median values depending on the distribution. When testing continuous variables, the Independent Samples t-test was used if the test's parametric assumptions were fulfilled. Otherwise, the Mann-Whitney U test was used. Demographic differences were calculated by using chi-square test. The alteration of anxiety scores and VAS scores regarding enlightenment were compared with paired samples t-test and Wilcoxon test. Statistical significance was defined for p less than 0.05.

Results

Of 235 patients eligible for research, a total number of 176 women were enrolled in the study. The rest 59 patients refused to participate except for 33 cases who did not fulfill the requirements of a scorable test. A total of 143 patients were randomized into two groups where 57 were informed (group 1) an 86 were not informed (group 2) of the US results. The demographic data of the patients are shown in Table 1.

Regarding the medical records, 44 % (n=63) of patients were submitted to radiology department for an oncologic follow-up. Among non-oncological patients, 26 % (n=38) were suspected of breast cancer in clinical breast examination (CBE), and 29 % (n=42) applied for a due breast screening programme. 52 % (n=75) of patients had scheduled mammography workup on the same day with the US, and this group showed higher levels of state anxiety before US (p=0.036). The state anxiety score before US was higher in the group with abnormal CBE and those who make breast self-examination. Oncological patients, including breast cancer, had significantly lower state anxiety scores (Table 2).

Enlightenment related anxiety alteration during US was evaluated by STAI scores (Table 3). The baseline level of anxiety was referred as the trait STAI score, which was obtained before the US examination. The trait anxiety was similar between the two groups (38.91 ± 4.97 in group 1 and 38.69 ± 5.21 in group 2) The state anxiety score before US was also similar among the groups (44.81 ± 5.13 in group 1 and 44.91 ± 5.27 in group 2). The state anxiety after US decreased significantly in group 1($p<0.001$).

About 46 % (n=66) of the patients were presented with breast pain. Patients who had mammography the same day and those in menstrual period had significantly higher pain scores before the US procedure (Table 4). The mean intensity of breast pain on VAS scale was 6.02 ± 1.90 before US and 5.62 ± 2.00 after US. Enlightenment related pain reduction after US procedure was statistically significant (p=0.03).

Table 1. Demographic data of study population.

	Group 1 (enlightenment) (n=57)	Group 2 (no enlightenment) (n=86)	p value
Age (years), mean±SD	49.07±13.08	49.91 ± 12.44	0.409*
Marital status			
Married	32	36	0.094Δ
Single	25	50	
Education			0.555Δ
High school or less	23	39	
University or higher	34	47	
Employment	27	36	0.516Δ
Offspring	25	30	0.280Δ
Breastfeeding	24	35	0.867Δ
Personal history of cancer	28	35	0.320Δ
Personal history of breast cancer	18	27	0.982Δ
Breast self-examination	26	35	0.561Δ
Abnormal CBE	19	25	0.589Δ
BI-RADS category			0.548Δ
BI-RADS 3 or less	36	50	
BI-RADS 4 or more	21	36	
Mammography	30	45	0.971Δ
Pain	32	34	0.051Δ
Present menstrual period	19	17	0.067Δ
Use of COCs	19	17	0.067Δ

SD, Standard deviation; CBE, clinical breast examination; BI-RADS, breast imaging and reporting and data system; COCs, combined oral contraceptives.
*Mann-Whitney U test
ΔChi-square test

Table 2. State STAI anxiety scores before breast ultrasound in different subgroups

	Mean state STAI score before US SD (n)		P value
Feature	Yes	No	
University graduate or more	43.98±4.99 (81)	46.03±5.28 (62)	0.020¶
Employment	43.49±4.78 (63)	45.95±5.29 (80)	0.004¶
Offspring	45.75±5.24 (55)	44.32±5.13 (88)	0.113¶
Breastfeeding	44.53±5.05 (59)	45.11±5.32 (84)	0.512¶
Personal history of cancer	43.24±4.95(63)	46.15±5.06 (80)	0.001¶
Personal history of breast cancer	42.87±4.39 (45)	45.79±5.30 (98)	0.002¶
Breast self-examination	45.97±4.70 (61)	44.05±5.43 (82)	0.029¶
Abnormal CBE	46.55±5.07 (44)	44.12±5.11 (99)	0.010¶
Mammography	45.73±5.07 (75)	43.91±5.22 (68)	0.036¶

STAI, state trait anxiety inventory; US, ultrasound; SD, Standard deviation; CBE, clinical breast examination.
¶Independent samples t-test

Table 3. Patient self-reported outcomes.

Outcome	Group 1 (enlightenment) (n=57)	Group 2 (no enlightenment) (n=86)	p value	p value (before and after US)	
				Group 1	Group 2
Anxiety scores (mean±SD)					
Trait STAI	38.91 ± 4.97	38.69 ± 5.21	0.804*		
State STAI (before US)	44.81 ± 5.13	44.91 ± 5.27	0.910¶		
State STAI (after US)	40.33 ± 5.95	45.83 ± 7.97	<0.001*	<0.001$^{\Delta}$	0.162$^{\Delta}$
Reduction in stateSTAI	4.51 ± 4.89	-1.44 ± 4.57	<0.001*		
Pain scores					
VAS (before US)	5.84 ± 2.25	6.18 ± 1.52	0.499*		
VAS (after US)	5.12 ± 2.12	5.09 ± 1.79	0.046*	0.030$^{\Sigma}$	0.669$^{\Sigma}$
Reduction in VAS	0.72 ± 1.57	0.09 ± 1.13	0.075*		

STAI, state trait anxiety inventory; US, ultrasound; SD, Standard deviation.
*Mann-Whitney U test
¶Independent samples t-test
ΔPaired samples t-test
∑Wilcoxon test

Table 4. Pain VAS scores in 66 patients before breast ultrasound in different subgroups

	Mean VAS scores before US SD (n)		P value
Feature	Yes	No	
Breastfeeding	6.00 ± 1.94 (21)	6.02 ± 1.91 (45)	0.939*
Personal history of cancer	6.06 ± 1.95 (32)	5.97 ± 1.89 (34)	0.922*
Personal history of breast cancer	5.73 ± 2.16 (22)	6.16 ± 1.77 (44)	0.424*
Present menstruation	6.53 ± 1.86 (32)	5.53 ± 1.84 (34)	0.041*
Abnormal CBE	5.56 ± 1.94 (18)	6.19 ± 1.88 (48)	0.336*
Mammography	6.35 ± 1.85 (51)	4.87 ± 1.68 (15)	0.009*
Use of COCs	6.13 ± 2.32 (23)	5.95 ± 1.67 (43)	0.791*

VAS, visual analog scale; US, ultrasound; SD, Standard deviation; CBE, clinical breast examination; COCs, combine combined oral contraceptives.
*Mann-Whitney U test

Discussion

Due to longer life expectancy and new diagnostic approaches, breast imaging workups and screening programmes are lately in demand amongst women. On the other hand, fear of breast cancer brings out the increment of anxiety related to the radiological procedure itself and its consequences (9). Our study emphasizes that women having breast US, especially those who were referred for an abnormal physical examination finding, are stressed out more than follow-up patients, either oncological group or patients due to a screening programme. Also, our results encourage the consideration of enlightenment during the US procedure, which reduces anxiety and pain.

It is previously reported that radiological diagnostic procedures induce emotional reactions which may eventually lead to disrupted patient cooperation (10, 11). Also, the quality of imaging is found to be inversely proportional to the degree of anxiety the patient experiences (12). In such a status where the procedure itself is the stressor, the anxiety level would proceed through the sonography session increasingly. Therefore, we hypothesized that the enlightenment of the patient during sonography at a certain necessity level would reduce the imaging related anxiety.

In a study of anxiety investigation among scheduled different radiological examinations, US revealed the highest level of anxiety scores. This finding was related to the quick delivery of the US reports rather than the other imaging modalities, or the fear of necessity for having another advanced type of imaging examination after US (9). In this context, anxiety seen in women awaiting breast US cannot be undervalued and should be supported by health professionals where necessary.

The possibility of having breast cancer eventually is the main stressor factor in women undergoing screening, which means to face big changes in one's life. The reason of anxiety in this population is related to the fear of both having a cancer

diagnosis and being exposed to its consequences considering the treatment. On the other hand, women who already have cancer diagnosis and visit radiology department for an oncological follow-up are reported to show lower anxiety (9). Similarly, our study revealed that women referred to radiology for breast US from clinics with abnormal CBE have higher state anxiety levels and oncological follow-up patients show lower stress levels. We think this is because the clinician's concrete physical finding is a stronger fact than the unknown results of a routine screening for breast cancer or a follow-up. Patients who had mammography before breast US on the same day showed higher levels of state anxiety. We thought that the reason of this induced anxiety was in parallel with the elevated number of examinations taken in a restricted time period, where the imaging workup related stressor factor multiplies. The state anxiety scores were also higher in patients who make breast self-examination. This is probably because the abnormality that the patient realizes on her own leads her to associate this fact with potential breast cancer. The presence of employment and high education level were features with the advantage of lower state anxiety scores. Lo Re et al. reported similar results and suggested that the more knowledge the patient has, the better understanding of the disease and treatment she will have, which would reduce anxiety. We think the employment has a similar effect where the patient would have the comfort of upcoming financial burden related to a possible cancer.

Several studies revealed that the more anxiety the patient has before surgery, the worse prognosis is followed after, including postoperative pain and treatment (9). Therefore, we think that other than the organic etiologies, breast pain could be associated with high levels of anxiety related to the scheduled breast imaging appointment. Health professionals working in radiology departments are not trained for managing screening related patient anxiety. Only MRI procedures, if needed, could be implemented with the scheduled collaboration of anesthesia department in many centers of our country. But most women undergoing breast US experience the stress of taking a diagnostical examination.

There is a variety of relaxation methods used to reduce patient's anxiety throughout a medical intervention. These methods include meditation, hypnosis, music and medication (13-16). The most practical, cheapest and noninvasive method among these supporting implementations is music. We tried to develop an alternative feasible method to music with this study. Unlike cross-sectional imaging modalities and X-rays, breast ultrasound is a workup of a kind, where the radiologist is present at the time of the procedure and is able to evaluate the severity of the case. Speaking for breast imaging, it is important to evaluate the patient as a whole, where other modalities, if necessary, should also be analyzed and concluded to the final decision. But in many patients that take a breast US, it is possible to speak of discrimination between BI-RADS 3 and BI-RADS 4, viva voce. We realized that informing the patient under this context brings out a relief, and we tried to support our hypothesis by measuring the anxiety levels before and after breast US in informed and control groups.

The development of breast cancer in patients with mastodynia is reported as a very small possibility (17). Several studies confirmed this finding with an estimated rate of 1.2-6.7%. Zarei et al. reported in their study that patients revealed less breast pain after even only implementing breast sonography. However, the population of this study was restricted to the cases who had only breast pain as a symptom, but also had normal CBE. They also commented that their study population included both menstrual cyclic and noncyclic pain (18). Our study comprises a larger range of population and we analyzed the impact of informing the patients during the sonography procedure, for both pain and anxiety related to the imaging. We think that the significantly reduced pain levels would not be the result of enlightenment effect only, but also could originate from the diversity of our study group. Some of our patients scheduled for breast US had a mammography session just before the US procedure. Therefore, mammography related mastodynia was not ruled out in this inhomogeneious study group, and this might have affected the overall pain experienced. Similarly, cyclic and noncyclic pain was not studied separately. The pain reduction could be the consequence of both the relief related to US implementation itself or enlightenment.

We had several limitations in this study. First, there was an inhomogeneious group of patients evaluated for breast pain. Patients both with various breast symptoms and normal CBE findings were included. Also, some patients were referred to mammography before the US procedure. These facts could be optimized with a larger study group, working on each subgroup seperately. Second, in our country the US procedures are all performed by the radiologists in person. However, in different countries, the sonographers are responsible for this task and it is impossible for such centers to inform the patient throughout a breast US procedure.

Conclusion

In conclusion, informing the patient throughout a breast US examination reduces the anxiety levels and pain. This

enlightenment makes a probable relief concerning the imaging workup related anxiety itself which also has an effect on pain perception.

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Research Article

Kidney Transplantation in the New Hospital Model in Turkey: 3 Years of Experience in Ankara City Hospital

Türkiye'de Yeni Hastane Modelinde Böbrek Nakli: Ankara Şehir Hastanesi'nde 3 Yıllık Deneyim

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Abstract

Aim: City hospitals, as a new model hospital, started to serve in approximately 20 different cities in Turkey. In this study, we aimed to present the 3 years experience of Ankara City Hospital kidney transplant unit, which has exceeded 100 cases, as a new hospital model.

Materials and Methods: We retrospectively collected the data of 101 end-stage renal disease patients who underwent live or cadaveric kidney transplantation in the Department of Urology at Ankara City Hospital. The demographic data of the recipient and donor, postoperative complications, patient survival and graft functions were recorded.

Results: Patient and graft survival rates of the recipients were 96% and 98% at 36 months follow-up, respectively. The median serum creatinine level at post-op first day, 1 months, 6 months, 12 months, 18 months, 24 months and 36 months posttransplantion was 1,3 (range, 0,7-5,7) mg/dl, 1,3 (range, 0,8-1,7) mg/dl, 1,3 (range, 0,8-2,5) mg/dl, 1,3 (range, 0,7-2) mg/dl, 1,2 (range, 0,8-1,9) mg/dl, 1,4 (range, 0,8-2,4) mg/dl and 1,4 (range, 1-2,4) mg/dl, respectively. 6 (5,9%) patients with urinoma were treated conservatively with urinary catheterization and percutaneous drainage. Renal artery stenosis was observed in 2 (2%) patients.

Conclusion: Kidney transplantation is still the most important treatment option for ESRD patients in Turkey as in the world. In our center, we observed that graft function results were acceptably good at 36 months follow-up.

Keywords: city hospital, graft function, kidney transplantation

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Öz

Amaç: Şehir hastaneleri, yeni bir model hastane olarak Türkiye'de yaklaşık 20 farklı ilde hizmet vermeye başlamıştır. Bu çalışmada, Ankara Şehir Hastanesi böbrek nakli ünitesinin 100 vakayı aşan 3 yıllık deneyimini sunmayı amaçladık.

Gereç ve Yöntemler: Ankara Şehir Hastanesi Üroloji Kliniğinde canlı veya kadavradan böbrek nakli yapılan 101 son dönem böbrek (SDBH) hastasının verileri retrospektif olarak toplandı. Alıcı ve vericinin demografik verileri ameliyat sonrası komplikasyonlar, hasta sağkalımı ve greft fonksiyonları kaydedildi.

Bulgular: Hasta ve greft sağkalım oranları sırasıyla %96 ve %98 idi. Post-op ilk gün, 1 ay, 6 ay, 12 ay, 18 ay, 24 ay ve 36 ay sonraki ortanca serum kreatinin düzeyi 1,3 (aralık, 0,7-5,7) mg/dl, 1,3 (aralık, Sırasıyla 0,8-1,7) mg/dl, 1,3 (aralık, 0,8-2,5) mg/dl, 1,3 (aralık, 0,7-2) mg/dl, 1,2 (aralık, 0,8-1,9) mg/dl, 1,4 (aralık, 0,8-2,4) mg/dl ve 1,4 (aralık, 1-2,4) mg/dl olarak bulundu. Ürinomu olan 6 (%5,9) hastalar üriner kateterizasyon ve perkütan drenaj ile konservatif olarak tedavi edildi. Renal arter stenozu 2 (%2) hastada gözlendi.

Sonuçlar: Böbrek nakli, dünyada olduğu gibi Türkiye'de de SDBH hastaları için halen en önemli tedavi seçeneğidir. Merkezimizde 36 aylık takipte greft fonksiyon sonuçlarının kabul edilebilir derecede iyi olduğunu gözlemledik.

Anahtar Kelimeler: böbrek nakli, greft fonksiyonu, şehir hastanesi

Introductıon

Kidney transplantation is the most effective and successful treatment method for end-stage renal disease (ESRD) [1]. Kidney transplantation not only improves the quality of life of patients, but also significantly reduces the loss of workforce compared to hemodialysis [2, 3]. The successful outcomes in kidney transplantation are rising day by day with the increase in knowledge organs and tissues, developments in surgical technique, and new and effective immunosuppressive drugs [4]. An accumulated clinical experience and harmonious teamwork including experienced surgeon, nephrologist and nursing care are important for obtaining of successful outcomes after kidney transplantation.

In 2017, city hospitals, as a new model that firstly executed in Mersin, Yozgat and Isparta, started to serve in approximately 20 different cities. In the city hospital model, many hospitals in that city were brought together under a single roof and a larger and more complex system was established. Ankara City Hospital (ACH) has emerged as a large complex hospital which structure formed by the combination of the Turkey Yüksek İhtisas Training and Research Hospital, Ankara Numune Training and Research Hospital, Ankara Atatürk Training and Research Hospital, Zekai Tahir Burak Women's Health Education and Research Hospital, Physical Therapy and Rehabilitation Hospital, Diskapi Child Health and Hematology Hospital. In addition to the disadvantages of such a structure, which has a bed capacity of approximately 4000 and consists of multiple sub-units, such as difficulty in coordinating, difficulties in working with different echools; it has advantages such as creating synergy arising from the coexistence of differences. In this study, we aimed to present the 3 years experience of xxxx Hospital kidney transplant unit, which has exceeded 100 cases, as a new hospital model.

Material and Methods

This study was conducted in accordance with the Declaration of Helsinki and all patients have given written informed consent. After obtaining approval from the institutional review board (IRB number: E2-22-2076 Date: 06/07/2022), we retrospectively collected the data of 101 ESRD patients who underwent live or cadaveric kidney transplantation in the Department of Urology at xxxxx Hospital. The demographic data of the recipient and donor (age, gender and body mass index-BMI) postoperative complications, patient survival and graft functions were recorded. Recipient serum creatinine levels were recorded at intervals up to 3 years after transplantation. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation [5]. Immunological suitability assessment of all patients was performed. Contrast-enhanced computer tomography was performed for kidney anatomy of living donors. In addition, 24-hour urine creatinine clearance (≥80 ml/min) and proteinuria (≤150 mg/day) were measured.

All living donors underwent laparoscopic transperitoneal donor nephrectomy. The left kidney was the first choice. The donated kidney was placed in the right iliac fossa of the recipient. Vascular anastomosis was performed to the external iliac artery and vein. Ureteroneocystostomy was performed with a double-J ureteral catheter using the antireflux Lich-Gregoir technique. The mean time for ureteral double-j stent removal was 3 weeks.

For the induction treatment, methylprednisolone and basiliximab/anti-thymocyte globulin-ATG were used as immunosuppression in the recipients. Patients who developed

acute cellular and vascular rejection were treated with pulse methylprednisolone (500 mg × 3/day). Plasmapheresis and IVIG (Intravenous Immunoglobulin) were applied in cases with acute humoral rejection.

Statistical analysis

Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc. Chicago, USA) computer package program was used for statistical analysis of the research data. In the descriptive statistics section, categorical variables are presented as numbers, percentages, and continuous variables are presented with median (smallest-largest value).

Results

Between March 2019 and June 2022, 101 patients with ESRD underwent renal transplantation in xxxxx Hospital. Table 1 shows the demographic and clinics characteristics of the study population. Of the donor kidneys, 76 (75.2%) kidneys were obtained from living donors and 25 (24.8%) kidneys obtained from cadaveric donors. Of 101 donors, 76 had single artery, 18 had 2, and 1 had 3 renal arteries. The median recipient age was 35 years (median, 15 –67 years) and male-to-female ratio of recipients was 68/33. The median donor age 43 was years (range, 19-68 years) and male-to-female of donors ratio was 56/45. The etiology of ESRD consisted of 49 (48.5) systemic disease (hypertension, diabetes mellitus), 12 (11.9%) glomerular disease, and 5 (5%) autosomal dominant polycystic kidney disease, 5 (5%) miscellaneous, 16 (15.8%) other diseases and 14 (13%) patient with unknown etiology.

Table 2 shows the post-operative complications of renal transplant recipients. No surgical complications were observed in the donors. Rejection developed in 12 patients with humoral rejection in 6 (5,9%), cellular in 3 (3%) and acute vascular in 3 (3%) patients. 2 of patients who developed rejection underwent graft nephrectomy. 6 (5,9%) patients with urinoma were treated conservatively with urinary catheterization and percutaneous drainage. Perirenal hematoma occured in 5 (5%) patients, but no surgical intervention was required. Perirenal hematomas resolved spontaneously with conservative follow-up. Seven cases (%6.9) that developed lymphocele were managed with percutaneous drainage. 20 (19,8%) patients who had infections for various reasons (urinary tract infections, wound infections, fever of unknown origin, upper respiratory tract infection and bacteremia) were treated with medical treatment; however, 2 needed peri-renal abscess drainage. Renal artery stenosis was observed in 2 (2%) patients who were conservatively followed. Deep vein thrombosis (DVT) occurred in one patient (1%) which was managed with anticoagulation. In one (1%) patient, ureteroneocystostomy (UNC) stenosis occured 3 months after the transplantation. 4 (4%) recipient deaths occurred after transplantation. 2 of the deaths occurred during the first and fourth month after transplantation due to severe sepsis. 1 patient died in the first week due to bleeding. The last patient died due to myocardial infarction (MI) in the 3rd month of follow-up.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variables	N=101
Recipient	
Sex	
Male/Female	68/33
Age, yr	35 (15-67)
BMI, kg/m2	23,7 (16,3-42)
Smoking, n(%)	15 (14,9)
ABO, n(%)	
A	35 (34,7)
B	19 (18,8)
O	42 (41,6)
AB	5 (5)
Dialysis time, m	12 (0- 156)
Hospital stay, day	21 (8- 55)
Etiology of ESRD, n (%)	
Systemic disease (diabetes mellitus or arterial hypertension)	49 (48,5)
Autosomal dominant polycystic kidney disease	5 (5)
Glomerular disease	12 (11,9)
Miscellaneous	5 (5)
Other	16 (15,8)
Unknown	14 (13,9)
Donor	
Sex	
Male/Female	56/45
Age, yr	43 (19- 68)
ABO, n(%)	
A	31 (30,7)
B	17 (16,8)
O	51 (50,5)
AB	2 (2)
Number of graft arteries, n (%)	
1	76 (75,2)
2	18 (17,8)
3	1 (1)
Nephrectomy side, n (%)	
Left	74 (73,3)
Right	27 (26,7)
Cadaveric donor, n (%)	25 (24,8)
Warm ischemia time, min	2 (1,5- 5)
HLA mismatch	4 (0-6)

BMI;body mass index, ESRD; end-stage renal disease , HLA; human leukocyte antigen

Table 2: Postoperative Complications	
Complications	n (%)
Humoral rejection	6 (5,9)
Cellular rejection	3 (3)
Acute vascular rejection	3 (3)
Acute tubular necrosis (ATN)	2 (2)
Urinoma	6 (5,9)
Hematoma	5 (5)
Lymphocele	7 (6,9)
Infection	20 (19,8)
UTI	6 (30)
Surgical wound infection	3 (15)
Fever of unknown origin	7 (35)
Upper respiratory tract infection	1 (5)
Bacteremia	1 (5)
Peri-renal abscess	2 (10)
BK virus nephropathy	1 (1)
Arterial stenosis	2 (2)
UNC stenosis	1 (1)
Cardiovascular (ACS and DVT)	2 (2)
Delayed graft function	1 (1)
Graft nephrectomy	2 (2)
Death	4 (4)
UTI; urinary tract infection, UNC; ureteroneocystostomy, ACS; Acute Coronary Syndrome, DVT; Deep Vein Thrombosis	

Table 3 shows the graft functions of the recipients at 36-month follow-up. Patient and graft survival rates of the recipients were 96% and 98%, respectively. The median serum creatinine level at post-op first day, 1 months, 6 months, 12 months, 18 months, 24 months and 36 months posttransplantion was 1,3 (range, 0,7 - 5,7) mg/dl, 1,3 (range, 0,8 - 1,7) mg/dl, 1,3 (range, 0,8 - 2,5) mg/dl, 1,3 (range, 0,7 - 2) mg/dl, 1,2 (range, 0,8 - 1,9) mg/dl, 1,4 (range, 0,8 - 2,4) mg/dl and 1,4 (range, 1 - 2,4) mg/dl, respectively.

Discussion

According to the United States Renal Data System Annual Data Report 2021, Turkey ranked 10th among countries with >50% residual incidence of renal transplantation between 2009 and 2019 [6]. From a historical perspective, the first living kidney transplant from a mother to her 12-year-old child was performed successfully at Hacettepe University Hospital on November 3, 1975 [7]. As it was not legally possible at that time, kidney transplantation from a cadaver using an organ provided by Eurotransplant was performed for the first time in Turkey in 1978 [7]. In 1979, with the preparation of the legal ground, kidney transplantation from a cadaver was performed for the first time [8]. Since then, kidney transplantations have been performed at an increasing rate in many centers in Turkey. As of

Table 3: Serum Creatinine, Glomerular Filtration Rate and Hemoglobin Values During the Follow-Up								
	Pre-op	Post-op first day	1th month	6th month	12th month	18th month	24th month	36th month
Hg (g/dl)	10,5 (6,1- 14,6)	9,2 (8,6- 10,2)						
SCr (mg/dL)	7 (2,8- 15,5)	1,3 (0,7- 5,7)	1,3 (0,8- 1,7)	1,3 (0,8- 2,5)	1,3 (0,7- 2)	1,2 (0,8- 1,9)	1,4 (0,8- 2,4)	1,4 (1- 2,4)
GFR (mL/ min/1.73 m2)	8 (3- 23)	71,5 (9- 104)	60 (47- 91)	58 (33- 101)	59,5 (44- 95)	63 (45- 83)	54,5 (34- 83)	60,5 (33- 67)
SCr; serum creatinine, GFR; glomerular filtration rate, Hg;hemoglobin								

2022, there are 78 kidney transplant centers in Turkey [9].

In 20% of transplantation centers in Turkey, kidney transplantation is performed by urologists [10]. Renal transplantation in Ankara City Hospital is primarily performed by urologists. The first patient with end-stage renal disease admitted to ACH on 07.02.2019 and the first kidney transplant was performed on 04.03.2019 as a living kidney transplant. Since 2019, kidney transplantation at ACH has exceeded 100 cases and is being successfully implemented. As one of the 78 kidney transplant centers in Turkey, in our center, GFR and serum creatinine values of renal transplanted patients at 36 months indicate that graft function is acceptably good in the mid-long term.

Complications after kidney transplantation are still important issues. Especially urologic and vascular complications are the most prominent problems. In studies conducted in the last 30 years, the incidence of urologic complications after renal transplantation ranged between 3.7%-6.0% [11]. The most important urologic complication is urinoma after urinary leakage. Urinary leakage has been reported up to 6% in the literature [11, 12]. Urinoma may compress the graft vascular structures and cause graft dysfunction [11]. In addition, urinoma can become infected and lead to perinephritic abscesses in the kidney recipient, which can endanger the patient's life [13]. In our study, urinoma was detected at a rate of 5.9%, which is consistent with the literature. Infected urinoma was not seen in any patient. Similarly, postoperative lymphocele formation is one of the most common postoperative complications in kidney recipients, with a rate of 12-40% [14]. The management of lymphocele includes the use of sclerotic agents or routine drainage [15]. In the present study, lymphocele occured in 7 (6.9%) patients in accordance with the literature. We preferred

to manage the lymphocele with percutaneous drainage.

Vascular complications are seen in 3-15% of kidney recipients [16]. The most common vascular complications are renal artery stenosis and vein thrombosis in kidney recipients [17]. The incidence of renal artery stenosis in kidney recipients has been reported to vary between 1-23% [18]. In the present study, renal artery stenosis in kidney recipients occured in the rate of 2% at acceptable rates compared to those reported in the literature. Furthermore, we did not observe renal vein thrombosis in any recipient patient. However, DVT occurred in one patient (1%). DVT was managed with anticoagulant therapy.

UNC stenosis can be seen in 2-10% of the patients within 3 months after kidney transplantation [19]. One patient (1%) in the present study who suffered from UNC stenosis managed with long-term double J stent application 3 months after kidney transplantation. UNC stenosis rate in the present study is also acceptable according to literature.

Study limitations

The present study has some limitations to be acknowledged. Our study was designed retrospectively. Furthormore, the study has different donor charachteristics and follow-up was not long-term. It should be noted that living donor kidney transplantation is more common in our center (75%), which leads to better graft outcomes.

Conclusion

Kidney transplantation is still the most important treatment option for ESRD patients in Turkey as in the world. In our center, we observed that graft function results were acceptably good at 36 months follow-up. We believe that the number of patients waiting on the kidney transplant list will decrease with the increase in medical centers that perform kidney transplantation like our center and with experienced transplant surgeons in these centers.

Ethics Committee Approval

Ankara City Hospital Institutional Review Board approved this study (IRB number: E2-22-2076 Date: 06/07/2022).

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Authorship Contributions

Concept – MY, MEP, EÖ; Design – MY, MK, MEŞ, EsÖ; Supervision – EÖ, MEŞ; Data collection and/or processing – MEP, MK, EsÖ; Analysis and/or interpretation – MY, MEP, MK; Literature review – MY, MK, MEŞ; Writing – MY, MEP, MK, MEŞ, EsÖ; Critical review – EsÖ, EÖ.

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Research Article

Diagnostic Accuracy and Safety Of Ultrasound Guided Omental Biopsy: Single Center Experience

Ultrason Kılavuzluğunda Omental Biyopsinin Diagnostik Doğruluğu ve Güvenliği: Tek Merkez Sonuçları

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Abstract

Aim: Omental biopsy has conventionally been performed using a surgical approach. The thickened omentum can serve as a useful target for ultrasonography guided percutaneous biopsy, in clinical practice. The objective of our study was to determine the diagnostic value and safety of ultrasound guided percutaneous biopsy of omental thickening. Additionally, we aim to investigate the correlation of biopsy results with the paracentesis fluid cytology.

Material and Methods: This retrospective study included 49 patients (33 women and 16 men; mean age, 64 ± 13.9 [SD] years) who underwent ultrasound guided omental biopsy between 2014 and 2022 at a single institution at which US served as the first-line modality for omental biopsy guidance. Post-biopsy clinical follow-up were reviewed for each patient. We compare the outcomes of biopsy and paracentesis fluid cytology results.

Results: Total 49 patients were included in our study. US-guided biopsy was diagnostic in 46/49 (93.8%) of patients. There were total 36 (73.4%) malignant cases, 5 (10.2%) chronic inflammation suggestive of tuberculosis, while 2 (4.1%) were chronic peritoneal infection. In 3 patients, the result of core biopsy was benign and reported as Ig4-related inflammatory pseudotumor, desmoid fibromatosis and fat necrosis-foreign body reaction. Out of 36 malignant cases, majority 17 (47.2%) had ovarian cancer. There were no major complications. In 21 of 25 patients (%84) who underwent paracentesis fluid sampling, cytology results (malign or bening cytology) were found to be consistent with omental biopsy results. The ascitic cytological evaluation was favourable for malignancy in 16/25 (64%) patients.

Conclusions: Ultrasound-guided percutaneous biopsy of omentum is less expensive, safe and effective method with a high diagnostic accuracy. Paracentesis fluid cytology results are highly sensitive in patients with omental thickening.

Keywords: Biopsy, Ultrasonography, Omental thickening

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Öz

Amaç: Omental biyopsi geleneksel olarak cerrahi bir yaklaşım kullanılarak yapılmaktadır. Kalınlaşmış omentum, klinik pratikte tanı koyulabilmesi için ultrasonografi eşliğinde perkütan biyopsi yapılabilir bir hedeftir. Çalışmamızın amacı, omental kalınlaşmanın ultrason eşliğinde perkütan biyopsisinin tanısal doğruluğunu ve güvenliğini incelemektir. Ek olarak, biyopsi sonuçlarının parasentez sıvısı sitolojisi ile ilişkisini araştırmayı amaçlıyoruz.

Gereç ve Yöntemler: Bu retrospektif çalışma, 2014-2022 yılları arasında ultrasonun kılavuz olarak kullanıldığı omental biyopsi yapılan 49 hastayı (33 kadın ve 16 erkek; ortalama yaş, 64 ± 13.9 [SD] yıl) içermektedir. Hastaların biyopsi sonrası klinik takip ve patoloji sonuçları değerlendirilmiştir. Ayrıca kor biyopsi ve parasentez sıvı sitolojisi sonuçları karşılaştırılmıştır.

Bulgular: Çalışmamıza toplam 49 hasta dahil edildi. Ultrason kılavuzluğunda biyopsi 49 hastanın 46'sında (%93,8) tanı koydurucuydu. Toplam 36 (%73,4) malign olgu, 5 (%10,2) tüberkülozu düşündüren kronik inflamasyon, 2 (%4,1) kronik periton enfeksiyonu vardı. 3 hastada kor biyopsi sonucu benign idi ve bunlar; Ig4 ilişkili inflamatuar psödotümör, desmoid fibromatoz ve yağ nekrozu-yabancı cisim reaksiyonu olarak rapor edildi. 36 malign vakanın 17'si (%47,2) ovaryen kanser olarak raporlandı. İşlemlerin hiçbirinde yakın dönem majör komplikasyon görülmedi. Parasentez sıvı örneklemesi yapılan 25 hastanın 21'inde (%84) sitoloji sonuçları (malign veya benign sitoloji) omental biyopsi sonuçları ile uyumlu bulundu. Sitolojik değerlendirmede 25 hastanın 16'sı (%64) malign sitoloji olarak raporlandı.

Sonuç: Ultrason eşliğinde perkütan omentum biyopsisi ucuz, güvenli ve etkili, tanısal doğruluğu yüksek bir yöntemdir. Omentum kalınlaşması olan hastalarda parasentez sıvısı sitolojisi sonuçları oldukça duyarlıdır.

Anahtar Kelimeler: Biyopsi, Ultrasonografi, Omental kalınlaşma

Introduction

The omentum is a multi-layered fold of the peritoneum. Because the peritoneal cavity contains a small amount of fluid, infections and cancer spread easily to the omentum.Numerous primary and metastatic neoplastic diseases frequently manifest in the peritoneum and omentum. Gastrointestinal and ovarian malignancies are the most common sources of metastasis to omentum[1]. Involvement of the omentum and peritoneum by non-neoplastic conditions, such as granulomatous diseases, hematomas, infections, or inflammatory disorders, occurs less frequently.

Conventional imaging techniques, such as ultrasound and CT scans, have low specificity and sensitivity for determining the etiology. As a result, a biopsy is frequently needed to confirm the diagnosis. The greater omentum is a frequently affected site for malignant peritoneal metastasis and can be a target for percutaneous biopsy [2].

Radiologists commonly conduct image-guided biopsies, which play a crucial role in clinical decision-making. These biopsies offer a high level of diagnostic accuracy, reliability, and are generally well-tolerated. Image-guided percutaneous biopsies have largely replaced excisional biopsy and surgery as primary diagnostic methods. In the context omental diseases, image-guided biopsies have also supplanted exploratory laparoscopy and laparotomy.

Among various guidance tools such as US, computed tomography (CT), and magnetic resonance (MR) imaging, US has a number of advantages for guiding percutaneous biopsy for intraabdominal lesions. These advantages include accessibility, portability, absence of ionizing radiation, shorter procedure duration, real-time visualization of the biopsy needle and target lesion during the entire procedure, capability to guide the procedure in nearly any anatomical plane, reduced occurrence of false-negative biopsies, and lower cost [3,4].

Traditionally, ultrasound (US) has been utilized for percutaneous biopsy guidance of solid abdominal organs, including the kidney, liver, and spleen [5–7]. While US remains a common method for guiding paracentesis to drain peritoneal fluid, CT is more frequently employed for guiding biopsies of peritoneal soft-tissue infiltrations and masses in clinical practice [2]. A correct diagnosis directs patient care and provides information on the prognosis. US-guided Core Biopsy can quickly and safely deliver the diagnosis.

The purpose of this study is to evaluate diagnostic accuracy and safety of ultrasound-guided percutaneous biopsy of omental thickening and to determine its underlying etiology. Furthermore, we aim to investigate the correlation between biopsy results and cytological analysis of paracentesis fluid.

Material and Methods

The institutional ethics review board approved this study and patient informed consent was waived for this retrospective study. The hospital database was used to analyze patients who underwent US-guided percutaneous biopsy for omental thickening over an eight-year period, from 2014 to 2022. We reviewed radiology database and medical records for pathology and cytology results. Patients with uncorrectable bleeding parameters and patients with missing pathology results were excluded from the study. The final study population included 49 participants (33 women and 16 men; a mean age of 64 years; an age range of 15–85 years).

Prior to the biopsy, all patients had a US examination to determine the omental thickness and feasibility of the biopsy. If the omentum was thicker than 10 mm, it was considered thickened. All patients' bleeding parameters, including prothrombin time (PT) and platelet count, were recorded. A platelet count of more than $50x10^9$/L was considered adequate for carrying out the procedure. For patients on oral anticoagulants, any PT value with an international normalized ratio (INR) less than 1.5 was considered acceptable and consistent with existing literature [8].

The procedure was carried out in supine position. Appropriate ultrasound probe depending on the lesions depth and patient habitus is used to identify the area of maximum thickness, determine the amount of ascites, and evaluate adjacent bowel loops. Color Doppler imaging was also used to assess vascularity in the omental lesions and nearby large vessels. We routinely tap before a biopsy if there is a large amount of ascites present.

Procedure site in the skin and the surrounding area was scrubbed with povidone iodine solution before administering 10 ml of local anesthetic (2% prilocaine hydrochloride) subcutaneously through the abdominal wall with a 22-gauge needle. A small incision was made in the skin (2–3 mm wide), and a biopsy needle was inserted directly into the deep layer of the abdominal wall. The biopsy was performed using semi-automatic biopsy guns and 18-gauge biopsy needles (TSK Laboratory, Japan) under real-time USG guidance using a free hand technique. The needle was advanced into the thickened omentum using real-time US guidance. As the needle tip reached the omentum under ultrasound guidance, two to four cores of tissue were routinely taken from each patient. The biopsy specimen was retained in formalin and sent for histopathological examination. Patients were observed for possible complications 4-6 hours following the procedure.

We compared the outcomes of US-Guided Core Biopsy to the results of primary malignancy, omental pathology following surgical excision, and preoperative paracentesis fluid analysis. Complications were categorized based on the guidelines provided by the Society of Interventional Radiology (SIR) for needle biopsy [9]. Technical success was determined by the successful collection of core specimens.

Results

In this study we included 49 patients who had undergone omental biopsy. An adequate sample was obtained in 100% of the cases. Positive histopathological results were obtained in 46 (93.8%) patients. In the other 3 patients, the biopsy result were reported as adipose tissue. Malignant involvement in the omentum was detected in 2 of these 3 patients as a result of surgery (excisional biopsy proven ovarian carcinoma involvement, gastric mucinous adenocarcinoma involvement). In the other 1 patient, no malignancy was detected in the follow-up.

There were 36 (73.4%) malignant cases, 5 (10.2%) cases of chronic inflammation suggestive of tuberculosis, and 2 (4.1%) cases of chronic peritoneal infection. In 3 patients, the result of core biopsy was benign and reported as Ig4-related inflammatory pseudotumor, desmoid fibromatosis and fat necrosis-foreign body reaction. Out of 36 malignant cases, 17 had ovarian 4 had uterine-cervical cancer, 4 had primary peritoneal carcinoma, 5 had gastrointestinal system cancer, 3 had breast and 2 had lung cancer. In 1 patient, the biopsy result was reported as hepatocellular carcinoma metastasis. There were no procedural complications reported.

Postoperative excisional biopsy results for 16 patients were obtained. Out of 16 cases, 7 (43.7%) had ovarian cancer, and 2 (12.5%) had chronic inflammation. Preoperative omental biopsy results were consistent with postoperative excisional biopsy results in 13 out of the 16 patients who had surgery. In 2 patients, no viable tumor cells were found in the excisional biopsy due to the regression of omental soft tissues secondary to treatment. In one patient, the excisional biopsy revealed adenocarcinoma, whereas the preoperative omental biopsy result indicated fibroadipose tissue without evidence of malignancy.

Paracentesis fluid samples were taken simultaneously with omental biopsies from 25 patients. The cytological evaluation was favorable for malignancy in 16 (64%) patients. When paracentesis fluids and omental biopsy results were compared, omental biopsy was positive for malignant cells in 15 of 16 patients. The omentum biopsy result was in favor of malignancy in 3 of the patients who have no malignant atypical cells in the paracentesis fluid.

Discussion

There is still limited literature available on the use of US guidance for omental biopsy [2,10–12]. Govindarajan et al. in their series of 173 patients, obtained diagnostic biopsy results in 140 (81%) patients [11]. In their study, Perez et al. reported that US-guided biopsy was diagnostic in 95% of their patients' group[2]. This study presents our institutional experience of utilizing US as the first-line method for guiding omental biopsy. The US-guided biopsy provided a diagnosis in 46 (93.8%) out of 49 patients, with no observed complications. These results demonstrate the safety and effectiveness of using ultrasound guidance for omental biopsy to obtain adequate tissue samples for diagnosis.

Omental thickening is a warning sign for abdominal pathologies such as malignancy and chronic inflammation. After tumor cells are seeded in the omentum, they spread intraperitoneally via the peritoneal reflection and ligaments, as well as hematogenously. The greater omentum, being a superficial and easily accessible intraabdominal structure, is well-suited for image-guided biopsy when it is affected by pathological processes resulting in infiltration and enlargement. Nevertheless, performing ultrasound-guided biopsy of the omentum typically necessitates a comprehensive understanding of its anatomy and the ability to correlate earlier CT findings, as certain details may be less distinct on ultrasound imaging. [2]. These factors, coupled with institutional preferences, may partially explain why the omentum is not a common target for biopsy and why CT guidance continues to be the preferred approach for omental biopsy in many medical practices [13–15]. However, with a thorough understanding of the sonographic appearance of abnormal omentum and the sampling technique is established, US-guided biopsy offers several advantages. It enables rapid real-time core tissue biopsy without the requirement of an introducer needle, with minimal needle traverse times lasting only a few seconds. Additionally, US provides the benefit of real-time compression during biopsy, which can help reduce the mobility and distance of the omental target and allow for the displacement of vulnerable structures such as the bowel [16].

The effectiveness of US guidance for omental biopsies appears to have been underreported thus far. This study emphasizes the value and usefulness of US guidance in performing omental biopsies. Based on our findings, we suggest that US should be considered as the primary choice for guiding omental biopsies in the majority of cases.

Although surgical biopsy is the gold standard in the diagnosis of omental thickening, US-guided core biopsies are becoming increasingly common because they can be performed quicker and are less expensive. Anterior peritoneal location and easy visibility make percutaneous ultrasound-guided omental biopsy feasible. It can be performed as a day-care procedure under local anesthesia without significant complications. These advantages make US-guided biopsy a preferable option compared to the conventional laparoscopic or laparotomy route [15].

In addition, it has advantages such as being able to see the omental thickening throughout the procedure in US-guided biopsies and not being exposed to radiation, although similar results are obtained in CT-guided biopsies. During these procedures, multiple CT scans are typically conducted to aid in procedure planning, instrument placement, and intra- and postprocedural assessments. Because of the longer scan times and increased number of scans performed, CT-guided interventional procedures often have a higher radiation dosage than conventional diagnostic scans [17,18].

Core biopsy is of greater diagnostic value than ascitic cytology, which has a reported sensitivity of 60% [19]. In this study, the ascitic cytological evaluation of patient with omental thickening was favourable for malignancy in 16/25 (64%) patients. Salman et al. reported the malignancy rate as 56% in a series of 100 patients with omental thickening as well as ascites [20]. In our study, we compared US-guided omental biopsies with paracentesis fluid samples in addition to surgical excision material. In 21 of 25 patients (%84) who underwent paracentesis fluid sampling, cytology results (malign or benign cytology) were found to be consistent with omental biopsy results. Although 3 of remaining 4 patients were defined as benign with cytological analysis, core biopsy results were malignant. Despite the presence of malignant atypical cells in the last patient, the omental biopsy result was reported as chronic inflammation. In woman we found 50% (n = 5) of all the positive cytology results were ovarian in origin. Other studies vary in this percentage from 7%–85% [21–24].

Conclusion

US-guided core biopsy is feasible, safe, and quicker method for the diagnosis of omental thickening. Paracentesis fluid cytology results are highly sensitive in patients with omental thickening.

Conflict of interest

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Araştırma Makalesi

Gelecek salgınlara ders olması gereken Covıd-19 deneyimi: bir üniversite hastanesinde görevli sağlık çalışanlarının enfekte olma kaygısı üzerine nitel bir çalışma

The Covid-19 experience as a learning opportunity for future outbreaks: a qualitative study on infection anxiety of health workers at a university hospital

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Öz

Amaç: Bu çalışmanın amacı COVID-19 pandemisinin erken dönemlerinde görev yapan sağlık çalışanlarının enfekte olma riskine ilişkin kaygısını incelenmektir.

Gereç ve Yöntemler: Bu nitel araştırmada durum çalışması deseni kullanılmış olup, görüşmeler 01 Haziran- 31 Temmuz 2020 tarihleri arasında bir üniversite hastanesinde pandemi polikliniği, servisi ve yoğun bakım ünitelerinde çalışan 32 sağlık çalışan ile gerçekleştirilmiştir. Katılımcılara görüşmenin sonunda COVID-19 bulaşması konusunda kaygı düzeyini değerlendirmek amacıyla Vizüal Analog Skala 10 ve depresyon, anksiyete, stres düzeyini ölçmek için Depresyon, Anksiyete, Stres Ölçeği-21 eş zamanlı uygulanmıştır. Elde edilen görüşmeler NVivo11 programına aktarılarak içerik analizi yapılmıştır.

Bulgular: Sağlık çalışanlarının enfekte olma kaygısını açıklayan dört tema (Kaygı Deneyimleri, Kaygı Nedenleri, Başa Çıkma Yolları ve Kaygının Etkileri), on üç ana kategori, sekiz alt kategori ve yüz otuz sekiz kod belirlenmiştir. Sağlık çalışanlarının kaygı deneyimlerinin enfekte olma ve enfekte etme riski, mesleki zorluklar, koruyucu donanım eksikliği, aileden ayrılık, temizlik ve hijyen gibi faktörlerden etkilendiği anlaşılmıştır. Kaygı nedenlerinin salgınla ilişkili, kişisel nedenler ve çalışma koşulları olduğu belirlenmiştir. Sağlık çalışanlarının kaygı ile başa çıkmak için çeşitli yöntemler kullandıkları belirlenmiştir. Sağlık çalışanları kaygının sağlık hizmetlerine, iş verimine ve psikolojilerine etkisinin olduğunu ifade etmişlerdir. Ayrıca çoğu sağlık çalışanının, kaygı ile ilgili duygularının olumsuz yönde etkilendiği ve somatik belirtilerinin ortaya çıktığı bulunmuştur.

Sonuç: Sağlık çalışanları COVID-19 salgınında hem enfeksiyon bulaşma ve hem de bulaştırma kaygısı ve buna bağlı stres yaşadıkları belirlenmiştir. Salgınlarda görev alacak sağlık personeli için tüm fiziksel, sosyal ve ruhsal tüm koruyucu önlemler alınmalıdır.

Anahtar Kelimeler: COVID-19 salgını, Sağlık Çalışanı, Bulaşma, Kaygı, Nitel araştırma, Durum çalışması

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Abstract

Aim: The aim of this study is to examine the anxiety of being infected by healthcare workers during the early stages of the COVID-19 outbreak.

Material and Methods: In this qualitative research, interviews were conducted with 32 healthcare workers who worked in a university hospital's in the pandemic departments between June 1st and July 31st, 2020. The Visual Analog Scale-10 (VAS-10) and the Depression, Anxiety, Stress Scale-21 (DASS-21) were administered simultaneously to measure anxiety about COVID-19 transmission. The interviews were transferred to the NVivo11 program and content analysis was made.

Results: Four themes (Anxiety Experiences, Causes of Anxiety, Coping Strategies, and Effects of Anxiety), thirteen main categories, eight subcategories, and one hundred and thirty-eight codes were determined to explain the anxiety of healthcare workers about being infected. It has been understood that healthcare workers' anxiety experiences were influenced by factors such as the risk of transmission, occupational challenges, lack of protective equipment, separation from family, cleanliness, and hygiene. The causes of anxiety were determined to be related to the outbreak, personal reasons, and working conditions. They expressed that anxiety impacted healthcare services, job performance, and psychological well-being. Furthermore, it was found that healthcare workers' emotions were negatively affected, and somatic symptoms appeared.

Conclusion: Healthcare workers experienced anxiety regarding both contracting and transmitting the infection during the initial phases of the COVID-19 pandemic, resulting in associated stress. It is crucial to implement comprehensive physical, social, and psychological protective measures for healthcare personnel involved in future outbreaks.

Keywords: COVID-19 outbreak, Healthcare workers, Transmission, Anxiety, Qualitative research, Case study design

Giriş

Aralık 2019'da Çin Wuhan'da başlayan sürecin sonunda, 2019-nCoV kaynaklı pandemi (COVID-19), 200'den fazla ülkeye yayılmış, etkisi iki yıldan uzun sürmüş ciddi bir halk sağlığı krizidir [1]. COVID-19 pandemisi 700 milyon insanı etkilerken, 6,5 milyondan fazla kişi hayatını kaybetmiştir [2,3]. Hastalık damlacık yoluyla bulaşmaktadır ve enfekte damlacıklar yüzeylerde birikebilir ve buralara temas ile enfeksiyon bulaşabilir [4]. Hastalık hafif durumlardan, akut solunum sıkıntısı sendromuna, çoklu organ yetmezliğine ve ölüme sebep olabilmektedir.

Hiç şüphesiz ki pandemi, dünya genelinde birçok sağlık çalışanının hayatını riske atarak mücadele ettiği ciddi bir sürece neden oldu. Onlar, en öndeki savaşçılar olarak, enfeksiyon riskinin en yüksek olduğu ortamlarda çalışmak zorunda kaldılar. Dönem dönem, salgının yayılma hızı ve yoğunluğu nedeniyle birçok ülkede sağlık sistemleri çoğu zaman kapasitelerinin ötesinde zorlandı. Bu nedenle, sağlık çalışanları uzun süreli çalışma saatleri, fiziksel ve psikolojik stres, personel eksiklikleri ve kişisel koruyucu ekipmanlarda yaşanan sıkıntılar, yorgunluk ve aşırı iş yükü gibi zorluklarla karşı karşıya kaldılar. COVID-19 birçok sağlık çalışanında ciddi stres, anksiyete ve tükenmişlik belirtilerine yol açtı ve bu psikolojik etkileri, bir dizi çalışmada dikkat çekici bir şekilde belgelendi [5-6]. Lai ve ark. yaptıkları çalışmada sağlık çalışanlarının önemli oranda psikolojik yük yaşadığını ve bu durumun özellikle doğrudan COVID-19 hastaları ile çalışan sağlık çalışanlarında daha belirgin olduğunu buldu [5].

COVID-19 sağlık çalışanları için aynı zamanda mesleki hastalığı riski de oluşturmaktadır. Her ne kadar ciddi korunma önlemleri alınsa da hastane içi yüksek bulaş nedeniyle birçok enfekte olan ve hayatını kaybeden sağlık çalışanı olmuştur [7,8]. COVID-19 pandemisi gibi büyük bir salgında çalışan sağlık personellerinin toplumdaki diğer bireylerden daha fazla enfekte olma kaygısı yaşadığı da ortadadır. COVID-19 salgının anlaşılmaya çalışıldığı erken dönemlerinde görev yapan sağlık personelinin enfekte olma kaygı düzeyini ve hizmet sunmaya yönelik kaygı durumunu belirlemek amacıyla bu nitel çalışma planlanmıştır. Bu nitel çalışmada farklı görev ve sorumlulukları olan sağlık çalışanlarının yaşadığı kaygı durumunu ve süreçten ne kadar etkilendiğini değerlendirmek ana amacımızdır. Özellikle bu kaygının hizmet sırasındaki davranışları ne derece etkilediğini ya da geliştirdiğini anlamak gelecekte yaşanacak salgınlara karşı mücadelede önemlidir.

Gereç ve Yöntemler

Araştırmanın Tipi, Yeri ve Zamanı

Bu nitel çalışmada 'durum çalışması' deseni kullanılmıştır. Araştırma, 01 Haziran- 31 Temmuz 2020 tarihleri arasında bir tıp fakültesi hastanesi pandemi polikliniği ve servisinde çalışmakta olan sağlık çalışanlarına yapılmıştır.

Araştırmanın Örneklemi

Çalışmamızda amaçlı örnekleme tekniği kullanılmıştır. Nitel araştırmalarda kesin bir örneklem büyüklüğü kuralı yoktur [9,10]. Evreni, tıp fakültesi hastanesinde pandemi polikliniği ve servisinde çalışmakta olan sağlık çalışanları oluşturmaktadır.

Çalışmaya gönüllü olan, en az 6 aydır hizmet veren ve pandemi sürecinde de çalışmaya devam eden, COVID-19 ile hiç enfekte olmamış 32 sağlık çalışanı (12 doktor, 10 hemşire/ebe, 10 diğer yardımcı ya da temizlik personeli) oluşturmuştur. İşitme ve konuşma zorlukları olanlar çalışmaya alınmamıştır.

Araştırmanın Kavramsal Çerçevesi ve Kaygının Boyutları

Görüşme sorularında kaygının kavramsal boyutlarına odaklanılmıştır. Kaygı, tehdit algısıyla ortaya çıkar ve iç sıkıntısı, anksiyete ve bunaltı gibi kavramlarla tanımlanan bir duygudur. Kontrol edilemez bir şekilde hissedilir ve iç ve dış olayları kapsayan olumsuz bir geri bildirim döngüsüdür [11,12]. Kaygı normal bir korunma mekanizmasıdır, ancak yaşam kalitesini düşüren sübjektif bulgulara dayanıyorsa patolojik bir durumdur ve tedavi gerektirir [12,13]. Kaygı, beden-zihin ilişkisini yansıtan fizyolojik bir haldir. Korkutucu durumlardan kaçınma eğilimi, anksiyete bozukluğu riskini artırır [14]. Korku, tehdit oluşturan bir uyarıcıya karşı gerçekleştirilen zihinsel bir değerlendirme sürecini ifade ederken, kaygı ise bu değerlendirmenin sonucunda ortaya çıkan duygusal yanıtı temsil eder [15]. Estes ve Skinner kaygının nedenini ortama verilen koşullanmış tepki olarak görmektedirler [16]. Kaygı, altı temel boyutla karakterize edilebilir [12], (Şekil 1). Algı, biliş, düşünce, duygu, davranış ve bedensel fizyolojik belirtiler. Bu altı boyut, kaygı durumlarının çeşitli yönlerini ifade eder ve bireylerin yaşadığı kaygıyı daha iyi anlamaya yardımcı olur.

Şekil 1. Kaygı kavram haritası

Veri Toplama Araçları

Sosyo-Demografik Özellikler Formu: Katılımcıların yaşı, cinsiyeti, eğitim durumu, mesleği, branşı, çalıştığı birim, meslekte geçirdiği süre, medeni durum, çocuk sayısı ve çocuklarının yaşları hakkında soruları içermektedir.

Yarı Yapılandırılmış Görüşme Formu: Literatür ışığında hazırlanmış 11 adet sorudan oluşan yarı yapılandırılmış görüşme formudur (Tablo 1).

Tablo 1. Yarı Yapılandırılmış Görüşme Soruları
1. COVID-19 salgını sürecinde sağlık personeli olarak çalıştığınız günler neler hissettiğinizi anlatır mısınız?
2. Enfekte olan bir hastaya 1 metreden daha az yaklaşmanız ya da temas etmeniz gerektiğinde kendinizi nasıl hissediyorsunuz? (2a. Fiziksel olarak nasıl hissediyorsunuz, fiziksel olarak bedeninizde ne gibi değişiklikler hissediyorsunuz?)
3. Özellikle çalışmadığınız günlerde hissettiğiniz hastalık bulaşma kaygısı ile ilgili nasıl hissediyorsunuz, hastalık bulaşma kaygısında değişiklik oluyor mu, nedenleri ile anlatır mısınız?
4. Çalışırken yaşamış olduğunuz kaygı düzeyiniz hakkında, sağlık personeli değil de başka bir mesleği yapıyor olsaydınız ne düşünürdünüz?
5. Çalışırken enfekte olursanız iyileşme süreciniz ile ilgili neler düşünüyorsunuz?
6. Çalışırken enfekte olursanız başkalarının size yaklaşımı nasıl olacaktır?
7. İş dışında olduğunuz zamanlarda sağlık çalışanı olduğunuzu bilenlerin size karşı davranışları nasıl, bahseder misiniz?
8. Sağlık personeli olarak çevrenizi enfekte etme ihtimaliniz konusunda ne düşünüyorsunuz?
9. Salgın nedeniyle çalışırken hissettiğiniz enfekte olma kaygısı sizi ve çalışma veriminizi nasıl etkiledi?
10. Çalışırken ya da iş dışında hissettiğiniz kaygı düzeyi ile nasıl baş ediyorsunuz?

Depresyon Anksiyete Stres Ölçeği-21 (DASÖ-21/DASS-21): Ölçek, Lovibond tarafından 42 maddelik uzun formun kısaltılmasıyla oluşturulmuştur [17,18]. Her iki versiyonun da depresyon, anksiyete ve stres seviyelerini ölçme konusunda güvenilir ve geçerli araçlar oldukları kanıtlanmıştır [19,20]. Sarıçam tarafından 2018'de Türkçe geçerliliği ve güvenilirliği test edilen 21 maddeli 4'lü Likert tipi ölçek, depresyon, anksiyete ve stres boyutlarını değerlendirir [21]. Ölçekteki her cevap, 'hiç uygulanmaz' anlamına gelen 0'dan, 'tamamen uygulanır' anlamına gelen 3'e kadar kodlanmıştır. Her boyut için en düşük puan 0, en yüksek puan ise 21'dir.

Vizüal Analog Skala (VAS): Bu ölçek hastaların semptomlarının yoğunluğunu ve sıklığını değerlendirmede ağrı başta olmak üzere birçok neden için kullanılabilir [22]. Bu çalışmada sağlık çalışanlarının kaygı düzeylerini ifade etmek için kullanılmıştır. Katılımcılardan yüz ifadelerini de dikkate alarak 0-10 arasında kaygı düzeylerini en iyi belirten bir dereceyi işaretlemeleri istenmiştir (Şekil 2).

Şekil 2. VAS-10 Kaygı değerlendirme aracı

Verilerin Toplanması

Araştırma çevrimiçi sesli ve görüntülü kayıt yapma özelliğine sahip ücretsiz bir video konferans uygulaması ile yürütülmüştür. Çalışmada "bireysel derinlemesine görüşme" yöntemi kullanılmıştır. Katılımcılara, görüşmeye başlamadan önce, araştırmanın amacı ve ses kaydının yapılacağı hakkında bilgi verilmiştir. Sağlık çalışanları, araştırmaya katılmayı kabul etmiş ve bu kabullerini hem sözlü hem de yazılı onaylarla belirtmişlerdir. Araştırmacılar ile örneklemi oluşturan katılımcılar arasında herhangi bir çıkar çatışması yoktur. Görüşmeler, iş saatleri dışında gerçekleştirilmiştir. Görüşme süreleri, 28 dakikadan 65 dakikaya kadar değişmiş ve her katılımcı ile yalnızca bir kez görüşme yapılmıştır. Sonrasında katılımcıların görüşme kayıtları araştırmacı tarafından olduğu gibi yazılı metin formatına aktarılmıştır. Ayrıca kayıtlar USB bellekte saklanmıştır ve araştırma raporu hazırlanır hazırlanmaz imha edilmiştir.

Verilerin Değerlendirilmesi

Alınan veriler, "içerik analizi"ne dayalı tümevarımcı bir metodoloji ile değerlendirilmiştir [23]. Tüm görüşmeler NVivo11 programına aktarılmıştır. Araştırmacı yanlılığını azaltmak ve tutarlı kalmak için hiçbir kod, kategori ya da tema önceden belirtilmemiştir. Geçerliliği artırmak için nitel veri analizinde deneyimli iki kodlayıcı (DY ve YDA) doygunluğa ulaşılana kadar kodları oluşturmuştur [24]. Kodlayıcılar arasında kappa uyum katsayısı hesaplanmıştır ve 0,85 bulunmuştur. Daha sonra bir araştırmacı (DY) kodları değerlendirerek temaları ve ana kategorileri çıkarmıştır. Tema ve ana kategorilerin görselleştirilmesi için MAXQDA 2022 programı kullanılmıştır.

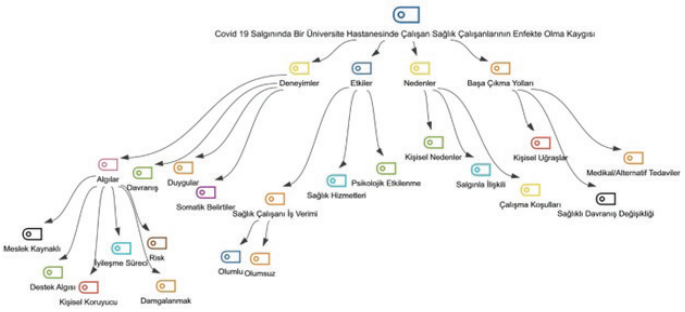
Bulgular

Demografik Bulgular

Araştırmaya katılan 32 sağlık çalışanının 12'si doktor, 10'u hemşire ya da ebe geriye kalanı ise diğer yardımcı personellerdir. Tanımlayıcı özellikler tablo 2'de sunulmuştur. Gruplar arasında cinsiyet açısından dağılım istatistiksel olarak anlamlı farklı bulunmuştur (p=0,002). Doktorların ortanca yaşı 29 (25-33) yıl, hemşire/ebe grubunun ise 42,5 (21-47) yıl iken diğer grubundakilerin 40 (32-50) yıl olarak hesaplanmıştır (p<0,001). Grupların ortanca VAS-10 kaygı düzeyleri salgın başındaki dönem için benzer bulunmuştur (p=0,059). Görüşme sırasındaki VAS-10 kaygı düzeyleri ortancası ise sırasıyla 5 (3-8), 6 (3-9) ve 3,5 (0-5) hesaplanmıştır (p=0,009). Ayrıca her üç grupta da salgın başlangıcına göre VAS-10 kaygı düzeylerinde istatistiksel anlamlı bir düşüş olduğu gözlenmiştir (sırasıyla, p=0,002, p=0,007 ve p=0,005). Katılımcıların DASÖ-21 puanları incelendiğinde gruplar arasında anksiyete düzeyleri haricinde (p=0,298) stres (p=0,017), depresyon (p=0,048) ve toplam puan (p=0,030) açısından istatistiksel farklılık olduğu ve hemşire/ebe grubundakilerin daha yüksek değerlere sahip olduğu saptanmıştır.

İçerik Analizi Sonuçları: Sağlık Çalışanlarının Enfekte Olma Kaygısı

Bu nitel çalışmada içerik analizi sonucunda, sağlık çalışanlarının enfekte olma kaygısını açıklaya bilecek dört tema altında (Kaygı Deneyimleri, Kaygı Nedenleri, Başa Çıkma Yolları ve Kaygının Etkileri) on dört ana kategori, sekiz alt kategori ve yüz otuz sekiz kod belirlenmiştir (Tablo 3, Şekil 3-4).



Şekil 3. COVID-19 Pandemisi Sırasında Sağlık Hizmeti Sunan Sağlık Çalışanlarının Enfekte Olma Kaygısı ile ilgili Temalar

Şekil 4. COVID-19 Pandemisi Sırasında Sağlık Hizmeti Sunan Sağlık Çalışanlarının Enfekte Olma Kaygısı ile kod bulutu

Tablo 2. Katılımcıların tanımlayıcı özellikleri

	Doktor n=12	**Hemşire/Ebe** n=10	**Diğer Yardımcı Personel** n=10
Cinsiyet, n(%)			
Kadın	5 (41,7)	10 (100)	5 (50)
Erkek	7 (58,3)	0	5 (50)
Yaş, yıl			
Ort±sd	28,9±2,3	40,7±7,4	40,4±5,8
Oranca (min-maks)	29 (25-33)	42,5 (21-47)	40 (32-50)
Eğitim durumu, n(%)			
Ortaokul	0	0	5 (50)
Lise	0	1 (10)	3 (30)
Meslek yüksekokulu	0	5 (50)	0
Üniversite	0	4 (40)	2 (20)
Yüksek lisans / Doktora	12 (100)	0	0
Medeni durum, n(%)			
Bekâr	2 (16,7)	1 (10)	1 (10)
Boşanmış	0	0	1 (10)
Evli	10 (83,3)	9 (90)	8 (80)
Çocuk, n(%)			
Var	5 (41,7)	9 (90)	9 (90)
Yok	7 (58,3)	1 (10)	1 (10)
Meslekte geçirdiği süre, yıl			
Ort±sd	4,5±1,9	20,5±8,2	12±6,7
Oranca (min-maks)	5 (2-8)	23 (1-29)	8 (7-26)
Salgın nedeniyle birim değişikliği, n(%)			
Var	8 (66,7)	4 (40)	7 (70)
Yok	4 (33,3)	6 (60)	3 (30)
Birlikte çalıştığı kişi enfekte olan, n(%)			
Var	6 (50)	10 (100)	8 (80)
Yok	6 (50)	0	2 (20)
Görüşme Salgının kaçıncı haftası, n(%)			
8. hafta	9 (75)	6 (60)	4 (40)
9. hafta	1 (8.3)	1 (10)	4 (40)
10. hafta	2 (16.7)	3 (30)	2 (20)
Salgının ilk haftasında VAS kaygı			
Ort±sd	7,5±1,1	8,7±1,1	7,4±1,8
Oranca (min-maks)	7 (6-10)	9 (7-10)	8 (4-10)
Görüşme sırasında VAS kaygı			
Ort±sd	5,2±1,5	6,1±1,9	3,4±1,5
Oranca (min-maks)	5 (3-8)	6 (3-9)	3,5 (2-5)
DASS-21 Stress			
Ort±sd	3,5±2	8,4±3,6	4,4±5,5
Oranca (min-maks)	3 (0-7)	10 (2-12)	2,5 (0-17)
DASS-21 Anksiyete			
Ort±sd	2,7±1,3	4,7±3,3	3±2,8
Oranca (min-maks)	3 (0-4)	3,5 (0-11)	3 (0-10)
DASS-21 Depresyon			
Ort±sd	4±3,4	7,6±3,9	3,6±3,5
Oranca (min-maks)	3 (0-10)	8 (0-15)	3,5 (0-11)
DASS-21 Toplam			
Ort±sd	10,2±5	20,7±9,7	11±10,5
Oranca (min-maks)	8 (4-19)	22 (7-37)	8,5 (0-32)

Tablo 3. İçerik Analizi Sonucu Oluşturulan Temalar, Ana Kategoriler, Alt Kategoriler ve Kodlar

Temalar	Ana Kategoriler	Alt Kategoriler	Kodlar	
Kaygı	Algılar	Risk	-Enfekte olma riski -Enfekte etme riski	-Birlikte Yaşanan Riskli gruptakiler
		Meslek Kaynaklı	-Zorunluluk -Sorgulamak -Sevmek -Pişmanlık -Mutluluk -Memnuniyet	-Kıymetli -İhtiyaç -Gurur duydum -Faydaları -Farksız
		Kişisel Koruyucu Donanım Kaynaklı	-Zor -Zaman alıcı -Yeterlilik	-Koruyuculuk -Güvenli -Alışmak
		İyileşme Süreci	-Tamamen iyileşeceğim -Rahat geçirmek -Hayati tehlike	-Asemptomatik -Ağır
		Destek Algısı	-İnanilmaz Bir Olay -Yönetim -Sosyal medya -Psikiyatrik destek ihtiyacı	-İş arkadaşları -Diğer meslek grupları -Çevreden destek -Aileden destek
		Damgalanmak	-Yüz üstü kalmak -Yanımda rahat hissetmezler -Uzak durmak	-Suçlanmak -Dışlanmak
	Davranış		-Veda etmek -Uzun ya da fazla duş almak -Sık el yıkama -Peçete ile dokunmak -Öcü görmüş gibi -Maske almak -Kat kat giyinmek -Her yerde virüs var	-Hastadan uzak durmak -Hasta yanında nefes tutmak -Hasta odasından dışarı çıkma isteği -El yıkama -Dikkatli olma -Tedbirler
	Duygular		-Karamsarlık -Korku -Panik	-Sitem etmek -Üzülmek
	Somatik Belirtiler		-Titreme -Terleme -Taşikardi -Öksürük -Nefes almada zorlanma	-Kas eklem ağrısı -Boğazda yanma, ağrı -Baş ağrısı -Ateş -Ağızda kuruluk
Kaygı Nedenleri	Salgın İlişkili		-Yayılım hızı -Tanısını bilmemek -Salgının Süresi -Personel bulaşı	-Medyadaki infodemik haberler -Bulaştırıcılığı yüksek -COVID ne?
	Kişisel Nedenler		-Kendisinde Kronik hastalık -Hastane dışında	-Evden ayrı kalmak -Ayrılık
	Çalışma Koşulları		-Hastanede, hasta yanında -Görev yeri değişikliği	-Çevreyi enfekte endişesi
Başa çıkma mekanizmaları	Kişisel Uğraşlar		-Yemek yapmak -Temizlik, ev işi yapmak -Şarkı söylemek -Sohbet -Pozitif düşünce -Örgü örmek -Müzik dinlemek -Kitap okumak	-Her şey olacağına varır -Fotoğraf ve video çekmek -Dua etmek -Dizi film izlemek -Bilimsel çalışmalar yapmak -Bilgisayar oyunu -Ailemle zaman geçirmek
	Medikal / Alternatif Tedaviler		-İlaç kullanmak	-Psikolojik yardım
	Sağlıklı Davranış Değişikliği		-Uyumak -Spor -Profesyonel -İyi dinlemmek -iyi beslenmek	-Evde izolasyon -El yıkamak -Duş almak -Dezenfektan kullanmak
Kaygının Etkileri	Sağlık Hizmetleri		-Hijyenin önemi -Gereksiz hastane başvuruları -Bulaşıcı hastalıkların önemi	-Gerçek acil başvuruları -Yoğunluk azaldı
	Sağlık Çalışanı İş Verimi	Olumlu	-Sağlık çalışanlarına saygı arttı -Daha dikkatli çalışmak -Öz verili	-İyi niyetli -İstekli -Daha hızlı -Aynı
		Olumsuz	-Yorgunluk -İsteksiz -Erteleyici	-Daha yavaş -Azaldı
	Psikolojik Etkilenme		-Zarar vermek -Obsesyonlar arta bilir -Uyku sorunları -Takıntılı -Tahamülsüz -Sinirlilik -Mutsuzluk	-Kilo kaybı -İştahsızlık -Huzursuzluk hissi -Baskı -Ağlamak -Sosyal hayatta mesafe

Tema 1: Kaygı Deneyimleri

Sağlık çalışanlarının kaygı deneyimleri dört ana kategoride incelenmiştir: Algılar, Davranışlar, Duygular ve Somatik Belirtiler. Her üç meslek grubu için de benzer içerikler gözlenmiştir. Algılar kategorisi, enfekte olma riskinin yüksek olduğu algısı, aile üyelerine hastalık bulaştırma korkusu, hastalarla yakın temas etme endişesi, çalışırken kendini güvende hissetmeme ve işe başlama-eyleme geçme süresinde uzama ve işin zorluğu algısını içermektedir. Davranışlar kategorisinde, koruyucu ekipmanlar kullanma ve hijyen önlemleri almakta titizlik gösterme, hastalarla mümkün olduğunca az yakınlaşma ve yanlarında kısa süre geçirme, evde izolasyon ve aile üyelerinden ayrı kalmaya çalışma gibi davranışlar yer almaktadır. Bazı katılımcıların, enfeksiyon riskiyle mücadele için çift eldiven ve maske kullanmak, hasta yanında nefesini tutmak gibi ekstra önlem aldığı anlaşılmıştır. Duygular kategorisinde ise, endişe ve korku, tedirginlik, yorgunluk, halsizlik, sinirlilik ve stres gibi duygusal tepkiler bulunmaktadır. Son olarak, somatik belirtiler kategorisi, baş ağrısı, ateş hissi, iştahsızlık ve kilo kaybı gibi fiziksel belirtileri içermektedir. Bu temaya ait bazı ifadeler aşağıda sunulmuştur (KH: Katılımcı Hemşire, KD: Katılımcı Doktor ve KYP: Katılımcı Yardımcı Personel).

"… Tüm koruyucu ekipmanları giysem de hastanın yanından çıktıktan sonra bulaştı mı diye endişe ediyordum. …Özellikle başlarda hastanın yanında nefes almamak için kendimi tutuyordum kendimi dışarıya zor atıyordum nefes alıp tekrar yanına gidiyordum." (KH3,Yoğunbakım, 45 yaş)

"…Bana hastalığın bulaşmasından değil çocuklarıma bulaştırmaktan korkuyorum." (KYP1, Pandemi Servisi, 48 yaş)

"Ama Allah'ın gücüne gitmesin arkamda çocuğumu bırakıp ölmek istemiyorum. Olacaksa ikimize birlikte bir şey olsun." (KYP6, Pandemi Servisi, 40 yaş)

Tema 2: Kaygı Nedenleri

Kaygı nedenleri 3 ana kategori altında değerlendirilmiştir: kişisel nedenler, salgınla/virüsle ilişkili nedenler ve çalışma koşullarına bağlı nedenler. Kişisel nedenler içerisinde kendisinde kronik hastalık olmasından dolayı hastalığın ağır geçeceğini belirtenler olmuştur. Sağlık çalışanlarının aile ve sosyal hayatlarının pandemi sürecinde önemli ölçüde bozulduğu, kendilerine bulaşması endişesinden ayrı olarak başkalarına bulaştırma endişesinin de önemli kaygılarından biri olduğu anlaşılmıştır. Ayrıca, salgının ve virüsün bilinmezlikleri, sürekli değişen bilgiler de sağlık çalışanlarını endişelendiren faktörler arasında yer almaktadır. Çalışma koşullarına bağlı nedenler kategorisinde, yoğun iş yükü, yetersiz ekipman ve koruyucu önlemler, pandemi sürecinin getirdiği stres önemli bir kaygı nedenidir.

"…ailemden ve çocuğumdan ayrı kaldık, eşimle birlikte ayrı ev tuttuk, çocuğuma anneannesi ve dedesi bakıyor. Sadece kapıdan görüyorum aile birliğim tamamen bozuldu." (KD4, Pandemi Servis, 30 yaş)

"…Aslında başlarda endişeden çok yoğunluk vardı. Enfekte olmaktan daha çok ailemi görememekten ve ilgilenememekten dolayı daha çok kaygılıyım." (KH4, Pandemi Servis, 42 yaş)

"…İşyerinde dokunduğum her yerde COVID varmış gibiydi. Yediğim şeylerde bile varmış gibi hissettim." (KYP2, Pandemi Servis, 32)

Tema 3: Başa Çıkma Yolları

Sağlık çalışanlarının enfekte olma kaygısı ile başa çıkma yolları üç ana kategoride incelenmiştir: kişisel uğraşlar, medikal / alternatif tedaviler ve sağlıklı davranış değişikliğidir. Sağlık çalışanları, yemek yapma, temizlik ve ev işleriyle meşgul olma, şarkı söyleme, sohbet etme, örgü örme, müzik dinleme, kitap okuma, fotoğraf ve video çekme, dua etme, dizi-film izleme, özellikle bazı doktorlar için bilimsel çalışmalarda bulunma, bilgisayar oyunları oynama ve aileleriyle zaman geçirme gibi kişisel aktivitelerle streslerini azaltmaya çalışmaktadırlar. Enfekte olma kaygısı yaşayan sağlık çalışanları, ilaç kullanma, psikolojik yardım ve profesyonel psikiyatrik destek alarak, bu süreci atlatmaya, kendilerini daha güçlü hissetmeye ve dayanıklılıklarını arttırmaya çalışmaktadırlar. Sağlıklı davranış değişikliği olarak sağlık çalışanları, uyumak, spor yapmak, iyi dinlemek, iyi beslenmek, evde izolasyon, duş almak ve dezenfektan kullanmak gibi sağlıklı davranış değişiklikleriyle enfekte olma riskini azaltmaya çalışmaktadırlar.

"…Bol bol dua ettim. Kendi kendimi pozitif telkin ettim." (KYP1, Pandemi Servis, 48 yaş)

"…Kendimi rahatlatmak için bol bol ev işi yapıyorum. Arkadaşlarımla telefonda konuşuyorum." (KYP3, Pandemi Yoğun bakım,45 yaş)

"…Bilimsel araştırmalara yoğunlaştım, evde ailemle zaman geçirdim, dizi film seyrettim." (KD3, Pandemi Servis, 32 yaş)

Tema 4: Kaygının Etkileri

Bu tema, kaygının sağlık çalışanlarının yaşamları ve çalışma ortamlarını nasıl etkilediğine dair bulgular içermektedir. Sağlık hizmetlerinde hijyen ve bulaşıcı hastalıkların öneminin artmasından çoğu katılımcı memnundur. Doktorlar, acil servise gereksiz başvuruların azaldığını, gerçek acil durumlar ile başvuruların ise arttığını ifade etmiştir. Enfekte olma

korkusu nedeniyle, gereksiz başvurular azalmış ve hastaların hastanelerden kaçınması, diğer polikliniklerin yoğunluğunun önemli ölçüde düşmesine yol açmıştır. Enfekte olma kaygısı, sağlık çalışanlarının iş veriminde hem pozitif hem negatif etkiler yaratmıştır. Bu kaygı, bazı çalışanların verimliliğini artırırken, bazılarında ise yorgunluk, isteksizlik, erteleme eğilimi ve iş veriminde genel bir düşüş gibi olumsuz etkilere sebep olmuştur. Ancak bu katılımcılar, pandeminin ilk iki haftasından sonra olumsuz etkilerin azaldığını belirtmiştir. Enfekte olma kaygısı, sağlık çalışanlarında çeşitli psikolojik etkilenimlere yol açmıştır. Bu etkilenimler obsesif düşünceler, uyku bozuklukları, sinirlilik, mutsuzluk, kilo kaybı, iştahsızlık ve huzursuzluk olarak kendini göstermiştir. Ayrıca, enfekte olma ve enfekte etme kaygıları sosyal ve toplumsal yaşamlarını da etkilemiştir, sosyal etkileşimlerini kısıtlama ve sosyal mesafeyi koruma eğilimi göstermişlerdir.

"…Başlarda ağlama ataklarım oldu. Hayatın anlamsız olduğunu dünyaya neden geldiğimi sorguluyorum. Ama şuan alıştım bu şekilde çalışmaya. Açıkçası güvenebileceğim bir psikiyatri uzmanıyla karşılaşsaydım ilaç almayı düşünürdüm. Ama kapsamlı destek olabileceklerini düşünseydim destek alırdım. (KYP, Pandemi Yoğunbakım, 45 yaş)"

Tartışma

Bu nitel çalışmada, özellikle COVID-19 pandemisinin ilk aylarının içeresinde hayatlarında ilk kez pandemide sağlık hizmeti verme deneyimi yaşayan üçüncü basamak bir sağlık kuruluşunda çalışanların hem enfeksiyon bulaşma kaygısı ve stresini hem de bulaş konusunda yüksek riskli şartlarda çalışmalarından dolayı yakın çevrelerini enfekte etme kaygısı yaşadıkları belirlenmiştir. Kaygı deneyimleri ile ilgili değişkenlerin bir arada incelenmesi ve aralarındaki ilişkilerin nitel olarak ortaya konulması bu çalışmanın özgün tarafıdır.

Bulgularımız, sağlık çalışanlarının kaygı deneyimlerinin enfekte olma ve enfekte etme riski, mesleki zorluklar, koruyucu donanım eksikliği, yakın çevreden ayrı kalma, temizlik ve hijyen gibi faktörlerden etkilendiğini göstermiştir. Ayrıca sağlık çalışanlarının kaygı ile ilgili duygularının olumsuz yönde etkilendiği ve somatik belirtilerinin de ortaya çıktığı bulunmuştur.

Literatüre uygun olarak, bulgularımız sağlık çalışanlarının salgınlarda kaygı yaşadığını göstermektedir. Ataç ve arkadaşları COVID-19 salgını sırasında çalışanların %52,3'ünde yaygın anksiyete bozukluğu, %53,1'inde uykusuzluk olduğunu belirtmişlerdir [25]. Benzer şekilde, Fırat ve ekibi de sağlık çalışanlarının pandemi sebebiyle endişe yaşadıklarını, ruhsal, fiziksel, sosyal ve ailevi bir dizi sorunla karşılaştıklarını belirtmişlerdir. Bu sorunlar arasında yorgunluk, uykusuzluk, gerginlik, huzursuzluk ve iştah kaybı bulunmaktadır [26]. Bulgularımız, sağlık çalışanlarının kaygılarının çeşitli faktörlere bağlı çok boyutlu bir olgu olduğunu teorik olarak belirlerken, pratikte de onların psikolojik sağlıklarını koruyup desteklemek için profesyonel yardım ve basit başa çıkma yöntemlerine ihtiyaç duyduklarını vurgulamaktadır. Sağlık çalışanlarının kaygı, depresyon ve stres düzeyleri, salgının ilk haftasında her toplumdaki her birey gibi yüksek bulunmuştur. Daha sonraki dönemde daha düşüktür.

Sağlık çalışanları kaygı ile başa çıkmak için yemek yapmak, uyumak, temizlik yapmak, şarkı söylemek, spor yapmak, sohbet etmek, pozitif düşünmek, örgü örmek, müzik dinlemek, kitap okumak, iyi dinlemek, iyi beslenmek, ilaç kullanmak, her şeyin olacağına varır demek, fotoğraf ve video çekmek, evde izolasyon yapmak, el yıkamak, duş almak, dua etmek, dizi film izlemek, dezenfektan kullanmak, bilimsel çalışmalar yapmak, bilgisayar oyunu oynamak ve aileleriyle zaman geçirmek gibi çeşitli yöntemler kullandıklarını belirtmişlerdir. Bulgularımız literatürle benzerlik göstermektedir. Tanrıverdi'nin çalışması, COVID-19 pandemisi sırasında sağlık çalışanlarının psikolojik travmalardan korunmasına yardımcı olabilecek bazı stratejileri belirtmiştir. Bu stratejiler, yeterli uyku almayı, yoga ve meditasyon gibi rahatlama tekniklerini uygulamayı ve stresi azaltmak için müzik dinleme veya resim çizme gibi aktiviteleri içermektedir [27].

Sonuç

Bu çalışmanın sonuçları hem ilgili literatüre hem de sağlık çalışanlarına kaygı ile başa çıkma yolları açısından katkı sağlamaktadır. Bu çalışma, sağlık hizmeti sunarken sağlık çalışanlarının yaşadığı kaygıların daha iyi anlaşılması ve bu kaygıların yönetimi için gerekli önlemlerin alınması açısından önemlidir. Ayrıca, pandemi sürecinde özellikle temizlik personeli gibi ön safta yer alan bir grup çalışanın deneyimlerine ışık tutmaktadır. Pandeminin başlangıcında elde edilen bu bulgular, gelecekte benzer olağanüstü durumlarla başa çıkmak için daha etkili stratejilerin belirlenmesine yardımcı olabilir. Bu çerçevede, sağlık yöneticileri ve politika yapıcılar, sağlık çalışanlarının ihtiyaçlarını ve kaygılarını daha iyi anlayarak, çalışma koşullarını iyileştirecek ve personelin psikolojik sağlığını destekleyecek önlemleri hayata geçirebilirler. Bu çalışmadan çıkarılan sonuçlar ışığında önerilen önlemler şunlardır:

1. Sağlık çalışanlarının duygusal ve psikolojik ihtiyaçları için destek hizmetlerine erişimin sağlanması ve aile ve sosyal yaşamlarını sürdürmelerine yardımcı olacak desteklerin sunulması önemlidir.

2. Enfeksiyon kontrolü ve bulaşma riskini azaltma hakkında eğitim ve bilgilendirme programları düzenlenmelidir.

3. Sağlık çalışanları için daha uygun çalışma saatleri, yeterli dinlenme süreleri ve güvenli çalışma ortamları oluşturulmalıdır.

4. Sağlık çalışanlarının kaygılarını ve endişelerini paylaşabilecekleri güvenli ve açık iletişim kanalları oluşturulmalıdır.

5. Sağlık çalışanlarına yönelik damgalanmayla mücadele ve farkındalık yaratma çalışmaları yapılmalıdır.

6. Sağlık çalışanlarının çalışmalarının takdir edilmesi ve motivasyonlarının artırılması gereklidir.

7. Sağlık çalışanlarının iş yükünün dengelenmesi için gerektiğinde ek kadro ve kaynak sağlanmalıdır.

8. Sağlık çalışanlarının sürekli eğitim ve profesyonel gelişim olanaklarına erişimi sağlanmalıdır.

9. Sağlık çalışanlarının görüşleriyle mevcut uygulama ve politikalar gözden geçirilmeli ve iyileştirilmelidir.

Sağlık çalışanlarının salgınlarda korunması için fiziksel, sosyal ve ruhsal tüm önlemler alınmalıdır. Bu tür önlemler, pandemide yaşanan zorlukları ve kaygıları etkin yönetmeye yardımcı olabilir. Bu sayede hem sağlık çalışanlarının hem de toplumun genel sağlığı ve refahı için olumlu etkiler sağlanabilir.

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Research Article

The Comparison of Selection Criteria and Results for Incisional and Excisional Biopsy in Breast Masses

Meme Kitlelerinde Eksizyonel ve İnsizyonel Biyopsi İşlemlerinin Seçim Kriterleri ve Sonuçları

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Abstract

Aim: The main purpose of this study is to clarify the biopsy selection criteria by revealing the biopsy methods and post-biopsy surgical treatment choices and pathology results in cases with biopsy indication.

Material and Methods: The study was carried out in cases who applied to the General Surgery Clinic between June 2020 and June 2022 and had biopsy indication.In fact;The records of 62 patients aged 18-70 years who were diagnosed with benign or malignant masses after excisional biopsy, tru-cut or incisional biopsy were retrospectively reviewed, and cases with incomplete or uncertain data were not included in the study.Descriptive statistics are given as mean±standard deviation, percentage and frequency.Student t test was used for continuous variables in the comparison of binary groups, $\chi 2$ test was used for comparison of binary variables, and the $p<0.05$ value in the 95% confidence interval was considered statistically significant.

Results: The total number of cases was 62.The mean age of the patients included in the study was 41.11±14.74.On the other hand, the mean age of the cases diagnosed as malignant after biopsy was found to be higher than the benign cases[(49.46±15.38)vs(39.31±14.10)($p<0.05$)].The number of cases with BI-RADS 4 was found to be significantly higher in the group who underwent trucut or incisional biopsy[(n=11(91.6%)].Biopsy incidences;n=12(19.4%) incisional or trucut biopsies were performed, and the remaining 50(80.6%) cases underwent excisional biopsy.It was seen that patients who underwent incisional or trucut procedure were statistically significantly malignant [n=11(91.6%) vs 1(8.4%)($p<0.05$)]. According to the total number of patients, the results of malignancy in cases who underwent incisional or trucut biopsy were significantly higher than those who underwent excisional biopsy[n=11(17.7%)vs51(82.3%)($p<0.0001$)].

Conclusion: We think that the cases diagnosed with breast cancer generally have masses that are not palpable as a result of mammography examinations performed in the preoperative period, and therefore, the cases with excisional biopsy are usually benign, and preoperative imaging is very important like physical examination.

Key words: Excisional biopsy, incisional biopsy , breast ,mass , biopsy selection

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ÖZ

Amaç: Bu çalışmanın temel amacı, biopsi endikasyonu görülen olgularda biopsi yöntemlerini ve biopsi sonrası cerrahi tedavi seçimleriyle patoloji sonuçlarını ortaya koyarak biopsi seçim kriterlerini netleştirmektir.

Gereç ve Yöntemler: Çalışma haziran 2020 ve haziran 2022 tarihleri arasında Genel Cerrahi Kliniğine başvuran ve biopsi endikasyonu konulan olgularda gerçekleştirildi. Esas olarak; Eksizyonel biopsi, tru-cut veya insizyonel biyopsi sonrası benign veya malign kitle tanıları konulan 18-70 yaş arası 62 hasta kayıtları retrospektif olerek incelemeye alınmış olup, verileri eksik ya da belirsiz olan olgular çalışmaya dahil edilmemiştir. Bu tanımlayıcı istatistikler ortalama±standart sapma, yüzde ve frekans olarak verilmiştir. İkili grupların karşılaştırılmasında sürekli değişkenler için bağımsız gruplarta student t test, ikili değişkenlerin karşılaştırılmasında $\chi 2$ testi kullanılmış ve %95 güven aralığındaki $p<0,05$ değeri istatistiksel olarak anlamlı kabul edilmiş olup nihai sonuçlara regresyon analizi yapılarak ulaşılmıştır.

Bulgular: Toplam olgu sayısı 62 idi. Çalışmaya alınan hastaların yaş ortalaması 41,11±14,74 idi. Diğer yandan biopsi sonrası malignite tanısı alan olguların yaş ortalaması, benign olgulura göre daha yüksek saptandı[(49,46±15,38) vs (39,31±14,10) ($p<0.05$)].BI-RADS 4 gelen olgu sayısı trucut veye iniszyonel biopisi yapılan grupta belirgin biçimde yüksek olarak bulundu[(n=11(91.6%)].

Biopsi insidansları; n= 12(19.4%) insizyonel veya trucut biopsisi yapılmış olup, geri kalan 50 (80.6%) olguya eksizyonel biopsi yapılmıştır.İnsizyonel veya trucut işlemi uygulanan hastaların istatistiki olarak anlamlı biçimde malign geldiği görülmüştür [n=11(%91.6) vs 1(8.4%)($p<0.05$)].Toplam hasta sayısına göre de insizyonel veya trucut biopsi yapılan olguların malignite ile sonuçlanmaları eksizyonel biopsi yapılan olgulara göre anlamlı olarak yüksektir[n=11(17.7%)vs 51(82.3%) ($p<0.0001$)].

Sonuç: Meme kanseri tanısı konan olguların genel olarak preoperatif dönemde yapılan mammografi tetkikleri neticesinde ele gelmeyen kitleler olduğu ve bu sebeple eksizyonel biopisi yapılan olguların belirgin olarak benigin geldiğini ,preoperatif görüntülemenin, fizik muayane gibi çok önemli olduğunu düşünüyoruz.

Anahtar Kelimeler: Eksizyonel biyopsi, insizyonel biyopsi, meme, kitle, biyopsi seçimi

Introduction

Although the diagnosis and diagnosis methods are much better day by day, on the other hand, breast cancers are increasing, unfortunately, and it was stated that the number of cases diagnosed all over the world in 2018 was around 2.2 million(1). On the other hand, it has been reported that the number of women with a history of breast cancer in the United States alone in 2022 is almost 4.1 million(2).As stated in the literature; Palpable breast lumps and sometimes nipple discharge are common symptoms that often bring patients to the doctor. Andrea M. Bodine et al. also stated that a careful anamnesis and a comprehensive approach including physical examination and laboratory imaging examinations are required when evaluating the cases with the above basic complaints(3). While breast cancer is increasing all over the world, early diagnosis and treatment are gaining importance. For this reason, biopsy can be performed if there is a suspicion of malignancy as a result of the patient's history, physical examination, and imaging studies. In addition, although the diagnosis of benign radiological disease is thought to be radiological, if there is a mass that impairs the patient's quality of life, its excision can be considered by investigating other causes. However, unnecessary excisional biopsies should be avoided, especially at early ages.Because by affecting the breast and therefore axillary lymph nodes; It may lead to skip axillary metastases, which are especially missed in sentinel lymph node biopsies. Charles E. Cox et al. In their study on sentinel lymph node biopsies, they stated that only 1 case among all patients had axillary skip metastases and this patient had a history of previous excisional biopsy(4).All the above factors, the importance of biopsy selection criteria becomes clear.

Material and Methods

The retrospective study was approved by Çukurova University Faculty of Medicine Ethics Committee dated February 4, 2023 the ethics committee decision the number of 130.The study was carried out in cases who applied to the General Surgery Clinic between June 2020 and June 2022 and had biopsy indication.

In fact;The records of 62 patients aged 18-70 years who were diagnosed with benign or malignant masses after excisional biopsy, tru-cut or incisional biopsy were retrospectively reviewed, and cases with incomplete or uncertain data were not included in the study. Descriptive statistics are given as mean±standard deviation, percentage and frequency.Student t test was used for continuous variables in the comparison of binary groups, $\chi 2$ test was used for comparison of binary variables, and the $p<0.05$ value in the 95% confidence interval was considered statistically significant.

Results

All of the patients consisted of female cases. The mean age of the entire patient population was 41.67±13.77 years. On the other hand, the mean age of patients diagnosed with malignant breast cancer was significantly higher than those with benign pathology results [(49.46±15.38) vs.(39.31±14.10) ($p<0.05$)] (Table 1).

As a result of the comparison of the postoperative malignancy results of the cases with BI-RADS 4 mammography and those who did not have mammography due to age or whose mammography was BI-RADS 3 and below;The all patients who diagnosed with mammografphy as BI-RADS 4 , as a result; Trucut was the group of patients diagnosed with fine needle aspiration or incisional biopsy (Table2). According to preoperative clinical staging of cases found to be malignant and surgery performed;

Of the malignant cases, 5 (45.5%) cases were left MRM, 2 (18.2%) cases were right MRMs, 4 (36.4%) cases were BCS. In the preoperative clinical staging of the cases; 1 case was defined as stage 0, 9 cases as stage 2, and 1 case as stage 3 (Table 3). Considering the postoperative staging of the cases found to be malignant, different from the preoperative stage, it is distributed as follows according to the surgery performed; It was understood that 4 cases with BCS and 2 cases with right MRM were stage 2, 2 patients with left MRM were stage 3, 3 cases were stage 3, and the difference between the groups was significant (Table4).

According the table 3; Of the malignant cases, 5 (45.5%) were LMRM, 2 (18.2%) were RMRM, 4 (36.4%) were BCS. In the preoperative clinical staging of the cases; 1 case was defined as stage 0, 9 cases as stage 2, and 1 case as stage 3.

It was understood that 4 patients who underwent BCS and 2 patients who underwent RMRM and 2 patients who underwent LMRM were stage II, 3 patients who underwent LMRM stage III, and the difference between the groups was significant.

Table 1: Comparison of the cases with malignant pathology after biopsy applied to the patients, with cases with benign pathology results in independent groups by Studen t t test.

	Applied surgical procedure	n	Mean±Std. Deviation	P<0.05
Age	1,00(Malign cases)	11	49,46±15,38	0.031
	2,00(Benign cases)	51	39,31±14,10	
	Total case	62	41,67±13.77	

1:After trucut or incisional biopsies for malignant results; Performed right modified radical mastectomy, left modified radical mastectomy, breast-conserving surgery)
2: Benign excisional biopsy or tru-cut biopsy results

Table 2 : The comparison of the postoperative malignancy results of the cases with BI-RADS 4 mammography and those who did not undergo mammography due to age or whose mammography was BI-RADS 3 and below

			BI-RADS		Total	P<0,05
			,00	4,00		
Malign vs.benign cases	+	n	0	11	11	0.0001
		% of Total	0,0%	17,7%	17,7%	
	-	n	51	0	51	
		% within BIRADS	100,0%	0,0%	82,3%	
		% of Total	82,3%	0,0%	82,3%	
Total number			51	11	62	

Table 3: Preoperative clinical staging of cases found to be malignant and surgery performed

			The distribution of surgery performed			Total number	P<0.05
			BCS	RMRM	LMRM		
Preoperative clinical stage	Stage 0	n	0	0	1	1	
		The percentage(%) of the distribution of surgery performed in Stage 1 cases	0,0%	0,0%	20,0%	9,1%	
	Stage 2	n	4	2	3	9	
		The percentage(%) of the distribution of surgery performed in Stage 2 cases	44,4%	22,2%	33,3%	100,0%	
		The percentage(%) of surgery performed according to total malignant cases for stage 2	100,0%	100,0%	60,0%	81,8%	
	Stage 3	n	0	0	1	1	
		The percentage(%) of the distribution of surgery performed in Stage 3 cases	0,0%	0,0%	20,0%	9,1%	
Total number		n	4	2	5	11	
		% Total-Consequently the percentage(%) of the distribution of surgery performed in cases for BCS, RMRM,LRMM	36,4%	18,2%	45,5%	100,0%	

BCS: Breast conserving surgery
RMRM: Right modified radical mastectomy
LRMM: Left modified radical mastectomy

Table 4 : Postoperative staging of the cases found to be malignant and their distribution according to the surgery performed are as belowed

			The distribution of surgery performed			Total number	P<0.05
			BCS	RMRM	LMRM		
Postoperative stage	Stage 2,00	n:The distribution of opeative stage II cases according to the surgery performed	4	2	2	8(72,7%)	0.046
		The distribution percentage(%) of postoperative stage II cases according to the surgery performed	50,0%	25,0%	25,0%	100,0%	
	Stage 3,00	n: The distribution of opeative stage III cases according to the surgery performed	0	0	3	3(27,3%)	
		The distribution percentage(%) of postoperative stage III cases according to the surgery performed	0,0%	0,0%	100%	100,0%	
Total number		The distribution of cases according to the surgery performed	4	2	5	11	
		The distribution percentage(%) of total cases according to the surgery performed	36,4%	18,2%	45,5%	100,0%	

Discussion

In the literature , approximately 30% of the cases diagnosed with breast cancer have modifiable risk factors such as excessive body weight, insufficient physical activation and alcohol consumption, and therefore, if these factors are corrected, underlined advantage can be available against to the breast cancer(5). Xiaoxian Li et al. In the study they shared in the literature on breast cancer, they emphasized that the age distribution was between 30 and 87. In our study, the age distribution was between the age group of 33 and 80, which is consistent with the literature. In addition, our average age value; It was significantly higher than the benign group and this was statistically significant. The malign cases mean age 49,46±15,38 and benign cases mean age was 39,31±14,10(p=0.03)(6). This is clearly seen in Table 1.On the other hand, as determined in our study, it has been reported that mammography tests provide significant decreases in mortality thanks to a secondary prevention mechanism against breast cancer and the chance of early diagnosis(7). This determination in our study is also clearly seen in Table 2. In the light of one of the current literature, it has been stated that especially Contrast-enhanced mammography (CEDM) technique provides superiority in preoperative accurate staging(8). We also agree with this view. Because while there

is only 1 case in stage III stage in table 3 showing preoperative staging, 3 cases in stage III stage in table 4 showing postoperative staging. Although we did not use contrast-enhanced mammography in our study, we were successful in detecting breast cancer in all our BI-RADS 4 cases, but we cannot say the same about preoperative staging. It is striking that the stages determined in the preoperative staging table 3 and the postoperative staging table in table 4 are different.To the American Congress of Obstetrics and Gynecology (ACOG) and the American Cancer Society (ACS); Other breast cancer among new cancer cases, 30% cases in women. They reported that you created (9). In addition, unfortunately, the lifetime rate of breast cancer in a woman is not to be underestimated, and 1 out of every 8 cases is likely to be breast cancer(10,11). Breast cancer is a common cancer in women (122.2/100.000) (12).; A very good evaluation absolutely must be done. Here, as an inclusive; Physical examination, radiological images, pathological diagnosis samples should be taken in the best way and followed up. In our study, as seen in both table 5 and figure 1, 82.3% of the patients were benign. However, since breast cancer is a common and fatal disease, we should carefully in diagnosisi process.

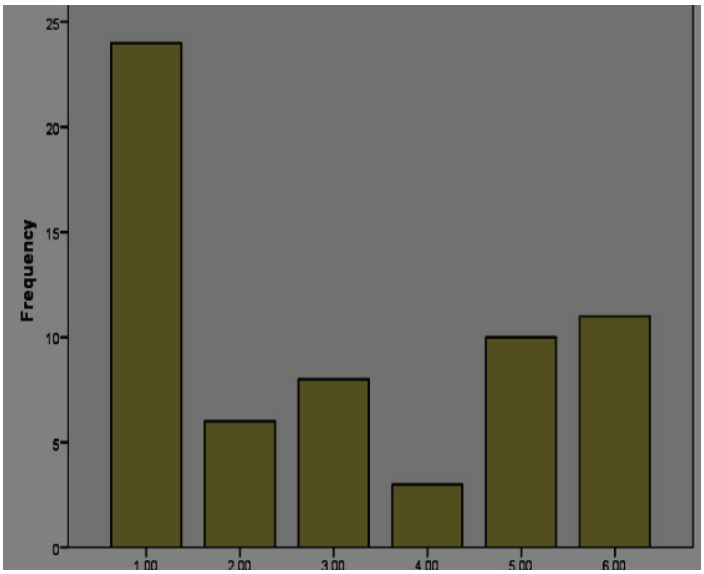

Figure 1: Schematic representation of the distribution of subgroup surgeries and postoperative diagnoses indicated in Table 5.

Distribution of the postoperative diagnosis;

1.Pure fibrocyst, fibrocystic lesion and fat necrosis, fibroadenoma, fibroepithelial polyp, accessory breast tissue, sclerosing adenosis and fibrocystic disease, tubular adenoma, tubular adenoma and fibroadenoma association

2.Coexistence of fibrocystic change, apocrine metaplasia and sclerosing adenosis, coexistence of chronic active mastitis and apocrine metaplasia in the breast, Coexistence of fibrocystic change sclerosing adenosis and apocrine metaplasia.

3.Chronic active inflammation, abscess and cyst formation in the breast, chronic active inflammation and granulation, abscess and chronic active inflammation

4. Pure epidermal cyst

5.Chronic active mastitis, ruptured epidermal cyst, granulomatous mastitis, non-caseating granulomatous mastitis, lymphocytic invasion and giant granulocytic structure

6. Primary malignant breast cancer [mucinous carcinoma, Iintraductal carcinoma(IDK), IDK+ carcinoma in situ]

Table 5: Distribution of subgroup surgeries and postoperative diagnoses

	Frequency	Percent	Cumulative Percent	
Subgroups	1,00	24	38,7	38,7
	2,00	6	9,7	48,4
	3,00	8	12,9	61,3
	4,00	3	4,8	66,1
	5,00	10	16,1	82,3
	6,00	11	17,7	100,0
	Total	62		100,0

Conclusion

We think that when biopsy is decided after the radiological and examination phases starting with breast examination, it is more necessary to prioritize trucut and incisional biopsies over excisional biopsies and even to prioritize trucut biopsy in order not to affect lymphatic drainage.

Ethic

In this retrospective study, national and international ethical rules were complied with.

Conflict of Interest

No conflict of interest was declared by the authors. In addition, no financial support was received for this study.

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Araştırma Makalesi

Koroner Endarterektomi ile kombine Koroner Arter Baypas Greftleme: Tek Merkez Deneyimi

Coronary Endarterectomy Combined with CoronaryArtery Bypass Grafting: Experience of a single centre

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Öz

Amaç: Koroner arterlerde yaygın ateroskleroz nedeniyle uzun segment oklüzyon veya çok ince lümen mevcudiyeti durumlarında revaskülarizasyon sağlayabilmek veya anastomozun kalitesini arttırabilmek için koroner arter endarterektomisi gerekli olabildiği bildirilmektedir. Koroner endarterektomi ile kombine koroner arter baypas greftlemede riskin sadece koroner arter bypass greftleme gerçekleştirilen hastalardan daha yüksek olduğunun bildirilmesine rağmen, revaskülarizasyon gerektiren hasta grubunda diffüz veya kompleks koroner kalp hastalığı insidansının artması nedeniyle tam revaskülarizasyon sağlayabilmek amacıyla endarterektomi uygulanabileceği ve cerrahi teknikteki ve perioperatif yönetimdeki ilerlemelerle sonuçların eskiye oranla daha iyi olduğu ifade edilmektedir.

Gereç ve Yöntemler: Retrospektif çalışmamız koroner arter baypas greftleme operasyonu uygulanmış hastalarda gerçekleştirildi. Çalışmaya ilk defa elektif izole koroner arter baypas greftleme operasyonu uygulanan (koroner endarterektomi ile kombine veya değil) hastalar dahil edildiler. Koroner arter baypas greftleme operasyonu ile eşzamanlı farklı bir kardiyak, karotis veya aort cerrahisi uygulanan hastalar, farklı bir açık kalp operasyonu uygulanan hastalar, ikinci defa açık kalp ameliyatı uygulanan hastalar çalışmaya dahil edilmediler.

Bulgular: Çalışmaya dahil edilen toplam 184 hastanın (142 tanesi erkek) yaş ortalaması 63.5+/-9.58 idi. Hastalardan 10 tanesine koroner arter endarterektomisi ile kombine koroner arter baypas greftleme operasyonu gerçekleştirilmişti. Sol ön inen arter ve Diagonal artere (koroner endarterektomi hastalarının %50'si) uygulanan endarterektomiler açık teknikle gerçekleştirilmişti. Koroner endarterektomi uygulananlardan 2 tanesinde erken dönem mortalite gözlendi.

Sonuç: Hedef koroner arterlerde özellikle uzun segment ciddi stenoz/oklüzyon varlığı gibi anastomoz kalitesini azaltan ve anastomozu zorlaştıran durumlarda koroner endarterektomi ile kombine koroner arter baypas greftleme yönteminin özellikle cerrahi tecrübe ve uygun hasta seçimi varlığında güvenli ve sonuçlarının kabul edilebilir olabileceğini düşünmekle birlikte daha fazla hasta sayılı çalışmaların yapılmasının yararlı olabileceğini düşünmekteyiz.

Anahtar kelimeler: endarterektomi, koroner arter hastalığı, koroner arter baypas greftleme, ateroskleroz

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Abstract

Aim: It has been reported that coronary artery endarterectomy may be necessary to provide revascularization or to improve the quality of anastomosis in cases of long segment occlusion or very thin lumen due to extensive atherosclerosis in the coronary arteries. Although it has been reported that the risk in coronary artery bypass grafting combined with coronary endarterectomy is higher than in patients who undergo coronary artery bypass grafting alone, due to the increased incidence of diffuse or complex coronary heart disease in the patient group requiring revascularization, endarterectomy can be applied to achieve complete revascularization and the results have been restored with advances in surgical technique and perioperative management.

Material and Methods: Our retrospective study was performed in patients who underwent coronary artery bypass grafting. Patients who underwent elective isolated coronary artery bypass grafting for the first time (combined or not with coronary endarterectomy) were included in the study. Patients who underwent a different cardiac, carotid or aortic surgery simultaneously with coronary artery bypass grafting operation, patients who underwent a different open heart operation, and patients who underwent open heart surgery for the second time were not included in the study.

Results: The mean age of 184 patients (142 males) included in the study was 63.5+/-9.58 years. Coronary artery endarterectomy combined with coronary artery bypass grafting was performed in 10 of the patients. Endarterectomies to the left anterior descending artery and diagonal artery (50% of coronary endarterectomy patients) were performed using the open technique. Early mortality was observed in 2 patients who underwent coronary endarterectomy.

Conclusion: We think that coronary artery bypass grafting combined with coronary endarterectomy may be safe and the results may be acceptable, especially in the presence of surgical experience and appropriate patient selection, in conditions that reduce anastomosis quality and complicate anastomosis, such as the presence of long segment severe stenosis/occlusion in the target coronary arteries, and we think that it would be useful to carry out studies too.

Keywords: endarterectomy, coronary artery disease, coronary artery bypass grafting, atherosclerosis

Giriş

Önemli bir mortalite ve morbidite nedeni olduğu bilinmekte olan koroner arter hastalığının (KAH) tedavisinde bir cerrahi revaskülarizasyon seçeneği olan koroner arter baypas greftleme (KABG) özellikle sol ana koroner arter lezyonu olan veya diyabetik koroner arter hastalarında önerilmektedir.[1,2] Bazen yaygın ateroskleroz nedeniyle koroner arterlerde uzun segment oklüzyon veya çok ince lümen mevcudiyeti durumlarında tam revaskülarizasyon sağlayabilmek veya anastomozun kalitesini arttırabilmek için koroner endarterektominin (KE) gerekli olabildiği ifade edilmektedir.[3,4] İlk kez 1950'lerde şiddetli ateroskleroz ve miyokardial iskeminin bir tedavisi olarak uygulandığı ifade edilen KE ile ilgili ilk çalışmalarda yüksek mortalite ve morbidite oranlarının yanı sıra KE'nin postoperatif akut miyokard enfarktüsü (MI) ile ilişkili olduğunun ve bu nedenlerle pek tercih edilmediğinin bildirildiği de ifade edilmektedir.[3,5] Literatürde KE ile kombine KABG'de riskin KE uygulanmaksızın gerçekleştirilen KABG'den daha yüksek olduğunun bildirilmesine rağmen, koroner arter cerrahi revaskülarizasyonu gerektiren hasta grubunda diffüz veya kompleks lezyon insidansının artması nedeniyle tam revaskülarizasyon sağlayabilmek amacıyla KE uygulanabileceği ve ayrıca, cerrahi teknikteki ve perioperatif yönetimdeki ilerlemelerle KE sonuçlarının eskiye oranla daha iyi olduğu bildirilmektedir.[3,6]

Çalışmamızda kliniğimizde gerçekleştirdiğimiz KE ile kombine KABG operasyonlarının erken dönem klinik sonuçlara etkilerini incelemeyi ve literatür eşliğinde değerlendirmeyi amaçladık.

Gereç ve Yöntemler

Retrospektif çalışmamız üçüncü basamak hastanemizde Eylül 2021-Ağustos 2022 tarihlerinde KABG cerrahisi uygulanmış olan hastalarda gerçekleştirildi. Çalışma için Etik Kurul onayı alındı, Helsinki deklarasyonu kriterlerine uyuldu. Çalışmaya araştırma verileri elde edilebilen ilk defa elektif izole KABG cerrahisi uygulanan (KE ile kombine olan veya olmayan) hastalar dahil edildiler. Acil KABG uygulanan hastalar, KABG operasyonu ile eşzamanlı farklı bir kardiyak, karotis veya aort cerrahisi uygulanan hastalar, KABG harici bir açık kalp

operasyonu uygulanan hastalar, ikinci veya üçüncü defa açık kalp ameliyatı uygulanan hastalar çalışmaya dahil edilmediler. Çalışmaya dahil edilen hastaların preoperatif (yandaş hastalıkları, laboratuvar tetkiki ve ekokardiyografi verileri…vs), intraoperatif (KE uygulanıp uygulanmadığı, KE uygulanan damarlar, kardiyopulmoner baypas (KPB) süresi, aortik klemp süresi, distal bypass sayısı…vs) ve postoperatif bulguları (istenmeyen olaylar, intraaortik balon pompası (İABP) kullanımı, mortalite…vs) hastane veri kayıt sisteminden incelenerek kayıt edildi. Erken dönem istenmeyen olay olarak postoperatif ilk 30 günde gerçekleşen olaylar kabul edildi.

Bu çalışmada sürekli değişkenler ortalama±standart sapma (SS), kategorik değişkenler ise frekans ve yüzde (%) olarak gösterildi. Tanımlayıcı veriler, hasta sayısı ve yüzde olarak ifade edildi. Bu tanımlayıcı çalışmada başka bir istatistiksel analiz yapılmadı.

Bulgular

Çalışma periyodunda hastanemiz Kalp Damar Cerrahisi kliniğinde gerçekleştirilen ve çalışma verileri değerlendirilebilen, yaş ortalaması 63.5+/-9.58 olan 184 koroner arter hastasında gerçekleştirilen elektif izole KABG ameliyatlarından 10 tanesinde eşzamanlı KE uygulandığı tespit edildi. Çalışma verilerine erişilebilen tüm elektif izole KABG hastalarının demografik verileri Tablo.1.'de ve KABG ile kombine KE uygulanmış olan hastaların verileri Tablo.2.'de gösterilmiştir. Sol ön inen arter (LAD) ve Diagonal artere açık teknikle KE uygulandığı saptanmış olup LAD anastomozlarının tamamı sol internal mamarian arter (LİMA) grefti kullanılarak gerçekleştirilmişti. KE ile kombine KABG operasyonlarından 1 tanesi off-pump tekniğiyle gerçekleştirilmişti. KABG ile kombine KE uygulanmış olan hastalardan 2 tanesinde erken dönem (postoperatif ilk 30 gün içerisinde) mortalite gözlenmiş olup bu hastaların klinik özellikleri Tablo.3.'te ayrıntılı olarak gösterilmiştir.

Tablo.1. Çalışma hastalarının demografik verileri

Değişken	n=184
Yaş (yıl)	63.5+/-9.58
Cinsiyet (erkek)(%)	142(%77.17)
Ağırlık (kg)	79.4+/-13.7
DM(%)	106(%57.6)
EF (%)	53+/-9.4
Ortalama distalanastomoz sayısı	3.64+/-1.08
IABP kullanılan hasta sayısı(%)	12(%6,52)
Off-pump KABG uygulanan hasta sayısı(%)	17(%9.23)
Ortalama KPB süresi (dakika)	121.71+/-33.30
Mortalite(%)	16(%8,69)

Tablo.2. Koroner Endarterektomi uygulanan hastaların verileri

Değişken	n=10
Yaş (yıl)	63,9+/-13.2
Cinsiyet(erkek)	9(%90)
Ağırlık (kg)	89+/-16.9
DM	4(%40)
EF (%)	52+/-7.9
Off-pump KABG sayısı	1(%10)
Ortalama KPB süresi (dakika)	167,11+/-47.17
Tek damara KE uygulanan hasta sayısı	8(%80)
İki damara KE uygulanan hasta sayısı	2(%20)
Ortalama distalanastomoz sayısı	3,8+/-1.13
IABP kullanılan hasta sayısı	1(%10)
Mortalite	2(%20)

Tartışma

KABG operasyonunun son dönemde özellikle diabetik hastalarda ve ana koroner hastalığı veya üç damar hastalığı olan hastalarda önerilen revaskülarizasyon seçeneği olarak halen yerini korumakta olduğu bildirilmektedir.[1] KABG uygulanmasında teknikte gelişmeler de halen devam etmekte ve intraoperatif ve postoperatif hasta yönetimindeki gelişmelerin mortalite ve morbidite üzerine olumlu etkileri

Tablo.3. Koroner Endarterektomi uygulanan hastaların klinik özellikleri

	Yaş (yıl)	Cinsiyet	Preoperatifkomor-bidite	Preoperatif EF(%)	KE uygulanan damarlar	KPB kullanımı	IABP kullanımı	Kom-plikasyon	Mortalite
Hasta 1	62	E	SVH	50	PDA	Evet	Hayır	Hayır	Hayır
Hasta 2	77	E	KBY	45	LAD	Evet	Hayır	SVH	Evet
Hasta 3	38	E	KBY	60	RCA	Evet	Hayır	Hayır	Hayır
Hasta 4	67	E	Hayır	35	LAD	Hayır	Hayır	AF	Hayır
Hasta 5	67	K	Hayır	55	Diagonal	Evet	Hayır	AF	Hayır
Hasta 6	79	E	Hayır	50	OM	Evet	Hayır	SVH	Evet
Hasta 7	71	E	Hayır	60	RCA	Evet	Hayır	Hayır	Hayır
Hasta 8	51	E	Hayır	55	LAD, OM	Evet	Evet	Kanama Revizyon	Hayır
Hasta 9	52	E	Hayır	60	OM, Diagonal	Evet	Hayır	Hayır	Hayır
Hasta10	75	E	Hayır	50	OM	Evet	Hayır	Hayır	Hayır

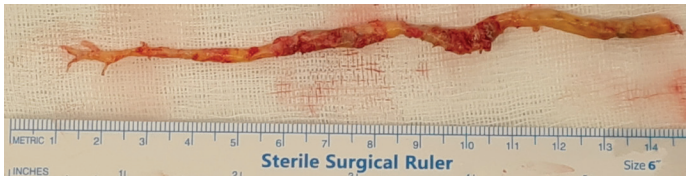
olduğu görülmektedir. Bununla birlikte kompleks koroner arter lezyonlarında başarılı revaskülarizasyon yapılabilmesindeki zorlukların yerini korumakta olduğu ve özellikle koroner arterlerin yaygın aterosklerozu nedeniyle uzun segment oklüzyon veya lümenin çok ince olması durumlarında başarılı bir revaskülarizasyon sağlayabilmek ve anastomoz kalitesini arttırabilmek amacıyla KE uygulamak gerekli olabildiği de ifade edilmektedir.[3,4] KE ile ilgili ilk çalışmaların sonuçlarının mortalite ve erken dönem istenmeyen olaylar açısından çok iyi olmaması nedeniyle bir süre pek tercih edilmediği bildirilmekte olup [3,5,7] cerrahi teknik ve yönetimdeki ve ilaç teknolojisindeki gelişmeler sonrasında KE sonuçlarının eskiye oranla daha iyi olduğu ifade edilmektedir. [3,6,8]

Daha önceleri yalnız başına bir revaskülarizasyon tekniği olarak uygulanabilen KE'nin KABG ile kombine edilmesi sonrasında sonuçların iyi ve kabul edilebilir olduğu [1,9-11], bu sonuçların gelişen cerrahi tekniklerle birlikte perioperatif yönetim ve etkili antitrombotik tedaviye bağlı olabileceği [12] ve KE ile kombine KABG'nin sonuçları açısından farklı merkezlerde yapılan daha büyük çalışmalara ihtiyaç olduğu da bildirilmektedir.[1] Diğer taraftan literatürdeki bazı çalışmalardan elde edilen sonuçların, KE ile kombine KABG operasyonlarının greft açıklığını azalttığı [12,13] ve KE uygulanmaksızın gerçekleştirilen KABG operasyonlarına göre erken ve geç dönem mortalite ve istenmeyen olay risklerini arttırdığı yönünde olduğu bildirilmektedir. [12,14,15] Bizim çalışmamızda biz de benzer şekilde özellikle uzun segment aterosklerotik lezyonu olan ve anastomoz lokasyonunda koroner arter lümeninin ince olduğu hastalarda KE ile kombine KABG tekniğini uyguladık.

Literatürdeki birkaç farklı çalışmada KE ile kombine KABG yöntemiyle revaskülarizasyon gerçekleştirilen hastalarda erken postoperatif mortalite oranlarının düşük (%5, %8) olarak bildirildiği ifade edilmekle birlikte [1] [2][3] yine hasta seçiminin ve cerrahi tecrübenin de KE ile kombine KABG operasyonunun sonuçlarının daha iyi olmasında etkili olduğunun bildirildiği ifade edilmektedir. [9] Diğer taraftan, KABG ile birlikte KE uygulanan hastalarda erken dönem mortalitenin %61 oranında arttığının ifade edildiği [12] ve DM, kadın cinsiyet, sol ana koroner hastalığı, akut myokard enfarktüsü ve şiddetli ventrikül disfonksiyonunun KE ile ilişkili mortalite için risk faktörlerinden olduğu bildirilmekte olup [1,16] çalışmamıza dahil edilen izole elektif KABG uyguladığımız toplam 184 hastada mortalite oranımız %8,69 olarak hesaplandı. Çalışmamıza dahil edilen KE ile kombine edilmiş KABG operasyonu uyguladığımız 10 hastadan 2 tanesinde (%20) erken postoperatif mortalite gerçekleşmişti ve hastalardan 1 tanesinde (%50) eşlik eden DM, KBY ve KKY, diğerinde ise eşlik eden SVH tanısı mevcuttu. Bizim çalışmamızda mortalite nedenleri SVH ve KBY olarak saptandı.

Sırasıyla sağ koroner arter ve LAD'nin en fazla KE uygulanan arterler olduğunu[1,2] ve 2 arterine KE uygulanan hasta oranını %5,4 olarak bildiren yayınlar [1] mevcut olup literatürdeki bir yayında KE işleminde en sık açık tekniği kullandıkları bildirilmektedir (%79).[2] Farklı bir çalışmada ise KE'yi hastaların %70,37'sinde sol koroner arter ve dallarına uyguladıkları [3] ve KE'nin özellikle LAD başta olmak üzere (%50'sinde) sıklıkla tek koroner artere uygulandığını ve LAD'ye uygulanan KE'nin özellikle de kapalı teknik tercih edilmişse artmış mortalite ve morbidite ile ilişkili olabileceği de bildirilmektedir.[3,17] Bizim çalışmamızda KE ile kombine KABG uyguladığımız hastaların 3 tanesinde (%30) LAD'ye, 2 tanesinde (%20) RCA'ya, 1 tanesinde PDA'ya (%10), 2 tanesinde (%20) Diagonal artere ve 4 tanesinde (%40) Optus Marginalis arterlerine endarterektomi uygulanmış olup bunlardan LAD ve Diagonal artere gerçekleştirilenler açık diğerleri ise kapalı endarterektomi tekniği ile yapılmıştı. Hastaların %70'inde sol koroner arter ve dallarına KE yapılmıştı ve %20'sinde 2 koroner artere KE yapılmıştı.

Literatürde KE işleminden sonra erken dönem mortalitenin açık veya kapalı teknik açısından genellikle benzer olduğunu[3], bu hasta grubunda LİMA grefti kullanımının önemli olduğunu ve hastaların çoğunda LİMA grefti kullandıklarını bildiren yayınlar bulunmakla birlikte[2,12], LAD anastomozlarının tamamında LİMA kullandıklarını ifade eden çalışmalar da mevcuttur.[9] Biz de KE ile kombine KABG operasyonu uyguladığımız hastaların tamamında LAD anastomozu için LİMA greftini kullandık. Uyguladığımız endarterektomi işleminde çıkartılan aterosklerotik plak boylarının tamamını kaydedememekle birlikte KE ile çıkarttığımz en uzun plak boyunun yaklaşık 13,5cm olduğunu belirtmek isteriz (Resim.1). Bizim bilgilerimize göre literatürde bu denli uzun KE plağı tanımlayan sadece bir çalışma mevcuttur.[9]



Resim.1. Çok uzun bir koroner arter endarterektomi plağı (yaklaşık 13.5cm uzunluğunda)

Bazı çalışmalarda KE uygulanan koroner arter sayısının fazlalığının KE uygulanmaksızın gerçekleştirilen KABG operasyonlarına kıyasla perioperatif kanama ve serebrovasküler hastalık (SVH) gibi istenmeyen olaylar ve mortalite ile daha fazla ilişkili olduğu bildirilmekte [3,5,8] olup Wang ve arkadaşlarının yayınlarında KE ile postoperatif inme arasında bir ilişki olduğu ve bunun önlenebilmesi için ikili antiplatelet tedavi kullanımının önerildiği ifade edilmektedir. [3,8] Yine bir çalışmada 2 koroner arterine KE uygulanan hastalardan 1 tanesinde (%50) iskemik inme geliştiği bildirilmektedir.[3] Bizim çalışmamızda KE ile kombine KABG uygulanmış hastalardan 1 tanesinde postoperatif erken dönem SVH ve diğerinde postoperatif renal yetmezlik sonrası mortalite gözlenmiş olup postoperatif hemoraji/tamponad nedeniyle revizyon gerektiren hasta oranını %10 (1 hasta-postoperatif 0.gün) olarak saptadık ve 2 koroner arterine (LAD ve Optus marginalis arter) KE uygulanan bu hastada mortalite gerçekleşmedi.

KE ile kombine KABG uygulanan hastalarda KPB süresinin KE uygulanmaksızın KABG uygulanan hastalara kıyasla daha uzun olduğu bildirilmekte olup [3,8,18] aortik klemp ve KPB süresinde oluşan artışın renal hipoperfüzyon ve pıhtılaşma gibi komplikasyonlarla ilişkili olduğu da bildirilmektedir.[3,19] KE ile kombine KABG operasyonlarında KPB süresinin bypass greftleme yapılan koroner arter sayısına göre değişebileceği, literatürde bu sürenin ortalama 4+/-0.95 koroner artere bypass uygulanan hastalar için 192+/-56.5 dak olarak bildirildiği bir çalışmada KPB süresinin diğer yayınlara göre nispeten uzun olmasının operasyon tekniği, aterosklerozun şiddeti ve lokalizasyonu, yüksek kalsifikasyon oranı ve hastaların %98'inde LİMA kullanımına bağlı olduğu ifade edilmektedir. [2]Bizim çalışmamızda KE ile kombine KABG uyguladığımız hastalarda ortalama distal baypas sayısı 3.8+/-1.13 olarak saptanmış olup KPB eşliğinde KABG gerçekleştirilen hastalar için (9 hasta, ortalama distal baypas sayısı 4.11+/-0.6) ortalama KPB süresi 167.11+/-47.17dak olarak tespit edilmiştir ve KPB eşliğinde KABG uygulanan tüm hastalar için hesaplanan KPB süresinden (167 hastanın ortalama distal baypas sayısı 3.84+/-0.89, ortalama KPB süresi 121.71+/-33.30dak) daha uzun olup bu açıdan literatürle benzerdir. Çalışma grubumuzdaki hastaların %50'sinde açık teknikle KE gerçekleştirilmiş ve LAD anastomozlarının tamamında LİMA grefti kullanılmıştır.

Çalışmamızın tek merkezli, nispeten az hasta sayılı, kontrol grubu olmayan ve hastane otomasyon sistemi temelinde retrospektif tasarımlı bir çalışma olması gibi sınırlılıkları bulunmaktadır.

Sonuç olarak, hedef koroner arterlerde özellikle uzun segment aterosklerotik ciddi stenoz/oklüzyon ve ciddi kalsifikasyon varlığı gibi anastomoz kalitesini azaltan ve anastomozu zorlaştıran durumlarda KE ile kombine edilmiş KABG yönteminin daha uzun KPB ve aortik klemp süreleri olmasına rağmen özellikle cerrahi tecrübe ve uygun hasta seçimi varlığında güvenli ve sonuçlarının kabul edilebilir olabileceğini düşünmekle birlikte yüksek riskli hastaları belirlemek ve sonuçlar açısından daha belirgin bilgiler edinebilmek için daha fazla hasta sayılı çalışmaların yapılmasının yararlı olabileceğini düşünmekteyiz.

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Research Article

Systemic immune inflammation index may predict mortality in dialysis patients

Diyaliz hastalarında sistemik immün inflamasyon indeksi mortaliteyi öngörebilir

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Abstract

Aim: Renal failure patients have increased inflammation. Serum ferritin is an acute phase reactant. Systemic immune inflammation index is a new marker calculated using lymphocyte, neutrophil, and platelet counts and have been shown to be a prognostic marker for cardiovascular disease and cancers.

This study aims to determine the availability of Systemic immune inflammation index in determining the mortality risk of dialysis patients and the relationship between mortality and ferritin levels.

Material and Methods: This retrospective, multicenter study enrolled 84 patients on peritoneal dialysis and hemodialysis. Baseline demographic, clinical and laboratory data, were obtained from medical records. Inflammatory indices were defined as NLR: absolute neutrophil count divided by absolute lymphocyte count and SII: absolute platelet count multiplied by NLR.

Results: Mean age was 51.3 ± 20.1 years and the mean follow-up time was 60 (6 ~ 85) months. During the follow-up period, 45 (53%) patients died.

Study population was analyzed according to median ferritin level. Kaplan-Meier curves showed higher mortality in patients in the high ferritin group (log-rank test, P = 0.029)

Study population was analyzed according to median SII values. Kaplan-Meier survival analysis showed higher mortality in the group with the higher SII (log-rank test, P = 0.029)

In multivariate regression analysis age (HR 1.060, P=0.00), Kt/V(HR 0.161,P=0.014), CRP(HR1.001,P=0.0429 and SII(HR 1.001, P=0.00), and ferritin (HR 1.001, P=0.013) were the most important determinants of all-cause mortality.

Conclusion: SII, a novel inflammatory marker, and ferritin are related to all-cause mortality in dialysis patients. We believe that inflammation can be followed with SII and ferritin levels.

Keywords: Dialysis, Inflammation, Systemic immune inflammation index

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Öz

Amaç: Böbrek yetmezliğinde artmış inflamasyon söz konusudur. Serum ferritini bir akut faz reaktanıdır. Sistemik immün inflamasyon indeksi, kardiyovaskuler hastalıklarda ve kanserlerde prognostic önemi olduğu gösterilen, nötrofil, lenfosit ve trombosit sayılarından hesaplanan yeni bir belirteçtir. Bu çalışma, sistemik immün inflamasyon indeksinin diyaliz hastalarının mortalite riskini belirlemede kullanılabilirliğini ve mortalite ile ferritin düzeyleri arasındaki ilişkiyi belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: Çalışmaya 84 hemodiyaliz ve periton diyaliz hastası alındı. Hastaların bazal demografik, klinik ve laboratuvar verileri, tıbbi kayıtlardan elde edildi. Mutlak nötrofil lenfosit oranının, mutlak platelet ile çarpımı ile sistemik immün inflamasyon indeksi elde edildi.

Tartışma: Yeni bir inflamatuar belirteç olan Sistemik immün inflamasyon indeks ve ferritin, diyaliz hastalarında tüm nedenlere bağlı ölümlerle ilişkilidir. Diyaliz hastalarında inflamasyonun Sistemik immün inflamasyon indeks ve ferritin düzeyleri ile takip edilebileceğini düşünüyoruz.

Sonuç: Hastaların ortalama yaşı 51.3 ± 20.1olup, ortalama takip süreleri 60 (6 ~ 85) aydı. Takip süresince hastaların 45(%53) ü öldü. Hastalar medyan ferritin düzeyine göre analiz edildi. Kaplan-Meier analizine göre ferritinin yüksek olduğu grupta mortalitenin daha yüksek olduğu saptandı (log-rank test, P = 0.029).

Yine hastalar medyan sistemik immün inflamasyon indeksine göre analiz edildi. Kaplan-Meier analizine göre sitemik immün inflamasyon indeksinin yüksek olduğu grupta daha yüksek mortalite oranları saptandı (log-rank test, P = 0.029).

Çok değişkenli regresyon analizinde yaş (HR 1.060, P=0.00), Kt/V (HR 0.161, P=0.014), CRP (HR1.001, P=0.0429) ve Sistemik immün inflamasyon indeksi (HR 1.001, P=0.00) ve ferritin (HR) 1.001, P=0.013) tüm nedenlere bağlı ölümlerin en önemli belirleyicileriydi.

Anahtar kelimeler: Diyaliz, Enflamasyon, Sistemik immün inflamasyon indeks

Introduction

CKD is a public health problem with a high risk of mortality and morbidity. Patients with CKD have increased inflammatory mediators, probably because of excessive oxidative stress and extracellular fluid overload (1).

Serum ferritin level is considered as an acute phase reactant that is increased in inflammatory conditions such as CKD, liver disease, and cancer (2-5). A high ferritin level can lead to macrophage accumulation causing an increase in reactive oxygen metabolites (6). The association between serum ferritin and mortality in hemodialysis patients has been reported before (6-7).

Several traditional inflammatory cytokines, such as C-reactive protein (CRP), interleukin-6, and tumor necrosis factor-α, are positively correlated with poor survival (7,8). The neutrophil-to-lymphocyte ratio is a marker of inflammatory status and is considered to be a predictor of mortality in cardiovascular disease, end-stage renal disease, and cancer (9-12). The systemic immune inflammation index (SII), on the other hand, is a new marker calculated using lymphocyte, neutrophil, and platelet counts and have been shown to be a prognostic marker for cardiovascular disease and cancers (13-16).

This study aims to determine the availability of SII in determining the mortality risk of dialysis patients and the relationship between mortality and ferritin levels.

Material and Methods

This retrospective, observational, multicenter study enrolled 84 patients with end-stage kidney disease (ESKD) on peritoneal dialysis and hemodialysis at……. and…….. All patients with anemia were treated with erythropoiesis-stimulating agents (ESA) and received iron supplementation (intravenously or orally) when transferrin saturation (TSAT) was ≤30% and ferritin ≤500 µg/L. This study was conducted at .....from November 2014 to November 2021. Patients with a duration of maintenance dialysis of fewer than three months, with known malignancy and chronic inflammatory diseases, were excluded.

The study protocol was approved by the Medical Ethics Committee. We reviewed and followed up on the medical data according to the guidelines of our ethics committee. The patients were analyzed retrospectively, and the time of the death was recorded if mortality occurred.

Baseline demographic and clinical parameters, including age, sex, body mass index (BMI), primary kidney disease, and laboratory data, were obtained from medical records. Blood samples at the dialysis initiation were obtained from the medical records. Available laboratory data included systolic blood pressure (SBP), diastolic blood pressure (DBP), Kt/V, blood urea nitrogen (BUN), creatinine, phosphorus, calcium, cholesterol, triglycerides, LDL-C, HDL-C, serum ferritin, uric acid, CRP, albumin, hemoglobin, neutrophil count, lymphocyte count, and platelet count. Inflammatory indices were defined as NLR: absolute neutrophil count divided by absolute lymphocyte count and SII: absolute platelet count multiplied by NLR. Laboratory tests are recorded from the patient files at the beginning of the dialysis.

Descriptive results of continuous variables are reported as mean ± standard deviation (SD), and categorical variables are reported as percentages and numbers. Comparisons between groups were analyzed using a one-way analysis of variance and the chi-square test. The Spearman rank test was performed to estimate correlations. All-cause mortality was determined by Kaplan-Meier survival analyses with the log-rank test. Multivariate Cox regression analysis with forwarding regression was performed to adjust for confounding factors. A P value < 0.05 was considered statistically significant. All statistical analyzes were performed with the Statistical Package for the Social Sciences (SPSS) version 25.0 for Windows (SPSS Inc, Chicago, IL, USA).

Results

A total of 84 patients were included in the study. Baseline demographic, clinical, and laboratory parameters are shown in Table 1. The mean age was 51.3 ± 20.1 years, the male/female ratio was 49/35, and the mean follow-up time was 60 (6 ~ 85) months. During the follow-up period, 45 (53%) patients died. The underlying renal diseases were chronic glomerulonephritis (16.7%), diabetic nephropathy (13.1%), hypertensive nephropathy (29.8%), polycystic kidney disease (4.8%), chronic pyelonephritis (8.3%), and unknown (27.4%).

The median ferritin level was 419 ng/ml. The study population was analyzed according to ferritin level (ferritin level (group 1: ferritin < 419, group 2: ferritin > 419). A comparison of the groups with low and high ferritin levels at baseline can be seen in Table 2. The number of patients receiving hemodialysis was higher in group 2 (31% vs. 87%; p=0.00). EPO consumption was higher in group 2 (54.8% vs. 81%; p=0.01). SBP was lower in group 1 (121.19±19.1 vs. 131.8±16.5; p=0.007). There was a statistically significant difference between the two groups in Hb level, blood glucose, and neutrophil to lymphocyte ratio (11.0±1.5 vs. 10.2±1;p=0.005, 87±22 vs. 80±23; p00.036 and 3.86±2.01 vs. 4.07±2.14,p00.019, respectively) (Table 2).

İn correlation analysis, ferritin was not correlated with CRP, NLR, albumin, SII, or Hb levels (Table 3).

Table 1. Demographic, clinical and labarotory parameters in study population

Parameter	patients (n=87)
Age (years)	51±20
Gender (male, n, %)	35(41.7%)
BMI (kg/m2)	24.6±4,8
Comorbidites	
Diabetes (n, %)	13(15%)
Hypertension (n, %)	47 (56%)
Ischemic heart disease (n, %)	22 (26.2%)
Cause of CKD (n, %)	
Diabetes	11 (13.1%)
Glomerulonephritis	14(16.7%)
Hypertension	25(29.8%)
Polycystic kidney disease	4(4.8%)
Chronic pyelonephritis	7 (8.3%)
Unknown	23 (27.4%)
SBP (mmHg)	126.7±18.5
DBP (mmHg)	79.1±10
Kt/V	1.73±0.44
Hemoglobin (g/dL)	10.6±1.3
Glucose (mg/dl)	83±22
Albumin (g/dL)	3.9±0.4
TC (mg/dl)	166±38
TG (mg/dl)	168±114
HDL-C (mg/dl)	40±14
CRP(mg/L)	8.58±8.1
Ferritin(ng/ml)	424±252
NLR	3.96±2.06
SII	1278.14±1105.86

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; CRP, C reactive protein; NLR; neutrophil lymphocyte ratio; SII, serum immune inflamation index

Table 2. Comparision of low and high ferritin groups at the baseline

	Group1 (ferritin<419)	Group2 (ferritin>419)	p
Parameter			
Age (years)	50±15	51±17	0.922
Gender (male, n, %)	19(45.2%)	16(38.1%)	0.567
Dialysis type(HD)	13(31%)	36(87%)	0.00
EPO	23(54.8%)	34(81%)	0.01
BMI (kg/m2)	25.1±5	24.2±4.6	0.269
Comorbidites			
Diabetes (n, %)	8(18%)	5(11.9%)	0.365
Hypertension (n,%)	24(57.1%)	23(54.8%)	0.826
SBP (mmHg)	121±19.1	131.8±16.5	0.007
DBP (mmHg)	77±12	80±23	0.104
Kt/V	1.94±0.46	1.51±0.28	0.00
Hemoglobin (g/dL)	11.0±1.5	10.2±1	0.005
Glucose (mg/dl)	87±22	80±23	0.036
Albumin (g/dL)	3.9±0.4	3.9±0.3	0.896
TC (mg/dl)	170±39	163±37	0.338
TG (mg/dl)	167±113	169±116	0.717
HDL-C (mg/dl)	41±16	38±11	0.312
LDL-C (mg/dl)	90±27	84±27	0.352
CRP (mg/L)	8.83±8.32	8.32±7.95	0.553
NLR	3.86±2.01	4.07±2.14	0.019
SII	1212.32±754.15	1343.95±776.65	0.774

Table 3. Cox regression analysis

	Sig.	Exp(B)	95,0% CI for Exp(B)	
			Lower	Upper
Hb	,948	,991	,746	1,316
NLR	,291	,892	,721	1,103
Alb	,916	1,085	,236	4,981
SII	,000	1,001	1,000	1,001
Ferritin	,013	1,001	1,000	1,002
Age	,000	1,060	1,028	1,094
Kt/v	,014	,161	,037	,693
Glucose	,670	1,004	,986	1,022
CRP	,042	,930	,867	,997

SII was found to be positively correlated with NLR and CRP and negatively correlated with albumin levels

The ability of serum ferritin to predict mortality during a median follow-up of 60 months was investigated. Of the 84 patients, 45 died during follow-up. Kaplan-Meier curves showed higher mortality in patients in the high ferritin group (log-rank test, P = 0.029 (Figure 1).

The median value of SII was 1091.67, and the study population was divided into two groups: < 1091.67 (group 1) and > 1091.67 (group 2). Kaplan-Meier survival analysis was performed to understand the effect of SII on survival, and higher mortality was found in the group with the higher SII (log-rank test, P=0.01) (Figure 2).

To determine the independent predictors of all-cause mortality in dialysis patients, a Cox proportional hazard model was applied. After adjustment for age, sex, and other confounders (factors with P < 0.10 in univariate analysis), multivariate analysis was performed.

Age (HR 1.060, P=0.00), Kt/V(HR 0.161,P=0.014), CRP(HR1.001,P=0.0429 and SII(HR 1.001, P=0.00), and ferritin (HR 1.001, P=0.013)were the most important determinants of all-cause mortality..

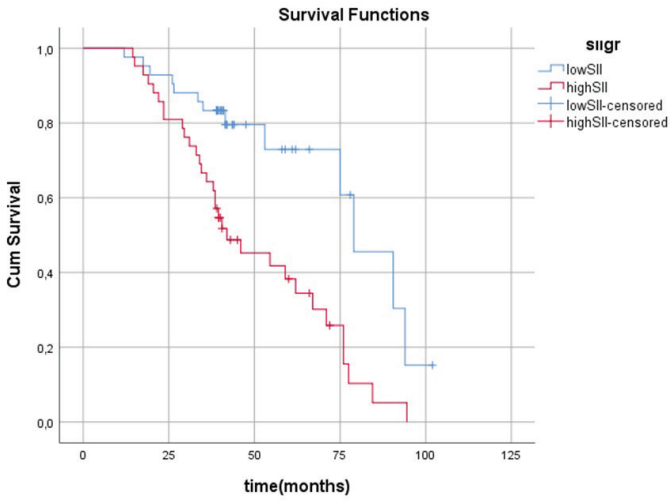

figure 1: Kaplan-Meier analysis of ferritin groups

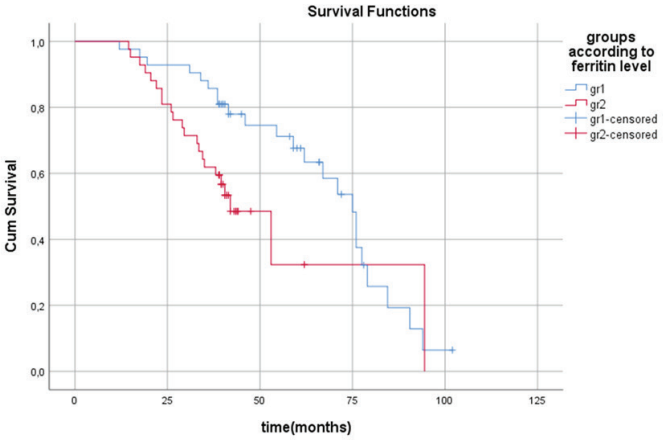

figure 2: Kaplan-Meier analysis of SII groups

Discussion

The most important finding of this study is the predictive value of ferritin and SII for mortality in dialysis patients.

Serum ferritin is an iron-containing protein. Apart from this function, it is an acute phase reactant and an inflammatory marker (4,17). It has been reported to be elevated in cancer with liver disease, coronary artery disease, and various immunological diseases (2,5,18,19). It is also associated with the rate of progression in patients with renal failure (20-22). Previous studies have demonstrated the association between high ferritin levels and mortality in dialysis patients (23-25).

The association between high ferritin levels and mortality is not fully known, but some mechanisms have been proposed. Serum ferritin escapes from damaged cells and loses most of the iron in the bloodstream. This free iron cannot be bound and increases cellular damage (26). In addition, aminolevulinate, a uremic toxin, can increase oxidative stress by causing the release of iron from ferritin (27).

The causes of inflammation in ESRD are diverse, and uremic toxins, concomitant comorbidities, and the dialysis process are some (28,29). It has been found that inflammation can indicate the long-term prognosis of ESRD patients based on some clinical indicators (30-32). Therefore, in this study, we investigated the use of ferritin as an inflammatory indicator and its effect on mortality.

A ferritin-mediated inflammatory cycle may explain why ferritin is a marker of mortality in dialysis patients. Ferritin molecule includes heavy (H) and light (L) chains. Inflammatory cytokines increase ferritin synthesis by increasing the synthesis of the H and L subunits (33). The increase in ferritin leads to a positive feedback loop with TLR9 activation, and inflammatory signals further increase (33). In addition, chronic inflammation in the uremic milieu has been reported to exacerbate vascular calcification and malnutrition and increase associated risk factors (14).

Although serum ferritin levels are almost always associated with inflammation, we did not find any correlation between inflammatory parameters and ferritin in correlation analysis. This could be the use of a single basal value, the use of iron supplements by patients, and the use of EPO.

The value of SII, an inflammatory marker, may be due to increased neutrophil and platelet counts and decreased lymphocyte counts. An increase in the neutrophil count has been shown to be associated with mortality in both cardiovascular disease and CKD (11-12).

Platelets are formed from the breakdown of megakaryocyte plasma. Megakaryopoiesis is regulated by inflammatory factors such as IL -6 and IL -1 (33). Similarly, inflammation in ESRD can also cause thrombocytosis through the action of cytokines (34). The authors suggested that SII is a more sensitive inflammatory marker because it is calculated with three cell types affected by inflammation (35).

Micro inflammation further accelerates the progression of atherosclerosis and is a crucial factor in the syndrome of malnutrition, inflammation, and atherosclerosis in ESRD patients (36). In inflammation, neutrophils are directly involved in tissue destruction (37). They do this through mediators such as myeloperoxidase and oxygen radicals (37). It has been reported that low lymphocyte count is associated with the progression of atherosclerosis and increased mortality, possibly caused by lymphocyte apoptosis (37).

Some limitations should be noted

1. This was a retrospective observational study conducted at a single center with a small sample size.

2. Only a single serum ferritin concentration was used, determined at baseline.

3. No other biomarkers of inflammation, including IL -1, TNF-α, and IFN-γ, were analyzed in addition to CRP.

Conclusion

Consequently, SII, a novel inflammatory marker, and ferritin are related to all-cause mortality in dialysis patients. We believe that inflammation can be followed with SII calculated from complete blood count parameters, which is a simple and inexpensive test. That ferritin measurement can also be a stimulating factor when the association between inflammation and mortality is considered. Prospective follow-up studies with a more significant number of patients are needed.

Ethics Committee Approval

Ethical Declaration Ethical permission was obtained from the Diskapi Yildirim Beyazit Training and Research Hospital Clinical Research Ethics Committee for this study with the date 12.09.2022 and number 146/10, and Helsinki Declaration rules were followed to conduct this study.

Author Contributions

All 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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Olgu Sunumu

Klinikopatolojik olarak tanı konan pulmoner odağı olmayan hepatobiliyer tüberküloz olgusu

A clinicopathologically diagnosed hepatobiliary tuberculosis case without pulmonary focal point

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Öz

Gelişmekte olan ülkelerde tüberküloz toplum sağlığını etkileyen büyük bir sorun olmaya devam etmektedir. Tüberküloz gibi kültür ortamında üretilmesi zor mikroorganizmaların neden olduğu enfeksiyonlarda, etken izolasyonu çok zor olabilmektedir. Tüberküloz pulmoner ve ekstrapulmoner olmak üzere iki ana grupta değerlendirilebilir. Pulmoner odağı olmayan hepatobiliyer tüberkülozda semptomların tipik olmaması ve tutulan organa ait bulgular ile karşımıza çıkması tanı konulmasını geciktirebilir. Bizim olgumuz buna güzel bir örnektir. Yirmibir yaşında erkek hasta kliniğimize kilo kaybı, iştahsızlık, yüksek ateş, bel ve sırt ağrısı şikayetleri ile başvurmuştur. Fizik muayene ve anemnez sonrasında hastada still, Brusellozis, Hepatit B virüs reaktivasyonu ön tanıları düşünülmüştür. Yapılan karaciğer biyopsisi ve histopatolojik değerlendirme sonucunda hepatobiliyer tüberküloz tanısı konulmuştur. Hastaya 3 ay süre ile 4'lü, takip eden 3 ay süreyle 2'li antitüberküloz tedavisi uygulanarak tam remisyon sağlanmıştır. Toplumda nadir görülen bu gibi olgularda hepatobiliyer tüberküloz ayırıcı tanıda göz ardı edilmemelidir. Ayrıca histopatolojik tanı yöntemlerinin unutulmaması gerekir. Tanıda biyokimyasal ve mikrobiyolojik yöntemlerin yetersiz kaldığı durumlarda ilk tercih olmasada invaziv girişimler ve histopatolojik tanı yöntemlerinin önemini göstermesi açısından sunulmuştur.

Anahtar kelimeler: tüberküloz; ekstrapulmoner tüberküloz; hepatobiliyer tüberküloz; histopatolojik tanı

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Abstract

Tuberculosis continues to be a major problem affecting public health in developing countries. Isolation of the causative agent can be very difficult in infections caused by microorganisms that are difficult to grow in culture media such as tuberculosis. Tuberculosis can be evaluated in two main groups as pulmonary and extrapulmonary. In hepatobiliary tuberculosis without a pulmonary focus, the absence of typical symptoms and the presence of findings related to the involved organ may delay the diagnosis. Our case is a good example of this. A 21-year-old male patient applied to our clinic with complaints of weight loss, loss of appetite, high fever, low back and back pain. After physical examination and anamnesis, preliminary diagnoses of still, Brucellosis, and Hepatitis B virus reactivation were considered. Hepatobiliary tuberculosis was diagnosed as a result of liver biopsy and histopathological evaluation. Complete remission was achieved by administering quadruple antituberculosis therapy for 3 months and double antituberculosis therapy for the following 3 months. Hepatobiliary tuberculosis should not be ignored in the differential diagnosis of such cases, which are rare in the community. In addition, histopathological diagnostic methods should not be forgotten. It is presented in terms of showing the importance of invasive interventions and histopathological diagnostic methods, although it is not the first choice in cases where biochemical and microbiological methods are insufficient in the diagnosis.

Keywords: tuberculosis; extrapulmonary tuberculosis; hepatobiliary tuberculosis; histopathological diagnosis

Giriş

Tüberküloz dünya genelinde büyük bir sağlık sorunudur ve gelişmekte olan ülkelerde %95'lik prevelansa sahiptir [1]. Türkiye'de yapılan bir çalışmada 1649 tüberküloz tanısı alan olgunun % 12,7'sinde (210) ekstrapulmoner tüberküloz (EPT) ve bunların sadece %0,95'inde hepatobiliyer tüberküloz saptanmıştır [2]. İzole hepatobiliyer tüberküloz nadir görülen bir hastalık olması ve bulguların spesifik olmaması nedeni ile hastaya tanı konması gecikebilir. Bizim olgumuzda da semptomların spesifik olmaması nedeni ile ayırıcı tanıda hepatobiliyer tüberküloz düşünülmemiştir. Bu nedenle hastanın şikayetlerinin başlamasından 3 ay sonra ve araştırıldığı üçüncü merkezde tanı konulmuştur.

Olgu Sunumu

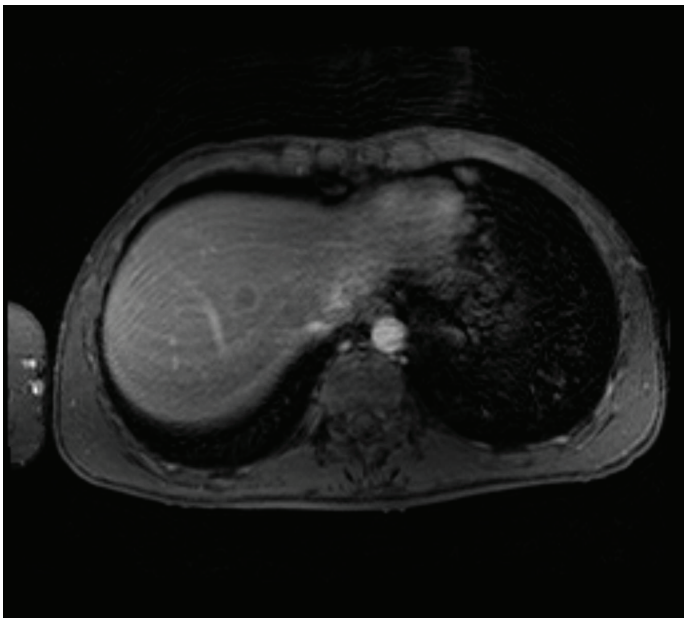
Yirmibir yaşında erkek hasta hastanemize müracatından iki ay önce kilo kaybı, bel ve yan ağrısı şikayetleri ile bulunduğu ilçe devlet hastanesine müracat etmiştir. Başlanan semptomatik tedaviye rağmen şikayetlerinde gerileme olmamıştır. Ateşi 38°C' yi geçen, iştahsızlık, kilo kaybı (6 ayda 6 kilo), eklem ağrısı olan hastanın şikayetleri artmaya başlayınca farklı bir merkeze müracat etmiştir. Yapılan tetkiklerinde Rose Bengal: Pozitif, HbsAg: Pozitif, Wright tüp aglütinasyon testi: Negatif, Lomber Ponksiyon: "BOS berrak, renksiz, hücre görülmedi" olarak sonuçlanmış. Still ön tanısı ile kolşisin tedavisi başlanmıştır. Torakoabdominal tomografide karaciğerde multiple hipodens alanlar saptanması üzerine ileri tetkik ve tanı için kliniğimize sevk edilmiştir.

Kliniğimizde yatırılarak takip edilen hastanın 4 yıldır bilinen Hepatit B Virüs taşıyıcılığı olduğu, 4 yaşında nefrolitiazis nedeni ile opere olduğu, taze peynir tüketiminin olduğu öğrenilmiştir. Aile içerisinde burusella öyküsü olması nedeni ile ayırıcı tanılar arasına Brusellozis eklenmiştir.

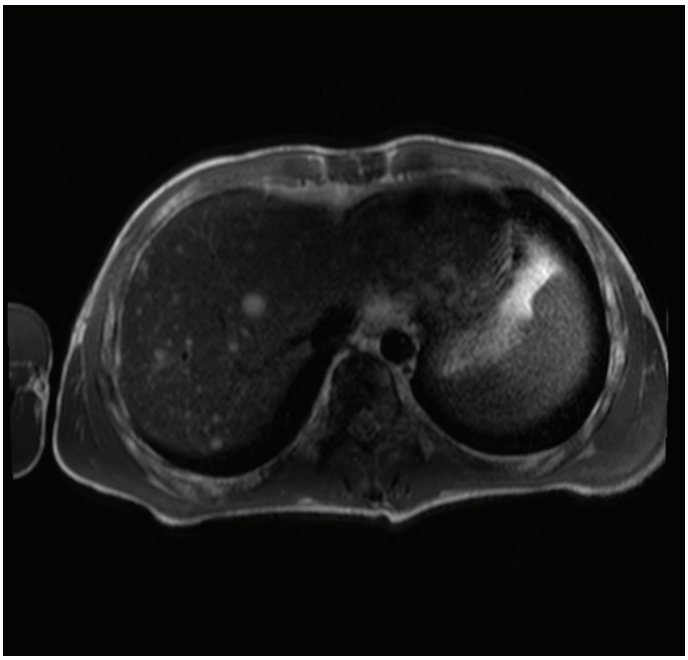
Yatışında 38°C üzerinde antipiretik tedaviye cevap vermeyen dirençli ateşi mevcut olan hastanın iştahsızlık, kilo kaybı, ateş, karın ve sırt ağrısı şikayetleri mevcuttu. Fizik muayenesinde umblikus çevresinde ve epigastrik bölgede hassasiyet, sağ kot altında hissedilen hepatomegali dışında bulguya rastlanmadı.

Yapılan görüntüleme ve laboratuvar tetkiklerinde, tüm batın ultrasonografisinde karaciğerde çok sayıda hipoekoik solid lezyon saptandı. Dinamik MRI da: "Hepatomegali (175 milimetre) saptanmış olup, tüm lob ve segmentlerde T1'de hipointens, T2'de hiperintens en büyüğü 15 mm'lik, bazılarında periferik tarzda kontrastlanma izlenen ayırıcı tanısında granülomatöz lezyonlar, hamartom ve hipovasküler metastazın göz önünde bulundurulması önerilir" [Şekil1-3]. Emisyon Tomografisinde (PET) malign bir lezyonla uyumlu olabilecek odak izlenememiştir. WBC:8750 K/uL, Hgb:11.1 g/dL, eritrosit sedimentasyon hızı:106 mm/saat, Üre:29 mg/dL, Kreatinin:0.7 mg/dL, AST:141 U/L, ALT:183 U/L, ALP:310 U/L, GGT:148 U/L, İNR:1.27, CRP:178 mg/L, HBV DNA: Negatif olarak saptanmıştır. Alınan kan kültüründe üreme olmadı, Tüberkülin Deri Testi (TDT): 10 mm altında (Negatif), Rose Bengal: Negatif, Mikoloji kültürü: Negatif, serolojik olarak TORCH: Negatif olarak sonuçlandı. Yapılan tüm tetkikler sonucunda tanı konamadı ve odağın hepatobiliyer sistem olduğu değerlendirildiği için hastaya karaciğer iğne biyopsisi planlandı. Karaciğer iğne biyopsisi sonucu patoloji raporunda "Yaygın nekroze alanlar mevcut, lenfosit infiltrasyonu ve hepatositlerde yaygın mitoz, kazeifikasyon nekrozu gösterir granülomlar

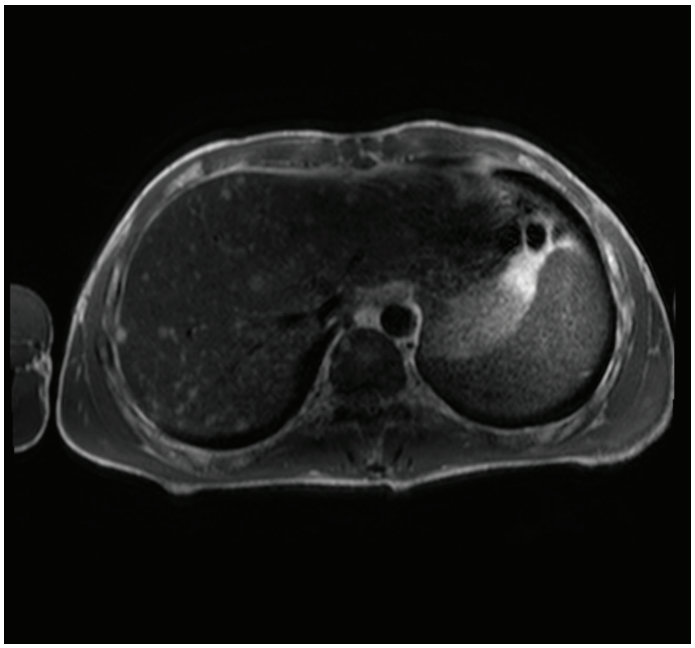
saptanmıştır" olarak raporlandı. Hastaya patoloji sonucuna göre hepatobiliyer tüberküloz tanısı kondu. Primer odak araştırmasında Akciğer dahil diğer organlarda odak saptanmadı. Hastaya 4'lü antitüberküloz tedavisi başlandı. Kontrollerinde 3 ay sonra hastanın şikayetlerinin geçtiği, karaciğer boyutlarının normal sınırlara gerilediği, lezyonların iyileştiği saptandı. Hastanın kontrollerinde herhangi bir sekel saptanmadı.



Şekil-1. Manyetik Rezonans Görüntülemede T1 sekansta karaciğer tutulumunu gösteren kesit



Şekil-2. Manyetik Rezonans Görüntülemede T2 sekansta karaciğer tutulumunu gösteren kesit



Şekil-3. Manyetik Rezonans Görüntülemede Karaciğerde çoklu odakları gösteren kesit

Tartışma

Tüberküloz, Mycobacterium tuberculosis'in neden olduğu tüm doku ve organları tutabilen enfeksiyöz bir hastalıktır. Pulmoner tutulum ve ekstrapulmoner tutulum olarak iki grupta değerlendirilebilir. EPT içerisinde pulmoner odak saptanmaksızın hepatik tutulum ile seyreden vakalar oldukça nadirdir. Türkiyede yapılan bir çalışmada 1649 tüberküloz tanısı konan hastanın % 12,7'sinde EPT ve bunların sadece %0,95'inde hepatobiliyer tüberküloz saptanmıştır [2]. EPT erkeklerde kadınlara göre 2 kat daha fazla görülür, her yaş grubunda saptanabilmesine karşın yapılan bir çalışmada en sık 11 ile 50 yaş aralığında saptandığı belirtilmiştir [3].

Tüberküloz basili karaciğere hematojen yayılım veya hepatopedal lenf damarları yoluyla ulaşır. Tüberküloz basili karaciğere hepatik arter yolu ile, fokal karaciğer tüberkülozu veya tüberküloz primer kompleksinde ise portal ven yoluyla ulaşır [4].

EPT olgularında pulmoner tüberküloza ait tipik semptomlar görülmez, sıklıkla tutulumun olduğu organa ait bulgular verir. Hepatobiliyer tüberküloz ise sıklıkla asemptomatik seyreder. Hepatobiliyer tüberkülozda en sık karşılaşılan semptomlar ise sağ üst kadran ağrısı (%65-%87), ateş, bulantı ve kusma gibi semptomatik bulgular (%55-%90), yaygın karın ağrısı (%50), sarılık (%20-%35), hepatomegali (%70-%96), splenomegalidir (%25-%55)[4]. Bu semptomlar karaciğerin diğer hastalıklarında görülebilen bulgulardır ve tüberkülozu düşündürecek özellikte değildir. Bizim olgumuzda olduğu gibi bu spesifik olmayan

bulgular nadir görülen hepatobiliyer tüberkülozun tanısının konmasını geciktirebilir hatta tanı konamamasına sebep olabilir.

Biyokimyasal tetkiklerde karaciğer transaminazlarındaki artışlar hepatik tüberküloza spesifik değildir. Hepatik tüberkülozlu hastaların %75'inde pulmoner tüberkülozu gösteren radyolojik bulgular saptanabilir. Ancak pulmoner tutulumu olmayan fokal hepatik tüberküloz olabileceği unutulmamalıdır [5]. Türkiyede 636 EPT olgusunda yapılan TDT'nin %95.5 i pozitif (10 milimetrenin üzerinde) saptanmıştır[6]. Türkiye'deki bir başka çalışmada ise aktif tüberkülozlu olguların % 32,7 sinde TDT 10 mm altında (negatif) saptanmıştır[7]. Bizim olgumuzda da TDT'de endurasyon çapı 10 milimetrenin altında (negatif) olarak saptanmıştır. TDT sonucunun negatif olarak sonuçlanmış olması tüberküloz tanısını dışlamaz.

Görüntüleme yöntemleriyle karaciğer odağının saptanması sonucu yapılan girişimsel radyolojik tetkik ve histopatolojik incelemeler sonucunda epiteloid granulom yapısı ve kazeifikasyon nekrozunun saptanması ile tanı konabilir. Türkiyede EPT tanılı hastalarda yapılan bir çalışmada olguların %36'sına tüberküloz tanısı histopatolojik olarak konulmuştur [6]. Bizim olgumuzda da tanı ancak biyopsi sonrası histopatolojik değerlendirme sonucunda konulmuştur. Tüberküloz tanısında kültürde mikroorganizmanın üretilmesi altın standart olsada, Mycobacterium tübercülosis'in üretilmesi zor bir bakteri olması nedeni ile birçok kültürde üretilememektedir. Olgumuza ait kan ve doku kültüründe tüberküloz basili üretilememiştir. Tanı sonrasında hastaya başlanan izoniazid, rifampisin, pirazinamid ve ethambutolden oluşan dörtlü antitüberküloz tedavisi ile yaklaşık 3 ay sonra hastanın tüm şikayetleri geçmiştir. Hastaya 3 ay daha ikili antitüberküloz tedavi verilmiştir. 6 ay sonrasında tam remisyon sağlanmıştır. Erken tanı ve tedavi ile sekelsiz iyileşme sağlanabilen, nadir bir hastalık olması önemlidir.

Sonuç

Toplumda nadir görülen bu gibi olgularda hepatobiliyer tüberküloz ayırıcı tanıda göz ardı edilmemelidir. Ayrıca histopatolojik tanı yöntemlerinin unutulmaması gerekir. Tanıda biyokimyasal ve mikrobiyolojik yöntemlerin yetersiz kaldığı durumlarda ilk tercih olmasada girişimsel ve histopatolojik tanı yöntemlerinin önemini göstermesi açısından sunulmuştur.

Hasta onamı

Hastadan vaka sunumu yapılacağına dair aydınlatılmış onam formu alınmıştır.

Çıkar Çatışması

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

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Case Report

Anesthesia Management in Emergency Cesarean Section of Pregnant with an Undiagnosed Neuromuscular Disease

Tanı Konulmamış Nöromüsküler Hastalığı Olan Gebenin Acil Sezaryen için Anestezi Yönetimi

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Abstract

A 30 year-old ASA II pregnant woman with an undiagnosed neuromuscular disease at 41 weeks of gestation was admitted to our hospital. Neurological examination is normal except lower extremity weakness that has been ongoing for the last 10 years. In this case report, we aimed to discuss general anesthesia management for emergency cesarean section of this particular pregnant woman.

Keywords: cesarean section; neuromuscular diseases; anesthesia

Öz

30 yaşında ASA II gebe kadın 41. gebelik haftasında tanı konmamış nöromusküler hastalık nedeniyle hastanemize başvurdu. Son 10 yıldır devam eden alt ekstremite güçsüzlüğü dışında nörolojik muayenesi normaldi. Bu olgu sunumunda, bu özel gebenin acil sezaryeninde genel anestezi yönetimini tartışmayı amaçladık.

Anahtar Kelimeler: sezaryen; nöromusküler hastalık; anestezi

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Introduction

Emergency cesarean section (CS) under anesthesia in a parturient with a history of neuromuscular disease carries high risk of morbidity and mortality due to increased risk of complicating respiratory muscle functions after general anesthesia or existing lower extremity weakness after spinal anesthesia [1]. In this case report, we aimed to discuss general anesthesia management in a pregnant woman with an undiagnosed neuromuscular disease history scheduled to undergo emergency CS.

Case

A 30-year-old ASA II pregnant woman (160 cm and 75 kg) at the 41 weeks of gestation in active labor was admitted to the emergency room and then immediately transferred to obstetric and gynecologic (OBGYN) clinic. The patient had a medical history of lower extremity weakness for the last 10 years. In the beginning of the pregnancy, the parturient was referred to rheumatology and neurology departments due to the pre-existing elevated creatinine kinase (CK) and liver function tests. The electromyography was reported as normal and examination of bilateral lower extremity iliopsoas muscle strength of the patient was noted as 3/5 but there was no weakness in the lower extremities. Thus, any connective tissue disease or myositis or vasculitis (monoclonal antibodies in the immunofixation and immune extraction electrophoresis in serum/plasma test were negative) was considered as a preliminary diagnosis. Consensus was made to wait for the postpartum period for further evaluations.

After emergency CS decision by the obstetricians due to the indication of non-progressed labor and cephalopelvic disproportion, written informed consent for operation and anesthesia, was obtained from the patient. In the preoperative anesthetic evaluation of the case, there is no known drug allergy, no history of anesthesia and surgery. Because of the undiagnosed neuromuscular disease history and current lower extremity weakness, we decided to perform general anesthesia using total intravenous anesthesia (TIVA) for this particular patient. We did not use inhalation anesthetics and depolarizing muscle relaxants because of the potential risk for malignant hyperthermia. We kept dantrolene ready in the operation room and monitored the patient's body temperature continuously [2]. After administering 10 mg of IV metoclopramide (Anti-Nausea 10mg/2ml, Onfarma, Samsun, Turkey) and 2 gram of cefazolin (Cezol 1g, Deva, İstanbul, Turkey®) IV before onset of surgery, 100% preoxygenation was followed by IV induction with propofol (Propofol-PF 1%, Polifarma,Tekirdağ,Turkey) (2.5 mg/kg) and 0.2 µg/kg/min remifentanil (Rentanil 2 mg ,Vem ilaç, Ankara, Turkey) infusion.

Adequate muscle relaxation was achieved using TOF (train of four) monitoring after giving 20 mg IV rocuronium (Muscuron 50mg/5ml, Koçak Farma, Tekirdağ, Turkey). When the TOF was 2, endotracheal intubation was facilitated with an ID of 7 mm endotracheal tube. Then, anesthesia was maintained with propofol (6-8 mg/kg/h) and remifentanil (0.1-0.2 mcg/kg/min) infusion. Four minutes after skin incision, a male baby (48.5 cm and 3070 grams) was born. Newborn's 1st and 5th minute APGAR scores were noted as 7/10 and 10/10, respectively. After umbilical cord clamping, oxytocin (Synpitan Forte 5 IU/ml, Deva, İstanbul, Turkey) 20 IU/1000 mL Ringer's lactate was administered by IV infusion. Uterine tone was achieved, bleeding control was done and CS operation was completed. For antagonizing residual neuromuscular block, IV sugammadex (Sugawake 200 mg/ 2 ml, Abdi İbrahim, İstanbul, Turkey) (2 mg/kg) was given. Then, the patient was extubated when spontaneous breathing returned. Meanwhile, the TOF ratio was greater than 0.9, and the patient was fully awake. For postoperative analgesia, 6 mg of IV morphine (Morfin Hidroklorür 0.01 gr/1 ml, Osel, İstanbul, Turkey) and 1 gram of IV paracetamol (Paracerol 10 mg/ml, Polifarma, Tekirdağ, Turkey) were administered. To prevent further nausea and vomiting, 1 mg of IV granisetron (Granitron 3 mg/3ml, Koçak Farma, İstanbul, Turkey) was added as an antiemetic. The case was followed in the recovery unit for about half an hour and then transferred to the ward for further follow up.

Discussion

Successful and uneventful management of general anesthesia using TIVA and TOF monitoring for an emergency CS of a pregnant woman with an undiagnosed neuromuscular disease history was presented.

Choice of anesthesia technique in a patient with a known neuromuscular disease is challenging but in case of an existing history of undiagnosed neuromuscular disease is more challenging [3]. Therefore, anesthesia technique should be selected with caution. We did not prefer spinal anesthesia for the present patient as it may complicate the existing lower extremity weakness. However, postoperative respiratory muscle functions of the patient may also be adversely affected after general anesthesia. Thus, we waited until the patient regained his muscle strength to start spontaneous respiration. We observed and confirmed the recovery of muscle strength

with TOF monitoring. We selected anesthetic drugs that could not result in further increase in creatinine kinase (CK) and liver enzymes. Considering the risk of respiratory distress in the postoperative period, we observed the patient closely because of a possible need for noninvasive or invasive mechanical ventilation during followed up in the PACU [4].

Conclusion

In a parturient with an undiagnosed neuromuscular disease plus increased liver enzymes, careful use of muscle relaxants via monitoring TOF under TIVA, seemed to be the appropriate approach for emergency CS with uneventful postoperative period.

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Letter To The Editor

Intracardiac Masses

İntrakardiyak Kitleler

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Öz

Budak ve arkadaşlarının yazısını ilgiyle okuduk. (1) "Atriyal Kitleyi Taklit Eden Spontan İntramural Sol Atriyal Hematomların Robot Yardımlı Yönetimi" başlıklı yazı derginin 1/2023 sayısında yayınlandı. Bu yazı için yazarları tebrik ederim.

Anahtar kelimeler: intrakardiyak, kitle, atriyal, ventriküler

Abstract

We read the article with great interest by Budak et al. (1) titled "Robot-Assisted Management of Spontaneous Intramural Left Atrial Hematoma Mimicking an Atrial Mass" published in the Issue 1/2023 of the journal. Congratulations to the authors for this article.

Keywords: intracardiac, mass, atrial, ventricular

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Intracardiac masses are one of the confusing issues in cardiac surgery. It is not easy to make a definite differential diagnosis of these masses. The reasons for this are; the heart is a dynamic organ in constant motion, difficulty in imaging due to circulating blood volume and cyclical shrinkage and enlargement, and difficulty in performing invasive procedures due to the risk of thromboembolism. For these reasons, the definitive diagnosis and treatment of intracardiac masses is usually surgical removal of the mass. However, recently, real-time sampling could be performed in two cases with left atrial masses by esophageal endoscopic ultrasound. Burkitt lymphoma was found in one case and synovial sarcoma in the other (2). Intracardiac echocardiography guided biopsy was also performed in a case with a mass in the left ventricle and stage 4 metastatic lung cancer was detected (3). Malignancies that spread hematogenously or lymphatic (such as lymphoma, leukemia, malignant melanoma, sarcoma) may form an intracardiac mass (4) and the primary treatment in these patients is usually chemotherapy, not surgery. Therefore, if there is a metastatic intracardiac mass due to a malignant disease, its treatment may not be primarily removed by open heart surgery. These patients should definitely undergo cardiac CT or MR imaging before surgery. These imaging methods can give an idea about whether the cardiac mass is a thrombus or a tumoral formation. Localization of the intracardiac mass is also important. For example, the mass in the right atrium may originate directly from the atrium wall or may extend through the inferior vena cava and reach the right atrium (5). Especially in tumors such as renal cell CA and intravascular leiomyoma, the mass may extend into the right atrium via the venous route. Direct spread can also occur in mediastinal cancers (thymus or lung cancers) (6).

In conclusion, the differential diagnosis of intracardiac masses is difficult and there is no definitive algorithm on this subject yet. When planning the operation, cardiac CT or MR imaging and even echocardiography guided biopsy should be performed if necessary, and if the mass is a thrombus or a primary tumor of the heart, it should be surgically removed. In metastatic or directly disseminated intracardiac masses, appropriate treatment should be performed according to the histopathological diagnosis of the tumor.

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TURKISH JOURNAL of CLINICS and LABORATORY

Türk Klinik ve Laboratuvar Dergisi

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

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

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

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

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

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

Dergi adının kısaltması: Turk J Clin Lab

Yazışma adresi: Yazılar e-mail yoluyla sorumlu yazar tarafından, Dergipark ta yer alan Turkish Journal of Clinics and Laboratory linkine girip kayıt olduktan sonra gönderilmelidir.

Makale dili: Makale dili Türkçe ve İngilizcedir. İngilizce makaleler gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanı tarafından düzeltilebilir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu amaçla, Türk Dil Kurumu Sözlük ve Yazım Kılavuzu yazım dilinde esas alınmalıdır.

Makalenin başka bir yerde yayımlanmamıştır ibaresi: Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. 400 kelimeden az özetler kapsam dışıdır. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

Değerlendirme: Dergiye gönderilen yazılar format ve plagiarism açısından değerlendirilir. Formata uygun olmayan yazılar değerlendirilmeden sorumlu yazara geri gönderilir. Bu tarz bir zaman kaybının olmaması için yazım kuralları gözden geçirilmelidir. Basım için gönderilen tüm yazılar iki veya daha fazla yerli/yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayıma kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir. Makalenin dergiye gönderilmesi veya basıma kabul edilmesi sonrası isim sırası değiştirilemez, yazar ismi eklenip çıkartılamaz.

Basıma kabul edilmesi: Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak basım sırasına alınır. Her yazı için bir doi numarası alınır.

Yayın hakları devri: http:/www.dergipark.ulakbim.gov.tr/tjclinlab adresi üzerinden online olarak gönderilmelidir. 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.

Etik kurallar: Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. Turkish Journal of Clinics and Laboratory gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Teşekkür yazısı: Varsa kaynaklardan sonra yazılmalıdır.

Maddi destek ve çıkar ilişkisi: Makale sonunda varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmelidir. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları "Cumulated Index Medicus" ta kullanılan stile uymalıdır. Kaynak sayısının araştırmalarda 25 ve derlemelerde 60, olgu sunumlarında 10, editöre mektupta 5 ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce köşeli parantez kullanılarak belirtilmelidir. Örneğin [4,5]. Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

Şekil ve tablo başlıkları: Başlıklar kaynaklardan sonra yazılmalıdır.

4. Şekiller: Her biri ayrı bir görüntü dosyası (jpg) olarak gönderilmelidir.

Makalenin basıma kabulünden sonra "Dizginin ilk düzeltme nüshası" sorumlu yazara e-mail yoluyla gönderilecektir. Bu metinde sadece yazım hataları düzeltilecek, ekleme çıkartma yapılmayacaktır. Sorumlu yazar düzeltmeleri 2 gün içinde bir dosya halinde e-mail ile yayın idare merkezine bildirecektir.

Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

Özpolat B, Gürpınar ÖA, Ayva EŞ, Gazyağcı S, Niyaz M. The effect of Basic Fibroblast Growth Factor and adipose tissue derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end to end anastomosis rat model. Turk Gogus Kalp Dama 2013; 21: 1010-19.

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Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

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Doktora/Lisans Tezinden alıntı;

Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

Sitenin adı, URL adresi, yazar adları, ulaşım tarihi detaylı olarak verilmelidir.

DOI numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of Complementary and Alternative Medicine into Family Practice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

Diğer referans stilleri için "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References" sayfasını ziyaret ediniz.

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