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ÖNSÖZ

Saygıdeğer Okurlar

A.Ü.Tıp Fakültesi Cerrahi Tıp Bilimleri Dergimizin 5. sayısı ile yine sizlerle buluşmaktan mutluyuz. Dergimize gönderilen makaleleri editoryal değerlendirmeler ve titiz bir hakemlik süreci ardından yayınlamaya devam ediyoruz. Yayınlarımızın daha geniş tabanlı ulaşılabilirliğini sağlamak ve kaliteli bilimsel indekslerde yer almak için büyük bir özen içindeyiz.

Ağustos 2023 sayımızda; 4 araştırma makalesi, 2 olgu sunumu bulunuyor.

-Önemli bir sağlık sorunu olarak karşımıza çıkan, diyabetik ayağın zorlu tedavi sürecini sağlık sistemine getirdiği mali boyut ile ele alan makalemiz,

-Periferik sinir yaralanmalarında asetik asitin nöroprotektif ve rejeneratif etkilerini histopatolojik, elektrofizyolojik olarak inceleyen ve asetik asitin antiinflamatuar, antioksidan ve nöroprotektif etkileri ile periferik sinir yaralanmalarının tedavisi için diğer çalışmalara da ışık tutacağı deneysel çalışma,

-Kadınlar için önemli bir sağlık sorunu olan ve cerrahi müdahale gerektiren makromasti olgularında WISE patern ve vertikal skarsız tekniğin sonuçlarının karşılaştırıldığı ve 8 yıllık cerrahi deneyimi sunan makalemiz literatüre değerli bilgiler sağlamakta.

-Tükrük bezi lezyonlarında preoperatif tanı, neoplastik ve non-neoplastik lezyonlarda farklılık gösteren tedavileri için önemlidir. Bu amaçla kullanılan en önemli tanı yöntemi olan İİAB sitolojilerinin tanı değerini ortaya koyan ve histopatolojik tanılarla karşılaştıran bu değerli çalışmayı da ilginize sunmaktan mutluyuz.

-Şiddetli mıtral yetersizliği olan miyokard enfarktüsü sonrası sol ventriküler anevrizma ve atipik yerleşimli dev soliter molluskum kontagiosum olgusunu ele alan olgu sunumları da dikkat çekici.

Editör ekibimize yurtdışı üniversitelerden hocalarımızın da dahil olmasının mutluluğu içindeyiz. California, San Francisco UCSF Tıp Fakültesi, Patoloji bölümünden ve Bilim Akedemisi üyesi Prof Dr. Tarık Tihan Hocamızın editöryel ekibimizdeki varlığından onur duymaktayız.

Makaleleri için dergimizi tercih eden yazarlarımıza, titiz çalışmaları için hakemlerimize ve editör kurulumuza, destekleri için Atatürk Üniversitesi Tıp Fakültesi Bilimsel Yayınlar koordüntörlüğümüze çok teşekkür ederim.

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İÇİNDEKİLER

OLGU SUNUMU

TREATMENT COST ANALYSIS IN PATIENTS WITH DIABETIC FOOT INFECTION: A RETROSPECTIVE STUDY

DİYABETİK AYAK ENFEKSİYONLU HASTALARDA TEDAVİ MALİYET ANALİZİ: RETROSPEKTİF BIR ÇALIŞMA

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Abstract

Introduction: Diabetic foot infection (DFI) and diabetic foot ulcer (DFU) are widespread complications of diabetes. The management and treatment of DFU, an important public health problem, can result in a significant economic burden on health systems. The purpose of this study was to reveal the general cost dimension in patients hospitalized in our clinic for treatment and care with diagnoses of DFI. **Materials and methods:** One hundred seventy-nine patients followed-up with diagnoses of DFI in our clinic between 1st of the January,2018, and 1st of the August, 2020, were included in this retrospective study. General cost totals including radiological imaging, laboratory tests, examination and consultation, bed costs, medical and surgical treatment (amputation, debridement), and dressing costs during patients' hospital stays were calculated. **Results:** The mean age of the 179 patients with DFI in this study was 61.5±10.9 years, and 122 (68.2%) were men. Mean duration of diabetes was 13.7±6.5 years. Based on the Infectious Disease Society of America classification, 55.9% of the cases with DFU were moderate, osteomyelitis was present in 41.3%, and 15.6% were receiving hyperbaric therapy. The general prevalence of amputation was 26.8%, with minor amputations representing 22.9%. Thirteen (7.3%) of the amputation cases had undergone more than one amputation. Repeat hospitalizations were observed in 54.7% of the patients during the study period. The general mortality rate was 2.8%. The mean treatment cost per capita among the patients with DFU was 9181.9±5155.3 Turkish lira. With the exception of the repeat hospitalization cases ($p<0.001$), no significant association was determined between per capita cost and any of the demographic and clinical variables investigated($p>0.05$ for all). **Conclusion:** There is a significant correlation between patients with repeated hospitalizations and cost. Awareness training programs including risk factors and foot care will contribute to a decrease in DFU development and related complications such as amputation in patients with diabetes mellitus.

Keywords: Diabetic foot infection, diabetic foot ulcer, cost

Özet

Giriş: Diyabetik ayak enfeksiyonu (DAE) ve diyabetik ayak ülserleri (DAÜ) diyabetin yaygın komplikasyonlarındandır. Önemli bir halk sağlığı sorunu olan DAÜ yönetimi ve tedavisi sağlık sistemlerinde önemli boyutlarda ekonomik yük oluşturmaktadır. Bu nedenle DAE tanısıyla kliniğimizde yatırılarak tedavi ve bakımı yapılan hastalardaki genel maliyet boyutunu ortaya koymayı amaçladık. **Materyal ve method:** Retrospektif olarak gerçekleştirilen bu çalışmada kliniğimizde 1 Ocak 2018 ile 1 Ağustos 2020 tarihleri arasında DAE tanısıyla takip edilen 179 hasta dahil edildi. Hastanede yattıkları süre içerisindeki radyolojik görüntüleme, laboratuvar tetkikleri, muayene ve konsültasyon, yatak masrafı, medikal ve cerrahi tedavi (ampütasyon, debridman), pansuman maliyetleri dahil olmak üzere genel maliyet toplamları hesaplandı. **Bulgular:** Çalışmaya dahil edilen 179 DAE'lu hastanın yaş ortalaması 61.5±10.9 yıl ve 122'si (%68.2) erkekti. Hastaların ortalama diyabet süresi 13.7±6.5 yıldı. DAÜ'li hastaların IDSA sınıflamasına göre %55.9'u orta derece olup, %41.3'ünde osteomiyelit bulunuyor ve %15.6'sı hiperbarik oksijen tedavisi alıyordu. Çalışmada genel amputasyon sıklığı %26.8 olup, %22.9'unu minör amputasyonlar oluşturuyordu. Amputasyonlu vakaların %7.3'ü (n=13) ise birden fazla amputasyon geçirmişti. Hastaların %54.7'sinin çalışma süresi kapsamında tekrarlayan hastane yatışları söz konusuydu. Vakalarda genel mortalite sıklığı ise %2.8 idi. DAÜ'li hastaların ortalama kişi başı tedavi maliyeti 9181.9±5155.3 TL idi. Kişi başı maliyet ile tekrarlayan hospitalizasyonu olan hastalar ($p<0.001$) hariç, incelenen değişkenlerin hiçbiri anlamlı ilişki göstermedi (tümü için $p>0.05$) **Sonuç:** Hastaneye tekrarlayan yatışı olan hastalarla maliyet arasında anlamlı bir korelasyon vardır. DAÜ oluşumuna neden olan risk faktörleri ve ayak bakımını içeren farkındalık eğitim programları DM'lu hastalarda DAÜ oluşumunu ve buna bağlı gelişen ampütasyon gibi komplikasyon oranlarının azalmasına katkı sağlayacaktır.

Anahtar Kelimeler: Diyabetik ayak enfeksiyonu, diyabetik ayak ülser, maliyet

1. INTRODUCTION

Diabetic foot infection (DFI) is one of the widespread complications of diabetes and is closely associated with morbidity, an increased risk of amputation, and high mortality (1). Several factors are involved in the development of diabetic foot ulcer (DFU). This particularly occurs as a result of weak glycemic control, neuropathy, and peripheral vascular disease or poor foot care (2). DFI develops as a result of complex interaction between these factors and the immune system (3).

DFIs lead to prolongation of hospital stays, impaired quality of life, morbidity, and even increased mortality rates in diabetic patients. Interestingly, DFU costs have been reported to be higher than the treatment costs for several forms of cancer (4). The management and treatment of DFU, an important health problem, impose a significant economic burden on health systems. The purpose of the present study was therefore to examine the general cost dimension in patients diagnosed with DFI hospitalized for treatment and care in our clinic in a center serving a large patient population in the east of Turkey.

2. MATERIAL AND METHOD

The data for patients followed-up with diagnoses of DFI at the Atatürk University Medical Faculty Infectious Diseases Clinic between 1 January, 2018, and 1 August, 2020, were included in this retrospective study. This study was started after the approval of the local ethics committee. One hundred seventy-nine patients whose records were suitable for the study, from the 414 individuals followed-up were enrolled. Patients' demographic characteristics, accompanying diseases, amputation status, and degrees of DFI were recorded. All ulcers were analyzed according to the severity of infection using the Infectious Disease Society of America (IDSA) and International Working Group on the Diabetic Foot (IWGDF) classification [5]. Grade 1, no symptom or sign of infection, Grade 2, local infection, Grade 3, local infection deeper than subcutaneous tissue without systemic inflammatory response symptoms (SIRS), and Grade 4, infections with SIRS. Patients with grade 2, 3, and 4 were included in the study. The patients with other relevant comorbid conditions requiring hospitalization (nephropathy, diabetic acidosis, etc.) were also excluded from the study.

Total general cost calculations were performed, including radiological imaging, laboratory tests, examinations and consultations, bed costs, medical and surgical treatment (amputation and debridement), and dressing costs during hospitalization. Cost calculations also included initial evaluations, and the diagnosis and treatment of underlying and accompanying diseases. Indirect costs, post-discharge treatment costs, post-amputation prosthesis, physiotherapy and wheelchair procurement are not included in the cost analysis.

All costs data were calculated in Turkish lira (TRY) then exchanged to US dollars using the Central Bank of the Republic of Turkey Exchange Rates-Banknotes (Converted to TRY) per year through 2018–2020. The exchange rate of US dollars to TRY for 2018, 2019, and 2020 were 4.81, 5.67, and 7.00, respectively.

Approval for the study was granted by the Ataturk University Medical Faculty Clinical Research Ethical Committee (no. B.30.2. ATA.0.01.00/368).

2.1. Statistical analysis

The study data were analyzed on SPSS version 22 software. Descriptive statistics were expressed as mean, standard deviation, number, and percentage. Compatibility with normal distribution was assessed using the Kolmogorov Smirnov Test, with graphing methods and z-values calculated for skewness and kurtosis coefficients.

3. RESULTS

The mean age of the 179 patients with DFI was 61.5±10.9 years, and 122 (68.2%) were men. The mean duration of diabetes was 13.7±6.5 years, and 36.65 % were active smokers or had histories of smoking. Patients had actively smoked for a mean 1.8±0.4 years. The three principal clinical features were peripheral neuropathy (34.4%), hypertension (21.1%) and cardiovascular diseases (15.5%). In terms of treatment for diabetes, 40.8% of patients were using insulin and 21.8% oral hypoglycemic (OH) medications. The patients' mean HbA1c level was 9.6±2.6. Based on the IDSA classification, 55.9% of the cases with DFU were moderate, osteomyelitis was present in 41.3%, and 15.6% were receiving hyperbaric oxygen therapy. The incidence of amputation was 25.8%, with minor amputations representing 22.9%. A history of more than one amputation was present in 7.3% (n=13) of cases. Soft tissue infection only was present in the remaining cases (73.2%). Repeated hospitalizations during the study period were present in 54.7% of patients. The general mortality rate was 2.8%. The patients' demographic and clinical characteristics are shown in Table 1, and Table 2.

The mean per capita treatment cost of the patients with DFU was 9181.9±5155.3 Turkish lira (TL). With the exception of patients with repeated hospitalizations ($p<0.001$), none of the variables exhibited a significant relationship with per capita treatment cost (for all $p>0.05$) (Table 3, 4).

Table 1: The patients' demographic characteristics

Variables		n (%)
Gender	**Female**	57 (31.8)
	Male	122 (68.2)
Education level	**Illiterate**	49 (27.4)
	Elementary/middle school	105 (58.7)
	High school	19 (10.6)
	University	6 (3.4)
Place of residence	**Village**	41 (22.9)
	District	55 (30.7)
	Urban center	83 (46.4)
Smoking status	**Smoker**	62 (34.6)
	Non-smoker	117 (65.4)
	Duration of smoking (years)	1.8±0.4

Table 2: The patients' clinical characteristics

Variables		n (%)
Clinical characteristics	**PNP**	122 (34.4)
	HT	75 (21.1)
	CVD	55 (15.5)
	Hypercholesterolemia	39 (11.0)
	PAD	32 (9.0)
	PVI	17 (4.8)
	Hemodialysis	15 (4.2)
Diabetes treatment	**Insulin**	73 (40.8)
	Oral hypoglycemic	39 (21.8)
	Insulin and oral hypoglycemic	67 (37.4)
IDSA	**Grade 2**	60 (33.5)
	Grade 3	100 (55.9)
	Grade 4	19 (10.6)
Osteomyelitis	**Yes**	74 (41.3)
	No	105 (63.1)
Hyperbaric therapy	**Yes**	28 (15.6)
	No	151 (84.4)
Amputation status	**None**	131 (73.2)
	Minor	41 (22.9)
	Major	7 (3.9)
Number of amputations	**Single**	35 (19.5)
	Multiple	13 (7.3)
Repeat hospitalization	**Yes**	98 (54.7)
	No	81 (45.3)
Mortality	**Yes**	5 (2.8)
	No	174 (97.2)

Table 3: The cost results according to the demographic characteristics of the patients

		General Cost Per Case		
		Mean±SD	**Median[Q1-Q3]**	**p**
Gender	Female	8366±9671.5	4875[2878.2-9449.2]	0.96
	Male	9563±16222.7	5177[2912.7-10133]	
Education level	Illiterate	9375±10944.4	7307[2883.1-10299.6]	0.681
	Elementary-middle school	9065±16659	4523.4[2908-9449.2]	
	High school	7919±7593.6	5971.2[3475.1-9929.8]	
	University	13647±16342.8	5857.7[5086.1-17819]	
Place of residence	Village	8255±7881.5	5648.1[2883.5-9974.1]	0.681
	District center	10361±21451.2	6016.7[3358.8-10133]	
	Urban center	8859±10867.7	4522.3[2643.8-9929.8]	
Diabetes treatment	Insulin	8998±9691.9	5571.9[3467- 10988.9]	0.369
	OH	6453±6097.6	4522.3[2562.5-8266.9]	
	Insulin+OH	10971±20763.7	5761.8[2883.5-10136.8]	
Smoking status	Smoker	9112±20655.4	4409.9[2608.7-7478.5]	0.91
	Non-smoker	9219±9787.6	5806.7[3111.2-10350.2]	

4. DISCUSSION

Cost analysis was performed for 179 patients with DFI over an approximately three-year period. No significant correlation was determined between total cost and patients' demographic characteristics, underlying diseases, degree of DFU, or amputation status. However, significant correlation with cost was determined in patients with repeated hospitalizations.

Diabetes mellitus (DM) is a chronic disease requiring lifetime resources in order to prevent complications developing over the course of time and for treatment. The costs entailed in diabetic foot lesions include interventions aimed at preventing foot ulcer development, treatments to shorten wound healing time, strategies to prevent amputation, the management of post-amputation disability, and patient care (6). Increasing numbers of individuals worldwide are being affected by DM, and patients' quality of life is compromised as a result of severe complications such as DFU and infection.

Various studies have reported amputation rates in DFUs in Turkey. In a study of 138 patients with DFI, Karagöz et al. reported a major amputation rate of 28.5% and a total amputation rate of 57% (7). Another study cited an amputation rate of 18% (8). The frequency of lower extremity amputation has been reported to be in decline over the last 30 years (9). However, there are also studies citing high amputation rates (10-12). The general amputation rate among patients with DFI in the present study was 26.8%, with a major amputation rate of 3.9%. A previous prospective study performed in our clinic determined an amputation rate of 28.5% among 137 patients followed-up due to DFI (13). Our clinic has been serving DFU patients on an intensive patients for approximately three years. Patients under follow-up are given instruction concerning wound care and prevention, and are informed about early presentation to health centers. Patients with DFI and repeated hospitalizations can thus be identified and treated early. This may explain our lower amputation rate compared to other studies. Awareness programs including the risk factors involved in DFU formation and foot care will contribute to reducing the development of DFU and rates of associated complication such as amputation in patients with DM.

Approximately half of DFUs become infected during treatment (14). Our mild, moderate, and severe DFU rates based on the IDSA-IWGDF classification system were 33.5%, 55.9% and 10.6%, respectively. In a study conducted in our country, DFIs were staged using the Wagner classification, and 15 of 63 patients were evaluated as stage 3 and 10 as stage 4 within a period of approximately one year. (15). According to an IDSA report using the IDSA-IWGDF system, 47% of cases were mild, 34% moderate, and 17.9% severe (5). The lower incidence of severe cases in the present study may be attributable to the earlier recognition of infection by patients and the prompt initiation of the necessary treatments.

Table 4: The cost results according to the clinical characteristics of the patients

		Mean Standard deviation	Median[Q1-Q3]	p
Hypercholesterolemia	Yes	8180±7836.5	5648.1[2912.7-9213.7]	0.532
	No	9461±15812.4	4908.5[2835.7-10065.1]	
Hemodialysis	Yes	8907±9914	5232.1[3130.7-11257.7]	0.807
	No	9207±14811.9	5140.2[2880.6-9985.6]	
CVD	Yes	11399±21788.4	6278.3[3111.2-13487.2]	0.166
	No	8199±9505	4908.5[2761-9557.2]	
HT	Yes	11545±20496.4	5806.7[2643.8-11938.9]	0.503
	No	7478±7193.5	4990.6[3125.4-9173.4]	
PAD	Yes	14472±28659.3	7447[3925.4-10844.8]	0.116
	No	8030±8515	4875[2793.3-9929.8]	
PVI	Yes	11632±14074.3	6540.2[4319.1-11257.7]	0.203
	No	8925±14501.2	5105.6[2793.3-9974.1]	
PNP	Yes	8408±9358.4	4908.5[2883.5-9449.2]	0.719
	No	10838±21676.1	5806.7[2931.6-10133]	
Amputation	None	9346±16284.7	4597.2[2412.8-10136.8]	0.091
	Minor	8986±7765.6	7118.5[4009.5-9929.8]	
	Major	7257±6054.7	4358.8[3468.7-8879.3]	
Number of amputations	1	7848±6625.8	5648.1[3577-9929.8]	0.107
	>1	11118±9380.6	8879.3[7067.8-9449.2]	
Osteomyelitis	Yes	11215±20177	5832.4[3358.8-10431.9]	0.166
	No	7749±8143.9	5086.1[2562.5-9004.7]	
IDSA	Grade 2	6814±7100.5	4475.3[2623.8-8498.1]	0.279
	Grade 3	10190±17446.6	5704.9[3011.9-10322.4]	
	Grade 4	11354±13948.3	6540.2[2951.1-11240.3]	

Hyperbaric therapy	Yes	17234±30614.1	6205.8[3969.7-17844.3]	0.061
	No	7689±8033.7	5039.2[2676.3-9213.7]	
Repeated hospitalization	Yes	12397±18569.7	7031[4009.5-13902.5]	*0.001*
	No	5292±4258.7	3824.9[2235.3-7415.5]	
Mortality	Yes	15482±19108.9	4009.5[2912.7-21871.6]	0.746
	No	9001±14319.5	5177[2883.5-9974.1]	

Table 5: Distribution of cost components by years

Cost components	**2018 (mean±SD)**	**2019 (mean±SD)**	**2020 (8 months) (mean±SD)**
Radiology	223.6±275.4	375.0±984.2	252.4±346.4
Tests	791.5±909.3	1073.6±1319.8	585.0±643.5
Examination/Consultation	75.2±95.6	102.2±128.5	57.4±51.0
Bed	1450.0±3029.7	1249.8±1488.0	848.4±1332.7
Other (dressings, local treatments, debridement)	3491.7±15632.2	2984.6±4289.4	2616.9±3100.6
Total	5963.6±16131.2	5736.0±6986.3	4314.3±4800.4

Several studies have investigated the economic outcomes of DFU and amputations. Although it is not possible to perform an exact comparison among such studies, diabetic foot cost rates in health spending appear to have risen significantly in recent years. The calculation of total costs resulting from extremity amputation should involve more than surgery and the care of hospitalized patients (6). They should also include outpatient services and topical wound treatments until full recovery, as well as the cost of workforce losses during the time that patients are not working. There are studies describing topical wound care and inpatient costs as the most important expenditures in patients with DFU (16, 17). Inpatient and topical wound care costs during hospitalization were included among the total cost results in the present study. However, topical care costs among discharged patients, physiotherapy, wheelchair provision, and costs arising from workforce losses were not included. Previous research and the present study show that diabetic foot lesions result in serious health spending. The total costs of the DFI patients in the present study, including beds, dressings, topical treatment, surgical debridement and amputation exceeded the cost involved for radiology, analysis, and examination/consultation (Table 5).

One study from Turkey reported a mean cost of $ 3880 (US dollars) for a patient with DFI hospitalized for treatment (7). Gonen et al. analyzed the costs for 80 patients and reported a mean per capita figure of $ 2573 (18). Another study calculated a mean cost of $ 976 per patient with diabetic foot (19). The primary risk factors for hospitalization and the development of complications in patients with DFU include an advanced degree of DFU and severe infection. Hospital stays are longer and direct costs higher in patients with moderate and severe infection in particular (20).

A Swiss study investigating DFI costs in 220 patients reported a mean healing time of 29 weeks in patients with no amputation requirement, and of 52 and 38 weeks in patients with minor and major amputation, respectively (6). A longer healing time was reported in minor compared to major amputations. The total cost per patient among those improving without amputation was $ 17,554, compared to $ 33,540 for patients with minor amputation and $ 30,135 for those with major amputation. Costs increased in patients with DFU as non-infected ulcers progressed toward infection, gangrene, and amputation (6). In the present study, treatment costs including local wound care, dressing, surgical debridement, and amputations in patients with DFI were greater than the radiology, analysis, examination/consultation costs. In addition, it was observed that the cost in patients without amputation was higher than in patients with amputation. We think that this situation causes a longer stay in the hospital and an increase in wound care costs, since most of our patients who require amputation do not accept surgical procedures. The decrease in treatment costs over the years may be attributable to the development of strategies aimed at preventing, the education of patients and relatives, and early detection and treatment of ulcer infection by the physician.

As a limitation of our study, Cost findings should now be further detailed through prospective studies that also evaluate the costs of transportation to health services, household spending, and financial losses caused by an inability to work, which are not reflected in national health calculations. In addition, the lack of cost analysis regarding the service received from an external center during hospitalization, external prescription, treatment cost after discharge, prosthesis after amputation, physiotherapy and wheelchair supply is another limitation of our study.

The care costs for diabetic foot exceed those of such major diseases as cancer, lung disease, and depression (21). It is estimated that by 2030 10% of the world population will be diabetic, and that that diabetic foot costs will also rise as a result (22). In conclusion, direct costs (such as diagnosis, treatment, and wound care) during inpatient treatment in patients with DFI are rising on a daily basis. In order to reduce the costs entailed by diabetic foot, the development of the condition must be prevented by providing awareness training concerning DFU and DFI for patients, relatives, and healthcare providers.

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Conflict of interest: None

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DENEYSEL OLARAK RATLARDA OLUŞTURULAN PERİFERİK SİNİR YARALANMALARINDA ASİATIK ASİT'İN ROLÜNÜN İNCELENMESİ

INVESTIGATION OF THE ROLE OF ASIATIC ACID IN EXPERIMENTALLY CREATED PERIPHERAL NERVE INJURIES IN RATS

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Özet

Amaç: Deneysel olarak aksonotmezis ve nörotmezis tipi yaralanma modellerinde Asiatik Asit'in (AA) nöroprotektif ve rejeneratif etkileri histopatolojik, elektrofizyolojik ve klinik olarak incelendi. **Gereç ve Yöntem:** 56 adet erkek Spraque-Dawley cinsi erkek sıçan, yedi alt gruba ayrıldı. Grup1 (kontrol), Grup2A (aksonotmezis sonrası 28 gün oral serum fizyolojik verilen grup), Grup2B (aksonotmezis sonrası 10/mg/kg/gün x 28 gün oral AA tedavisi verilen grup), Grup2C (aksonotmezis sonrası 20/mg/kg/gün x 28 gün oral AA tedavisi verilen grup), Grup3A (nörotmezis sonrası oral serum fizyolojik verilen grup), Grup3B (nörotmezis sonrası 10/mg/kg/gün x 28 gün oral AA tedavisi verilen grup) ve Grup3C (nörotmezis sonrası 20/mg/kg/gün x 28 gün oral AA tedavisi verilen grup) olarak tanzim edildi. Fonksiyonel değerlendirme için yürüme testi, siyatik fonksiyon indeksi, ektansör postural thrust ve gastroknemius kası ağırlık indeksi parametrelerine bakıldı. Elektrofizyolojik değerlendirme için elektromyografi (EMG) yapıldı. Tüm gruplar 28.gün sonunda sakrifiye edildi. Siyatik sinirler ve gastroknemius kasları eksize edildi. Siyatik sinirler hemotoksilen-eozin ve toloudin mavisiyle, gastroknemius kası ise masson trikrom ile histopatolojik olarak boyandı. Siyatik sinirler; anti-TNF-alfa, anti-TGF-beta, anti-NGF ve anti-S100 ile immünohistokimyasal olarak da boyandı. Boyamalar sonrası preperatlar semikantitatif ve stereolojik yöntemlerle incelendi. Sonuçlar istatiksel olarak analiz edildi. **Bulgular:** Aksonotmezis ve nörotmezis yapılan gruplarda klinik, elektrofizyolojik ve histopatolojik olarak güncel literatür ile paralel patolojik bulgular elde edildi. AA verilen tüm grupların, ilaç verilmeyen travma gruplarına göre histopatolojik, klinik ve elektrofizyolojik değerlendirmede istatiksel olarak anlamlı olduğu gözlendi. Ayrıca tedavi grupları içerisindeki doz farklılıklarının histopatolojik iyileşmede istatiksel olarak anlamlı bir fark oluşturmadığı görüldü. **Sonuç:** Analizler sonucunda oral asiatik asit verilen gruplarda; rejenere akson sayısı, miyelin formasyonu ve denerve kas atrofisinin restorasyonunda pozitif yönde anlamlı görüntüler tespit ve klinik testlerle teyit edildi. Bu nedenle asiatik asitin antiinflamatuar, antioksidan ve nöroprotektif etkileriyle periferik sinir yararlanmalarının tedavisine katkılar sağlayacağı ve periferik sinir yaralanmalarının tedavisi için yapılacak diğer çalışmalara ışık tutacağı kanaatindeyiz.

Anahtar kelimeler: Asiatik asit, periferik sinir yaralanmaları, travma, sıçan modeli

Abstract

Objective: The neuroprotective and regenerative effects of Asiatic Acid (AA) were examined histopathologically, electrophysiologically and clinically in axonotmesis and neurotmesis type injury models experimentally. **Material and Method:** 56 male Spraque-Dawley male rats were divided into seven subgroups. Group1 (control), Group2A (the group that received oral saline for 28 days after axonotmesis), Group2B (the group that received 10 / mg / kg / day x 28 days of oral AA treatment after axonotmesis), Group2C (the group that received 20 / mg / kg / day x 28 days of oral AA treatment after axonotmesis), Group3A (the group that received oral saline for 28 days after neurotmesis), Group3B (the group that received 10 / mg / kg / day x 28 days of oral AA treatment after (neurotmesis) and Group3C (the group that received 20 / mg / kg / day x 28 days of oral AA treatment after neurotmesis). For functional evaluation; walking test, sciatic function index, extensor postural thrust and gastrocnemius muscle weight index parameters were measured. Electromyography (EMG) was performed for electrophysiological evaluation. All groups were sacrificed at the end of the 28th day. Sciatic nerves and gastrocnemius muscles were excised. Sciatic nerves were histopathologically stained with hemotoxylin-eosin and toloudin blue, and gastrocnemius muscle with masson trichrome. Sciatic nerves; It was also stained immunohistochemically with anti-TNF-alpha, anti-TGF beta, antiNGF and anti-S100. After staining, the preparations were examined by semi quantitative and stereological methods. Results were analyzed statistically.**Results:** Clinical, electrophysiological and histopathological pathological findings were obtained in parallel with the current literature in the groups that underwent axonotmesis and neurotmesis. It was observed that all groups given AA were statistically significant in histopathological, clinical and electrophysiological evaluation compared to the trauma groups that were not given medication. In addition, it was observed that the dose differences within

the treatment groups did not make a statistically significant difference in histopathological improvement. **Conclusion:** As a result of the analysis, in groups given oral asiatic acid; Significant positive images in the restoration of regenerated axon count, myelin formation and denervated muscle atrophy were detected and confirmed by clinical tests. Therefore, we believe that asiatic acid will contribute to the treatment of peripheral nerve injuries with its anti-inflammatory, antioxidant and neuroprotective effects and will shed light on other studies for the treatment of peripheral nerve injuries.
Keywords: Asiatic acid, peripheral nerve injuries, trauma, rat model

1. GİRİŞ

Periferik sinir sistemi (PSS), merkezi sinir sistemi (MSS) ile nihai organlar arası her türlü duyusal, motor, endokrin iletişimin ve koordinasyonun sağlandığı çok gelişmiş bir ağdır. Bu sistemde meydana gelebilecek bir hasar canlı organizma için ciddi kayıplara yol açabilir. Periferik sinir yaralanmalarının etyolojisinde; travma, ezilme, bası, laserasyon, gerilme ve kimyasallar gibi bir takım sebepler vardır (1, 2). Periferik sinir hücresinin; wallerian dejenerasyon, aksonal dejenerasyon ve segmental demiyelinizasyon olmak üzere yaralanma tipleri mevcuttur. Sinir lifi travma sonrası hücreden ayrı kalan kısımda morfolojik, kimyasal ve fonksiyonel olarak gelişen değişikliklerin tümüne sinir dejenerasyonu denir. Sinirde meydana gelen bu değişikliklere wallerian dejenerasyon (WD) adı verilir. WD'ye uğramış bir sinirin iyileşip normal fonksiyonunu kazanmasına rejenerasyon denir (3). Wallerian dejenerasyonun da immün süreçte nötrofiller, makrofajlar ve T hücreleri de dahil olmak üzere çok sayıda immün hücrenin, patojenik süreçlere katkıda bulundukları sinir hasarını takiben yaralı bölgelere alındığı bilinmektedir. Periferik sinir yaralanmaları sonrası inflamatuar sürecin tetiklenmesiyle oksidatif stresin artması ve inflamatuar mediatörlerin salınımı artmaktadır. Asiatik asit (AA) doğal bir pentasiklik triterpenoid olup geniş farmakolojik etkileri sayesinde oldukça umut vaad eden bir bileşiktir. Yapılan çalışmalarda AA' nın antioksidan, antienflamatuvar ve analjezik etkileri olduğu gösterilmiştir. Çalışmalarda AA'nın NOS enziminin aktivitesini etkileyerek antiinflamatuar ve süperoksit dismutaz gibi antioksidan enzim aktivitelerini artırarak da antioksidan etkiye sahip olduğu görülmüştür. Yine yapılan çalışmalar da NF-kB'nin 'downregülasyonu' ve MAPK fosforilasyonunun baskılanması ile NOS, COX2, İL-1b, İL-6 ve TNF-a ekspresyonun inhibisyonu ile AA'nın antiinflamatuar etki gösterdiğini rapor edilmiştir (4, 5). Bir çalışmada ise nöroprotektif etkisini, beyinde kan-beyin bariyerini stabilize ederek ve mitokondriyal metabolizmayı düzenleyerek sağladığı gösterilmiştir (6). Asiatik asitin periferik sinirde aksonotmezis ve nörotmezis tipi yaralanmalarda sinir rejenerasyonunda rolü ve katkısı ilk kez gösterilecektir. Çalışmamızda asiatik asitin dozlarını daha önceki çalışmalara göre belirledik (7). Asiatik asit antiinflamatuar, antioksidan, nöroprotektif ve analjezik etkilerinden dolayı periferik sinir yararlanmalarında muhtemel yeni katkılar sağlayacaktır.

2. MATERYAL VE METOD

Erzurum Atatürk Üniversitesi Hayvan Deneyleri Yerel Etik Kurulu'nun 18.02.2020 tarihli ve 42190979-000-E.2000053833 sayılı izni ile yapıldı. Denekler Erzurum Atatürk Üniversitesi Deney Hayvanları Laboratuvarından temin edildi. Ağırlıkları 200- 250 gr arasında olan 56 tane erkek Spraque-Dawley rat kullanıldı. Deneklerin sağlıklı, daha önce ilaç verilmemiş ve herhangi bir deneyde kullanılmamış olmalarına dikkat edildi. Denekler cerrahi işleme başlamadan 12 saat önce aç bırakıldı ve ağırlıkları ölçülerek kaydedildi. Deneklerin 28 günlük deney boyunca ağırlıkları günlük ölçüldü ve ilaç doz ayarlamaları ağırlıklarına uygun olarak hassas terazide yapıldı ve gavajla oral yolla deneklere verildi. Deneyler mikroskop eşliğinde ve mikrocerrahi ekipmanları ile yapıldı. Deneyler sırasında kullanılan Asiatic Asit ürün bilgileri; Alfa Aesar™ Asiatic acid, %97 500 mg, H60149. ME, Code: NEW, Additional Details: CAS Number: 464-92-6, product of China, ThermoFisher (Kandel) /Germany şeklindedir. Üretici firma tarafından iyofilize halde -20°C'de soğuk zincirde teslim edilen AA, oda sıcaklığında Atatürk Üniversitesi Tıp Fakültesi Biyokimya Laboratuvarı'nda deneklerin ağırlıklarının ölçülmesini takiben günlük doz miktarına uygun olarak dimetil sülfoksit (DMSO) yardımı ile çözüldü.

Denekler öncelikle 3 ana gruba ayrıldı. Grup1 (kontrol grubu) :8 rat, Grup2 (aksonotmezis grubu): 24 rat, Grup3 (nörotmezis grubu): 24 rat ile oluşturuldu. Sonrasında Grup2 ve Grup3 kendi içerisinde eşit olarak üç gruba ayrılarak (2A: 8 rat, 2B: 8 rat, 2C:8 rat, 3A:8 rat, 3B:8 rat, 3C:8 rat) toplamda herbiri sekizer denek içeren 7 alt grup oluşturuldu. Deneklere Ketamin Hidroklorür (Ketalar® flakon, Parke-Davis lisansı ile Eczacıbaşı İlaç Sanayi İstanbul) 50 mg/kg ve Xylazin (Rhompun® enjektabl flakon, Bayer Türk Kimya Sanayi İstanbul) 10 mg/kg intraperitoneal olarak uygulanarak genel anestezi sağlandı. Deneğe operasyon tahtası üstünde prone pozisyon verildi. Denek kan dolaşımını bozmayacak şekilde dört ekstremiteden bağlanarak sabitlendi. Sağ gluteal ve uyluk lateral bölgesi traş edildi. Povidon iodine ile insizyon yeri temizliği yapıldı. Operasyon sahası siyah steril örtü ile örtüldü. Sağ alt ekstremitede kalça eklemi hizasından femoral kemiğe paralel sekilde oblik gluteal 3 cm'lik insizyon yapıldı. Cilt sıyrılarak biseps femoris kasına ulaşıldı. Biseps femoris ve gluteus superficialis komşuluğundan girişim yapıldı. Vastus lateralis görüldü. Biceps

femoris posteriora doğru ekarte edildi. Siyatik sinir ortaya çıkarıldı.
Aksonotmezis hasar modeli için, sıçan siyatik sinir ezilme tarzı yaralanma modeli kullanıldı. Aksonotmezis tipi yaralanma oluşturmak amacıyla; siyatik sinir üzerine 180 gr'lık kuvvet [1,76 Newton (N)] uygulayan 5 cm uzunluğunda 13 mm uç uzunluğuna sahip Dietrich bulldog klemp (Tekno-Cer® AC-123-20) 1 dakika süreyle yerleştirilip, lezyon oluşturuldu ve klemp çıkarıldı. Kas fasiası 4/0 vicryl sütür, cilt ise 4/0 prolen sütür ile kapatıldı. Nörotmezis tipi yaralanma oluşturmak amacıyla, cerrahi olarak eksplore edildi, cerrahi mikroskop kesi alanı üzerine getirilerek, 25'lik büyütme yapılarak mikromakas yardımı ile kesildi. Sonrasında mikrocerrahi teknikle tüm sinirler uç uca aynı cerrah tarafından yapılmak üzere 10/0 naylon sütur ile epinöral olarak dikildi. Kas fasyası ve cilt daha önce tarif edildiği gibi kapatıldı.
Yaraya 10 gün boyunca pansuman yapıldı. Denekler post-operatif dönemde kafeslerinde, normal oda sıcaklığında, günlük povidon iyot ile pansumanları yapılarak veteriner hekim kontrolünde tutuldular. Proflaktik antibiyotik olarak yeme karıştırılmış vaziyette amoksisilin klavulonik asid verildi. Günlük beslenmeleri ve su ihtiyaçları karşılandı. İlk operasyondan 28 gün sonra denekler reeksplore edildi. 28. günün sonunda deneklerin yaralanma oluşturulan sağ siyatik sinirleri hasar bölgesinin proksimal ve distalini de içine alacak şekilde çıkarıldı. Bilateral gastroknemius kasları da eksize edildi. Tüm deney aşamalarından geçen denekler daha sonra karbonmonoksit kutusu kullanılarak uyutuldu.
Her deneğe ait sinir ve kas dokuları, içinde %10'luk formalin solüsyonu bulunan kaplarına konuldu. Solüsyon içinde bir gün bekletildi. Sinir örneklerinden alınan ardışık tranvers kesitler Thermo Fisher Scientific marka, Shandon Excelsior ET model takip cihazında parafinle bloklandı. Her bir hayvana ait parafin bloktan 5 µm kalınlığında kesitler alındı. Denek başına 5 kesit, toplamda 270 kesit alındı. Sinir morfolojisi, inflamasyon, ödem ve konjesyonunu göstermek maksadıyla hematoksilen – eozin (H&E) ve WD'yi göstermek için Toloudin Blue ile boyandı. Gastroknemius kası numuneleri ise sinir inervasyonunun bozukluğunu ve atrofiye gittiğini histopatolojik olarak göstermek amacıyla masson trichrome 59 (MTC) ile boyandı ve fibrozis durumları derecelendirildi. Hazırlanan preparatlar Carl Zeiss marka Axio Scope. A1 model polarize ışık mikroskobunda değerlendirildiler. Stereorolojik analiz için bir yazılım (Stereoinvestigator, Microbrightfield; USA) ve kamera ataçmanı kullanıldı. İlk olarak her bir rat için siyatik sinir örnekleri düşük büyültmede çizildi. İkinci olarak, uygun grid büyüklüğü ve unbiased sayım çerçeve 60 büyüklüğü belirlendi. Çizili alanlar Fractionator probe aracılığı ile sistematik ve randomize bir şekilde örneklendi ve miyelinli aksonlar yüksek büyültmede sayıldı. Son olarak, ortalama miyelinli akson sayısal yoğunluğu şu formül ile hesaplandı [8].

$$Nv=\Sigma Q/\Sigma Sx\ A$$

(Nv: Sayısal yoğunluk Q: Sayılan toplam markerlar S: Örneklenen tarafların sayısı A: Sayılan çerçeve alanı)
Sinir dokusuna ait kesitlerden miyelinli akson yoğunluğu, miyelin kılıf kalınlığı, myelinli akson çapı, gastrokinemius kas dokusuna ait kesitlerden gastroknemius kas lifi çapı ve kollajen lif alan yüzdesi stereolojik olarak hesaplandı. Preparatların histopatolojik değerlendirilmesinde; fibrozis, wallerian dejenerasyon, ödem ve inflamatuar hücre infiltrasyonu parametrelerine gire 3 puan üzerinden skorlama yapılan modifiye histopatolojik gradeleme skalası kullanıldı [9-11] .(Tablo 1)

2.1. İstatistiksel Analiz

İstatistiksel analizler IBM-SPSS Statistics 22 (IBM, USA) programı kullanılarak yapıldı. İstatistiksel değerlendirmede $p<0.05$ değeri anlamlı farklılık olarak kabul edildi. İkiden fazla bağımsız grup için normal dağılım ve varyans homojenliği varsayımları sağlandığında tek yönlü varyans analizi (ANOVA) Tukey HSD uygulandı. Korelasyon incelemelerinde Pearson Ki – kare ve ANOVA testleri kullanıldı. P değerinin 0.05'ten küçük olması durumunda sonuçlar istatistiksel olarak anlamlı kabul edilmiştir.

3. BULGULAR

28 günlük deney süresince deney gruplarından toplamda 2 rat (ikisi de nörotmezis IIIa grubundan kanibalizm sonucu) öldüğünden 54 rat değerlendirmeye alındı. Makroskobik olarak bacak postürü, ayak basma özellikleri, bacak fleksör kaslarında atrofi gelişip gelişmediği, bası yaralarının olup olmadığı ve insizyon hattı özelliklerine dikkat edildi. Haricen yara yeri problemi tespit edilmedi.
Çalışmaya dahil edilen 54 deneğe ait siyatik sinir dokularının cerrahi eksplorasyon sonrası yapılan makroskobik değerlendirmesinde; kontrol grubunda yer alan deneklerde çevre dokuya yapışıklık ve nöroma izlenmezken, çalışma gruplarına ait sinirlerde sütür hattına uyan bölgelerde çevre dokuya yapışıklık görüldü. Nöroma oluşumu saptanmadı.
Deney gruplarına ait periferik sinir dokuları H&E boyama sonrasında değerlendirildi. Grup 1'de sinir liflerin düzenli olduğu, SC' ye ait nukleuslar ve düzenli akson yapıları ile tüm bölümlerde normal histolojik yapıda olduğu izlendi. Fibrozis, WD, ödem ve inflamatuar hücre infiltrasyonu tespit edilmedi (Şekil 1).
Grup2A'daki deneklerde periferik sinir doku bütünlüğünün kaybolduğu görüldü. Dejeneratif zeminde akson yoğunluğunun azaldığı, myelin kaybı

olduğu ve sinir liflerinin irregüler dağıldığı tespit edildi (Şekil 2) .

Grup2A'daki Denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 1 - 2 - 3, WD bakımından Grade 2 - 3, ödem bakımından Grade 1 - 2 - 3, inflamatuar hücre infiltrasyonu bakımından Grade 2 - 3 düzeyinde tespit edildi (Tablo 2). Değerler istatistiksel olarak anlamlı idi ($p<0.05$).

Grup2B'deki deneklerde akson ve miyelin yapısının düzenlenmeye başladığı, fibrotik alanların ve konjesyonun azaldığı gözlendi. Grup2B' deki denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 1 - 2, WD bakımından Grade 1 - 2, ödem bakımından Grade 1 - 2, inflamatuar hücre infiltrasyonu bakımından 76 Grade 0 - 1 - 2 düzeyinde tespit edildi (Tablo 2). Değerler istatistiksel olarak anlamlı idi ($p<0.05$).

Grup2C'deki deneklerde dejeneratif değişikliklerde ve konjesyonda azalma, akson ve miyelin organizasyonununda iyileşme tespit gözlendi. Grup2C' deki denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 1 - 2, WD bakımından Grade 0 -1 - 2, ödem bakımından Grade 0 - 1 - 2, inflamatuar hücre infiltrasyonu bakımından Grade 0 - 1 düzeyinde tespit edildi (Tablo 2). Değerler istatistiksel olarak anlamlı idi ($p<0.05$).

Grup3A'daki deneklerde çok yoğun inflamatuar hücre infiltrasyonu, belirgin
konjesyon sahaları, yoğun kollajen lifler, aksonal bütünlükte bozulma miyelin kaybı ve
yabancı cisim reaksiyonu gözlendi (Şekil 3). Grup3A' daki denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 2 - 3, WD bakımından Grade 2 - 3, ödem bakımından Grade 2 - 3, inflamatuar hücre infiltrasyonu bakımından Grade 2 - 3 düzeyinde tespit edildi (Tablo 3). Değerler istatistiksel olarak anlamlı idi ($p<0.05$). Grup3B' deki deneklerde akson yapısının ve miyelin organizasyonunun kısmen düzenlendiği, fibrotik alanların, inflamatuar hücre infiltrasyonunun ve konjesyonun azaldığı gözlendi. Grup3B' deki denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 1 - 2 - 3, WD bakımından Grade 1 - 2, ödem bakımından Grade 1 - 2, inflamatuar hücre infiltrasyonu bakımından Grade 1 düzeyinde tespit edildi (Tablo 3). Değerler istatistiksel olarak anlamlı idi ($p<0.05$). Grup3C' deki deneklerde akson yapısının ve miyelin organizasyonunun kısmen düzenlendiği, fibrotik alanların, inflamatuar hücre infiltrasyonunun ve konjesyonun azaldığı gözlendi. Grup3C' deki denekler Modifiye Histopatolojik Skorlama Tablosuna göre fibrozis bakımından Grade 1 - 2 , WD bakımından Grade 1 - 2, ödem bakımından Grade 1 - 2, inflamatuar hücre infiltrasyonu bakımından Grade 0 - 1 düzeyinde tespit edildi (Tablo 3). Değerler istatistiksel olarak anlamlı idi ($p<0.05$). Grup1'de sinir liflerin düzenli olduğu, SC' ye ait nukleuslar ve düzenli akson yapıları ile tüm bölümlerde normal histolojik yapıda olduğu izlendi. Aksonal organizasyon düzenliydi ve WD gözlenmedi (Şekil 4). Yaralanma yapılan kontrol gruplarında (Grup2A ve Grup3A) wallerian dejenerasyon, miyelin kaybı, konjesyon, kollajen lif ve inflamatuar hücre infiltrasyonu belirgindi, kısmen Schwann hücre hiperplazisi gözlendi. Grup2B, Grup2C, Grup3B ve Grup3C' de rejenere aksonlar ve Schwann hücre artışı ön plandaydı (Şekil 5). Grup1' deki deneklerin miyelinli akson yoğunluğu ortalama 0.00426 ± 0.00106 n/µm ^{3}, en düşük 0.00332 n/µm ^{3}, en yüksek 0.00667 n/µm ^{3} olarak saptandı. İstatistiksel olarak anlamlı farklılık saptanmadı ($p>0.05$). Grup2A' daki deneklerin miyelinli akson yoğunluğu ortalama 0.00103 ± 0.00025 n/µm ^{3}, en düşük 0.00076n/µm ^{3}, en yüksek 0.00139 n/µm ^{3} olarak saptandı. İstatistiksel olarak anlamlı düşüklük saptandı ($p<0.001$). Grup2B'deki deneklerin miyelinli akson yoğunluğu ortalama 0.00239 ± 0.00100 n/µm ^{3}, en düşük 0.00136 n/µm ^{3}, en yüksek 0.00433 n/µm ^{3} olarak saptandı. İstatistiksel olarak anlamlı yükseklik saptandı ($p<0.05$). Grup2C' deki deneklerin miyelinli akson yoğunluğu ortalama 0.00322 ± 0.00149 n/µm ^{3}, en düşük 0.00186 n/µm ^{3}, en yüksek 0.00646 n/µm ^{3} olarak saptandı. İstatistiksel olarak anlamlı yükseklik saptandı ($p<0.001$). Grup3A' daki deneklerin miyelinli akson yoğunluğu ortalama 0.00050 ± 0.00015 n/µm ^{3}, en düşük 0.00025 n/µm ^{3}, en yüksek 0.00065 n/µm ^{3} olarak saptandı. İstatistiksel olarak anlamlı düşüklük saptandı $p<0.001$). Grup3B' deki deneklerin miyelinli akson yoğunluğu ortalama 0.00088 ± 0.00045 n/µm ^{3}, en düşük 0.00046 n/µm ^{3}, en yüksek 0.00167 n/µm ^{3} olarak saptandı. Miyelinli akson yoğunluğundaki artış istatistiksel olarak anlamlı değildi ($p>0.05$). Grup3C' deki deneklerin miyelinli akson yoğunluğu ortalama 0.00122 ± 0.00102 n/µm ^{3}, en düşük 0.00042 n/µm ^{3}, en yüksek 0.00330 n/µm ^{3} olarak saptandı. Miyelinli akson yoğunluğundaki artış istatistiksel olarak anlamlı değildi ($p>0.05$) (Tablo 4,5).

Grup1'e ait deneklerin gastrokinemius kas örneklerinde çizgili kas demetleri nizami idi ve kollajen lif saptanmadı. Grup2A ve Grup 3A' ya ait deneklerin kas demetlerinde atrofi ve fibrozis ve kollajen lif oranında artış saptandı. Grup2B, Grup2C, Grup3B ve Grup3C' ye ait deneklerde fibrozis ve kollajen lif oranında azalma saptandı. (Şekil 6) Grup1'e ait deneklerin kollajen lif alan yüzdesi ortalama 1.50 ± 1.23, en düşük 0.26, en yüksek 4.21 idi. İstatistiksel olarak anlamlı değildi ($p>0.05$). Grup2A'ya ait deneklerin kollajen lif alan yüzdesi ortalama 4.60 ± 1.67, en düşük 1.12, en yüksek 6.14 idi. İstatistiksel olarak anlamlı

Tablo 1. Modifiye Histopatolojik Skorlama Kriterleri

Skor	Kriter (Kesit alanda x40 büyütmede)
Fibrozis	
Grade 1	< 150 fibroblast
Grade 2	100 – 150 fibroblast
Grade 3	> 150 fibroblast
Wallerian dejenerasyon	
Grade 1	< %25 dejenerasyon
Grade 2	%25-%75 dejenerasyon
Grade 3	> %75 dejenerasyon
Ödem	
Grade 1	< %25 ödem
Grade 2	%25- %75 ödem
Grade 3	> %75 ödem
İnflamatuar hücre infiltrasyonu	
Grade 1	0 – 10 nötrofil
Grade 2	10 – 50 nötrofil
Grade 3	> 50 nötrofil

Tablo 2. Grup2 Deneklerin Siyatik Sinir Hasarının Modifiye Histopatolojik Skorlama Tablosuna Göre Değerlendirilmesi

Denekler	Fibrozis			WD			Ödem			İnflamatuar hücre infiltrasyonu		
	(1-2-3)			(1-2-3)			(1-2-3)			(1-2-3)		
	2A	2B	2C	2A	2B	2C	2A	2B	2C	2A	2B	2C
1	1	1	1	2	1	0	1	1	0	2	0	0
2	3	1	1	3	1	1	3	1	0	2	1	0
3	2	1	1	3	1	1	3	1	1	2	1	0
4	3	1	1	2	1	1	3	1	1	2	1	0
5	2	1	1	3	1	1	3	1	1	3	1	1
6	1	1	1	3	2	1	3	2	1	3	1	1
7	3	2	1	3	2	2	2	2	1	3	1	1
8	3	2	2	3	2	2	3	2	2	3	2	1

yükseklik tespit edildi ($p<0.05$). Grup2B'ye ait deneklerin kollajen lif alan yüzdesi ortalama 3.44 ± 1.50, en düşük 1.09, en yüksek 6.23 idi. Kollajen lif alan yüzdesindeki azalma anlamlı değildi ($p>0.05$). Grup2C'ye ait deneklerin kollajen lif alan yüzdesi ortalama 1.84 ± 1.30, en düşük 0.96, en yüksek 4.84 idi. Kollajen lif alan yüzdesindeki azalma istatistiksel olarak anlamlıydı ($p<0.05$). Grup3A'ya ait deneklerin kollajen lif alan yüzdesi ortalama 6.61 ± 3.18, en düşük 2.26, en yüksek 11.62 idi. Kollajen lif alan yüzdesindeki artış istatistiksel olarak anlamlıydı ($p<0.05$). Grup3B'ye ait deneklerin kollajen lif alan yüzdesi ortalama 4.72 ± 1.86, en düşük 1.96, en yüksek 7.76 idi. Kollajen lif alan yüzdesindeki azalma anlamlı değildi ($p>0.05$). Grup3C'ye ait deneklerin kollajen lif alan yüzdesi ortalama 4.49 ± 1.82, en düşük 2.12, en yüksek 8.01 idi. Kollajen lif alan yüzdesindeki azalma istatistiksel olarak anlamlı değildi ($p>0.05$) (Tablo 6, 7).

4. TARTIŞMA

Günümüzde trafik ve iş kazalarının artması, sporun hayatımızda daha fazla yer almaya başlaması, toplumsal şiddet olaylarının artması sonucu ateşli silah ve kesici-delici aletle oluşan yaralanmalara bağlı olarak periferik sinir yaralanmaları daha sık gözükmektedir. Avrupada periferik sinir yaralanmasının insidansının yılda yaklaşık 300.000

vaka olduğu tahmin edilmektedir (12). Multitravma hastalarının yaklaşık % 2,8' inde meydana gelen periferal sinir hasarları; motor, duyusal ve otonom işlevlerinin kısmi veya tam kaybına yol açmaktadır. Bu durum önemli ölçüde iş ve güç kaybına neden olmaktadır (13). Direkt travma, kontüzyon, bası, iskemi, ısı, elektrik ve enjeksiyon uygulamaları gibi nedenler periferik sinir yaralanmalarının etiyolojisinde yer almaktadır (14, 15). Sinir kesilerinin olduğu yaralanmalar, yarattıkları morbidite sebebiyle aşılmaya çalışılan önemli bir sağlık sorunudur. Periferik sinir yaralanmalarının tedavisi; yaralanmanın şekli, lezyonun yeri, çevre dokuların durumu ve eşlik eden yaralanmalara bağlı olarak değişiklik göstermektedir. Proksimal seviyedeki yaralanmalarda dorsal kök ganglionlarında ve ön boynuzda çok sayıda hücre ölümü de fonksiyonel iyileşmenin kısıtlayıcı etkenlerindendir (16). Literatür incelendiğinde deneysel rat modelinde sinir yaralanması yapılıp, kullanılan maddelerin sinir iyileşmesi üzerine etkinliğinin araştırıldığı birçok çalışma vardır (17). Çalışmamamızda; insana en yakın deneysel model olması, uygulamada ve teknikte kolaylık sağlaması nedeniyle deney modeli olarak rat modeli seçilmistir. Özellikle rat siyatik siniri, uzun seyri, orta uyluk bölgesinde kolay diseksiyona izin vermesi ve manipülasyon için uygun bir alana sahip olması, bu siniri sinir çalışmalarında vazgeçilmez kılmaktadır. Periferik sinir yaralanmasında hasar patogenezinde oksidatif stres ve inflamasyon önemli bir rol oynar (18). Oksidatif stres yaralanma sonrası nöral hasarın ana nedenlerinden biridir ve periferik sinir yaralanması sonrası fonksiyonel iyileşmede olumsuz rol oynar (19,20). Periferik sinir yaralanmalarının farklı türleri farklı derecelerde oksidatif strese yol açabilir (21). Son araştırmalar, periferik sinir yaralanmasından sonra oksidatif stresin inhibisyonunun, fonksiyonel işlevin artmasına ve onarım sürecinde hızlanmaya neden olabileceğini göstermiştir (22, 23). Periferik sinir yaralanmasını takiben gelişen hızlı proinflamatuar yanıt, doku artıklarının ortadan kaldırılması ve etkin bir sinir rejenerasyonu için gereklidir (24). Ancak inflamasyon devam ederse ve zamanında etkili bir şekilde baskılanmazsa fonksiyonel iyileşme etkilenir. Periferik sinir hasarından sonra inflamatuar yanıtın baskılanması iyileşmeye katkıda bulunur (25). Sonuç olarak, oksidatif stresin ve inflamasyonun baskılanması oksidatif stres ve inflamatuar yanıta sekonder oluşan nöral hasarın önlenmesini sağlayarak sinir rejenerasyonuna ve fonksiyonel rekonstrüksüyona katkıda bulunabilir (26). Yaralı sinirin aksonal parçalanmasıyla başlatılan inflamatuar yanıt hem humoral (kompleman sistemi, siklooksijenaz-lipoksijenaz yolakları, sitokinler/ kemokinler) hem de hücresel (kan-sinir bariyeri permeabilizasyonu, SC aktivasyonu, makrofaj göçü) komponentler içerir. Sitokinler klasik olarak immun sistemin aktivasyonu ve inflamatuar yanıtla ilişkili heterojen bir grup polipeptid mediatör içerir. Son zamanlarda sitokinlerin sinir sistemi hasarı sonrası ekspresyonlarında artış olduğuna dair artan kanıtlar vardır (26).

Çalışmamızda ilk kez deneysel olarak ratlarda oluşturulan siyatik hasar modelinde AA' nın yaralanmış sinir üzerine antiinflamatuar ve nöroprotektif etkilerinin gösterilmesi için histopatolojik incelemeler yapıldı. İnflamatuar hücre infiltrasyonu, ödem, wallerian dejenerasyon ve fibrozis semikantitatif yöntemlerle, miyelinli akson yoğunluğu, miyelin kılıf kalınlığı, miyelinli akson çapı, gastroknemius kas lifi çapı ve gastroknemius kası kollajen lif alan yüzdesi stereolojik olarak değerlendirildi.

Grupların fibrozis dereceleri istatistiksel olarak değerlendirildiğinde Grup2C ve Grup2B'de Grup 2A'ya kıyasla anlamlı düşüklük tespit edildi (sırasıyla $p=0.004$, $p=0.01$). Grup2C ve Grup2B arasında ise anlamlı farklılık saptanmadı ($p>0.05$). Grup3C ve Grup3B'de fibrozis açısından Grup3A'ya kıyasla anlamlı düşüklük tespit edildi (sırasıyla $p=0.03$, $p=0.048$). Grup3C ve Grup3B arasında ise anlamlı farklılık saptanmadı ($p>0.05$). Bu duruma göre sinir yaralanması olan gruplarda fibrozisin ciddi olarak arttığı, AA verilen gruplarda ilaç doz artışından bağımsız olarak fibrozis derecelerinde belirgin azalma olduğu gözlendi.

Bu analizler doğrultusunda AA' nın, periferik sinir yaralanmasında NGF ve S100 düzeylerini artırıp, TNF-α ve TGF-β düzeylerini azaltarak; nöroprotektif, antiinflamatuar ve antioksidan etki gösterdiği ilk kez gösterildi. AA' nın bu mekanizmalarla fonksiyonel olarak, düşük ayak gelişimini azalttığı, siyatik fonksiyon indeksini (SFİ), basma kuvveti (EPT) ve gastroknemius kas ağırlık indeksini artırdığı tespit edildi. Elektrofizyolojik olarak amplitüd ölçümlerini artırdığı gösterildi. Histopatolojik olarak ise fibrozis, wallerian dejenerasyon (WD), ödem, inflamatuar hücre infiltrasyonu ve kollajen lif yoğunluğunu azalttığı; miyelinli akson yoğunluğunu, miyelin kılıf kalınlığını, miyelinli akson çapını ve gastrokinemius kas lifi çapını artırdığı gösterildi.

Sonuç olarak; periferik sinir yaralanmalarından sonra uygulanan uygun dozda asiatik asitin periferik sinir rejenerasyonunda olumlu etkileri gözlenmiştir. Analizler sonucunda oral asiatik asit verilen gruplarda; rejenere akson sayısı, miyelin formasyonu ve denerve kas atrofisinin restorasyonunda pozitif yönde anlamlı görüntüler tespit ve klinik testlerle teyit edildiğinden dolayı, asiatik asitin antiinflamatuar, antioksidan ve nöroprotektif etkileriyle periferik sinir yararlanmalarının tedavisine katkılar sağlayacağı ve periferik sinir yaralanmalarının tedavisi için yapılacak diğer çalışmalara ışık tutacağı kanaatindeyiz

Tablo 3. Grup3 Deneklerin Siyatik Sinir Hasarının Modifiye Histopatolojik Skorlama Tablosuna Göre Değerlendirilmesi

Denekler	Fibrozis			WD			Ödem			İnflamatuar hücre infiltrasyonu		
	(1-2-3)			(1-2-3)			(1-2-3)			(1-2-3)		
	3A	3B	3C	3A	3B	3C	3A	3B	3C	3A	3B	3C
1	3	1	1	2	1	1	2	1	1	3	1	0
2	2	1	1	3	2	1	3	1	1	2	1	0
3	2	2	1	3	2	2	3	1	1	2	1	1
4	3	2	1	2	2	2	3	2	2	3	1	1
5	3	2	2	3	2	2	3	2	2	3	1	1
6	3	2	2	3	2	2	3	2	2	3	1	1
7	*	2	2	*	2	2	*	2	2	*	1	1
8	*	3	2	*	2	2	*	2	2	*	1	1

(* işaretli ratlar öldüğünden değerlendirmeye alınamamıştır)

Tablo 4: Grupların Miyelinli Akson Yoğunluğu (n/µm ³) Verileri

Denek	Grup-1	Grup-2			Grup-3		
		2A	2B	2C	3A	3B	3C
1	0.00332	0.00076	0.00136	0.00186	0.00025	0.00046	0.00042
2	0.00344	0.00084	0.00146	0.00222	0.00040	0.00050	0.00047
3	0.00374	0.00087	0.00189	0.00240	0.00049	0.00051	0.00050
4	0.00379	0.00088	0.00208	0.00243	0.00059	0.00074	0.00075
5	0.00423	0.00095	0.00228	0.00294	0.00060	0.00083	0.00075
6	0.00444	0.00119	0.00238	0.00334	0.00065	0.00089	0.00154
7	0.00444	0.00138	0.00333	0.00412	*	0.00142	0.00203
8	0.00667	0.00139	0.00433	0.00646	*	0.00167	0.00330
Ort	**0.00426**	**0.00103**	**0.00239**	**0.00322**	**0.00050**	**0.00088**	**0.00122**
±SD	**±0.00106**	**±0.00025**	**±0.00100**	**±0.00149**	**±0.00015**	**±0.00045**	**±0.00102**

(* işaretli ratlar öldüğünden değerlendirmeye alınamamıştır)

Tablo 5: Grupların Ait Miyelinli Akson Yoğunluğu (n/µm ³) Ortalama Değerleri

Gruplar	Minimum	Maksimum	Ortalama ± SD
1	0.00332	0.00667	**0.00426 ± 0.00106**
2A	0.00076	0.00139	**0.00103 ± 0.00025**
2B	0.00136	0.00433	**0.00239 ± 0.00100**
2C	0.00186	0.00646	**0.00322 ± 0.00149**
3A	0.00025	0.00065	**0.00050 ± 0.00015**
3B	0.00046	0.00167	**0.00088 ± 0.00045**
3C	0.00042	0.00330	**0.00122 ± 0.00102**

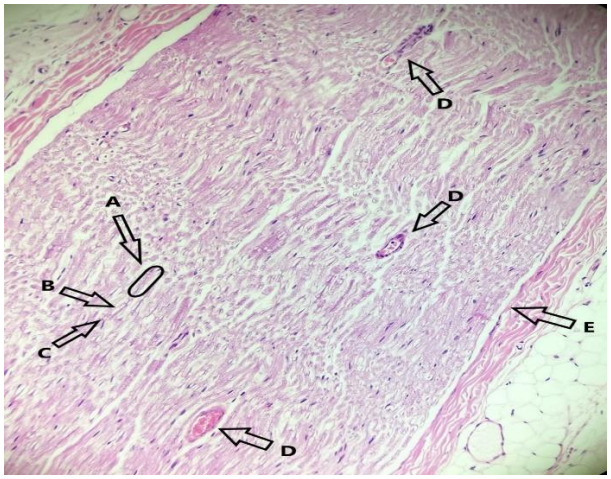
Tablo 6: Grupların Kollajen Lif alan Yüzde Verileri

Denek	Grup-1	Grup-2			Grup-3		
		2A	2B	2C	3A	3B	3C
1	0.26	1.12	1.09	0.96	2.26	1.96	2.12
2	0.56	3.25	2.41	0.99	4.87	2.43	2.96
3	0.99	4.48	2.87	1.12	5.56	4.51	3.56
4	1.23	5.23	2.96	1.25	7.23	4.86	4.02
5	1.24	5.25	3.84	1.32	8.14	4.99	4.44
6	1.36	5.62	3.96	1.96	11.62	5.12	5.13
7	2.22	5.77	4.17	2.28	*	6.15	5.74
8	4.21	6.14	6.23	4.84	*	7.76	8.01
Ort ± SD	**1.50 ± 1.23**	**4.60 ± 1.67**	**3.44 ± 1.50**	**1.84 ± 1.30**	**6.61 ± 3.18**	**4.72 ± 1.86**	**4.49 ± 1.82**

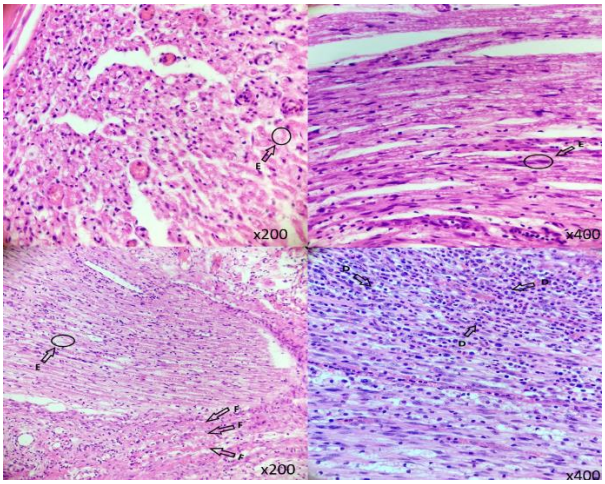
(* işaretli ratlar öldüğünden değerlendirmeye alınamamıştır)

Tablo 7: Grupların Kollajen Lif alan Yüzdelerinin Ortalama Değerleri

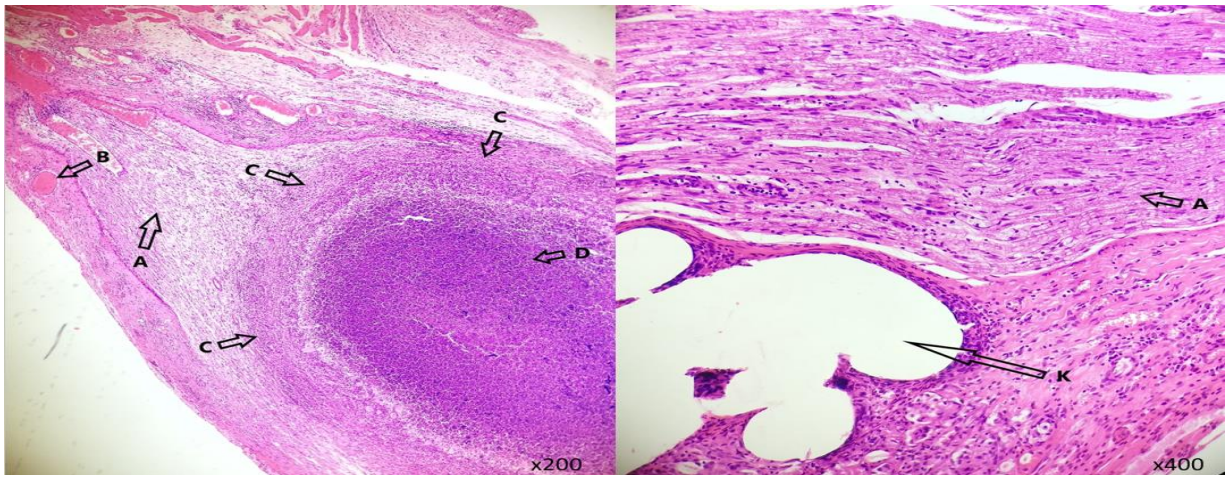
Gruplar	Minimum	Maksimum	Ortalama ± SD
1	0.26	4.21	**1.50 ± 1.23**
2A	1.12	6.14	**4.60 ± 1.67**
2B	1.09	6.23	**3.44 ± 1.50**
2C	0.96	4.84	**1.84 ± 1.30**
3A	2.26	11.62	**6.61 ± 3.18**
3B	1.96	7.76	**4.72 ± 1.86**
3C	2.12	8.01	**4.49 ± 1.82**



Şekil.1 Kontrol grubuna ait sağlam sinir lifleri, H&E, x200 (A: Sinir Lifi, B: Miyelin C: Schwan hücresi, D: Vasküler yapı, E: Perinöryum)

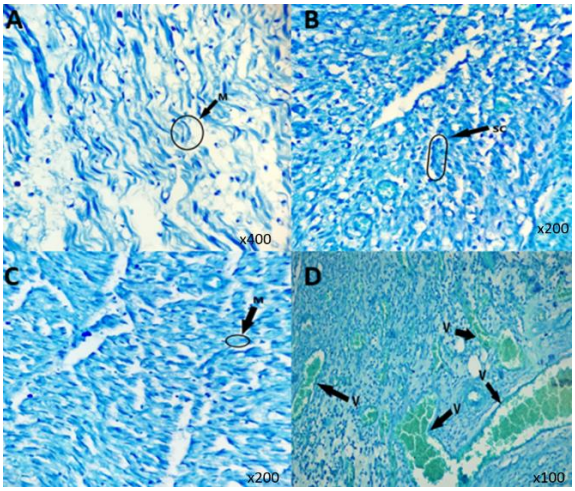


Şekil 2: Grup2A'ya ait sinir lifleri, H&E (E: Miyelin kaybı, F: Kollajen lifler D: İnflamatuar hücreler)

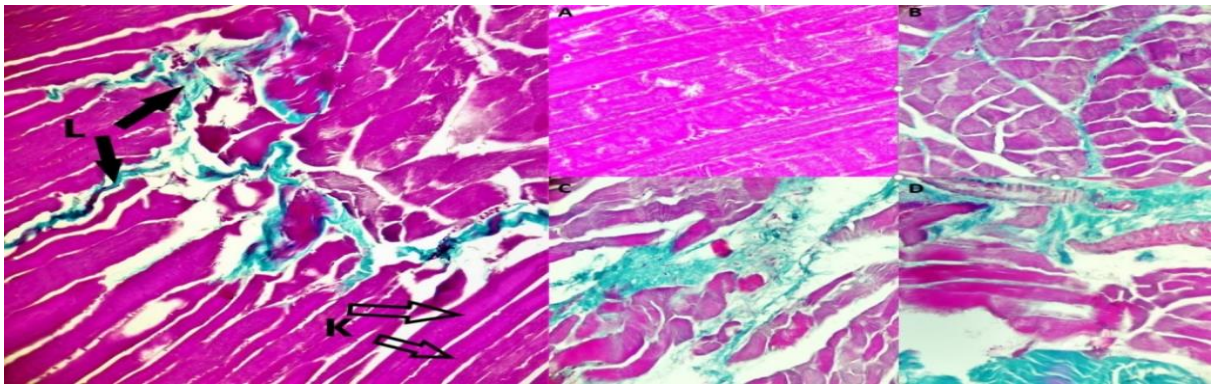


Şekil 3: Grup3A'ya ait Sinir dokusunda belirgin inflamasyon ve hasar bulguları, H&E (A: Sinir lifleri, B: Vasküler yapı, C: Fibrozis, D: İnflamatuar hücreler, K: Yabancı cisim reaksiyonu)

Şekil 4: Kontrol grubuna ait siyatik sinir kesiti, toluidin mavisi x200 (P: Perinöryum, V: vasküler yapı, S: sinir lifi, SC: Schwann hücresi)



Şekil 5: Grup3A' ya ait hasarlı sinir lifinde belirgin myelin kaybı, toluidin mavisi (M:Myelin Kaybı, SC: Schwann hücre artışı, V:Vasküler yapı



Şekil 6: Kas gruplarında fibrozis değerlendirmesi MTC boyası x200 (L: Kollajen lif, K: Çizgili kas, A: Normal kas, B: Hafif fibrozis, C: Orta derecede fibrozis, D: İleri derecede fibrozis)

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A COMPARISON OF OUTCOMES BETWEEN WISE PATTERN REDUCTION MAMMAPLASTY AND NO VERTICAL SCAR REDUCTION MAMMAPLASTY: EIGHT YEARS OF EXPERIENCE.

MEME KÜÇÜLTME OPERASYONUNDA WISE PATTERN VE VERTİKAL SKARSIZ TEKNİĞİN SONUÇLARININ KARŞILAŞTIRILMASI: SEKİZ YILLIK DENEYİM

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Abstract

Objectives: Macromastia or breast hypertrophy is a significant health problem for women that requires surgical correction. Many procedures have been described for reduction mammaplasty (RM) with specific skin incisions (such as inverted T scar, vertical scar, no vertical scar, circumareolar scar, snowball shape incision), or blood supply to the nipple-areolar complex (NAC) (such as inferior, superior, medial, lateral, superomedial, superolateral pedicle or horizontal bipedicle, vertical bipedicle). Since each method has its advantages and disadvantages there is no standard guideline to be applied. Patient expectations, the shape, and size of the breast, as well as the surgeon's knowledge, and experience, are important in decision-making. **Material and Methods:** In the study, 65 patients underwent RM operations from 2012 to 2020. All the surgeries were performed by a single surgeon. While 20 cases were operated by the no vertical scar (NVS) technique, the operations of 45 cases were performed by the inverted T scar, wise pattern (WP) technique. The inferior pedicle technique was chosen as a pedicle in all NVS cases. Although all pedicles can be used easily with a WP, only cases using the inferior pedicle are included in this study. The patients were followed up as outpatients at 1, 6, 12 months, and yearly afterward. In the follow-up controls, the subjective criteria such as relief of symptoms and patient satisfaction were checked along with the objective criteria such as early and late complications. **Results:** The average age of the patients was 42.7 years (42 years for WP; 44.2 years for NVS). The average total reduction for patients was 2594 g for WP and 2248 g for NVS. Preoperatively, the average distance from the sternal notch to the nipple was 33.1 cm for WP and 32.5 cm for NVS. While the early complication rate in patients operated with WP was 17.7%, and the late complication rate was 18.8%. On the other hand, the early complication rate of NVS patients was 2.5%, and the late complication rate was 15%. It was found that the total early complication rate was 13%, and the total late complication rate was 17.6% considering all cases. In total, complications occurred in 30% of all patients. Among the patients who underwent WP operations, 75.5% were very satisfied, 22.3% were satisfied, and 2.2% were not satisfied. The complaint of the dissatisfied patient was permanent pain. 80% of the patients who underwent NVS were very satisfied, and 20% were satisfied. **Conclusion:** Patient and surgeon satisfaction was very high in both techniques.

Keywords: reduction mammaplasty, wise pattern, no vertical scar, inferior pedicle

Özet

Amaç: Makromasti veya meme hipertrofisi kadınlar için cerrahi müdahale gerektiren önemli bir sağlık sorunudur. Spesifik cilt insizyonları (ters T skar, dikey skar, dikey skar yok, çevresel skar, kartopu şeklinde insizyon gibi) veya meme başı-areolar kompleksine (NAC) kan temini ile meme küçültme ameliyatı (RM) için birçok prosedür tanımlanmıştır. alt, üst, medial, lateral, süperomedial, süperolateral pedikül veya yatay ikipedikül, dikey ikipedikül gibi). Her yöntemin avantaj ve dezavantajları olduğundan uygulanacak standart bir kılavuz yoktur. Karar vermede hastanın beklentileri, memenin şekli ve büyüklüğü kadar cerrahın bilgi ve deneyimi de önemlidir. **Gereç ve Yöntem:** Araştırmada 2012-2020 yılları arasında 65 hastaya RM ameliyatı uygulandı. Ameliyatların tamamı tek cerrah tarafından gerçekleştirildi. Olguların 20'si dikey skarsız (NVS) teknikle, 45'i ise ters T skarlı, bilge desen (WP) tekniğiyle ameliyat edildi. Tüm NVS vakalarında pedikül olarak alt pedikül tekniği seçildi. WP ile tüm pediküller rahatlıkla kullanılabilse de bu çalışmaya sadece alt pedikülü kullanan vakalar dahil edilmiştir. Hastalar 1, 6, 12. ay ve sonrasında yıllık olarak ayaktan takip edildi. Takip kontrollerinde semptomların azalması, hasta memnuniyeti gibi subjektif kriterlerin yanı sıra erken ve geç komplikasyonlar gibi objektif kriterlere de bakıldı. **Bulgular:** Hastaların ortalama yaşı 42,7 (WP için 42, NVS için 44,2) idi. Hastalar için ortalama toplam azalma WP için 2594 g ve NVS için 2248 g idi. Ameliyat öncesinde sternal çentikten meme başına ortalama mesafe WP için 33,1 cm, NVS için 32,5 cm idi. WP ile ameliyat edilen hastalarda erken komplikasyon oranı %17,7, geç komplikasyon oranı ise %18,8 olarak belirlendi. NVS hastalarında ise erken komplikasyon oranı %2,5, geç komplikasyon oranı ise %15 olarak belirlendi. Tüm olgular dikkate alındığında toplam erken komplikasyon oranının %13, toplam geç komplikasyon oranının ise %17,6 olduğu belirlendi. Toplamda, tüm

hastaların %30'unda komplikasyon meydana geldi. WP operasyonu geçiren hastaların %75,5'i çok memnun, %22,3'ü memnun, %2,2'si memnun değildi. Memnun olmayan hastanın şikayeti kalıcı ağrıydı. NVS yapılan hastaların %80'i çok memnun, %20'si memnun kaldı. **Sonuç:** Her iki teknikte de hasta ve cerrah memnuniyeti oldukça yüksekti.

Anahtar Kelimeler: küçültme mammaplastisi, wise pattern, vertikal skar, alt pedikül

1. INTRODUCTION

Macromastia or breast hypertrophia is an important health problem for women. Complaints of macromastia patients include severe back and neck pain, inframammarian skin eruptions, persistent shoulder groove from the bra, chest discomfort, and unpleasant appearance of the body. Patients also experience psychological and social discomfort because of body image problems. It causes a decrease in the quality of life.

Reduction mammaplasty (RM) aims to alleviate these issues by reducing excessive breast volume while preserving arterial circulation and nipple sensation, ultimately providing an aesthetically pleasing outcome.

Macromastia is a complaint that surgeons have been trying to resolve for a long time. Nowadays, the task has become a bit easier with the demonstration of the nipple blood supply and definition of pedicles. However, a perfect method that answers all problems once is still not available.

There are roughly three decisions to be made before operation (1).

First of all, a technique to be used for skin excision is decided. For this purpose, inverted T (wise pattern) is the most commonly used technique which is easy to learn and apply. All pedicle applications are easily performed with this method. The only drawback is that it leaves a large scar. The other technique that has been applied commonly in recent years is the vertical scar technique. The vertical scar technique gives an aesthetically pleasing shape to the breast and increases projection (2,3). On the other hand, the temporary breast misshape in addition to the vertical scar appearance are disadvantages of the vertical scar RM technique (4,5). In addition, with the vertical scar RM technique, better results are more easily achieved for small to moderate reduction volumes (<800 g per breast). At the same time it can be difficult to achieve a satisfactory cosmetic result when a larger reduction is required (5). Another method known as the no vertical scar (horizontal) technique has been on the rise in recent years (6). The biggest advantage of this method is that it does not leave a visible scar. This can result in an "unoperated" appearance after the surgery. While the periareolar scar is concealed by the junction of the areolar skin and breast skin the inframammarian scar is concealed beneath the breast (6,4). On the other hand, the horizontal RM technique has been criticized for several reasons. It can give a boxy appearance to the breast (7). The scar on the chest wall can extend more laterally than it does with the WP (6) and, it is not ideal for all breast types. It is best suited for breasts that are exceedingly ptotic (normal skin of 5 cm or more between the areola and new areola) (6). Additionally, some critics argue that there is a postoperative loss of projection (6). Many modifications have been proposed to address all those criticisms (4,6,7,8).

The second decision to be made is determining the appropriate pedicle. Surgeons are generally aware of the blood supply to the breast, which comes from branches of the internal mammary (thoracic), the lateral thoracic, and the thoracoacromial arteries (3,9). A pedicle is selected for the protection of the NAC blood supply. Unfortunately, there is no consensus among surgeons as to which pedicle to choose. NAC necrosis is a very serious complication and to avoid it, the surgeons select an appropriate pedicle they trust.

The last decision to be made is the amount and location of the tissue to be removed. Excision is performed to provide the desirable breast shape and projection. Careful consideration of the selected pedicle is of utmost importance in this regard.

2. MATERIAL AND METHOD

Erzurum Health Sciences University ethics committee approval (37732058-514.10) was obtained before surgery.

Many factors including the size of the breast, the amount of tissue excised, skin quality, and the patient's request were taken into consideration when deciding on skin incisions in patients. When the techniques were explained to the patients, it was observed that younger patients tended to choose the horizontal scar technique. The pedicle selection is made according to the nipple position in patients who applied the WP technique. As it is suggested in the literature, all pedicles can be freely selected when the WP is used. If the nipple length is longer than 34 cm an inferior pedicle is selected for pedicle safety. If the nipple length is less than 28 cm, an inferior pedicle is selected for projection. Other pedicles are selected in cases with a nipple length of 28-34 cm. In that case, if the nipple is lateral to the breast meridian, a superomedial pedicle is selected, while a superolateral pedicle is selected, if the nipple is medial to the breast meridian. Only inferior pedicle cases were included in the scope of this study. The inferior pedicle technique was applied to all patients undergoing a horizontal scar pattern.

2.1 OPERATIVE TECHNIQUE:

2.1.1 Preoperative Preparation:

The operation was discussed with the patients in detail before the surgery. Requests and expectations of the patient were asked. What happens during and after the operation was clearly explained to the patient. The active participation of the patient in the operation method was ensured. Thus, the expectations of the patients were realistically leveled, and their postoperative satisfaction increased. Prior to surgery, all patients underwent breast ultrasonography, and for patients aged 40 and above, mammography was also performed. Benign radiological findings were carefully considered during the operation. Sometimes these benign findings required a change in the pedicle selection. Standard pre-anesthetic blood tests were performed for all patients while blood sugar level was carefully monitored and regulated in diabetic patients.

2.1.2 Wise Pattern:

First of all, the patient was marked in the standing position before the surgery. Marking started with finding the suprasternal notch and breast meridian. The most important step in marking is the determination of the new nipple position. The distance to the suprasternal notch is important for deciding the new nipple position. The new nipple position must also be compatible with the inframammary fold of the patient. The new nipple should be positioned on the breast meridian, slightly above the projection of the inframammarian line and 19-23 cm from the suprasternal notch. The WP was placed after the new nipple position was set (Picture 1a, Picture 1b). When the base was 8 cm wide and centered on the breast meridian.

2.1.3 No Vertical Scar (Horizontal) Technique:

Before the operation, marking was performed in a standing position. The design used in the NVS technique was accomplished as described by Lalonde (6). Similar to the WP technique, nipple position was decided first. Then areola was shaped to be 3 cm in diameter. The new inframammarian sulcus was shaped 6 cm below the new areola. While the incision line was extended to the medial and lateral. The anterior axillary line was not crossed. The diameter of the areola was adjusted to be transposed as 3.5 cm. Lalonde recommends 4-5 cm for relaxing closure and minimized scar (Picture 2a, Picture 2b). The pedicle width was kept at 8 cm.

All operations were performed under general anesthesia with the patients lying supine with abducted arms at 90 degrees. The surgical field was then sterilized and tumescent infiltration was applied to each patient for bleeding control and desepithelization. After the primarily planned pedicle was shaped, the breast tissue and skin were removed en bloc. The Pectoralis fascia was not exposed. Pedicle-shaping sutures were placed in both methods. If the pedicle was too long, it was shortened with sutures, and the pedicle was fixed from the medial and lateral to the pectoral fascia. Pedicle shaping sutures were avoided from being too tight for nipple viability. Areola was placed in its new position with 4-0 and 5-0 monocryl sutures. Skin and subcutaneous tissue were sutured with 3-0 and 4-0 monocryl sutures. The drain was applied to each patient and removed on the 3rd day. A compression dressing was applied after surgery. Antibiotic therapy was administered in the immediate preoperative phase and continued until the postoperative fifth day (first-generation cephalosporin). The physical activity of the patients was instructed to be limited for 3 weeks after the surgery. Patients were advised to wear a special bra (lateral supported) for 6 weeks.

3. RESULTS

Between January 2012 and June 2020, 65 macromastia patients (130 breasts) were operated. Patient characteristics including age, amount of tissue removed, preoperative distance from the sternal notch (SN) to the nipple, breast ptosis, preoperative and postoperative macromastia-related symptoms, and postoperative complications were analyzed. Patients underwent postoperative evaluations at 1 month, 6 months, and 1 year after surgery, followed by annual check-ups thereafter. Patients were interviewed at 1 month and 1 year. Annual breast cancer evaluation of patients over 35 years old was also performed in the same hospital. A satisfaction survey was administered during the first year follow-up, and patients were asked to rate their satisfaction with the surgery on a scale of 1 to 3.

1: not satisfied, there was no improvement in symptoms

2: satisfied, improvements in symptoms

3: very satisfied, complete improvement in symptoms

34 out of 45 patients who were operated the WP technique were very satisfied, 10 were satisfied and 1 was not satisfied. On the other hand, there were 16 very satisfied and 4 satisfied patients out of 20 patients with the NVS technique. Satisfaction results are shown in figure 1 and figure 2.

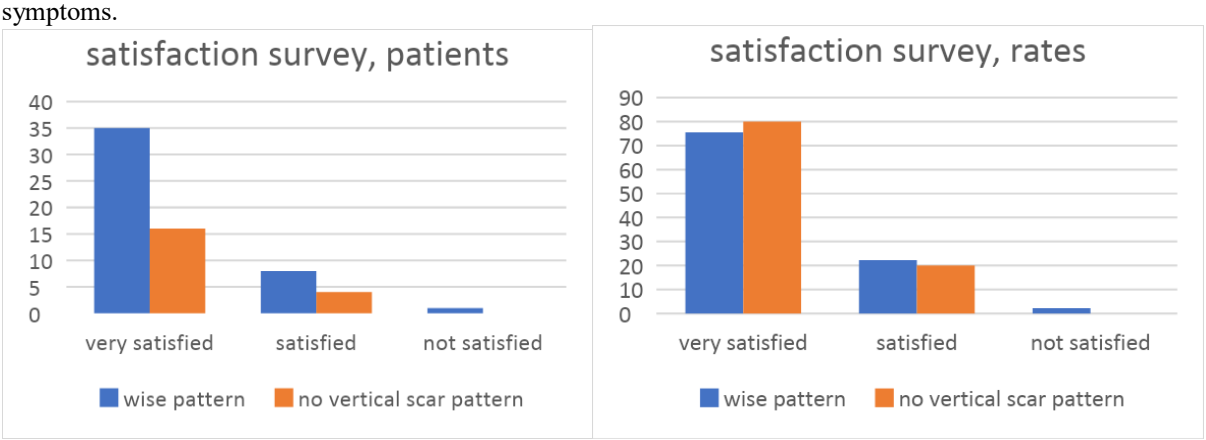
The average age of the patients was 42 (range, 19-65) for WP and 44.2 years (range,24-66) for the NVS pattern. The average total reduction in the patients was 2594 g (range, 860-5850 g) for WP and 2248 g (range 1290-3740 g) for the NVS pattern. The average specimen weight was 1316 g (range, 480-3202g) for right breast WP; 1116 g (range, 640-1840g) for right breast NVS pattern, and 1278 g (range, 380-3050g) for left breast WP; 1132g (range, 650-1900g) for left breast NVS pattern. Preoperatively, the average distance from the sternal notch to the nipple was 33,1 cm (range, 24-51 cm) for WP and 32,5 cm (range,26-41 cm) for the NVS pattern. Seven patients who underwent the NVS technique were found to have 2nd-degree ptosis and

13 patients had 3rd-degree ptosis. Among the patients who underwent the WP technique, 15 had 2nd-degree ptosis, and 30 had 3rd-degree ptosis.
The early complications of RM include hematoma, seroma, infection, wound dehiscence, and nipple areola necrosis. Among the cases operated with the WP technique, two breasts developed hematoma, six had wound dehiscence and partial nipple-areola necrosis, one had an infection, and one breast had total nipple areola necrosis. Patients with wound dehiscence and partial nipple areola necrosis were followed up by repeated dressing with topical ointments. Afterward, secondary healing was observed in wound dehiscence and nipple areola necrosis. There was no need for a secondary operation. Although hematoma is an early complication, in one case, hematoma developed after the 2nd week at the patient's one breast. This case was reoperated, but total nipple necrosis occurred (Picture 3). The second hematoma case was not reoperated since it was limited. Late complications of RM are abnormal scarring, dog ear deformities, over-reduction, under-reduction, and nipple sensory loss. Six patients who were operated with WP had nipple sensory loss in the early period, but it was not permanent. Among six patients (12 breasts) with hypertrophic scar, and two with dog ear deformity (4 breasts), only one patient requested correction. In addition, one patient can be classified to be under reduction but this was due to the patient's request. This patient was very satisfied with the operation even six years after surgery (Picture 4a, Picture 4b).
Partial nipple areola necrosis developed in one of the breasts operated with the NVS technique.
Other early complications have not been observed with the use of this technique. Abnormal scarring from late complications was observed in three patients (6 breasts). None requested correction. Other late complications have not been observed.
It was determined that for those undergoing an RM with the WP technique, the early and late complication rates were 17.7% and 18.8%, respectively.
On the other hand, the early complication rate in patients who were operated with the NVS technique was 2.5% and the late complication rate was 15%.
The total early complication rate was 13% and the total late complication rate was 17.6%. The overal complication rate was found to be 30%.

Table 1: Mammary ptosis was classified according to Regnault's (10) classification

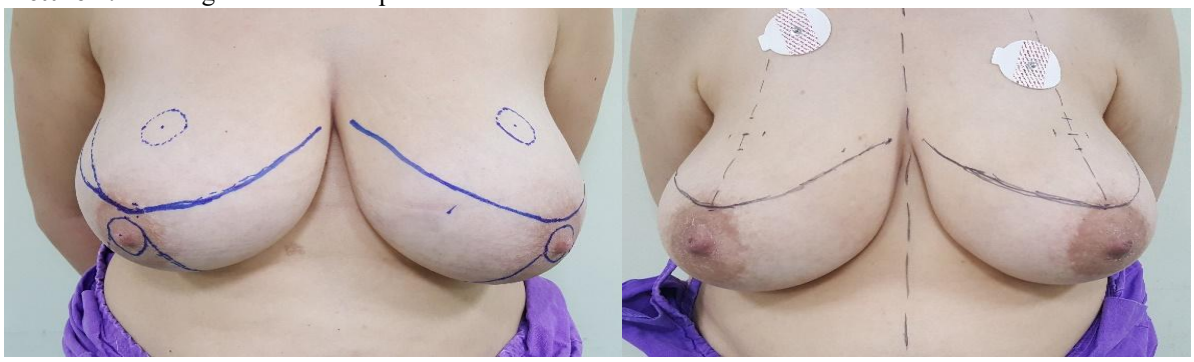
	1st degree mild	2nd degree moderate	3rd degree severe
Breast ptosis			
Wise	0	15	30
NVS	0	7	13
	0	22	43

Figure 1: Satisfaction survey, patients, Both methods provide significant improvement for macromastia-related symptoms.



Picture 1: new nipple position and wise pattern.

Picture 2: Marking for no vertical pattern



Picture 3: Patient 10 after 2 weeks hematoma developed and total NAC necrosis occurred.

Picture 4: Patient 52 wise pattern, inferior pedicule technique. Preoperative, postoperative 7. years. It can be classified under resection but the patient is still very satisfied.

Table 2: Early and late complications

	Wise Skin Resection Pattern Breast (90)	%	No Vertical Scar Pattern Breast (40)	%
Early Complications				
Hematoma	2	%4,4	0	%0
Infection	1	%1,1	0	%0
Seroma	0	%0	0	%0
Dehiscence at T junction	6	%6,6	0	%0
Nipple areola necrosis				
Partial	6	%6,6	1	%2,5
Total	1	%1,1	0	%0
Late Complications				
Abnormal scarring	12	%13,3	6	%15
Dog ears	4	%4,4	0	%0
Nipple-areola sensory loss	0	%0	0	%0
Under- reduction	0	%0	0	%0
Over- reduction	1	%1,1	0	%0

4. DISCUSSION

Macromastia has been a problem that surgeons have been working on for a long time. The earliest studies started in the late 19th century, but these studies aimed only to reduce the tissue mass. Billroth (11) and Pousson (12) who were among the pioneers in the treatment of macromastia, did not concern themselves with the aesthetic results. In the early 20th century aesthetic results gained importance with the work of Morestin (13), Hollander (14), Lexer (15), and Kraske (16).

In 1922, Thorek defined the method of removing the lower pole of the breast and carrying the nipple as a graft (17).

The skin excision pattern was defined in 1956 by Wise, who made a significant contribution to its prevalence (18,19). The wise pattern is still widely used in the world. Robbins described the inferior pedicle technique in 1977 (20). This technique still has a wide range of applications due to its pedicle safety, ease of learning, and application, and successful aesthetic outcomes. The only disadvantage of the inferior pedicle technique is that it can lead to bottoming out deformity with tissue accumulation in the lower pole (21). Many modifications have been described to prevent this complication (22).

Pitanguy (23) described the horizontal dermal pedicle and superior dermal pedicle. Skoog (24), described lateral dermal pedicle. McKissock (25), described vertical dermal bipedicle. Hester (26), described the central pedicle. And the combinations and modifications of pedicle selection were defined. Thus comprehensive freedom in pedicle selection was gained.

Recently, the vertical pedicle technique has been introduced and popularized by Arie (27), Lassus (28), Lejour (2), and Hall-Findlay (3) for use in RM. There is no inframammarian incision in this technique. The no-vertical scar technique, which was proposed by Passot (29) in 1925 has long escaped attention. The method, which was re-described by Yousif et al (30) in 1992 and used by Savaci (31) in 1996, gained a wide application area with Lalonde in 2003. Lalonde (6) published no vertical scar operation technique as a modification of the wise pattern. In this method, only inframammarian and periareolar incisions are made. In this way, it is attempted to avoid a visible scar. The vertical scar technique is one of the best techniques that provide aesthetic breast shape (2) but leaves a permanent visible scar. In contrast, the no vertical scar technique does not leave a visible vertical scar. However, a disadvantage of this technique is the challenge in achieving breast projection. Various modifications have been suggested to overcome this difficulty.

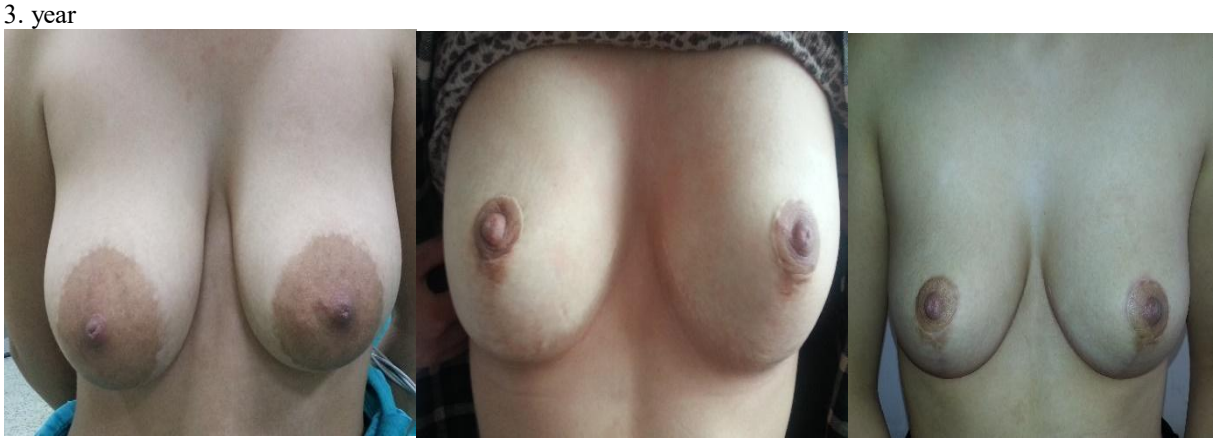
When the RM is applied, the remaining tissue and pedicle are usually placed in the new skin pocket. Especially if the inferior pedicle is left unshaped, there is a possibility of developing bottoming-out deformity. This deformity can be prevented by shaping the pedicle and suspending it from the pectoral fascia. In our case series, pedicle shaping was performed for all cases, and as a result, no bottoming-out deformity was observed.

The most common complications associated with RM are wound dehiscence, delayed wound healing,

infection, seroma, hematoma, and skin and NAC necrosis. Current literature has demonstrated complication rates in RM to ranging from 7.1% to 53% (32,33). In the adolescent population, overall complication rates are similar, ranging from 10% to 55% (34,35). In the present study, the overall complication rate was 30%. The most common complication to be seen was an abnormal scar.

Picture 5: Patient 28. Four years after operation (wise pattern). The vertical scar was perfectly healed, but there was a slight irregularity in the inferior of areola. The patient did not experience any wound-healing problems,and there were no irregularities in the areola during the early period.

Picture 6: Patient 63 wise pattern, inferior pedicule technique. Preoperative, postoperative 1. year, postoperative 3. year



Picture 7: Patient 65 wise pattern, inferior pedicule technique. Preoperative, postoperative 1. Year

In a study by Dancey et al. patients were subdivided based on the weight of breast tissue resection into two groups: macromastia (<1500 g resection per breast) and gigantomastia (>1500 g resection per

breast)(36). Degeorge et al. reported that there was no significant difference in terms of major complications between the two groups. However minor complications were observed more frequently in the gigantomastia group (37). In our study, 30 breasts (13 patients with bilateral gigantomastia, and 4 patients with unilateral gigantomastia) can be classified to be gigantomastia. A wound-healing problem occurred in a patient with unilateral gigantomastia, and partial nipple areola necrosis was observed in a patient with bilateral gigantomastia.

Picture 8: Patient 54 wise pattern, inferior pedicule technique. Preoperative, postoperative 1. month. Bilateral partial nipple-areola necrosis.

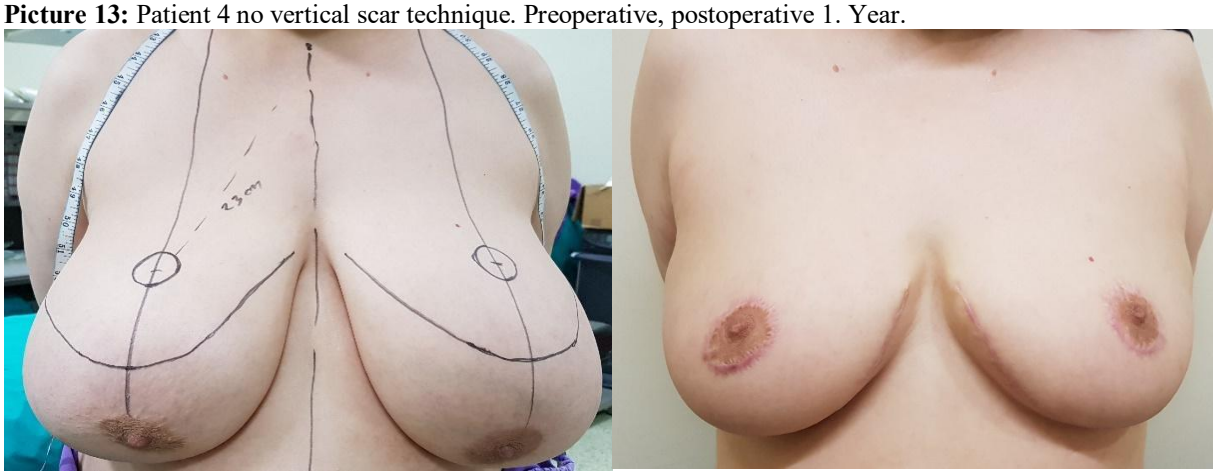
Picture 9: Patient 59 wise pattern, inferior pedicule technique. Preoperative, postoperative 1. Month. The patient has diabetes mellitus and excellent healing was observed.

Picture 10: Patient 58 wise pattern, inferior pedicule technique. Preoperative, postoperative 7. years.

Picture 11: Patient 28 wise pattern, inferior pedicule technique. Preoperative, postoperative 4. years. The patient has breastfed.

Picture 12: Patient 2 no vertical scar technique. Preoperative, postoperative 1 year.

Picture 13: Patient 4 no vertical scar technique. Preoperative, postoperative 1. Year.

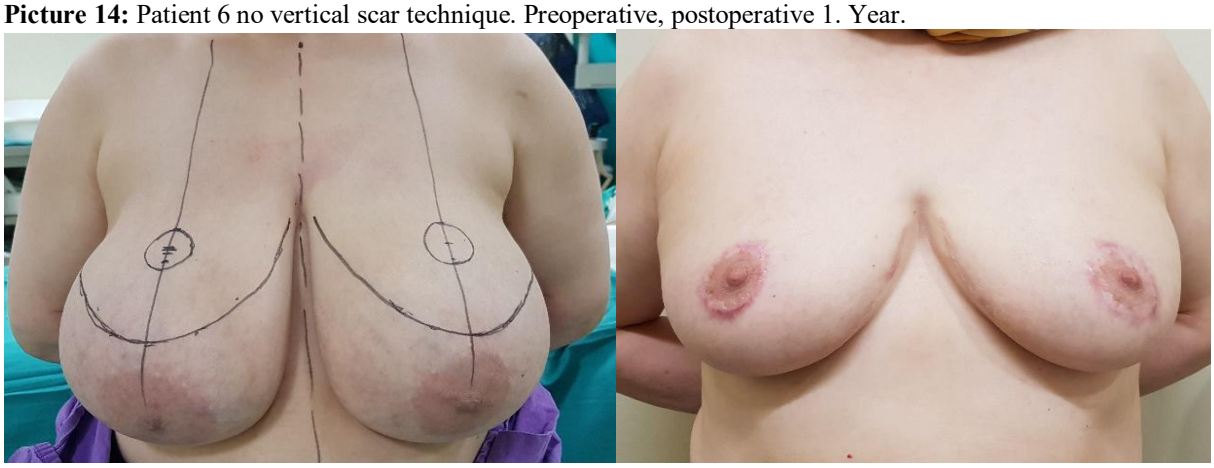


If wound healing problems occurred in the patients who underwent WP, irregular scars were observed in the inferior of the areola. Lalonde suggested that a vertical incision caused unaesthetic appearance of the areola (6). Our experience indicated that in cases without wound healing problems, the wise pattern also yielded satisfactory/desired aesthetic results.

It was observed in the study that even if the vertical scar healed well in the wise pattern RM, there was a possibility that irregularity can develop in the inferior of the areola (Picture 5). Our personal opinion is that the wise pattern inferior pedicle technique is applied due to excessive tissue tension in the upper and lower areas of the T junction.

A significant advantage of the inferior pedicle technique is that it does not interfere with breastfeeding. Four patients who became pregnant after the operation were able to breastfeed. Since all those patients were operated on using the wise pattern, a comparison was not possible.

Picture 14: Patient 6 no vertical scar technique. Preoperative, postoperative 1. Year.



In the study, there were 11 patients with type 2 diabetes mellitus, and all of them operated using the WP technique. Among the RM patients with diabetes, only one experienced a wound-healing problem. Smoking is considered to be a risk factor for wound complications after RM operations. There were a total of 7 patients who smoked, and no complications were observed in those patients.

Although many studies have shown that the use of prophylactic antibiotics is inefficacious (38), many surgeons still use them. The reason could be related to the forejudgement of the surgeon or the fears due to the observation of the developing infection. In the study, prophylactic antibiotherapy was applied to all cases to avoid any complications related to the development of any infection.

The most important criticism of the NVS technique is its inability to provide adequate breast projection. Horndeski and Gonzales (39) proposed that the perfect projection can be achieved in the no-vertical scar technique by shaping the pedicle. They also pointed out that successful shaping could give the appearance of a prosthetic implanted breast and the patient's expectation of not having a vertical scar. It was also found in present cases that shaping the pedicle rather than releasing it in the pocket had a greater contribution to projection.

One limitation of the vertical scar technique is that it can be applied to ptotic breasts. There must be at least 6 cm between the new NAC location and the NAC that the patient has. Shin et al. (40) overcame this restriction with the semicircular skin island prepared from the lower breast.

Whatever method is chosen, RM eliminates pain, restores physical activities, improves the quality of life, and has the highest patient satisfaction rates (41,42). In our study, very high satisfaction rates of the patients were observed for both techniques.

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THE ROLE OF FINE-NEEDLE ASPIRATION BIOPSY IN THE DIAGNOSIS OF SALIVARY GLAND LESIONS: A COMPARATIVE HISTOPATHOLOGICAL STUDY

TÜKÜRÜK BEZI LEZYONLARININ TANISINDA İNCE İĞNE ASPİRASYON BİYOPSİNİN YERİ: HİSTOPATOLOJİK KARŞILAŞTIRMALI ÇALIŞMA

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Abstract

Objective: As the treatment of neoplastic and non-neoplastic lesions of salivary gland differs, their differentiation in preoperative period is crucial. Fine-needle aspiration biopsy (FNAB) is among the common diagnostic methods for this purpose. We intended to compare the cytological-histopathological diagnosis of salivary gland lesions, and evaluate sensitivity, specificity, predictive value (PV) and diagnostic accuracy of the FNAB results. **Methods:** 156 cases examined in our department, having FNAB and excision material, were compared with their cytological-histopathological diagnosis. **Results:** Lesions were localized in parotid gland in 132 cases, in submandibular gland in 22 cases, and in minor salivary gland in 2 cases. FNABs were categorized based on their cytomorphological results into nondiagnostic (7.05%), benign (78.21%), suspicious (7.05%) and malignant (7.69%) groups. When the cytological-histopathological diagnosis of cases was compared, the diagnosis of 12 cases among malignant lesions (100%, 12/12) and 121 among benign lesions (99.2%, 121/122) were found to be compatible. One false negative case (0.8%) (warthin tumor→mucoepidermoid carcinoma) was detected, but no false positive (0%) was the case. Histopathological examinations of three cases among suspicious lesions resulted in diagnosis of ectopic thyroid tissue, sialadenitis and pleomorphic adenoma. Results of sensitivity, specificity, positive PV, negative PV and accuracy analysis examinations were respectively 92.3%, 100%, 100%, 99.2% and 99.3%. **Conclusion:** Evaluating FNABs with sufficient sampling minimizes false positive/negative results, leading to accurate diagnosis in preoperative period. Wide range of salivary gland lesions and overlapping cytomorphological findings should also be minded.

Keywords: Salivary gland, fine-needle aspiration biopsy, pleomorphic adenoma, mucoepidermoid carcinoma

Özet

Amaç: Tükürük bezi non-neoplastik ve neoplastik lezyonlarının tedavileri farklılık gösterdiği için, preoperatif dönemde ayrımlarının yapılması önemlidir. İnce iğne aspirasyon biyopsisi (İİAB) bu amaçla en yaygın kullanılan tanı yöntemlerinden biridir. Burada tükürük bezi lezyonlarının sitolojik-histopatolojik tanılarının karşılaştırılması, İİAB sonuçlarının sensitivite, spesifite, prediktif değer (PV) ve tanısal doğruluğunun değerlendirilmesi amaçlandı. **Materyal ve metod:** Bölümümüzde incelenen İİAB ve eksizyon materyali olan 156 olgu sitolojik-histopatolojik tanıları ile karşılaştırıldı. **Bulgular:** Lezyonlar 132 (%84.6) olguda parotis bezinde, 22 (%14.1) olguda submandibuler bezde ve 2 (%1.3) olguda minör tükürük bezinde lokalizeydi. İİAB'lerin sitomorfolojik sonuçlarına göre % 7.05'i (n=11) nondiagnostik, %78.21'i (n=122) benign, % 7.05'i (n=11) kuşkulu ve % 7.69'u (n=12) malign olarak sınıflandırıldı. Olguların sitolojik-histopatolojik tanıları karşılaştırıldığında; malign lezyonlar içinde 12 olgunun (12/12; %100) ve benign lezyonlar içinde 121 olgunun (121/122; %99.2) tanıları uyumluydu. False negatif bir olgu (%0.8) (warthin tümör→mukoepidermoid karsinom) saptandı. False pozitif olgu saptanmadı (%0). Kuşkulu lezyonlar içinde üç olgunun histopatolojik incelemeleri ektopik tiroid dokusu, sialadenit ve pleomorfik adenom tanıları ile sonuçlandı. Sensitivite, spesifite, pozitif PV, negatif PV ve doğruluk analizi değerlendirmesinde sırasıyla % 92.3, % 100.0, % 100.0, % 99.2 ve % 99.3 sonuçları elde edildi. **Sonuç:** İİAB'lerinde yeterli örnekleme ile birlikte değerlendirmelerindeki deneyim, çalışmamızda olduğu gibi false pozitif/negatif sonuçları en aza indirgeyecek ve preoperatif dönemde doğru tanıya ulaştıracaktır. Bununla birlikte tükürük bezi lezyonlarının geniş yelpazesi ve örtüşebilecek sitomorfolojik bulguların varlığı da akılda tutulmalıdır.

Anahtar Kelimeler: Tükürük bezi, ince iğne aspirasyon biyopsisi, pleomorfik adenom, mukoepidermoid karsinom.

1. INTRODUCTION

Salivary gland lesions including a wide variety of tumor-like lesions and tumor types have a broad morphological pattern (1,2). It is important to distinguish neoplastic and non-neoplastic lesions in the preoperative evaluation due to the fact that neoplastic lesions are usually excised surgically, while non-neoplastic lesions are treated conservatively with clinical follow-up (3).

Fine needle aspiration biopsy (FNAB) is one of the most widely used first-stage diagnostic methods for this purpose. FNAB is a method that can provide rapid morphological evaluation in determining the origin (salivary gland or not), nature (benign or malignant), and possible grade (low or high) of the lesions (1,4,5). However, there are also limitations of FNAB (1,5-7). Sampling errors, presence of cystic components, lesions with morphological heterogeneity and overlapping cytomorphological findings are among the related limitations which lead to a wide range of sensitivity (81-100%) and specificity (90-100%) in cytological diagnosis (4,8-12).

In our study, we aimed to compare the cytological and histopathological diagnoses of salivary gland lesions, and to evaluate the sensitivity, specificity, predictive value as well as diagnostic accuracy of the FNAB results.

2. MATERIAL AND METHOD

This study was found ethically appropriate according to the local ethical committee with its decision number 2019-1137.

2.1. FNAB and histopathological data of the patients:

The FNAB samples and excision material of patients with lesions located in the salivary gland (parotid, submandibular and minor salivary glands) which were sent to our department between 2014-2019 were evaluated with their clinical information. All the FNABs were performed with real-time ultrasound guidance. Demographic characteristics (age, gender) of the patients, the localization of the FNABs, cytomorphological findings and diagnoses of FNABs were recorded.

The FNAB results according to the cytomorphological findings were classified into four groups as nondiagnostic, benign, suspicious for malignancy, and malignant. Insufficient, acellular or hypocellular smears, cyst contents consisting of only macrophages without diagnostic cells or smears containing elements of peripheral blood were interpreted as nondiagnostic. When characteristic cytomorphological findings of benign epithelial and mesenchymal neoplasia of the salivary gland (pleomorphic adenoma, warthin tumor, etc) were observed, it was interpreted as benign. On the other hand, it was interpreted as malignant when significant malignancy findings such as atypical cells with increased nuclear/cytoplasmic ratio, pleomorphic and hypercromatic nucleus which forms sheets or three-dimensional groups, and frequent mitosis, necrotic background and specific findings for malignant tumor type (for example matrix globules and basal cells for adenoid cystic carcinoma) were in question. Although suggestive of malignancy, smears that did not meet all the criteria for specific diagnoses were interpreted as suspicious for malignancy.

Histopathological diagnoses of excision materials were classified into three groups as non-neoplastic, benign and malignant.

2.2. Evaluation of compliance between FNAB and histopathological diagnoses:

The histopathological diagnoses of excision materials and FNAB diagnoses were compared in order to evaluate the cytological-histopathological compatibility. The obtained true negative and true positive, and false negative and false positive results were evaluated.

When evaluated together with histopathological results, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy rates were analyzed for the FNAB findings. Analyzes were made in two separate groups. In the first group, patients with nondiagnostic results and suspicious for malignancy were not included. While nondiagnostic patients were not included in the second group, patients suspicious for malignancy were included in the malignant group and evaluated. All the analyses were evaluated separately and totally based on the localizations of the lesions (parotid and submandibular gland). Due to two patients with minor salivary gland lesions, they were not included in the analysis performed based on localization but were evaluated in the total group.

2.3. Statistical analysis

The data were transferred to IBM SPSS Statistics 23 package program. While evaluating the study data, frequency distribution (number, percentage) for categorical variables and descriptive statistics (mean, standard deviation) for numerical variables were given. Chi-square test was used to examine the relationship between gender and localization, and cytological and histological categories. By comparing the FNAB results with the histopathology results, sensitivity, specificity, PPV, NPV and accuracy values were calculated.

3. RESULTS

3.1. FNAB findings of the lesions:

One hundred fifty-six patients with excision material out of 417 patients whose FNAB was examined were included in the study. 85 (54.5%) of the patients were

male, whereas 71 (45.5%) were female, with the male/female (M/F) ratio being 1.2: 1. The mean age was 52.65 ± 14.21.

The lesions were localized in the parotid gland in 132 (84.6%) patients, in the submandibular gland in 22 (14.1%) patients, and in the minor salivary gland in 2 (1.3%) patients.

Of the lesions of the patients, 7.05% were in the nondiagnostic group, 78.21% in benign group, 7.05% in suspicious for malignancy group, and 7.69% in malignant group (Table 1).

3.2. Histopathological findings of the lesions:

Of the lesions in the nonneoplastic diagnosis group (12.2%), 68.4% were located in the parotid gland and 31.6% were in the submandibular gland. Among this group, sialadenitis was the most common etiology (47.4%).

Of the patients with benign neoplasia (73.1%), 93% of the lesions were located in the parotid gland, 6.1% were in the submandibular gland and 0.9% were in the minor salivary gland. Pleomorphic adenoma was the most common benign neoplasia (55.3%).

Of the lesions in the malignant group (14.7%), 56.5% were located in the parotid gland, 39.1% in the submandibular gland and 4.4% in the minor salivary gland. Mucoepidermoid carcinoma (MEC) was the most common primary malignant neoplasia (21.7%). Other tumors were acinic cell carcinoma (ACC), lymphoma, poorly differentiated carcinoma, undifferentiated carcinoma, adenoid cystic carcinoma (AdCC), carcinoma ex pleomorphic adenoma, lymphoepithelial carcinoma, and leiomyosarcoma. MEC showed moderate differentiation in three patients, while it was of low or high grade in the other patients. High-grade transformation was not detected in all three patients with a diagnosis of ACC. The carcinoma component detected in the patient with carcinoma ex pleomorphic adenoma was high grade squamous cell carcinoma (SCC). Both patients with a diagnosis of lymphoma were of high grade. Leiomyosarcoma was well differentiated. SCC metastasis was the most common among the metastatic tumors in this group. Others were renal cell carcinoma, malignant melanoma and breast carcinoma metastases. While primary carcinoma and metastasis diagnoses were made simultaneously in two patients with SCC, the time to occurrence of the metastatic lesion varied between 12 and 72 months in other patients.

While benign lesions in the parotid gland were detected at a higher rate than malignant lesions, the rate of malignant lesions in the submandibular gland was higher than the rate of benign lesions ($p=0.000$). There was no statistically significant relationship between gender and benign and malignant lesions ($p> 0.05$).

The distribution of histopathological diagnoses based on the localizations of the lesions is given in Table 2.

3.3. Compatibility of cytological and histopathological diagnoses of the lesions:

When cytological and histopathological diagnoses were compared in the study, 12 true positive results (100%), 121 true negative results (99.2%) and one false negative result were found (0.8%). The false negative one was benign cytologically (warthin tumor), being localized in the parotid gland and diagnosed as malignant tumor (MEC) as a result of the histopathological examination (Figure 1). No false positive results were found in the study (0%).

Incompatibility between cytological and histopathological diagnoses was detected in three patients in the suspicious for malignancy group. As a result of the histopathological examination, two of the patients were diagnosed as having non-neoplastic lesions (ectopic thyroid tissue (Figure 2) and sialadenitis) and one was diagnosed as having benign tumor (pleomorphic adenoma).

Sensitivity, specificity, PPV, NPV and accuracy analysis results are included in Table 3

Table 1: The distribution of the cytological-histopathological categories of the cases

FNAB categories	Histopathological categories			
	Nonneoplastic (N,%)	**Benign (N,%)**	**Malignant (N,%)**	**Total (N,%)**
Nondiagnostic	2 (1.28)	7 (4.49)	2 (1.28)	11 (7.05)
Benign	15 (9.62)	106 (67.95)	1 (0.64)	122 (78.21)
Suspicious	2 (1.28)	1 (0.64)	8 (5.13)	11 (7.05)
Malignant	0	0	12 (7.69)	12 (7.69)
Total (N,%)	19 (12.18)	114 (73.08)	23 (14.74)	156 (100)

Table 2: The distribution of the histopathological diagnosis of the cases based on their localizations

Parotid gland	**N (%)**	**Submandibular gland**	**N (%)**	**Minor salivary gland**	**N (%)**
Nonneoplastic lesion		***Nonneoplastic lesion***			
Sialadenitis	5 (3.2)	Sialadenitis	4 (2.6)		0 (0)
Granulomatous infl.	2 (1.3)	Branchial cyst	1 (0.6)		
Lymphoepithelial cyst	2 (1.3)	Ectopic thyroid tissue	1 (0.6)		
Necrotizing SM	1 (0.6)				
Oncocytosis	1 (0.6)				
Sjögren syndrome	1 (0.6)				
Epidermoid cyst	1 (0.6)				
Benign		*Benign*		*Benign*	
PA	56 (35.9)	PA	6 (3.8)	PA	1 (0.6)
Warthin tumor	45 (28.8)	Lipoma	1 (0.6)		
Basal cell adenoma	2 (1.3)				
Lipoma	2 (1.3)				
Canalicular adenoma	1 (0.6)				
Malignant		*Malignant*		*Malignant*	
MEC	3 (1.9)	MEC	2 (1.3)	Leiomyosarcoma	1 (0.6)
ACC	3 (1.9)	Lymphoma	2 (1.3)		
Ca-ex-PA	1 (0.6)	Poorly diff. carcinoma	2 (1.3)		
Undifferentiated carcinoma	1 (0.6)	AdCC	1 (0.6)		
SCC metastasis	2 (1.3)	Lymphoepithelial carcinoma	1 (0.6)		
RCC metastasis	1 (0.6)	SCC metastasis	1 (0.6)		
BC metastasis	1 (0.6)				
MM metastasis	1 (0.6)				
Total	132 (84.6)		22 (14.1)		2 (1.3)

Table 3: Sensitivity, specificity, PPV, NPV and accuracy results

	Sensitivity	Specificity	PPV	NPV	Accuracy
*Total	92.3%	100%	100%	99.2%	99.3%
Parotid gland	87.5%	100%	100%	99.1%	99.2%
Submandibular gland	100%	100%	100%	100%	100%
**Total	95.2%	97.6%	87%	99.2%	97.2%
Parotid gland	91.7%	99.1%	91.7%	99.1%	98.4%
Submandibular gland	100%	80%	81.8%	100%	89.5%

PPV: Positive predictive value, NPV: Negative predictive value.
*: The group in which nondiagnostic and suspicious for malignancy in FNABs were not included
**: The group in which nondiagnostic FNABs were not included

4. DISCUSSION

Due to the findings that can overlap between non-neoplastic, benign and malignant salivary gland lesions, it is sometimes difficult to make a definitive diagnosis in the histopathological examination (5-7). The traps at the diagnosis stage in the FNABs may also be due to sampling errors that may cause false negative results (5,11,12). False negative results can be observed in mostly small lesions, tumors with cystic components such as pleomorphic adenoma, Warthin tumor or low grade MEC, and tumors such as sialadenitis or Warthin tumor with regenerative epithelial hyperplasia and squamous metaplasia (11,13). In the literature, false negative rates are reported up to 37% (11,14,15). In our study, the false negative rate was 0.8%. The low false negative rate compared to the literature may be related to the increasing experience in this regard with adequate sampling and increased use of FNAB in salivary gland.

The histopathological examination of the patient with a lesion localized in the parotid gland whose FNAB was interpreted as Warthin tumor resulted in the diagnosis of MEC. There are studies in the literature reporting false-negative results with similar diagnoses (6,16-18). MEC is one of the lesions that is difficult to diagnose accurately with FNAB. Diagnostic cytological findings are a dirty background of mucus and debris with intermediate cells, mucin-producing cells, and squamous epithelial cells. However, in about 20% of these tumors, oncocytic cells, the presence of many lymphocytes on the background with cystic debris, may be misinterpreted as a Warthin tumor. Moreover, mucinous differentiation may be seen in Warthin tumor, which may further complicated differentiate from mucoepidermoid carcinoma (8).

The false positive rate reported in the literature is lower than the false negative rate, and this varies between 0-10% (14,15). In our study, we did not have a false positive result, and accordingly PPV was high (100%), which is consistent with the rates reported in the literature (6,10,11).

The diagnostic accuracy rates evaluated in two separate groups in our study were 99.3% and 97.2%, respectively. Wide ranged rates are reported in studies for sensitivity (81-100%) and specificity (90-100%) (4,6,8-11,18). Our findings were consistent with those reported in the literature. In particular, the specificity was higher than the sensitivity, and the result obtained above 95% showed us that the accuracy rate of FNAB in the diagnosis of benign lesions was high. When we evaluated the parotid gland and submandibular gland separately, it was observed that the sensitivity rate in the submandibular gland was higher than the rate found in the parotid gland (100% vs 87.5% -91.7%). This finding showed us that FNAB was more reliable in detecting the malignant lesions in the submandibular gland. This reliability may also be the case since the lesions observed in the submandibular region are more malignant (1,19).

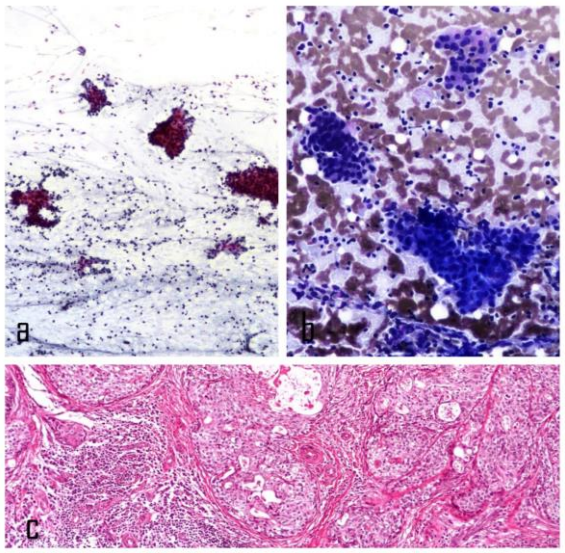

Figure 1: In the patient who was diagnosed as Warthin tumor cytologically, MEC was found as a result of resection. a-b: Epithelial cell groups with oncocytoid appearance on a background containing lymphoid cells (PAP, x100; MGG, x200), c: Tumor tissue consisting of squamoid islands containing keratinous material in their lumen and lymphoid cell infiltration around it (H&E, x100).

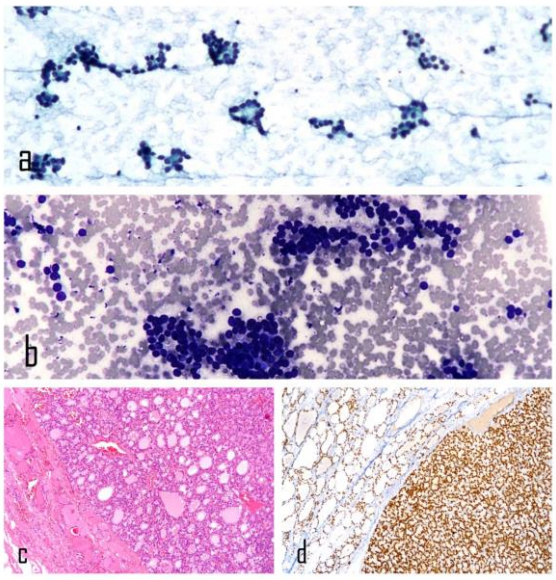

Figure 2: In the patient who was diagnosed as suspicious for malignancy group cytologically, ectopic thyroid tissue was found as a result of resection. a-b: Cellular smears containing microfollicle-like structures consisting of cells in uniform appearance (PAP, x200; MGG, x200), c: Adenoma with normal thyroid tissue (H&E, x100), d: TTF-1 positivity in surrounding the thyroid tissue and adenoma (x100).

For FNAB, which is widely used in the diagnosis of salivary gland lesions, it is important that FNAB is sufficient and of good quality, besides the experience of the evaluating pathologist (20). Nondiagnostic cytology in FNAB is generally reported with a rate varying between 2-34% in the literature (14,15,20,21). Nondiagnostic cytologies that do not contain sufficient cellular elements may depend on the experience of the person performing the procedure, the cytomorphological character of the lesion such as bleeding, necrosis, or low cellularity, as well as the location of the lesion. The rate we found in this group in our study was compatible with the one in the literature, and it was 7.05%.

Studies have reported that 30-60% of lesions suspicious for malignancy are found malignant in histopathological examinations (8,22,23). In our study, this rate was 73%, which was above the rate in the literature. However, histopathological examinations of two lesions originating from the submandibular gland in this group resulted in the diagnosis of ectopic thyroid tissue and sialadenitis, while the lesion originating from the parotid gland was also diagnosed as pleomorphic adenoma. Ectopic thyroid tissue localized in the submandibular region may not be clinically differentiated from the other pathologies such as salivary gland tumors or cysts, as in our study (24).

In the FNAB of sialadenitis, which is one of the non-neoplastic lesions, ductal epithelial cell groups and mononuclear inflammatory cells as well as mucous and squamous metaplastic cells can be observed (8). These metaplastic cells play an important role in the misinterpretation of FNAB, and low-grade MEC should primarily be kept in mind in the differential diagnosis of sialadenitis, as it was the case in our patient (11,13,25). Pleomorphic adenoma is the parotid gland tumor that we encounter most frequently and diagnose in FNAB (2,8,19). Ductal epithelial cells, myoepithelial cells and mesenchymal matrix are observed in varying proportions in smears. Due to the different components, AdCC from matrix-producing tumors, epithelial/myoepithelial carcinoma, solid variant AdCC in the presence of highly cellular smear without matrix, and low-grade MEC when it contains a mucoid matrix may be included in the differential diagnosis (1,8).

Of salivary gland tumors, 60-80% are localized in the parotid gland. Most of the tumors are benign and the most common benign tumor is pleomorphic adenoma. Malignant tumors are in the submandibular gland at a rate of 45% and in the sublingual gland at a rate of 90%. They are observed less frequently (%30) in the parotid gland. The most common malignant tumor is MEC (1,2,5,19,26). The findings of higher rate of benign tumors in the parotid gland and higher rate of malignant tumors in the submandibular gland in our study were consistent with those in the literature. Pleomorphic adenoma was the most common benign tumor, and MEC was the most common among the malignant tumors.

5. CONCLUSION:

The high sensitivity and specificity results we obtained in our study showed that FNAB was a reliable diagnostic tool in salivary gland lesions. However, the wide spectrum of salivary gland lesions and the presence of overlapping cytomorphological findings should also be kept in mind and taken into consideration.

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Conflict of interest: None

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LEFT VENTRICULAR SACULAR ANEURYSM AFTER MYOCARDIAL INFARCTION WITH SEVERE MITRAL REGURGITATION

ŞİDDETLI MİTRAL YETERSİZLİĞİ OLAN MİYOKARD ENFARKTÜSÜ SONRASI SOL VENTRIKÜLER SAKÜLER ANEVRIZMA

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Abstract
Introduction: One significant consequence of acute transmural myocardial infarction(MI) is left ventricular aneurysm (LVA). It is commonly known that patients with LVA are more likely to experience problems such congestive heart failure, thromboembolic events, and arrhythmias. **Case report:** In this paper, we describe the case of diabetic man who was admitted to our cardiology department for severe mitral valve regurgitation. He had undergone percutaneous coronary angioplasty. A saccular aneurysm of the inferio-lateral left ventricular wall was observed along with Coronary artery stenosis. The decision to do surgery was made. The patient had mechanical mitral valve replacement, coronary artery bypass grafting. **Conclusion:** The care of the late mechanical consequence of myocardial infarction, left ventricular aneurysm, is challenging. Surgery is generally beneficial and is followed by a noticeable increase in function, although it comes with a high postoperative mortality rate.
Anahtar kelimeler: Venticular aneurysm, MI
Özet
Giriş: Akut transmural miyokard enfarktüsünün (MI) önemli sonuçlarından birisi sol ventrikül anevrizmasıdır (SVA). LVA'lı hastaların konjestif kalp yetmezliği, tromboembolik olaylar ve aritmiler gibi problemler yaşama ihtimalinin daha yüksek olduğu yaygın olarak bilinmektedir. **Olgu sunumu:** Bu yazıda, kardiyoloji bölümümüze şiddetli mitral kapak yetersizliği nedeniyle başvuran diyabetik bir erkek olgusu anlatılmıştır. Perkütan koroner anjiyoplasti geçirmişti. Koroner arter stenozu ile birlikte sol ventrikül alt yan duvarında sakküler anevrizma izlendi. Ameliyat kararı verildi. Hastaya mekanik mitral kapak replasmanı, koroner arter baypas greftleme uygulandı. **Sonuç:** Miyokard enfarktüsünün geç mekanik komplikasyonu olan sol ventrikül anevrizması gelişen hastalarda cerrahi yönetim zordur. Bizim sunduğumuz vakada sol ventirkül anevrizması cerrahi olarak başarılı bir şekilde tamir edildi ve ameliyat sonrası kardiyak fonksiyonlarında transtorasik ekokokardiyografide gözle görülür bir artış izlendi..
Keywords: Ventiküler anevrizma, MI

1. INTRODUCTION

One of the leading causes of mortality and morbidity in the globe is myocardial infarction. Coronary atherosclerosis is a chronic condition with phases of stability and instability. Patients may experience a myocardial infarction when there are unstable periods of activated inflammation in the arterial wall Myocardial infarction can be a little, undiscovered incident in a lifetime chronic condition, or it can be a huge catastrophe resulting in a sudden death or severe hemodynamic impairment. Myocardial infarctions can happen frequently in people with preexisting illness or they might be the initial sign of coronary artery disease.

Acute myocardial infarction is sometimes followed by acute mitral regurgitation (MR). It can happen when the papillary muscles rupture (primary MR), or it can happen when the infarcted portions reconstruct quickly, causing geometric alterations and tethering of the leaflets. (secondary or functional MR). When combined with pulmonary edema and refractory cardiogenic shock, the clinical picture might be disastrous.

One significant consequence of acute transmural myocardial infarction(MI) is left ventricular aneurysm (LVA). We now have a better

understanding of LVA's natural history. The increased use of noninvasive methods has enabled earlier identification and a greater understanding of the pathophysiology and etiology of LVA. More successful LVA surgery has been achieved as a consequence of advancements in surgical anesthetic and approaches. 7.6% of patients with coronary artery disease (CAD) who had been referred for coronary angiography reported LVA (1).

Figure 1: Ventricular aneurysm seen in angiography.

In this paper, we describe the case of a 53-year-old diabetic man who was admitted to our cardiology department for severe mitral valve regurgitation. He had undergone percutaneous coronary angioplasty with stenting of the mid segments of the left anterior descending artery (LAD) for myocardial infarction one year prior. On the ECG, there were abnormal Q waves in the inferolateral leads and sinus rhythm at 90 beats per minute. A sacular aneurysm of the infero-lateral left ventricular wall, significant mitral valve regurgitation, and fibrosis were all seen on transthoracic and transesophageal echocardiography, but no thrombus reported. A mildly decreased ejection fraction (EF) of 50% was seen along with LV hypertrophy and dilation. The ultrasound results and observable diffuse coronary stenosis at the ending point of the LAD stent application were verified by coronary angiography (figure1). Other coronary arteries did not show any noticeable stenosis. The decision to do surgery was made. Gaint aneurysm was seen in posteriolateral wall (figure 2). The patient had mechanical mitral valve replacement, coronary artery bypass grafting of the left anterior descending (LAD) with the left internal mammary artery (LIMA), and ventricular aneurysm repair (figure 3). In the early stages of his recovery in the intensive care unit after the surgery, he required an intra aortic balloon pump. A negligible MR and an improvement in LVEF to 55% were seen on the postoperative echocardiographic control.

Figure2: Intraoperative image of aneurysm.

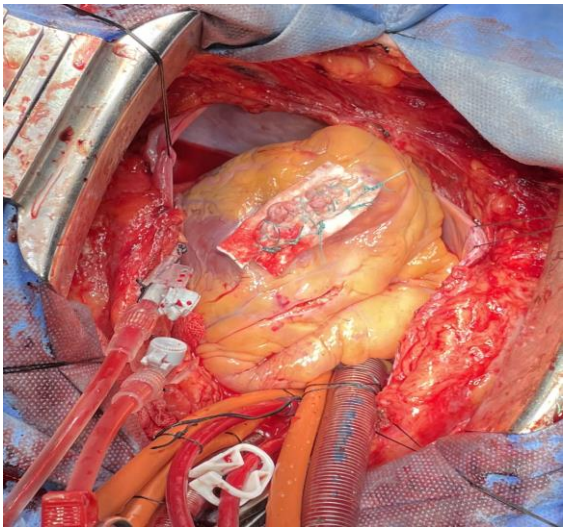
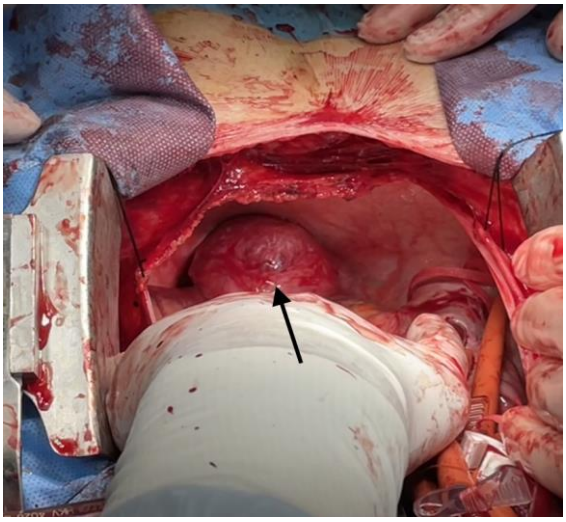


Figure3: post repair image of ventricular aneurysm.



2. DISCUSSION

After an acute MI, LV aneurysm and pseudoaneurysm development are recognized side effects, especially in cases of severe MI and late presentation (2), however because percutaneous reperfusion treatment is widely available, its prevalence has significantly decreased (3). Due to their increased propensity for progressive development and rupture, LV pseudoaneurysms require prompt surgical intervention in contrast to true aneurysms, which are frequently treated conservatively (3) as well as the need of early and

routine echocardiography reevaluation, particularly in patients who continue to show symptoms and have significant LV failure. Additionally, weeks after the index event, pseudoaneurysms and myocardial rupture may develop (4). It is difficult to treat the late mechanical complication of myocardial infarction, left ventricular aneurysm. Surgery has a high postoperative mortality rate but is often helpful and results in a considerable improvement in function.

Çıkar çatışması: Yazar bu çalışma için çıkar çatışması bildirmemişlerdir.

Mali Destek: Yok

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ATİPİK YERLEŞİMLİ DEV SOLİTER MOLLUSKUM KONTAGİOSUM OLGUSU

A CASE OF GIANT SOLITER MOLLUSCUM CONTAGIOSUM WITH ATYPICAL LOCATION

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Özet

Molluskum kontagiosum; deri ve mukozada yerleşen, tipik olarak tek ya da çok sayıda ortası çöküк, deri renginde veya saydam yuvarlak nodüller ile karakterize viral bir enfeksiyondur. Etkeni Poxvirüs grubundan bir DNA virüsü olan molluskum kontagiosum(MK) virüstür. Biz burada, öz bakımı kötü 78 yaşındaki hastamızın el sırtında oluşan molluskum kontagiosum olgusunu nadir görülen bir görünümde ve lokalizasyonda olması nedeniyle sunmaktayız. 78 yaşında erkek hasta, sağ el üzerinde oluşan ağrısız lezyon ile polikliniğimize başvurdu. Hasta lezyonun yaklaşık 6 aydır olduğunu ve giderek büyüdüğünü, daha önce doktora başvurduğunu, verilen kremlerden fayda görmediğini ifade etmekteydi. Olgumuza mevcut klinik bulgularla molluskum kontagiosum tanısı konarak lezyon total eksize edildi, sekonder iyileşmeye bırakıldı. Molluskum kontagiosumun atipik lokalizasyonları 1 cm büyüklüğüne ulaşabilir ve bunlara dev molluskum kontagiosum denir. Olgumuzda sunmuş olduğumuz gibi klinikle gelen vakalarda hekimlerin aklına ön planda bazal hücreli karsinom, keratoakantom, trikoepitelyoma gibi tümöral lezyonlar gelmektedir. Bu nedenle bu tarz lezyonlar muhakkak palpe edilmeli, palpasyona bağlı olarak ve klinik öykü sonucu ayırıcı tanıda dev molluskum kontagiosum da düşünülmelidir.

Anahtar kelimeler: Eksizyon, Molluskum, Poxvirüs

Abstract

Molluscum contagiosum; It is a viral infection of the skin and mucous membranes, characterized by single or multiple sunken, skin-colored or transparent round nodules. The causative agent is (molluskum contagiosum)MK virus, a DNA virus from the Poxvirus group. Here, we present a case of molluscum contagiosum on the back of the hand of our 78-year-old patient with poor self-care because of its rare appearance and localization. A 78-year-old male patient was admitted to our outpatient clinic with a painless lesion on his right hand. The patient stated that the lesion had been around for 6 months and was growing gradually, that he had consulted a doctor before, and that he did not benefit from the creams given. Our case was diagnosed as molluscum contagiosum based on the current clinical findings, and the lesion was excised completely and left for secondary healing. Atypical localizations of molluscum contagiosum can reach 1 cm in size and are called giant molluscum contagiosum. As we have presented in our case, physicians think of tumoral lesions such as basal cell carcinoma, keratoacanthoma, trichoepithelioma in clinical cases. Therefore, such lesions should be palpated, and giant molluscum contagiosum should be considered in the differential diagnosis depending on palpation and clinical history

Keywords: Excision, Molluscum, Poxvirus

1. GİRİŞ

Molluskum kontagiosum; deri ve mukozada yerleşen, tipik olarak tek ya da çok sayıda ortası çöküк, deri renginde veya saydam yuvarlak nodüller ile karakterize, genellikle gövde, aksilla, genital bölge ve yüzde ortaya çıkan, çoğu aylar içerisinde kendiliğinden iyileşen viral bir enfeksiyondur. Etkeni Poxvirüs grubundan bir DNA virüsü olan MK virüstür[1,2]. Enfeksiyon genellikle çocuklarda görülmekle beraber immün yetmezlikli ve atopik bireylerde, kortikosteroid kullananlarda, malignitesi olan hastalarda da çok sayıda ve atipik yerleşimli olgular bildirilmiştir[2]. İnsan bilinen tek konak olmakla beraber bulaş deri teması ve cinsel ilişki yoluyla gerçekleşir. Sıcak iklimli, gelişmekte olan ve kişisel hijyenin kötü olduğu toplumlarda, yüzme havuzu, sauna ve spor merkezlerinden bulaş olguları sık olarak bildirilmiştir[1]. Biz burada altta yatan bir hastalığı, herhangi bir ilaç kullanımı ve cinsel birliktelik öyküsü bulunmayan öz bakımı kötü 78 yaşındaki hastamızın el sırtında oluşan molluskum kontagiosum olgusunu nadir görülen bir görünümde ve lokalizasyonda olması nedeniyle sunmaktayız.

2. OLGU

78 yaşında öz bakımı iyi olmayan erkek hasta, sağ el üzerinde oluşan ağrısız lezyon ile polikliniğimize başvurdu. Hasta lezyonun yaklaşık 6 aydır olduğunu ve giderek büyüdüğünü, daha önce doktora başvurduğunu, verilen kremlerden fayda görmediğini ifade etmekteydi. Sistemik muayenesi doğaldı. Yapılan dermatolojik muayenesinde yalnızca sağ el sırtında soliter, yaklaşık 3 cm çaplı pembe renkli üzeri sarı krutlu nodüler lezyon görülmekteydi. Hastanın altta yatan bir immunosüpresif hastalığı, lokal ya da sistemik herhangi bir ilaç kullanımı, cinsel birliktelik öyküsü, havuz-sauna ve hamam kullanım öyküsü yoktu fakat yaşlı ve öz bakımı kötü bir hastaydı. Lezyon palpe edildiğinde hafif yumuşaktı. Üzerinde sarı krut kaldırıldığında lezyon içerisinden sıvı kazeöz materyal boşaldı. Olgumuza mevcut klinik bulgularla molluskum kontagiosum tanısı konarak lezyon total eksize edildi, sekonder iyileşmeye bırakıldı. Mevcut klinik takiplerinde rekürrens gözlenmedi.

Resim 1: Üzeri sarı krutlu, pembe, yumuşak kıvamlı nodüler lezyon

Resim 2: Lezyonun eksizyon sonrası görünümü

3. TARTIŞMA

Molluskum Kontagiosum, ilk kez 1871'de Bateman ve arkadaşları tarafından klinik olarak tanımlanmıştır. Poxvirüs sınıfından çiftsarmal DNA yapılı MK virüsünün sebep olduğu hastalık, sıklıkla çocuklarda görülmekle birlikte; cinsel açıdan aktif, immunsupresif yapılı bireylerde de bildirilmiştir[3,4]. Virüs epitel hücreleri içinde çoğalabilmektedir. Tipik lezyonlar yaklaşık 3-5 mm çapa ulaştıktan sonra hücresel hasar mekanizması ile merkezde çukurluk oluşturur ve beyaz renkli, içi kazeöz materyal ile dolu, merkezi deprese görünüme ulaşır[1]. Lezyonlar genellikle gövde, aksilla, genital bölge ve yüzde ortaya çıkmaktayken; atopik dermatit, kortikosteroid ve immünosupresif tedavi kullanımı, sarkoidoz, lösemi, Wiskott Aldrich sendromu ve Edinilmiş İmmün Yetmezlik Sendromu(AIDS) gibi hastalıklara sahip immunsupresif bireylerde, molluskum atipik lokalizasyonlar gösterebilir, 1 cm büyüklüğüne ulaşabilir ve bunlara dev molluskum kontagiosum denir[3]. Tanı, çoğunlukla klinik görünümle konulmasına rağmen kesin tanı konulamayan olgularda, histopatolojik inceleme, tzanck smear , PCR tanıda yardımcı olabilir. Ayırıcı tanıda tek sayıda lezyonu olanlarda keratoakantom, bazal hücreli karsinom, sebase hiperplazi, dermal nevüs, trikoepitelyoma; çok sayıda lezyonu olan hastalarda ise siringom, milyum, hidrokistoma, kondilom düşünülülebilir. Molluskum kontagiosum sıklıkla kendi kendini sınırlayarak birkaç ay içerisinde kendiliğinden iyileşse de tedavide kriyoterapi, küretaj, trikloroasetik asit, topikal tretinoin ve

imikimod, podofilotoksin, gümüş nitrat, fenol, 5-florourasil ve potasyum hidroksit(KOH), oral simetidin kullanılabilmektedir[2].

4. SONUÇ

Olgumuzda sunmuş olduğumuz gibi klinikle gelen vakalarda hekimlerin aklına ön planda bazal hücreli karsinom, keratoakantom, trikoepitelyoma gibi tümöral lezyonlar gelmektedir. Bu nedenle bu tarz lezyonlar muhakkak palpe edilmeli; palpasyona bağlı olarak ve klinik öykü sonucu ayırıcı tanıda dev molluskum kontagiosum da düşünülmelidir.

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