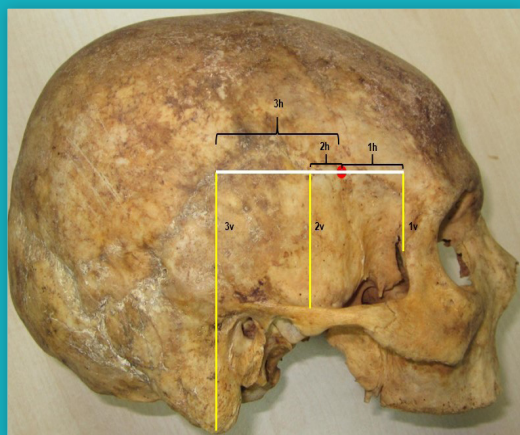




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▼ ***The Effects of *Lucilia sericata* Larval Secretions on The Expressions of MicroRNAs that are Suggested to be Related with Wound Healing in Experimental Diabetic Rat Wound Model***

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▼ ***Investigation of Plantar Pressure Distribution in Overweight and Obese Individuals***

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EDITORIAL

Dear Readers,

I wish 2020 to be a year of new hope and beauty. With our increasing efforts and successes every day, I think that we achieved a lot of success on behalf of our journal last year. We start the new year with a new cover face. We will change the color and design of our cover in the first issue. For each issue, we will include a figure to be determined by our editorial board from among the figures of the articles to be published in that issue, and the name of this article will appear on the cover. In our last issue, I mentioned about the new indexes we joined and that our language of publication would be English. We continue to accept Turkish articles. We translate accepted articles without charge. I think this will be an attraction for our researchers, who have a shortage of language.

In this issue; the article entitled "Inner Surface of Pterion in Terms of Surgical Approaches: an Anatomical Cadaveric Study" by DEVELİ et al., the article entitled "The Effects of *Lucilia Sericata* Larval Secretions on The Expressions of MicroRNAs that are Suggested to be Related with Wound Healing in Experimental Diabetic Rat Wound Model" by KILINÇ et al., the article entitled "Investigation of Plantar Pressure Distribution in Overweight and Obese Individuals" TAŞ et al., and the article entitled "Retrospective Analysis and Family Feedback of Patients Who Underwent Tracheostomy in Pediatric Intensive Care Unit: Single Center, 10 Years of Experience" by KOÇOĞLU et al. are the articles that are prominent. Increasing publication demands honor us and we are pleased to see new articles coming from domestic and international institutions.

With our new issue, there have been changes in our editorial board and new friends have joined us. I offer my heartfelt thanks to all our friends who supported us. I would like to welcome our new friends and thank them in advance for their contributions to our journal.

I celebrate your new year again, I wish it to be an occasion of beauty for our country and the world.

See you in the next issue....

Kindest regards

Prof. Dr. Adem AKCAKAYA

Editor-in-Chief



Clinical-histopathological Features of Paratesticular Masses and Factors Affecting Survival: Single Center Experience

Paratestiküler Kitlelerin Klinik-histopatolojik Özellikleri ve Sağkalıma Etki Eden Faktörler: Tek Merkez Deneyimi

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ABSTRACT

Objective: As paratesticular masses constitute 2-3% of all scrotal and inguinal masses, published cases in the literature are limited. We aimed to present our experiences of nine cases which we have treated and followed up in our department.

Methods: Between January 2013 and February 2017, we retrospectively analyzed the data of nine patients with paratesticular mass in our department.

Results: Seven (77.8%) patients presented with scrotal mass or swelling, while two (22.2%) patients had swelling in the inguinal region. Histological types of malign tumors were rhabdomyosarcoma [(RMS), 2 cases, 22.3%], liposarcoma [(LPS), 1 case, 11.1%], leiomyosarcoma [(LMS), 1 case, 11.1%]] and malignant fibrous histiocytoma [(MFH), 1 case, 11.1%]. Bening tumors were fibroma (1 case, 11.1%), adenomatoid tumor (1 case, 11.1%), cystadenoma (1 case, 11.1%) and inflammatory myofibroblastic tumor (1 case, 11.1%). During median 23.5 (4-62) months of follow-up of paratesticular sarcomas, the rates of recurrence-free and progression-free survival were 60%, overall survival rate was 60%. LMS and MFH had poor prognosis. No recurrence or progression was observed in the follow-up of LPS and RMS. Among them, LPS had the best prognosis. The disease-free survival was 100% at the median 49 (36-64) months follow-up of four benign masses without any

ÖZ

Amaç: Paratestiküler kitleler, tüm skrotal ve inguinal kitlelerin %2-3 gibi oldukça az bir kısmını oluşturduğundan, literatürde bildirilmiş olgular kısıtlıdır. Kliniğimizde paratestiküler kitle nedeniyle takip ve tedavisini gerçekleştirdiğimiz dokuz olguya ait deneyimlerimizi sunmayı amaçladık.

Yöntemler: Ocak 2013-Şubat 2017 arasında, kliniğimizde paratestiküler kitle nedeniyle takip ve tedavi ettiğimiz 3-72 yaş arasındaki dokuz olgunun verilerini, postoperatif takip sürecindeki bulgularını retrospektif olarak inceledik.

Bulgular: Yedi (%77,8) olgu skrotal kitle, şişlik yakınması ile başvururken, iki (%22,2) hasta inguinal bölgede şişlik nedeniyle başvurdu. Patolojik tanısı malign gelen tümörlerin histolojik tipleri rhabdomyosarkom [(RMS), 2 olgu, %22,3], liposarkom [(LPS), 1 olgu, %11,1], [leiomyosarkom (LMS), 1 olgu, %11,1]] ve malign fibröz histiyostom [(MFH), 1 olgu, %11,1]] idi. Benign patolojili tümörler ise, fibroma (1 olgu, %11,1), adenomatoid tümör (1 olgu, %11,1), kistadenom (1 olgu, %11,1) ve enflamatuvar miyofibroblastik tümör (1 olgu, %11,1) olarak saptandı. Beş sarkom olgusunun medyan 23,5 (4-62) aylık takibinde nüksüz ve progresyonsuz sağkalım oranı %60 iken, genel sağkalım oranı %60 idi. Bu beş olgudan en kötü prognozlu olanlar LMS ve MFH idi. LPS ile RMS olgularının takibinde nüks ve progresyon gözlenmezken, en iyi prognoz LPS'ye aitti. Adjuvan tedavi gereksinimi olmayan

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need for adjuvant treatment. According to FNCLCC Classification, times of local recurrence-free survival and overall survival in grade II sarcomas were significantly higher than those with grade III ($p=0.039$).

Conclusion: It is difficult to differentiate clinically benign paratesticular masses from sarcomas. LPS has better prognosis and high-grade sarcomas have poor prognosis. If adjuvant treatments are not added, local recurrence or progression may be observed in a short time.

Keywords: Benign paratesticular masses, FNCLCC grading system, local recurrence free survival, overall survival, paratesticular sarcomas

dört benign kitlenin median 49 (36-64) aylık takibinde hastalıksız sağkalım %100'dü. FNCLCC sınıflandırması'na göre derece 2 sarkomlarda lokal nüksüz sağkalım ve genel sağkalım süreleri, derece 3'e göre anlamlı olarak daha fazla saptandı ($p=0,039$).

Sonuç: Benign paratestiküler kitleleri, sarkomlardan klinik olarak ayırt etmek zordur. Paratestiküler sarkomlarda histolojik alt tipler içerisinde LPS daha iyi prognoza sahiptir. Yüksek dereceli sarkomların prognozu daha kötüdür. Adjuvan tedaviler eklenmezse, kısa sürede lokal nüks veya progresyon gözlenebilmektedir.

Anahtar Sözcükler: Benign paratestiküler kitleler, FNCLCC derecelendirme sistemi, genel sağkalım, lokal nüksüz sağkalım, paratestiküler sarkomlar

Introduction

Paratesticular area consists of embryological remains such as epididymis, spermatic cord, tunica vaginalis, appendix testis, and inguinal canal and supporting tissues (1). Although tumors originating from this region are rare, they have a wide distribution in terms of pathological diversity due to the different anatomical structures they contain (2). Paratesticular masses account for 2-3% of all scrotal masses (1,3). Although the rate of malignancy is lower than intratesticular masses, it is difficult to distinguish precisely with clinical findings. When the suspicion of malignancy cannot be ruled out in benign masses, radical orchiectomy is often performed (3). On the other hand, malignant masses can be interpreted as benign inguinoscrotal masses such as hernia, lipoma, epididymal cyst, and incomplete resections of malignant masses which are thought to be benign, can lead to tumor recurrence in up to 50% of patients (4).

Paratesticular sarcomas are tumors with poor prognosis, originating from embryonic mesenchymal cells. The incidence of soft tissue sarcoma is 5 in 100.000 per year, of which less than 5% is due to the genitourinary system. It accounts for 1-2% of all genitourinary malignancies (4). Since paratesticular sarcoma is rare, studies with a large population of patients in the literature are very few (5,6). Therefore, our knowledge of its natural course and prognosis is limited, and no definitive follow-up and treatment protocols have been established. To our knowledge, the largest patient series belong to Ap Dafydd et al. (4) whose study was performed on 77 patients.

Tumor stage, degree, histopathological subtype and size are important in predicting resectability and survival in paratesticular sarcomas (5,6). Complete surgical resection, known to increase survival rates, is the recommended treatment to be done in the first stage. Adjuvant treatment protocols have not yet been standardized and their contribution to survival varies in different studies (6). Since our knowledge of paratesticular masses is limited, we aimed to examine the clinical-pathological characteristics of benign and malignant patients in our clinic and to evaluate the prognostic factors that may have an effect on oncological outcomes in cases with sarcoma.

Methods

We examined the pathological data of patients who underwent radical orchiectomy due to intratesticular or extratesticular mass in our clinic between January 2013 and February 2017. Nine patients with ages of 3-72 years who were treated and followed up due to paratesticular masses were included in the study. The clinical and histopathological data of the patients and their findings in postoperative follow-up were evaluated retrospectively. Demographic data, presenting symptoms, side of the tumor, localization of the tumor in the paratesticular area, the status of metastasis at diagnosis, pathological tissue diagnosis, pathological tumor size, the performed surgical treatments, surgical resection status (complete/incomplete), surgical margin positivity, adjuvant therapy given during postoperative follow-up, postoperative follow-up period, local recurrence, progression and survival status were recorded.

The French Fédération Nationale des Centers de Lutte Contre le Cancer (FNCLCC) Grading system was used for the pathological examination of patients with sarcoma and the pathological rating of each patient was recorded according to this system. In this system, three parameters including tumor differentiation, mitotic activity and tumor necrosis degree are scored separately and according to the total score, patients are classified as grades I, II, III (low, medium, high grade) in terms of sarcoma grade (7,8).

Statistical Analysis

Before comparing the differences between benign and malignant pathologies, normality status was evaluated with Kolmogorov-Smirnov and Shapiro-Wilk tests. When there was normal distribution, Independent Sample t-test was used to compare age and tumor size, which are independent continuous variables. While Kaplan-Meier method was used for survival analysis in malignant patients, differences between patient subgroups were evaluated by the log rank test. This study was not suitable for the multivariate model, due to the small size of the sample. The analyses were done using IBM SPSS Statistics 21 (IBM, Armonk, NY USA) software. $P<0.05$ was considered statistically significant.

Results

The mean age at diagnosis of the nine male patients included in the study was 38.67 ± 22.18 years. Seven patients (77.8%) were admitted with scrotal mass or swelling, while two patients (22.%) were admitted with swelling in the inguinal area. Histological types of malignant tumors were rhabdomyosarcoma [(RMS), 2 cases, 22.3%], liposarcoma [(LPS), 1 case, 11.1%], leiomyosarcoma [(LMS), 1 case, 11.1%] and malignant fibrous histiostoma [(MFH), 1 case, 11.1%]. Benign tumors were fibroma (1 case, 11.1%), adenomatoid tumor (1 case, 11.1%), cystadenoma (1 case, 11.1%) and inflammatory myofibroblastic tumor (1 case, 11.1%). Since the suspicion of malignancy could

not be ruled out clinically, surgical excision was applied in all patients. Surgical boundary positivity was observed in only one (11.1%) of all patients undergoing complete resection. Preoperative serum tumor markers (alpha fetoprotein, beta human chorionic gonadotropin, lactate dehydrogenase) were normal in all patients.

No metastasis was detected at the time of diagnosis in any of the five patients with sarcoma. Neoadjuvant therapy was not applied to the patients; adjuvant chemotherapy (CT) was administered in three patients, adjuvant radiotherapy (RT) was administered in one case, and one case was followed up. The recurrence-free and progression-free survival rate was 60%, while the overall

Table 1. Demographic, clinical, pathological data and oncological results of patients gender

1	19	Male	Right scrotal swelling	Testis-epididymis	Spindle cell variant RMS grade 2	55x45x45	Right inguinal orchiectomy + 7 cycles of CT for left paraaortic 10x8 mm-diameter lymph node (vincristine, actinomycin D, cyclophosphamide)	63 months	No relapse, Alive
2	59	Male	Right scrotal swelling	Spermatic cord-epididymis	LPS grade 2	45x40x27	Right inguinal orchiectomy + follow up	49 months	No relapse, Alive
3	72	Male	Swelling in the left inguinal region	Spermatic cord	LMS grade 3	50x40x30	Left inguinal orchiectomy + inguinal mass excision + adjuvant RT due to surgical boundary positivity	4 months	Relapse in the 4 th month, The patient voluntarily left the follow-up, It was learnt that he died in the 28 th month
4	3	Male	Right scrotal swelling	Testis-epididymis	Embryonal RMS grade 2	11x10x5	Right inguinal orchiectomy + 12 cycles of CT (vincristin)	40 months	No relapse, Alive
5	60	Male	Left scrotal swelling	Spermatic cord-epididymis	Malignant fibrous histiocyotoma grade 3	50x49x45	Left inguinal orchiectomy + 4 cycles of CT (ifosphamide, mesna, Adriamycin)	8 months	Relapse in the 8 th month, The patient voluntarily left the follow-up, It was learnt that he died in the 33 rd month
6	45	Male	Swelling in the right inguinal region	Spermatic cord	Fibroma	32x23x10		47 months	No relapse, Alive
7	26	Male	Left scrotal mass	Epididymis	Adenomatoid tumor	19x18x16		51 months	No relapse, Alive
8	30	Male	Left scrotal mass	Epididymis	Cystadenoma	16x14x12		36 months	No relapse, Alive
9	24	Male	Left scrotal mass	Epididymis	Inflammatory myofibroblastic tumor	15x12x11		64 months	No relapse, Alive

RMS: Rhabdomyosarcoma, LPS: Liposarcoma, LMS: Leiomyosarcoma, CT: Chemotherapy

survival rate was 60% in 5 patients with sarcoma during a median 23.5-month follow-up (4-62 months). Among these cases, those with the worst prognosis were LMS and MFH. In the case with LMS, after radical orchiectomy, adjuvant RT was applied due to surgical boundary positivity, but in the early stage (in the 4th month) there was local recurrence. In our case with MFH, local recurrence was detected in the 8th month. We do not know about the state of progression in these patients due to lack of follow up. However, the overall survival times of these patients were 28 and 33 months, respectively. In the follow-up of patients with LPS and RMS, recurrence and progression were not observed. We determined LPS as the histopathological type with better prognosis, because that patient with LPS did not show recurrence and progression during 49 months of follow-up, even though we did not administer adjuvant therapy.

The disease-free survival rate was 100% during the median 49-month follow-up (36-64 months) of four patients with benign masses without need of adjuvant therapy. While the mean tumor size was 43.00 ± 18.04 mm in patients with sarcoma, the tumor size in benign masses was significantly smaller (20.25 ± 8.09 mm) ($p=0.047$). No significant difference was observed between benign and malignant patients in terms of mean age at diagnosis (33.75 ± 8.18 and 42.60 ± 29.83 , respectively) ($p=0.555$). The characteristics of the cases are seen in Table 1.

The oncological results of five patients with sarcoma were evaluated in terms of patient age, histopathological subtype of tumor, FNCLCC rating system and tumor size (>5 or <5 cm). In Kaplan-Meier analysis, local survival time without recurrence and overall survival time were significantly higher in grade II sarcomas than in grade III sarcomas according to FNCLCC classification ($p=0.039$, Figure 1, 2). No significant effects of other parameters were observed on survival without local recurrence and overall survival (Figure 3, 4, 5).

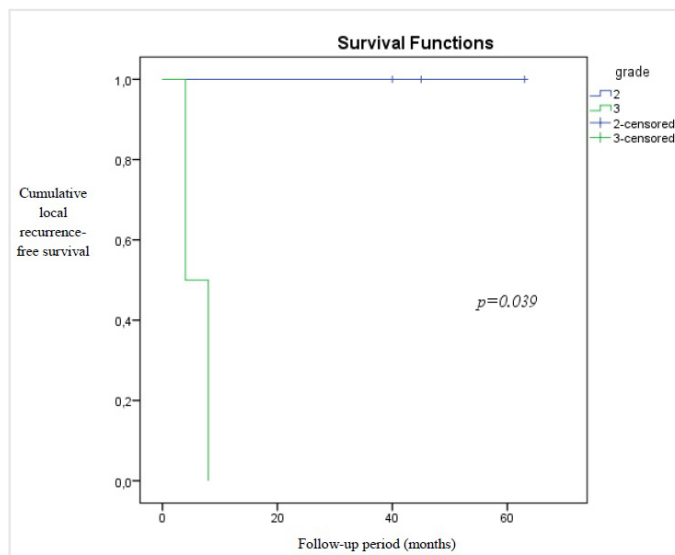


Figure 1. Kaplan-Meier graph of local recurrence-free survival curves according to histopathological grade

Discussion

It is known that there is a lower rate of malignancy in paratesticular masses than intratesticular masses (3). When we examined our patient data, we detected germ cell tumors in 75 (87.2%) of 86 cases who underwent radical orchiectomy due to testicular mass in our clinic, while we observed malignancy in five (55.5%) of nine paratesticular masses. The incidence of paratesticular sarcoma was reported as 6.7% in radical orchiectomies performed with suspicion of testicular tumor (9), whereas in our radical orchiectomy series, this rate was 5.2%. Paratesticular benign tumors are more common in the third and fourth decades, while malignant tumors occur in the sixth and

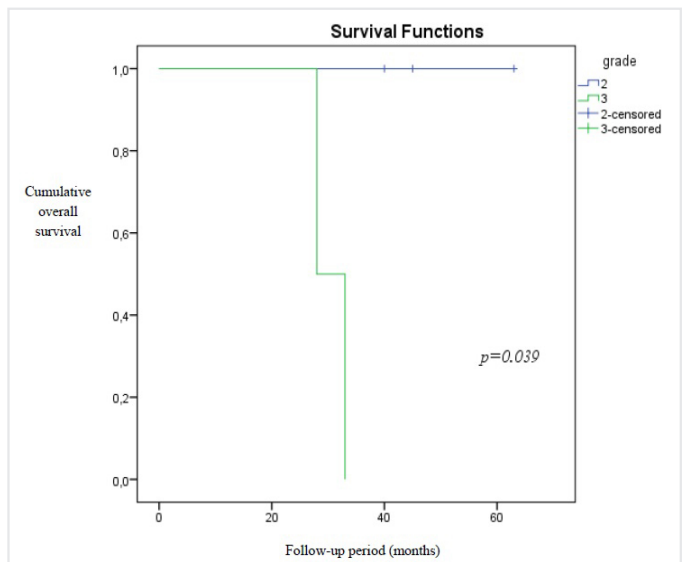
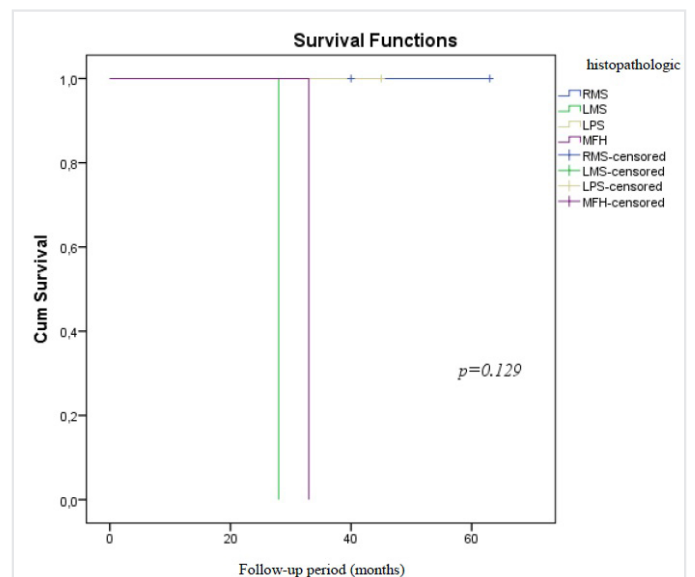


Figure 2. Kaplan-Meier graph of overall survival curves according to histopathological grade



Kaplan-Meier survival graph according to histopathological tumor type

RMS: Rhabdomyosarcoma, LMS: Leiomyosarcoma, LPS: Liposarcoma, MFH: Malignant fibrous histiocytoma

seventh decades (10). Similarly, the mean age at diagnosis was 33.75 ± 8.18 years in benign patients and 42.60 ± 29.83 years in malignant patients in our study.

Paratesticular masses constitute 2-3% of all scrotal masses, 30% of these masses are sarcomas, more than half are benign tumors (11). Adenomatoid tumors, the most common benign mesothelial tumors of the paratesticular region, constitute 30% of all paratesticular neoplasms and 60% of all benign neoplasms (12). The second most common benign tumor is cystadenoma. Both tumors originate mostly from the epididymis (13). Synonym names such as inflammatory pseudotumor, atypical myofibroblastic tumor, and pseudosarcomatous myofibroblastic proliferation are also used for inflammatory myofibroblastic tumors (IMT), which account for about 6% of paratesticular masses (14). While there were no reported relapses in follow-

up, distant metastasis was observed in less than 5% of non-epididymic IMT cases (15). Fibromas, which constitute 6% of paratesticular tumors, originate from tunica vaginalis in 75% of cases and from epididymis in 10% of cases, and spermatic cord involvement is much rarer (16).

Since benign tumors with paratesticular placement do not show recurrence and progression, total mass excision with using a testicular protective approach is sufficient treatment method (2). However, it is often difficult to distinguish malignancy with clinical examination and radiological methods. Radical orchiectomy may be preferred especially in patients with involvement of tunica albuginea, rete testis and spermatic cord (2).

Since our information on paratesticular sarcomas belongs to series with a limited number of patients published in the literature; there is still no consensus on optimal treatment regimens and follow-up protocols (17,18). The most common type among all soft tissue sarcomas is LPS, while the most common types among genitourinary-derived sarcomas are LMS (29%), LPS (26%) and RMS (18%) (6), respectively. The most common types among paratesticular sarcomas are LPS (20-32%), LMS (19-32%) and RMS (11-24%) (19). We observed RMS in two cases (40%), LPS in one case (20%), LMS in one case (20%) and MFH in one case (20%) in patients with paratesticular sarcomas. However, because we have few cases, our rates do not match the literature. Embryonal type RMS is the most common paratesticular sarcoma in children and adolescents (19) and our 3-year and 19-year-old patients with RMS are compatible with the literature in this respect.

The admission complaint in paratesticular sarcomas is mostly painless scrotal mass and they develop from the mesenchymal elements of the spermatic cord, epididymis and testicular sheath. About 70% of them settle on spermatic cord (10). Of the five patients with sarcoma in our study, three (60%) originated from the spermatic cord.

When all genitourinary sarcomas are examined in the literature, survival rates of paratesticular sarcomas and sarcomas originating from bladder are reported to be higher than those originating from other organs (6). This was attributed to early admission of patients due to scrotal swelling in paratesticular sarcoma and hematuria in bladder sarcoma and to diagnosis in earlier stages (5). All nine cases in our study were admitted with noticeable swelling in the scrotal or inguinal region, and none of the five patients diagnosed as having sarcoma had metastasis at the time of diagnosis.

RMS is the most common primary paratesticular malignant neoplasia between 7 and 36 years of age (average age at diagnosis is 10 years) (20). It accounts for 80% of paratesticular tumors seen under the age of 21 and 24% of those detected in adults (21). The histopathological types; "embryonal type" and "spindle cell variant", found in two cases with paratesticular RMS in our study had a better prognosis than the other RMS subtypes (22). In fact, no recurrence and progression were observed in the mean 50.5-month (39-62 months) follow-up of both cases.

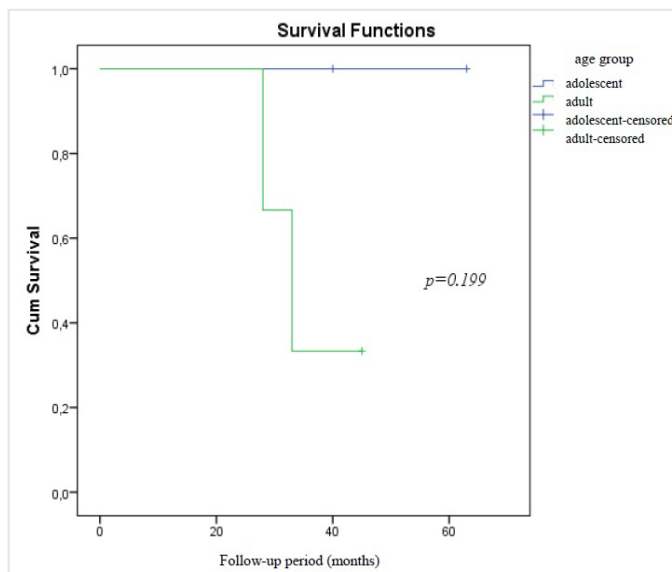


Figure 4. Kaplan-Meier survival graph according to patient age groups

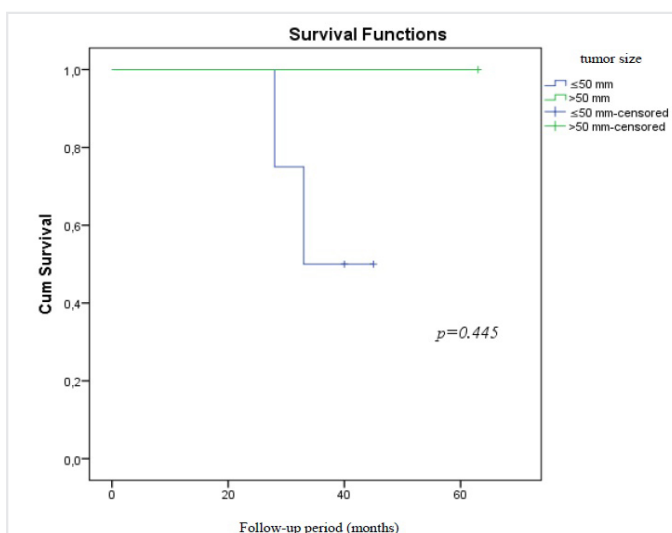


Figure 5. Kaplan-Meier survival graph according to tumor size

There are fewer reported cases with paratesticular LMS and LPS in the literature (23,24). Fisher et al. (23) showed that development of recurrence and metastasis can be prevented with radical orchiectomy in patients with low-grade paratesticular LMS. In our case, surgical boundary positivity was observed after complete excision and he received adjuvant RT. Despite multimodal treatment, development of local recurrence in the 4th month could not be prevented. Paratesticular LPS is mostly well differentiated and expected survival is longer in patients with paratesticular LPS (24,25). In our case with grade II paratesticular LPS, no recurrence or progression were observed during 48-month follow-up without adjuvant treatment.

There is still debate about the role of retroperitoneal lymphadenectomy (RPLND) in paratesticular sarcomas (25-27). At the time of diagnosis, only CT was applied instead of RPLND as adjuvant treatment for our RMS patient with a 10x8 mm diameter lymph node with a 10x8 mm diameter lymph node in the left paraaortic area. No recurrence or progression was observed during 62 months of follow-up.

The frequency of MFH, which is very rare and fast progressive, is 4.5% in all genitourinary sarcomas and 11.1% in paratesticular sarcomas (5). The size and histopathological characteristics of the tumor are important factors for development of metastasis. Despite multimodal treatment, 3-year survival is approximately 40% (28). The overall survival was 33 months in our patient with grade III paratesticular MFH. Despite adjuvant CT, he developed local recurrence in the 8th month.

There are very few reported studies regarding long-term follow-up results of paratesticular sarcomas. Since there is a greater incidence of RMS in the pediatric age group, most of the survival results were obtained from multicenter publications of RMS cases (9). Korkes et al. (9) indicated that overall survival was 27.8±6.2 months and overall survival rate was 50% after a median 31.4 (6-60) months of follow-up. In the same study, lung metastasis was observed in 50% of cases with LMS, while recurrence or progression was not detected in cases with LPS, and metastasis rate in RMS was found to be 50%. They found no difference between sarcoma types in terms of disease-free survival (9). In another study with a median 32.18 months (1-142) of follow-up, overall survival rate was 12.5% (29). Dotan et al. (6) showed that increased tumor size, incomplete surgical resection, positive surgical boundary and metastasis at the time of diagnosis in all genitourinary sarcomas were identified as negative factors that reduce disease-specific survival. Although the 5-year local recurrence rate was reported as 32%, metastasis-free survival rate as 60% and disease-specific survival rate as 69%; no subgroup analysis was performed for paratesticular sarcomas in this study (6).

Having the largest known series of patients (188 patients) with all kinds of genitourinary sarcomas, Dotan et al. (6) showed that 5-year disease-free survival rate was 12.5% and cancer-specific survival was 25%. In subgroup analyses of 56 patients with paratesticular sarcoma. The negative factors that affect recurrence-free survival are renal placement, female gender,

presence of metastases at diagnosis, and positive surgical margin and the negative factors that affect metastasis-free survival are the presence of incomplete surgical resection and positive surgical margin. During a median 23.5 (4-62) months of follow-up, we observed recurrence-free and progression-free survival as 60% and overall survival as 60% in five patients with sarcoma. In addition, we found local recurrence-free survival time and overall survival time were significantly higher in grade II sarcomas than in grade III sarcomas according to FNCLCC classification, while we were unable to show any significant effect of other parameters on oncological outcomes.

While complete surgical excision is the recommended treatment in the first step, the location of adjuvant CT and RT is still unclear. Although adjuvant treatments have been reported to reduce local recurrence and extend overall survival (9,30), in two cases with grade III tumor in our study, recurrence and progression were observed in a short period of time despite adjuvant CT and/or RT.

Study Limitations

The retrospective design of our study, the inability to create randomization, the limited statistical analysis due to the small number of patients, short follow-up times and the follow-up results belonging to one center are the main limitations of our study.

Conclusion

As a result, paratesticular masses are rare and low malignant pathologies, but it is often difficult to distinguish them with clinical findings. In cases where the suspicion of malignancy cannot be ruled out, radical orchiectomy is inevitable. In sarcomas of this region, complete surgical excision is often not sufficient for disease-free survival. Adjuvant treatments, on the other hand, do not increase overall survival in every case. According to our findings, tumor grade is the most important prognostic factor determining relapse and overall survival. It is necessary to better identify the prognostic factors that have effect on survival and to establish specific adjuvant treatment protocols according to the tumor subtype with other prospective, randomized, controlled, multicenter with large patient numbers and long follow-up.

Ethics

Ethics Committee Approval: Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: İ.S., Design: İ.S., Data Collection or Processing: İ.S., Analysis or Interpretation: İ.S., H.B., Literature Search: İ.S., Writing: İ.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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The Effects of *Lucilia sericata* Larval Secretions on The Expressions of MicroRNAs that are Suggested to be Related with Wound Healing in Experimental Diabetic Rat Wound Model

Deneyisel Diyabetik Sıçan Yara Modelinde *Lucilia sericata* Larva Salgılarının Yara İyileşme Süreci ile İlişkilendirilmiş MikroRNA'ların Ekspresyon Seviyeleri Üzerine Etkisi

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ABSTRACT

Objective: Normal wound healing is achieved by a cascade of many cellular activities. This process is affected by some of the metabolic diseases like Diabetes Mellitus (DM). DM causes bad prognosis and is one of the major contributors to chronic wound healing problems. Recently, *Lucilia sericata* larvae are used for wound healing as they are very effective agents in wound healing process. It's still unclear that how the larvae affect the molecular mechanisms and signaling pathways of chronic wound healing. MicroRNAs (miRNAs) can induce gene expression in post-transcriptional mechanisms. In this study, our aim was to determine whether the larvae secretions could change the expression patterns of selected miRNAs on the diabetic microenvironment.

Methods: Wistar Albino rats were classified as diabetic and non-diabetic, then full thickness cutaneous wounds were created at the dorsal region of rats. Wound tissues were collected on days 0, 3, 7 and 14 post wounding. The association between *miR21*, *miR146a*, *miR146b* and *miR29a* gene expression profiles and wound healing

ÖZ

Amaç: Normal yara iyileşmesi bir çok hücrel faaliyetin zincirleme tepkimeleri ile gerçekleşmektedir. Diabetes Mellitus gibi metabolik hastalığa sahip kişilerde ise bu süreç olumsuz etkilenmekte, kötü iyileşen ya da iyileşmeyen kronik yaraların meydana gelmesine neden olmaktadır. *Lucilia sericata* larvalarının yara iyileşmesinde etkin rol oynamakta olduğu bildirilmiştir ancak kronik yara iyileşmesinin moleküler mekanizmasında ve ilgili yollarındaki etkileri hala bilinmemektedir. RNA türlerinden biri olan mikroRNA'ların (miRNA) bir bölümünün yüksek glukoz düzeylerinde ekspresyonlarının değiştiği gösterilmiştir. Bu sebeple çalışmamızda; yara iyileştirmesinde rolü olduğu bildirilen bazı miRNA'ların ekspresyonlarının diyabetik şartlarda larva salgısı uygulaması ile deri iyileşmesi süresince ne yönde etkilendiği incelenmiştir.

Yöntemler: Deneyisel çalışmamızda kullanılan Wistar Albino türü sıçanlar diyabetik ve diyabetik olmayanlar olarak gruplandırıldıktan sonra sırt bölgesinde tam kat yara oluşturulmuştur. Oluşturulan yara bölgelerinden 0., 3., 7. ve 14. günlerde biyopsi örneği alınmıştır. Çalışmamızda literatür taraması yapılarak yara iyileşmesi ile ilişkilendirilmiş *miR21*, *miR146a*, *miR146b* ve *miR29a* genlerinin

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process was investigated by using Real Time polymerase chain reaction method.

Results: The increase in expression of *miR21* gene in diabetics treatment group was seen most on 3rd day compared with diabetics control group. An increase in expression profiles of *miR146a*, *miR146b* and *miR29* genes was seen most in larval treatment group compared with diabetics control group.

Conclusion: Our results have shown that larval secretion in wounds formed in diabetic rats affects the expression of miRNAs associated with wound healing process. Larval secretion therapy has been shown to increase wound healing and reduce inflammatory response by altering the expression of miR146a in diabetic rats

Keywords: Normal wound healing, diabetic wound healing, maggot debridement therapy, *Lucilia sericata*, microRNA expression

ifade analizleri, gerçek zamanlı polimeraz zincir reaksiyonu ile değerlendirilmiştir.

Bulgular: *miR21* geninin diyabetik kontrole göre diyabetik tedavi grubundaki ifade artışı en fazla 3. günde görülürken, *miR146b*, *miR146a* ve *miR29a* genlerindeki ifade artışı diyabetik kontrol grubuna göre kıyaslandığında en fazla larva salgısı tedavisi uygulanan gruplarda olduğu görülmüştür.

Sonuç: Sonuçlarımız ile diyabetik sıçanlarda oluşturulmuş yaralarda larva salgısının yara iyileşme süreci ile ilişkilendirilmiş miRNA'ların ifadelerini etkilediği bulgulanmıştır. Larva salgısı tedavisinin diyabetiklerde miR146a'nın ifadesini değiştirerek yara iyileştirmesini arttırdığı ve enflamatuvar yanıtı azalttığı gösterilmiştir.

Anahtar Sözcükler: Normal yara iyileşmesi, diyabetik yara iyileşmesi, larva debridman tedavisi, *Lucilia sericata*, mikroRNA ekspresyonu

Introduction

Although inadequate wound healing in diabetic patients is not fully understood, several studies in various diabetic human and animal models have shown that some disruptions have occurred in various stages of the wound healing process. It has been shown that the diabetic microenvironment significantly affects keratinocyte and fibroblast functions, and can alter extracellular matrix (ECM) structure and function (1-3).

MicroRNAs (miRNAs), known as small non-coding RNAs, are single-stranded RNA molecules that act negatively on genes at the translational level. In various studies, it has been observed that the release of cytokines and interleukins in chronic wounds contributes to various molecular stages such as angiogenesis and cell proliferation (4-6). The wound healing is delayed as a result of the negative factors that occur in the healing process of chronic wounds. Treatments applied to shorten this process are effective. The studies have revealed that larval secretion treatment is successful in debridement of chronic wounds (7,8).

Considering that miRNAs are required for the various phases of chronic wound healing and that miRNA levels change as a result of various treatments that accelerate chronic wound healing, larval secretions can affect miRNAs during the period of acceleration of healing by affecting the various phases of wound healing in diabetic microenvironment (9). However, there is no study concerning the effect of larval secretions on the expression of miRNAs associated with wound healing in diabetic subjects. In our study; it is predicted that the expression of miRNAs associated with wound healing may also change. For this reason, we aimed to determine whether or not *Lucilia sericata* larval secretions change the expression of miRNAs, miR21, miR146a, miR146b and miR29a, which were shown in bioinformatics studies to have a critical potential in effective healing (10).

Methods

Animal Experiments and Tissue Preparation

In our study, 20 male Wistar Albino rats weighing 300-350 g were obtained. Male rats were preferred in our study, as processes such

as breeding period, birth, nursing care, lactation period in the female rats would affect the results of the experiment. Our study was approved by the İstanbul University Animal Experiments Ethics Committee (decision no: 2013/44). Under standard conditions, the rats were given free access to water and food, and 4 groups of 5 animals were separated. The first two groups were separated into treatment groups while the other two groups were divided into control groups. Pre-experimentally, the rats were fasted overnight and were injected 60 mg/kg streptozotocin (STZ) intraperitoneally, pH=4.5 in 0.1 M citrate buffer, to form diabetes. Diabetes Mellitus formation was checked 3 days after the injection of STZ by measuring the blood glucose level in the rat's tail vein. Those with blood glucose levels above 250 mg/dL were considered diabetic and included in the study (11,12). The rats to be used in the experiment were anesthetized with intraperitoneal (i.p.) Pental sodium (Pentobarbitone sodium) (IU Ulgay Medicine Industry Co. Inc., İstanbul, Turkey) with a dose of 40 mg/kg and then dorsal fur was shaved. The biopsy "Punch" tool was used to create a full-layer excisional wound model. Four 12 mm-diameter tissues of epidermis and dermis were excised at equal distances of about 1 cm from each other on dorsal thoracic region. The day of wound formation was accepted as day 0. Both PBS and larval secretions were absorbed into the surgical sponges and placed on the wound. Biopsy materials were taken in the 3rd, 7th and 14th days after the wound was formed. Tissue fragments were homogenized with a homogenizer (Next advance, USA) by placing 500 µL of Qiazol lysis buffer (Qiagen, USA) and 3 times of tissue weight of zirconium beads (Next advance, USA) for use in RNA isolation method and kept at -80 °C.

Real-time PCR (RT-PCR)

After isolation of the RNA from the homogenized tissue, the purity and quantity of the samples were measured on a nanodrop spectrophotometer. Following cDNA synthesis, samples were used for real time polymerase chain reaction (PCR) procedures to detect the expression levels of miRNAs that were previously associated with wound healing. In our study, four genes that were found to be effective in the wound healing process in the literature were identified as miR21, mir29a, mir146a, mir146b.

A real-time PCR run was made for each of the 70 cDNA samples and was repeated 2 times. Inconsistent results were not evaluated. Coefficients calculated by the $2^{-\Delta\Delta CT}$ method, and values less than 2 and greater than -2 were considered to be insignificant.

Results

Results from biopsy samples taken at days 0, 3, 7, and 14 days of wound healing were evaluated separately for *miR21*, *miR146a*, *miR29a* and *miR146b* genes. For the 3rd, 7th and 14th days, fold changes of the treatment group compared with the control group were calculated in both diabetic and normal groups (Figure 1).

According to the findings obtained by real-time PCR study, fold changes of *miR146a*, *miR21*, *miR29a* and *miR146b* genes in diabetic rat skins compared to normal rat skins were examined separately in day 0. Accordingly, expression of *miR146a* gene decreased 3.75 fold, *miR29a* gene decreased 4.43 fold, *miR21* gene decreased 9.37 fold, and *miR146b* gene decreased 12.57 fold in diabetic group compared to normal group. When four genes were compared among themselves, it was seen that fold change value was highest in *miR146b* gene (Figure 2).

The expression of *miR21* gene in the 3rd day increased 42.75-fold in diabetic therapy (DT) group compared with diabetic

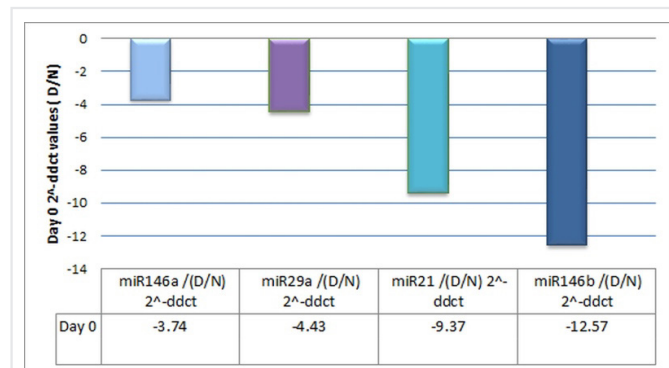


Figure 1. Representation of *miR146a*, *miR146b*, *miR21*, and *miR29a* gene expression in the diabetic skin and the normal skin. Expressions of related genes are shown as fold change

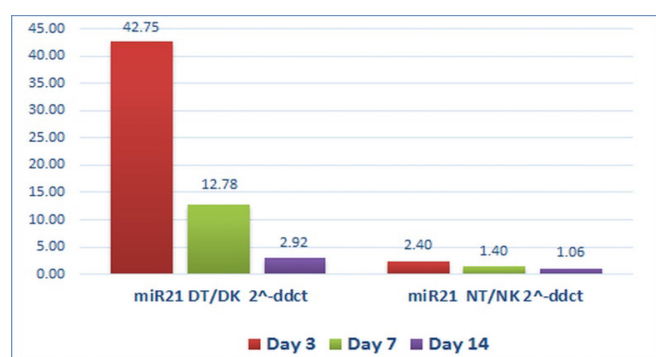


Figure 2. Changes in expression of *miR21* gene in the larval secretion applied wound tissues in 3rd, 7th and 14th days, compared to the control group. Expression of the genes involved is shown as fold change, and diabetic and normal groups are evaluated within themselves

control (DC) group, whereas it increased 12.78-fold in the 7th day. In the DT group, the *miR21* expression increased 2.92-fold more than the DC group in the 14th day. In the healthy group, the expression of *miR21* in the 3rd day was 2.40-fold higher in the normal therapy (NT) group than in the normal control (NC) group, whereas it was 1.40-fold in the 7th day and 1.06-fold in the 14th day (Figure 3).

While the *miR146a* gene showed a 9.79-fold increase in DT compared to the DC group in the 3rd day, it increased 4.11-fold in the 7th day. The DT group showed a 7.45-fold increase in expression of *miR146a* in day 14 compared to the DC group. In the diabetic group, it was seen that the increase of folds was highest in 3rd day, while it was lowest in 7th day, when the 3rd, 7th and 14th days were compared within themselves. In the healthy group, the expression of *miR146a* gene in the 3rd day increased 3.19-fold. The expression of the *146a* gene in the 7th day decreased 1.51-fold in NT compared to the NC group, but decreased 4.22-fold in the 14th day. When the days 3, 7 and 14 were evaluated in the normal group, it was seen that the expression of *miR146a* showed the highest increase in the third day (Figure 4).

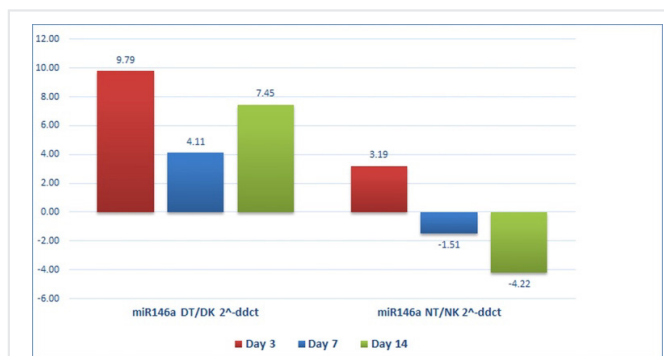


Figure 3. Changes in expression of *miR146a* gene in the larval secretion applied wound tissue in the 3rd, 7th and 14th days, compared to the control group. Expression of related genes is shown as fold change, and diabetic and normal groups are evaluated within themselves

DT: Diabetic therapy, NT: Normal therapy



Figure 4. Changes in expression of *miR146b* gene in the larval secretion applied wound tissue in the 3rd, 7th and 14th days, compared to the control group. Expression of related genes is shown as fold change, and diabetic and normal groups are evaluated within themselves

DT: Diabetic therapy, NT: Normal therapy

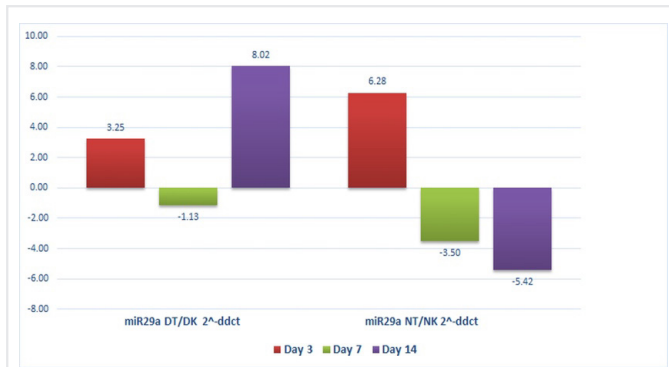


Figure 5. Changes in expression of *miR29a* gene in the larval secretion applied wound tissue in the 3rd, 7th and 14th days, compared to the control group. Expression of related genes is shown as fold change, and diabetic and normal groups are evaluated within themselves

DT: Diabetic therapy, NT: Normal therapy

When the *miR146b* gene was compared with the DC group in the 3rd day, the increase in the DT group was 8.12-fold, while the increase in the 7th day was 1.97-fold and 9.79-fold in the 14th day. It was seen that the fold increase was the highest in 14th day and the lowest in 7th day. In the healthy group, the expression of *miR146b* in the 3rd day increased 5.95-fold in the NT group compared to the NC group, whereas it decreased 5.91-fold in the 14th day in the NT group compared to the NC group. It decreased 2.51-fold in the NT group compared to the NC group in the 7th day. When the days 3, 7 and 14 were evaluated in the normal group, the expression of *miR146b* increased the most in the 3rd day, whereas in the 14th day it showed down regulation and the expression decreased 5.95-fold (Figure 5).

The expression of *miR29a* showed a 3.25-fold increase in the DT group compared to the DC group in the 3rd day, a 1.13-fold decrease in the 7th day and 8.02-fold increase in the 14th day. It was observed that the maximum fold increase was in the 14th day. In the healthy group, the expression of *miR29a* in the 3rd day increased 6.28-fold in the NT group compared to the NC group, decreased 3.50-fold in NT group compared to the NC group in the 7th day, and decreased 5.42-fold in the 14th day. When the 3rd, 7th, and 14th days in the normal group were evaluated within themselves, the expression of *miR29a* increased the most in day 3, whereas in day 14 it decreased by 5.42-fold with down regulation.

Discussion

It is well known that the wound healing process is a highly orchestrated series of mechanisms and biological cascades, although its complex molecular mechanisms are not yet discovered completely (13,14). Recent studies indicate that miRNA levels are altered during normal skin wound healing and these alterations lead to wound healing defects in pathological stages such as diabetes (3). Although there are a large number of miRNA species expressed in wound microenvironment during different phases of wound healing, bioinformatics studies showed that *miR21*, *miR146a*, *miR146b* and *miR29a* target the

mRNAs encoding many wound healing-related proteins, all of which show critical potential in effective healing (10,15-18). Also we know that high glucose levels significantly affects the expression of a large set of miRNAs (19). Since the larvae of *Lucilia sericata* improve the healing process, the study of the changes in the larvae secretions-induced miRNA expression in wound microenvironment may yield insights into understanding the molecular mechanisms that regulate wound healing and may provide new and more efficient treatment for wounds (20). Therefore, the present study was conducted to investigate the effects of the larvae secretions on wound healing in diabetic rats in relation to the expression levels of *miR21*, *miR146a*, *miR146b* and *miR29a*.

For this purpose, it was aimed to observe the effect of larval secretion on open wounds in diabetic and normal Wistar albino rats, and to represent the relatively open wound as the wound type, a full layer excisional wound model was used. Three pieces of 12 mm-diameter tissues including dermis and epidermis, each with an equal distance of about 1 cm were taken from each rat on dorsal thoracic region with a punch biopsy instrument. Scar tissue was removed in days 0, 3, 7, and 14 after wound formation. Some of the tissues underwent real-time PCR for the purpose of carrying out expression assays of *miR146a*, *miR146b*, *miR29a* and *miR21*.

The migration of fibroblasts to the wound site facilitates the synthesis of growth factors in ECM which leads migration of other cell types to the wound site. In a study by Madhyastha et al. (21), it was investigated that how different miRNAs associated with cell growth and proliferation contributed to the healing of diabetic wounds. The differences in expression of the selected miRNAs in diabetic and normal wound healing were compared. It was shown that *miR21* expressed by fibroblasts, keratinocytes, melanocytes and inflammatory cells, had significant effects on the migration of fibroblasts to the wound area. In the same study, it was also reported that the expression of the *miR21* gene varied in wound healing process. In our study, it was observed that the expression of *miR21* increased 42.75-fold in the group treated with larval secretion compared to the untreated diabetic group in the 3rd day. When the role of fibroblasts in wound healing is taken into account, observing a good course of wound healing in the diabetic group on which the larval secretion is applied is possible. In the same study, it was stated that the expression of *miR21* gene changed during different days of wound healing. In our study, results supporting this finding were obtained, whereas fold change values of the expression of *miR21* gene differed in days 3, 7, and 14.

Yang and colleagues investigated the HaCaT cell line to monitor the effect of *miR21* on keratinocyte migration during wound healing and observed the change of expression of the *miR21* gene in the presence of Transforming growth factor beta1 (TGFβ1), which stimulates the cellular uptake of growth factors by facilitating cellular movements of monocytes, lymphocytes, macrophages, keratinocytes. The expression of *miR21* increased as a result of treatment with the HaCaT cell line, which caused

in vitro TGF β mediated keratinocyte migration. The same study also showed that the cause of delay in re-epithelialization was related to the down regulation of miR21. These findings suggest that the increase in expression of *miR21* gene in diabetic treatment group compared to DC group may occur as a result of TGF β increase in the environment with the therapeutic effect of larval treatment when in the third day of our study (22).

Studies have shown that miR29a is down-regulated in systemic sclerosis dermal fibroblasts, which leads to many forms of fibrosis, compared with the normal group (23).

Collagen synthesis and regulation are very important events occurring at the maturation stage of wound healing. In healthy skin fibroblasts, miR29a directly affects collagen synthesis in the post transcriptional stage. It is also known that the synthesis of miR29a is in control of TGF β , platelet derived growth factor-B and interleukin (IL)-4 in healthy skin (24). Some studies showed that the miR29 family has an effect on the wound-specific cellular functions and the cytokine network (25,26). Ramachandran noted that miR29a is crucial in the regulation of fibrosis, which is down-regulated in the final stage of ECM synthesis. In the same study, it was mentioned that miR29a is in the target position for many proteins required for ECM synthesis. (27).

In studies conducted by Wang et al. (28), TGF β increased angiogenesis by upregulating miR29a. In our study, expression of the *miR29a* gene was observed to decrease 5.42-fold in day 14 in normal treatment group compared to NC group. This indicates that the angiogenesis, which is now a feature of the proliferative phase, has completed and the wound healing has begun to terminate in the 14th day in the normal treatment group compared with the NC group. In day 7, similarly to day 14, the *miR29a* gene expression decreased 5.42-fold in normal treatment group compared to NC group.

Although the expression of the *miR146a* and *miR146b* genes, members of the *miR146* gene family, involved in regulation of immune and inflammatory responses, has been reported to change in many pathological conditions; miR146a dysregulation has also been associated with many chronic inflammatory diseases such as psoriasis and rheumatoid arthritis (25,29). In our study, in the diabetic group treated with larvae compared to DC group, the expression of *miR146a* gene was observed to increase 9.79-fold in the 3rd day, 4.11-fold in the 7th day, and 7.45-fold in the 14th day. This upregulation has been shown to be associated with downregulation of *IRAK1*, *TRAF6*, and other pathways associated with these genes and *NF κ B*, *IL-6* and *MIP2*, the target genes of *miR146a* (30). These data suggest that secretion of larvae in the treatment group promotes wound healing in diabetics and changes the *miR146a* expression and appears to reduce the inflammatory response.

Conclusion

In summary, our results have shown that larval secretion in wounds formed in diabetic rats affects the expression of miRNAs associated with wound healing process.

Larval secretion therapy has been shown to increase wound healing and may reduce inflammatory response by altering the expression of miR146a in diabetics.

Ethics

Ethics Committee Approval: Our study was approved by the İstanbul University Animal Experiments Ethics Committee (decision no: 2013/44).

Informed Consent: Patient approval has not been obtained as it is performed on animals.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.Ö., F.A., E.P., İ.O., Design: A.Ö., İ.O., E.P., Data Collection or Processing: Ö.K., F.A., M.T., Analysis or Interpretation: A.Ö., M.T., F.A., H.A., Literature Search: Ö.K., H.A., Writing: A.Ö.

Conflict of Interest: There is no conflict of interest between the authors.

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Investigation of Plantar Pressure Distribution in Overweight and Obese Individuals

Aşırı Kilolu ve Obez Bireylerde Plantar Basınç Dağılımının İncelenmesi

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ABSTRACT

Objective: The increase in the incidence and prevalence of orthopaedic foot diseases may be related to changes in the plantar pressure distribution in overweight/obese individuals. Therefore, the purpose of the present study was to investigate the plantar pressure distribution in overweight/obese individuals.

Methods: The study included a total of 94 individuals between the ages of 19 and 62 years. Individuals were divided to two groups according to body mass index (BMI) as normal weight (BMI<25 kg/m²) and overweight/obese (BMI≥25 kg/m²). Static plantar pressure distribution and force measurement were assessed using MatScan System (Tekscan, Inc., South Boston, Massachusetts, USA).

Results: The total contact area (p<0.001) and midfoot maximum force (p<0.001) increased in overweight/obese individuals compared to normal weight individuals. Weight of individuals had a low correlation with peak pressure (r=0.23, p=0.026), mean pressure (r=0.24, p=0.018), midfoot maximum force (r=0.35, p=0.001) and metatars maximum force (r=0.36, p<0.001), and a moderate correlation with heel maximum force (r=0.47, p<0.001), and a strong correlation with contact area (r=0.79, p<0.001).

Conclusion: Obtained results show that total contact area and midfoot maximum force in overweight/obese individuals increased compared to normal weight individuals.

Keywords: Foot, pressure, obesity, body mass index

ÖZ

Amaç: Aşırı kilolu/obez bireylerde ortopedik ayak hastalıkları insidansı ve prevalansındaki artış, bu bireylerin plantar basınç dağılımındaki değişiklikler ile ilişkili olabilir. Bu nedenle, bu çalışmanın amacı, aşırı kilolu/obez bireylerde plantar basınç dağılımının araştırılmasıdır.

Yöntemler: Bu çalışma 19-62 yaş aralığında 94 sağlıklı bireyin katılımı ile gerçekleştirildi. Bireyler vücut kütle indekslerine (VKİ) göre normal kilolu (18,5 kg/m² <VKİ <25 kg/m²) ve aşırı kilolu/obez (VKİ≥25 kg/m²) olmak üzere iki gruba ayrıldı. Değerlendirilen bireylere ait statik ayak plantar basınç dağılımı ve kuvvet ölçümleri MatScan Sistemleri kullanılarak değerlendirildi (Tekscan, Inc., South Boston, Massachusetts, USA).

Bulgular: Aşırı kilolu/obez grubun total temas alanı (p<0,001) ve orta ayak tepe kuvvet değerinin (p<0,001) normal kilolu gruba göre yüksek olduğu bulundu. Kilo ile tepe basınç (r=0,23, p=0,026), ortalama basınç (r=0,24, p=0,018) ve orta ayak tepe kuvvet (r=0,35, p=0,001) arasında düşük düzeyde ilişki; kilo ile topuk tepe kuvvet (r=0,47, p<0,001) arasında orta düzeyde ilişki; kilo ile total temas alanı (r=0,79, p<0,001) arasında ise kuvvetli ilişki olduğu tespit edildi.

Sonuç: Elde edilen sonuçlar, aşırı kilolu/obez bireylerin total temas alanı ve orta ayak tepe kuvvetinde normal kilolu bireylere göre artış olduğunu göstermektedir.

Anahtar Sözcükler: Ayak, basınç, obezite, vücut kütle indeksi

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Introduction

The incidence of foot pain is reported as 14% in the adolescent population and 42% in geriatric individuals over 65 years of age (1,2). Foot pathologies and foot pain are associated with many factors, one of which is excessive weight and obesity (3,4). The increase in incidence and prevalence of foot diseases or pain in overweight/obese individuals may be associated with changes in plantar pressure distribution in these individuals. Plantar pressure distribution can significantly affect foot and ankle function. Changes in plantar pressure distribution may cause loss of support and flexibility of the foot during functional activities such as walking, running or standing (5-7). In addition, lower extremity posture is associated with plantar pressure distribution (8) Therefore, changes in plantar pressure distribution may cause changes in lower extremity posture, abnormal loading on the foot and foot-related structures, causing orthopedic diseases such as plantar fasciitis and anterior knee pain (5-9).

In overweight/obese individuals, plantar pressure distribution in static posture in standing is the subject of very limited research (10-13). Besides, the results of these studies are quite different. To give an example, some of these studies reported increased plantar pressure in overweight and/or obese individuals (12,13), while other studies reported similar plantar pressure distribution in obese individuals and individuals with normal weight (10,11). Exhibiting the changes in plantar pressure distribution in overweight/obese individuals can help developing new preventive and therapeutic approaches by providing better understanding of the increased foot and lower extremity orthopedic injuries in these individuals. Therefore, the aim of this study was to evaluate plantar pressure distribution in overweight/obese individuals and compare it with individuals with normal weight. The hypothesis of the study is that peak pressure, mean pressure and maximum force values in overweight/obese individuals will be higher than individuals with normal weight.

Methods

Power Analysis

Power analysis was conducted to determine the number of cases in this study. In order to perform this study with 80% power and 5% error margin, it was found that a minimum of 39 individuals in each group are needed to notice 10 cm² deviation in the contact area in case the average contact area of the control group is 81.8 cm² and the standard deviation (SD) is 16.7 cm² (13).

Participants

This study was conducted with the participation of 94 asymptomatic individuals in the 19-62 age range (35.2±11.5 years), including 68 females and 26 males. In the study, individuals with lower extremity injuries such as achilles tendinitis, plantar fasciitis and meniscopathy; with a history of major trauma or surgery of lower extremity; with a diagnosis of a rheumatic disease such as osteoarthritis or gout; with marked postural disorder such as hallux valgus and hammer toe; and with neurological diseases which may affect lower extremity were

not included. This research was conducted after it was approved by the Toros University Clinical Research Ethics Committee (decision no: 2018-02/08). The research was conducted on individuals who read and signed the consent form which was approved by the ethics committee.

Body Composition Analysis

Measuring the height of the individuals was done using a standard stadiometer, in a standing upright position. Individuals' weight and body mass index (BMI) were measured using a standard scale (Tanita BC-418 MA, Tanita Corporation, Tokyo, Japan). Individuals were grouped according to their BMI as normal weight (18.5 kg/m²<BMI<25 kg/m²) and overweight/obese (BMI≥25 kg/m²) (14).

Plantar Pressure Analysis

Plantar pressure distribution measurements of individuals in static posture in standing were evaluated using the MatScan system, which was reported to be reliable and valid (Tekscan, Inc., South Boston, Massachusetts, USA) (15). The device has a measuring area of 17.16x14.52" (435.9x368.8 mm). It also allows pressure measurement up to 862 kPa. After the calibration of the device, the measurements were performed at 50 Hz in bare feet and standing upright position for 30 seconds, as the manufacturer suggested. The peak pressure (kPa), mean pressure (kPa), heel maximum force (lbs), metatars maximum force (lbs), forefoot maximum force (lbs) and total contact area (cm²) values of each individual were calculated and recorded. Analysis of the data was done using FootMat™ software (Tekscan, Inc., FootMat™ for Clinicians software, South Boston, Massachusetts, USA) (Figure 1).

Statistical Analysis

Statistical analyses were done using special software (SPSS for Windows-version 18, IBM, USA). The parameters evaluated were given as mean ± SD. The Mann-Whitney U test was used to compare parameters without normal distribution between groups. The relationship level between parameters was evaluated

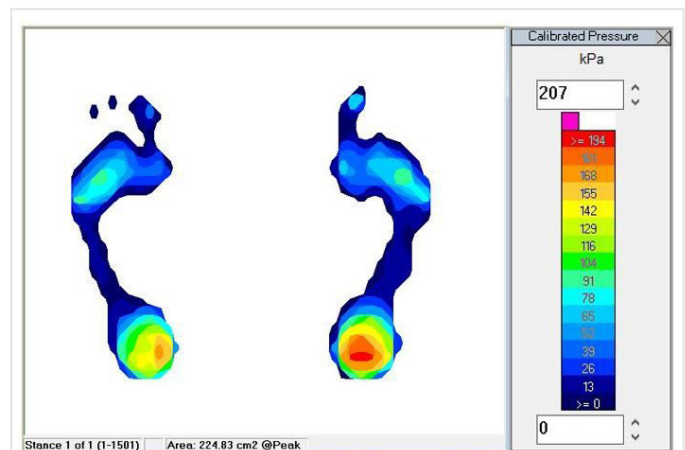


Figure 1. Plantar pressure distribution map obtained from pedographic analysis

by the Spearman test. Type 1 error level below 5% was interpreted as statistically significant. In correlation analyses, the relationship level was rated as 0-0.20 (weak correlation), 0.21-0.40 (low correlation), 0.41-0.60 (moderate correlation), 0.61-0.80 (strong correlation), and 0.81-1.00 (very strong correlation).

Results

There was no difference between groups in terms of age ($p=0.402$) and height ($p=0.550$) (Table 1). Total contact area ($p<0.001$) and metatars maximum force values ($p<0.001$) of the overweight/obese group were found to be higher compared to the normal weight group. The peak pressure ($p=0.239$), mean pressure ($p=0.190$), heel maximum force ($p=0.164$), forefoot maximum force ($p=0.215$) and change in center of force ($p=0.558$) values of both groups were found to be similar (Table 2).

When we examined the results of correlation analysis between

the parameters evaluated, there were low correlation between weight and peak pressure ($r=0.23$, $p=0.026$), mean pressure ($r=0.24$, $p=0.018$), metatars maximum force ($r=0.35$, $p=0.001$) and forefoot maximum force ($r=0.36$, $p<0.001$); moderate correlation between weight and heel maximum force ($r=0.47$, $p<0.001$); strong correlation between total contact area and weight ($r=0.79$, $p<0.001$). There were low correlation between BMI and heel maximum force ($r=0.25$, $p=0.015$) and forefoot maximum force ($r=0.21$, $p=0.048$); moderate correlation between BMI and metatars maximum force ($r=0.48$, $p<0.001$); and strong correlation between BMI and total contact area ($r=0.62$, $p<0.001$) (Table 3).

Discussion

This study was planned to investigate possible changes in plantar pressure distribution in overweight/obese individuals. The hypothesis of this study was that peak pressure, mean pressure and

Table 1. Demographic data of the patients.

Parameters	Control group (n=54)	Obese group (n=40)	p
	Mean $\pm$ SD (min-max)	Mean $\pm$ SD (min-max)	
Age (years)	34.5 $\pm$ 11.6 (19-62)	36.3 $\pm$ 11.5 (19-58)	0.402
Gender (female/male)	41/13	27/13	
Height (m)	1.66 $\pm$ 0.09 (1.51-1.87)	1.67 $\pm$ 0.09 (1.48-1.86)	0.550
Weight (kg)	60.6 $\pm$ 10.4 (43.3-85.4)	77.3 $\pm$ 12.0 (54.8-107.0)	<0.001
BMI (kg/m ²)	21.9 $\pm$ 2.2 (16.7-24.8)	27.8 (25.0-42.1)	<0.001

m: Meter, kg: Kilogram, SD: Standart deviation, Min: Minimum, Max: Maximum, BMI: Body mass index

Table 2. Plantar pressure analysis results of the groups

Parameters	Control group (n=54)	Obese group (n=40)	p
	Mean $\pm$ SD (min-max)	Mean $\pm$ SD (min-max)	
Peak pressure (kPa)	136.5 $\pm$ 44.1 (80.0-253)	143.2 $\pm$ 38.5 (81-223)	0.239
Mean pressure (kPa)	111.2 $\pm$ 39.4 (55-234)	116.9 $\pm$ 33.3 (51-196)	0.190
Heel maximum force (lbs)	36.5 $\pm$ 17.6 (14.7-126.4)	40.5 $\pm$ 16.8 (16.8-88.0)	0.164
Metatars maximum force (lbs)	19.7 $\pm$ 9.9 (4.0-60.5)	29.8 $\pm$ 14.5 (11.2-93.0)	<0.001
Forefoot maximum force (lbs)	35.2 $\pm$ 12.3 (10.5-78.3)	37.5 $\pm$ 12.4 (12.1-62.8)	0.215
Contact area (cm ²)	90.0 $\pm$ 16.9 (71.0-168.3)	101.5 $\pm$ 11.8 (75.9-126.1)	<0.001
Change in the center of force (cm)	7.2 $\pm$ 2.5 (1.6-13.2)	7.0 $\pm$ 2.6 (1.4-12.5)	0.548

kPa: Kilopascal, lbs: Pound, SD: Standart deviation, Min: Minimum, Max: Maximum

Table 3. Results of analyses of correlation between parameters

	Age	Height	Weight	BMI
Peak pressure	-0.18	0.15	0.23*	0.17
Mean pressure	-0.19	0.16	0.24*	0.19
Heel maximum force	-0.06	0.52**	0.47**	0.25*
Metatars maximum force	-0.02	-0.03	0.35*	0.48**
Forefoot maximum force	0.05	0.31*	0.36**	0.21*
Contact area	-0.01	0.58**	0.79**	0.62**
Change in the center of force	-0.02	-0.14	0.09	0.04

* $p<0.05$, ** $p<0.001$, BMI: Body mass index

maximum force values in overweight/obese individuals would be higher compared to individuals with normal weight. Unlike the hypothesis of the study, the results showed that peak pressure, mean pressure, heel maximum force and forefoot maximum force values for overweight/obese and normal weight groups were similar. However, similar to the study's hypothesis, it was found that the total contact area and metatars maximum force of overweight/obese individuals were higher than individuals with normal weight. It was also found that there were varying correlations between the increase in total contact area and force parameters and the increase in weight and BMI, ranging from low to strong. Similar to our results, Yoon et al. (10) found that there was no change in forefoot and hind-foot pressure in obese individuals. Birtane and Tuna (13) reported that total contact area and forefoot pressure values increased in obese individuals, but heel pressure was similar in obese individuals and individuals with normal weight. Unlike our results, Hills et al. (12) reported that heel, middle foot and forefoot plantar pressure values were higher in obese individuals compared to individuals with normal weight. Cimolin et al. (11) reported that in obese adolescents, the contact area of the forefoot and metatars increased, but the peak pressure value did not change. There appear to be significant differences between studies in the literature. Differences between the study results may be related to differences in the populations of the studies (adolescents (11), adults (12) and geriatric individuals (13) and differences in the obese individuals included in the studies (obese individuals (13) and individuals with morbid obesity (11,12)).

Obese individuals may be expected to have an increase in peak and mean pressure values due to an increase in body mass. The increase in metatars maximum force values in overweight/obese individuals indicates an increased load on the foot of these individuals, but this increased load caused an increase in total contact area and did not cause a change in mean and peak pressure values. In addition, the increase in metatars maximum values of overweight/obese individuals suggests that the increase in total contact area of these individuals was more associated with a decrease in medial longitudinal arch height. Similarly, many studies in the literature report a decrease in medial longitudinal arch height in overweight/obese individuals (16,17).

Our results show changes in the total contact area and force distribution of overweight/obese individuals. Changes in foot pressure distribution are known to be associated with orthopedic foot diseases such as foot pain, plantar fasciitis and achilles tendinitis (18-20). The increase in incidence of foot diseases in overweight and obese individuals may be associated with changes in plantar pressure distribution in these individuals. In addition to the increased loading of feet due to increased body weight in obese individuals, changes in plantar pressure distribution in these individuals are likely to cause abnormal loading on some parts of the foot, causing different orthopedic foot injuries (18,19). For this reason, foot posture should be evaluated in obese individuals and orthotic approaches such as medial longitudinal arch reinforcement should be applied to correct pressure distribution where appropriate. It is also thought that directing overweight

and obese individuals to physical activities and diet programs to lose weight could reduce the risk of possible foot injury.

Study Limitations

This study has some limitations. First of all, foot pressure distribution was evaluated only in static standing posture in this study. If plantar pressure distribution could be measured during different activities such as walking and standing on one foot, the effects of excess weight and obesity on plantar pressure distribution could be explained in more detail. Only adult young and/or middle-aged individuals were evaluated in the study. In different populations, such as geriatric, adolescent, recreational athletes or professional athletes, the effects of excess weight and obesity on plantar pressure distribution could have been more different.

Conclusion

As a result, mid-foot peak force and total contact area were found to increase in overweight/obese individuals. In addition, peak pressure, mean pressure, heel maximum force, forefoot maximum force and change in center of force were found to be similar in both groups. When the results of the correlation analysis were examined, it was determined that the increase in weight and BMI was related to the increase in maximum force and total contact area.

Ethics

Ethics Committee Approval: This research was conducted after it was approved by the Toros University Clinical Research Ethics Committee (decision no: 2018-02/08).

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: S.T., Y.S., Design: S.T., Y.S., Data Collection or Processing: S.T., Y.S., Analysis or Interpretation: S.T., Y.S., Literature Search: S.T., Y.S., Writing: S.T., Y.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Retrospective Analysis and Family Feedback of Patients Who Underwent Tracheostomy in Pediatric Intensive Care Unit: Single Center, 10 Years of Experience

Çocuk Yoğun Bakımda Trakeostomi Açılmış Hastaların Geriye Dönük Analizi ve Aile Geri Bildirimleri: Tek Merkez, 10 Yıllık Deneyim

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ABSTRACT

Objective: The aim of this study was to investigate the patients who had undergone tracheostomy during hospitalization in our pediatric intensive care unit (PICU), to learn the satisfaction of the families, and to evaluate the effect of tracheostomy on the number of hospitalizations.

Methods: The medical records of 80 patients who underwent tracheostomy in the PICU between 2006-2016 were retrospectively analyzed.

Results: Forty-one of our patients were male (51.25%) and 39 were female (48.75%). The mean age of males was 46.98 months (1-209 months) and girls was 43.44 months (1-205 months). Neurological system diseases (42.5%) were on the first place according to the current chronic diseases. Seventy-five patients (93.75%) were followed up with invasive mechanical ventilation and the mean duration of mechanical ventilation was 22.47±13.91 days. Only one patient (1.25%) had complication in early period. Forty one patients were contacted via telephone. Twenty-three families (56%) were satisfied with tracheostomy and 10 (24.5%) were not. The mean age of the dissatisfied group was statistically lower than the satisfied group (p=0.018). Of the 41 patients, 18 (44%) reported

ÖZ

Amaç: Bu çalışmada çocuk yoğun bakım birimimizde (ÇYBB) yatarken trakeostomi açılan hastaların incelenmesi, aile memnuniyetlerinin öğrenilmesi ve trakeostominin hastane yatış sayısına etkisinin değerlendirilmesi amaçlanmıştır.

Yöntemler: ÇYBB'de 2006-2016 yılları arasında yatarken trakeostomi açılan 80 hastanın tıbbi kayıtları geriye dönük olarak incelendi. Ailelere ulaşılarak trakeostomiden memnun kalıp kalmadıkları, trakeostomi açılmadan önce ve sonra hastane yatış sayısı arasında fark olup olmadığı ile ilgili bilgi alındı.

Bulgular: Hastalarımızın 41 tanesi erkek (%51,25), 39 tanesi kızdı (%48,75). Erkeklerin yaş ortalaması 46,98 ay (1-209 ay), kızların yaş ortalaması 43,44 aydı (1-205 ay). Mevcut kronik hastalıklara göre ilk sırayı nörolojik sistem hastalıkları (%42,5) almaktaydı. Yetmiş beş hasta (%93,75) invaziv mekanik ventilasyonda takip edilmisti ve mekanik ventilasyonda kalış süreleri ortalama 22,47±13,91 gündü. Erken dönemde sadece bir hastada (%1,25) komplikasyon gelişmişti. Toplam 80 hastanın 9'u (%11,25) kaybedilirken 71'i (%88,75) eve taburcu edilmişti. Kırk bir hastanın ailesine telefon ile ulaşıldı. Yirmi üç aile (%56) trakeostomiden memnun olduğunu, 10 aile (%24,5) ise memnun olmadığını belirtti. Memnun olmayan grubun yaş ortalaması memnun gruptan istatistiksel olarak anlamlı

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a decrease in the number of hospitalizations between before and after the tracheostomy and four (10%) reported an increase in the number of hospitalizations. The group with an increased number of hospitalizations had a significantly higher number of hospitalizations before the tracheostomy ($p=0.028$).

Conclusion: The satisfaction levels of the families will be increased by increasing the tracheostomy care trainings given before discharge from the hospital, improving the home care services and ensuring the ease of transportation of these patients to the hospitals.

Keywords: Child, intensive care, satisfaction, tracheostomy

derecede düşüktü ($p=0,018$). Ulaşılan 41 hastanın 18'i (%44) trakeostomi öncesi ve sonrası arasında yatış sayısı bakımından azalma olduğunu, dört hasta (%10) ise artma olduğunu belirttiler. Yatış sayısı artmış olan grupta trakeostomi açılmadan önce de hastane yatış sayısı yüksek bulundu ($p=0,028$).

Sonuç: Taburculuk öncesi verilen trakeostomi bakım eğitimlerinin artırılması, evde bakım hizmetlerinin geliştirilmesi ve bu hastaların hastanelere ulaşım kolaylığının sağlanması ile ailelerin memnuniyet düzeyleri artacaktır. Trakeostomi açılmadan önce zaten sık hastane yatışı olan hastalarda ise yatış sayısını azaltmak için başka tedbirlerin alınması bu hastalar için daha fazla yarar sağlayabilir.

Anahtar Sözcükler: Çocuk, yoğun bakım, memnuniyet, trakeostomi

Introduction

Tracheostomy is one of the oldest surgical methods for providing airway clearance (1). The first successful tracheostomy intervention was published by Brassolva in the beginning of 15th century (2). In children, it is most commonly applied in case of prolonged endotracheal intubation due to systemic or upper and lower respiratory diseases in order to reduce sedation time, to relieve mechanical ventilator dependence and thus to increase patient comfort (3). While in the early 1900s, tracheostomy was made in infectious diseases causing upper airway obstruction, nowadays there has been an increase in the number of patients undergoing tracheostomy and change in indications for tracheostomies with the development of intensive care units (4,5).

Telling parents about the need for tracheostomy in appropriate language and getting consent is often one of the most difficult situations we all face. Especially in traditional societies like our country, tracheostomy seems to be a practice that is initially opposed by families. Chen et al. (6) also noted that it is difficult to get families to accept the need for tracheostomy in Taiwan and that this leads to very long periods of invasive and non-invasive mechanical ventilator stays. In this study, we aimed to summarize our 10-year data and to find out what effect tracheostomy has on the quality of life of patients and their parents, whether it reduces the number of hospitalizations of patients and the positive-negative situations experienced by parents in general.

Methods

This study was carried out in our third level pediatric intensive care unit (PICU) which has a capacity of 16 beds. The study was approved by the Ethics Committee on 11.12.2017 (2017/386). The medical records of 80 of the 86 patients who underwent tracheostomy were retrospectively examined from 2602 patients who were admitted to the PICU between 01.01.2006 and 31.12.2016. Six patients were excluded from the study because their files could not be reached. Patients' ages, genders, current diseases, causes of admission to intensive care unit, number of hospitalizations, mechanical ventilation durations, reintubation numbers, pre-and post-tracheostomy hospitalizations, and early complications were recorded. The patients' families were

contacted by telephone to determine whether they were satisfied with the tracheostomy, whether there was a difference between the number of hospitalizations before and after the tracheostomy was opened, and the positive-negative situations they experienced in general.

Statistical Analysis

In this study, statistical analysis was done with Number Cruncher Statistical System 2007 Statistical Software (Utah, USA) package program. For data analysis, descriptive statistical methods (mean, standard deviation) were used, one way analysis of variance in comparison between groups with variables with normal distribution, independent t-test in binary comparisons between two groups, Kruskal Wallis test in comparisons between groups with variables without normal distribution, Mann-Whitney U test in binary comparisons between groups, and chi-square test in comparisons of quantitative data were used. The results were evaluated at the level of significance $p<0.05$.

Results

Of 80 patients, 41 were male (51.25%) and 39 were female (48.75%). Boys' average age was 46.98 months (1-209 months) and girls' average age was 43.44 months (1-205 months). According to the etiology, 34 (42.5%) had diseases of the neurological system; 20 (25%) skeletal system diseases; nine (11.25%) congenital metabolic diseases; four (5%) syndromic conditions; (3.75%) malignancies; one (1.25%) trauma; one (1.25%) chronic lung disease; one (1.25%) hereditary hematologic disorders; one (1.25%) chronic kidney disease; one (1.25%) had infectious disease. Five patients (6.25%) were admitted to intensive care unit without any disease. The current diseases of our patients, the reasons for hospitalization, the number of former hospitalizations, the mode of ventilation applied, the number of reintubation, early complications, the location and timing of tracheostomy, discharge and satisfaction are shown in Table 1.

The average duration of stay in mechanical ventilator of 75 patients was 22.47±13.91 days and the average hospitalization day of our patients before tracheostomy was 24.41 days (3-67 days) and 29.76 days after tracheostomy (1-169 days).

Table 1. Diagnosis and clinical features of patients undergoing tracheostomy in the pediatric intensive care unit

		n	%
Current diseases	Neurological diseases	34	42.5
	Cerebral palsy	15	44.12
	Neuromotor retardation	5	14.71
	Epilepsy	4	11.76
	Guillain-Barre syndrome	2	5.88
	Microcephaly	2	5.88
	Hydrocephalus + shunt	2	5.88
	Hypoxic ischemic encephalopathy	2	5.88
	Hereditary polyneuropathy	1	2.94
	Subacute sclerosing panencephalitis	1	2.94
	Diseases of the musculoskeletal system	20	25
	Spinal muscular atrophy	11	55
	Hypotonia	7	35
	Myopathy	1	5
	Severe kyphoscoliosis	1	5
	Congenital metabolic diseases syndromes	9	11.25
	Down syndrome	4	5
	Others	2	50
	Malignancies	3	3.75
	Intracranial tumors	2	66.67
	Acute myeloid leukemia	1	33.33
	Trauma		
	Car accident	1	1.25
	Chronic lung diseases		
	Bronchopulmonary Dysplasia	1	1.25
	Hereditary hematological disorders		
	Factor 5 leiden mutation	1	1.25
	Nephrological diseases		
	Chronic kidney failure	1	1.25
	Infectious diseases		
	Tetanus	1	1.25
	None	5	6.25
Cause of hospitalization	Respiratory distress	75	93.75
	Shock (hypovolemic or septic shock)	3	3.75
	Post-cardiopulmonary resuscitation	1	1.25
	Planned	1	1.25

Number of hospitalization	None	27	33.75
	1	15	18.75
	2	8	10
	>3	30	37.5
Mechanical ventilation	Invasive	75	93.75
	Non-invasive	5	6.25
Number of reintubation	None	51	63.75
	1	9	11.25
	2	15	18.75
	>3	5	6.25
Complication	No	79	98.75
	Yes	1	1.25
Place and timing	Planned/in the operating room	78	97.5
	Emergent/at bedside	2	2.5
Discharge status	Survived	71	88.75
	Exitus	9	11.25

The families of 41 patients in the study were reached by phone. According to this, eight families (19.5%) were unable to assess their tracheostomy status after discharge either because they had to be admitted to another intensive care unit or because they had losses shortly afterwards. Twenty-three families (56%) said they were satisfied with tracheostomy, while 10 families (24.5%) were dissatisfied. The only difference between the dissatisfied and satisfied groups was in mean age. The mean age of the dissatisfied group was statistically significantly lower than that of the satisfied group ($p=0.018$). There were no statistically significant differences between sex, present disease, cause of hospitalization, number of hospitalizations, duration of hospitalizations before and after tracheostomy, mechanical ventilation and duration, number of reintubation, early complications, location and timing of tracheostomy, and manner of discharge. A comparison of our patients' satisfaction levels is shown in Table 2.

Thirteen of the 41 patients (32%) were unable to make an assessment due to their initial admission to our service, while 18 patients (44%) reported a decrease, four patients (10%) reported an increase and six patients (14%) reported no changes in terms of number of hospitalizations before and after tracheostomy. The only difference between the declining, increasing, and unchanged groups was in the distribution of the number of hospitalizations before and after tracheostomy. The number of hospitalizations was higher before tracheostomy ($p=0.028$) in the group with increased hospitalizations. There were no statistically significant differences between groups in terms of age, sex, current illness, cause of hospitalization, duration of hospitalization before and after tracheostomy, duration of mechanical ventilation, number of reintubation, early complications and satisfaction distributions. The evaluation of the number of hospitalizations before and after tracheostomy in our patients is shown in Table 3.

Table 2. Comparison of the satisfaction level of the families whose children underwent tracheostomy

		Satisfied (23)	Dissatisfied (10)	p
Age (months)		51.48±54.99	10.90±8.49	0.018
Gender	Male	12 (52%)	2 (20%)	0.086
	Female	11 (48%)	8 (80%)	
Current disease	Neurological diseases	12 (52%)	6 (60%)	0.533
	Musculoskeletal diseases	7 (31%)	3 (30%)	
	Syndromes	1 (4%)	0	
	Car accident	1 (4%)	0	
Cause of hospitalization	Chronic pulmonary diseases	2 (9%)	1 (10%)	0.897
	Respiratory distress	22 (95%)	10 (100%)	
	Shock	1 (5%)	0	
Number of hospitalization	None	9 (40%)	4 (40%)	0.174
	1	1 (4%)	3 (30%)	
	2	1 (4%)	0	
	>3	12 (52%)	3 (30%)	
Duration of hospitalization before tracheostomy (days)		20.61±16.96	23.5±11.76	0.272
Duration of hospitalization after tracheostomy (days)		21.57±13.92	21.2±10.79	0.984
Mechanical ventilation	Invasive	21 (91%)	9 (90%)	0.905
	Non-invasive	2 (9%)	1 (10%)	
Duration of mechanical ventilation (days)		18.29±12.97	23.78±10.76	0.189
Number of reintubation	None	15 (65%)	6 (60%)	0.956
	1	3 (13%)	2 (20%)	
	2	2 (9%)	1 (10%)	
	>3	3 (13%)	1 (10%)	
Complication	No	22 (96%)	10 (100%)	0.503
	Yes	1 (4%)	0	
Place/Timing	Planned	22 (96%)	10 (100%)	0.503
	Bedside	1 (4%)	0	
Discharge status	Survived	23 (100%)	10 (100%)	

Discussion

The frequency of performing tracheostomy in intensive care units varies from unit to unit and according to which patients the unit encounters more. Pizza et al. (4) found that the frequency of performing tracheostomy was 1.94% and we determined our frequency as 3.3%. In our study, we found in line with the literature that neurological system diseases were the most common disease group in which tracheostomy was performed (7). This is because these children are in the higher risk group in terms of mechanical ventilator duration, ventilator-related pneumonia incidence and mortality rates than other children in intensive care unit (8-10). In 93% of our patients, the reason for admission to our service was respiratory distress. Since tracheostomy is an application aimed at providing respiratory access, and since the most common two groups of diseases requiring tracheostomy were neurological system and musculoskeletal system diseases, it was considered normal to get this result. In this study, we

found high incidence of tracheostomy in children with frequent hospitalizations and high reintubation frequency as well as in children with first-time hospitalization (33.75%) and first-time intubation (63.75%).

Tracheostomy is performed in the operating room under normal conditions, under general anesthesia and after intubation (11,12). In our unit, 78 patients (97.5%) underwent tracheostomy in elective conditions under operating room conditions and 2 patients (2.5%) underwent tracheostomy at the bedside. These two patients were emergency patients who could not be intubated due to difficult intubation. The majority of our patients were in the group of patients we decided to perform tracheostomy due to prolonged mechanical ventilation. There is no conclusive consensus in the literature on the timing of tracheostomy and how long the patient will remain intubated before tracheostomy (13,14). This period varies between 4.3 days and 30.4 days in the United States, with an average of 14.4 days (13-15). In a 1989

Table 3. Evaluation of the number of hospitalizations before and after tracheostomy

		Decreased	No change	Increased	p
Age (months)		56.64±70.14	21.75±13.05	37.67±44.41	0.598
Gender	Male	5 (45%)	1 (25%)	2 (67%)	0.544
	Female	6 (55%)	3 (75%)	1 (33%)	
Current disease	Neurological diseases	7 (63%)	2 (50%)	2 (67%)	
	Musculoskeletal diseases	4 (36%)	1 (25%)	0	0.135
	Malignancies	0	1 (25%)	0	
Cause of hospitalization	Hematological diseases	0	0	1 (33%)	
	Respiratory distress	10 (91%)	4 (100%)	3 (100%)	0.714
	Shock	1 (9%)	0	0	
Number of hospitalization	None	1 (9%)	0	0	
	1 ve 2	1 (9%)	2 (50%)	6 (67%)	0.028
	>3	9 (82%)	2 (50%)	1 (33%)	
Duration of hospitalization before tracheostomy (days)		16.27±10,15	22±15.34	14.33±4.16	0.597
Duration of hospitalization after tracheostomy (days)		1864±13.05	11.75±9.74	36±24,27	0.114
Mechanical ventilation	Invasive	11 (100%)	4 (100%)	3 (100%)	
Duration of mechanical ventilation (days)		14.82±10.66	18.75±17.46	14.33±4.16	0.834
Number of reintubation	None	8 (73%)	2 (50%)	3 (100%)	0.672
	1	1 (9%)	1 (25%)	0	
	2	2 (18%)	1 (25%)	0	
Complication	No	10 (91%)	4 (100%)	3 (100%)	0.714
	Yes	1 (9%)	0	0	
Place/timing	Planned	11 (100%)	4 (100%)	3 (100%)	
Discharge status	Survived	11 (100%)	4 (100%)	3 (100%)	0.342
	Satisfied	7 (78%)	1 (50%)	1 (33%)	
Satisfaction	Dissatisfied	2 (22%)	1 (50%)	2 (67%)	

consensus report, The American National Association of Medical Directions of Respiratory Care recommended tracheostomy in patients who have been on a mechanical ventilator for longer than 21 days (16). In children, Holscher et al. (17) and Lee et al. (18) recommended that this period be kept shorter (7 and 14 days) as it provides a decrease in sedation amount, increases in patient comfort and causes a shorter leaving from mechanical ventilator. In the studies from our country, Oğuz and Deniz (19) found the ventilation period before tracheostomy as an average of 30 days and Tolunay et al. (20) found as an average of 29.6 days. The average duration of stay in mechanical ventilator in our patients was 22.47±13.91 days, the average number of hospitalization days before tracheostomy was 24.41 days (3-67 days) and 29.76 days after tracheostomy (1-169 days).

Early complications such as pneumothorax, pneumomediastinum or subcutaneous emphysema began to decrease with performing of tracheostomy under general anesthesia in operating room conditions (21), but high rates of 53-61% were reported in some series (22,23). Pneumothorax developed in the early postoperative period in only one patient (1.25%) was controlled by early diagnosis and intervention in our study. Mortality rates ranging from 8% (24,25) to 42.9% (3) have been reported in

the literature associated with underlying disease unrelated to tracheostomy. Deaths due to tracheostomy are below 1% (26,27). Nine of our patients (11.25%) were lost due to their underlying diseases, while 71 of them (88.75%) were discharged to home. There was no mortality due to the tracheostomy procedure.

There are not many studies about the families of children with tracheostomy in the literature. Some surveys to date have shown that the quality of life of parents with children with tracheostomy has decreased, which has a negative impact on the mental health of parents (28). The same surveys highlighted that the stress and fear experienced by parents can be best reduced by communication with experienced families with children with tracheostomy. Margolan noted that only 60% of parents felt they had received their full pre-discharge tracheostomy training and that they had many concerns (29). Mc Cormick noted that many parents expressed dissatisfaction after discharge and believed that all family members should receive emergency training before being discharged (30). The limitation of our study was that it included patients in the last 10 years and that we did not follow up patients after tracheostomy, so we were able to reach only 41 parents. No surveys could be conducted because we did not meet with the families face to face. However, they were asked to

make comparisons between the first speech made by us about the necessity of performing a tracheostomy to their children and the period after they started living alone at home after the tracheostomy was performed. In general, they stated that they were satisfied with the tracheostomy and that their fears were lost after they started to live with the tracheostomy, compared to the anxiety and fear they experienced when the first conversation about tracheostomy was made with the families. They explained their levels of satisfaction with decreased complaints about their children's respiratory system, in particular. The dissatisfied group was a particularly small aged group and the reasons for dissatisfaction included inadequate education, difficulty in reaching a hospital when there is a problem, and failure in closing the tracheostomy at follow up. Tracheostomy training is provided by experienced nurses in our unit. However, we believe that establishing tracheostomy training teams, improving the quality of education and providing intermittent home care services to these patients will be better for patient and parental health.

In our study, we found that tracheostomy decreased the number of hospitalizations in 44% of patients and increased the number of hospitalizations in 10% of patients. The group with an increased number of hospitalizations was also the group with a higher number of hospitalizations prior to tracheostomy. Although tracheostomy is performed in cases of prolonged mechanical ventilation, it is intended to reduce hospitalizations due to respiratory problems, especially in chronically ill children. However, in these children who are already hospitalized frequently, we believe that the development of respiratory protective methods other than tracheostomy will be more comfortable. After discharge, follow-up of patients with tracheostomy in our hospital is performed by the otorhinolaryngology clinic. The fact that our study covered a period as long as 10 years and that patient follow-up was carried out by another clinic caused the number of patients that could be reached to be limited. Therefore, the satisfaction and hospitalization data after tracheostomy that we aimed for in the study needs to be supported by wider studies.

Conclusion

Increasing the quality of education given to parents before discharge, especially in the younger age group, and ensuring that these patients have access to hospitals in case of any problem will increase the comfort of life and satisfaction of children and families. In addition, we believe that home care services should be developed and necessary measures should be taken regarding tracheostomy care. In chronic patients who already have frequent hospitalizations, the number of hospitalizations can be reduced by developing other respiratory protective methods.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee on 11.12.2017 (2017/386).

Informed Consent: Our work is retrospective.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: H.S.K., O.Y., M.T.P., Design: Ü.K.B., E.Ş., N.A., Data Collection or Processing: O.Y., N.A., Ü.K.B., Analysis or Interpretation: E.Ş., M.T.P., Ü.K.B., Literature Search: H.S.K., E.Ş., N.A., Writing: M.T.P., Ü.K.B., O.Y.

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Inner Surface of Pterion in Terms of Surgical Approaches: An Anatomical Cadaveric Study

Cerrahi Yaklaşımlar Açısından Pterionun İç Yüzeyi: Anatomik Kadavra Çalışması

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ABSTRACT

Objective: Aim of this study was to evaluate the morphometric features and the inner surface of the pterion in terms of surgical procedures for neighboring anatomical structures.

Methods: Thirty five skeletally mature craniums were included in the present study. Fifteen of the craniums were belonged to cadavers, 20 of the craniums were dry bones. All specimens were obtained from the department of anatomy. Type of pterion and distance of midpoint of pterion to palpable surface landmarks were noted. Inner surface of pterion was marked by translumination of a laser pointer. Overlap of pterion with important anatomical structures and its closest distance to them was evaluated.

Results: The most common type of pterion was sphenoparietal-type (80%) and the least common type was epipteric (1.4%) type. The mean thickness of the calvaria on the pterion was 4.2±0.16 mm. Pterion is located approximately 4 cm superior and 2.5 cm anterior to midpoint of arcus zygomaticus; 3 cm superior and 1.5 cm posterior to tuberculum marginale; 7 cm superior and 6.5 cm anterior to the tip of processus mastoideus. In 61.4% (n=43) of samples, inner surface of pterion was found to be associated with groove of a. meningeal media. In 81.4% (n=57) of specimens, inner projection was coincided with sinus sphenoparietalis. Foramen spinosum was located posteroinferior to inner projection and the mean closest distance was 39.8±6.53 mm. Meckel cave was located posteromedial to inner projection and the mean closest distance was 40.6±3.18 mm.

ÖZ

Amaç: Bu çalışmanın amacı pterionun morfometrik özelliklerini ve pterionun iç yüzeyini, komşu anatomik yapılar için yapılan cerrahi prosedürler açısından değerlendirmektir.

Yöntemler: Çalışmaya, iskelet gelişimi tamamlamış 35 kafatası dahil edildi. Kafataslarından 15'i kadavralara aitti, 20 tanesi kuru kemik idi. Tüm örnekler anatomi anabilim dalından alınmıştır. Pterion tipi ve pterionun orta noktasının palpabl yüzey işaret noktalarına olan uzaklığı kaydedildi. Pterionun iç yüzeyi, bir lazer işaretçinin translüminasyonu ile işaretlenmiştir. Pterionun önemli anatomik yapılarla örtüşmesi ve onlara olan en yakın mesafesi değerlendirildi.

Bulgular: Pterionun en yaygın görülen tipi sphenoparietal tip (%80), en az gözlemlenen tipi epipteric tip pterion (%1,4) idi. Kalvaria'nın pterion üzerindeki ortalama kalınlığı 4,2±0,16 mm olarak ölçüldü. Pterion, arcus zygomaticus'un orta noktasına göre yaklaşık 4 cm üstte ve 2,5 cm önde; tuberculum marginale'ye göre 3 cm üstte ve 1,5 cm arkada, processus mastoideus'a göre 7 cm üstte ve 6,5 cm önde yer alıyor olarak bulunmuştur. Örneklerin %61,4'ünde (n=43) pterionun iç yüzeyi a. meningeal media'nın oluğu ile ilişkili bulunmuştur. Örneklerin %81,4'ünde (n=57) ise sinüs sphenoparietalis ile çakışmaktaydı. Foramen spinosum posteroinferior yerleşimde ve ortalama en yakın mesafesi 39,8±6,53 mm idi. Meckel oluğu posteromedial yerleşimde ve ortalama en yakın mesafe 40,6±3,18 mm idi.

Sonuç: Sinüs sphenoparietalis ve a. meningeal media'nın frontal dalı, pterionun iç yüzeyi ile çakışan başlıca anatomik yapılarıdır.

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Conclusion: Sinus sphenoparietalis and frontal branch of a. meningeal media are the main anatomical structures overlapping with internal aspect of pterion. In order to minimize complications, these anatomical structures should be kept in mind during pterional craniotomies.

Keywords: Pterion, arteria meningeal media, sinus sphenoparietalis

Komplikasyonları en aza indirmek için pterional kraniyotomiler sırasında bu anatomik yapılar akılda tutulmalıdır.

Anahtar Sözcükler: Pterion, arteria meningeal media, sinüs sphenoparietalis

Introduction

Cranial part of the central nervous system is enclosed by neurocranium. In the adult cranium, bones form the neurocranium articulate by joining with each other via sutural joints. In the embryo, junctions of these sutural joints are not calcified. Membranes covering spaces between these junctions are called fontanelles. In human fetus, six fontanelles are found in the neurocranium. Two of them are seen on the superior of the skull which are called anterior and posterior fontanelles. Four of them are located on the lateral side of cranium. Anteriorly located ones are called sphenoid fontanelles and the posteriorly located ones are called mastoidal fontanelles (1).

In the adult, the sphenoid fontanelle becomes pterion by calcification which is the junction of the suture on the anterolateral side of the neurocranium (1). Pterion is also known as the thinnest part of the calvaria (2). Pterion is often used as surgical landmark especially for the transsylvian approach in order to reveal frequently seen vascular or parenchymal lesions (3,4). On the other hand, pterion is also used as marking point for the branches of a. meningeal media, in terms of epidural hemorrhage during lateral craniotomies (5).

In this study, we aimed to reveal the morphometric features of the pterion and its relationship with the vascular and dural anatomical structures which is important for lateral surgical approaches.

Methods

Ethics committee approval was taken from the local ethical committee (KEAH - 2017 - 1564).

A total of forty skeletally mature adult craniums were included in the present study. Twenty of the craniums were dry bones, twenty of the craniums belonged to adult cadavers. Cadavers were obtained from the department of anatomy. Cadavers were fixed with formaldehyde and they belonged to Caucasian subjects. Age of the cadavers were unknown. Five of the craniums with fracture or previous dissection regarding pterion region were excluded from the study. A total of thirty five craniums and seventy sides (fifteen dry bones, twenty cadaveric) were included for the study.

Pterion was revealed on the lateral side of the cranium. Formation pattern of the pterional junction was noted according to the Murphy Classification which was described in 1956 (6). In order to locate the position of the pterion, mid-point of arcus zygomaticus, tuberculum marginale, and tip of the processus

mastoideus were used as bony landmarks. Since these landmarks are palpable under the surface of skin, location of the pterion can be found easily during surgeries without any further skin incisions. External cranial landmarks and measurement points are shown in Figure 1.

Inner surface of the pterion is in close relationship with a. meningeal media and sinus sphenoparietalis. In order to assess this relationship, translumination with laser pointer was used and inner projection of the pterion was marked. The relationship of the inner projection of pterion with a. meningeal media and sinus sphenoparietalis was evaluated. Distance of the inner projection to foramen spinosum and Meckel cave, and thickness of the calvaria on the pterion were also measured. A digital caliper was used for measurements on the specimens. All measurements were repeated 3 times and mean value of three measurements was accepted as the final distance. Photographs were taken by digital camera (Canon Ixus 115).

Statistical Analysis

Descriptive analyses were made for all variables. Statistical results were represented as mean $\pm$ standard deviation. Student's t-test was performed to compare the measurements of left and right

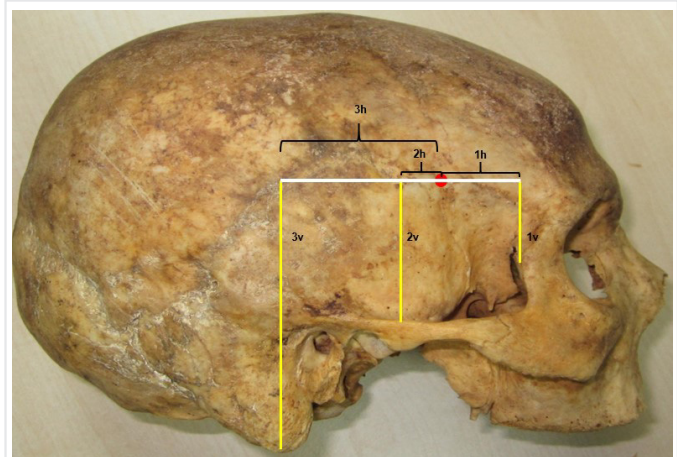


Figure 1. Landmarks used for morphometric measurements. Easily palpable surface landmarks are used for measurements.

1: Tuberculum marginale, 1v: Vertical distance to pterion, 1h: Horizontal distance to pterion, 2: Midpoint of arcus zygomaticus, 2v: Vertical distance to pterion, 2h: Horizontal distance to pterion, 3: Tip of processus mastoideus, 3v: Vertical distance to pterion, 3h: Horizontal distance to pterion

sides. All analyses were done using SPSS (version 15) software with a statistically significance level of $p < 0.05$. This study was conducted after it was approved by the local ethical committee.

Results

The most common type of the pterion was sphenoparietal type in the present study (80%) (Figure 2A). The least observed pterion type was the epipteral type of pterion (1.4%) (Figure 2B). The frequencies of pterion types are given in Table 1. The mean thickness of the calvaria on the pterion was measured as 4.2 ± 0.16 mm.

In order to locate pterion easily during surgeries, palpable bony landmarks were chosen. Vertical and horizontal distances between pterion and these landmarks are given in Table 2. According to our results, pterion was located approximately 4 cm superior and 2.5 cm anterior to midpoint of the arcus zygomaticus, 3 cm superior and 1.5 cm posterior to tuberculum marginale, 7 cm superior and 6.5 cm anterior to the tip of the processus mastoideus.

Inner surface of the pterion was marked by translumination from the exterior of the cranium. Relationship of the inner surface of the pterion with vascular and dural structures was observed. In 61.4% ($n=43$) of the samples, inner surface of the pterion was found to be associated with groove of a. meningea media (Figure 3). This relationship was associated with the frontal

ramus of the a. meningea media in all of the samples. Bifurcation of the a. meningea media to frontal and parietal branches was 17.3 ± 1.6 mm inferior to inner projection. In 81.4% ($n=57$) of the specimens, inner projection was coincided with sinus sphenoparietalis (Figure 3, 4). Foramen spinosum was located posteroinferior to the inner projection and the mean closest distance was 39.8 ± 6.53 mm. Meckel cave where the trigeminal ganglion is found was located posteromedial to inner projection and the mean closest distance was 40.6 ± 3.18 mm.

Statistical analyses of the data revealed that no significant difference was found between right and left sides ($p > 0.05$).

Discussion

The pterion which is located on the anterolateral side of the cranium is the junction of four neurocranium bones: Temporal, frontal, sphenoid and parietal bones (1). Since inner surface of the pterion is associated with important anatomical structures such as a. meningea media or Sylvian fissure, it is commonly used as an important extracranial landmark (3). The appearance of the conjunction of the pterion varies. The most common classification used for the appearance of the pterion is the Murphy classification (6). The sphenoparietal type pterion (Type A according to Murphy Classification) is the most common observed pterion type and our findings are consistent with the literature. The rarest type of pterion varies due to ethnic differences (2,7). In the current study, epipteral type was the least observed type (Type C).

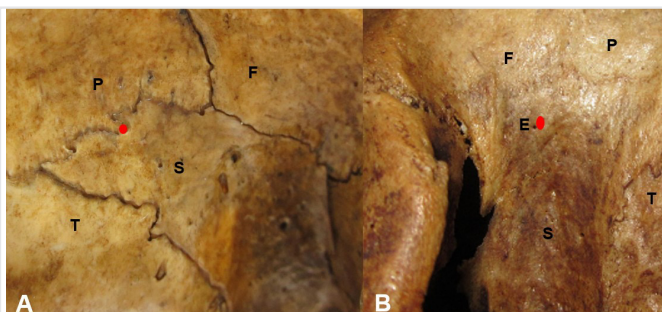


Figure 2. The most common and the least common types of pterion
A) Sphenoparietal type is the most common observed type, B) Epipteral type is the least common observed type in this study

Table 1. Frequency of Pterion types

Sphenoparietal	Frontotemporal	Epipteral	Stellate
80% ($n=56$)	15.7% ($n=11$)	1.4% ($n=1$)	~2.9% ($n=2$)

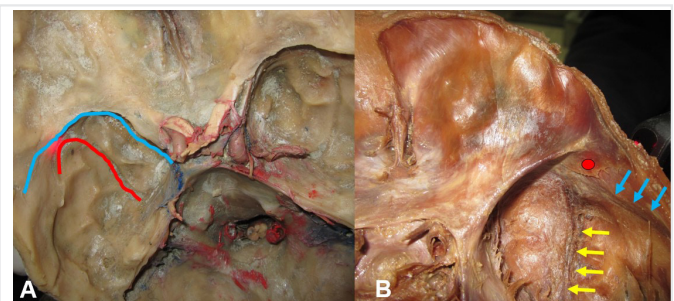


Figure 3. Internal aspect of the pterion
A) Overlapping of sinus sphenoparietalis and a. meningea media on the pterion. Blue line indicates the course of the sinus sphenoparietalis. Red line indicates the groove of the a. meningea media, B) Inner surface of the pterion does not coincide with dural sinus or meningeal vessels. Blue arrows: sinus sphenoparietalis, yellow arrows: meningeal vessels. Red circle indicates the inner surface of the pterion

Table 2. Distances between pterion and bony landmarks

	Tuberculum marginale		Midpoint of arcus zygomaticus		Tip of processus mastoideus	
	Vertical distance to pterion	Horizontal distance to pterion	Vertical distance to pterion	Horizontal distance to pterion	Vertical distance to pterion	Horizontal distance to pterion
Midpoint of pterion	31.46 ± 1.25	14.73 ± 0.37	42.58 ± 3.62	24.81 ± 2.49	69.14 ± 5.02	65.48 ± 4.24

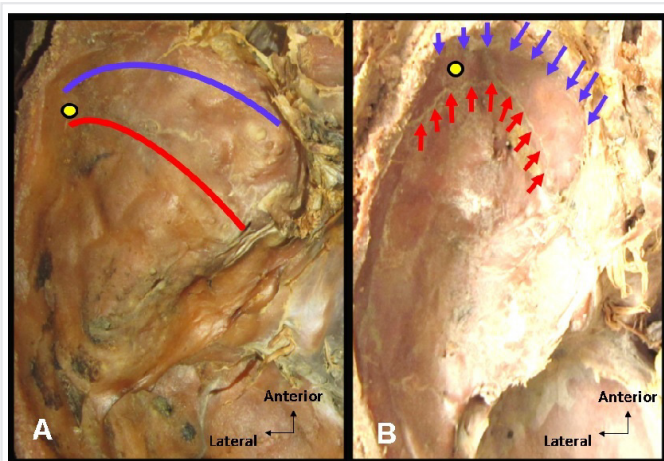


Figure 4. Course of the sinus sphenoparietalis and a. meningeal media according to pterion

A) Overlapping of sinus sphenoparietalis and a. meningeal media on the pterion. Blue line indicates the course of the sinus sphenoparietalis. Red line indicates the groove of the a. meningeal media. Yellow circle indicates the inner surface of the pterion, B) Inner surface of the pterion and its overlapping with the dural sinus and meningeal vessels. Blue arrows: sinus sphenoparietalis, red arrows: Meningeal vessels. Yellow circle indicates the inner surface of the pterion

In order to locate the pterion, different landmarks have been described in the literature, such as arcus zygomaticus or frontozygomatic suture (2,7). In the present study, palpable landmarks under the surface of the skin without any further skin incision were chosen to locate the pterion, such as tuberculum marginale and processus mastoideus. Despite the majority of the previous studies had described the location of the pterion according the closest distance to the landmarks, we used vertical and horizontal distances of pterion to palpable landmarks in order to locate the position more effectively. We think that, according to closest distances, two dimensional description is more effective, especially during surgeries but we do not suggest any superiority of this method.

Thickness of the pterion was reported to be 3-4 mm which was consistent with our results (8,9). Despite it was reported to be thicker on the left side in Korean population, no significant difference was found in terms of right and left sides in the present study (9).

Internal aspect of the pterion is closely related with Sylvian fissure which is called as sulcus lateralis in Nomina Anatomica. Opercular cortex, Broca's motor speech area, some of the anterior subarachnoid cisterns such as Sylvian cistern are in close neighborhood with inner surface of the pterion (1). In addition, distance of pterion to trigeminal ganglion and its branches, insular cortex, branches of anterior and posterior circulation in the anterior and middle cranial fossa are short.

The pterional approach is one of the most commonly used surgical procedures in neurosurgery. Due to close distance to

important anatomical structures, pterional craniotomy was described as an advantageous and functional approach (10). Main objective of the present study was to reveal the relationship of important anatomical structures with inner surface of the pterion. According to our findings, a. meningeal media and the sinus sphenoparietalis were the main anatomical structures to be affected in pterional approaches.

In classical anatomy textbooks, a. meningeal media was reported to be overlying the inner surface of the pterion (1,11,12). Rather than the main stem of the a. meningeal media, anterior or frontal ramus of the artery courses on the internal aspect of the pterion. There is limited metric data about pterion and a. meningeal media in the literature. The closest distance between pterion and the stem of the a. meningeal media was reported to be 1 cm by Kalthur et al. (13). Ma et al. (8) reported that the branches of the a. meningeal media travels within a 1 cm diameter circle around pterion. In the present study, foramen spinosum was found to be approximately 4 cm posteroinferior to pterion. The closest distance of pterion to bifurcation of the artery was found to be 1.7 cm, which was longer than the South Indian population (13). Ma et al. (8) reported that internal aspect of the pterion coincided with the branches of the a. meningeal media in 68% of the samples. In the current study, in 61.4% of the samples, overlapping of the vessel with pterion was found which was lower than but similar with the previous results.

Trigeminal ganglion is located on the impressio trigeminalis which is at the petrous apex of temporal bone. Layers of the dura mater cover this area and a space is formed between the layers of the dura mater in this region. This space is called the Meckel cave which contains trigeminal ganglion and its branches. This dural space is also in the neighborhood of the parasellar region (14). Thus, Meckel cave is an important surgical intervention area for trigeminal ganglion and cavernous sinus. Distance of Meckel cave to the inner surface of the posterior root of the arcus zygomaticus and lateral tip of the petrous ridge was reported as 26.5 mm and 38.4 mm, respectively in a previous study (14). In the current study, closest distance of internal aspect of the pterion to Meckel cave was found as 40.6 mm which was consistent with the literature.

To our knowledge, no previous study has reported the relationship of sinus sphenoparietalis with pterion. The sinus sphenoparietalis courses along the lesser wing of the sphenoid bone. During its course from posterior to medial part of sinus cavernosus; middle meningeal veins, superficial middle cerebral vein, anterior temporal diploic veins, and ophthalmic veins may be drained into sinus sphenoparietalis and larger sinuses are seen in these cases (1). A larger sinus sphenoparietalis may cause complications during pterional approaches. In the present study, overlapping of the dural sinus with inner surface of pterion was found in 81.4% of the samples.

Main limitation of our study was relatively low sample size. We believe that further studies with larger samples will provide more detailed results.

Conclusion

In conclusion, sinus sphenoparietalis and the frontal branch of the a. meningea media are the main anatomical structures overlapping with the internal aspect of the pterion. Since the metric data about the internal aspect of pterion and neighboring anatomical structures are limited in literature, we hope that percentage of the overlapping dural sinus (81.4%) and meningeal vessel (61,4%) that we showed would contribute to the literature. In order to minimize complications, these anatomical structures should be kept in mind during pterional approaches.

Ethics

Ethics Committee Approval: Ethics committee approval was taken from the local ethical committee (KEAH - 2017 - 1564).

Informed Consent: It was not taken because it was a cadaver work.

Peer-review: Externally peer-reviewed.

Author Contributions

Concept: S.D., R. M., Design: S.D., R. M., Data Collection and Processing: S.D., R.M., Analysis and Interpretation: S.D., R. M., Literature Search: S.D., R.M., Writing: S.D., R.M.,

Conflict of Interest: The authors have no conflicts of interest to declare.

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The Relation of The Duration of Work in Dentists with Postural Problems, Range of Motion and Pain

Diş Hekimlerinde Çalışma Süresinin Postüral Problemler, Eklem Hareket Açıklığı ve Ağrı ile İlişkisi

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ABSTRACT

Objective: The aim of this study is to determine the relationship between cervical and lumbar range of motions, pain and postural problems with the time spent in the occupation in dentists.

Methods: A total of 56 dentists (27 males, 29 females), participated in this research as a volunteer (age=29.55±9.5 years). Firstly, the participants were divided into 3 groups according to the working years in their life and the time spent at unit during the day; they were also divided into 2 groups according to the intermittent or uninterrupted working conditions during the day. Cervical and lumbar joint range of motions were measured to determine limitations. The McGill pain scale survey was used to evaluate the pain. Kruskal Wallis and Mann-Whitney U tests with a posthoc Bonferroni test were used for all statistical analyses.

Results: It was seen that the cervical and lumbar joint range of motions decreased, and the postural deformities in the spine and knee were observed and the level of pain increased significantly in comparatively to the excess of the time spent in the profession. However, in the analysis according to the time spent at the unit during the day, only the decrease in the range of motion of the regions was determined with the increase of the time spent at the unit during the day.

ÖZ

Amaç: Bu çalışmanın amacı; diş hekimlerinde meslekte geçirilen süreye bağlı postür problemlerini belirleyerek, bu sürenin vücutta oluşan ağrı, servikal ve lumbal bölgedeki eklem hareket açıklıkları ile ilişkisinin ortaya koymaktır.

Yöntemler: Araştırmaya 27'si erkek, 29'u kadın toplam 56 diş hekimi (yaş=29,55±9,5 yıl) gönüllü olarak katıldı. Demografik bilgi anketinin uygulandığı katılımcılar; çalışma yıllarına (0-4, 5-9 ve ≥10 yıl) ve gün içinde unit başında geçirdikleri süreye göre (0-5, 6-8 ve ≥9 saat) 3'er gruba; gün içinde ara vererek ve ara vermeden çalışma durumuna göre 2 gruba ayrıldı. Postür analizi ve servikal-lumbal bölge eklem hareket açıklığı ölçümleriyle var olan limitasyonlar belirlendi. Ağrıyı değerlendirmek için McGill Ağrı skalası anketi uygulandı. Gruplar arası farklılıkların belirlenmesinde Kruskal-Wallis ve Mann-Whitney U testleri; post hoc analizlerde ise Bonferroni düzeltmesi kullanıldı.

Bulgular: Meslekte geçirilen sürenin fazlalığı ile orantılı olarak servikal ve lumbal eklem hareket açıklığının azaldığı, omurgada ve dizde postüral deformitelerin gözlemlendiği ve ağrı düzeyinin anlamlı bir şekilde arttığı görüldü. Ancak gün içinde unit başında geçen süreye göre yapılan analizlerde, sürenin artışı ile sadece servikal ve lumbal bölge eklem hareket açıklığında azalmaların varlığı belirlendi.

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Conclusion: With the increase in the working years in the dentists, it was revealed that the limitation of the range of motion increased and posture disorders and pain were formed. It is thought that all these problems will be caused by working in non-ergonomic environments for a long time. In this respect, it is important to include experts in the field of physiotherapy in the courses given under the name of preventive medicine. As a result, it can be said that the health problems encountered with the increase in time spent in the profession have increased.

Keywords: Pain, dentists, range of motion, posture

Sonuç: Diş hekimlerinde çalışma yıllarının artış göstermesi ile birlikte eklem hareket açıklığı kısıtlılıklarının geliştiği, postür bozukluklarının ve ağrının oluştuğu ortaya konuldu. Tüm bu problemlere, uzun süre ergonomik olmayan ortamlarda çalışmanın neden olacağı düşünülmektedir. Bu doğrultuda, koruyucu hekimlik adı altında verilen derslerde fizyoterapi alanında uzman eğitimcilerin yer alması önem taşımaktadır. Sonuç olarak, meslekte geçirilen sürenin artışı ile karşılaşılan sağlık problemlerinin arttığı söylenebilir.

Anahtar Sözcükler: Ağrı, diş hekimleri, eklem hareket açıklığı, postür

Introduction

Dentists may use some parts of their body systems more or less functionally because of their profession. In this profession, ergonomic working conditions are important. The characteristics of the environment in where dentists work during the day can play an active role on the body systems (1). Ergonomically unsuitable areas of work decrease the maneuverability of dentists and increase the risk of improper movement patterns of the body (2). With unsuitable clinical environment; lighting of the environment, inadequate isolation and disturbing odors, poor air quality, humidity-temperature ratio, noise from the environment and a crowded environment constitute ergonomic risk factors (3).

Dentists remain in the same static posture for a long time during work. Even if the person has the appropriate sitting posture, there is minimal mobility between the joints in the spine as half of all muscles in the body contract statically. These small changes cause some musculoskeletal disorders in the neck, back and shoulders (4,5).

The World Health Organization introduced an ergonomic international standard to the treatment approaches of dentists in 1977. The most important aspect of these applications is the adoption of ergonomic working posture. Working by sitting for too long decreases the feeling of fatigue on the lower part of the body, especially in the pelvis and legs (6). Flattening of lumbar lordosis is observed in dentists in the position of sitting without support. The bone infrastructure provides less support to the spine and the spine is supported by the muscles, ligaments and connective tissue behind it, causing tension, ischemia and trigger point formation in the tissues. This flattening of the Lumbar curve also causes the movement of the nucleus of the vertebral disc towards the back, that is, the spinal cord. Over time, the back wall of the disc begins to weaken and disc herniation may occur. Therefore, the physician should be able to provide the most appropriate lumbar lordosis position (6).

It was found that physicians who performed the majority of clinical procedures with an assistant were less likely to experience shoulder and neck pain than those who worked alone (3). Studies have been done on ergonomic working conditions and

what the negative effects are in case of lack of ergonomic working conditions. However, it is noteworthy that there is no study on the limitations of range of motion (ROM) caused by active duty in the profession for long periods of time.

In this context, the purpose of our study is to determine whether the time which dentists spent in the profession has an effect on posture, cervical and lumbar ROM and pain, and to make protective rehabilitative recommendations in line with the results.

Methods

The sample size of the study was calculated using the G*power Analysis Program according to confidence interval 80%, alpha 5% and 80% power. According to the calculation, the sample size was determined to be at least 54. A total of 56 dentists, of whom 27 (48.2%) were men and 29 (51.8%) were women, were selected randomly and were included in the study.

The study group whose mean age was 29.55 ± 9.5 years included PhD students from the faculty of dentistry and dentists who were currently working in public universities and continued their profession in dental clinics or private practice. The study was conducted in accordance with the "Ethical Principles for Medical Research Involving Human Subjects" of the World Medical Association Declaration of Helsinki (amended in October 2013). Students who were students of the faculty of dentistry and have not yet started working at the clinic were not included in the study. Informed consent forms were distributed to 56 dentists who were asked to participate in the study and their approval was obtained and the purpose of the study was explained to them. The demographic information questionnaire used in the evaluation was used to generate general data of the participants (Table 1). After evaluating the results, participants were divided into various groups:

- According to the working years (1st group: 0-4 years/24 dentists, 2nd group: 5-9 years/18 dentists, 3rd group: ≥ 10 years/14 dentists),
- According to the time spent at the unit during the day (1st group: 0-5 hours/19 dentists, 2nd group: 6-8 hours/22 dentists, 3rd group: ≥ 9 hours/15 dentists)

C. Whether or not to work continuously during the day (1st group: 32 dentists working intermittent, 2nd group: 24 dentists working uninterrupted)

Following the demographic information survey, we used the McGill Pain Questionnaire, cervical and lumbar ROM and posture analysis. The short-form McGill Pain Questionnaire (MPQ) which is commonly used and was developed by Melzack in 1987 was used to evaluate pain in the study. The validity ($r=0.637-0.700$, $p<0.001$) and reliability ($r=0.836$) of its Turkish version were shown by Yakut et al. (7). The first part of the questionnaire (MPQ is consisted of 4 parts) showing pain on body diagram, the second part containing 20 pairs of words featuring sensory and perceptual evaluation and the fourth part containing descriptive words for determining severity of pain were used in the study. In the fourth part, the total pain intensity of the patient was evaluated with a Likert type scale of 6 points (0=no pain, 1=mild, 2=discomforting, 3=distressing, 4=horrible, 5=excruciating) (7). The excess of the total score indicates that the severity of pain is high. In statistical analysis, the participants' areas marked on the diagram of the human body where they felt pain and their Likert values were used.

Cervical ROM was tested using the cervical range of motion model 12-1156 (Fabrication Enterprises, White Plains, NY) deluxe device developed by the University of Minnesota by measuring extension, flexion, left-right lateral flexion and rotation values (8).

Lumbar ROM -lumbar flexion, extension, right and left lateral flexion angles- was measured using standard plastic goniometer (Msd Europe Bvba, Londerzeel, Belgium). All values were evaluated as normal or limited in line with normal joint ROM limits (9).

A symmetric graph-like back floor with a special drawing with 1 cm spaces in horizontal and vertical dimensions which was fixed to the wall was used in visual posture analysis. Participants were

placed in front of this floor and the layout of their body parts (head, neck, shoulder, elbow, back, waist, hip, knee and ankle) was examined anteriorly, posteriorly and laterally. The presence of postural deformities was recorded as "present (1)" and "absent (2)" and the differences between the groups were determined.

Statistical Analysis

In statistical analyses, the Shapiro-Wilk test was used to test the normality of distributions of all parametres and non-parametric tests were selected because these parameters did not show a normal distribution ($p<0.05$). The Kruskal-Wallis test was used to determine the differences between independent groups (pain intensity determined by Likert measurement method and ROM). The paired group comparisons were preferred for parameters there were found significant with the Kruskal-Wallis test and the results were formed using the the Mann-Whitney U test. Bonferroni test for post-hoc statistics was used to determine the source of the significant difference between the groups ($p<0.05$). The Bonferroni correction was determined by the formula p/k (level of significance/number of groups). The significance level was evaluated as $0.05/3=0.017$ with the Bonferroni correction, as the number of groups was 3 for the time spent at the unit during the day and working year. Therefore, after the Kruskal-Wallis analysis, the significance level of the Mann-Whitney U test, which was used to test the difference in the analysis of intergroup data on the time spent in the profession and the time spent at the unit during the day, was taken as $p<0.017$. The Bonferroni correction was not used because the number of groups was 2 in the data for intermittent and uninterrupted working during the day, and $p<0.05$ was evaluated as significant. In postural evaluations made through observation, "present (1)" or "absent (2)" was used to determine if there was an abnormal posture. Descriptive statistical analyses were used for postural problems and the results were presented in percentages.

In the analyses using SPSS version 24, p value <0.05 was considered as statistically significant.

Table 1. Analysis of the demographic characteristics of dentists depending on the time spent in the profession

Dentists' data according to time spent in the profession

Parameters	1 st group (0-4 years)		2 nd group (5-9 years)		3 rd group (≥ 10 years)		Kruskal-Wallis		Mann-Whitney U		
	Mean $\pm$ SD	Min - max	Mean $\pm$ SD	Min - max	Mean $\pm$ SD	Min - max	X ²	P	1 st and 2 nd groups	2 nd and 3 rd groups	1 st and 3 rd groups
Age (years)	23.75 $\pm$ 1.42	22-29	26.56 $\pm$ 1.65	24-30	43.36 $\pm$ 10.08	30-69	43.498	*0.001	*0.001	*0.001	*0.001
Height (cm)	169,2 $\pm$ 7.18	157-185	175.5 $\pm$ 9.65	160-191	175.9 $\pm$ 7.42	163-185	7.477	0.024	0.032	0.746	*0.016
Weight (kg)	62.5 $\pm$ 15.6	46-100	68.7 $\pm$ 12.9	51-94	78.1 $\pm$ 13.1	50-100	10.387	*0.006	0.073	0.065	*0.003
BMI (kg/m ²)	21.62 $\pm$ 4.18	16.5-32.7	22.35 $\pm$ 2.56	19.3-27.8	24.95 $\pm$ 3.28	18.10-29.5	8.428	*0.015	0.147	0.025	*0.013

BMI: Body mass index, *: Denotes p values that are considered significant. * $p<0.017$, SD: Standart deviation, Min: Minimum, Max: Maximum

Results

The results of the analysis were presented under 3 different headings according to the time spent in the profession, the time spent at the unit and intermittent or uninterrupted working during the day.

Time Spent in the Profession

According to the time spent in the profession; there were differences between groups in terms of cervical right lateral flexion, cervical right rotation, cervical left rotation, lumbar flexion, lumbar extension, lumbar right lateral flexion, lumbar left lateral flexion ROMs; right lumbar pain and left lumbar pain levels ($p<0.05$, Table 2).

According to the Paired Comparisons:

1. Comparison Between 1st and 2nd Groups: Cervical right rotation, lumbar flexion and lumbar right lateral flexion ROMs were higher in the 1st group (0-4 years) than the 2nd group (5-9

years). The differences between the two groups were statistically significant ($p<0.017$).

2. Comparison Between 2nd and 3rd Groups: Cervical right lateral flexion, cervical left rotation, lumbar extension, lumbar right lateral flexion, lumbar left lateral flexion ROMs and right-left lumbar pain levels were higher in the 2nd group (5-9 years) than in the 3rd group (≥ 10 years). The differences between the two groups were statistically significant ($p<0.017$).

3. Comparison Between 1st and 3rd Groups: Cervical right lateral flexion, cervical right rotation, cervical left rotation, lumbar extension, lumbar right lateral flexion, lumbar left lateral flexion ROMs and right-left lumbar pain levels were higher in the 1st group (0-4 years) than in the 3rd group (≥ 10 years). The differences between the two groups were statistically significant ($p<0.017$).

The kyphosis (K), genu varum (GVR) and genu valgum (GVL) rates in the groups according to the time spent in the profession:

Table 2. Significant differences in ROM and pain level according to the time spent by dentists in the profession

According to time spent in the profession											
Variables according to time spent in the profession (°)	1 st group (0-4 years)		2 nd group (5-9 years)		3 rd group (≥ 10 years)		Kruskal-Wallis		Mann-Whitney U		
	Mean $\pm$ SD	Min-max median	Mean $\pm$ SD	Min-max median	Mean $\pm$ SD	Min-Max median	X ²	p	1 st and 2 nd groups	2 nd and 3 rd groups	1 st and 3 rd groups
Cervical right lateral flexion	45.4 $\pm$ 3.87	30-50 45	43.3 $\pm$ 5.14	25-45 45	38.5 $\pm$ 8.41	20-45 45	12.577	*0.002	0.041	*0.135	*0.009
Cervical left lateral flexion	45.8 $\pm$ 2.40	40-50 45	42.2 $\pm$ 6.69	25-50 45	42.5 $\pm$ 5.45	30-45 45	7.063	0.029	0.035	0.925	0.082
Cervical right rotation	76.2 $\pm$ 2.65	70-80 75	70.5 $\pm$ 6.61	60-80 75	66.4 $\pm$ 8.86	50-80 70	18.600	*0.001	*0.001	0.168	*0.001
Cervical left rotation	74.7 $\pm$ 1.02	70-75 75	73.6 $\pm$ 4.47	60-80 75	65.7 $\pm$ 7.30	50-75 70	25.680	*0.001	0.0290	*0.001	*0.001
Lumbar flexion	66 $\pm$ 5.31	60-75 70	59.4 $\pm$ 6.39	50-70 60	60.3 $\pm$ 8.42	50-70 60	10.227	*0.006	*0.002	0.808	0.047
Lumbar extension	27 $\pm$ 3.58	25-35 25	24.7 $\pm$ 7.94	10-50 25	17.8 $\pm$ 5.78	10-25 17.5	22.200	*0.001	0.046	*0.007	*0.001
Lumbar right lateral flexion	26.2 $\pm$ 2.21	25-30 25	22.7 $\pm$ 3.91	15-25 25	15.3 $\pm$ 4.98	10-25 15	31.731	*0.001	*0.001	*0.001	*0.001
Lumbar left lateral flexion	26.2 $\pm$ 2.21	25-30 25	23.8 $\pm$ 3.66	10-25 25	19.2 $\pm$ 5.49	10-25 20	23.563	*0.001	0.126	*0.011	*0.001
Left shoulder pain	0.67 $\pm$ 1.09	0-3 0	1.11 $\pm$ 1.18	0-3 1	0.29 $\pm$ 1.07	0-4 0	5.656	0.059	0.237	0.059	0.235
Right lumbar pain	0.58 $\pm$ 1.10	0-4 0	0.78 $\pm$ 1.06	0-3 0	2.29 $\pm$ 1.44	0-4 3	13.816	*0.001	0.475	*0.004	*0.001
Left lumbar pain	0.58 $\pm$ 1.10	0-4 0	0.78 $\pm$ 1.06	0-3 0	2.29 $\pm$ 1.44	0-4 3	13.816	*0.001	0.475	*0.004	*0.001
Pain in the trapezius	0.91 $\pm$ 1.38	0-4 0	1.33 $\pm$ 1.24	0-3 1.5	0.43 $\pm$ 1.09	0-4 0	4.772	0.092	0.232	0.041	0.448

ROM: Range of motion, *: Denotes p values that are considered significant, * $p<0.017$, Min: Minimum, Max: Maximum, SD: Standart deviation

First group (0-4 years): K: 12.5%, GVR: 14.3%, GVL: 16.7%

Second group (5-9 years): K: 37.5%, GVR: 50%, GVL: 16.7%

Third group (≥ 10 years): K: 50%, GVR: 35.7%, GVL: 66.77%

Time Spent at the Unit

According to the time spent at the unit; there were differences between groups in terms of cervical left rotation and lumbar flexion ROMs ($p < 0.05$, Table 3).

According to the Paired Comparisons:

1. Comparison Between 1st and 2nd Groups: There were no differences between groups in terms of ROMs and pain parameters ($p > 0.017$).

2. Comparison between 2nd and 3rd groups: Lumbar flexion ROM was higher in the 2nd group (6-8 hours) than in the 3rd group (≥ 9 hours). The difference between the two groups was statistically significant ($p < 0.017$).

3. Comparison Between 1st and 3rd Groups: Cervical left rotation ROM was higher in the 1st group (0-5 hours) than in the 3rd group (≥ 9 hours). The difference between the two groups was statistically significant ($p < 0.017$).

K, GVR and GVL rates in the groups according to the time spent at the unit:

First group (0-5 hours): K: 25%, GVR: 28.6%, GVL: 16.7%

Second group (6-8 hours): K: 50%, GVR: 28.6%, GVL: 50%

Third group (≥ 9 hours): K: 25%, GVR: 42.9%, GVL: 33.3%

Intermittent or Uninterrupted Working During the Day

According to intermittent or uninterrupted working during the day; there were differences between groups in terms of cervical left lateral flexion and lumbar right lateral flexion ROMs ($p < 0.05$, Table 4).

Table 3. Significant differences in ROM and pain according to the time spent at the unit in dentists

Significant findings based on time spent at unit

Variables according to the time spent at the unit (°)	1 st group (0-5 hours)		2 nd group (6-8 hours)		3 rd group (≥ 9 hours)		Kruskal-Wallis		Mann-Whitney U		
	Mean $\pm$ SD	Min-max median	Mean $\pm$ SD	Min-max median	Mean $\pm$ SD	Min-max median	X ²	p	1 st and 2 nd groups	2 nd and 3 rd groups	1 st and 3 rd groups
Cervical right lateral flexion	42.8 $\pm$ 7.13	30-50 45	43.8 $\pm$ 5.54	25-50 45	42 $\pm$ 6.21	30-50 45	1.233	0.540	0.731	0.267	0.477
Cervical left lateral flexion	43.9 $\pm$ 5.42	30-50 45	44.5 $\pm$ 4.60	25-50 45	42.6 $\pm$ 5.62	30-50 45	2.066	0.356	0.814	0.133	0.336
Cervical right rotation	72.1 $\pm$ 8.21	50-80 75	73.4 $\pm$ 6.05	60-80 75	69.6 $\pm$ 7.18	60-80 70	3.385	0.184	0.703	0.076	0.183
Cervical left rotation	73.4 $\pm$ 5.01	60-80 75	73.1 $\pm$ 3.63	60-75 75	69 $\pm$ 8.06	50-80 70	6.245	*0.044	0.339	0.061	*0.029
Lumbar Flexion	62.1 $\pm$ 7.13	50-70 60	65.4 $\pm$ 5.75	55-75 70	58.8 $\pm$ 7.43	50-70 60	7.421	*0.024	0.144	*0.008	0.178
Lumbar extension	25 $\pm$ 8.16	10-50 25	25.2 $\pm$ 4.21	15-35 25	21 $\pm$ 7.60	10-35 25	4.325	0.115	0.485	0.043	0.175
Lumbar right lateral flexion	23.1 $\pm$ 5.32	10-30 25	23.4 $\pm$ 5.43	10-30 25	20 $\pm$ 5.97	10-30 20	3.892	0.143	0.914	0.075	0.105
Lumbar left lateral flexion	23.6 $\pm$ 4.66	10-30 25	24.7 $\pm$ 3.26	15-30 25	22.3 $\pm$ 5.93	10-30 20	1.529	0.465	0.504	0.220	0.558
Left shoulder pain	0.42 $\pm$ 0.77	0-2 0	0.86 $\pm$ 1.25	0-3 0	0.87 $\pm$ 1.36	0-4 0	1.141	0.565	0.302	0.899	0.436
Right lumbar pain	0.84 $\pm$ 1.30	0-4 0	1.00 $\pm$ 1.31	0-3 0	1.47 $\pm$ 1.51	0-4 1	1.941	0.379	0.720	0.307	0.180
Left lumbar pain	0.84 $\pm$ 1.30	0-4 0	1.00 $\pm$ 1.31	0-3 0	1.47 $\pm$ 1.51	0-4 1	1.941	0.379	0.720	0.307	0.180
Pain in the trapezius	0.39 $\pm$ 1.04	0-4 0	1.28 $\pm$ 1.39	0-3 0.5	1.07 $\pm$ 1.28	0-4 1	5.669	0.059	0.028	0.715	0.038

*: Denotes p values that are considered significant, * $p < 0.017$, Min: Minimum, Max: Maximum, SD: Standart deviation, ROM: Range of motion

Table 4. Significant differences in ROM and pain according to whether dentists worked intermittent or uninterrupted

Significant findings according to whether working intermittent or uninterrupted

Variables according to whether working intermittent or uninterrupted	Dentists working intermittent		Dentists working uninterrupted		Mann-Whitney U	P values
	Mean $\pm$ SD	Min-max median	Mean $\pm$ SD	Min-max median	Z	
Cervical right lateral flexion	42.1 $\pm$ 6.46	40-45 45	44.1 $\pm$ 5.83	30-50 45	-1.907	0.057
Cervical left lateral flexion	42.5 $\pm$ 6.09	25-50 45	45.6 $\pm$ 2.68	40-50 45	-2.159	*0.031
Cervical right rotation	70.7 $\pm$ 6.85	55-80 75	73.5 $\pm$ 7.44	50-80 75	-1.940	0.052
Cervical left rotation	72.3 $\pm$ 5.38	60-80 75	71.8 $\pm$ 6.39	50-75 75	-0.029	0.977
Lumbar flexion	61.4 $\pm$ 6.86	50-70 60	63.9 $\pm$ 7.36	50-75 65	-1.405	0.160
Lumbar extension	23.2 $\pm$ 7.36	10-50 25	25 $\pm$ 6.07	10-35 25	-1.242	0.214
Lumbar right lateral flexion	21.0 $\pm$ 5.64	10-30 25	24.1 $\pm$ 5.24	10-30 25	-2.322	*0.020
Lumbar left lateral flexion	22.9 $\pm$ 4.72	10-30 25	24.7 $\pm$ 4.29	10-30 25	-1.579	0.114
Left shoulder pain	0.91 $\pm$ 1.81	0-4 0	0.46 $\pm$ 0.88	0-3 0	-1.242	0.214
Right lumbar pain	1.19 $\pm$ 1.40	0-4 0	0.92 $\pm$ 1.32	0-4 0	-0.675	0.499
Left lumbar pain	1.19 $\pm$ 1.40	0-4 0	0.92 $\pm$ 1.32	0-4 0	-0.675	0.499
Pain in the trapezius	1.23 $\pm$ 1.36	0-4 1	0.54 $\pm$ 1.10	0-4 0	-2.039	*0.041

SD: Standart deviation, Min: Minimum, Max: Maximum, ROM: Range of motion

K, GVR and GVL rates in the groups according to intermittent or uninterrupted working during the day:

First group: K: 62.5%, GVR: 78.6%, GVL: 83.3%

Second group: K: 37.5%, GVR: 21.4%, GVL: 16.7%

In dentists working intermittent during the day, 21.9% were in the first group (0-4 years), 50% were in the second group (5-9 years), and 28.1% were in the third group (≥ 10 years). It was found that 70.8% of the participants who worked uninterrupted during the day were in the first group (0-4 years), 8.3% were in the second group (5-9 years), and 20.8% were in the third group (≥ 10 years).

Discussion

In this study, postural problems, ROM restrictions, painful areas and degree of pain that may occur in dentists according to the time (hours) spent at the unit, the time (years) spent in

the profession and intermittent or uninterrupted working during the day were determined. With the increase in time spent in the profession, there were reductions in ROMs in the cervical and lumbar regions. The presence of GVL in the knees and K in the spine attracted attention and pain was found to be at most in the lumbar region. It was determined that only cervical left rotation and lumbar flexion ROMs decreased with increased time spent at the unit. Cervical left and lumbar right lateral flexion ROMs were found lower in dentists working intermittent than in dentists working uninterrupted.

In our study, it was determined that height, body weight and BMI values increased in parallel with the professional experience times of the dentists included in the study and that there were physical differences between the groups. When BMI values of all three groups were taken into account, it was observed that they were within normal limits according to the World Health Organization's assessment (10). In addition, in our study, the decrease in ROM observed in vertebrae in servical and lumbar

regions was more prominent as the time spent in the profession was longer. Our results showing that the increase in body weight and BMI with increasing age was associated with pain in the lumbar region were in line with the results of the studies by Lindfors et al. (11), Chamani et al. (12) and Rafie et al. (13); however, the results of the study by Motamayel et al. (14) were different from our results.

In our research, it was determined that postural health problems were seen more with the increase in working time in the profession, but it was noteworthy that lumbar flexion ($66^{\circ} \pm 5.31^{\circ}$) and lumbar right-left lateral flexion ($26.2^{\circ} \pm 2.21^{\circ}$) ROMs were lower than normal values (9) (lumbar flexion: 90° ; lumbar lateral flexion: 35°) even in the first group who spent the least time in the profession. In addition, the presence of pain in the lumbar region and postural problems such as lumbar lordosis were important details seen in the dentists who spent the least time in profession. We believe that these problems, which may have been settled during the student period, may also be related to the long and intensive work performed by dentists in clinical conditions without having an indirect working perspective.

Besides challenging movements done without rest during the work, technical tools used in the working environment and static posture are important factors in the formation of pain in musculoskeletal system in dentists (15,16). Being exposed to these factors for a long time leads to undesirable health problems. It is observed that most of the symptoms of occupational disease in dentists occur due to periods of 6-10 years in the profession and these symptoms increase as the number of years spent in profession increases (17,18). Our finding that the dentists who worked for ≥ 10 years had the most severe pain was in parallel with the literature (17,18). In our study, depending on the increase in time spent in the profession, the most pain seen in dentists and on the literature shows parallels. Furthermore, the reductions in ROM observed especially in cervical and lumbar regions and the postural problems that triggered pain in those regions support the findings in the literature (15-18).

Another issue that was examined in our research was the comparison of the effect of intermittent or uninterrupted working during day on ROM and pain levels in the dentists. Contrary to our expectations, the intermittent working group showed a decrease in cervical left and lumbar right lateral flexion ROMs and increased pain in the trapezoidal region. It was found that 21.9% of the dentists who worked intermittent during day were in the first group (0-4 years), 50% were in the second group (5-9 years) and 28.1% were in the third group (≥ 10 years). We think that with the increase in the number of years in the profession, the awareness of intermittent working emerged; however, this situation was realized after the emergence of pain and limitation in ROM. We think that this situation is related to the emergence of working awareness in dentists after the first 4 years in the profession.

It was found that 70.8% of the dentists who worked uninterrupted during day were in the first group (0-4 years), 8.3% in the second group (5-9 years) and 20.8% in the third group (≥ 10

years). This result suggests that especially in the first four years in the profession, dentists tend to work without rest and that postural problems may occur in the first years of the profession and that they may become basis to deformities that may develop in the following years. In these working conditions, dentists take part in an unhealthy working environment, leaving their comfort and ergonomics in second place. Under normal conditions, damaged tissues recover during rest, but often these damages pass the repairable stage due to insufficient resting times (4). A study conducted by Szymanska (18) found that 29.9% of dentists worked approximately 8 hours without a break and most of them took a break 1 time per day. In order to prevent this situation, the students should be informed about healthy working conditions and correct posture before going to the clinic. The majority of the participants in our study did not have sufficient awareness of the postural problems observed in the spine and knee. Although it is known that ergonomics lessons are given in universities, it can be said that it is important to carry out different studies on the use of this information in everyday life. There are also studies in the literature that emphasize the importance of gaining awareness about preventive practices for dentists (19). In this context, it is important to include experts in the field of physiotherapy and rehabilitation in the courses given for ergonomics under the name of preventive medicine in dentistry education.

Conclusion

The small number of dentists involved in the research can be evaluated within the limitations of this study. As a result, postural disorders seen in dentists are usually seen in cervical, thoracic and lumbar areas of the spine and knees. This may be due to the body position that dentists take when treating their patients. As a result of all these analyses, it can be said that postural disorders do not occur immediately, they occur later in the profession due to prolonged exposure to non-ergonomic working conditions and inappropriate posture. Dentists are at risk for pain due to their work in narrow and limited areas, making repetitive movements that require force, using some technical tools that create mechanical stress in the musculoskeletal system and staying in a certain position for a long time (15,16). It is recommended that dentists receive training on body awareness, correct posture, healthy working environment and preventive rehabilitation from the first years of education and be informed about practicing in their daily work lives.

Ethics

Ethics Committee Approval: Ethical Principles for Medical Research Involving Human Subjects” of the World Medical Association Declaration of Helsinki (amended in October 2013).

Informed Consent: A consent was completed by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: D.T., M.K., Design: D.T., Data Collection or Processing: M.K., Analysis or Interpretation: D.T., M.K., Literature Search: D.T., M.K., Writing: D.T.

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Determination of the Alexithymia in Patients with Myocardial Infarction

Miyokard Enfarktüsü Geçiren Hastalarda Aleksitiminin Belirlenmesi

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ABSTRACT

Objective: The aim of this study was to determine alexithymia and related factors in patients with myocardial infarction.

Methods: A cross-sectional and descriptive study including 211 patients was conducted between June and November 2016. Data were collected using a face-to-face interview method with "Patient Information Form" and Toronto Alexithymia scale-20. The number, percentage, mean, standard deviation, t-test, Mann-Whitney U test, Kruskal-Wallis and Bonferroni test were used to evaluate the data.

Results: Patients with myocardial infarction have alexithymic features. Gender, educational level, place of residence, working status, income level, duration of coronary artery disease and hypertension affected the "Toronto Alexithymia scale-20" point average ($p<0.05$). Also, gender, education level, working status, income level and tell someone else about disease affect patients' "difficulty in recognizing emotions"; the use of alcohol affects the "difficulty of expressing emotions", the age and working status affect the "externally-oriented thinking" ($p<0.05$).

Conclusion: Attention should be paid to the effect of alexithymic features on the diagnosis and treatment of myocardial infarction due to the presence of alexithymic features in patients with myocardial infarction and the presence of many factors affecting these features.

Keywords: Myocardial infarction, alexithymia, patient

ÖZ

Amaç: Bu çalışmanın amacı miyokard enfarktüsü geçiren hastalarda aleksitimi ve ilişkili faktörleri belirlemektir.

Yöntemler: Kesitsel ve tanımlayıcı nitelikteki bu çalışma, Haziran-Kasım 2016 tarihleri arasında 211 hasta ile yapıldı. Veriler, yüz yüze görüşme tekniği kullanılarak "Hasta Bilgi Formu" ve "Toronto Aleksitimi ölçeği-20" ile toplandı. Verilerin değerlendirilmesinde sayı, yüzde, ortalama, standart sapma, Mann-Whitney U, Kruskal-Wallis ve Bonferroni testi kullanıldı.

Bulgular: Miyokard enfarktüsü geçiren hastalar aleksitimik özelliklere sahiptir. Cinsiyet, eğitim düzeyi, yaşanılan yer, çalışma durumu, gelir düzeyi, koroner arter hastalığı süresi ve hipertansiyon, "Toronto Aleksitimi ölçeği-20" toplam puan ortalamalarını etkilemektedir ($p<0.05$). Ayrıca, cinsiyet, eğitim düzeyi, çalışma durumu, gelir düzeyi ve hastalığını anlatma hastaların "duygularını tanıma güçlüğü" etkilerken; alkol kullanımı "duygularını ifade etme güçlüğü", yaş ve çalışma durumu ise "dışa dönük düşünmeyi" etkilemektedir ($p<0.05$).

Sonuç: Miyokard enfarktüsü geçiren hastaların aleksitimik özellikler göstermesi ve bu özellikleri etkileyen fazla sayıda faktörlerin varlığı nedeniyle aleksitimik özelliklerin miyokard enfarktüsünün tanı ve tedavi sürecindeki etkisine dikkat edilmelidir.

Anahtar Sözcükler: Miyokard enfarktüsü, aleksitimi, hasta

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Introduction

Myocardial infarction (MI) is still one of the most important health problems today despite improvements in diagnosis and treatment. In recent years, the interaction between emotional diseases and heart diseases has been noted, and the connection of mental disorders with cardiac diseases has been pointed out (1).

Alexithymia affects the onset, course and recovery of the disease, especially when it occurs with psychological and physical syndromes. In Greek, the concept of alexithymia, which consists of a combination of words meaning a=no, lexis=word, thymos=feeling, is defined as “absence of words for emotions”. The ability to regulate signals coming from the body is impaired due to the inability to recognize and understand emotions in alexithymide, and problems with experiencing, recognizing and understanding physical and psychological symptoms develop (2,3). People with alexithymia have difficulty in recognizing their feelings, putting them into words, distinguishing one emotion from another, paying more attention to details by moving away from their inner world due to limitations in their ability to dream, and arranging their actions and thoughts according to external stimuli. Their inability to distinguish their emotional arousal from their physical arousal is often explained by their use of physical symptoms to express their feelings (3,4). They may also face the risks of not being able to receive effective treatment on time in the event of a physical and emotional illness (5,6). Therefore, sensitivity to bodily symptoms and emotions plays an important role in symptom perception, treatment and care process (2).

Different studies have reported a close relationship between cardiac diseases and alexithymia (1,7-9). Oxygen deprivation in MI requires urgent medical attention and causes damage to heart tissue and death of tissue, which requires urgency for early diagnosis and reperfusion treatment for good prognosis. Therefore, it is necessary for patients to be aware of their symptoms, to recognize and distinguish their symptoms as soon as possible, to seek help and to reach medical intervention (5,10). However, alexithymic features in MI increase medical admissions by causing higher perception of physical symptoms and increase mortality by preventing patients from taking appropriate treatment (1). Furthermore, the tendency for low somatic and emotional awareness in alexithymia reduces the perception and/or reporting of cardiac symptoms, thus causing excessive delays in receiving medical attention (4). Early recognition of symptoms such as chest pain, respiratory distress, sweating, nausea and vomiting, which are the first symptoms in MI, is very important for the initiation of life-saving interventions (5). However, patients with alexithymia may lose the chance of early treatment due to their inability to recognize cardiac symptoms (1,5). The ability of patients to accurately and timely describe their cardiac problems facilitates treatment and care possibilities. For this reason, it is very important for patients having MI to recognize and describe their feelings (5,10). A study found a significant relationship between somatic and emotional awareness and delay in admission of patients having MI, and it was determined that patients who were unable to describe their emotions, bodily

sensations and internal experiences were admitted to the hospital later for MI symptoms (10). In another study, alexithymia scores of patients who had previous MI were significantly higher than those who had acute MI (7).

It has been reported that recognizing and expressing emotions are important factors affecting the outcome of treatment and care, and therefore alexithymia is a guiding factor in the clinical treatment of patients (11). For this reason, the physical and psychological symptoms of patients with physical and emotional problems should be examined, and the contribution of the characteristics of alexithymia to these symptoms should be determined. In addition, it is thought that the determination of alexithymia is important in assessing treatment compliance and treatment outcomes in MI. The aim of this study was to determine the relationship of alexithymic characteristics with sociodemographic and disease characteristics of patients having MI.

Methods

Type and Location of Research

This cross-sectional and descriptive study was carried out at the coronary intensive care unit (CICU) of the Ahi Evren Chest and Cardiovascular Surgery Training and Research Hospital in Trabzon.

Universe and Sample Size of Research

The universe of the study consisted of 1200 patients staying in CICU with a diagnosis of MI between January 1, 2015 and December 31, 2015 at The Trabzon Ahi Evren Chest and Cardiovascular Surgery Training and Research Hospital. Statistical analysis was performed using the OpenEpi program to determine the sample size of the study with a strength of 80% in the 95% confidence interval and it was found that at least 211 patients should be included in the study (12). The sample of the study was composed of patients who were aged 18 or over, were staying in CICU due to diagnosis of MI and whose discharge was planned, who could communicate in Turkish, did not have a previous psychiatric condition that required treatment, had orientation to person, place and time.

Data Collection Tools

The data was collected using the “Patient Data Form” and the “Toronto Alexithymia scale (TAS-20)”.

Patient Data Form

The Patient Data Form which was created by the researchers by scanning the literature consisted of two parts (1-11). The first section contained 10 questions to determine the characteristics of the patients (gender, age, marital status, education level, living place, working status, income level, people living together, smoking and alcohol use) ; the second section contained a total of 16 questions, including six questions to determine the patient's disease characteristics [duration of coronary artery disease (CAD)], previous hospitalization due to MI, number of MI episodes, being able to describe the disease, being able

to recognize the symptoms of MI and seek help, presence of diabetes and hypertension).

Toronto Alexithymia Scale (TAS-20)

TAS-20 is a likert type, self-assessment scale consisting of 20 items which are rated between 1-5. TAS-20 was developed by Bagby et al. (13). The Turkish validity and reliability study of TAS-20 was performed by Sayar et al. (14). It was found that the cut-off score was 61 and the cronbach alpha internal consistency coefficient was 0.78 (14). TAS-20 explores alexithymia, which means that the individuals cannot be aware of their emotions and excitement. TAS-20 has three subscales: "difficulty in recognizing emotions (TAS-1)", "difficulty in expressing emotions (TAS-2)", and "outward thinking (TAS-3)". The TAS-1 subscale consists of seven questions (questions: 1,3,6,7,9,13,14;7-35 points) evaluating difficulty in identifying emotions and distinguishing them from the bodily sensations that accompany emotional arousal (I cannot fully describe the feelings I have). The TAS-2 subscale consists of five questions (questions: 2,4,11,12,17;5-25 points) evaluating difficulty in transferring emotions to others (it is very difficult for me to find the right words for my feelings). The TAS-3 subscale consists of eight questions (questions: 5,8,10,15,16,18,19,20;8-40 points) evaluating the presence of an extroverted cognitive structure, the weakness of introverted thinking and imagination (I prefer to talk about people's daily life activities rather than their emotions). The individual is asked to mark the most appropriate of the "never", "rarely", "sometimes", "often" and "always" options for each question. The total score is between 20-100. High scores indicate a high alexithymic level. The alpha internal consistency coefficient of TAS-20 for this study is 0.65.

Implementation of Data Collection Tools

The patient data form and TAS-20 were applied to patients who were aged 18 or over, were staying in CICU due to diagnosis of MI and whose discharge was planned, who could communicate in Turkish, did not have a previous psychiatric condition that required treatment, had orientation to person, place and time with face-to-face interview method between June-November 2016. The face-to-face interview with the patients was conducted in a special room reserved for the interview with each patient in the CICU. The questions in the patient data form and TAS-20 were asked by the researcher and the responses were recorded in the relevant forms. The patient data form and TAS-20 took about 20 minutes to complete.

Evaluation of Data

Statistical analysis of data was done with SPSS Software for Windows (version 18.0; SPSS Inc., Chicago, IL) Statistics Package Program. Continuous variables were given as mean, standard deviation, (minimum-maximum values), and categorical variables as numbers (percentages). Normal distribution of the data was evaluated by Kolmogorov-Smirnov test and Homogeneity of variance analysis. The Mann-Whitney U test was used to compare binary groups without normal distribution and the Kruskal-Wallis test was used to compare three or more

groups without normal distribution. In comparison of three or more groups, the Bonferroni correction was performed to determine from which two subgroups this difference originated. $P < 0.05$ was accepted as statistical significance value.

Ethical Aspect of Research

The study was approved by the Ethics Committee for Clinical Research of the University of Health Sciences Kanuni Training and Research Hospital (number: 23618724/03.06.2016). In addition, informed consent was obtained from the patients participating in the study and the necessary institution permission was obtained from the hospital where the research was conducted by submitting a data form containing the purpose and scope of the research (number: 96975576/10.05.2016). Considering the principle of "respect for human dignity" in the study, the participants were informed that data about themselves would not be disclosed to others and adhered to the "principle of confidentiality". In addition, volunteerism was based on the participation of patients in the study, and patients who did not agree to participate in the study were not included in the study.

Results

The average TAS-1 score was 18.4 ± 7.1 , TAS-2 score 16.5 ± 3.3 , TAS-3 score 30.8 ± 4.5 and TAS-20 total score was 65.2 ± 11.6 (Table 1).

The Mann-Whitney U test showed that TAS-1 score ($U = 3083.5$, $p = 0.012$) and TAS-20 total score ($U = 3027.0$, $p = 0.008$) were significantly higher in men than in women. When patients were examined for alexithymic characteristics according to their age, there was a significant difference between the groups in terms of the TAS-3 subscale ($X^2_{kw} = 7.266$, $p = 0.026$) and the Bonferroni test performed to determine from which group this difference originated showed that this difference was due to those aged 60 or below and those in the 61-69 age range ($p = 0.024$). The Kruskal-Wallis test was performed to determine if the difference between TAS-20 subscale and total score averages was significant according to the level of education variable, and a significant difference was found between education level and TAS-1 score ($X^2_{kw} = 19.106$, $p = 0.001$). This difference was caused by college graduates and illiterate ones ($p = 0.000$). In addition, there was a significant difference between the educational level and the TAS-20 total score average ($X^2_{kw} = 18.290$, $p = 0.001$) and the Bonferroni test results showed that this difference was found between university graduates and primary school graduates ($p = 0.009$), and between

Table 1. TAS-20 subscale and total score averages of patients (n=211)

TAS-20	X $\pm$ SD	Med (Min-max)
TAS-1	18.4 $\pm$ 7.1	17 (7-35)
TAS-2	16.5 $\pm$ 3.3	17 (8-25)
TAS-3	30.8 $\pm$ 4.5	31 (15-40)
TAS-20 total	65.2 $\pm$ 11.6	64 (1-92)

TAS-1, difficulty in recognizing emotions, TAS-2, difficulty in expressing emotions, TAS-3, outward thinking, TAS-20, Toronto alexithymia scale-20 total, SD: Standart deviation, Min: Minimum, Max: Maximum

university graduates and illiterates ($p=0.000$). It was determined that there was a significant difference between the groups in terms of TAS-20 total score average according to the places where they were living ($X^2_{kw}=6.393$, $p=0.041$) and that this difference was due to those living in the province and those living in the village ($p=0.038$). The TAS-1 score ($U=3289.0$, $p=0.005$), TAS-3 score ($U=3094.0$, $p=0.001$) and TAS-20 total score averages ($U=2826.5$, $p=0.000$) were significantly higher in working patients than in non-working patients. There was a significant difference between different income levels in terms of TAS-1 ($X^2_{kw}=16.911$, $p=0.000$) and TAS-20 score averages ($X^2_{kw}=18.806$, $p=0.000$). The Bonferroni test showed that the

differences in terms of TAS-1 score were between those whose income was higher than expense and those whose income was lower than expense ($p=0.006$ and $p=0.001$, respectively) and that the differences in terms of TAS-20 total score were between those whose income was equal to expense and those whose income was lower than expense ($p=0.003$ and $p=0.008$, respectively). The Mann-Whitney U test showed a significant difference between patients with alcohol use and patients without alcohol use in terms of the scores of TAS-2 ($U=820.5$, $p=0.027$).

Marital status, smoking and people they were living together did not significantly affect the TAS-1, TAS-2 and TAS-3 score averages and TAS-20 total score average ($p>0.05$) (Table 2).

Table 2. TAS-20 subscale and total score averages according to the characteristics of the patients (n=211)

Features	n (%)	TAS-1 X ± SD	TAS-2 X ± SD	TAS-3 X ± SD	TAS-20 total X ± SD
Gender					
Woman	50 (23.7)	22.0±21.2	17±16.9	32±31.6	69±69.4
Man	161 (76.3)	17±17.5	17±16.4	31±30.5	64±63.9
	U	3083.5	3609.5	3338.0	3027.0
	p	0.012*	0.267	0.067	0.008**
Age					
≤60 years	88 (41.7)	18.2±7.2	16.2±3.4	30.0±4.2	63.2±12.3
61–69 years	55 (26.1)	17.7±7.3	16.5±3.3	32.1±3.8	66.2±10.3
≥70 years	68 (32.2)	19.3±6.8	16.8±3.3	30.8±5.1	66.9±11.5
	X^2_{kw}	1.883	1.122	7.266	2.751
	p	0.390	0.571	0.026*	0.253
Marital status					
Married	204 (96.7)	17.0±18.5	17.0±16.5	31.0±30.9	65.0±65.5
Single	7 (3.3)	16.0±15.8	17.0±15.4	28.0±28.8	62.0±57.0
	U	579.5	593.5	493.5	490.5
	p	0.396	0.445	0.163	0.159
Education level					
Illiterate	35 (16.5)	23.0±22.5	17.0±16.8	32.0±31.0	70.0±70.4
Literate	9 (4.2)	20.0±21.1	15.0±15.7	30.0±30.1	67.0±61.4
Primary school	119 (56.3)	17.0±18.2	17.0±16.8	31.0±31.4	65.0±66.1
Secondary school	21 (9.9)	17.0±16.8	17.0±16.9	29.0±29.9	64.0±61.9
College	27 (13.1)	13.0±14.5	14.0±14.7	28.0±28.8	58.0±58.2
	X^2_{kw}	19.106	7.831	7.920	18.290
	p	0.001**	0.098	0.095	0.001**
Place of residence					
Village	40 (18.9)	20.7±7.3	17.3±3.3	31.3±4.2	69.6±10.4
Town	75 (35.5)	17.6±6.6	16.5±3.2	31.1±4.5	64.1±12.1
City	96 (45.6)	18.1±7.2	16.1±3.4	30.4±4.5	64.1±11.4
	X^2_{kw}	4.616	3.820	1.750	6.393
	p	0.099	0.148	0.417	0.041*
Working status					
Working	57 (27.0)	16.1±6.2	16.1±3.3	29.2±4.2	59.5±12.6
Not working	154 (73.0)	19.3±7.2	16.7±3.3	31.4±4.4	67.3±10.5

Table 2 continued

	U	3289.0	3926.0	3094.0	2826.5
	p	0.005**	0.236	0.001**	0.000***
Income level					
Income higher than expense	19 (9.0)	14.8±6.3	15.0±3.9	29.1±3.5	56.7±11.6
Income equal to expense	61 (28.9)	16.1±5.4	16.3±3.1	30.4±4.6	62.3±8.5
Income lower than expense	131 (62.1)	20.1±7.4	16.8±3.3	31.2±4.5	67.7±12.1
	X ² kw	16.911	3.691	5.434	18.806
	p	0.000***	0.158	0.066	0.000***
People living together					
Alone	23 (10.9)	21.2±8.2	17.4±2.9	31.7±4.5	69.6±15
Partner	121 (57.3)	18.2±6.9	16.6±3.5	31.1±4.6	65.7±10.6
Partner and kids	57 (27.0)	17.8±7.1	15.8±3.1	30.1±4.0	62.4±12.1
Partner, kids and family elders	10 (4.8)	18.3±6.5	16.3±3.3	29.5±4.7	64.1±9.4
	X ² kw	2.718	3.964	3.535	7.283
	p	0.437	0.265	0.316	0.063
Smoking status					
Smoking	94 (44.5)	17.6±6.7	16.1±3.4	30.5±4.4	63.5±12
Not smoking	117 (55.5)	19.1±7.3	16.8±3.2	31.1±4.5	66.5±11.2
	U	4899.5	4825.0	5015.5	4886.0
	p	0.173	0.123	0.271	0.164
Alcohol use					
Using	13 (6.1)	18.2±3.4	14.6±2.9	29.4±4.1	58.4±11.6
Not using	198 (93.9)	18.4±7.3	16.6±3.3	30.9±4.5	65.6±11.1
	U	1196.5	820.5	1041.0	1062.5
	p	0.671	0.027*	0.247	0.292

TAS-1, difficulty in recognizing emotions, TAS-2, difficulty in expressing emotions, TAS-3, outward thinking, TAS-20, Toronto alexithymia scale-20 total, U: Mann-Whitney U test, X²kw: Kruskal-Wallis test, *p<0.05, **p<0.01, ***p<0.001, SD: Standart deviation

The difference between CAD duration and TAS-20 subscale and total score averages was evaluated by the Kruskal-Wallis test and significant difference was found between CAD duration and TAS-20 total score average (X²kw=9.701, p=0.021). In further analysis, it was determined that this difference was between patients with CAD duration less than one year and patients with CAD duration of 1-5 years (p=0.019). The Mann-Whitney U test showed that the TAS-1 score average (U=231.5, p=0.035) was significantly higher in patients who could describe their disease than in patients who could not and that TAS-20 total score average (U=4334.0, p=0.035) was significantly higher in patients with hypertension than in patients without hypertension.

The patients' previous hospitalization due to MI, the number of MI episodes, the ability to recognize MI symptoms and seek help, and the presence of diabetes did not significantly affect the TAS-1, TAS-2 and TAS-3 score averages and TAS-20 total score average (p>0.05) (Table 3).

Discussion

In our study, patients having MI were found to have alexithymic features. This result suggested that patients were not adequate

in recognizing and correlating their bodily sensations, tended to focus on somatic sensations and reported these sensations as physical discomfort or other distinct symptoms. However, it is very important for patients with MI to recognize and explain their feelings in order to reach treatment on time. For this, patients need to be aware of their symptoms as soon as possible, recognize and distinguish their symptoms, seek help and reach medical intervention (4). Similar to our study, Valkamo et al. (8) found the TAS-20 total score average in the alexithymic group in patients with CAD as 65.7±0.6 and Meloni et al. (5) found it in 28% of patients admitted to the emergency room due to MI as 64.8±3.4. Alexithymic people who have problems in recognizing, understanding and arranging their feelings have characteristics such as not being able to name their feelings, not being able to distinguish their feelings from each other and from their physical feelings, and not being aware of their feelings (15). In our study, patients experienced difficulty in recognizing their emotions. The tendency of low somatic and emotional awareness to alexithymia is thought to reduce recognition and perception of cardiac symptoms. Unlike our results, the average TAS-1 scores in patients with CAD were 23.54±6.29 (9), 22.6±2.4 (8) and 21.83±6.00 (1) in other studies.

Table 3. TAS-20 subscale and total score averages according to the disease characteristics of the patients (n=211)

Disease characteristics	n (%)	TAS-1 X ± SD	TAS-2 X ± SD	TAS-3 X ± SD	TAS-20 total X ± SD
CAD duration					
<1 year	129 (61.1)	17.8±7.0	16.1±3.2	30.4±4.6	63.5±11.9
1-5 years	32 (15.1)	21.4±8.0	17.4±2.8	32.0±4.2	70.6±11.6
6-10 years	18 (8.5)	18.1±6.2	17.5±4.2	31.3±4.3	66.7±9.6
≥11 years	32 (15.3)	18.1±6.6	16.8±3.7	30.8±4.2	65.7±9.7
	X ² kw	5.656	6.573	3.666	9.701
	p	0.130	0.087	0.300	0.021*
Previous hospitalization due to MI					
Yes	73 (34.5)	18.4±7.0	16.8±3.8	31.3±4.3	66.3±10.7
No	138 (65.5)	18.4±7.2	16.3±3.1	30.5±4.5	64.6±12.1
	U	4994.0	4699.5	4536.5	4682.0
	p	0.919	0.420	0.234	0.400
MI episoded					
1 time	142 (67.2)	18.5±7.3	16.3±3.2	30.6±4.5	64.7±12.1
2 times	46 (21.8)	17.2±6.6	16.7±3.5	31.8±3.8	65.1±11.1
≥3 times	23 (11.0)	20.4±6.4	17.0±4.1	30.3±5.0	68.1±9.8
	X ² kw	3.667	0.483	2.377	2.466
	p	0.160	0.786	0.305	0.291
Being able to tell about his/her disease					
Yes	206 (97.6)	18.6±7.1	16.5±3.4	30.8±4.5	65.3±11.7
No	5 (2.4)	12.2±3.7	17.0±1.8	30.8±3.9	60.4±3.6
	U	231.5	476.0	503.5	344.5
	p	0.035*	0.771	0.932	0.206
Being able to recognize MI symptoms and seek for help					
Yes	79 (37.4)	18.1±6.7	16.4±3.7	30.7±4.2	64.2±12.3
No	132 (62.6)	18.6±7.3	16.5±3.1	30.8±4.6	65.7±11.2
	U	5130.0	5045.0	5098.0	5046.5
	p	0.845	0.692	0.786	0.696
Diabetes Mellitus					
Yes	73 (34.5)	19.8±7.6	16.7±3.2	30.0±4.8	66.2±12.8
No	138 (65.5)	17.7±6.7	16.3±3.4	30.8±4.2	64.6±10.9
	U	4301.5	4830.0	5000.5	4424.5
	p	0.081	0.621	0.931	0.146
Hypertension					
Yes	131 (62.0)	19.1±7.4	16.8±3.2	31.1±4.5	66.8±10.7
No	80 (38.0)	17.3±6.4	16.1±3.5	30.3±4.3	62.5±12.6
	U	4604.5	4710.0	4644.5	4334.0
	p	0.139	0.215	0.165	0.035*

TAS-1, difficulty in recognizing emotions, TAS-2, difficulty in expressing emotions, TAS-3, outward thinking, TAS-20, Toronto alexithymia scale-20 total, CAD: Coronary artery disease, MI: Myocardial infarction, U: Mann-Whitney U test, X²kw: Kruskal-Wallis test, SD: Standart deviation
*p<0.05

Patients with MI with alexithymia tend to focus on bodily sensations due to their limitations in cognitive processing of emotions, leading to situations that can be misinterpreted as symptoms of physical illness (1). In this study, patients had difficulty in explaining and expressing their feelings. Failure to adequately express emotions leads to the development of different physical symptoms (15). In different studies, similar to our results, average TAS-2 scores in patients with CAD were 15.25 ± 3.92 (9), 15.00 ± 5.30 (1) and 17.7 ± 1.8 (8).

The difficulty in recognizing, describing and expressing emotions in people with alexithymic characteristics decreases the ability to dream and the tendency to think solid, and causes them to do their actions and thoughts more in line with external stimuli (3). In our study, the TAS-3 score average was high showing the difficulty of outward thinking of the patients. This conclusion reinforced the fact that patients with MI focused more on external events when their internal experiences were damaged. Nekouei et al. (9) showed that the TAS-3 score average in patients with CAD was 21.59 ± 3.48 ; Silva et al. (1) showed that it was 23.43 ± 4.96 and Valkamo et al. (8) showed that it was 25.5 ± 2.2 , which were all lower than our results.

Mattila et al. (2) reported that alexithymic features were associated with female sex. In our study, female patients had more difficulty in recognizing, distinguishing and making sense of their emotions showed more alexithymic characteristics than male patients. In parallel with our study, Meloni et al. (5) noted that female patients admitted to the emergency room due to MI had significantly higher alexithymic characteristics, that women waited longer for MI symptoms to pass, and that they were not able to assess their symptoms seriously/urgently.

In our study, patients in the 61-69 age range thought more outwardly and had difficulty in dreaming. This suggested that patients in our study group placed much greater emphasis on environmental factors and detail in the problems they experienced. Silva et al. (1) found significant differences between TAS-1 and TAS-3 score averages and TAS-20 total score average and age of the patients with MI. Oktay and Batıgün (16) stated that there was a relationship between age and TAS-3 and that the ability to dream decreased as age increased. Valkamo et al. (8) found the mean age of patients with CAD with alexithymic characteristics as 60.4 ± 1.6 ; Meloni et al. (5) as 60.8 ± 11.9 ; and Kojima et al. (7) as 60.8 ± 10.9 years.

Mattila et al. (17) found that education level was negatively associated with alexithymia, and that alexithymic features were seen in 3.3% of highly educated people and 16.5% of low educated people. In our study, illiterate patients experienced more difficulty in recognizing their emotions and their alexithymic characteristics increased as their level of education decreased. This result was interpreted as follows: As education level decreased interpersonal communication decreased, difficulties in recognizing and distinguishing emotions occurred, and difficulty in finding appropriate words to express emotions occurred. Similar to our study, Oktay and Batıgün (16) found that alexithymia decreased as education level increased; Kojima

et al. (7) found that 39.9% of post-MI patients with alexithymia had an educational level of ≤ 7 years.

It was argued that alexithymic features arise as a result of learning in the sociocultural environment in which individuals were present (18). In our study, the patients living in the village had high alexithymic characteristics. The reason for this was that the patients living in the village had more patriarchal family structure. It was stated that alexithymia was a condition learned in the process of social development and that the traditional patriarchal approach provided the basis for alexithymic features in adult life (18). In addition, societies in underdeveloped regions are more controlling and oppressive, which can lead to poor social life, personality development, and therefore emotional development. Parallel to our study, Kokkonen et al. (19) also found high alexithymia in people living in the village.

In this study, patients who did not work experienced more difficulty in recognizing their emotions than those who did, thought more outwardly, and had higher alexithymic characteristics. This has been associated with decreased interactions of non-working patients with people in their lives that contribute to the recognition and expression of emotions and with lack of adequate social support. Similar to our results, Kokkonen et al. (19) found non-workers to be more alexithymic than employees, and noted that alexithymia was associated with unemployment. Valkamo et al. (8) showed that the sick leave/retirement rate was 78% in the group without alexithymia and 97% in the group with alexithymia in patients with CAD.

In our study, it was found that patients with decreased income levels had more difficulty in recognizing their emotions and increased alexithymic characteristics. It was thought that as income levels decreased, it became difficult to deal with problems and social support decreased. Parallel to our study, Kokkonen et al. (19) found that alexithymia was associated with low income levels; people with low income levels had higher alexithymia score averages than those with high income levels. Again, Mattila et al. (2) found that people with low income had a higher average score of TAS-20.

It is very important to realize the feelings experienced and to put them into words in order to establish healthy and balanced relationships. In emotional situations, such as alcohol and drug use, it is stated that losses in the process of regulating emotions are likely to negatively affect emotional health (4). In our study, patients who did not use alcohol had more difficulty expressing their feelings than those who did. This result suggested that patients who used alcohol could express themselves more freely by creating social environments in terms of meaningful interpersonal relationships, self-acceptance, attractiveness, and recognition, and that they used alcohol as a relief tool in coping with stressful situations. In a study of inpatient alcohol addicts in Turkey, anxiety and avoidance subscales of the Liebowitz Social Anxiety scale were found to correlate with TAS-1, TAS-2 and TAS-3 subscales, while the anxiety subscale was associated with TAS-1 subscale (20).

In our study, patients with CAD duration of 1-5 years had higher alexithymic characteristics. This result suggested that patients were unable to relax even though the acute period had passed, and were unable to cope with the complex nature of MI in daily life and were unable to reduce painful emotions. It was stated that the duration of the disease affected daily life and emotions, and that patients needed time to learn how to adapt to the disease and how to cope with it (7). Kojima et al. (7) noted that high alexithymic characteristics developed in patients who had MI in three and six months after discharge, and those who had previously CAD were more alexithymic than those who had acute MI. It was also stated that there was a limitation in the imagination activities and emotional expression of patients who experienced a life-threatening fatal condition or received treatment in the intensive care unit (5).

The fact that MI is a stressful event causes the patient to tell those around him/her (family, friends) what he/she feels and to seek help (6). Meloni et al. (5) noted that 22.2% of patients with high alexithymic characteristics with ST-segment elevation MI consulted a family member for the disease. In our study, it was thought that telling about the disease might play an important role in accelerating the recovery of the cardiac condition, but on the contrary, these patients experienced more difficulty in recognizing their emotions. We could relate this to the fact that patients were still in critical period of MI. It was also thought that patients were unable to convert their emotions into meaningful feelings and were unable to fully describe their emotions. It was stated that people with alexithymia had impaired ability to establish personal intimate relationships, cognitive losses occurred in their emotions, and that they had difficulty in properly recognizing and responding to other people's feelings have (6). Nekouei et al. (9) noted that alexithymia reduced social support in patients with CAD, and that alexithymic patients did not receive adequate social support from their families and/or friends.

There are studies showing that in alexithymia which can be effective on physical health, emotional status is associated with traditional risk factors for CAD, such as emotional sedentary lifestyle, high body mass index and essential hypertension (5,11). Hypertension and CAD make it necessary for the individual to develop a certain lifestyle. This causes patients to lead stressful lives and therefore develop various emotional responses (11). In our study, patients with hypertension had high alexithymic features. Many studies have shown a close relationship between alexithymia and hypertension. Meloni et al. (5) showed that 44.4% of patients with hypertension and ST-segment elevation had high and 48.5% of them had low alexithymic features. Grabe et al. (21) showed that there was a clear association between alexithymia, hypertension and carotid atherosclerosis in the general population. Kojima et al. (7) showed that alexithymic features were more common in patients with essential hypertension and CAD compared with healthy individuals.

Study Limitations

The limitation of the study was that only patients hospitalized in the CICU of Trabzon Ahi Evren Chest and Cardiovascular

Surgery Training and Research Hospital were included in the study. The results of this study are therefore directed at patients receiving treatment in this unit. The results of this study cannot be generalized to all patients.

Conclusion

The patients who had MI included in the study were shown to have alexithymic characteristics. In our study, it was found that the "alexithymic characteristics" of the patients were influenced by sex, age, education level, place of residence, working status, income level, alcohol use, CAD duration, being able to tell about their disease and the presence of hypertension. Patients with MI with alexithymic features may require more support and individual attention. Patients with MI should be monitored for alexithymic features and sociodemographic and disease-related features should be taken into consideration during this process. In addition, it is recommended to carry out comparative studies between the alexithymic characteristics and sociodemographic and disease-related characteristics of the patients having MI.

It is thought that the results of the study may increase awareness of the alexithymic characteristics of patients having MI and the factors affecting their alexithymic characteristics, and contribute to the planning, implementation and monitoring of health care in the diagnosis and treatment of MI. In addition, considering that it is very important for patients having MI to express themselves, it is thought that further investigation of this issue will be useful in developing new recommendations.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee for Clinical Research of the University of Health Sciences Kanuni Training and Research Hospital (number: 23618724/03.06.2016).

Informed Consent: A consent form was completed by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: A.T., S.H., Design: A.T., S.H., Data Collection or Processing: A.T., S.H., Analysis or Interpretation: A.T., S.H., Literature Search: A.T., S.H., Writing: A.T., S.H.

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Additional Preoperative Parameters to Enable the Decision of Partial Orchiectomy in Small Testicular Masses

Küçük Testiküler Kitlelerde Parsiyel Orşiektomi Kararını Vermeyi Sağlayacak Ek Preoperatif Parametreler

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ABSTRACT

Objective: We aimed to determine the predictive value of additional parameters for differentiating benign-malign tumors and to identify optimal patients for partial orchiectomy in unilateral, small (≤ 2 cm) testicular masses.

Methods: The data of 31 patients who underwent radical orchiectomy between January 2010 and December 2017 due to unilateral and small testicular masses were retrospectively analyzed. Demographic data, histopathological tumor types, serum tumor markers, neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV), red cell distribution width (RDW), the presence of testicular dysgenesis syndrome (TDS) and its components, postoperative follow-up outcomes were recorded. Patients were divided into two groups as benign and malignant.

Results: There was no significant difference between groups in terms of AFP ($p=0.116$), β -hCG ($p=0.205$), LDH ($p=0.606$), MPV ($p=0.087$) and RDW ($p=0.266$); while MLR ($p=0.001$), NLR ($p=0.036$) and PLR ($p=0.001$) were significantly higher in malignant group. The presences of testicular microlithiasis ($p=0.719$), undescended testis ($p=0.254$), hypospadias ($p=0.645$), atrophic testis ($p=0.409$) were not different between groups; while the rate of disorders of semen parameters ($p=0.043$) and presence of TDS ($p=0.043$) were significantly higher in malignant cases.

ÖZ

Amaç: Tek taraflı, küçük (≤ 2 cm) testiküler kitlelerin preoperatif değerlendirmesinde, benign-malign ayrımını yapabilmeye kullanılabilecek ek klinik parametrelerin öngörü değerini araştırarak, parsiyel orşiektomi uygulanabilecek hastaları belirlemeyi amaçladık.

Yöntemler: Ocak 2010-Aralık 2017 tarihleri arasında radikal orşiektomi yapılan tek taraflı, küçük testiküler kitleye sahip 31 hastanın verileri retrospektif olarak incelendi. Hastaların demografik verileri, histopatolojik tümör tipleri, serum tümör belirteçleri, nötrofil/lenfosit oranı (NLR), monosit/lenfosit oranı (MLR), platelet/lenfosit oranı (PLO), ortalama platelet hacmi (MPV), eritrosit dağılım genişliği (RDW), testiküler disgenезis sendromu (TDS) ve bileşenlerinin varlığı, postoperatif takip verileri kaydedildi. Hastalar tümör histopatolojisine göre benign ve malign olarak iki gruba ayrılarak karşılaştırıldı.

Bulgular: Ortalama tanı yaşı $29,39 \pm 5,90$ olan 31 hastanın 11'i benign, 20'si malign patolojiye sahipti. İki grup arasında AFP ($p=0,116$), β -hCG ($p=0,205$), LDH ($p=0,606$), MPV ($p=0,087$) ve RDW ($p=0,266$) açısından anlamlı fark görülmezken; malign grupta MLR ($p=0,001$), NLR ($p=0,036$) ve PLR ($p=0,001$) anlamlı olarak daha yüksekti. Testiküler mikrolitiazis ($p=0,719$), inmemiş testis ($p=0,254$), hipospadias ($p=0,645$), atrofik testis ($p=0,409$) saptanma oranları gruplar arasında farklılık göstermezken; semen parametresi bozukluğu oranı ($p=0,043$) ve TDS varlığı ($p=0,043$) malign olgularda belirgin olarak yüksek bulundu. Çok değişkenli

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In multivariate analysis, MLR and PLR were found as predictive factors for benign-malign distinction of small testicular masses.

Conclusion: In the patients in whom preoperative malignancy suspicion could not be excluded, we think that PLR, MLR, NLR, disorders of semen parameters and presence of TDS may have high predictive value for benign-malign distinction. Partial orchiectomy may be recommended in patients with suspicion of benign lesions according to these parameters.

Keywords: Partial orchiectomy, serum hemogram parameters, small testicular masses, testicular dysgenesis syndrome

analizde, MLR ve PLO'nun ≤ 2 cm boyutlu testiküler kitlelerde malign-benign ayrımını öngörmeye prediktif faktörler olduğunu gözledik.

Sonuç: Preoperatif olarak malignite şüphesinin dışlanamadığı olgularda, PLO, MLR, NLR, semen parametresi bozuklukları ve TDS varlığının benign-malign ayrımını yapma gücünün yüksek olabileceğini; benign olma olasılığı yüksek olgularda, parsiyel orşiektominin önerilebileceğini düşünmekteyiz.

Anahtar Sözcükler: Parsiyel orşiektomi, serum hemogram parametreleri, küçük testiküler kitleler, testiküler disgenezis sendromu

Introduction

Testicular germ cell tumor (TGCT) is a relatively rare neoplasm that accounts for 1-2% of all malignancies (1), but is the most common genitourinary malignancy detected, especially in males between the ages of 15-44. It accounts for 98% of all testicular malignancies (2). The standard approach to treatment is radical orchiectomy. As a result of the developments in chemotherapy (CT) applications in recent years, high cure rates are provided in patients with TGCT. However, adjuvant CT or radiotherapy (RT) applied with orchiectomy and its continuation may lead to a decrease in fertility rates in this young male population. In addition, due to the lack of testosterone production caused by testicular loss; decrease in sexual function, deterioration in muscular body structure, osteoporosis due to decrease in bone mineral density can be seen in the following years (3,4).

Testicular sparing surgery has been introduced to protect fertility rates and testosterone levels. Partial orchiectomy for this purpose is recommended only in patients with bilateral testicular tumors or in the presence of a tumor in the solitary testis, if the testosterone level is normal and the tumor size is < 2 cm (4,5). Since the majority of testicular masses have malignant characteristics, this approach is not recommended in patients with stable contralateral testis, with the concern that the chance of cure may be reduced in patients with inadequate or incomplete resection (5).

Most of the palpable masses detected in the physical examination, which is the first approach to diagnosis of testicular masses, are large in diameter (> 2 cm). Although scrotal ultrasonography (USG) used as imaging method increases the accuracy of diagnosis, the exact diagnosis is made by orchiectomy following inguinal exploration (3). However, the diagnosis-treatment algorithm to be applied in small testicular masses that are not easily palpable and detected only by USG is still a subject of debate (6). Benign pathology has been reported in 60-80% of small testicular masses with normal tumor markers, and current studies suggest that radical orchiectomy is an extreme treatment in these cases (4,6,7). As a result, we have seen recent studies advocating the applicability of partial orchiectomy in small, unilateral tumors (6,8).

Since our knowledge on diagnostic and therapeutic approach to be applied in unilateral, small (≤ 2 cm) testicular masses

is still controversial, in this study, we aimed to investigate the predictive value of additional parameters that can improve diagnostic accuracy in preoperative evaluation by examining clinical-pathological characteristics of benign and malignant cases diagnosed in our clinic.

Methods

The pathological data and oncological results of 96 patients who were admitted in our clinic between January 2010-December 2017 due to testicular mass and were treated with radical orchiectomy for suspected malignancy after physical examination, measurement of tumor markers, scrotal ultrasonography and even magnetic resonance imaging (MRI) were performed, were evaluated retrospectively. Among 74 patients with histopathological diagnosis of TGCT and 13 patients with all other benign pathologies, 31 patients with pathological tumor diameter ≥ 2 cm and whose treatment and follow-up data could be fully accessed were included in the study. A total of 31 patients, 20 of whom had TGCT and 11 with benign pathology, were analyzed. All the procedures in our study were carried out in accordance with the principles of the Helsinki Declaration and this study was not approved by the Ethics Committee due to its retrospective design.

Demographic data of the patients (age), clinical findings (undescended testis, hypospadias, atrophic testis with testicular volume < 12 mL, testicular microlithiasis, semen parameter disorders), histopathological features (tumor subtypes, clinical tumor stage, tumor size, pathological prognostic factors of tumor), serum levels of tumor markers [alpha-fetoprotein (AFP), beta human chorionic gonadotropin (β -hCG), lactate dehydrogenase (LDH)], hemogram, serum parameters [(neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLO), mean platelet volume (MPV), erythrocyte distribution width (RDW)], oncological results (follow-up duration after orchiectomy, local recurrence, distant metastasis and cancer-specific mortality rates) were recorded.

In the presence of oligospermia [hazard ratio (HR): 11.9], decreased vitality (HR: 6.6), impaired sperm morphology (HR: 4.2), or low numbers of total motile sperm (HR: 6.9), it is known that there is a higher risk of testicular cancer (9). Therefore, we

evaluated the patients, in whom we detected any impairment in semen parameters in terms of number, motility, morphology or vitality, as decreased spermatogenesis. The definition of testicular dysgenesis syndrome (TDS) includes the presence of at least two components of the undescended testicle, hypospadias, decreased spermatogenesis, atrophic testis and TGCT. In preoperative evaluation, we considered four parameters other than TGCT when describing the presence of preoperative TDS, since it would not be possible to know if TGCT was present in the testicular mass in patients without pathology results. Based on anamnesis and clinical examination findings, we evaluated patients with at least two of these four clinical findings as TDS.

Clinical tumor stages of patients with TGCT were evaluated according to the 2009 tumor-node-metastasis classification and histopathological tumor subtypes according to the World Health Organization's classification. Pathological prognostic risk factors were assessed as set out in the European Association of Urology 2019 guideline. Accordingly, the presence of Rete testis involvement and tumor size greater than 4 cm in seminomas; the presence of lymphovascular invasion, the percentage of embryonal carcinoma >50% and the proliferation rate >70% in non-seminomas were noted as poor prognostic factors (5). However, in all patients in our study, the tumor size was ≤ 2 cm.

Patients were divided into two groups, benign and malignant, according to tumor histopathology. Eleven patients with benign pathological diagnosis were classified as group I and 20 patients with TGCT diagnosis were classified as group II. Both groups were compared in terms of clinical findings, prognostic risk factors, serum hemogram parameters and oncological outcomes.

Statistical Analysis

To compare the differences between the two groups, normality status was evaluated with Kolmogorov-Smirnov and Shapiro-Wilk tests. Pearson chi-square or Fisher's exact test was used for categorical variables; independent sample t-test or Mann-Whitney U test was used for continuous variables. The Kaplan-Meier method could not be used because there were not enough cases to perform survival analysis in the malignant group. Univariate and multivariate logistic regression analyses were used to determine the predictive factors that could predict malignant-benign mass differentiation. The analyses were done using IBM SPSS Statistics 21 (IBM, Armonk, NY USA) software. $P < 0.05$ was considered statistically significant.

Results

The mean age of diagnosis of 31 patients with tumor size ≤ 2 cm was 29.39 ± 5.90 years. In total, TGCT was detected in 20 patients, while histopathology of 11 patients was benign. Detected benign testicular tumors were epidermoid cyst ($n=2$, 18.2%), myofibroblastic inflammatory tumor ($n=2$, 18.2%), benign cystic teratoma ($n=3$, 27.2%), benign Leydig cell tumor ($n=2$, 18.2%), and fibroma ($n=2$, 18.2%) (Table 1).

In a median 44-month (9-117) follow-up, only in a single case with stage IIIC nonseminoma, recurrence in retroperitoneum

and visceral metastasis in the lung were observed 4 months after orchiectomy and cancer-specific mortality occurred 9 months after the diagnosis despite adjuvant CT was given. The pathological characteristics and oncological outcomes of all patients are shown in Table 1.

There were no significant differences between the benign and malignant groups in terms of AFP ($p=0.116$), β -hCG ($p=0.205$) and LDH ($p=0.606$), which were tumor markers evaluated in the preoperative period. MLR ($p=0.001$), NLR ($p=0.036$) and

Table 1. The pathological characteristics and oncological outcomes of testicular masses

Parameters	Group I (n=11) benign	Group II (n=20) malignant
Histopathological tumor type (n,%)		
-Seminom		10 (50.0)
-Non-seminom	-	8 (40.0)
-Mixed	-	2 (10.0)
-Epidermoid cyst	-	
- Inflammatory myofibroblastic tumor	2 (18.2)	-
- Benign cystic teratoma	2 (18.2)	-
- Benign Leydig cell tumor	3 (27.2) 2(18.2) 2(18.2)	-
-Fibroma		-
Tumor stage (n,%)		
IA	-	7 (35.0)
IB	-	7 (35.0)
IS	-	0 (0.0)
IIA	-	1 (5.0)
IIB	-	1 (5.0)
IIC	-	0 (0.0)
IIIA	-	0 (0.0)
IIIB	-	1 (5.0)
IIIC	-	3 (15.0)
Intratubular germ cell neoplasia (n,%)	-	13 (65.0)
Rete testis involvement (n,%)	-	7 (35.0)
Lymphovascular invasion (n,%)	-	6 (30.0)
Rate of embryonal carcinoma >50% (n,%)	-	6 (30.0)
Proliferation rate >70% (n,%)	-	2 (10.0)
Local recurrence rate (n,%)	-	1 (5.0)
Distant metastasis rate (n,%)	-	1 (5.0)
cancer-specific mortality rate (%)	-	1 (5.0)

PLR ($p=0.001$) were significantly higher in the malignant group, while there were no differences between the groups in terms of MPV ($p=0.087$) and RDW ($p=0.266$) (Table 2).

Although the detection rates of testicular microlithiasis ($p=0.719$), the rates of undescended testis ($p=0.254$), hypospadias ($p=0.645$) and atrophic testis ($p=0.409$) were higher

Table 2. Demographic and clinical data of patients

Parameters	Group 1 (n=11)	Group 2 (n=20)	Total (n=31)	p
Age				
Average $\pm$ standard deviation	28.27 $\pm$ 5.14	30.00 $\pm$ 6.32	29.39 $\pm$ 5.90	$\dagger$ 0.445
Tumor diameter (cm)				
Average $\pm$ standard deviation	1.61 $\pm$ 0.27	1.55 $\pm$ 0.29	1.57 $\pm$ 0.28	$\dagger$ 0.530
Tumor side (n,%)				
-Left	5 (45.5)	11 (55.0)	16 (51.6)	$\dagger$ 0.611
-Right	6 (54.5)	9 (45.0)	15 (48.4)	
AFP (ng/mL)	1.50	2.05	1.80	
Median (25.-75. percentile)	(1.20-2.70)	(1.52-7.45)	(1.30-5.70)	$\S$ 0.116
β-hCG (mIU/mL)	1.50	2.25	1.50	
Median (25.-75. percentile)	(0.00-1.60)	(0.22-31.40)	(0.10-4.50)	$\S$ 0.205
LDH (U/L)	165.00	183.50	167.00	
Median (25.-75. percentile)	(132.00-202.00)	(143.00-220.50)	(140.00-210.00)	$\S$ 0.606
Monocyte/lymphocyte ratio (MLR)				
(Average $\pm$ standard deviation)	0.19 $\pm$ 0.07	0.32 $\pm$ 0.10	0.28 $\pm$ 0.11	$\dagger$ 0.001*
Neutrophil/lymphocyte ratio (NLR)	1.67	2.35	2.12	
Median (25.-75. percentile)	(1.33-2.12)	(1.55-4.19)	(1.38-3.39)	$\S$ 0.036*
Platelet/lymphocyte ratio (PLO)				
(Average $\pm$ standard deviation)	94.33 $\pm$ 21.29	162.12 $\pm$ 58.54	138.06 $\pm$ 58.38	$\dagger$ 0.001*
Mean platelet volume (fL) (MPV)	3.12	3.91	3.75	
Median (25.-75. percentile)	(2.67-4.15)	(3.22-5.18)	(3.08-4.44)	$\S$ 0.087
Red cell distribution width (fL) (RDW)				
(Average $\pm$ standard deviation)	13.24 $\pm$ 0.72	13.70 $\pm$ 1.22	13.54 $\pm$ 1.08	$\dagger$ 0.266
Presence of testicular microlithiasis (n,%)				
Yes	1 (9.1)	2 (10.0)	3 (9.7)	
No	10 (90.9)	18 (90.0)	28 (90.3)	$\P$ 0.719
Undescended testis (n,%)				
Yes	0 (0.0)	3 (15.0)	3 (9.7)	
No	11 (100.0)	17 (85.0)	28 (90.3)	$\P$ 0.254
Disorder of semen parameter (n,%)				
Yes	0 (0.0)	6 (30.0)	6 (19.4)	
No	11 (100.0)	14 (70.0)	25 (80.6)	$\dagger$ 0.043*
Hypospadias (n,%)				
Yes	0 (0.0)	1 (5.0)	1 (3.2)	
No	11 (100.0)	19 (95.0)	30 (96.8)	$\P$ 0.645
Atrophic testis (n,%)				
Yes	0 (0.0)	2 (10.0)	2 (6.5)	
No	11 (100.0)	18 (90.0)	29 (93.5)	$\P$ 0.409
Presence of TDS (n,%)				
Yes	0 (0.0)	6 (30.0)	6 (19.4)	
No	11 (100.0)	14 (70.0)	25 (80.6)	$\dagger$ 0.043*

AFP: Alpha-fetoprotein, β -hCG: Beta human chorionic gonadotropin, LDH: Lactate dehydrogenase, TDS: Testicular dysgenesis syndrome

$\dagger$ Independent sample t-test, $\S$ Mann-Whitney U test, $\dagger$ Chi-square test, $\P$ Fisher's Exact test, * $p<0.05$ (There is a significant difference between the groups.)

in the malignant group, these differences were not statistically significant. Impairment rate of semen parameters ($p=0.043$) and presence of TDS ($p=0.043$) were significantly higher in patients with TGCT (Table 2).

Due to the low number of patients in both groups, ROC analysis could not be performed to determine the predictive values for hemogram parameters. Instead, median values were used as predictive values. According to our analysis, we determined the predictive values as 0.27 for MLR, 2.12 for NLR and 124.04 for PLO.

In univariate analysis, MLR, NLR, PLO, semen parameter disorders and presence of TDS were found as independent predictive factors in predicting benign-malignant differentiation in testicular masses with size ≤ 2 cm. In multivariate analysis, we observed that PLR and MLR were more significant (Table 3).

Discussion

It is known that hypogonadism develop in 10-20% of patients after radical orchiectomy. For this reason, partial orchiectomy is a treatment strategy that has been tried to be popularized in order to protect fertility, reduce the need for lifelong androgen supplementation and psychosexual problems that may occur, especially in young patients without children (8). It was stated that sufficient Leydig cell reserves could be maintained to ensure testosterone production with partial orchiectomy (8). However, the main drawback in this practice is insufficient or incomplete resection of the tumor due to microinvasions that may be overlooked. In addition, the high rate of detection of intratubular germ cell neoplasia (ITGCN), a precancerous lesion that accompanies tumors in the peripheral testicular parenchyma, also limits the applicability of partial orchiectomy in every case (11). However, there are also studies advocating the application of this method in well-selected cases (3,8). Bojanic et al. detected local recurrence in one (11.1%) patient who underwent partial orchiectomy in median 45-month follow-up of 9 patients (12). Xiao et al. (8) reported that in the median 78-month follow-up, oncological results were similar in patients who underwent radical orchiectomy and those who underwent partial orchiectomy, but

fertility rates were better maintained in the follow-up in the patients who underwent partial orchiectomy.

The main problem with small testicular masses is the application of radical orchiectomy because those with benign pathology cannot be distinguished in preoperative examination. In recent years, clinical diagnostic accuracy of testicular tumors has greatly increased thanks to advances in diagnostic imaging techniques such as USG and MRI, in addition to serum tumor markers (5). However, due to its low incidence, there are still no predictive models with high predictive value in making the benign-malignant tumor distinction. Preoperative biopsy is not recommended because there may be tumor seeding.

The most important stage in partial orchiectomy applied to small testicular masses is intraoperative frozen examination following inguinal exploration. Intraoperative histopathological diagnosis can be made in this way. In various publications, the sensitivity of frozen examination to detect benign tumors was stated as 81-90% and specificity as 99-100%; sensitivity to detect malignant tumors was found as 93-100%, specificity as 98-100%, positive predictive value as 94.2%, negative predictive value as 92.6% (3,13,14). However, in some tumors with very small size (<8 mm), it may be difficult to obtain enough tissue samples for frozen examination. In addition, it is not easy to distinguish benign and malignant tumors in some pathologies such as Sertoli cell tumor, Leydig cell tumor, epidermoid cyst, Brenner tumor, testicular tubular adenomas (6). For this reason, one of the accepted approaches is to perform radical orchiectomy in patients who have malignancy as a result of frozen examination (7).

Song et al. (11) detected benign tumors in 24% of 325 patients who underwent radical orchiectomy with suspicion of TGCT. They showed that the increase in tumor size increased the risk of malignancy (for a 1 cm increase in tumor size, $HR=1.284$, $p=0.036$). However, since the mean tumor diameter was 4.9 ± 0.2 (min=0.5 - max=230 cm) in the patients included in that study, it was not a study evaluating the benign-malignant separation in small testicular masses. Examining publications in the literature, Shilo et al. (15) reported that 38.5% of tumors smaller than

Table 3. Factors predicting malignancy in small testicular masses

	Univariate model				Multivariate model			
	OR	95% CI		p	OR	95% CI		p
		Lower	Upper			Lower	Upper	
MLR>0.27	6.222	1.212	31.937	0.028*	14.118	1.239	160.936	0.033*
NLR>2.12	8.357	1.400	49.883	0.020 *				
PLO>124.04	23.333	2.417	225.223	0.006*	23.333	2.417	225.223	0.006*
Semen parameter disorder	1.929	0.317	11.739	0.025*				
Presence of testicular dysgenesis syndrome	3.333	0.337	32.959	0.033*				

MLR: Monocyte/lymphocyte ratio, NLR: Neutrophil/lymphocyte ratio, PLO: Platelet/lymphocyte ratio

* $p<0.05$ shows a statistically significant difference, OR: Odds ratio, CI: Confidence interval

Logistic regression analysis

18.5 mm in size and 2% of tumors of larger size were benign. In other 60-77% of tumors smaller than 20 mm were benign, while this rate rised to 80% in masses less than 5 mm (3,16). On the other hand, the incidence of benign pathology in paediatric patients has been reported to increase up to 74%, and testicular protective surgical approach is more on the agenda, especially in the puberty and postpubertal age groups (4). We found that 35.4% of 31 patients with testicular mass size ≤ 2 cm received a benign diagnosis.

Song et al. reported that the increase in β -hCG values, regardless of tumor size, was a strong determinant in predicting malignant testicular masses (HR=10.550, $p<0.001$) and that AFP was not effective in making this distinction ($p>0.05$) (11). They showed that the AFP level was normal in patients with seminoma and that seminoma was detected in 44.5% of cases. We found no significant difference between benign and malignant groups in terms of all three tumor markers in a more specific subgroup with tumor size ≤ 2 cm. This finding suggests that the use of tumor markers in terms of predicting malignancy may not be useful, especially in preoperative clinical evaluation of small testicular masses.

The most commonly used method in clinical evaluation today is the combination of scrotal gray scale USG and colored doppler USG. Evaluation of tumor diameter, parenchyma echogenity and testicular blood flow may be decisive in the differential diagnosis of malignancy (17,18). In this low-cost, easily accessible, non-invasive method, increased blood flow (HR=3.320, $p<0.001$) and decreased parenchyma echogenity (HR=3.191, $p=0.001$) were reported to be decisive for malignant masses (11). Although the sensitivity of colored doppler USG is high in small testicular masses, its specificity is very low, which may lead to the accidental evaluation of benign masses as malignant (7). In suspected cases where USG is insufficient, MRI and contrast-enhanced ultrasound may be the guide with high accuracy rates for determining tumoral blood flow, with the advantage of evaluating soft tissues. However, these methods are not easy to reach everywhere (19). Ates et al. (7) detected TGCT in 6.7% of 15 testicular masses <25 mm in size. They performed partial orchiectomy, because they excluded suspicion of malignancy by preoperative clinical evaluation. This suggests that more reliable parameters are needed in clinical evaluation. In our study, although scrotal USG, doppler USG and scrotal MRI were performed due to suspected malignancy in ≤ 2 cm sized masses, radical orchiectomy was performed because the possibility of malignancy could not be ruled out. In 11 (35.4%) of 31 patients, the histopathological diagnosis was benign and perhaps unnecessary organ loss was experienced in these patients. This leads us to the search for better diagnostic parameters.

In recent years, several studies have been reported evaluating the relationship between inflammatory markers, hemogram parameters, and oncological outcomes in patients with genitourinary cancer. In TGCT, the effects of NLR and platelet levels on disease prognosis, metastasis development, and disease-specific survival have been studied in some studies (20-22). Platelets have been shown in various animal experiments to affect

the immune system by secreting various bioactive molecules and cytokines, contributing to tumor proliferation and metastasis development (23,24). We, on the other hand, evaluated the reliability of various non-invasive hemogram parameters in making benign-malignant separation in ≤ 2 cm sized testicular masses, unlike those reported in the literature. According to our findings, the predictive values were 0.27 for MLR, 2.12 for NLR and 124.04 for PLO. We predict that the masses with values higher than those predictive values are more likely to be malignant. We were unable to show that MPV and RDW values were significant in predicting the presence of malignancy.

Embryonal hormonal disorders associated with androgens are thought to lead to abnormal differentiation in primordial germ cells and gonocytes (25). Based on this hypothesis, disorders in androgen production and receptor expression and exposure to anti-androgenic or estrogenic effects have been shown to negatively affect genitourinary system development in animal experiments (26,27). Impairment in testicular differentiation and development provides the basis for irreversible genital malformations (such as hypospadias and undescended testicles), impaired spermatogenesis, and development of TGCT (28). All of these abnormalities called TDS include the components of undescended testis, hypospadias, decreased spermatogenesis, atrophic testis and TGCT components. It is stated that testicular dysgenesis may occur in the presence of at least two of these pathologies (10). Since it is known that the undescended testis and decreased spermatogenesis, two of these components, are also predisposing factors in the development of TGCT; patients with TDS with these components are more likely to be accompanied by TGCT. In our study, only the decreased spermatogenesis rate, which was one of TDS-forming components, was significantly higher in the malignant group, while the incidence of TDS was higher in the malignant group. Decreased spermatogenesis and the presence of TDS were also determined as independent predictive factors for malignancy in univariate analysis. Our findings coincided with publications reporting that testicular neoplasia was more common in patients with impaired spermatogenesis and that male infertility might be a biomarker for testicular malignancies (9,28).

Of patients undergoing radical orchiectomy, 80-90% have simultaneous ITGCN in adjacent testicular tissue (29). This suggests that ITGCN would be more likely to be present in the peripheral testicular parenchyma next to the excised tumor during partial orchiectomy. For this reason, taking biopsy from peripheral parenchyma and even from contralateral testis during partial orchiectomy is recommended and 20 Gy adjuvant RT is recommended in patients with ITGCN (5). In thirteen (65%) of the 20 patients with TGCT included in our study, ITGCN was detected, while in four (30.8%) of these thirteen patients the presence of TDS was observed. ITGCN was observed in four (66.7%) of six patients with TDS. This finding showed us that if partial orchiectomy was planned, it would be necessary to obtain a biopsy from the peripheral testicular parenchyma as well as a frozen tissue examination from the tumor base and to ensure the presence of ITGCN; if there was a presence of TDS in

the patient's anamnesis during preoperative evaluation, ITGCN detection rate might be higher.

Testicular microlithiasis is a rare condition detected by chance in the scrotal USG. It is often asymptomatic and seen at a rate of 2.4-5.6%. The incidence rate in men with scrotal symptoms is 0.6-9.0% (28). The incidence rate may be up to 18.1% in the presence of accompanying pathologies such as undescended testicles, atrophic testicles, or infertility, while the rate is 6-46% in the presence of accompanying TGCT (30). Although the presence of testicular microlithiasis alone does not carry a risk for malignancy, there is an increased risk for development of TGCT in the presence of an accompanying history of TGCT, undescended testis, testicular atrophy and infertility. This risky group requires close monitoring (30). In our study, we observed testicular microlithiasis in 9.7% of 31 patients in total, consistent with the literature. The incidence rate did not differ significantly between benign (9.1%) and malignant (10%) cases.

Study Limitations

The retrospective design of our study, the inability to perform randomization, the limited statistical analysis due to the low number of patients, short follow-up durations and the fact that the follow-up results belonging to one center are the main limiting factors.

Conclusion

Although benign pathology is high in small (≤ 2 cm), unilateral testicular masses with normal levels of tumor markers and contralateral intact testis, the suggestion of testicular protective approach is still not accepted. However, in cases where preoperative imaging methods cannot clearly rule out the suspicion of malignancy, we think that increased PLR and MLR levels may be more reliable, as well as increased NLR level, semen parameter disorders and the presence of TDS may have high accuracy to predict malignancy. Therefore, using these parameters, we argue that partial orchiectomy, which is a fertility and organ sparing approach, may be recommended in cases with high probability of benign tumor. However, we believe that our findings should be supported by other prospective, randomized, controlled, multicenter studies with larger number of patients and longer follow-up durations.

Ethics

Ethics Committee Approval: All the procedures in our study were carried out in accordance with the principles of the Helsinki Declaration and this study was not approved by the Ethics Committee due to its retrospective design.

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: İ.S., H.B., Design: İ.S., H.B., Data Collection or Processing: İ.S., H.B., Analysis or Interpretation: İ.S., H.B., Literature Search: İ.S., H.B., Writing: İ.S., H.B.

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The Results of Arteriovenous Graft Placement in Hemodialysis Patients: Single Center Experience

Hemodiyaliz Hastalarında Arteriyovenöz Greft Uygulama Sonuçları: Tek Merkez Deneyimi

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ABSTRACT

Objective: Arteriovenous grafts (AVG) are the options of vascular access to be used in hemodialysis patients who do not have an arteriovenous fistula option in the upper extremity. In this study, we evaluated the graft survival and complication results of 39 patients who underwent AVG in our center.

Methods: Between 2010 and 2013, a total of 55 patients underwent AVG. As the records of 16 patients could not be reached, 39 patients were included in the study. The cases were retrospectively evaluated in terms of demographic data, AVG sites, survival with or without revision, factors affecting graft survival, and reasons for graft termination.

Results: The mean duration of graft use without revision was 9.9±8.5 months and the mean total graft use was 13.6±11.6 months. The total graft survival rates were 82.1%, 74.1%, and 35.3% at the end of the 2nd, 12th, and 24th months, respectively. The demographic data of the patients and the use of catheter or vascular access in the same side of the graft did not have a significant effect on graft survival or early complications. There was no significant difference in terms of survival time between the graft locations. The most common cause of AVG termination was thrombosis (43.6%).

Conclusion: Although the rate of AVG which developed early functional loss was high in our study, first and second year survival rates in working grafts were similar with the literature. In conclusion, AVG is one of the important vascular access options with similar survival results with fistula in hemodialysis patients. Early graft loss can be reduced with preoperative venography.

Keywords: Arteriovenous graft, vascular access, hemodialysis

ÖZ

Amaç: Üst ekstremitede arteriyovenöz fistül seçeneği bulunmayan hemodiyaliz hasta grubunda, uygulanması gereken damar yolu seçeneği arteriyovenöz greftlerdir (AVG). Bu çalışmamızda, merkezimizde AVG uygulanmış 39 hastanın greft sağ kalım ve komplikasyon sonuçlarını değerlendirdik.

Yöntemler: 2010-2013 yılları arasında toplam 55 hastaya AVG uygulandı. On altı hastanın kayıtlarına ulaşamadığı için 39 hasta çalışmaya alındı. Olgular; demografik veriler, AVG uygulanma bölgeleri, revizyonlu ve revizyonsuz sağ kalım süreleri, greft sağ kalımına etki eden faktörler ve greft sonlanma nedenleri açısından geriye dönük olarak değerlendirildi.

Bulgular: Revizyonsuz greft kullanım süresi ortalama 9,9±8,5 ay, toplam greft kullanım süresi ortalama 13,6±11,6 aydı. İkinci ay sonunda toplam greft sağ kalımı %82,1, 12. ayda %74,1, 24. ayda %35,3'tü. Hastalara ait demografik verilerin, greft ile aynı taraf katater ya da damar yolu ameliyatı uygulanmış olmasının greft sağkalımına veya erken dönem komplikasyon gelişmesine anlamlı etkisi yoktu. Greft uygulanma bölgelerine göre sağ kalım süreleri açısından anlamlı fark saptanmadı. En sık AVG sonlanım nedeni tromboz gelişmesiydi (%43,6).

Sonuç: Çalışmamızda erken dönemde fonksiyon kaybı gelişen AVG oranı yüksek olmasına rağmen, çalışan greftlerde birinci ve ikinci yıl sonu sağ kalım oranları literatürle benzer sonuçlara sahiptir. Sonuç olarak, AVG, fistüle yakın sağkalım sonuçlarıyla hemodiyaliz hastaları için önemli damaryolu seçeneklerinden biridir. Erken dönem greft kaybı ameliyat öncesi yapılacak olan venografi ile azaltılabilir.

Anahtar Sözcükler: Arteriyovenöz greft, damar yolu, hemodiyaliz

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Introduction

In patients undergoing hemodialysis due to end stage renal disease, priority should always be given to autogenous arteriovenous fistulas (AVF) within the vascular access options (1). For some patients, on the other hand, AVF is not the most suitable vascular access option. In particular, 30-50% of the forearm region fistulas are reported to have maturation problems that do not provide the blood flow required for hemodialysis (2,3). Arteriovenous graft (AVG) can be used in patients in whom arteriovenous fistula option is not available or who do not have superficial vein (4), who are diabetic or elder and do not have vascular access, whose vascular access is damaged due to inappropriate and who is admitted for a new vascular access lately (5). A matured AVF has higher primary and secondary survival rates compared to graft (6,7). However, low AVG survival in studies may be due to the fact that the patient group in whom AVG is placed is about 10 years older, have higher co-morbidities such as diabetes, cardiovascular disease and lupus, and has worse vascular anatomy (8). Also there are studies with large patient groups indicating that AVF and graft have equal survival outcomes (9). Therefore, the most important point to keep in mind is that in people who do not have the chance of AVF, the best option is graft, not catheter. The decision to create arteriovenous graft should be taken according to the detailed history of catheter and previous vascular access surgeries, a full physical examination and vascular mapping done by doppler ultrasound (10). Detailed vascular mapping, if possible, done by a vascular surgeon is the most important factor in finding autogenous vascular access options that have been overlooked and/or can be repaired and in reducing the number of unsuccessful surgical interventions.

Methods

Patients who underwent AVG in our clinic between January 2010 and June 2013 were retrospectively examined. Records for 16 of the total 55 patients could not be reached. Demographic data (age, gender and body mass index), area of the graft, survival times with and without revision, the patient's previous history of vascular surgery and catheter insertion from the same extremity, complications seen early after AVG administration and the reasons for the termination of the graft were recorded. The cumulative and individual effects of the the creation of graft in the forearm, upper arm or thigh on graft survival and effects of other data on graft survival were statistically analyzed. Grafts that stopped functioning in the first two months after surgery or that did not function at all were considered as primary failure.

Surgical Technique

The surgeries were performed with local anesthesia accompanied by sedation. A single dose of antibiotic prophylaxis was administered before the incision. Loop graft between brachial artery and antecubital vein in forearm (Figure 1), "C" graft between brachial artery in upper arm and basilic vein or parabrachial vein in axilla (Figure 2), and loop graft between femoral artery and femoral vein in thigh region were preferred. The grafts that were thrombosed were evaluated with imaging methods and if appropriate underwent a surgical revision. After

thrombectomy, the narrowed venous drainage end of the graft was repaired with patch angioplasty or a jump graft.

Statistical Analysis

The SPSS 15.0 for Windows package program was used for statistical analysis. Descriptive statistics were given as mean, standard deviation, minimum and maximum for numerical variables, and number and percentage for categorical variables. The comparison of the categorical variables between groups was tested by the chi-square test. The comparison of numerical variables between two independent groups was done with the Student t-test when there was normal distribution and with the Mann-Whitney U test when there was not normal distribution, and with the Kruskal-Wallis test in more than two groups. The relationship between numerical variables was examined with the Spearman correlation analysis because the conditions for parametric tests were not met. Graft survival rates were examined with the Kaplan-Meier analysis. Statistical alpha significance level was considered $p < 0.05$.

Results

Twenty of the patients were female (51.3%), the average age was 58.6 ± 11.7 years, and the average body mass index was 25.6 ± 4.3 kg/m². The demographic data of the patients, their AVG regions and their post-operative clinical results are shown in Table 1.



Figure 1. Forearm loop graft



Figure 2. Upper arm C graft

During the follow-up period, 21 patients had graft failure due to thrombosis, infection or arm edema. The two-month primary survival rate of patients with graft was 82%, one-year 55.1%, and two-year 26.4%. Estimated median graft survival time was 17 months (95% confidence interval=10.5-23.5 months) (Chart

Table 1. Demographic data, locations of AVG placement and postoperative clinical results of the patients

		n	%
Gender	Female	20	51.3
	Male	19	48.7
Age (year) Mean ± SD (Min-max)		58.6±11.7 (39-84)	
BMI (kg/m²) Mean ± SD (Min-max)		25.6±4.3 (18-33.3)	
Graft type	Upper arm	28	71.8
	Forearm	8	20.5
	Thigh	3	7.7
Revision	No	28	71.8
	Yes	11	28.2
Revision	No	33	84.6
	Yes	6	15.4
Primary survival time (month) Mean ± SD (Min-max)		9.9±8.5 (0-37)	
Secondary survival time (month) Mean ± SD (Min-max)		13.6±11.6 (0-44)	
History of catheter in the same side before graft	No	18	47.4
	Yes	20	52.6
History of surgery in the same side before graft	Fistula	31	81.6
	Graft	2	5.3
	No	5	13.2
Early complication after graft	No	26	66.7
	Yes	13	33.3
	Thrombosis	6	15.4
Reason for graft termination	Infection	5	12.8
	Ischemia	1	2.6
	Thrombosis	17	43.6
Reason for graft termination	Infection	2	5.1
	Arm edema	2	5.1
	Exitus	7	17.9
	Transfer	1	2.6
	Continue	10	25.6

SD: Standart deviation, Min: Minimum, Max: Maximum, AVG: Arteriovenous grafts

1). With the revision, secondary one-and two-year graft survival rates increased to 74.1% and 35.3%, respectively. There was no statistically significant difference between the groups when the survival rates of the AVGs were evaluated according to the areas where AVGs were placed ($p=0.848$) (Table 2, Chart 2). During the follow-up period, survival time was determined to be 9.9 ± 8.5 months when no revision was applied to AVG, and total graft survival time with revisions was 13.6 ± 11.6 months. Eleven (28.2%) of the grafts that were terminated were found eligible for revision surgery after imaging was performed. Graft survival time was significantly higher in the patient group with revision than in the patient group without revision ($p=0.001$) (Table 3).

In 33.3% of cases after the placement of AVG, complications such as thrombosis, ischemia or infection developed in the early period. However, there was no significant relationship between early complications and demographic data, catheter insertion to the same extremity, or history of previous vascular surgery (Table 4). In addition, there was no statistically significant difference in terms of AVG survival between patients with a history of catheter

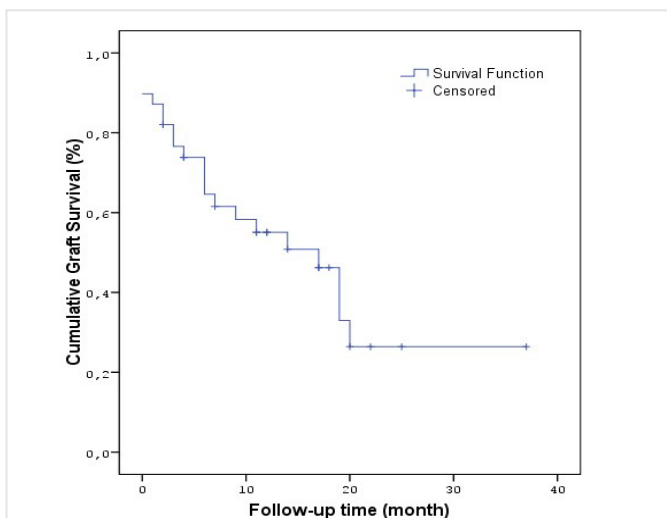


Chart 1. Assessment of cumulative AVG survival by Kaplan-Meier analysis

AVG: Arteriovenous grafts

Table 2. AVG survival results by placement locations

	Upper arm	Forearm	Thigh
Estimated median Life Span -95% CI	17 months (7.7-26.3 months)	20 months (-)	11 months (-)
Time (month)	Cumulative graft survival (%)	Cumulative graft survival (%)	Cumulative graft survival (%)
2 months	82.1%	75.0%	100%
12 months	58.0%	60.0%	0.0%
24 months	31.6%	-	-
36 months	31.6%	-	-

CI: Confidence interval, AVG: Arteriovenous grafts

insertion and patients without a history of catheter insertion ($p=0.848$) (Chart 3).

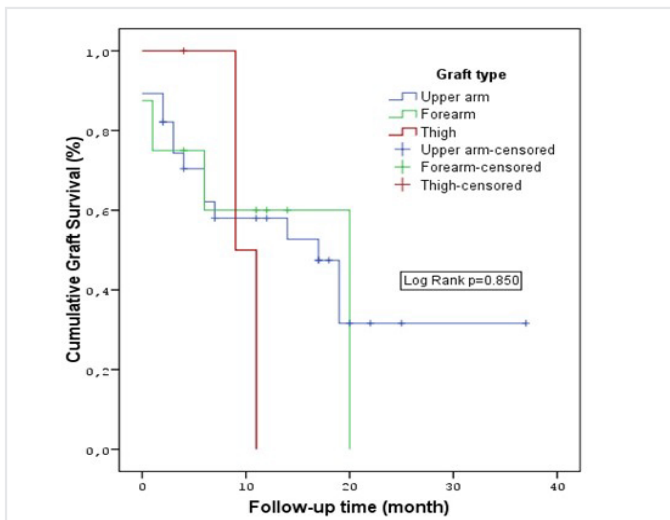


Chart 2. Evaluation of cumulative AVG survival by placement locations with Kaplan-Meier analysis

AVG: Arteriovenous grafts

Table 3. Primary and secondary cumulative AVG survival

Estimated median graft life span -95% CI 17 months (95% CI 10.5-23.5 months) 20 months (95% CI 13-27 months)

Time (month)	Cumulative primary graft survival (%)	Cumulative secondary graft survival (%)
2 months	82.1%	82.1%
12 months	55.1%	74.1%
24 months	26.4%	35.3%
36 months	26.4%	28.2%

CI: Confidence interval, AVG: Arteriovenous grafts

Discussion

Arteriovenous graft is often placed in the upper extremity and, more rarely, in the lower extremity. Although there are no differences in terms of primary and secondary patency times and complications between pre-arm and upper arm graft placement in upper extremity placements (11), it is recommended that priority be given to pre-arm graft placement in order to protect subsequent vascular access options (12). In our study, the ratio of upper arm graft placement was 71.8%. The most important reason for this high ratio was that no available deep and superficial vascular access options were detected during the evaluation with doppler ultrasonography. In the lower extremity, AVG is usually placed in the thigh area. This is an important option for patients who do not have a chance of having a vascular access in

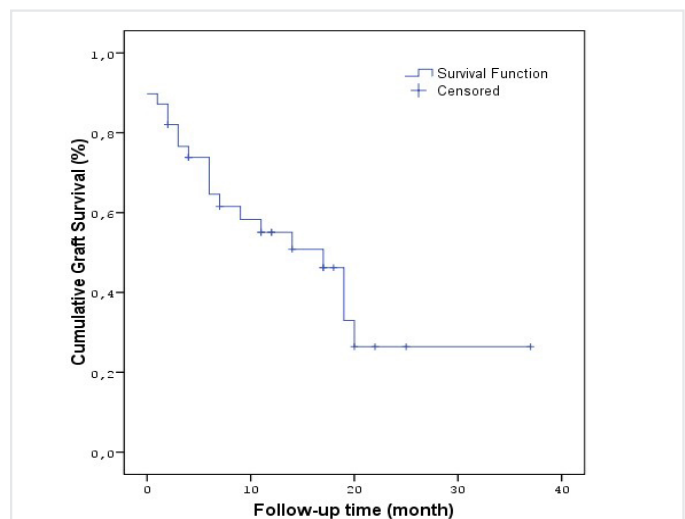


Chart 3. Evaluation of the effect of same-side extremity catheter placement on cumulative AVG survival by Kaplan-Meier analysis

AVG: Arteriovenous grafts

Table 4. Relationship between early complication and demography, catheter and previous vascular access surgery

		Early complication after graft				p
		No	%	Yes	%	
Gender	Female	15	57.7	5	38.5	0.257
	Male	11	42.3	8	61.5	
Age	59.5±12.8 (39-84/64)			57.0±9.6 (45-74)		0.488
BMI	25.6±4.6 (18-33.3/25.3)			25.4±3.7 (20.3-31/25.4)		0.887
Location of graft placement	Upper arm	17	65.4	11	84.6	0.551
	Forearm	6	23.1	2	15.4	
	Thigh	3	11.5	0	0.0	
History of catheter in the same side before graft	No	12	46.2	6	50.0	0.825
	Yes	14	53.8	6	50.0	
History of vascular access surgery in the same side before graft	Fistula	21	80.8	10	83.3	1.000
	Graft	1	3.8	1	8.3	
	No	4	15.4	1	8.3	

BMI: Body mass index

the upper extremity, even though it is not preferred due to the risk of infection. In our study, only 3 (7.7%) patients had AVG placed in the thigh area. Studies have shown shorter primary and secondary patency times in AVGs placed in the thigh region (13,14). Thigh grafts had shorter survival times in our study, although there was not a statistically significant difference in terms of graft survival times between placement areas of grafts.

The Kidney Disease Outcome Quality Initiative recommends that the rate of grafts that stop working within the first 30 days or the rate of grafts that never work should be less than 5% in the upper arm and 10% in the forearm (15). In two separate studies involving 289 and 128 patients with AVG, this ratio was given as 15% and 19%, respectively (16,17). This rate was 17.9% and 25% for the first two months in our study, respectively. This rate can often be associated with surgery-related technical problems, early cannulation-related hematoma or patient-related problems. In addition, we believe that one of the important factors to explain this high ratio is graft placement without imaging in order to prevent catheter use in patients who cannot undergo hemodialysis due to vascular access thrombosis. Akoh (10) showed in their systematic review that one-year and two-year cumulative AVG survival rates were 59-90% and 47-85%, respectively. In a different study, one-and two-year primary survival rates were reported as 74% and 50%, and secondary survival rates were reported as 82% and 66% in patients who underwent AVG with systematic follow-up program (18). In our study, these rates were 55.1% and 26.4% for one-year primary and secondary survival, and 74.1% and 35.3% for two-year primary and secondary survival, respectively. We believe that the most important reason why our graft survival results were low was that the primary failure rate seen in the first two months was high.

Complications such as bleeding, thrombosis, and distal limb ischemia developed in one third of the cases in the early period after AVG placement. Shingarev et al. (19) examined the results of AVF and graft in patients having catheter placed in the same extremity in their study. They stated that catheter did not have an effect on primary failure in the early period, but that catheter might have a negative effect on long-term vascular access survival. Similarly, when the causes of these early complications were examined in our series, neither demographic data nor history of having catheter or AVF placed in the same extremity were found related with complications. However, in our study, when we evaluated the patients with and without catheter placed in the same extremity, no adverse effects of catheter were observed on long-term graft survival. At the end of the follow-up period, in 21 cases (53.8%), AVG was terminated due to complications.

Conclusion

Arteriovenous graft placement is an important option that does not have maturation period, can easily be cannulated, has similar secondary survival time with AVF and allows long-term hemodialysis for patients with end-stage renal disease and it should be preferred before catheter. We believe that imaging of

the central venous system before placement will reduce primary failure rates, but the results need to be supported by prospective studies with larger patient populations.

Ethics

Ethics Committee Approval: The article has an ethical committee.

Informed Consent: Most of the patients in the group were not alive due to their disease when the article was written. Therefore, it is not possible to receive informed consent from those patient later.

Peer-review: Internally peer-reviewed.

Financial Disclosure: The authors declared that this study received no financial support.

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Relationship Between the Level of Pain and Quality of Sleep in Women After a Cesarean-section

Sezaryen Sonrası Kadınlarda Ağrı Düzeyi ile Uyku Kalitesi Arasındaki İlişki

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ABSTRACT

Objective: The aim of this study was to examine the effect of the level of pain on quality of sleep in women after a cesarean section. This study was designed as a cross-sectional study.

Methods: The study was conducted in the obstetrics clinic of a university hospital in Ankara between May-July 2018. No sample selection was done, and the women who had underwent a cesarean section in the six-month period were included in the study. The study was conducted with 320 women. Visual Analogue scale was used to determine the level of pain and sufficiency level of sleep in the women. The Form of Factors that Affect Sleep Pattern (FFASP) was used for the purpose of determining early-stage sleep problems in the women.

Results: It was found in the our study that age, work status, and the type of the room (staying alone or with two or more patients) affected the severity of pain and sleep quality in women after a cesarean section. As the severity of pain in women who underwent a cesarean section increased, it was found that the FFASP scores increased and sleep quality decreased.

Conclusion: There is a relationship between the severity of pain in women after a cesarean section and the level of sleep sufficiency and quality.

Keywords: Cesarean section, level of pain, quality of sleep, women

ÖZ

Amaç: Bu çalışma, sezaryen sonrası hastanede yatan kadınların ağrı düzeyinin uyku kalitesine etkisini incelemek amacıyla kesitsel tipte dizayn edilmiştir.

Yöntemler: Çalışma Mayıs-Temmuz 2018 tarihleri arasında Ankara ilinde bulunan bir üniversite hastanesinin kadın hastalıkları ve doğum sonu servisinde yapılmıştır. Çalışmada, örneklem seçimine gidilmemiştir ve altı aylık sürede sezaryen operasyonu uygulanan kadınlar çalışmaya dahil edilmiştir. Araştırma, 320 kadın ile yürütülmüştür. Kadınların ağrı düzeylerini ve uyku yeterlilik düzeylerini belirlemek için görsel analog skala kullanılmıştır. Kadınların erken dönemde uyku sorununu belirlemek amacıyla Uyku Düzenini Etkileyen Etmenler Formu (UDEEF) kullanılmıştır.

Bulgular: Çalışmada sezaryen sonrası kadınların ağrı şiddeti ve uyku kalitesini yaş, çalışma durumu ve oda şeklinin etkilediği belirlenmiştir. Sezaryen uygulanan kadınların ağrı şiddeti arttıkça UDEEF puan ortalamalarının arttığı, uyku düzen ve kalitelerinin azaldığı belirlenmiştir.

Sonuç: Sezaryen sonrası kadınların ağrı şiddeti ile uyku yeterliliği ve kalitesi arasında ilişki vardır.

Anahtar Sözcükler: Sezaryen, ağrı düzeyi, uyku kalitesi, kadınlar

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Introduction

Pain control after a cesarean section carries a distinct importance in terms of the quality of patient care (1). The pain that develops after a cesarean section can prevent the mother from engaging with her baby under optimal conditions by negatively affecting the early-stage communication (breastfeeding, baby care etc.) (1,2). However, the post-cesarean-section pain can lead to the development of problems in women such as irregular sleep pattern, constraint in physical activities (movement, etc.), increase in sensitivity to sounds and noises and inability to rest sufficiently due to anxiety and tiredness (1,3). For this reason, effective control of pain in the period after a cesarean section carries great importance in terms of preventing problems that may develop, primarily in sleep patterns and the quality of sleep. Sleep is among the most fundamental daily activities of life and is necessary for an individual to meet physical, psychological, sociocultural, and intellectual needs. Sleep encompasses one-third of the lives of humans (4,5). Accordingly, women meeting their needs for sleep in a balanced and adequate manner are able to maintain current level of health (6,7). However, pain that develops after surgical operations such as birth by cesarean section can lead to unfavorable outcomes in the pattern and quality of sleep due to care-treatment procedures, being in a foreign environment, inability to rest because of breastfeeding in 2-3 hour intervals, and inability to maintain daily routines (4). A previously conducted study determined that 45.5% of patients admitted to the hospital experienced a change in their patterns of sleep (4-8). Other studies reported that the total duration of sleep decreased by 80% in patients in the first night after surgical operations, that patients experienced sleep-related problems, and that the most important factor that caused sleep problems was pain (8,9). The literature also reports that the deterioration in sleep patterns in patients triggers a decrease in pain tolerance and an increase in the severity of pain (10). For this reason, the effective evaluation of the pain scores of women after a cesarean, optimal and effective management of pain and impaired sleep patterns, the formation of the conditions necessary for adequate rest, and the maintenance of sleep quality should be among the nursing activities that must be handled with care. In the stage of creating a qualified nursing care plan for women after a cesarean section; the patient's expectations, perception of care, capacity to assess care, and satisfaction with the care should be considered (8,10). Care and treatment beginning from the first day after a cesarean section should be adjusted based on the levels of pain and cycles of sleep/wakefulness. Pain should be taken under control, and foreign surroundings, voices, lights, and noises should be reduced. Infant care can interrupt the sleep of women and inhibit their sleeping while they are breastfeeding. In this stage, women should be supported in caring for infants while they are sleeping.

Methods

Purpose and Type

This study was designed as a cross-sectional study for the purpose of examining the effect of the level of pain on quality of sleep

in women giving birth in the hospital after a cesarean section. The study was conducted in the obstetrician and maternity ward of the hospital of a university in Ankara between May and July 2018.

Samples and Participants

No sample selection was done, and women who had underwent a cesarean section in the six-month period were included in the study. The study was conducted with 320 women. The criteria for women to be included in the study were being above the age of 18, agreeing to participate in the study and having no verbal communication problem.

Data Collection Tools

A 12-question data collection form containing some descriptive characteristics for women who underwent a cesarean section (age etc.) was used for the purpose of gathering data in the study. The researchers developed the data collection form after reviewing the literature, considering expert views (4,6,10). The 10 centimeter (cm) horizontal visual analogue scale (VAS) in pain was used for the purpose of determining the level of pain and sleep sufficiency in the first and second day after the cesarean section in the women. The Form of Factors that Affect Sleep Pattern (FFASP) that aimed to evaluate the quantitative and qualitative quality of sleep in the mornings of the first and second days after the cesarean section was used for the purpose of determining early-stage sleep problems in the women (11). The highest score that can be received from the score is 120 and the lowest is 24. The factors that affected the sleep of the patients such as pain, bed, light, heat, and sound, whether sufficient information was provided about the disease, and psychological factors such as level of anxiety were recorded in the FFASP. The Cronbach Alpha reliability coefficient for the FFASP was found to be 0.70.

Data Collection

Women who would undergo a cesarean section were admitted to the hospital one night before the operation. The data collection form was subsequently administered to the women. The VAS was implemented to determine the hourly level of pain after the patient was readmitted to service following the cesarean section procedure on the day that the cesarean section operation was performed, and the average VAS score at the end of the day was recorded. The VAS was implemented for the evaluation of the sleep sufficiency at the earliest opportunity in the second morning after the cesarean section procedure and the FFASP was implemented to determine the pattern and quality of sleep. The VAS was implemented to determine again the level of pain and sleep sufficiency on the second day after the cesarean section. Also, all women after giving birth received postnatal care from the routine obstetricians and nurses. Postnatal care consisted of checking the state of consciousness and vital signs, assessing bleeding and uterus involution, assessing the patient with extreme pain in terms of hematoma (incision line), starting breastfeeding as soon as possible and helping the mother breastfeed her baby and providing her with training on breastfeeding.

Ethical Dimension

Institutional ethics committee approved the study, and written informed consents were obtained from the patients who agreed to participate in the study.

Analysis of the Data

The Statistical Package for Social Sciences (SPSS) version 22.0 was used for the analysis of data. Frequency, t-tests, Pearson correlation and ANOVA were used for the analysis.

Results

A total of 320 women monitored in the maternity ward after a cesarean section were included in the study. The mean age of the women was 30.6 ± 5.5 years. When the descriptive characteristics of the women were examined, it was determined that 62.4% had an educational level of high school and above, that 73.5% expressed their income level as “moderate”, and that 62.8% were housewives. When the characteristics of the participants regarding sleep were examined, it was reported that 74.6% generally expressed their sleep patterns as “sufficient”. Of the women included in the study, 48.7% were primipara and 67.2% were staying in rooms with two or more people (Table 1). All of the women were married, and it was determined that 27.9% had previously underwent a surgical procedure (cesarean section).

In the present study, while the mean of the VAS pain score on the first day after the cesarean section was found 6.97 ± 2.4 , the mean of VAS pain score on the second day was found 4.70 ± 2.17 . While the mean of the VAS sleep sufficiency score on the first day after the cesarean section was determined to be 5.12 ± 2.68 , the mean of the VAS sleep sufficiency score on the second day was determined 5.48 ± 2.39 (Figure 1).

The mean of FFASP scores of the women was found to be 77.17 ± 16.73 . When the FFASP scale was examined, it was determined that pain, medical devices attached to the body and the noisy environment were the factors that negatively affected the sleep patterns of the women after the cesarean section (Figure 2).

According to Table 1, in the current study, it was determined that the mean of FFASP and VAS pain scores of the women in the 18-30 age group were higher compared with that of those in the 31-44 age group, and the mean of VAS sleep sufficiency scores were lower ($p < 0.05$). In our study that it was found the mean FFASP, VAS pain, and VAS sleep sufficiency scores of the women who worked were higher than those of the housewives

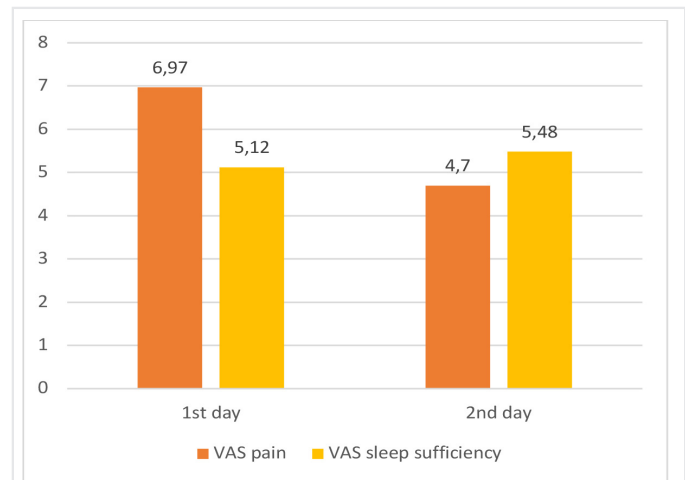


Figure 1. Relationship between VAS pain and VAS sleep sufficiency measurements

VAS: Visual analogue scale

Table 1. Distribution of form of factors that affect sleep pattern, visual analogue scale pain and visual analogue scale sleep sufficiency scores according to some descriptive features of women who had underwent a cesarean section (n=320)

Some Characteristics	n (%)	FFASP Mean ± SD	p	VAS pain 1 st day Mean ± SD	p	VAS pain 2 nd day Mean ± SD	p	VAS sleep sufficiency 1 st day Mean ± SD	p	VAS sleep sufficiency 2 nd day Mean ± SD	p
Age (year)											
18-30	160 (50.0)	85.35±16.94	0.042	7.01±2.42	0.001	4.98±2.19	0.005	4.77±2.47	0.021	5.34±2.46	0.003
31-44	160 (50.0)	78.98±16.97		6.93±2.38		4.51±2.14		5.46±2.84		5.99±2.78	
Working status											
Laboring	119 (37.2)	81.91±14.83	0.001	7.20±2.32	0.043	4.99±2.20	0.025	5.30±2.70	0.002	5.80±2.41	0.001
Housewives	201 (62.8)	74.36±17.19		6.84±2.44		4.53±2.13		4.81±2.62		4.96±2.78	
Effect of pain on sleep quality within the last 24 hours											
Yes	171 (53.4)	79.01±15.50	0.014	7.78±2.19	0.019	5.26±1.99	0.049	5.08±2.70	0.001	5.37±2.31	0.037
No	149 (46.6)	75.05±17.87		6.13±2.37		4.05±2.18		5.95±2.70		5.62±2.40	
Type of room											
Single	121 (37.8)	72.10±16.09	0.001	6.73±2.56	0.001	4.29±2.25	0.004	5.33±2.68	0.002	5.70±2.28	0.016
Room where two or more people staying	199 (62.2)	84.17±16.44		7.36±2.06		4.93±2.02		4.73±2.63		5.13±2.53	

VAS: Visual Analogue scale, FFASP: Form of Factors that Affect Sleep Pattern, SD: Statistical deviation, p: Statistical analysis

($p<0.05$). In the present study, it was determined that the mean FFASP and VAS pain scores of women who stated that the status of pain in the previous 24 hours affected their sleep patterns were higher compared with those of the women who stated that it did not and the mean VAS sleep sufficiency score was lower ($p<0.05$). It was found in our study that the mean FFASP and VAS pain scores of women staying in single-person private rooms were lower compared with women staying in rooms with two or more people and that the average VAS sleep sufficiency score was higher ($p<0.05$).

In our study, a highly negative correlation was found between the the mean of VAS pain and the mean of VAS sleep sufficiency scores on the first day following the cesarean section ($r=-0.730$; $p=0.001$) and a highly positive correlation was found between the mean of VAS pain scores and the mean of FFASP scores on the first day following the cesarean section ($r=-0.872$; $p=0.001$), and these correlations were statistically significant. A moderately negative correlation was found between the the mean of VAS pain and the mean of VAS sleep sufficiency on the second day

following the cesarean section ($r=-0.440$; $p=0.001$), and a highly positive correlation was found between the the mean of VAS pain and the mean of FFASP on the second day following the cesarean section ($r=0.682$; $p=0.001$), and these correlations were statistically significant. Based on our data, as the levels of pain of the women who underwent a cesarean section increased, the mean of FFASP scores increased, and sleep sufficiency decreased (Table 2, Figure 1).

Discussion

Many women (50-70%) experience severe or moderate pain after a cesarean section (9,12-14). Of women, 40% report that they experience standard pain after a cesarean section at moderate or severe levels while resting despite treatment (15-18). We found that women experienced severe pain on the first day after the cesarean section, and it was observed that the pain gradually subsided. We found that the sleep insufficiency of women on the first day after the cesarean section decreased considerably and, although not much, sleep sufficiency partially increased on the second day. The mean FFASP scores of women in our study were

Table 2. The correlation between the mean scores of visual analogue scale pain, visual analogue scale sleep sufficiency and form of factors that affect sleep pattern of women (n=320)

Scale	VAS sleep sufficiency 1 st day	VAS sleep sufficiency 2 nd day	Total FFASP
VAS pain 1 st day	-	-	-
r	-0.730	*	0.872
p	0.001	*	0.001
VAS pain 2 nd day	-	-	-
r	*	-0.440	0.682
p	*	0.001	0.003

VAS: Visual analogue scale, FFASP: Form of factors that affect sleep pattern

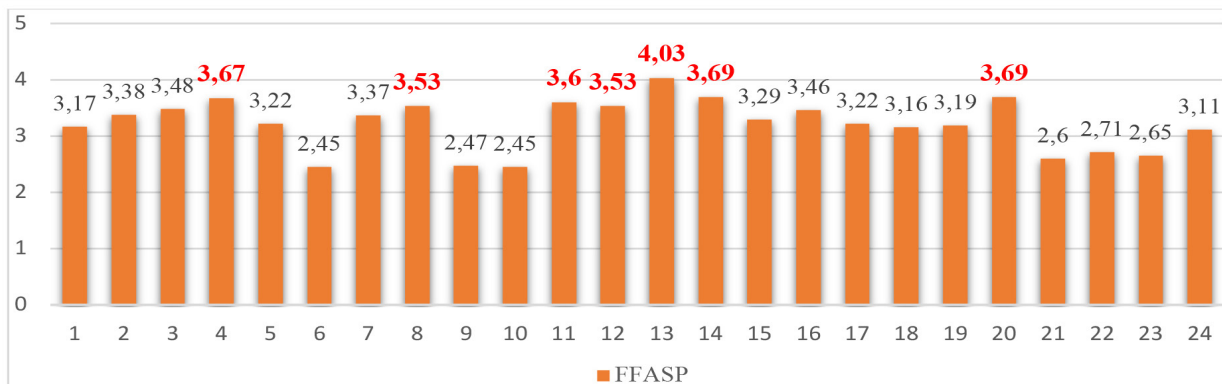


Figure 2. Distribution of factors affecting sleep patterns of women

1. The bed is uncomfortable, 2. The pillow is uncomfortable, 3. Bedding is dirty and uneven, 4. The room is airless, 5. There is much light in the room, 6. The room is dark, 7. The temperature of the room is inappropriate, 8. The room is crowded, 9. Being alone in the room, 10. Having a companion beside her, 11. Entering and exiting the room frequently, 12. Interventions made during sleep time, 13. Having pain, 14. Medical devices fitted to the body, 15. Being hungry or satiated, 16. Having concerns about the disease, 17. Not having enough information about the disease, 18. Thinking of home or work, 19. Not feeling safe, 20. Noise in the surrounding area, 21. Inability to exercise and sport, 22. No activity to do during the day, 23. Inability to apply pre-sleep habits, 24. Hours of sleeping and waking up in the hospital.

FFASP: Form of factors that affect sleep pattern

also found to be high. In the study that Yılmaz et al. (2008) conducted, the mean FFASP scores of the women was found to be high (17). Our study found that the sleep insufficiency based on severe pain of women on the first day after the cesarean section decreased and, together with the decrease of pain, sleep sufficiency partially increased on the second day. We found that the presence of medical devices attached to the body affected the quality of sleep apart from pain. Previously conducted studies reported that medical devices attached to the body led to pain and position constraint in patients and that these problems led to difficulty in sleeping and deterioration of sleep quality in 16.8% of patients (2,13,14). It was reported that age possessed a strong influence in the threshold of pain perception (19). We found that the pain levels on the first and second days following the cesarean section of women in the 18-30 age group were quite a bit higher than those of women in the 31-44 age group, that women did not get enough sleep, and that their sleep patterns deteriorated ($p<0.005$). Beebe and Lee (15) reported in their study that the birth rate by cesarean section in young women who experienced sleep problems was higher, that the pain they experienced after the cesarean section was higher, and that their quality of sleep decreased as the severity of pain increased. Our study determined that the severity of the pain in working women compared with housewives was higher on first and second days after the cesarean section and that their sleep sufficiency and sleep patterns deteriorated in relation to this ($p<0.05$). It was reported in the literature that the expectations regarding pain, experiences, perceptions of pain, and capacities to assess the effectiveness of the performed procedure of women who worked and who had high levels of education were influential in expressing their problems (13,20,21). In the present study we found the mean score of pain severity to be higher and sleep sufficiency to be lower in women who stated that their pain problems in the past 24 hours affected their sleep pattern on first and second days after the cesarean section than in the women who stated that it did not ($p<0.05$). Özkaya et al. (22) (2013) determined in their study that the pain affected the sleep patterns of the patients mostly on the first day after the surgery. Our study detected that the severity of pain in the women staying in rooms with two or more people increased, that the sleep sufficiency based on the pain decreased, and that their sleep patterns significantly deteriorated. The excessive number of patients in the room leads to triggering of the pain and the patients are unable to sleep comfortably at night (5,7,12,19). According to the results of the analysis for the correlation between the VAS pain, VAS sleep insufficiency and FFASP scale in our study, it determined that as the severity of pain after a cesarean section increased, sleep sufficiency and sleep quality decreased. A highly negative relationship was found between the severity of pain and the sleep sufficiency and sleep quality of women after a cesarean section.

Study Limitations

This study was conducted in a small group of women in one hospital. The results were interpreted according to the patients' self-reports. Therefore, the results of this study cannot be generalized.

Conclusion

It was found in our study that age, work status, status of pain in the previous 24 hours affecting sleep, and the type of the room (staying alone or with two or more patients) affected the severity of pain, sleep insufficiency, and sleep pattern and quality in women after a cesarean section. As the severity of pain in women who underwent a cesarean section increased, it was found that the mean of FFASP scores increased and sleep quality decreased. There was a relationship between the severity of pain in women after a cesarean section and the level of sleep sufficiency and sleep pattern and quality. Based on this data, the effective control of pain after a cesarean section carries great importance in terms of better quality of sleep for the patient.

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Ethics

Ethics Committee Approval: The necessary permissions were obtained from the hospital where the research and from the Ufuk University Social and Humanities Scientific Research and Publication Ethics Committee (protocol number: 2017/35).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: D.A., Ö.İ., M.G.T., Design: D.A., Ö.İ., M.G.T., Data Collection or Processing: D.A., Ö.İ., M.G.T., Analysis or Interpretation: D.A., Ö.İ., M.G.T., Literature Search: D.A., Ö.İ., M.G.T., Writing: D.A., Ö.İ., M.G.T.

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Results of the Local Steroid Injections in the Simple Bone Cyst

Basit Kemik Kistinde Lokal Steroid Enjeksiyonlarının Sonuçları

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ABSTRACT

Objective: Steroid injections represent one of the simple treatment alternatives for simple bone cysts (SBC). The aim of this study was to evaluate the results of local steroid injections in the treatment of SBC.

Methods: Seventeen patients (11 males, 6 females; mean age 12.4 years; range=2 to 39 years) with SBC were treated with injection of methylprednisolone acetate (MPA) with the use of the two-needle technique. The cysts were localized in the proximal humerus (n=6), the calcaneus (one patient had bilateral lesions) (n=2), proximal femur (n=7) and the tibia (n=2). Pathological fractures occurred in three patients before steroid injection. These three patients with pathological fractures were treated with injection of MPA after fractures healed. Each patient received a maximum of four injections at eight week intervals, each consisting of 40-160 mg of MPA. The patients were followed up with plain radiographs obtained in the first month, third month, sixth month, and at the end of a year. After the first year, patients were followed up with plain radiographs once a year. The mean follow-up duration was twenty two months (range=3 to 48 months). Cyst healing was assessed according to the modified Neer classification.

Results: Treatment with MPA resulted in complete recovery in ten cysts (55%) and recovery with residual lesions in three cysts (17%). Three cysts (17%) did not respond to steroid treatment and two patients (11%) developed recurrence. The results were satisfactory (72%) in patients with complete recovery and partial recovery with residual lesions, and unsatisfactory in five patients (28%). The patients with recurrence were treated with curettage

ÖZ

Amaç: Basit kemik kistin (BKK) tedavi alternatiflerinden biri olan lezyon içine steroid uygulamasının etkinliğini araştırmaktır.

Yöntemler: BKK saptanan 17 hasta (11 erkek, 6 kız ; ortalama yaş 12,4 yıl; dağılım 2-39 yıl) iki iğne tekniği kullanılarak kist içine metilprednisolon asetat (MPA) enjeksiyonuyla tedavi edildi. Kist altı olguda humerus proksimaline, iki olguda kalkaneusa (olgulardan biri bilateral), yedi olguda proksimal femura ve iki olguda da tibiaya yerleşmişti. Üç hastada steroid enjeksiyonu öncesinde patolojik kırık oluşmuştu. Patolojik kırığı olan bu üç hastaya kırıkları iyileştikten sonra MPA enjeksiyonu yapıldı. Hastalara sekiz hafta arayla, herbiri 40-160 mg MPA içeren en fazla dört enjeksiyon uygulandı. Hastalar enjeksiyon sonrasında birinci, üçüncü, altıncı aylarda ve birinci yılda çekilen direkt grafiler ile takip edildi. İlk yıldan sonra hastalar yılda bir kez düz grafilerle takibe alındı. Hastaların ortalama takip süresi 22 ay (dağılım=3-48 ay) idi. Kist iyileşmesi modifiye Neer sınıflandırmasına göre değerlendirildi.

Bulgular: MPA enjeksiyonu ile 10 kistte (%55) tamamen, üç kistte (%17) rezidüel lezyonla iyileşme sağlandı. Üç kistte (%17) steroidle hiç yanıt alınamadı, iki hastada lezyon tekrarladı (%11). Tamamen veya rezidüel lezyonla iyileşen hastalardaki sonuçlar tatminkar bulunurken (%72), beş hastada (%28) steroid tedavisi başarısız bulundu. Bu hastalar küretaj ve greftleme veya sementleme ile tedavi edildi. İşlemlerle ilgili hiçbir hastada komplikasyon görülmedi.

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and grafting or cementation. No procedure-related complications were encountered.

Conclusion: Our findings suggest that, the treatment with local steroid injection in SBC provides satisfactory results, thus this treatment with low morbidity can be applied to these patients before aggressive treatment.

Keywords: Simple bone cyst, intralesional injection, methylprednisolone, steroid

Sonuç: BKK tedavi alternatiflerinden olan intralezyonel steroid enjeksiyonu ile tatmin edici sonuçlar elde edilebilmektedir. Agresif tedaviler öncesinde düşük morbiditeli ve etkili olan bu tedavinin uygulanabileceği kanısındayız.

Anahtar Sözcükler: Basit kemik kisti, intralezyonel enjeksiyon, metilprednizolon, steroid

Introduction

Simple bone cysts (SBC) are the most common benign bone lesions in children and young people, making up 3% of all bone tumors that have been biopsied (1,2). These lesions are usually asymptomatic and their exact incidence and prevalence are unknown since they are detected incidental in radiology (3).

Patients with mechanical symptoms and the possibility of pathological fractures should be treated surgically to prevent cyst involution and catastrophic complications, although asymptomatic lesions that are detected as incidental in radiological examinations and do not carry the risk of pathological fractures may be followed up. Methylprednisolone acetate (MPA) injection for the treatment of SBC is a method used after being defined by Scaglietti in 1979. In traditional surgical treatment, grafting/cementing is applied after curettage of the lesion (4).

The aim of our study was to question the results of percutaneous drainage and MPA injection treatment in SBC and determine the effectiveness of the treatment. Our hypothesis was that MPA injection was an effective alternative treatment to be tried before open surgery having more complications in the treatment of SBC.

Methods

Prior to the study, permission was taken from the Academic Lectern Council (no: 839, date: 15.01.2019). Eighteen cysts of 17 patients were included in the study who were diagnosed as having SBC and underwent MPA injection into the cyst using two-needle technique in our hospital between January 2010 and December 2015. Their data were obtained with retrospective archival scan.

The diagnosis of SBC was based on clinical experience, the radiological typical appearance of the cyst (concentric localization on the metaphysical region of long bones (2,5), expansion in all directions, presence of a thinned cortex not penetrated into the physis), and the characteristic seroanguinous colored fluid that came through the cyst during surgery. Patients with atypical radiologic appearance and patients who underwent biopsy due atypical material that came through the cyst during surgical drainage, were not included in the study.

Lesion volume before surgery was calculated with the Fujifilm's Picture Archiving and Communication System program according to plain radiograph and CT sections. Volume was calculated with the formula $\frac{4}{3} \pi \cdot d_1/2 \cdot d_2/2 \cdot d_3/2$ (5).

The surgeries were performed under spinal, general anesthesia or a laryngeal mask, depending on the patient's condition. The procedure was performed under sterile conditions following proper surgical cleaning and age-appropriate prophylactic IV antibiotics (cephasoline 1-2 g) followed by fluoroscopy using two Jamshidi biopsy needles. After the location of the cyst was determined by fluoroscopic examination, the Jamshidi needle was carefully passed through the skin, subcutaneous tissue, muscle and periosteum and placed into the cyst (Figure 1). The presence of seroanguinous fluid that came from the cyst was considered to support the diagnosis of simple bone cyst. This seroanguinous fluid was sent for pathological examination in all patients. The inside of the cyst was washed with an average of 500 mL of saline until the flow of seroanguinous fluid through the cyst ended and the flow of clear fluid began (Figure 2). After washing, the second Jamshidi needle was withdrawn and a steroid injection of 40-160 mg was given through the other needle, enough to overflow from the cyst, according to the size of the cyst, and the procedure was terminated. The patients were discharged in the day after the surgery.

The patients were given at least one and at most four times MPA injections eight to ten weeks apart. In the follow-up after injection, not seeing trabeculation which determined bone tissue formation in the cyst on plain radiographs was considered as indication of subsequent injection. Patients were followed up with plain radiographs performed in 1st, 3rd and 6th months and in the 1st year after injection (Figure 3). While the improvement in controls was evaluated radiologically, the Neer classification developed by Capanna et al. (6) was used. Stage I and II were evaluated as successful results and Stage III and IV as unsuccessful results (Table 1).

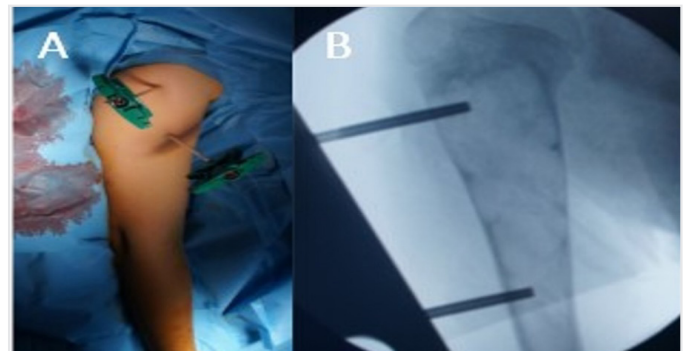


Figure 1. A) Application of two Jamshidi needles to simple bone cyst in proximal humerus and B) Fluoroscopic image

Statistical Analysis

Statistical analysis of the data was done with IBM SPSS v20 (Statistical Package for the Social Sciences, version 20.0, IBM, Armonk, NY, USA) package program. The normal distribution of the data was evaluated by the Shapiro-Wilk test. The mean $\pm$ standard was used to express continuous variables with normal distribution, median (minimum-maximum) was used to express continuous variables without normal distribution, and frequency (n) and percentage (%) were used to express categorical variables. The Mann-Whitney test was used to compare two independent groups of continuous variables with normal distribution. Relations between variables without normal distribution were examined with Spearman's Rank Correlation Coefficient.

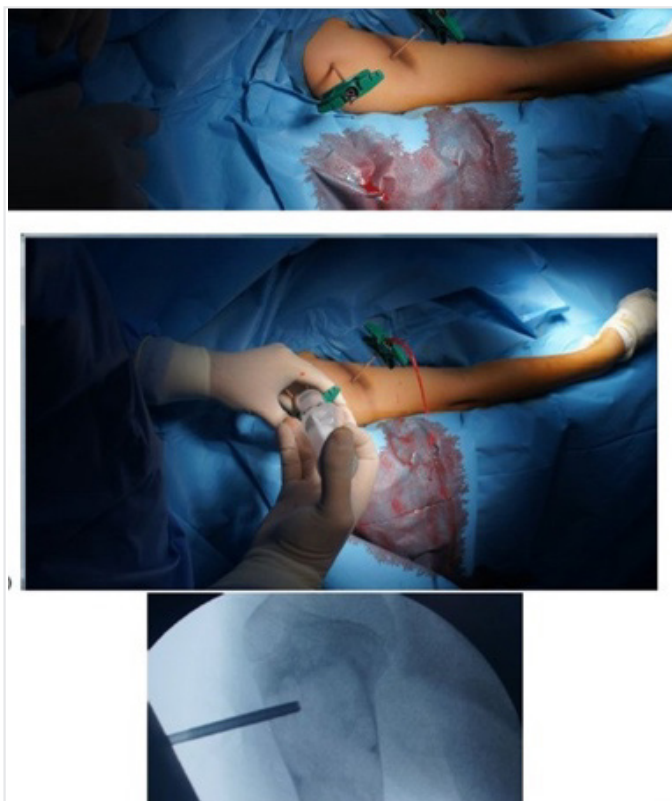


Figure 2. Discharge of seroanginous fluid in the cyst while the cyst cavity is washed with saline

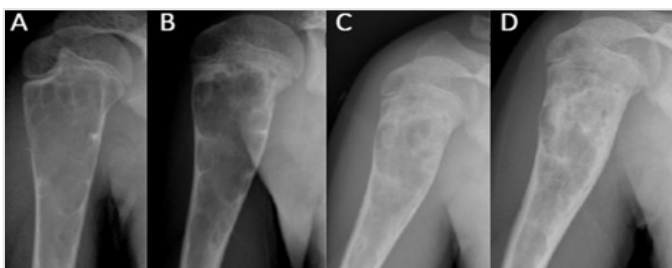


Figure 3. Type 2 improvement in follow-up plain radiographs of a patient with percutaneous steroid injection A) Preoperative plain radiograph B) Follow-up plain radiograph after injection C) Follow-up plain radiograph after injection D) Follow-up plain radiograph after injection

Results

The mean age of 11 male and 6 female patients included in the study was 12.4 years (range= 2-39) and the mean follow-up period was 22.8 months (range= 3-48). In six patients, the cyst was located to the proximal humerus, in two patients to the calcaneus (bilateral in one patient), in seven patients to the proximal femur, in one patient to the proximal tibia, and in one patient to the distal tibia. Three patients had pathological fractures prior to steroid injection. These three patients were treated with steroids after their pathological fractures in the proximal humerus were healed by conservative methods. In pathological fractures with lower extremity placement, first, surgical treatment (curettage + cementing) was applied.

MPA treatment resulted in complete recovery in ten cysts (55%) and in partial recovery with residual lesions in three cysts (17%). Three patients (17%) did not respond to MPA; two patients had repeated cysts (11%). While results were satisfactory in patients with complete recovery or partial recovery with residual lesions (72%), MPA treatment was found to be unsuccessful in five cysts (28%) (Neer classification Table 1).

The average age of the patients with satisfactory results was 10.5 years, while the average age of the patients with unsuccessful results was 17 years. No statistically significant relation was found between age and injection result ($p=0.458$). In the five cysts where MPA treatment did not produce positive results, the average cyst volume was 24.6 cm^3 , while in the 13 cysts with satisfactory results, the average cyst volume was 21.9 cm^3 . No statistically significant relation was found between tumor volume and injection result ($p=0.961$). The average number of injections was 2 in the patients with satisfactory results and the average number of injections was 2.4 in the five patients with failure. No statistically significant relation was found between the number of injections and the result of the injection ($p=0.681$). None of the five patients with a successful result had a pre-treatment pathological fracture, and all three patients with a pathological fracture had a successful outcome. No statistically significant relation was found between the pathological fracture and the results ($p=0.522$). There was no significant relation between localization and injection success when lesions were divided into two groups as lesions localized to upper and lower extremities ($p=0.615$) (Table 2).

In one of the two patients where the cyst relapsed, the lesion was in the proximal femur and the cyst volume was 9.85 cm^3 . In the other patient with relapse, the cyst was located in the distal

Table 1. The Modified Neer classification (6)

Stage I	Consolidation with completely new bone and thickening of cortical borders
Stage II	Residual defect with partial recovery (cortical thickening and consolidation)
Stage III	Despite consolidation after treatment, development of osteolysis in follow-up (recurrence)
Stage IV	No signs of cyst healing

tibia and was 10.3 cm³ in size. One of three patients with no response to MPA therapy had simple bone cysts in the bilateral calcaneus. The cyst on the left side of this patient, which did not respond to steroid treatment, was 7.1 cm³ in size and was cured with grephonage after curettage. The cyst on the right side of the patient was 26.2 cm³ in size and responded well to MPA treatment. In the second patient, who never responded to steroid treatment, the cyst was settled into the calcaneus and it was 18.8 cm³ in size. This patient was also treated with curettage and grephonage. In the third patient who did not respond to steroid treatment, the cyst was located in the proximal humerus and its size was 75.6 cm³. In this patient, the cyst relapsed despite curettage and grephonage. Curettage and cementing were performed in this patient. No complications related with the procedure were seen in any patients.

Discussion

Simple bone cyst treatment continues to be challenging for orthopedists, despite numerous studies on this subject and many treatment options available. Although curettage of SBC and bone grafting is a conventional treatment for SBC, this treatment has some disadvantages (4,7). Some of these are; long surgical duration, relatively greater risk of infection, longer hospitalization, being a more morbid procedure than MPA injection. For this reason, surgeons have directed to alternative percutaneous and open treatments (8). Alternatively, methods such as intracystic injection (steroid, bone marrow, demineralized bone matrix, calcium sulfate), decompression of the cyst (multiple drilling, pin, nail) and structural support (flexible intramedullary nail) can be used. The superiority of these treatments against each other has not been demonstrated (9).

The etiology of SBC is not clear. Significant relation has been shown between SBC and bone modeling, failure in hematoma resorption, osteomyelitis, tumor degeneration, and venous obstruction (10-14). The most valid of these theories is that intra-lesional pressure secondary to venous obstruction is higher than bone marrow pressure (15,16). Prostaglandin E2, interleukin-1 β and gelatinase in cyst fluid are known to cause resorption of bone. Trepanation of bone has been shown to reduce pressure inside bone, regulate venous circulation and reduce the factors

that cause bone resorption and induce new bone formation (17). In MPA injection, cortical trepanation is performed using two Jamshidi needles. Lesion decompression is achieved by opening holes. Even if the healing mechanism associated with this technique is not fully explained, it can also be thought that the anti-inflammatory mechanism play a role.

MPA injection for the treatment of SBC is a method used after being defined by Scaglietti in 1979 (18). There are different results about MPA injection in the literature. Capanna et al. showed that the success of MPA injection was 90% in cysts located in diaphysis and 94% in monolocular cysts (6). Oppenheim et al. reported a success rate of 95% (19). On the contrary, Wright et al. showed unsuccessful results in 22 (58%) of 38 patients (20). In our study, ten patients (55%) recovered completely and three patients (17%) recovered with residual lesions. Three patients (17%) did not respond to MPA treatment; two patients had repeated cysts (11%). While results were satisfactory in patients with complete recovery or recovery with residual lesions (72%), MPA treatment was found to be unsuccessful in five cysts (28%). (Neer classification Table 1)

Scaglietti et al. (21) found 24% improvement in SBC with single injection. Campanacci et al. showed recurrence and no recovery in 32% of patients after the first injection (19). In our study, single injection was enough in only 4 (22%) of 18 cysts. The average number of injections was 2 in the patients with satisfactory results and the average number of injections was 2.4 in the five patients with failure. No statistically significant relation was found between the number of injections and recovery.

There have been authors who have generally argued that SBC will resorb spontaneously as age progresses (22,23). Donaldson et al. showed that there was no spontaneous resorption in 87% of 24 paediatric patients who were followed up for an average of seven years due to SBC (24). Although the average age of the patients with satisfactory results was 10.5 years and the average age of the patients with unsuccessful results was 17 years, there was no statistically significant relation between age and satisfactory results.

Although successful results with MPA injection in the cysts in the proximal humerus were shown, the success rate of this treatment in the cysts in the calcaneus is low (25,26). Glasser et al. reported that 66% of patients who underwent steroid injection required open surgery (25). Cakar et al. (27) reported 82% improvement in proximal humerus lesions with this treatment. In our study, when we divided the patients into two groups as patients having cysts in the upper and lower extremities, we found no significant relation between the cysts in upper and lower extremities in terms of the success of this treatment.

The limitations of our study are that the patient group is heterogeneous, the number of patients is limited and there is no long follow-up period. However, the possibility of recurrence of the disease is open to debate in patients who show satisfactory recovery in a short time. Further studies in large number of patients involving control groups can be planned to show long-term results.

Table 2. Relation between non-parametric results

		Age	Result	Postoperative follow up	Cyst volume
Result	rs	0.259			
	p	0.299			
Postoperative follow up	rs	0.232	0.355		
	p	0.355	0.149		
Cyst volume	rs	0.518	0.043	0.020	
	p	0.028	0.865	0.938	
Number of injections	rs	0.376	0.214	0.335	0.013
	p	0.124	0.395	0.174	0.959

Conclusion

Intralesional MPA application is an effective treatment alternative that can be applied in the treatment of SBC. The antiprostaglandin effect of steroids is the basis of steroid therapy in SBC. We believe that this treatment, which is cost effective, is minimally invasive, has low morbidity, requires a short hospitalization period and is effective, can be tried before aggressive treatments. Supporting this study with studies having more homogenous patient and control groups and having long-term follow-up results will shed light on the treatment of SBC in the later period.

Ethics

Ethics Committee Approval: Prior to the study, permission was taken from the Academic Lectern Council (no: 839, date; 15.01.2019).

Informed Consent: Our study is retrospective.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: V.U., A.P., A.C.E., M.K., V.G., Design: V.U., A.P., A.C.E., M.K., V.G., Data Collection or Processing: V.U., A.P., A.C.E., M.K., V.G., Analysis or Interpretation: V.U., A.P., A.C.E., M.K., V.G., Literature Search: V.U., A.P., A.C.E., M.K., V.G., Writing: V.U., A.P., A.C.E., M.K., V.G.

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Home-based Palliative Care

Ev Temelli Palyatif Bakım

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ABSTRACT

Palliative care (PC) is defined as the approach that improves quality of lives of patients and their families who face up with the problems accompanied with life-threatening conditions. Provided usually in an inpatient setting, PC services are considered as an appropriate caregiving model for patients with critical illnesses. As the need for such services increases, many healthcare systems has been developing novel programs that integrate PC to their healthcare services in-hospital, outside the hospital, and home-based settings. Home-based PC is the care approach that provides meeting of physical, psychological, and moral needs of the patients with chronic and disabling health problems such as advanced cardiac, renal, respiratory, malignant, and neurological conditions in home-based setting. It is provided by a multidisciplinary team that has training in PC and that consists of physicians, nurses, public health professionals, and volunteers in line with PC programs of hospitals. Patients in need of PC have higher mortality and length of stay at intensive care units (ICU) with increased costs; in fact, they often live their terminal days in ICU. Even though it is considered as a model of care for those with life-limiting conditions in developed countries, home-based PC is still not sufficient. In our country, population gets older year by year. However, PC and home-care services are quite new and both are not yet up to the level to meet the needs. Therefore, PC services should be integrated into home-care services bearing in mind the sociocultural structure and national health policies of our country.

Keywords: Home care, palliative care, chronic critical illness

ÖZ

Palyatif Bakım (PB) yaşamı tehdit eden hastalığa bağlı sorunla karşılaşan hasta ve ailelerinin yaşam kalitesini artıran bir yaklaşım olarak tanımlanmaktadır. PB hizmetleri, yoğunlukla hastanelerde yataklı tedavi birimlerinde verilmekte olup ciddi hastalığı olan hastalar için uygun bir bakım verme modeli olarak kabul görmektedir. PB ihtiyacının artmasıyla birlikte, birçok sağlık sistemi, hastane, hastane dışında ve evde bakım hizmetlerine PB'yi entegre ederek yeni programlar geliştirmektedir. Ev temelli PB ileri dönem kalp, böbrek, solunum yolu hastalıkları, kanser ve kronik nörolojik bozukluklar gibi kronik, yaşamı sınırlayıcı sağlık sorunları olan, hastaların yaşadığı evde, fiziksel, psikolojik ve manevi ihtiyaçlarının karşılanmasını sağlayan, bakım yaklaşımıdır. Doktor, hemşire vb. sağlık çalışanları ve gönüllülerinden oluşan, PB konusunda eğitilmiş multidisipliner bir ekip tarafından hastanelerin PB programlarına bağlı olarak verilir. PB ihtiyacı olan bu hastalar genellikle yaşam sonu dönemlerini yoğun bakım ünitelerinde (YBÜ) geçirmekte olup YBÜ'de kalış süreleri ve mortalitelerinin yüksek olduğu, ayrıca maliyelerinin de fazla olduğu bilinmektedir. Ev temelli PB gelişmiş ülkelerde yaşamı sınırlayıcı hastalıkları olanlar için bir bakım modeli olarak görülse de henüz yeterli değildir. Ülkemizde de nüfusumuz her geçen gün yaşlanmaktadır. Bununla birlikte PB ve evde bakım hizmetleri oldukça yeni olup her ikisi de ihtiyacı karşılayacak düzeyde değildir. Bu nedenle ülkemizin sosyokültürel yapısı ve sağlık politikalarına göre PB hizmetlerinin evde sağlık hizmetlerine entegre edilmesi gereklidir.

Anahtar Sözcükler: Evde bakım, palyatif bakım, kronik kritik hastalık

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Introduction

The increase in the elderly population in the world leads to an increase in patients with chronic critical illnesses (CCI) in need of palliative care (PC) (1,2). The majority of CCI is comprised of patients with dementia, heart failure (HF), and diseases with high mortality and symptom burden such as cancer (3,4). CCI is the patient group that needs the services of the PC that is most focused on improving the quality of life, and these patients are known to have complex needs such as relieving symptoms and end-of-life care in the clinical management plan (3-5). The World Health Organization (WHO) defined PC as an approach that improves the quality of life of patients and their families experiencing problems related to life-threatening disease (6). PC programs mostly function as inpatient treatment units and consultation services in hospitals (1). As the need for PC services increases, many healthcare systems has been developing novel programs that integrate PC to their healthcare services in the hospital, outside the hospital, and home-based settings (7). In recent years, PC services have been suggested to be integrated into the patient’s routine care along with therapeutic approaches beginning from the diagnosis of the disease (1,8,9). Today, too, PC services are provided in hospitals, polyclinics, nursing homes, or home environments, and they are considered as a basic care model especially in the end-of-life period (10,11).

What is Home-Based PC?

Home-based PC is the care approach that provides meeting of physical, psychological, and moral needs of the patients with chronic and disabling health problems such as advanced cardiac, renal, respiratory tract diseases, cancer, and chronic neurological conditions in a home-based setting (12,13). It is provided by a multidisciplinary team which has training in PC and consists of physicians, nurses, public health professionals, and volunteers in line with PC programs of hospitals (14). Home care patients with newly diagnosed serious diseases are candidates for PC. As the symptoms of these patients start affecting the quality of life, the burden of the disease increases, and thus, while the treatment for the disease continues, an advanced care planning that would increase the comfort of patients and that involves the symptoms is needed (15). PC interventions are an integral part of the care plan for these patients, and the patients have been reported to benefit more from the inclusion of the PC team in home-based

healthcare institutions (12). Table 1 shows home-based PC characteristics (12). In order to provide PC at home, it is necessary to evaluate the patient’s home environment. This includes assessment of living conditions such as nutrition, cleanliness, ambient temperature, access to water, electricity, and telephone, safety, and the availability of equipment (12). Most patients feel more comfortable in their homes than in hospitals or nursing homes. In addition, home-based PC enables family members to integrate into the process (13). The provision of PC services for patients with severe disease was reported to be more effective in providing care to patients, families, and health systems (16,17). Although patients with CCI have more PC requirements during the end of life period, only 1/10 of those in need of PC has access to this service according to the WHO’s data (18). Patients in need of PC generally spend their end of life period at the intensive care units (ICU), and it is common that they have long ICU stays and high mortality rates in addition to their highcosts (4). Even though it is considered as a model of care for those with life-limiting conditions in developed countries, home-based PC is still insufficient (15). In our country, due to the lack of PC awareness in addition to the insufficient number of PC centers where end of life care is provided and to it being a new care model, most of the deaths occur in ICUs which cause higher spending. This situation is not peculiar to Turkey, and only a minority of patients can benefit from home-based PC services in developed countries as well (18). Studies conducted on home-based PC practice has been on an increase in recent years, and it was reported that home-based PC services increased patient satisfaction and reduced spending (17,19). It was reported in studies that outpatient or home-based PC practice at the early stages of the disease would increase the quality of life, in addition, that emergency and acute care applications were reduced thanks to training provided to patient and their families on drug use at home, crisis intervention, and patient care (16,20-22). In 2014, WHO noted that PC should be integrated into other healthcare services as the fundamental element of healthcare continuity, and it also emphasized the necessity for healthcare team and primary care physicians to have PC training in order to integrate home-based care and PC services (8). In addition to the patient and the family, home-based care team are required to receive training on symptom management and psychosocial support in order to provide PC service to patients beginning from diagnosis through a multidisciplinary team approach comprising physician, nurse,

Table 1. Home-based PC properties (12)

- 1. Patients with CCD who have functional disorders preventing PC polyclinic follow-ups,
- 2. Compliance with home-based PC is determined by need and not by prognosis,
- 3. Concomitant PC application with the patient’s curative treatment,
- 4. Patient and family focused care by a multidisciplinary team consisting of a trained physician, nurse, social worker, and psychologist, physiotherapist, spiritual care specialist and home health assistant according to patient needs,
- 5. Home visits by all team members, including physicians to provide pain control, other symptom management, psychosocial support, and training to meet patient and family needs,
- 6. 24/7 phone support,
- 7. Informing about end-of-life care of patients and families and planning care together,
- 8. The PC team needs to check and control caregivers, home environment and family.

PC: Palliative care

and social service expert. The home PC team is responsible for the coordination and management of care and provides services for the evaluation of patients, planning, care delivery, follow-up monitoring and continuous reassessment of care (10,18). It has been reported that the effects of the disease and symptoms on the quality of life are less, physically and psychologically and patient satisfaction is higher in patients with home-based PC (22).

Requirements For Home-Based PC Service:

Home-based PC service can be set up quite simply. Minimum requirements for home care are given in Table 2 (23). The home environment should be a safe and accessible place for the team to store drugs and equipment, as well as to discuss patients and plan visits. In addition to transportation needs, teams need mobile phones to communicate with patients and their families 24 hours a day. A full-time nurse and part-time physician are minimum requirements for home-based PC, and the multidisciplinary team should have a psychologist, social worker and trained volunteer or community health worker. Team training should include both theoretical and practical components (23). In home-based PC, family and caregivers have duties and responsibilities that include advanced skills such as symptom and opioid management (24). Information and training should be provided to families and caregivers on the practical aspects of home-based care, such as symptom and pain management and nursing care (15). A caregiver's responsibilities include helping with housework, personal care, helping the patient's daily life activities and managing physical symptoms such as pain. Caregivers can also provide emotional and social support to the patient, as well as help in making decisions about their care (25). For many families, the diagnosis of a life-threatening disease in a family

member is the first confrontation with death, leading to major psychosocial conflicts (26). At the same time, patient receiving care by their family can be exacerbated by the restrictions on time and space as well as physical, emotional, financial and social burden of care (15,26). Discussions on the clinical status, prognosis and care objectives of the patients are important, and it is very significant to inform them with family meetings, to clarify the problems, to clarify the current situation, and to set goals for care (15). Counselling and psychological support may be required to help family members and caregivers to cope with possible distress, hopelessness, unresolved relationship issues, and other emerging concerns (15,26). Standard forms should be used to document the status of patients, and patient/family must sign a consent form. For each patient, a health record should be kept and records of drugs (especially morphine) should be maintained in accordance with local laws and regulations (23). The list of equipment that may be required in the home-based PC is quite long (Table 3) (23,27).

Home-Based Palliative Care Examples

Kaiser Permanente (KP) home-based PC Program

The KP home-based PC program was first launched in 1997 as a California-based pilot project and was launched in 1998 as an official program (14,28). In order to provide better care to home care patients and their families, the PC program integrated into the home health department comprises five fundamental components (14,28,29).

- Providing pain control, symptom management and psychosocial support to the patient and family by a team of physicians, nurses and social workers,

Table 2. Things to do to set up a home-based PC service (23)

1. PC evaluation of needs and resources

Starting the PC network by evaluating existing resources including potential voluntary human resources

2. Official establishment of home-based PC

Application to the competent authorities

3. Setting up an action plan

Determining which resources are required and what services will be provided.

4. Home care team to start the work by providing training

If at least one doctor and nurse are not locally available for training, provide training in connection with a training center in another area.

5. Employing and training of volunteers or community health workers

Voluntary or community health workers are needed to provide supportive care.

6. Taking action to use resources

Resources can be money or non-money (transport, storage space, etc.) and can be shared with other organizations.

7. Contacting local health providers

Providing links with primary care health centers and regional hospitals for referral or inpatient support.

8. Introduction of home-based PC service

Use of networks and media to raise awareness about PC

9. Promoting wider participation

Inclusion of wider community groups (association members, students and politicians)

PC: Palliative care

- Home visits by all team members, including physicians, to provide medical care, support and training that the patient needs,
- Planning care continuity to meet patient's medical, social and emotional care needs in an uninterrupted manner,
- 24/7 telephone support for patient and family when needed,
- Improved care planning for patients and their families to make informed decisions and choices about end of life care.

Admission Criteria For KP Home-Based PC Program: (14,28)

- Patients should have a life-threatening disease (cancer, KY, and chronic obstructive pulmonary disease (COPD) etc.,

- Life expectancy of 12 months or less,
- Need for symptom management in a worsening clinical condition ,
- The patient should have an emergency service application or hospitalization 1-2 times a year,
- Patient and the family accepting home care other than aggressive treatment.

Acceptance Process (28): Admission to the program comprises four stages

- The patient and the families are interviewed by PC nurse via telephone or face to face,

Table 3. Medical equipment and medicines that should be in the home care kit for home-based PC (23,27)

1. Medical equipment and supplies	2. Supporting equipment
Stethoscope Sphygmomanometer Thermometer Tongue depressor Forceps	Alternating air mattress Aspirator Nebulizer Wheel chairs Walking aids Bathroom chairs
3. Tools	
Dressing materials Cotton Scissors Gauze Gloves Plaster Transfusion materials	IV infusion sets Cannula and butterfly needle Injector and needle Aspirator probes Urinary catheters Bladder Feeding tubes
4. Medicines	
Pain management Paracetamol Ibuprofen Diclofenac Codeine Tramadol Morphine Gabapentin Psychological symptom management Diazepam Halperidol Amitriptyline Wound therapy Betadine solution and ointment Metrogil gel Hydrogen peroxic PC: Palliative care	Gastrointestinal symptom management Metoclopramide Domperidone Dexamethasone Bisacodil Loperamide Oral rehydration salts Ranitidine Antibiotics and antifungals Ciprofloxacin Metronidazole Oxacillin Fluconazole Nutritional supplements High protein and calorie food supplements Iron, vitamin and mineral supplements

- The PC nurse makes the first assessment of the patient in the patient's home. Physical evaluation, medications used, patient preferences and care planning related to DNR, home security, evaluation of needed medical equipment, education and training needs,
- Based on this assessment, patient admission and a necessary care plan are established,
- All other physicians and assistants to provide patient care will be included in the program.

Care Plan: The care plan developed after admission is updated at regular intervals. The PC nurse prepares a self-care plan and helps patients to create personal goals. During the evaluation, the patient and family members will learn more about their disease and prognosis. They are trained on managing the patient's home care and advanced care directives (17,28). What are the patient's treatment and care preferences? What additional services are needed to support the family? Is there a need for education and training? A maintenance plan is prepared considering all this information. It is updated by reviewing the maintenance plan every 60 days or more frequently when necessary (28). PC physician conducts home follow-up visits once a week or when required. The PC physician makes an assessment of the patient's medical condition and sets advanced care plans and treatment goals (28). The PC nurse makes a home visit according to the care plan and as often as the patient wants. A nurse visits 2-3 times a week to establish a strong relationship with the patient and to help manage home care can then visit less frequently. However, a few weeks before death, patients and families may need to be visited more frequently due to their increased psychosocial support (28,30). Among the nursing services are the assessment of the patient's medical needs as well as the effectiveness of the care management and the prescribed medical treatment in addition to the provision of emotional support to the patient and the family (28,30). Social workers provide advice and support to help patients and their families meet their economic, psychosocial and emotional needs. The social worker completes the initial assessment of the patient and their family within one week. They then conduct a telephone consultation or home visit at least once a month or more often if necessary (28,29).

Additional Services

Home Health Assistance Services: Certified personnel provide personal hygiene and personal care services to help patients stay comfortable at home. They also assist in creating a safe and healthy environment for patients. Under the observation and supervision of the nurse, such services as bathing, food preparation, shopping, etc. are provided (28,30).

Spiritual Care Services: These services are offered by an emotional care professional to help patients and families maintain their hopes and deal with changes. At the same time, they help the dying patient and their family to reach the meaning and goal of the spiritual values associated with the belief system. Spiritual care services can also be used for bereavement counselling and funerals or memorial services (28).

Rehabilitation Services: Such therapies as physiotherapy, occupational therapy and speech therapy help the patient to maintain basic functional skills and symptom control that support the daily life activities and physical and psychosocial independence of the patient (28,31).

Pharmacist Consultation: Since patients often have multiple co-morbid conditions that require multiple drugs, they provide guidance in preventing adverse effects of complex drug regimens, and in managing pain and other symptoms (28).

Diet/Dietician Services: Many patients have a negatively affected nutrition due to side effects and symptoms. With the support of a dietician, team members can be supported by educating the patient and their family about practical diet interventions that increase comfort and nutrition satisfaction (28).

Social Workers: For the evaluation and fulfillment of the needs of the family, it is necessary to develop a care plan both before and after the patient's death and these services are provided to the surviving family members for at least one year after the death of the patient (28,29).

Voluntary Services: The volunteers who are supervised by the KP home-based PC team provide support to patients and their families and accompany them. They also provide care for the patient during their stay with the patient to reduce the burden of caregivers. They offer support to family members after the patient's death. All volunteers receive training before serving (28,29).

Patient Care in Inpatient Wards: In case of inability to home care or to manage terminal care, patient care is also provided in inpatient wards. It is at the lowest possible level in accordance with the patient's care plan and, if possible, given in a nursing home or hospital. If the patient needs acute care, the patient is transferred to an inpatient institution as soon as possible, if consistent with his/her preference and therapeutic goals (28,29).

Medical Supplies: The equipment, oxygen and drugs needed can be provided 24 hours a day and 7 days a week (28).

Sutter Health Care Program

Sutter Health is an integrated care system that is participated by 24 hospitals and 5.000 physicians, oriented towards increasing the terminal patient care and decreasing the use of acute care facilities, and that provides PC in between hospital and home transitions (32). In 2000, it began as a service to provide symptom management and care planning for home care patients with advanced stage diseases, and in time, a chair management model was established that would cover patient/care participation, and bounced care planning, and care transitions (33). For home care, service is provided to patients with a life expectancy of 1 year or less that meet the criteria for medicare compliance, and patients' care plans and current situation of their drugs are coordinated on real-time information exchange upon assigning the caregivers of the patients to the established program network (33). With this care model, it was reported that patient's requests and goals were better adapted, and that a decrease in hospital stays

and an increase in patient/caregiver satisfaction were ensured (9,33). First of all, this model is not a PC program consists of a multidisciplinary team comprising a home care team, hospital doctors and caregivers. Close cooperation with inpatient care teams is provided to ensure smooth transition of patients from hospital to home. The multidisciplinary team identifies care goals with patients and their families and improves care plan (33). Sutter patients that are eligible for advanced disease management have more than one hospitalization, emergency room service, and clinical, functional or nutritional problems in the last 12 months. The care plan created after the patient is registered to the care system is shared with the whole team supporting the patient through the common network and the patient is followed up regularly.

Home-based Primary Care Model

The home-based primary care program was initiated in 1983, and in 1998, the program was expanded and a new program titled "care of veterans with life-limiting disease" was initiated in order to provide end-of-life care for the veterans and to meet the needs of these patients (34,35). A comprehensive home-based care service has been created by including PC and hospice care in the home care program. Patients can be reached 24 hours a day and 7 days a week through a call program managed by nurses, and nurses are provided medical support from the geriatrics clinic if needed and then nurses observe patients at home (34). Services such as telephone support to patients, infusion therapy, ventilator, patient monitoring, wound care and counselling are given (36). In the home-based primary care program, patients often have cerebrovascular diseases, HF and COPD, and in 30% of the patients, diabetes is the secondary diagnosis and 26% had dementia. Home care is provided for patients requiring ventilator and oxygen-dependent infusion therapy and total parenteral nutrition and enteral nutrition (34,37). In addition, there are nurses and dieticians certified in terms of chemotherapy and diabetes. Patients and caregivers have access to home-based primary care program for 7 days/24 hours. Data on patients in the program that reach office during working hours, and that reach nurses out of working hours, weekends, and at night via a phone are accessed via a computer, and their anxieties are relieved, in addition to medical issue resolutions; and if needed, a home visit is made to solve any problems. Nurses can access the geriatrics department academia when they see it necessary. Medications of patients may be prescribed by doctors (34). Physical therapist apply physiotherapy to patients at first at home two days a week, and then, at the hospital in groups if the patient is mobilized (34). For home-based primary care program services, patients get in touch with program staff and receive intensive health training after admission to the program. The purpose of this program is to improve the ability of patients to manage their diseases on their own, to reduce hospitalization and admission to the emergency department (36). Patients and families are monitored by the supervisor or physician and the information is recorded and the scope of service and clinical privileges and protocols are determined. Treatment plans are regularly reviewed by the program team, and necessary procedures are established,

including admission and discharge criteria (34,38). Patients are evaluated with a functional assessment form called the Katz Functional Daily Living Activities, and the functional status of the patient is evaluated at the beginning and at least every 90 days, and the treatment plan is reviewed and documented (34).

In our country, PC has not been put into practice in home care services, despite the rapid spread and necessary in-service trainings while especially taking part in the health services group due to the health policies in recent years. PC services are provided in hospitals, and PC services are not offered in consultation and home health services. Home health services such as PC have also gained momentum in the last 10 years, and the Regulation on the Presentation of Home Care Services dated 10 March 2005 and No. 25751 entered into force after being published in the Official Gazette (39). The Regulation on the Implementation Procedures and Principles of Home Health Care Services came into force on 01.02.2010 for the delivery of home health services by health institutions and organizations affiliated to the Ministry of Health (40). Home health services are presented in family and home settings especially to bedridden patients, patients with respiratory diseases, advanced muscle diseases, terminal cancer, and to newborns. Home health services are provided in coordination with Turkish Public Health Association through family physicians community health centers, and Turkish Public Hospitals Authority within the health institutions (training and research hospitals, general hospitals or branch hospitals) and are also offered through units established oral and dental health centers (40,41). Inspection and consultation within the scope of home health services, renewal of health board reports, prescription of medicines, examination and treatment (dressing, wound care, probe applications), rehabilitation, oral and dental health services, home to hospital or hospital to home transportation, training and support are the services that are provided. Medical devices that patients need, that may be of help for the treatment, and that are routinely used are provided for the use of the patients as entrusted to them. Necessary coordination with relevant institutions and organizations is provided by determining the patients' needs for social services (42).

Conclusion

Considering the benefits of home-based PC, together with the ageing population, the increase in CCD, and limited inadequate health resources, the integration of home-based PC into health systems becomes important. It is necessary to develop and implement PC policies and to ensure integration of PC with primary care, community and home based health services. Patients with CCD and PC need to be evaluated by a multidisciplinary team and referred to a hospital or home-based PC. Hospital-based PC is a more appropriate choice for patients who need more intensive symptom management or are unable to cope with the family's burden of care. In order to implement home-based PC; the health care team, the patient and the family must agree that the patient can be adequately managed at home, and the treatment plan should be approved by all parties. Depending on the patient's medical condition in home-based PC, it is necessary

to evaluate patients with home visits at intervals determined by a specialized PC team, to take samples for the necessary tests and to arrange the treatment protocol. However, the necessary actions should be directed to the PC centers if they cannot be performed adequately in the home environment. Consequently, it is necessary to create and implement national health policies that integrate PC services into home health services.

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The Cell Membrane: A Historical Narration

Hücre Membranının Keşfi: Tarihsel Bir Bakış

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ABSTRACT

The discovery of the structural elements of the cell has been entirely dependent on technological inventions. Although the discovery of cell membranes is thought to be in parallel with the discovery of microscopes, this is not exactly true. In the early 1660s, Robert Hooke made his first observation using a light microscope. In 1665, he examined a piece of fungus under a light microscope and he called each space as “*cellula*”. It was not already possible for him to see cell membranes with the primitive light microscope he used in this study. Also because the cells he was trying to study were plant cells, the lines that actually bounded the “*cellula*” were not the cell membrane, but the cell wall. In the following years, in addition to the microscopic observations, various physio-chemical studies were done in order to explore the structural and functional properties of the plasma membranes. In this review, the historical journey of the plasma membrane was summarized.

Keywords: Plasma membrane, history, light microscope

ÖZ

Hücrenin yapısal elemanlarının keşfi tamamen teknolojik buluşlara bağımlı olmuştur. Her ne kadar hücre membranlarının keşfinin mikroskopların keşfiyle paralel olduğu düşünülse de bu tam olarak doğru değildir. Bin altı yüz altmışı yılların başında Robert Hooke ilk ışık mikroskopik gözlemini gerçekleştirmiştir. 1665 yılında ışık mikroskop altında bir mantar parçasını inceleyerek gördüğü boşlukları “*cellula*” olarak isimlendirmiştir. Bu incelemede kullandığı ilkel ışık mikroskobu ile hücre membranlarını görmesi zaten mümkün değildi. Ayrıca incelemeye çalıştığı hücreler bitki hücreleri olduğu için, aslında hücreleri sınırlayan çizgiler hücre membranı değil, hücre duvarıydı. İlerleyen yıllarda mikroskopik gözlemlere ilaveten çeşitli fizyokimyasal çalışmalarla hücre membranlarının yapısal ve fonksiyonel özellikleri açıklanmaya çalışıldı. Bu derlemede hücre membranlarının keşfi ile ilgili çalışmalar tarihsel bir bakış açısı ile özetlenmiştir.

Anahtar Sözcükler: Hücre membranı, mikroskopi, tarih

Introduction

Molecular Properties of Cell Membrane: Eukaryotic cells are surrounded by cell membranes consisting of various molecules (1). In addition to protecting cells from various harmful factors, cell membranes create a regulated internal environment. The main components of membranes are phospholipids, proteins and carbohydrates. A double layer of phospholipids forms the main membrane skeleton. Proteins can be found either sprinkled

inside this layer or clinging to the outer faces. Carbohydrate molecules cling to integral proteins or phospholipids (2). The current membrane model describing the structure and functions of membranes is the “Fluid mosaic model” (Figure 1). This description was first used by Singer and Nicolson (3) in the early 1970s. The fluid mosaic model has been modified by various researchers after its initial identification and has become the final form that is valid today (1).

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According to the fluid mosaic model, membranes are basically composed of lipids, proteins and carbohydrates. The main skeleton of the membranes is formed by phospholipids, which are organized into two layers. Each phospholipid molecule has one hydrophilic and one hydrophobic region (4). The hydrophobic region or apolar region of each molecule is located facing the center of the membrane. Conversely, hydrophilic tip settles facing out of the layer (5). Membrane proteins are classified according to their location. One of these, integral membrane proteins (also called intrinsic proteins), is fully or partially embedded in the phospholipid layer. Integral membrane proteins that move across the membrane and extend from one end of the membrane to the other are called “transmembrane proteins”. Peripheral membrane proteins (also called extrinsic proteins) hold onto the surfaces of the membrane temporarily by weak connections. According to the fluid mosaic model, the third main element of the membrane is carbohydrates. These molecules form glycoproteins by clinging to proteins and glycolipids by clinging to lipids (6). There are many important features described by Singer and Nicolson (3) in relation to the fluid mosaic model. Some of these are fluidity, viscosity, continuity and asymmetry. Due to its fluidity property, molecules in the membrane can move in the lateral or vertical direction (7). The movement of molecules is regulated in such a way as to provide an optimum environment for the full function of membrane-bound enzymes and receptors, thanks to the viscosity, which is defined as the resistance of a liquid to flow. Membrane viscosity may vary according to the arrangement of membrane components (3,8). The inner and outer media are selectively separated from each other by means of continuity, which is another membrane feature, and a regulated inner environment is created. Thus, the integrity of the cell is maintained (3). Asymmetry is a natural result of asymmetric placement of membrane components including phospholipids, proteins (structural, enzyme-specific or receptor-qualified proteins) and carbohydrates (9).

Membranes are seen as three layers at the electron microscopic level. In the middle of the two dense layers located on the outside is a less dense third layer. This appearance of membrane is called “unit membrane”. This view is entirely related to the arrangement of membrane molecules (Figure 1).

History of Cell Membranes: Before the discovery of the cell and membranes, the discovery of systems to display these structures was necessary. The first in history was in 1590 when Zacharias Jansen, a German eyewear manufacturer, invented a prototype light microscope (10). Nineteen years after that, Galileo Galilei, an Italian scientist, made a light microscope (11). Despite the invention of the microscope, viewing the cells took place years later. For identification of the cell membrane, a wide variety of research has been done between the 16th and 19th centuries (12). The great scientist considered to be the father of optics is Robert Hooke (13). Microscopically, he studied plants, molds, sands

and fleas. He discovered the cell and named it. He also pioneered the studies of elasticity. He made significant contributions to the fields of physics, chemistry, meteorology, geology and biology (14). In the early 1660s, together with Robert Hooke, Christopher Wren, Thomas Willis and several other researchers in the Oxford experimental group, they made their first observations using a light microscope. Hooke emigrated to London in 1663, where he began writing his novel “Micrographia” (15). In 1665, while examining a piece of fungus under a light microscope, he saw gaps and gave them the name “*cellula*”, which naturally meant space (16). Six years after the publication of the book “Micrographia”, two important papers were sent to the Royal Society of London by the English botanist Nehemiah Grew (1641-1712) (17,18) and the Italian anatomist Marcello Malpighi (1628-1694) (19). Unbeknownst to each other, these two scientists had described the micro-anatomy of plants. Malpighi had also described the micro-anatomy of animal cells. Because the cell structures of plants were more prominent than those of animals, initial investigations were conducted in plants (20).

In 1672, Nehemiah Grew made the description of “mass of bubbles” in relation to plant parenchyma (17). In 1682 he reported that the cell membrane resembled a lace-like material (18). In Grew’s view, not only the fibers in the tissue but also the gaps between the fibers were consistent with each other. During the same period, he suggested that the plant cell wall was an uninterrupted layer that enveloped the cell (21). Malpighi predicted that cells were not simply distances located between membranes, but separate units surrounded by the cell wall (19,12). The strongest supporter of Grew’s view was the French botanist Brisseau de Mirbel. This researcher also acknowledged that both plant cavities and their fibers showed continuity, that all plant organisms had membrane systems, and that the cells observed between membranes were parts of this continuum

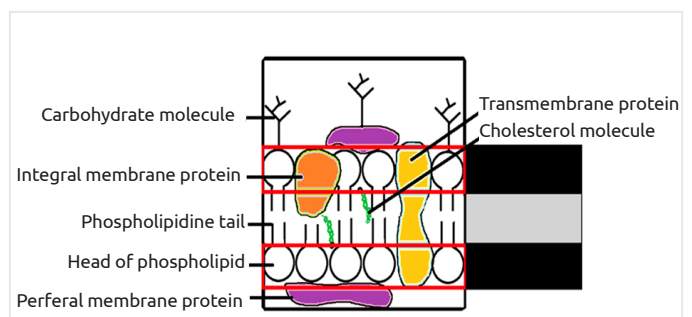


Figure 1. The relationship of membrane molecules with the three-layer unit membrane structure is clearly seen. The outer dark regions correspond to the hydrophilic heads of phospholipid molecules, while the lighter region in the middle corresponds to the hydrophobic tail regions of these molecules. Proteins are found in the membrane or on the periphery of the membrane; carbohydrates can be found bound on proteins or lipids (Illustration: M. Eşrefoğlu)

Table 1. Only a fraction of membrane-related studies have been shown (Table: M. Eşrefoğlu)

Researcher	Date	Research/result
Zacharias Jansen	1950	He developed the prototype light microscope
Robert Hooke	1660	He first made microscopic observation
Christopher Wren	1660	He made the first observation at light microscopic level
Thomas Willis	1660	He made the first observation at light microscopic level
Robert Hooke	1663	He wrote the book ' Micrographia'
Robert Hooke	1665	He studied and named the plant cell
Galileo Galilei	1969	He developed light microscope
Nehemiah Grew	1669	He described the micro-anatomy of plants
Marcello Malpighi	1669	He described the micro-anatomy of plants and animals
Nehemiah Grew	1672	He suggested the concept of 'mass of bubbles' for plants
Nehemiah Grew	1682	He likened the cell membrane to lace
Jean-Baptiste Lamarck	1809	In his book "Philosophie Zoologique" he wrote that membranes were the product of cellular tissues
Charles François Brisseau de Mirbel	1809	In his book "Expositioni de la Theorie de l'Organization Vegetale" he wrote that plants were made up of cells
Ludolph Christian Treviranus	1811	He isolated plant cells
Matthias Jakob Schleiden	1837	He showed that every plant cell had a nucleus
Matthias Jakob Schleiden	1837	He suggested that there was a general mechanism of development for all plant cells
Theodor Schwann	1839	He suggested that there was a universal mechanism related to the development of animal cells
Carl von Nägeli	1844	He observed that the volumes of algae varied in hypertonic and hypotonic solutions (membrane permeability studies)
Nathaniel Pringsheim	1854	He showed that there was a membrane around protoplasts of which permeability varied depending on conditions
Carl von Nägeli and Karl Cramer	1855	They showed that the volumes of plant cells varied in hypertonic and hypotonic solutions (membrane permeability studies)
Franz Von Leydig	1857	He rejected the existence of cell membranes
Franz Von Leydig	1860s	He accepted cell membranes as secondary structures resulting from hardening of the cell surface
Franz Von Leydig	1860s	He described the cell as a soft substance containing the nucleus, wrapped in a membrane
Wilhelm Hofmeister	1867	He reported that the protoplasts that made up the beetroot shrank in concentrated NaCl solution
Moritz Traube	1867	He developed Traube's presipitation membrane, conducted osmotic studies on the membrane
Wilhelm Pfeffer	1877	He was able to produce more robust precipitation membranes, conducted osmotic studies on the membrane and suggested that the membrane was semi-permeable
Hugo De Vries and Hartog Jakob Hamburger	1884	They showed that many solutions applied equal osmotic pressures at equal concentrations in plant and animal cells
Lord Rayleigh	1890	He examined the distribution of olive oil on the surface of the water and measured its thickness
Hartog Jacob Hamburguer	1896	He developed Hamburger's solution and conducted osmotic studies with erythrocytes

Table 1 continued

Charles Ernest Overton	1899	He showed that the membrane was in lipid structure, conducted studies on necrosis and became the first “membranologist”
Nathanson	1904	He proposed the mosaic membrane theory
Irving Langmuir	1917	He showed that hydrocarbon chains were flexible, not spread flat on the surface of the water, but curled. His study was fundamental to understanding the bilayer structure of the cell membrane
Fricke	1923	He calculated that the cell membrane was only 4-nm thick
Evert Gorter and Françoise Grendel	1925	They dissociated lipids from the erythrocyte membrane, suggesting the molecules could make double or single layers
Harvey and Kennet S. Cole	1932	They suggested the membrane was surrounded by proteins
James Frederic Danielli and Hugh Davson Fricke	1935	They developed the “Paucimolecular” membrane model
James Danielli and Hugh Davson	1935	They developed the sandwich membrane model
James Danielli	1936	He developed a series of additional membrane models
J. David Robertson	1959	He identified the unit membrane and its corresponding molecules (though not exactly accurate) by electron microscopic examination
Brady RO and Trams EG	1964	They described some properties of the current membrane model (proteins enter the lipid layer, the membrane is fluid, etc.)
Seymour Jonathan <i>Singer</i> and Garth L. <i>Nicolson</i>	1972	They proposed Singer and Nicholson’s fluid mosaic membrane model

structure (20). In the 2nd edition of the book “Philosophie Zoologique” prepared by Lamarck in the early 1800s, one section was reserved for cellular tissue. In this section, Lamarck wrote: “Membranes, known for many years to form the covering of the brain, nerves, all types of veins, glands, organs, muscles and muscle fibers, and even the skin of the body, are products of cellular tissues in general” (22). Charles François Brisseau de Mirbel published the 2nd edition of his book “Expositioni de la Theorie de l’Organisation Vegetale” in 1809 when Lamarck’s book was published. The general conclusion of this book was: “Plants are composed of cells, and all sections are caused by membranous tissue that is continuous with each other” (23). This hypothesis finally gained acceptance at the beginning of the 19th century when Treviranus, Moldenhawer and Dutrochet managed to separate plant cells using different methods century (12). Ludolph Christian Treviranus (24) and Johann Jacob Paul Moldenhawer (25) claimed that the cells were individually separable units. All opinions enabled Henri Dutrochet to form the basic doctrine of the modern cell theory. According to this, “Cells are the basic elements of organization” (26). Johann Heinrich Friedrich Link stated that pigments could not pass from one cell to the neighboring cell unless the cell wall broke down. This opinion contradicted Mirbel’s view that the gaps were continuous (12,27). Seeing the limits of most living cells except mature plant cells was unlikely at the light microscopic

level (28). It was extremely difficult to detect the fine structure of cells with primitive light microscopes at that times. A large number of studies were done in the 1800s, especially with plant cells. Matthias Jakob Schleiden (1804-1881), a Hamburg-born botanist, shifted the focus of plant Studies from classification research to structural research. Schleiden suggested that each plant cell had a nucleus, which was evidence of the cell’s existence. In 1837 Schleiden adopted the idea that there was a general mechanism of development for all plant cells (29). In 1838, while Schleiden and Theodor Schwann enjoyed sipping their coffee after dinner, Schleiden began excitedly talking about the universality of plant cells. Theodor Schwann, born in Neuss in 1810, was a professor of physiology at the University of Louvain. Schwann suddenly realized how much Schleiden’s work resembled his own. He himself had observed that all the species he was working on were composed of distinguishable units or cells (28). In 1839, Schwann adapted Schleiden’s hypothesis to animal cells, suggesting that there was a universal mechanism related to cell development (30). Several contradictory opinions have been raised over the years following Robert Hooke’s miraculous description of the cell. The fact that animal cells did not contain the cell wall seen in plant cells, even though they contained nuclei and protoplasm, caused confusion about the definition of cell (31).

In the early 1890s, cell membranes were generally considered

to be mandatory or elective secondary structures. In 1857, the first author to explicitly reject the existence of cell membranes was Franz Von Leydig. Leydig then reassessed cells and cellular structures as a result of a series of observations (12,32). He described the cell as a soft substance containing the nucleus, wrapped in a membrane (33). He attributed this view to the fact that membranes were not always visible. He simply depicted the cell as “A substance resembling a sphere in shape, with an object called a nucleus in its middle” (12). He considered cell membranes to be secondary structures caused by hardening of the cell surface. In these times, various methods were used to show the presence of cell membranes. These methods were generally osmotic study methods that assumed that cell membranes were semi-permeable (34).

In 1844, Carl von Nägeli and observed that protoplasts of some algae (e.g. *Nitella* and *Bryopsis*) moved away from their walls when placed in various condensed solutions, and when dilute solutions replaced condensed solutions, they returned back to their former size. Nägeli and Nathaniel Pringsheim (1854), who understood that protoplasts had osmotic properties which were defined for animal bladder by Jean-Antoine Nollet and Henri Dutrochet, concluded that there must be a membrane around protoplasts whose permeability varies depending on conditions (33). In the second half of the 19th century, a simple experimental idea launched a new hypothesis regarding cell boundaries (35). In 1855, Nägeli and Karl Cramer reported their observation that when plant cells were put into a hypertonic solution, they shrunk and the protoplasm moved away from the cell wall. On the contrary, when they were put into a hypotonic solution, the cytosol swelled and almost burst (36). In 1867, Wilhelm Hofmeister reported that the protoplasts forming the beetroot shrink in concentrated NaCl solution. Soon after, Hugo de Vries conducted similar plasmolytic studies in *Tradescantia discolor* epidermal cells. He also observed protoplasts moving away from the cell wall during the experiment. Hugo de Vries called this event “plasmolysis” (33). Not long after, another German scientist, Hartog Jakob Hamburger studied the entrance and exit of water into red blood cells based on the osmotic pressure of the solution in which they were found. He specifically investigated the effects of dilution leading to hemolysis at the last point. Osmotic studies, which took place in a similar way over time, began to be done more. In 1884, Hugo de Vries and Hamburger succeeded in using plant and animal cell models to show that many solutions applied equal osmotic pressures at equal concentrations (37). Although today the analysis of these results seemed to be very simple, at that time it was not considered decisive as the membranes still could not be displayed (12).

In 1867, Moritz Traube designed special membranes to create “artificial cells” with the aim of studying events such as growth and osmosis in living cells (33). The ‘Traube precipitation

membrane’ contained molecules at the interface of a potassium ferrocyanide solution and a copper sulfate solution. This membrane was semi-permeable. Traube cells were able to spread rapidly towards bud-like living cells, but the artificial membranes were not strong enough to resist the osmotic pressure that arose within them. They were therefore easily disintegrated. Working to overcome this problem, Wilhelm Pfeffer was able to produce more robust precipitation membranes in 1877. He conducted a series of experiments explaining the connection between these membranes and osmotic pressure, concentration and temperature of the solution (38). In 1877 Pfeffer, a botanist, was influenced by physiochemical studies and suggested that a plasma membrane or skin covered the outer face of the protoplasm (33). According to this scientist’s idea, the membrane he was referring to was similar to the artificial membrane. Pfeffer concluded that the cell barrier must be thin and semi-permeable with data from his studies on the osmotic properties of plasma membranes that have not yet been imaged (39). With these results he revealed that the barrier acted like an invisible skin, allowing water to selectively freely pass into and out of the cell, but limiting the passage of salt and sugar (40). In 1896, the German physiologist Hartog Jacob Hamburger invented a crystalloid solution (normal saline solution), which took the name “Hamburger’s solution”. This salt solution, thought to be in osmolality equal to human blood, did not naturally lead to hemolysis in red blood cells (37). Nearly 20 years after Wilhelm Pfeffer came up with his ideas, Overton showed that the permeability barrier -the cell membrane- was in the lipid structure. Charles Ernest Overton (1899) was regarded as the first true ‘membranologist’ with this view. Overton’s main work on understanding membranes was permeability studies (40). Overton carried out many important studies in this area. According to this scientist, a saturated outer boundary layer of a cell was the determinant of the osmotic properties of a living cell. Active events related to diffusion and metabolism played a role in the exchange of soluble matter between the cell and its environment. Na/P exchange was important in muscle and nerve stimulation. Overton also added important milestones to science about the theory of necrosis. In times when Overton did these studies, physics studies for cell surface properties in addition to the plasmolysis studies were also developing (40). In the late 1700s, Benjamin Franklin described for the first time that a drop of oil was emitted on the surface of the water in the form of a thin layer (35). In 1890 Lord Rayleigh observed the movement of olive oil on the water surface and estimated the thickness of this layer to be 10-20 Å (41). Agnes Pockels, a German pioneer in chemistry, conducted experiments using kitchen bowls, wires and buttons in the kitchen sink. He developed his own device to precisely measure the thickness of the oil layer on the water surface (42). In 1904 Nathanson put forward a mosaic membrane theory. According to this theory, the cell membrane was not a simple membrane, but rather contained mosaic domains with properties similar to Traube’s precipitation membrane (artificial

membrane). Such a mosaic membrane could provide different pathways for the entry of soluble or insoluble materials (43).

Development of the Unit Membrane Model: In 1917, Irving Langmuir discovered that with the help of a decoy, the oil molecules spontaneously spread across the water and air interfaces. By measuring the thickness of this layer, he presented the first evidence that this area had a monomolecular characteristic. In an excellent article on the subject, he stated that the propagation in this way created a monomolecular layer on the surface of the water. He calculated the field of each molecule with a simple arithmetic. He also showed that hydrocarbon chains were flexible, not spread flat on the water surface, but rather curl. This study was fundamental to understanding the bilayer structure of the cell membrane. Langmuir membranes were a key model of experimentation with historical characteristics associated with our modern perspective of biological membranes. In 1925, Evert Gorter and Francoise Grendel dissociated lipids from red blood cells. They calculated that the surface area of the lipid molecules they decomposed was about twice the surface area of the cells themselves. They showed that molecules could make single or double layers (45). The work of these scientists made the concept of the lipid double layer popular at the time. It also opened the door to the identification of the molecular structure of the membrane.

Studies on the membrane continued between 1920 and 1930. Fricke showed that the cell membrane was only 4-nm thick in his study on the measurement of the resistance of the cell membrane. As a result of their studies of membrane surface resistance in various cells, Harvey and Cole suggested that the membrane surface was not bare, but rather surrounded by proteins. This model was detailed in a review article by Danielli and Davson in 1935. In 1935, James Frederic Danielli and Hugh Davson Fricke developed a 'paucimolecular' model, in which molecular details were kept to a minimum by compiling the results of Gorter, Grendel and other scientists. Danielli and Davson proposed that there was a nonpolar lipid center between the bilayer amphipathic lipid molecules in the model. They noted that on both sides of the membrane there were protein layers at least one molecule thick above the lipid layer, this placement was due to the inability of proteins to be found stably within the membrane. Danielli and Davson came up with a sandwich membrane model in the same year (Davson-Danielli model or protein--protein model). According to this model, the surfaces were surrounded by a thin layer of protein on both sides. This observation was an important advance in a better understanding of the compositional nature of biological membranes (46). In 1936 Danielli introduced several membrane models in addition to the paucimolecular model he had created. . He divided the membranes into three as continuous, lipoprotein and mosaic membranes. He said that ion transport in membranes occurred depending on pores, a number of ion transporters, and simple

diffusion (47). Although electron microscopy was invented in 1930, it was not possible to study cell membranes in detail until the 1950s, when higher resolutions were achieved. The transverse sections of the membranes revealed the three-layer membrane structure known as the 'railway'. In this view, which would later be called "Unit membrane", there was a third layer between the two dense layers which was less dense (Figure 1). At that time, it was not yet known which layer of the unit membrane corresponded to which molecule. In 1959, J. David Robertson evaluated the paucimolecular model and suggested that the dark regions were protein layers, while the open area in the middle was equivalent to the lipid layer. That prediction was not exactly accurate. Robertson renamed the paucimolecular membrane model as the "Unit membrane model". In a review in 1964, Brady and Trams noted some of the features of the fluid mosaic model that was valid today. In that paper, they reported that the membrane was composed of lipids and proteins, that proteins entered the membrane and that the lipid component was fluid (48). With the development of freeze-breaking techniques and immuno-electron microscopy techniques, scientists identified isolated membrane proteins and membrane-embedded proteins through antibodies. So, Singer and Nicolson introduced the famous fluid mosaic membrane model in 1972. This model is the most important model in membrane science which has changed and developed until today. Although it has not changed much since its identification, it has been modernized and named as "Modified fluid mosaic model" in the light of the newly obtained data. The fluid mosaic model still holds the distinction of being the most explanatory hypothesis in understanding biological membranes. As is known, the word "mosaic" emphasizes that the membrane is composed of various molecules such as phospholipids, proteins and carbohydrates; the word "fluid" refers to the fact that most of these molecules are mobile (49). This model, which developed in the 1970s and whose foundation remained unchanged, will continue to exist until a new proposal is put forward. Future studies on the cell membrane; It will include membrane modifications to improve certain dysfunctions, including membrane signaling, transport, remodeling, and membrane biosynthesis.

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Authorship Contributions

Concept: M.E., K.T.K., Design: M.E., K.T.K., Data Collection or Processing: M.E., K.T.K., Analysis or Interpretation: M.E., K.T.K., Literature Search: M.E., K.T.K., Writing: M.E., K.T.K.

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Oro-dental and Radiographic Findings of Weyers Acrofacial Dysostosis: Report of a Rare Case

Weyers Akrofasiyal Disostozis'in Ağız-diş ve Radyografik Bulguları: Nadir Bir Olgu Sunumu

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ABSTRACT

Weyers acrofacial dysostosis is a rare type of ectodermal dysplasia syndrome characterized by mild short stature, postaxial polydactyly, dystrophic nails, and dental anomalies (hypodontia, microdontia, taurodontism). In this case report, we present the oral and radiographic findings of a 7-year-old girl consistent with the diagnosis of Weyers acrofacial dysostosis. Through this detailed discussion, we aim to contribute to the literature.

Keywords: Oral findings, polydactyly, syndrome, Weyers acrofacial dysostosis

ÖZ

Hafif boy kısalığı, postaksiyal polidaktili, distrofik tırnaklar ve dental anomaliler (hipodonti, mikrodonti, taurodontizm) ile karakterize otozomal dominant bir bozukluk olan Weyers akrofasiyal disostozis, ektodermal displazi sendromunun nadir görülen bir tipidir. Bu olgu raporunda, 7 yaşındaki kız çocuğunun Weyers akrofasiyal disostozis tanısı ile örtüşen oral ve radyografik bulguları sunulmuştur. Bu ayrıntılı tartışma sayesinde literatüre katkıda bulunmak amaçlanmıştır.

Anahtar Sözcükler: Ağız bulguları, polidaktili, sendrom, Weyers akrofasiyal disostozis

Introduction

Ectodermal dysplasia is a well-known hereditary disorder associated with the abnormal development of structures such as teeth, nails, hair, nerve cells, and sweat glands (1). Weyers acrofacial dysostosis (WAD) is a rare type of ectodermal dysplasia syndrome characterized by mild short stature, postaxial polydactyly, dystrophic nails, and dental anomalies (2). It has been reported to be caused by heterozygous mutation in the *EVC2* and *EVC* genes located on chromosome 4p16.2 (3).

Many phenotypic features of WAD are similar to Ellis-van Creveld (EVC) syndrome, an autosomal recessive disorder. However, WAD is a milder condition compared to EVC and does not include features such as short ribs, thoracic dysplasia,

and congenital heart disease, which are commonly observed in patients with EVC (4).

In this case report, we present the oral and radiographic findings of a 7-year-old girl consistent with the diagnosis of WAD. In the limited number of accessible reports of WAD, oro-dental findings have rarely been encountered. Through this detailed discussion, we aim to contribute to the existing literature.

Case Report

A 7-year-old girl was brought to our clinic by her parents for a dental examination. Her history revealed no consanguinity between the mother, father and the first of the two daughters of the family. The patient showed normal growth with a height of 122

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cm, a weight of 26 kg and no mental retardation. It was observed that the patient had a straight face profile with a marked lower jaw sulcus and dystrophic changes in the hands and toenails. The patient's parent stated that she had one more fingers on both hands and feet at birth, and underwent surgical correction at 9 months of age. Upon questioning, we learned that there was a family history of polydactyly at birth in the hands and feet of the patient's mother, grandfather, as well as her 3-year-old sister, who underwent surgery at 8 months of age.

During the intraoral examination, we observed multiple wide labial frenula and a unilateral posterior crossbite. The saliva flow rate was measured to be 1 mL/min with a pH value of 6. The patient had microdontia with cone-shaped primary incisors and primary molars with atypical cusps. The newly erupting upper incisors, however, were abnormally large with talon cusps. The patient had wide diastemas between the teeth as well as gingival recession in the vestibule in association with the primary canines. Radiographic evaluation showed congenitally missing teeth (permanent mandibular right and left central, right lateral),

taurodontism (permanent mandibular and maxillary first molars), and changes in the direction of tooth germs (permanent mandibular right and left second premolars).

The patient's 3-year-old sibling had an open bite due to the continued use of a pacifier. She also displayed microdontia with cone-shaped primary incisors and primary molars with atypical cusps, large diastemas between the teeth, similar to the patient.

Clinical and radiographic examination of the father showed no oral findings similar to the daughters. Although the patient's mother was found to have a history of polydactyly, she refused our invitation to visit the clinic for clinical examination and did not consent to genetic diagnostic testing.

Dental treatment planning was done and the patients were provided with all the necessary information. The importance of oral care and regular check-ups for maintaining oral health was explained to the patient.

Discussion

Many disorders that require special attention in childhood are described in the literature. One such syndrome is WAD, a rare type of ectodermal dysplasia characterized by polydactyly, dystrophic nails, and dental anomalies. Patients with WAD have been reported to have a normal facial appearance, short stature, dysplastic finger and toenails separated by thick vertical lines, and the presence of extra digits in the feet and hands (2,4-7). Although there was no growth retardation in our patient, the other findings were observed. Family history revealed polydactyly at birth in the hands and feet of the patient's mother, grandfather, and sister.

WAD is usually characterized by dental findings including multiple labial hyperplastic frenula, hypodontia, microdontia, taurodontism, conical teeth, and enamel hypoplasia (2). The patient displayed all these dental findings except enamel hypoplasia, suggesting a diagnosis of WAD.

The differential diagnosis for WAD includes EVC, Witkop and Orofacial Digital syndromes.

It has previously been reported that cardiac malformations occur in approximately 50-60% of patients with EVC with

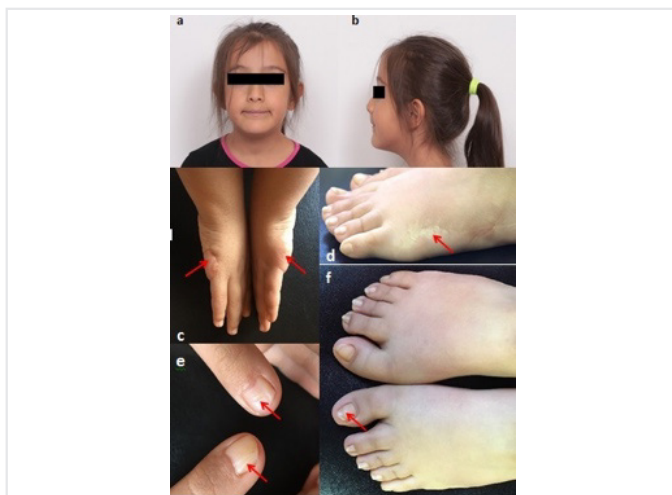


Figure 1. Facial appearance a) Frontal view, b) lateral profile, c, d) Bilateral postaxial polydactyly were removed at birth by surgical operations on both hands and feet, only scars (red arrows) were seen, e, f) Dystrophic hands and toenails



Figure 2. a, b) Intra-oral examination of the patient and (c, d) her sibling



Figure 3. The panoramic radiograph of the patient and periapical film showing the talon cusps

characteristic features of short ribs, thoracic dysplasia, and acromesomelic dwarfism (4). Our patient did not show these characteristic features and there was also no cardiac disturbance. The patient also showed polydactyly, a characteristic of WAD patients. It has previously been reported that polydactyly occurs commonly in the hands of EVC patients but occurs in the feet of only 10% of patients with EVC (4). Oral findings such as multiple hyperplastic frenula, diastemas, taurodontism, and hypodontia (mandibular and maxillary anterior region) observed in our patient are also observed in patients with EVC (8). However, natal and supernumerary teeth are seen in 25-30% of patients with EVC (8) and were not observed in our patient.

Although hypodontia and nail dysplasia, which are known to be characteristic features of Witkop syndrome (9) are seen in our patient, the presence of supernumerary digits helps to differentiate WAD from Witkop syndrome.

Orofacial digital syndrome (OFDS1) is a developmental genetic disorder frequently seen in girls with X dependent dominant transition and characterized by malformation of the oral cavity, face, and fingers (10). While our patient had multiple hyperplastic frenula, a finding commonly seen in OFDS1 patients, she did not show other features characteristic of OFDS1, including the lack of development, hypoplasia of the nasal limbs, mental disability, and polycystic kidney disease. Another distinguishing feature was the presence of dystrophic nails, a finding not observed in patients with OFDS1.

Due to the presence of dental anomalies (hypodontia, taurodontism, macrodont incisors) in the patient, it was explained that the protective and preventive treatments (fluoride and fissure sealant applications, dietary control), oral hygiene procedures, regular dental follow-up were important and necessary dental treatments were performed. It has been stated that there should be periodic follow-up of the teeth due to the changes in the direction of tooth germs. Since there were no parental and patient complaints due to the size and appearance of the anterior teeth, the model analysis was performed, and then necessary tooth interproximal strippings were done.

Although genetic analysis would provide a definitive diagnosis of WAD, the patient's mother did not give consent for genetic testing. The diagnosis of WAD in our patient was supported by family history as well as oral and radiographic findings.

Ethics

Informed Consent: Consent was obtained from the parents of the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Z.K., E.Ö., Design: Z.K., E.Ö., Data Collection or Processing: Z.K., E.Ö., Analysis or Interpretation: Z.K., E.Ö., Literature Search: E.Ö., Writing: Z.K., E.Ö.

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Fournier Gangrene Caused by Migration of Foreign Body from Rectum to Bladder

Rektumdan Mesaneye Migrate Olan Yabancı Cisim Nedeniyle Gelişen Fournier Gangreni

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ABSTRACT

Fournier gangrene is a serious infectious disease with high mortality and morbidity rates characterized by rapidly progressive skin necrosis. Immediate debridement of infected necrotic tissue and broad spectrum antibiotic therapy are the main principles of the treatment. Size of the debrided area, advanced age, colorectal predisposition and renal insufficiency are the factors affecting the mortality. In this case report, we present a rare case of Fournier gangrene caused by migration of foreign body from rectum to bladder.

Keywords: Fournier gangrene, rectum, bladder, foreign body

ÖZ

Fournier gangreni morbidite ve mortalite oranları yüksek, hızlı ilerleyen ve deri nekrozuyla karakterize ciddi bir enfeksiyöz hastalıktır. Acil olarak enfekte nekrotik alanların debridmanı ve geniş spektrumlu antibiyoterapi tedavinin ana prensipleridir. Debride edilen alanın büyüklüğü, ileri yaş, kolorektal predispozisyon varlığı, böbrek yetmezliği mortaliteyi etkileyen faktörler olarak sayılmaktadır. Bu olgu sunumunda çok nadir görülen rektumdan mesaneye migrate olmuş yabancı cisme bağlı Fournier gangreni anlatılmıştır.

Anahtar Sözcükler: Fournier gangreni, rektum, mesane, yabancı cisim

Introduction

Fournier gangrene (FG), first described in 1883, is rapidly progressive necrotizing fasciitis of perineal, perianal and genital areas that requires immediate treatment and rarely seen in women and children (1,2). Although it was first described as idiopathic rapidly progressive gangrene of scrotum and penis in young healthy men, it is more common in middle-aged and older men.

Case Report

An 82-year-old male patient with inadequate self-care who was living alone was brought to our emergency service with decreased

general condition. We could not obtain any information about patient's medical history. The body temperature of the patient was measured as 38.6 °C and laboratory tests revealed an urea level of 210 mg/dL, creatinine level of 4 mg/dL and white blood cell (WBC) level of 21.17 (10³/uL). Patient was diagnosed as having pneumonia and respiratory insufficiency and he was admitted to the intensive care unit as he required respiratory support and intravenous ceftriaxone treatment was started. Four days after admission, extended-spectrum beta-lactamase (+) *E. coli* was isolated from urine culture and antibiotic treatment was changed to intravenous imipenem. Five days after admission, patient had a WBC level of 12.62 (10³/uL) and was consulted to urology

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clinic after detection of a necrotic area in scrotum. Physical examination revealed a 5x5 cm necrotic area with edema and crepitus and we decided to perform urgent surgical debridement.

The necrotic area in the scrotum was debrided. During debridement, a large defect starting from the middle part of corpus spongiosum and urethra was observed and transurethral foley catheter was exposed in this region. Irrigation was performed with physiological saline solution via urethral catheter and it was seen that solution was leaking from anus. On digital rectal examination, rigid, elastic, uniformly contoured tubular foreign body was palpated in rectum. A lower abdominal median incision was made to perform a colostomy. It was observed that bladder was severely contracted and indurated. After the incision of bladder, a rigid pipe 6 cm in length and 5 mm in diameter was detected. It was thought that tube was placed rectally and later migrated to bladder. Object was removed from bladder by applying a small force. Apart from the described object, a 25x20 cm transparent bag and 3 stones approximately 1 cm in diameter were removed from bladder and a 14F Foley catheter was placed as cystostomy (Figure 1). Hartman colostomy was performed and a drain was placed inside abdomen. Wound dressings were changed daily and drain was removed in the postoperative 3rd day. Patient could not recover from life support and died in the postoperative 11th day.

Discussion

FG is a rapidly progressive infectious disease with high morbidity and mortality that requires immediate treatment and more

commonly observed in middle-aged and older men. Disease is usually originated from an infection in the anorectum, urogenital system or skin of the genital regions (3). It has been reported that many factors, such as Diabetes Mellitus, chronic alcoholism, lymphoproliferative diseases, cytotoxic drugs, immunosuppression, poor perineal hygiene, trauma, diseases that disturb urethral integrity as well as urinary tract infections and interventions to the urinary tract have predisposing effects on FG development (4,5). Only one type of microorganism may cause the infection but usually different types of microorganisms coexist at the same time and Streptococcus, staphylococcus and escherichia species are the most common strains in cultures (6). Infection causes obliterative endarteritis in the peripheral vascular structures which results in deterioration of the blood supply of surrounding tissues and in necrosis but necrosis does not progress to the tissue below the fascia. Pain, swelling and hyperemia in the scrotal region are the most common symptoms, accompanied by fever and tachycardia (7). The diagnosis process begins with bringing the disease to mind. On physical examination, detection of skin necrosis and crepitus suggests FG. Imaging methods such as X-ray, ultrasonography and computerized tomography may contribute to the diagnosis by demonstrating air in the tissue. FG is a disease with high morbidity and mortality rates, patients with suspicion of FG should be closely monitored and immediately treated with broad spectrum antibiotics and surgical debridement of necrotic tissue (8). It should be remembered that if there is necrosis in the perineal region, colostomy may be necessary. There is evidence that hyperbaric oxygen therapy can be beneficial after debridement in some patients (9). Frequent and appropriate care of the wound, stabilization of the patient's hemodynamics, blood sugar regulation and nutritional support have significant effects on healing. The size of the debrided area, advanced age, presence of colorectal predisposition, and renal insufficiency are counted as factors affecting the reported mortality rate of 29% (10). Although we performed adequate surgical debridement and gave broad spectrum antibiotics in our case, the patient died. We could not obtain any information about the medical history of the patient but presence of possible comorbidities and the fact that FG etiology was bladder and rectal injury had significant effect on mortality.

Conclusion

Although FG is rare disease that can be treated with immediate surgical debridement and broad spectrum antibiotics, it is a urological emergency with high morbidity and mortality rates. When there is a clinical suspicion of Fournier gangrene, radiological imaging is useful in detecting or excluding possible etiological factors even in patients without a history of genital or anal trauma.

Ethics

Informed Consent: Consent should be obtained for the orphaned, homeless street patient, and exits because of his illness.

Peer-review: Internally and externally peer reviewed.



Figure 1. 25x20 cm transparent bag, rigid pipe 6 cm in length and 5 mm in width, and 3 stones approximately 1 cm in diameter which were removed from bladder

Authorship Contributions

Concept: B.D., M.O.Ş., Design: V.Ş., Literature Search: C.E., B.D., A.İ., Writing: B.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Porcelain Laminate Veneer Applications in Upper Anterior Region: Case report

Üst Ön Bölgede Porselen Laminate Veneer Uygulamaları Olgu Bildirimi

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ABSTRACT

Recently, effects of rapidly developing technology have been seen in the dentistry. Advances in materials enable minimally invasive treatments in which dental tissue is preserved in order to provide esthetics. Porcelain laminate veneer technique, one of the minimally invasive treatments, is the most popular treatment today. Porcelain laminate veneers stand out with having translucency close to tooth and high biocompatibility properties. In this case report, stages of porcelain laminate veneer technique are described in detail.

Keywords: Porcelain, laminate, esthetic

ÖZ

Son zamanlarda hızla gelişen teknolojinin dişhekimliği alanında da yansımaları görülmektedir. Materyallerdeki gelişmeler estetiğin sağlanabilmesi için diş dokusunun korunduğu minimal invaziv tedavileri mümkün kılmaktadır. Minimal invaziv tedavilerden biri olan porselen laminate veneer tekniği günümüzde en popüler olan tedavi şeklidir. Porselen laminate veneerler dişe yakın translüsite göstermeleri ve yüksek biyouyumluluk özellikleriyle öne çıkmaktadır. Bu olgu sunumunda, porselen laminate veneerlerin yapım aşamaları ayrıntılarıyla anlatılmaktadır.

Anahtar Sözcükler: Porselen, lamina, estetik

Introduction

Esthetic problems in the front area are usually caused by gaps between teeth, discoloration, anomalies of shape, structure and position disorders that occur due to various reasons. These aesthetic problems can be treated with composite or porcelain laminate veneers, complete ceramic restorations, vital and devital whitening methods and combined methods. Porcelain laminate veneer technique is a conservative method and can meet esthetic expectations at a high rate due to its longer life than composite laminate veneers and it results in more esthetic appearance compared to composite laminate veneers (1,2).

In this case report, all stages of treatment, involving porcelain laminate veneer, of a female patient, who was admitted to our clinic with the request of removing the esthetic complaints on her front teeth, was described

Case Report

A 30-year-old female patient was admitted to our clinic because the old composite restorations on her upper front incisors did not meet her esthetic expectations (Figure 1).

An intra-oral examination of the patient revealed that old restorations had lost edge alignment and secondary bruises had formed. After occlusion control, radiographic examination and evaluation of the patient's habits, it was decided to perform laminate veneer restorations on teeth 11-12-21-22 using lithium disilicate glass ceramic material. First, the consent form was taken from the patient. The tooth color was determined by using the Vitapan Classical Shade Guide (Vita Zahnfabrik, Germany) in daylight before the teeth were introduced to the preparation stage. Before starting the preparation, local anesthesia was performed to

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the related teeth. After all of the old composite restorations were removed, the rotten tissues were cleaned (1,3). Preparations were made using chamfer frez (G&Z Instruments, Austria), just above the gum, approximately 0.5 mm wide (Figure 2). After gingival retraction cord with the number #00 (Ultradent, A.B.D.) was placed, final cutting was done and lacquer discs (Sof-Lex, 3MEspe, A.B.D.) were used to ensure smooth cutting. Plaster was transferred to the model with occlusal records by making measurement with additional type of silicone measuring agent (Variotime, Kulzer, Germany) after the preparation was completed.

The cementation process was performed using the Variolink Esthetic LC (Ivoclar,Vivadent, Liechtenstein) set. To check the color harmony before starting the simentation process, the color selection of the bonding cement with the testing cement was made. To the inner surface of the veneers, 10% hydrofluoric acid (Ultradent, A.B.D.) was applied for 20 seconds, then washed, and then dried with veneers air spray. Then cement (Monobond Plus, Ivoclar Vivadent, Liechtenstein) was applied to the veneers for 60 seconds. To teeth surfaces, 37% phosphoric acid (Total Etch, Ivoclar Vivadent, Liechtenstein) was applied for 15 seconds, then washed and dried. Then bonding agent was applied to all tooth surfaces and polymerized with 20 sec light according to the manufacturer's instructions. The bonding cement suitable for tooth color was applied to the inner surface of the veneers and placed on the tooth surface with a slight finger

pressure and initial polymerization was made with a LED light source (Valo, Ultradent, A.B.D) for 3 sec. The residue of the bonding cement was removed, the gingival sulcus was checked with dental floss, glycerin was applied to the gingival margin area and polymerization was completed by applying 40 sec light to each area (Figure 3). Edge alignment of laminate veneers was re-checked with eye and sond and occlusal alignment was re-checked with articulation paper (Figure 4, 5). The patient was called to control laminate veneers at the end of one year. Surface roughness, border alignment and coloration of laminate veneers, and secondary caries were evaluated (Figure 6).No problems were observed between restorations and teeth in terms of edge alignment.The restorations were determined to be esthetically good.

Discussion

Both composite and porcelain laminate veneer restorations can be applied in esthetic applications in the anterior region. Porcelain laminate veneer causes less material removal from the surface of the teeth, shows better color stability and biocompatibility and has more esthetic appearance compared with composite laminate veneer and it is a quite frequently used type of restoration (1,2).

Although more successful results are obtained with porcelain laminate veneers in terms of meeting esthetic expectations; they require more precise work, their repair is more difficult, they



Figure 1. Intra-oral image of the patient before treatment



Figure 2. The image of the prepared teeth



Figure 3. Cementation phase



Figure 4. Post-cementation image of porcelain laminate veneers

are more sensitive to breakage and their cost is higher compared with composite veneers which are among the disadvantages of porcelain laminate veneers (4,5).

Direct composite veneer applications may be preferred due to lack of laboratory stages, fast results and low cost in patients whose economic status is taken into account (6). However, although composite laminate veneers provide an acceptable esthetic result, they cannot provide as much light transmission as porcelain laminate veneers.

When evaluated in terms of microleakage and edge alignment, it is accepted that porcelain laminate veneers are superior to composite veneers (7,8). In addition to these, porcelain laminate veneers have more resistance to erosion, show higher attachment to enamel and are more resistant to stress and shear forces compared with composite veneers (8,9). These are the reasons why porcelain laminate veneers are more preferred.

Compared to full ceramic crowns, they are preferred because they require a smaller amount of cutting.

The most important stage affecting the success of porcelain laminate veneers in the long term is adhesive cementation. The structure and properties of the adhesive used should be well known and applied accordingly. When light-activated adhesive systems and dual cure systems are compared, light-activated

adhesives have a prolonged curing times and very good color stability which are among the reasons why they are preferred more than dual cure systems (10). During the cementation phase, it is also very important to remove the residue of the bonding cement which can cause excessive irritation in gums.

Porcelain laminate veneer restoration is a conservative approach resulting in good esthetic results, especially in patients with limited pathology to enamel tissue in case of determining correct indication in esthetic rehabilitation of the anterior region and of careful performing the application stages.

Ethics

Informed Consent: First, the consent form was taken from the patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Z.B.K., N.D., Design: Z.B.K., N.D., Data Collection or Processing: Z.B.K., N.D., Analysis or Interpretation: Z.B.K., N.D., Literature Search: Z.B.K., N.D., Writing: Z.B.K., N.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Figure 5. Finished porcelain laminate veneers



Figure 6. Image of porcelain laminate veneers at the end of 12 months follow-up



Spina Iliaca Anterior Superior Avulsion Fracture: A Case Report and Review of the Literature

Spina İliaka Anterior Superior Avülsiyon Kırığı: Olgu Sunumu ve Literatüre Genel Bakış

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ABSTRACT

Spina iliaca anterior superior (SIAS) avulsion fracture is a type of injury that is rare and possible to be overlooked in emergency services. SIAS is the insertion area of the Tensor fascia lata and Sartorius muscles, which are two of the hip flexor muscles and forceful contractions of these muscles which can be observed while kicking a ball, can lead avulsion fractures of SIAS, especially among adolescents. In our case, a 16-year-old male athlete attended the emergency service with a movement restriction and severe pain causing limping that started as an instant pain in the left hip after kicking the ball during a soccer game. It was misdiagnosed as soft tissue injury and no radiological imaging was performed. After plain radiography of the hip was performed in control appointment, the patient was diagnosed as having SIAS avulsion fracture, and a complete and pain-free range of motion was achieved after a conservative treatment of nonsteroid anti-inflammatory drugs, three weeks rest along with cold therapy and walking with crutches without full weight bearing. Even though SIAS fractures are generally treated with conservative methods, they can be misdiagnosed as soft tissue injury in case of poor physical examination and especially displaced fractures may cause clinical problems.

Keywords: Avulsion fracture, pelvis, apophysis, spina iliaca anterior superior

ÖZ

Spina iliaca anterior superior (SIAS) avülsiyon kırıkları nadir ve acil servis değerlendirmesinde gözden kaçabilecek yaralanmalardır. SIAS, kalça fleksör kaslarından olan tensor fasia lata ve sartorius kaslarının başlangıç bölgesidir. Özellikle adölesanlarda topa vurma esnasında bu kasların kuvvetli kontraksiyonlarıyla avülsiyon kırıkları gözlemlenebilir. Olgumuz, 16 yaşında erkek sporcu, futbol oynarken topa vurma sonrası sol kalçasında ani ağrı başlayan, topallamaya neden olacak ağrı ve hareket kısıtlılığı nedeniyle acil polikliniğe başvurmuş ve fizik muayenede yumuşak doku travması olarak değerlendirilmiştir. Tarafımıza başvuran hastanın poliklinik kontrollerinde çekilen grafilerinde SIAS avülsiyon kırığı tanısı konuldu. Hastaya non-steroidal anti-enflamatuvar ilaç, tam yük vermeden koltuk değnekleriyle mobilizasyon ve soğuk uygulama ile yaklaşık 4 hafta konservatif tedavi uygulandı. Birinci ay kontrolünde tam ve ağrısız eklem hareket açıklığı olduğu ve palpasyonda ağrı olmadığı saptandı. SIAS avülsiyon kırıkları çoğunlukla konservatif olarak tedavi edilse de iyi fizik muayene yapılmadığında yumuşak doku travması ile karışabilmekte ve özellikle deplasman miktarı fazla olan kırıklar klinik sorunlara sebep olabilmektedir.

Anahtar Sözcükler: Avülsiyon kırığı, pelvis, apofiz, spina iliaca anterior superior

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Introduction

Spina iliaca anterior superior (SIAS) avulsion fractures are rare and often affect young athletes with non-ossified cartilaginous growth plates during the adolescent period. In this age group, the anterior and posterior edges of the pelvis have lower trabecular density and the growth plates are more susceptible to trauma due to the relative strengthening of the musculotendinous junction with hormonal status (1).

Diagnosis can be made with good anamnesis, physical examination and X-ray. However, these injuries can often be confused with soft tissue trauma. This can lead to improper treatments and a delay in returning to the sport. Although conservative treatments involving rest, non-steroidal anti-inflammatory drugs (NSAIDs), mobilization with crutches without full weight bearing and cold therapy are sufficient, surgical treatment is rarely required (2).

Case Report

An amateur, male, 16-year-old football player with 178 cm tall, 70 kg weight and no known additional disease felt a sudden and sharp pain in the left hip after kicking the ball while he was playing football on the field. He could not continue playing and was admitted to the emergency orthopedics outpatient clinic. The patient was assessed as soft tissue trauma during physical examination and the patient was offered outpatient control. The patient was admitted in the outpatient clinic with complaints of pain in the left hip and difficulty walking. The patient's physical examination revealed painful left hip joint movements, painful limping when walking, and sensitivity on the iliac wing, especially on the left SIAS. The patient was in the 4th stage according to the Tanner's classification.

An avulsion fracture of the left SIAS apophysis with minimal displacement was detected in the X-ray of the patient (Figure 1). The degree of skeletal maturation was stage 3 according to the Risser's classification. Magnetic resonance imaging showed avulsion fracture in the left SIAS apophysis, and no additional soft tissue trauma was detected (Figure 2).

When the patient's examinations were evaluated, the displacement of approximately 3 mm was found to be suitable for conservative treatment. During the acute period, NSAIDs, cold application and mobilization with crutches without full weight bearing after the first 3 days of bed rest were recommended. The first-month control examination showed that the left hip joint range of motion was complete and the left SIAS was painless with palpation. The control X-ray showed that the apophysis of SIAS fully healed (Figure 3).

Discussion

Apophyses are specialized ossification centers that enable the transverse growth of bones and respond to tensile strengths. Sticking places of the major muscle groups and the tendons are located on the apophyses. These regions are the weakest regions of the musculoskeletal junction in the adolescent age group, and trauma mechanisms that cause muscle injury in adults result in



Figure 1. Pelvis AP X-ray image of the patient in his initial arrival. Avulsion fracture is observed in the apophysis of the left SIAS

SIAS: Spina iliaca anterior superior

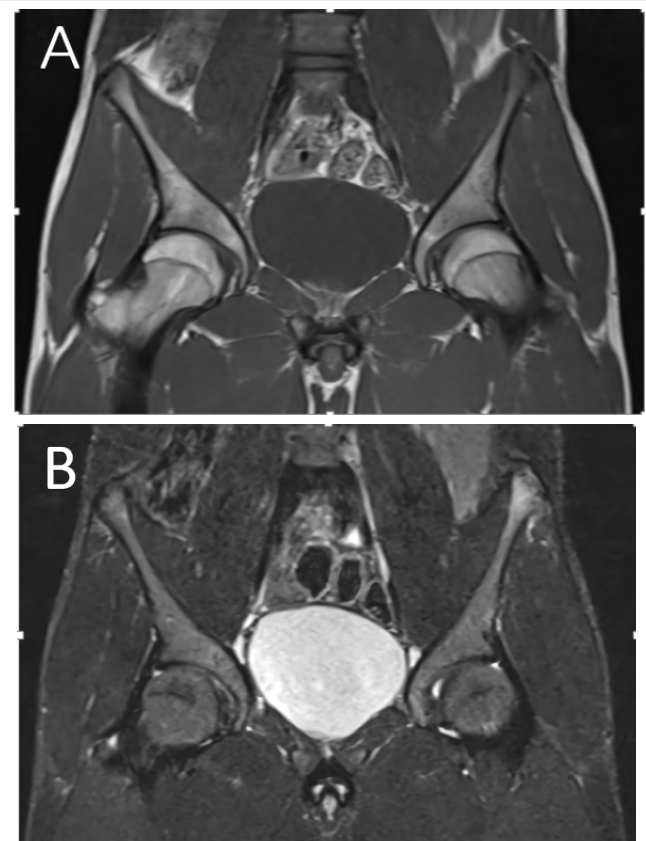


Figure 2. A) Pelvis MRI T1 sequence of the patient in his initial arrival. The fracture line evident on the left SIAS is seen as hypointense B) In pelvic MRI T2 sequence, the edematous region on the left SIAS is seen as hyperintense

SIAS: Spina iliaca anterior superior, MRI: Magnetic resonance imaging

apophyseal cartilaginous avulsion damage in this age group (3). Characteristics including age of 16 and Tanner Stage 4 in our patient were in accordance with the literature.

Pelvic avulsion fractures are among the hardest to diagnose because they are rare. In addition, in recent years, more young people engaged in professional sports have increased the frequency of these fractures relatively. SIAS avulsion fractures account for 15-19% of rare pelvic avulsion injuries (4). Avulsion fractures of this region are caused by severe contractions of the muscles that hold here, especially during kicking the ball in football players or during the initial phase of running in tennis players (Figure 4). Our patient also suffered an injury while kicking the ball while playing football.

Pelvic avulsion fractures are rare and often confused with muscle spasm or soft tissue trauma. It has been reported in the literature that these fractures can even be mixed with tumor in later times (4). Increased pain with activity, edema and tenderness on the bone during clinical examination should bring avulsion fractures to mind (5). Misdiagnosing these fractures in professional

athletes who want to return to the sport early can cause chronic unknown hip pain and make this pain last longer.

Surgical or conservative treatment methods may be preferred in SIAS avulsion fractures. Although the long-term results of these two methods are similar, conservative treatment comes to the fore (6). After 3 days of bed rest, satisfactory results can be obtained with mobilization with crutches and conservative treatment with NSAIDs. The most common complications of conservative treatment are heterotopic ossification and pseudoarthrosis. Surgical treatment is preferred in cases where the fracture displacement is more than 1.5-2 cm and the separated part is larger (6-8). Although surgical treatment has the advantage of early return to sport, especially in athletes, the need for general anesthesia and the possibility of development of mareljia paraesthetica are among the disadvantages (7). In our patient, pain-free recovery was observed in a month with conservative treatment and sportive activities were started. The clinical outcome of our patient is similar with the literature showing that conservative treatment is sufficient for pelvis avulsion fractures with minimal displacement in athletes.

Since SIAS avulsion fractures can often be confused with soft tissue trauma, diagnosis is not always possible. Proper recognition and treatment of these injuries are important for preventing morbidity such as osteonecrosis and lack of bone repair (9).

Ethics

Informed Consent: A consent form was completed by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: M.A.P., C.B.D., M.U., İ.T., Design: M.A.P., C.B.D., M.U., İ.T., Data Collection or Processing: M.A.P., C.B.D., M.U., İ.T., Analysis or Interpretation: M.A.P., C.B.D., M.U., İ.T., Literature Search: M.A.P., C.B.D., M.U., İ.T., Writing: M.A.P., C.B.D., M.U., İ.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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Figure 3. Pelvis AP X-ray in the first month. The left SIAS avulsion fracture appears to heal
SIAS: Spina iliaca anterior superior

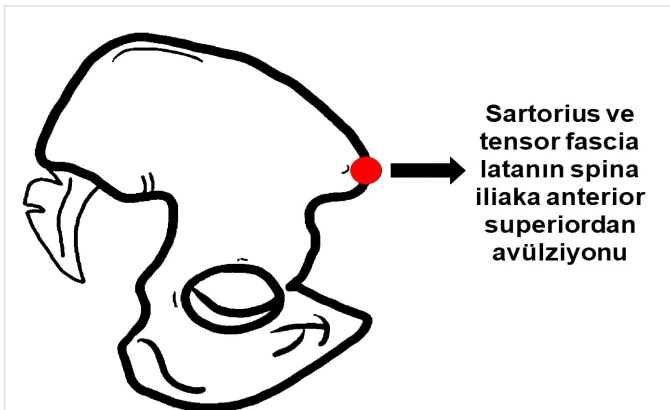


Figure 4. Schematic view of SIAS avulsion fractures.
SIAS: Spina iliaca anterior superior

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Boneless Maxillary Reconstruction

Kemiksiz Maksilla Rekonstrüksiyonu

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ABSTRACT

Objective: Although the midface is supported by maxillary bone, reconstruction of maxillary bony defects does not always require osseous reconstruction. A series of maxillary facial defects of moderate to severe sizes (Brown and Shaw 4-6) uniformly reconstructed with myocutaneous free flaps is presented.

Methods: Retrospective analysis was done for consecutive 10 cases between 2013-18. Seven of the cases had defects caused by oncological resection and 3 defects caused by trauma. Free vertically oriented rectus abdominis (fVRAM) flap was used to reconstruct these defects.

The mean age of patients was 42.9 years (range=20-71 years). All flaps survived and 2 flaps had small skin island problems. Rapid recovery, low morbidity, acceptable oral competency, and satisfactory cosmetic appearance were obtained with the reconstruction using fVRAM flaps.

Conclusion: According to our limited experience, acceptable reconstruction of extensive maxillary defects can be done with using only soft tissue flap, which is versatile and safe.

Keywords: Maxillectomy, midface, rectus abdominis myocutaneous flap, facial defect, soft tissue reconstruction

Level of Evidence: IV

ÖZ

Amaç: Maksiller kemik orta yüzün iskeletsel desteğini oluşturmakla beraber, kemik doku kullanılmadan da orta yüz rekonstrüksiyonu yapılabilir. Bu amaçla orta yüz bölgesinin orta ila şiddetli boyutlardaki (Brown ve Shaw 4-6) defektlerinde kas deri serbest flebini kullandık

2013-18 yılları arasında ardışık 10 vaka için retrospektif analiz yapıldı. Olguların yedisi onkolojik rezeksiyon, üçü travma nedenli idi. Tüm olgularda serbest vertikal rektus abdominis kas deri flebi kullanıldı

Yöntemler: Hastaların yaş ortalaması 42,9 idi (20-71). İki flepte deri adasında küçük problemler dışında tüm flepler sorunsuz iyileşti. Bu çalışmada, hızlı iyileşme, düşük morbidite, kabul edilebilir oral yetkinlik ve tatmin edici kozmetik görünüm elde edildi

Sonuç: Sınırlı tecrübemize göre, orta yüzün kemik içeren orta-geniş defektlerinde sadece yumuşak doku içeren rekonstrüksiyon kabul edilebilir bir seçenektir.

Anahtar Sözcükler: Maksillektomi, orta yüz, rektus abdominis kas deri flebi, defekt, yumuşak doku onarımı

Kanıt Düzeyi: IV

Introduction

The maxilla is the most important bony structure of the midface, extending between the zygomatic bone, the orbit, and the upper teeth, which is like a six-walled pyramide. It is vulnerable to

midfacial trauma because of the buttresses that extend around the bone and inside there is a sinus contains 2-4 mL of air. Midfacial tissue losses caused by trauma or oncological resections of skin, soft-tissue, and bone may not be life-threatening, but can have

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serious functional and esthetic consequences (1,2). The complex three-dimensional structure of the region requires careful and specialized reconstruction to obliterate dead space and re-establish the support features.

Bony deficiency can be filled with a bulky soft tissue flap to obliterate the dead space and to provide the competency of the oral cavity without any osseous component. The major aesthetic challenge is the provision of adequate cheek volume to improve the hollow and retracted skin appearance. Reconstruction of palatomaxillectomy defects using only soft tissues were presented and good functional and cosmetic outcomes were reported. This approach is not only a salvage option, but also (in selected cases) a quick, durable, and safe primary reconstructive procedure associated with minimal donor site morbidity and good resistance to the side-effects of later adjuvant radiotherapy (RT) (3).

We presented the use of a free vertical rectus abdominis myocutaneous (fVRAM) flap for reconstruction of Class IV, V, and VI midfacial defects according to the Brown and Shaw (B&S) classification (4).

Methods

Retrospective analysis was done for consecutive 10 cases, treated in Bezmalem Vakıf University Hospital, Department of Plastic, Reconstructive and Aesthetic Surgery, between 2013-2018. All patients had class IV, V, or VI midface defects according to the B&S classification accompanied by large losses of soft tissue and skin. All patients received fVRAM flaps with variable size of skin island. Resection and reconstruction were performed by the same plastic surgery team. Polypropylene mesh was used for donor site closure in all patients

This study was approved by the Bezmalem Vakıf University Hospital Institutional Review Board and all participants signed an informed consent agreement.

Results

The male:female ratio was 1:1. Seven defects were associated with tumor resection and 3 were secondary to trauma. Three out

of 7 oncology patients had squamous cell carcinomas, 2 soft-tissue sarcomas and 2 basal cell carcinoma. The mean ages of the oncological and trauma patients were 51 (range=28-71) and 24 (20-27) years, respectively. The overall mean age was 42.9 (20-71) years. B&S class VI defects were present in 4 cases, class V defects in 4, and class IV defects in 2. The mean hospitalization period was 28.7 (14-61) days (Table 1).

One flap skin island was lost on day 6 postoperatively because of neck hyperextension and rupture of the anastomosis during ocular examination. He was a Syrian civil war victim, who was injured by a gunshot. However, some of the muscle bulk remained healthy and the skin defect was reconstructed using a Mustardé cheek flap. In second case, early re-exploration was required at the day after surgery, because of venous congestion of the flap. A hematoma was encountered and although appropriate drainage was done, the skin island was lost. All other flaps survived without any complications (Figures 1, 2). No donor site morbidity was seen.

All oncological cases received postoperative RT. Late tumor recurrences developed in two patients with sarcoma who were then threatened with adjuvant chemoradiotherapy. Both eyes were



Figure 1. Above are the preoperative, immediate postoperative and postoperative (after 1 month) views of Case 3. Below are the preoperative, early postoperative and postoperative (after 12 months) views of Case 6

Table 1. Patients' demographics, defect sizes, orbital status, hospitalization, follow-ups and flap results

No	Sex	Age	Etiology	Defect (B & S)	Orbita	Hospital stay	Follow-up	Results Flap survival	Fonctional	Aesthetic
1	M	27	Gunshot	VI	Preserved	32 d	2 m	Partial loss	Good	Fair
2	M	25	Gunshot	IV	Exanterated	29 d	2 m	N/A	Good	Good
3	M	20	Gunshot	V	Preserved	16 d	1 m	N/A	Good	Good
4	M	56	SCC	IV	Preserved	28 d	4 m	Partial loss	Good	Fair
5	F	53	Sarcoma	V	Exanterated	61 d	5 m	N/A	Good	Fair
6	M	49	SCC	IV	Preserved	26 d	14 m	N/A	Good	Good
7	F	71	BCC	VI	Exanterated	14 d	3 m	N/A	Good	Fair
8	F	39	SCC	IV	Preserved	15 d	6 m	N/A	Good	Good
9	F	61	BCC	V	Preserved	17 d	3 m	N/A	Good	Good
10	F	28	Sarcoma	V	Exanterated	49 d	3 m	N/A	Fair	Fair

SCC: Squamous cell carcinomas, BCC: Basal cell carcinoma



Figure 2. Above are the preoperative, intra-operative, early postoperative and postoperative (after 5 months) views of Case 5. Below are the preoperative, intra-operative, early postoperative and postoperative (after 3 months) views of Case 7

preserved with normal visual function in 6 cases, remaining 4 cases underwent one sided orbital exenteration. Although no dental rehabilitation was done, acceptable aesthetic appearance with oral competency was obtained in all cases.

Discussion

The midface is one of the most important facial regions, playing major roles in terms of function and appearance. The complex structure of the maxilla must be considered while choosing a method of midface reconstruction (2-6). Osseous reconstruction is not necessary for functional and supportive features (7). Moreover, structural bony repair can be ignored and cavity obliteration using healthy soft tissue may in fact be ideal. The important steps leading to successful midface reconstruction may be counted as proper wound closure, obliteration of the palatamaxillectomy defect, supporting of orbital base (if the globe is preserved), obliteration of the orbital cavity (if the globe is exenterated), provision of a barrier between the anterior cranial fossa and the nasal sinuses, separation of oral-nasal cavities and restoration of the facial contour, respectively.

Extensive midfacial defects are usually caused by high-energy gunshots or major tumor resections. Reconstructions that respect the anatomical extensions and appearance of the midface afford reliable and effective results (8). A large number of pedicled and free flaps have been used by plastic surgeons to reconstruct complex defects (5-7,9-12). Fasciocutaneous flaps may be adequate to repair defects involving minimal soft-tissue loss (8). Osteocutaneous flaps (11,13-15), myocutaneous flaps (1,4), osteomyocutaneous flaps (16-18), or combined flaps (10,19) have been used according to the defect components. We prefer to use boneless soft tissue flaps in all cases.

Massive tumor resection and RT are always associated with long-term risks of complications such as collapse, contraction, entropion/ectropion, and contour irregularities (1,5,7). Adjuvant RT triggers soft-tissue contraction, fibrosis, and osteoradionecrosis. Bulky soft tissue flaps may improve the negative effects of radiation (20). Osteocutaneous flaps afford

the best osseous support for future dental reconstruction but adjuvant RT is a factor which complicates outcome and is also associated with a risk of osteoradionecrosis (1,13,20). In high energy gunshot injuries more efforts should be required to find appropriate vessel for free flaps.

However, osteocutaneous flaps yield good esthetic and functional results after maxillary reconstruction, the soft-tissue component of it lacks adequate bulk and the pedicle is not sufficiently long to allow contact with neck vessels in the absence of vein grafting or placement of a flow-through flap, but a boneless soft tissue flap has a long pedicle enables graft anastomosis to the neck vessels without the need for vein grafting or a flow-through flap. Many of our cases underwent adjuvant RT without any side-effects. Even our follow-up period was not long enough to get late conclusion, it was enough in duration to see the ultimate effects of radiation on the flap. In addition to that, soft-tissue flaps afford simple, rapid, and effective wound-healing.

Large muscle flaps, such as rectus abdominis (RA) and latissimus dorsi (LD) are used to reconstruct large defects. Disadvantages of the LD musculocutaneous flap are requirement of patient repositioning and increasing of the operation time. Superiorities of the RA flap are sufficient bulk of muscle and skin, reliable pedicle anatomy and 2-team work to save time (21-23).

The anterolateral thigh (ALT) flap is considered to be a workhorse flap for reconstruction of maxillary defects. However, the use of ALT flap to repair extensive defects is associated with significant donor site morbidity, but mismatch of the texture and color and in extensive cases insufficient bulk are potential problems.

We prefer to use fVRAM flaps to avoid patient repositioning during operation, and long pedicle of it. If it is the first choice for patients scheduled for later RT, some volume lose can be expected.

In patients with massive defects that expose the base of the skull, construction of a barrier between the oropharyngeal area and the base of the head is essential to prevent bacterial contamination of the brain. Muscle-skin flaps with well-vascularized tissue are ideal in this context; the bulky soft tissue forms a strong barrier supported by the robust blood supply (24).

We did not compare outcomes by defect site or size, because substantial amount of cases were successful. Since all cases were treated with the same type of flap, no statistical analysis was performed. However, our data presented here provided subjective measurements of outcomes, since evaluations were done qualitatively, not quantitatively. We found acceptable support in this study to our initial hypothesis regarding the important aspects of the reconstructive process in terms of oral competence, globe support, obliteration of the defect i.e., palatal reconstruction.

In conclusion, maxillary defects require different levels of skin, soft-tissue, and bone reconstruction, depending on the type of defect. Free tissue transfer is the most effective and reliable method when treating complex defects. The fVRAM flap allows

reconstruction in three dimensions and is safe and versatile when placed in cases with class IV, V, and VI midfacial defects involving extensive loss of soft tissue.

Ethics

Informed Consent: This study was approved by the Bezmalem Vakif University Hospital Institutional Review Board and all participants signed an informed consent agreement.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Concept: O.K., E.G., İ.M.K., K.Y., Design: O.K., E.G., İ.M.K., K.Y., Data Collection or Processing: O.K., E.G., İ.M.K., K.Y., Analysis or Interpretation: O.K., E.G., İ.M.K., K.Y., Literature Search: O.K., E.G., İ.M.K., K.Y., Writing: O.K., E.G., İ.M.K., K.Y.

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