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All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

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Book section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR,

editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.

Books with a single author: Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or technical report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study KidneyInt: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki Öğrencilerin Beslenme Durumları, Fiziksel Aktivitelerive Beden Kitle İndeksleri Kan Lipidleri Arasındaki Ilişkiler. H.Ü. SağlıkBilimleriEnstitüsü, DoktoraTezi. 2007.

Manuscripts accepted for publication, not published yet: Slots J. The microflora of black stain on human primary teeth. Scand J Dent Res. 1974.

Epub ahead of print articles: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. DiagnIntervRadiol. 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Manuscripts published in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlElD/cid.htm.

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CASE REPORTS

RESEARCH / ARAŞTIRMA
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RETROSPECTIVE ANALYSIS OF PEDIATRIC HYDROCEPHALUS PATIENTS TREATED WITH ENDOSCOPIC THIRD VENTRICULOSTOMY

PEDİATRİK YAŞ GRUBUNDA ENDOSKOPİK ÜÇÜNCÜ VENTRİKÜLOSTOMİ YAPILAN HASTALARIN RETROSPEKTİF ANALİZİ

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ABSTRACT

Objective: Ventriculoperitoneal (VP) shunt and endoscopic third ventriculostomy (ETV) are commonly utilized surgical interventions for managing hydrocephalus. This study aimed to analyze ETV procedures performed on patients under 17 years of age, focusing on demographic factors such as age and gender, etiological considerations, surgical complications, and the necessity for VP shunt placement.

Material and Method: A retrospective study was conducted on pediatric patients who underwent ETV for hydrocephalus at the Department of Neurosurgery, Istanbul Faculty of Medicine, Istanbul University, spanning from January 2015 to June 2022. The study encompassed 44 patients aged 17 years or younger, with assessments made retrospectively based on clinical and radiological outcomes.

Result: Among the 44 patients subjected to ETV for hydrocephalus, 24 were female (54.5%) and 20 were male (45.4%), with a mean age of 7.3 years. The most prevalent presenting symptom was headache, reported by 11 patients (25%), followed by increased head circumference in 10 patients (22.7%). The primary etiology of hydrocephalus was intracranial tumors (34%). In five patients (11.3%), ETV was performed to address shunt malfunction following a prior VP shunt procedure. Regression of hydrocephalus occurred in 30 patients (68.1%), while 14 patients (31.8%) necessitated a subsequent VP shunt placement. Postoperative wound complications were documented in five patients (11.3%).

ÖZET

Amaç: Hidrosefali ameliyatlarında ventrikülo-peritoneal (V/P) şant ve endoskopik üçüncü ventrikülostomi (EÜV) sıklıkla tercih edilen cerrahilerdir. Çalışmamızda 17 yaş altında EÜV yapılan hastaların yaş ve cinsiyete göre dağılımlarını, cerrahi komplikasyonlarını ve V/P şant ihtiyaçlarının incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Ocak 2015-Haziran 2022 tarihleri arasında İstanbul Üniversitesi İstanbul Tıp Fakültesi, Beyin ve Sinir Cerrahisi Anabilim Dalı'nda 17 yaş altında EÜV ameliyatı yapılan 44 hasta çalışmaya dahil edilmiştir. Hastaların klinik ve radyolojik sonuçları retrospektif olarak değerlendirilmiştir.

Bulgular: Endoskopik üçüncü ventrikülostomi yapılan hastaların 24'ü kadın (%54,5), 20'si erkekti (%45,4). Hastaların ortalama yaşları 7,3 idi. En sık hastaneye başvuru şikâyetleri 11 hastada saptanan (%25) baş ağrısı ve 10 hastada saptanan(%22,7) baş çevresinde artıştı. İncelenen hastalar arasında hidrosefalinin en yaygın nedeni intrakraniyal tümördü (%34). Daha önce V/P şant operasyonu yapılan ve takiplerinde şant disfonksiyonu gelişen beş (%11,3) hastaya EÜV yapıldı. EÜV yapılmış 44 hastanın 30'unda (%68,1) hidrosefalinin gerilediği görülürken, 14 hasta (%31,8) ikinci kez opere edilerek V/P şant takıldı. EÜV sonrası ikinci kez opere edilerek V/P şant takılan 14 hastanın 7'sine (%50) ilk ayda, 4'üne (%28,5) ise EÜV sonrası 1-3 aylık süreçte V/P şant takıldı. EÜV yapılan hastaların beşinde (%11,3) postoperatif yara yeri problemi geliştiği görüldü.

Sonuç: Geleneksel şant cerrahisine kıyasla EÜV komplikasyon riskinin daha düşük olması ve operasyon sonrası yaşam kalitesini

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Conclusion: ETV offers distinct advantages over traditional shunt surgery, including reduced complication risks and enhanced quality of life. Although the success of ETV in children can be affected by various factors, the procedure was demonstrated as safe and effective in many pediatric patients.

Keywords: Hydrocephalus, endoscopic third ventriculostomy, ventriculoperitoneal shunt

arttırması gibi birçok avantaj sunar. Çocuklarda ETV'nin başarısı çeşitli faktörlerden etkilenebilmesine rağmen prosedürün birçok pediatrik hastada güvenli ve etkili olduğu gösterilmiştir.

Anahtar Kelimeler: Hidrosefali, endoskopik üçüncü ventrikülostomi, ventrikülоperitoneal şant

INTRODUCTION

Pediatric hydrocephalus can arise from various causes such as congenital defects, infections, tumors, or brain injuries. If left untreated, hydrocephalus can lead to developmental delays, impaired cognitive function, and potentially fatal outcomes (1). Therefore, it is essential to promptly diagnose and manage this condition to prevent long-term complications (2-4). Endoscopic third ventriculostomy (ETV) is a minimally invasive surgical technique wherein an endoscope is allowed to visualize the third ventricle and create an opening in its floor, facilitating the unrestricted flow of cerebrospinal fluid (CSF) and bypassing any obstructions (5). ETV is increasingly favored over traditional ventriculoperitoneal (VP) shunt procedures due to its lower risk profile. While shunts have historically been utilized, they pose risks of complications such as infections, disconnections, and malfunctions (6). In contrast, ETV is a one-time intervention that does not involve the insertion of foreign materials into the body (7). In this study, we present a series of pediatric hydrocephalus cases treated with ETV at a single center.

MATERIALS and METHODS

Patient population

We conducted a retrospective analysis involving pediatric patients who received treatment with ETV for hydrocephalus at the Department of Neurosurgery, Istanbul Faculty of Medicine, Istanbul University, spanning from January 2015 to June 2022. A study comprised a total of 44 patients aged 17 years or younger. Data for the analysis were sourced from hospital records, encompassing details such as age, gender, family medical history, presenting symptoms, neurological examination results, preoperative and postoperative radiological findings, postoperative complications, and follow-up outcomes. Patients who underwent ETV and those lacking adequate follow-up at our institution were excluded from the study. Approval for this research was obtained from the ethics committee of İstanbul University, İstanbul Faculty of Medicine (Date: 11.05.2023, No: 1755581), ensuring the confidentiality of patient identities.

Surgical technique

The ETV procedure is conducted under general anesthesia on a patient positioned supine, without requiring head fixation. The procedure commences with planning a U-shaped incision centered at Kocher's point, located 3 cm laterally from the midline and 1–2 cm anterior to the coronal suture. Sterile precautions are observed during preparation and draping of the surgical site. A burr hole is then created slightly lateral to the designated Kocher's point, with the careful removal of the medial part of the burr hole in a semicircular manner to access to an ultrasound-guided working channel. Intraoperative ultrasound is utilized to visualize the lateral ventricles, third ventricle, and third ventricular floor. A trajectory starting from the foramen of Monro and extending toward the third ventricular floor is chosen. The puncture adapter is connected to the working channel and adjusted accordingly. Visualization of the ventricular entry is confirmed, often accompanied by a distinct popping sensation (8). Identification of the foramen of Monro is facilitated by the convergence of the thalamostriate vein, anterior septal vein, caudate vein, and choroid plexuses. Once the endoscope is advanced through the foramen of Monro, the third ventricular floor is punctured at a site between the infundibular recess and mammillary bodies, where the floor is the thinnest. Care is taken to identify and avoid the basilar artery to prevent bleeding and injury. Blunt penetration of the third ventricular floor is achieved using a monopolar coagulator tip to minimize vascular risk. Subsequently, a specialized NeuroBalloon catheter with two balloon compartments or a Fogarty two-French balloon catheter is inserted through the initial fenestration. The balloon is gradually inflated within the fenestration to enlarge the opening, then deflated and withdrawn. Finally, the fenestration allows visualization of structures in the prepontine cistern (Figure 1) (9).

Postoperative criteria for determining success

Clinical success is defined as the resolution of preoperative signs indicating elevated intracranial pressure, including improved levels of consciousness, relief from headaches, stabilization or reduction in head circumference, and cessation of seizures.

Radiological success is determined by observing either a decrease or stabilization in ventricular size during follow-up evaluations, as assessed by the Evans ratio index (9).

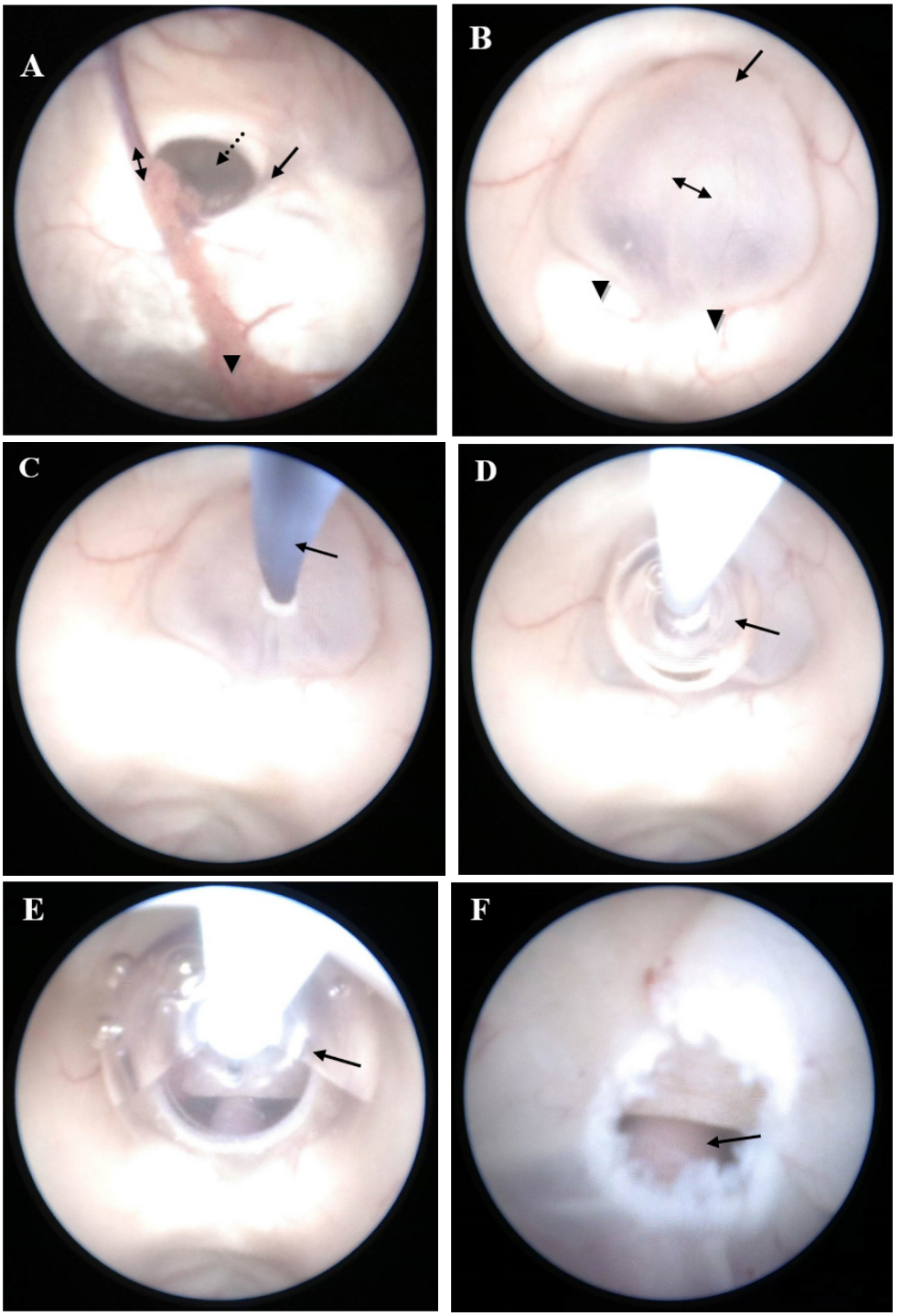

Figure 1: Intraoperative images during ETV
(A) Visualization of the right foramen of Monro (indicated by dashed arrow) featuring the thalamostriate vein (arrow), septal vein (double arrow), and choroid plexus (arrowhead).
(B) Observation of the floor of the third ventricle displaying the intermammillary membrane (double arrow), bilateral mammillary bodies (arrowheads), and anterior infundibular recess (arrow).
(C) Puncture of the floor of the third ventricle using a Fogarty balloon catheter (arrow).
(D, E) Image showing the inflated Fogarty balloon catheter (arrow).
(F) Final depiction of the third ventriculostomy with the prepontine cistern, alongside the basilar artery (arrow)

RESULTS

Among the cohort of 44 patients, 24 (54.5%) were female and 20 (45.4%) were male, with a mean age of 7.3 years. Males had a mean age of eight years, while females had a mean age of 6.8 years. The average duration of operations was 64 min, and patients were followed up for an average of 12 months (Table 1). The most frequently reported symptoms included headache (11 patients, 25%), increased head circumference (10 patients, 22.7%), nausea and vomiting (nine patients, 20.4%), dizziness (five patients, 11.3%), and seizures (four patients, 9%), and somnolence (four patients, 9%).

The study identified that 15 patients (34% of the total) developed hydrocephalus due to intracranial tumors, with 11 tumors situated infratentorially and four supratentorially. Biopsy via ETV was performed in two patients. Additionally, five patients (11.3%) had hydrocephalus associated with myelomeningocele, three (6.8%) had meningitis, and three (6.8%) had arachnoid cysts. Moreover, five patients (11.3% of the total) had a history of premature birth and germinal matrix bleeding (Table 1).

Among the 44 patients who underwent ETV, 30 (68.1%) experienced regression of clinical symptoms. In 11 of these patients, no radiological changes in ventricular size were observed, despite symptomatic improvement. The overall success rate of ETV in our study was 68.1%.

However, 14 patients (31.8%) still had persistent hydrocephalus after ETV and required VP shunt insertion. Among these, seven (50%) had the shunt inserted within the first month after ETV, while four (28.5%) had it inserted within 1–3 months post-ETV. Furthermore, five patients (11.3%) who underwent ETV for hydrocephalus had previously undergone VP shunt placement and required ETV due to shunt dysfunction. Additionally, five patients (11.3%) experienced postoperative wound complications.

Table 1: Patient demographics

Age		
Number of patients	44	
Average age	7.36 (min 1-max 17)	
Gender	**n (%)**	
Male	20 (45)	
Female	24 (55)	
Presenting complaints	**n (%)**	
Headache	11 (25)	
Head circumference growth	10 (22.7)	
Nausea–vomiting	9 (20.4)	
Dizziness	5 (11.3)	
Seizure	4 (9)	
Somnolence	4 (9)	
Incidental	3 (6.8)	
Cause of hydrocephalus	**Total n (%)**	**Success rate n (%)**
Intracranial tumor	15 (34)	12 (80)
Infratentorial	11 (25)	9 (81.8)
Supratentorial	4 (9)	3 (75)
Myelomeningocele	5 (11.3)	2 (40)
Germinal matrix bleeding	5 (11.3)	3 (60)
Meningitis	3 (6.8)	1 (33.3)
Arachnoid cyst	3 (6.8)	2 (66.6)

DISCUSSION

Numerous studies have established that ETV is an effective and safe treatment option for pediatric hydrocephalus (10). The success rate of ETV in children varies from 58% to 90%, depending on factors such as the underlying cause of hydrocephalus, the child's age, and the surgical technique employed (10-13). Moreover, ETV has been linked to a lower incidence of complications and a shorter hospital stay compared to traditional shunt surgery (14). However, ETV may not always be suitable for every pediatric patient with hydrocephalus, and careful patient selection and preoperative planning are essential for optimal outcomes. Overall, ETV can serve as a valuable treatment choice for pediatric hydrocephalus, but the decision to proceed with this surgery should be based on individual patient consideration (15). In our study, the overall success rate of ETV, encompassing both radiological and clinical outcomes, was 68.1%. In 11 out of 30 patients, there were no radiological changes observed in ventricular size; nonetheless, clinically, the patients experienced symptom improvement. Emphasizing clinical correlation over radiological findings is prioritized in determining successful outcomes. While imaging can provide valuable insights into the patient's condition, solely relying on it may be insufficient (15).

ETV offers several advantages over traditional VP shunt surgery, including a decreased risk of infection, a reduced need for revision surgery, and an enhanced quality of life (16). Notably, one of the primary benefits of ETV in children is its capacity to circumvent the potential complications associated with long-term shunt dependency. Shunts can malfunction, become infected, or obstruct, necessitating additional surgeries for replacement or revision (17). In contrast, ETV establishes a new pathway for CSF

circulation, eliminating the requirement for an implanted device (18). This can significantly mitigate the risk of complications linked to shunt surgery and enhance overall outcomes for children with hydrocephalus (19). Generally, the procedure is well-tolerated in pediatric patients, with few serious complications reported. Among the individuals in our study, five (11.3%) who underwent ETV for hydrocephalus had previously undergone VP shunt placement. Subsequently, there was no indication of shunt dependency among these patients during the follow-up period.

Shunt dependency can arise after ETV if the procedure fails to provide sustained alleviation of hydrocephalus symptoms (20). Several factors may increase the likelihood of shunt dependency following ETV, including younger age and the presence of concurrent comorbidities like spina bifida or aqueductal stenosis (21). The effectiveness of ETV may also be influenced by the underlying cause of hydrocephalus, with superior outcomes documented in cases of obstructive pathologies such as aqueductal stenosis compared to other etiologies (22). While the risk of shunt dependency following ETV exists, it is important to underscore that ETV can still serve as an effective treatment option for many hydrocephalus patients. Despite the potential for shunt dependency post-ETV, patients should not be discouraged from considering ETV as a viable treatment option (23). Our analysis revealed that patients undergoing surgery for intracranial tumors achieved a success rate of 80%, surpassing that of other pathologies.

Similar to any medical procedure, ETV carries potential risks and complications. Despite being deemed minimally invasive, complications of ETV can range from minor to life-threatening (24). Common complications include CSF leakage, bleeding, infection, and postoperative headache. CSF leakage, occurring in approximately 5%–10% of ETV cases, is a relatively frequent complication (24-26). Conservative measures like bed rest and antibiotics are typically employed to manage this complication, although surgical repair may be warranted in some instances (27). While bleeding is rare, infection rates range from 0.5% to 4% (28). Postoperative headache, though common, usually resolves within a few days. More severe complications, such as the development of a subdural hematoma, are extremely rare, occurring in less than 1% of cases (29). Nonetheless, they can lead to significant consequences like permanent brain damage or death. Despite these potential risks and complications, ETV remains a valuable treatment option for many hydrocephalus patients (30). In our study, postoperative wound problems were observed in five out of 44 patients (11.3%).

CONCLUSION

In summary, ETV stands as a beneficial treatment choice for pediatric hydrocephalus. It presents numerous advantages over traditional shunt surgery, notably a reduced risk of complications and enhanced quality of life. Although the success of ETV in children may be impacted by various factors, it has demonstrated safety and efficacy in a substantial proportion of pediatric cases.

Ethics Committee Approval: The study has ethical approval from the İstanbul University, İstanbul Faculty of Medicine (Date: 11.05.2023, No: 1755581).

Informed Consent: All patients signed the informed consent form.

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THE RELATIONSHIP BETWEEN LYMPHEDEMA AFTER AXILLARY DISSECTION FOR MALIGNANT SKIN TUMORS OF UPPER EXTREMITY AND NUMBER OF LYMPH NODES REMOVED

ÜST EKSTREMİTE KAYNAKLI MALİGN DERİ TÜMÖRLERİNE YÖNELİK YAPILAN AKSİLLER DİSEKSİYON SONRASI GELİŞEN LENFÖDEM İLE ÇIKARILAN LENF NODU SAYISI ARASINDAKİ İLİŞKİ

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ABSTRACT

Objective: Skin cancers are the most common malignant cancers. For the surgical treatment of skin cancer, there are cases where axillary dissection should be performed, and secondary lymphedema after axillary dissection is not uncommon. The study examined the number of lymph nodes removed in the dissection materials to evaluate the factors that may predict the development of lymphedema.

Material and Method: Our study included patients who underwent axillary lymph node dissection for malignant skin tumors originating from the upper extremities between 2019 and 2022. Age, gender, type of primary malignancy, localization of the lesion, total number of lymph nodes removed in the dissection material, number of metastatic lymph nodes detected in the dissection material, history of SLNB, and the difference in measurements between the operated and non-operated extremity were recorded preoperatively and at the first year postoperatively.

Result: In our study, there was a statistically significant positive correlation between the total number of lymph nodes removed and the diameter difference between the dissected and non-dissected arms. At the same time, there was a statistically significant positive correlation between the number of metastatic lymph nodes and the diameter difference between the dissected limb and the metacarpophalangeal joints of the other limb.

Conclusion: Lymphedema is a complication that is difficult to treat and whose prognosis can be alleviated if detected early. By evaluating the number of excised and metastatic lymph nodes

ÖZET

Amaç: Deri kanserleri en sık görülen malign kanserlerdendir. Cilt kanserinin cerrahi tedavisi için aksiller diseksiyon yapılması gereken durumlar mevcuttur ve aksiller diseksiyon sonrası sekonder lenfödem nadir değildir. Çalışmada, lenfödem gelişimini öngörebilecek faktörleri değerlendirmek için diseksiyon materyallerinde çıkarılan lenf nodu sayısı incelenmiştir.

Gereç ve Yöntem: Çalışmamıza 2019-2022 yılları arasında üst ekstremite kaynaklı malign deri tümörü nedeniyle aksiller lenf nodu diseksiyonu yapılan hastalar dahil edildi. Yaş, cinsiyet, primer malignite tipi, lezyonun lokalizasyonu, diseksiyon materyalinde çıkarılan toplam lenf nodu sayısı, diseksiyon materyalinde saptanan metastatik lenf nodu sayısı, SLNB öyküsü, opere edilen ve edilmeyen ekstremite arasındaki ölçüm farkı preoperatif ve postoperatif birinci yılda kaydedildi.

Bulgular: Çalışmamızda, çıkarılan toplam lenf nodu sayısı ile diseke edilen ve edilmeyen kol arasındaki çap farkı arasında istatistiksel olarak anlamlı pozitif korelasyon bulunurken, metastatik lenf nodu sayısı ile diseke edilen uzuv ile diğer uzvun metakarpofalangeal eklemleri arasındaki çap farkı arasında istatistiksel olarak anlamlı pozitif korelasyon bulunmuştur.

Sonuç: Lenfödem, tedavisi zor olan ve erken teşhis edildiğinde prognozu hafifletilebilen bir komplikasyondur. Diseksiyon materyallerinde eksize edilen lenf nodu sayısı ve metastatik lenf nodu sayısı değerlendirilerek lenfödem gelişebilecek hastalarda erken önlem almak, hastaları eğitmek, bireysel tedavi

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in the dissection materials, it may be possible to take early precautions, educate patients, develop individual treatment modalities, and avoid unwanted complications in patients who may develop lymphedema.

Keywords: Axillary lymph node dissection, melanoma, secondary lymphedema, non-melanoma skin cancer

modaliteleri geliştirmek ve istenmeyen komplikasyonlardan kaçınmak mümkün olabilir.

Anahtar Kelimeler: Aksiller lenf nodu diseksiyonu, melanom, sekonder lenfödem, melanom dışı cilt kanseri

INTRODUCTION

Skin cancer is the most common type of malignancy in the world, and its incidence is significantly increasing (1). Skin cancer types are classified as melanoma and nonmelanoma skin cancers (NMSC). Basal and squamous cell carcinoma are the main forms of NMCS (2). The etiologic factors for skin tumors are multifactorial; thereby, the mechanistic pathways differ. Nevertheless, significant factors include UV radiation, leading to genetic mutation (3).

Treatment modalities vary by the type of skin tumors, and they can be treated by surgery, chemotherapy, or radiotherapy. The gold standard for the management of skin cancer is surgical excision with histopathological control of excision margins (3).

Sentinel lymph node biopsy (SLNB) and regional lymph node dissection are complementary treatment modalities for managing SCCs and melanomas. SCC of the skin has low incidence rates of nodal metastasis. Therefore, regional lymphadenectomy is generally not recommended in clinically node-negative patients (4). In the case of lymph node involvement by SCC, regional lymph node dissection should be preferred. Patients who have melanomas should be investigated for the stage of the disease. When the disease is in its early period, wide surgical excision and the evaluation of the lymph nodes are the essential steps for managing the disease. Patients with clinically node-negative stage I or II melanoma that is 0.8 mm in thickness and located on the trunk or extremities should be allowed to discuss SLNB to provide staging and prognostic information (5). In the case of SLN positivity, completion lymph node dissection (CLND) is performed (6). Axillary, cervical, or inguinal completion lymph node dissection is performed after SLN positivity detection or clinically node-positive situations for metastatic skin tumors. CLND for the skin tumor is a curative process that aims to remove all lymph nodes and metastatic disease in a lymphatic basin. CLND helps to eliminate regional lymph node recurrences and the associated morbidity (7).

Lymphedema is a severe complication for the patient who is already trying to cope with the diagnosis of cancer. Physiologically and psychologically, disturbances will appear during the management of the lymphedema. After all, chronic lymphedema may lead to recurrent infection and even the development of lymphangiosarcoma (8). Postoperative lymphedema following axillary dissection has been studied in depth for breast cancer patients. Hence, while describing the risk factors for lymphedema after axillary dissection, breast cancer-related lymphedema studies must be investigated. Even though the operative techniques are different, the risk factors will be similar. Age, BMI, radiotherapy, sex, race, stage, diabetes, chemotherapy, and number of nodes removed are some of the main risk factors for lymphedema development after axillary dissection due to breast cancer (9).

In this study, we aim to evaluate the risk factors for the development of lymphedema in patients who underwent axillary lymph node dissection (ALND) due to upper extremity skin tumors. In addition, the study aims to evaluate the association between the number of nodes removed during dissection and postoperative lymphedema development. This study retrospectively examines pathology records in patients with ALND, and during follow-ups, our team evaluates lymphedema development by measuring arm circumferences.

MATERIALS and METHODS

In this study, patients who underwent axillary lymph node dissection (ALND) for malignant skin tumors originating from the upper extremities between 2019 and 2022 in the Plastic, Reconstructive, and Aesthetic Surgery Department were included. The study included patients who underwent ALND for cutaneous malignant tumors originating from the upper extremities in our clinic, who were followed up at the physical therapy and rehabilitation center for the prevention of lymphedema in the postoperative period, and in whom we measured the circumference of the relevant upper extremity in the first postoperative year. Exclusion criteria included having undergone ALND in a center other than our clinic, being under 18 years of age, having a history of preoperative trauma or infection in the relevant upper extremity, not attending postoperative follow-up for various reasons (comorbidity, death due to existing disease, etc.), and having undergone ALND for cutaneous malignant tumors located in regions other than the upper extremities (thorax, periumbilical region, etc.).

Patient's age, gender, type of primary malignancy, primary location of the lesion, total number of removed lymph nodes in the dissection material, number of positive lymph nodes detected in the dissection material, history of SLNB, and the difference in measurements between the operated and non-operated extremities in centimeters were recorded preoperatively and at the first year postoperatively. Circumferences of the bilateral arms (15 cm proximal to the elbow), forearms (10 cm distal to the elbow), wrists, and metacarpophalangeal (MCP) joints level were measured in centimeters two weeks before the operation and recorded on a chart. After the operation, a compression garment was applied to the relevant extremity on the first postoperative day, and rehabilitation was performed to prevent lymphedema. Circumferences were measured in centimeters at the bilateral arms (15 cm proximal to the elbow), forearms (10 cm distal to the elbow), wrists, and MCP joints level and recorded on the chart at the first postoperative year. Patients were instructed to refrain from activity before measurement. No patient received radiotherapy after the study.

Axillary lymph node dissection surgery involved removal of level 1-2-3 lymph nodes in the axillary region, while the long thoracic and thoracodorsal nerves were preserved. The total number of lymph nodes removed during the operation and the number of positive lymph nodes were recorded by reviewing the previous medical pathology report records.

The normality assumption of continuous variables was tested by the Shapiro-Wilk test. Categorical variables were presented as frequency (%), and continuous variables were presented as mean±SD, median, and range. Comparisons between two groups in continuous variables were performed with the Mann-Whitney U test. The Spearman correlation test analyzed the level of correlation between two continuous variables. Statistical calculations were performed with SPSS software version 25 (IBM Corp., Armonk, NY, USA). Results were evaluated at a 95% confidence interval, and significance was evaluated at $p<0.05$.

The study protocol was approved by the Medical Ethics Committee of Istanbul University (Date: 17.03.2023 No: 06). All data was anonymized, and the informed consent for every patient was recorded.

RESULTS

This study included 16 patients who underwent axillary lymph node dissection (ALND) for malignant skin tumors originating from upper extremities between 2019 and 2022 in our Plastic, Reconstructive, and Aesthetic Surgery department. Considering the exclusion criteria and the survival rate following melanoma disease, the number of patients included in the study was reduced to eight. The study included eight patients with skin tumors, five males and three females, with a mean age of 63.1±6.9 (Range: 52-73) years. The lesion was localized in the hand in three, forearm in two, arm in two, and axilla in one of the patients. Sentinel lymph node biopsy was performed in four patients, and axillary lymph node dissection was performed in all patients (100%). In axillary lymph node dissection, a mean of 23.4±6 (Range: 14-35) lymph nodes were removed, and carcinoma metastasis was detected in five patients. Lymphedema was observed in four patients during clinical follow-up, with a mean difference of 1.38±1.30 cm (4.4%) between the dissected and the other extremity (Table 1). The circumference measurement results of the patients are presented in detail in Table 2.

There was a statistically significant positive correlation between the number of lymph nodes removed and the diameter difference between the dissected and non-dissected arm ($r=0.734$; $p=0.038$), while there was a statistically significant positive correlation between the number of metastatic lymph nodes and the diameter difference between the dissected extremity and the MCP joints of the other extremity ($r=0.889$; $p=0.044$) (Table 3).

Table 1: Patients' demographic characteristics

Variables (n=8)	**n (%)**
Age, mean (SD)	63.1 (6.9)
Gender	
Male	5 (62.5)
Female	3 (37.5)
Localization of the lesion	
Hand	3 (37.5)
Forearm	2 (25)
Arm	2 (25)
Axillary region	1 (12.5)
SLNB prior to ALND	
Yes	4 (50)
No	4 (50)
Total number of removed lymph nodes, mean (SD)	23.4 (6.0)
Pathological lymph nodes	
Negative	3 (37.5)
Positive	5 (62.5)
Lymphedema	
Yes	4 (50)
No	4 (50)

SLNB: Sentinel lymph node biopsy, ALND: Axillary lymph node dissection, SD: Standard deviation

Table 2: Circumferential difference between operated and non-operated extremities and joints

Circumference measurements	Mean (SD)	Median	Min.-Max.
Arms (cm)	1.38 (1.30)	1	0-4
Forearms (cm)	0.75 (0.707)	1	0-2
Wrists (cm)	0.50 (0.756)	0	0-2
MCP joints (cm)	0.50 (0.535)	0.5	0-1

SD: Standard deviation, MCP: Metacarpophalangeal

Table 3: The relationship between the measurements and total number of removed lymph nodes and total number of metastatic lymph nodes

	TNRLN		TNMLN	
Variables	**r**	**p-value**	**r**	**p-value**
Arms (cm)	**0.734**	**0.038***	-0.433	0.467
Forearms (cm)	0.494	0.213	-0.148	0.812
Wrists (cm)	0.070	0.868	0.344	0.571
MCP joints (cm)	-0.112	0.792	**0.889**	**0.044***

*p<0.05, r: Spearman correlation test, TNRLN: Total number of removed lymph nodes, TNMLN: Total number of metastatic lymph nodes, MCP: Metacarpophalangeal

In patients who underwent SLNB prior to ALND, no significant changes were found in postoperative follow-up circumferential measurements at the arm (p=0.549), forearm (p=0.343), wrist (p=0.405) and MCP joint (p=1.000) level.

DISCUSSION

Skin tumors are common malignancies that require close follow-up after treatment. Our study evaluated the development of lymphedema after axillary dissection, one of the treatment modalities for skin tumors. In our patient group, a significant positive correlation was found between the diameter difference at the arm level of the extremity in which axillary dissection was performed for cutaneous malignant tumor in the upper extremity and the other extremity, as well as the total number of lymph nodes removed in the dissection material. There was also a statistically significant positive correlation between the number of metastatic lymph nodes found in the dissection material and the diameter difference between the MCP joints of the dissected extremity and the other extremity.

Depending on the subtype of skin tumor and the patient's clinical findings, there may be cases where SLNB should be performed before ALND. In the study group, some patients underwent SLNB before ALND; there was no significant difference between the circumferential measurements of the relevant extremity in these patients compared to patients who did not undergo SLNB, and the history of SLNB before dissection did not affect the outcome.

While the number of patients included in our study was 16 in the first phase, the number of patients followed up in the first postoperative year decreased to eight due to the effect of the survival of patients with melanoma, an aggressive skin tumor, and the death of patients due to additional comorbidities, etc. These factors led to a limited number of patients being analyzed. All patients were followed up in physical therapy centers to prevent lymphedema in the postoperative period, and appropriate compression garments were applied. Despite close physical therapy follow-up, a difference in diameter between the extremities with and without dissection was observed.

In the literature, there are studies evaluating lymphedema developing in patients who underwent axillary dissection for breast cancer. In these studies, when the risks for the development of lymphedema were examined, it was observed that the number of resected lymph nodes and the number of pathological lymph nodes were risk-increasing factors (10, 11). In a study conducted for melanoma treatment, it was observed that the total number of resected lymph nodes and the number of pathological lymph nodes were not associated with an increased prevalence of lymphedema. The same study observed that the history of SLNB was not a risk-increasing factor in the development of lymphedema (8). Our study observed that a history of SLNB did not increase the risk of lymphedema after ALND. However, the correlation between the total number of lymph nodes removed, the number of metastatic lymph nodes, and limb diameter differences resulted in different results from the aforementioned study.

Lymphedema is a severe complication after ALND and can be difficult to treat. While cellulitis caused by lymphedema is the main complication, there is a spectrum of complications extending to lymphangiosarcoma, and physiological and psychological disorders are also frequently observed in these patients (12). It is important to take precautions to reduce the development of lymphedema in the early postoperative period. For this purpose, necessary lymphedema training can be tailored individually and by cancer treatment (13). In our study, we focused on the factors we can evaluate in the early period regarding lymphedema development. The pathology report document examined in our outpatient clinic during the postoperative follow-up period was aimed at predicting the development of lymphedema and taking necessary measures to reduce the development of lymphedema by considering the total number of lymph nodes removed in the dissection material and the number of

metastatic lymph nodes. There are limitations within the scope of our study. First of all, the small number of cases constituted a limitation in our study. In addition, limb diameter measurements were used to evaluate the development of lymphedema in the patients, and volume change measurement was not applied, but the study by Taylor et al. showed that limb diameter measurements appropriate to anatomical points have high reliability (14). In addition, evaluating the quality of life of the patients could have helped us to better consider the clinical lymphedema complaints of the patients.

CONCLUSION

According to the results obtained from our data, there is a correlation between the total number of removed lymph nodes and metastatic lymph nodes and limb diameter differences. It may be beneficial to determine cut-off values for the total number of removed lymph nodes and the number of metastatic lymph nodes and to predict the development of lymphedema in a larger case series. Thus, it may be possible to predict the development of lymphedema, evaluate the results, establish appropriate communication with patients, and detail a personalized treatment.

Ethics Committee Approval: The study has ethical approval from the Istanbul University (Date: 17.03.2023, No: 06).

Informed Consent: All data was anonymized, and the informed consent for every patient was recorded

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- E.G., E.K.; Data Acquisition- E.G., E.K., A.A.; Data Analysis/Interpretation- E.G., E.K., Ö.B., A.Arıncı; Drafting Manuscript- E.G., E.K., A.A.; Critical Revision of Manuscript- E.G., E.K., Ö.B., A.Arıncı; Final Approval and Accountability- E.G., E.K., A.A., Ö.B., A.Arıncı

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JOINT LINE CHANGES AND PATELLA BAJA INFLUENCE CLINICAL OUTCOMES OF REVISION TOTAL KNEE ARTHROPLASTY

EKLEM ÇİZGİSİ DEĞİŞİKLİĞİ VE AŞAĞI YERLEŞİMLİ PATELLA REVİZYON TOTAL DİZ PROTEZİ KLİNİK SONUÇLARINI ETKİLEMEKTEDİR

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ABSTRACT

Objective: The purpose of our study was to determine joint line (JL), posterior condylar offset ratio (PCOR), and patellar height alterations following revision total knee arthroplasty (RTKA) and evaluate the functional results according to the critical limits defined in the literature.

Material and Method: Fifty-one patients with a minimum of two years of follow-up were retrospectively reviewed. Demographic data and operative reports were evaluated. Joint line change was measured according to the method of Figgie. Patellar height was measured using the Insall–Salvati Index and the Blackburn–Peel Index. The effect of JL, patellar height alteration, and PCOR on functional outcomes was analyzed using the Knee Society Score (KSS), knee range of motion (ROM), SF-12, and visual analog scale score as functional results.

Result: Patients whose joint lines were not reconstructed had a lower KSS than those whose JLs were restored in accordance with the crucial limit of 5 mm. The other functional results were similar. Functional outcomes were similar between patients with PCORs under 0.44 and those with PCORs higher than 0.44. There was also no significant difference in functional results for the group of patients whose PCOR was lower than 0.5 and those whose PCOR was higher than 0.5. The patients with patella baja had significantly lower knee ROMs, KSS, and SF-12 PCS scores than those without patella baja (p:0.012,p:0.03, and p:0.01, respectively).

Conclusion: In this study, joint line change >5 mm and patella baja negatively affected clinical outcomes after RTKA.

Keywords: Revision knee arthroplasty, joint line, prognostic factors, functional results, patella baja

ÖZET

Amaç: Çalışmamızın amacı revizyon total diz artroplastisi (RTKA) sonrası eklem hattı (JL), posterior kondiler ofset oranı (PCOR) ve patellar yükseklik değişikliklerini belirlemek ve fonksiyonel sonuçlara etkisini literatürde tanımlanan kritik sınırlara göre değerlendirmektir.

Gereç ve Yöntem: Takip süresi en az iki yıl olan 51 hasta retrospektif olarak incelendi. Demografik veriler ve ameliyat raporları değerlendirildi. JL değişimi Figgie'nin yöntemine göre ölçüldü. Patellar yükseklik hem Insall-Salvati İndeksi hem de Blackburn-Peel İndeksi kullanılarak ölçüldü. JL, patellar yükseklik değişikliği ve PCOR'un fonksiyonel sonuçlar üzerindeki etkisi, fonksiyonel sonuçlar olarak Knee Society Score (KSS), diz hareket açıklığı (ROM), SF-12 ve visüel analog skala skoru kullanılarak analiz edildi.

Bulgular: JL'si kritik sınır olan 5 mm'ye göre yeniden yapılan hastaların KSS'larının, eklem seviyesi rekonstrükte edilemeyen hastalara göre anlamlı derecede yüksek olduğu belirlendi. Diğer fonksiyonel sonuçlar benzerdi. PCOR'u 0,44'ün altında olan hasta grubu ile PCOR'u 0,44'ün üzerinde olan hasta grubunun fonksiyonel sonuçlar benzerdi. Hem PCOR'u 0,5'in altında olan hasta grubu hem de PCOR'u 0,5'in üzerinde olan hasta grubu arasında fonksiyonel sonuçlarda da anlamlı fark yoktu. Patella baja'lı hastaların diz ROM'ları, KSS ve SF-12 PCS skorları patella baja'sız hastalara göre anlamlı derecede düşüktü (sırasıyla p:0,012, p:0,03 ve p:0,01).

Sonuç: Bu çalışmada RTKA sonrası >5 mm eklem seviyesi değişikliği ve patella baja gelişmesinin fonksiyonel sonuçlara olumsuz etkisi bulunduğu tespit edilmiştir.

Anahtar Kelimeler: Revizyon total diz protezi, eklem seviyesi, prognostik faktörler, fonksiyonel sonuçlar, patella baja

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INTRODUCTION

Restoration of the native joint line (JL) is one of the key points in achieving natural knee biomechanics and successful functional results in total knee arthroplasty (TKA) (1, 2). Balancing the collateral ligaments and joint isometry is associated with good outcomes in revision total knee arthroplasty (RTKA) (3-6). Joint line alteration may result in increased component wear, lower survival rates, increased patellofemoral contact forces, patellar malalignment, decreased range of motion, and mid-flexion instability (7-9).

There are different landmarks to determine the native JL in RTKA. Comparing preoperative and postoperative distances according to prominent anatomical structures is one of the most known methods. However, when the surgeon has no pre-TKA X-ray of the affected knee and the patient has bone defects distorting the bony anatomy, it becomes hard to estimate the native JL during surgery, so JL changes may occur.

There needs to be a consensus about the critical limit of JL changes in primary TKA and RTKA. Figgie et al., and Partington et al. showed that a JL change of more than 8 mm was associated with inferior clinical results (8, 10). However, Hoffman et al. found that a ±4 mm critical limit of JL alteration was correlated with inferior clinical results, while Porteous et al. found that the critical limit was ±5 mm (6, 11). In addition to the change in the JL, the patellar height may also change and affect the functional results postoperatively in RTKA (12). Patella baja may occur due to shortening of the patellar tendon following revision surgery. Pseudo-patella Baja can also occur due to joint-level alterations (13, 14). Posterior condylar offset (PCO) is also one of the parameters affecting functional scores in revision surgery, such as JL restoration. It was first described by Bellemans et al. for TKA, and Johal et al. described a ratio for PCO (Posterior Condylar Offset Ratio: PCOR) (15, 16). It is also found that PCOR has the most significant impact on postoperative range of motion after TKA (17).

Our study aimed to determine JL, PCOR, and patellar height alterations in RTKA and evaluate the functional results according to the critical limits in the literature.

MATERIAL and METHODS

The study was found ethically appropriate by the Ethics Committee of Istanbul University, Istanbul Faculty of Medicine (Date: 25.06.2021, No: 2021/1110). In this retrospective study, the principles of the Declaration of Helsinki were applied. Informed consent was obtained from all the patients. Our study included patients who underwent RTKA at a single tertiary referral center from January 2011 to May 2018. Patients were excluded based on the following criteria: (1) having had a tibial insert change only with femoral and tibial stem retained in the revision procedure, (2) having <2 years follow-up period, (3) having missing or ineligible data, (4) having prior knee surgery other than arthroscopic meniscus surgery before primary knee arthroplasty (5) periprosthetic infection following RTKA. Twenty-two patients were excluded because of missing data (radiologic or demographic), unwillingness to participate in the study, and refusal to come to the hospital for their last follow-up because of the COVID-19 pandemic. All revision procedures were performed by one senior surgeon (C.S.). Medical records were analyzed for clinical findings of age, gender, follow-up period, diagnosis requiring revision arthroplasty, operative reports, knee range of motion, and preoperative functional results (Figure 1). The bone loss of the tibia and femur was classified according to the Anderson Orthopaedic Research Institute (AORI) bone defect classification system (18).

The radiographic measurements were performed using a picture archiving and communication system. Radiographic measurements were performed at three time points: 1) on the preoperative radiographs before the primary TKA or the non-operated contralateral knee radiograph if the patient was operated on in another hospital for primary TKA, 2) on preoperative radiographs for the RTKA, 3) at the last follow up following RTKA. The JL was defined as the superior surface of the tibial component, which is, due to the radiolucency of the tibial insert, the most distal part of the femoral component or distal femoral joint surface. Joint line height was measured according to the method of Figgie as the distance between the top of the tibial tubercle and the JL on a lateral X-ray of the knee (10) (Figure 2). The patellar position was evaluated using the Insall–Salvati ratio (ISR) and Blackburne–Peel index (BPI) on lateral radiographs taken at 30° of flexion. ISR was defined as the ratio of the patella tendon length to the length of the patella. BPI was defined as the ratio of the distance between the horizontal line and the inferior aspect of the patellar articular surface and the distance of the patellar articular surface. The patella baja was defined as ISR<0.8, and the pseudo-patella baja was defined as ISR > 0.8 and BPI<0.5 (19-21). PCOR was determined as the ratio between the distance from the femoral diaphysis posterior cortex to the posterior condylar margin and the maximum anteroposterior diameter of the distal femur on the actual lateral knee radiograph (16).

Functional results were evaluated by Knee Society Score (KSS) and SF-12 (Short Form-12; both physical [PCS] and mental scores [MCS]) preoperatively before RTKA and at the final follow-up postoperatively following RTKA (22, 23). A goniometer measured the knee range of motion (ROMs). The degree of pain was evaluated using a visual

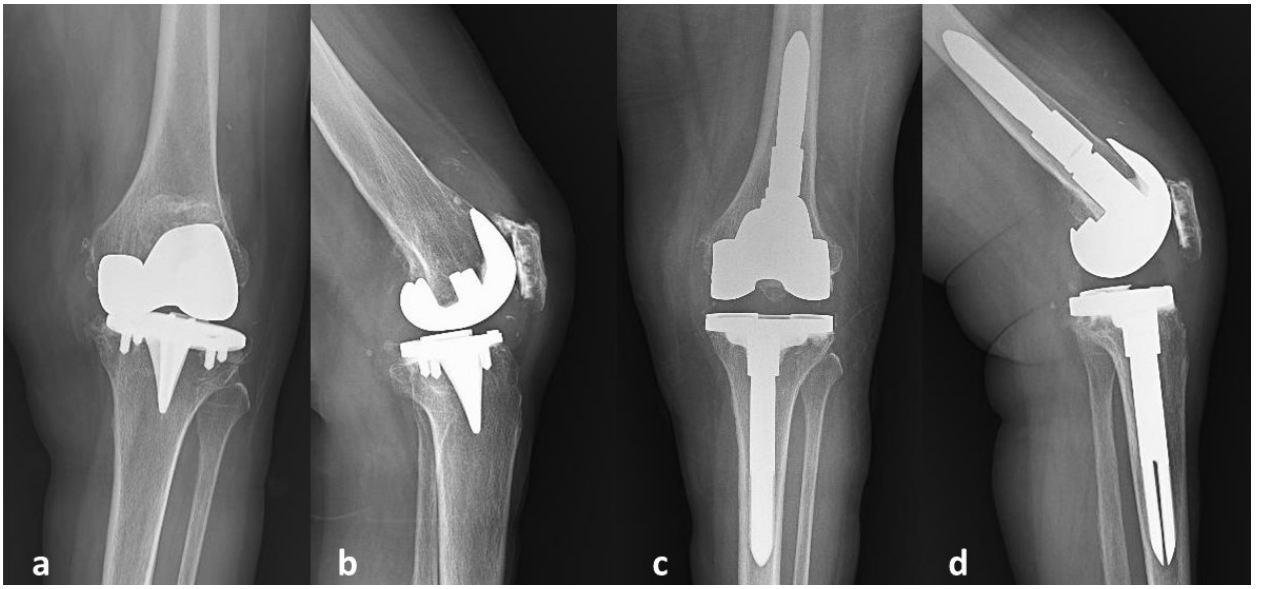

Figure 1: Preoperative (a and b) and postoperative (c and d) X-rays of a patient who underwent revision total knee arthroplasty

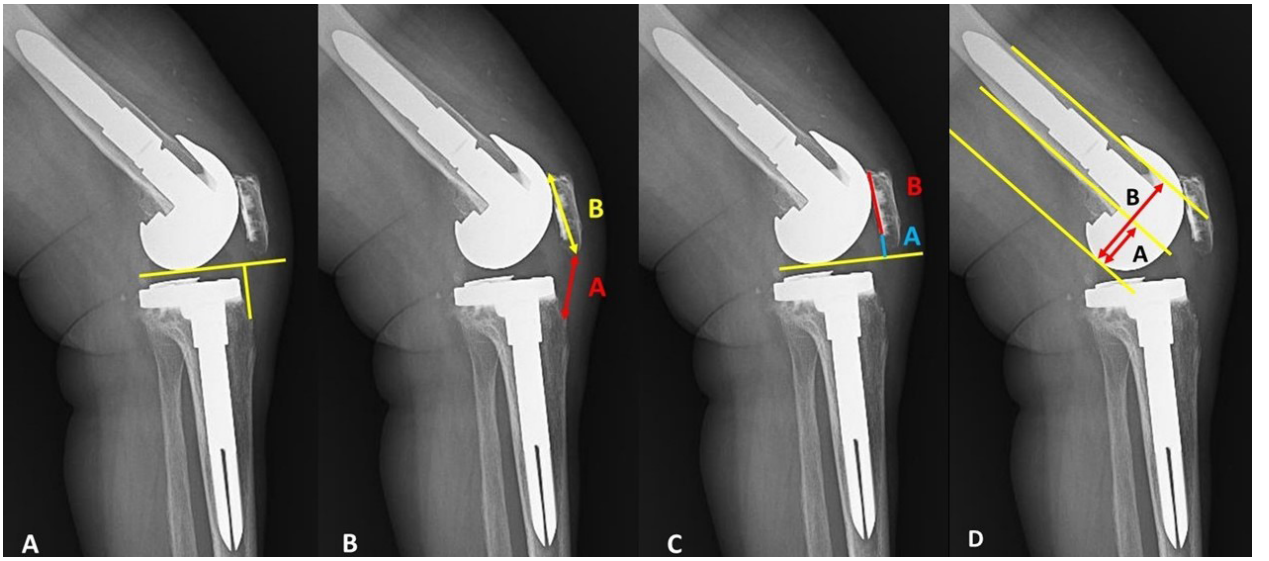

Figure 2: Demonstration of the radiographic measurements, A: Patients joint line height according to the method of Figgie (the distance between the top of the tibial tubercle (TT) and the joint line (JL) on a lateral X-ray of the knee), B: Patellar height measurement according to Insall-Salvati method (A/B), C: Patellar height measurement according to Blackburn-Peel index(A/B), Posterior condylar offset ratio measurement (A/B)

analog scale (VAS). Functional knee scores were calculated by independent orthopedic surgeons both preoperatively and at the final visit.

Joint line change was the difference between the measurements performed before primary TKA or contralateral knee and the last follow-up following RTKA. After calculating the changes in the patient's knee joint level using the Figgie method, patients were divided into two groups in different ways (10). Threshold values previously defined in the literature were used for grouping patients according to the change in joint level. The most accepted of these were 4 mm and 5 mm (6, 11). First, the patients were divided into two groups: those with JL change of more than 4 mm and those with less than 4 mm. Functional scores of the patients (postoperative ROM, KSS, SF-12 PCS, and MCS, and VAS scores) were compared between these two groups. Then, the same categorization and grouping procedure was performed again, considering the JL change with the limit of 5 mm.

Hence, two different comparisons were performed considering the JL alteration.

Since functional scores of patients with a PCOR value of less than 0.44 were reported in the literature, the patients were divided into two groups: those with a PCOR value of less than 0.44 and those with a PCOR value greater than 0.44 (15, 16). Functional scores were also compared between these two groups. Comparisons of functional scores were also performed, grouping the patients by considering the critical limit of 0.5 for PCOR, based on the critical limit of 0.5 for PCOR in the literature (24).

The statistical analysis was performed using SPSS software version 23.0 (IBM SPSS Corp., Armonk, NY, USA) for Windows. A p-value of <0.05 was considered statistically significant. The Shapiro-Wilk test was employed to determine the distribution's normality. Paired samples t-test and independent samples t-test were used to evaluate normally distributed data. The Wilcoxon signed-rank test was used to study dependent variables that were not normally distributed, whereas the Mann-Whitney U test was used to analyze independent variables. The Friedman Test was used to assess the significance of changes in non-normally distributed variables at different time points. Inter- and intraobserver reliability for radiographic classifications was assessed using the intraclass correlation coefficient (ICC). Each group was evaluated twice with repeat classifications on all radiographs with at least a one-week interval for each measurement by three independent observers (ME, KS, and SK). The agreement was excellent for ICC values >0.80.

RESULTS

Seventy-three patients had undergone revision knee surgery in our institution. Finally, 51 patients (40 women, 11 men; mean age 69.9±5.94 [range 56–82]) were included in the study. The mean follow-up period was 40.58±15.32 (24-68) months. The diagnosis for primary TKA was primary degenerative osteoarthritis for 48 knees (94%) and rheumatoid arthritis for three knees (6%). The diagnoses for RTKA were aseptic loosening (n:12, 23.5%), periprosthetic infection (n:37, 72.5%), and periprosthetic fracture (n:2, 4%) (Table 1).

Average knee ROM was 81.82±17.64 degrees before RTKA and significantly improved to 99.17±12.27 degrees (p<0.001) after revision surgery. KSS, SF-12 PCS, and SF-12 MCS scores also increased significantly (all p<0.001). The ICC for all functional outcomes and radiological data was more than 0.80 (range 0.86 to 0.94), showing strong agreement on all parameters evaluated by the three independent observers.

Table 1: Demographic and clinical data of 51 revision total knee arthroplasties

Age (years)	69.9±5.94 (56-82)	
Gender (Male/ Female)	11/40	
Age at primary TKA (years)	63.23±5.83 (48-74)	
Age at revision TKA (years)	66.6±5.9 (52-77)	
Follow-up period (months)	40.58±15.32 (24-68)	
Interval primary-revision TKA (months)	40.88±21.44 (34-46)	
Diagnosis for revision TKA		
Aseptic loosening	12 (23.5%)	
Periprosthetic infection	37 (72.5%)	
Periprosthetic fracture	2 (3.9%)	
Bone defect (AORI)		
Femur (1/2a/2b/3)	23.5%/41.2%/ 35.3%/0%	
Tibia (1/2a/2b/3)	19.6%/52.9%/ 27.5%/0%	
Range of motion (ROM)		p<0.001*
Pre-Revision TKA ROM	81.82±17.64	
Post-Revision TKA ROM	99.17±12.27	
Knee Society Score (KSS)		p<0.001*
Pre-Revision TKA KSS	46.25±4.78	
Post-Revision TKA KSS	72.39±6.82	
SF-12 PCS		p<0.001*
Pre-Revision TKA	31.03±7.48	
Post-Revision TKA	49.09±9.18	
SF-12 MCS		p<0.001*
Pre-Revision TKA	38.92±9.35	
Post-Revision TKA	52.15±9	

TKA: Total Knee Arthroplasty, AORI: Anderson Orthopaedic Research Institute, ROM: Range of motion, *: Statistically significant

In the last follow-up X-rays, patella baja was observed in 4 (7.8%) patients according to the Insall–Salvati index and 13 (25.5%) according to the Blackburn–Peel index. The incidence of pseudo-patella baja was 24% (n:12). The patients with patella baja had significantly lower knee ROM, KSS, and SF-12 PCS than the patients without patella baja (p:0.012, p:0.03, and p:0.01; respectively). Howev-

er, the functional results were similar for both groups of patients when patients were grouped according to the pseudo-patella baja (Table 2, 3).

Twenty-two knees (43.1%) showed a JL change of more than 4 mm, and 16 knees (31.4%) showed a JL change of more than 5 mm. When knee JL was reconstructed within the limit of 4 mm according to the method of Figgie, all postoperative functional results (ROM, KSS, SF-12 PCS, MCS, and VAS score) were similar for both the group where JL was reconstructed within the limit of 4 mm and the group where it was not. When the critical limit in JL reconstruction after RTKA was accepted as 5 mm, it was found that the KSS of the patients whose JLs were reconstructed according to this limit were significantly higher than the patients whose JL change was more than the limit of 5 mm (p:0.02). The other functional results were similar (Table 4). The patients whose JL changed more than 5 mm had higher pain and less knee ROM clinically. There was a trend, but it was not significant.

However, functional results were similar for the group of patients whose PCOR was lower than 0.44 and the group of patients whose PCOR was higher than 0.44. There was also no significant difference in functional results for the patients whose PCOR was lower than 0.5 and those whose PCOR was higher than 0.5 (Table 5).

DISCUSSION

Restoration of the JL in knee arthroplasty is one of the important factors affecting post-op functional results. In RTKA surgery, after bone loss that may occur for various reasons, it may not always be possible to maintain the joint level to the native JL, and alterations may occur in the JL (5, 25, 26). In our study, we aimed to evaluate the critical limit values of the JL change and PCOR affecting the functional results in RTKA, previously described in the literature. The main finding of the present study was that JL alteration of more than 5 mm is significantly associated with poorer KSS following RTKA. Although functional results were reported to be poor in patients with a PCOR below 0.44 in the literature, our findings showed similar

Table 2: Radiographic measurements

Insall-Salvati Index	
Pre-TKA	1.19±0.15
Pre-revision TKA	1.14±0.2
Post-revision TKA	1.1±0.22
Blackburn-Peel Index (BPI)	
Pre-TKA	0.84±0.15
Pre-revision TKA	0.66±0.18
Post-revision TKA	0.63±0.21
Joint line level according to Figgie	
Pre-TKA	24.54±2.49
Pre-revision TKA	26.12±6.77
Post-revision TKA	26.14±6.82
Posterior condylar offset ratio (PCOR)	0.46±0.06
Patella baja following RTKA (ISI<0.8) n (%)	4 (7.8%)
Pseudo-patella baja following RTKA n (%) (BPI<0.5 and ISI>0.8)	12 (24%)

TKA: Total Knee Arthroplasty, ISI: Insall-Salvati Index, BPI: Blackburn-Peel Index, PCOR: Posterior condylar offset ratio, RTKA: Revision total knee arthroplasty

Table 3: Functional results according to the patellar height

	Patella baja (ISI<0.8) Yes n (%) 4 (7.8%) No n (%) 47 (92.2%)		**p**	**Pseudo Patella baja (ISI≥0.8 and BPI<0.5) Yes n (%) 12 (24%) No n (%) 39 (76%)**		**p**
Post-RTKA ROM	Yes	90.21±12.2	**0.012***	Yes	91.25±13.25	0.5
	No	102.5±6.45		No	91.25±8.82	
Post-RTKA KSS	Yes	66.82±6.65	**0.03***	Yes	66.41±6	0.47
	No	74±5.48		No	67.69±7.1	
Post-RTKA SF-12 PCS	Yes	42.19±8.8	**0.013***	Yes	42±5.64	0.31
	No	53.75±7.22		No	43.43±10.1	
Post-RTKA SF-12 MCS	Yes	51.61±9.1	0.097	Yes	52.12±9.81	0.78
	No	52.63±8.08		No	52.25±5.92	
Post-RTKA VAS	Yes	2.93±1.07	0.266	Yes	3.16±0.7	0.31
	No	2.25±1.25		No	2.79±1.17	

RTKA: Revision Total Knee Arthroplasty, ISI: Insall-Salvati Index, BPI: Blackburn-Peel Index, ROM: Range of motion, KSS: Knee Society Score, SF-12: Short form-12, PCS: Physical score, MCS: Mental score, VAS: Visual Analogue Scale, *: Statistically significant

Table 4: Evaluation of the knees according to different levels of joint line alterations

	Joint line changing >4 mm Yes n (%) 22 (43.1%) No n (%) 29 (56.9%)		p	Joint line changing >5 mm Yes n (%) 16 (31.4%) No n (%) 35 (68.6%)		p
Post-RTKA ROM	Yes	89.82±14.3	0.41	Yes	89.57±13.46	0.20
	No	92.95±8.9		No	94.68±8.45	
Post-RTKA KSS	Yes	65.68±7.45	0.66	Yes	65.82±6.9	**0.02**
	No	69.63±5.25		No	70.81±5.38	
Post-RTKA SF-12 PCS	Yes	41.68±9.56	0.27	Yes	42±9.72	0.31
	No	44.95±8.51		No	45.5±7.61	
Post-RTKA SF-12 MCS	Yes	51.79±9.75	0.91	Yes	51.37±9.84	0.52
	No	52.63±8.08		No	53.87±6.75	
Post-RTKA VAS	Yes	3.06±1	0.15	Yes	3.08±1.01	0.64
	No	2.64±1.17		No	2.43±1.15	

RTKA: Revision Total Knee Arthroplasty, ROM: Range of Motion, KSS: Knee Society Score, SF-12: Short Form-12, PCS: Physical score, MCS: Mental score, VAS: Visual Analogue Scale

Table 5: Evaluation of functional results according to the posterior condylar offset ratio

	Posterior condylar offset ratio <0.44 n (%) 14 (27%) >0.44 n (%) 37 (73%)		p	Posterior condylar offset ratio <0.5 n (%) 37 (73%) >0.5 n (%) 14 (27%)		p
Post-RTKA ROM	<0.44	90.13±13.71	0.26	<0.5	90.54±12.06	0.62
	>0.44	93.92±6.84		>0.5	92.85±13.11	
Post-RTKA KSS	<0.44	67.18±6.8	0.65	<0.5	67.32±6.54	0.62
	>0.44	68±7.1		>0.5	67.57±8.42	
Post-RTKA SF-12 PCS	<0.44	42.69±9.28	0.79	<0.5	42.37±9.36	0.25
	>0.44	43.57±9.25		>0.5	45±8.73	
Post-RTKA SF-12 MCS	<0.44	51.18±9.48	0.36	<0.5	52.05±9.4	0.84
	>0.44	54.71±7.21		>0.5	52.42±8.12	
Post-RTKA VAS	<0.44	3±1.17	0.51	<0.5	3±1.3	0.54
	>0.44	2.83±1.06		>0.5	2.83±1	

RTKA: Revision Total Knee Arthroplasty, ROM: Range of Motion, KSS: Knee Society Score, SF-12: Short Form-12, PCS: Physical score, MCS: Mental score, VAS: Visual Analogue Scale

functional results when the patients were grouped according to the PCOR with the critical limit of 0.44 and 0.5.

There are different opinions regarding the effect of JL restoration on functional results in RTKA. Clave et al. and Hoffman et al. found that significantly lower functional outcome scores were associated with the JL change of more than 4 mm (5, 11). Partington et al., declared that the cut-off value of JL elevation in which functional scores are worse was 8 mm, while Porteous et al., stated the limit as 5 mm in RTKA (6, 8). However, Clement et al. and Seon et al. stated that the change in the JL did not significantly affect the functional scores following RTKA (27, 28). In our study, the critical limit of JL change is 5 mm. While there was no significant difference in clinical results when there was a 4 mm limit of JL change, the KSS of the patients was significantly poorer when the JL change was more than 5 mm.

Patella baja is one of the complications after RTKA and may cause inferior clinical results (6, 29). It can occur because of patellar tendon shortening with scar tissues with multiple operations. Additionally, JL elevation can cause pseudo-patella baja without patellar tendon shortening in RTKA (6, 14, 27). Our study observed patella baja and pseudo-patella baja after RTKA in 4 cases (7.8%) and 13 cases (24%), respectively. Patella baja incidence is lower

than in the study of Han et al. (14). In our study, no significant difference was found in the functional scores of patients with pseudo-patella baja and those without pseudo-patella baja, contrary to the study of Vandeputte et al. (30). However, the knee ROM and postoperative KSS of patients with patella baja was found to be significantly lower (p:0.012 and p:0.03, respectively). These results are consistent with the literature (6, 8).

There are several studies about PCOR and its effect on the functional results following knee arthroplasty (17, 26, 31). While Clement et al. and Malviya et al. suggested that PCO is one of the factors significantly influencing functional scores after knee arthroplasty, Ishii et al. reported that PCO does not affect functional scores (17, 26, 31). In the present study, we defined the critical limit of PCOR as 0.44 and 0.5 based on the literature (16, 24). When the patients were divided into two groups according to the PCOR of 0.44 and 0.5, no significant difference could be found in functional results between the two groups in our study. Our results are consistent with the study of Ishii et al.; however, Benazzo et al. did not evaluate the functional results according to the PCOR in their study (24, 31).

In the present study, the mean knee ROM was increased to 99 degrees from 82 degrees following RTKA. RTKA aims to restore native knee kinematics and joint level, and changes in these parameters can affect postoperative functional results (14, 32). Although the mean knee ROM increased after revision surgery in our study, knee ROM was lower, and the pain was higher in patients whose joint level was more than 5 mm.

Our study has several limitations, mostly due to the heterogeneous patient population and the retrospective design. Also, the reason for revision surgery in the present study was mostly periprosthetic joint infection (72.5%). Due to the higher probability of bone loss in the revision surgery after periprosthetic joint infection, restoration of the JL may be more difficult in this patient group and may cause bias in the results. The low number of patients in our study was another limitation. Lastly, all the radiological measurements performed on standard X-rays and measurement errors may be present because of the rotational position of the knee.

CONCLUSION

In this study, JL change >5 mm and patella baja were the prognostic factors affecting functional results after RTKA. The patients with patella baja had significantly lower knee ROM, KSS, and SF-12 PCS than those without patella baja.

Ethics Committee Approval: The study has ethical approval from the Istanbul University, Istanbul Faculty of Medicine (Date: 25.06.2021, No: 2021/1110).

Informed Consent: Informed consent was obtained from all the patients included in our study.

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AN INVESTIGATION REGARDING NUTRIENT FORAMEN OF THE RADIUS

RADIUS'UN FORAMEN NUTRİCİUM'U İLE İLGİLİ BİR ARAŞTIRMA

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ABSTRACT

Objective: Arteries that provide nutrition to the long bones pass through openings called nutrient foramen (NF). The number of studies on NFs of the radius is quite scarce. Therefore, this study aimed to determine the presence, number, direction, and anatomical localization of NFs of the radius.

Material and Method: A total of 133 dry adult human radii were investigated in this study. The presence, number, position, and direction of NFs of the radii were determined. The shortest distance of NF to the most proximal point of the radius (DPE), the transverse diameter of the radius at the level of the NF (TD), and the shortest distance of the NF to the most prominent point of the dorsal tubercle (DDT) were measured. Furthermore, the foraminal index (FI) was calculated.

Result: A single NF was found in 130 (97.7%) bones, and 3 (2.3%) radii did not have NF. The NFs were most commonly on the anterior surface (80%, 104 bones) and middle 1/3 (78.5%, 102 bones) part of the bones. All NFs were towards the elbow. The DPE, TD, and DDT were meanly 82.72±11.4 mm, 129.99±15.41 mm, and 14.6±1.97 mm, respectively. The average FI was 35.6±4.64.

Conclusion: This paper provides additional information, such as the distance of nutrient foramen to the dorsal tubercle. Our results may help clinicians during applications related to the NF of the radius.

Keywords: Nutrient foramen, radius, foraminal index

ÖZET

Amaç: Uzun kemiklerin beslenmesini sağlayan arterler, foramen nutricium (FN) adı verilen açıklıklardan geçer. Radius'taki FN'ler ile ilgili yapılan çalışma sayısı oldukça azdır. Bu nedenle,bu çalışmada FN'lerin radius üzerindeki varlığını, sayısını, yönünü ve anatomik lokalizasyonunu belirlemek amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmada toplam 133 adet yetişkine ait kuru radius kemiği incelendi. FN'lerin radius üzerindeki varlığı, sayısı, konumu ve yönü belirlendi. FN'nin radius'un en proksimal noktasına olan en kısa mesafesi (PM), FN'nin bulunduğu seviyedeki transvers çap (TÇ), FN'nin tuberculum dorsale'nin en belirgin noktasına olan mesafesi (TDM) ölçüldü. Ayrıca foraminal indeks (FI) hesaplandı.

Bulgular: 130 (%97,7) radius'ta tek FN vardı, 3 (%2,3) radius'ta ise FN yoktu. FN'ler en sık radius'un facies anterior'unda (%80; 104 kemik) ve orta 1/3 (%78,5; 102 kemik) kısmındaydı. Tüm FN'lerin yönü dirseğe doğruydu. PM, TÇ ve TDM sırasıyla ortalama 82,72±11,4 mm, 129,99±15,41 mm ve 14,6±1,97 mm olarak hesaplandı. Ortalama FI 35,6±4,64 olarak kaydedildi.

Sonuç: Bu çalışma, nutrient foramenin dorsal tüberküle olan uzaklığı gibi ek bilgiler sağlamaktadır. Çalışma sonuçlarımızın, radius'taki FN ile ilgili uygulamalarda klinisyenlere yardımcı olacağı öngörülmektedir.

Anahtar Kelimeler: Foramen nutricium, radius, foraminal indeks

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INTRODUCTION

The nutrient foramen (NF) is the opening through which blood vessels play a role in the arterial supply and growth of bones (1, 2). One or two nutrient arteries supply the bone tissue by passing through the NF in an oblique course from the body to the bone. The entry and angulation positions of the NFs rarely vary, and the location is far from the epiphysis (3).

The anterior interosseus artery mainly provides the arterial supply of the forearm bones, and this artery supplies the radius through its branch, called the nutrient artery of radius (4, 5). The nutrient artery of the radius can branch from the posterior interosseous artery (5). Knowing the localization of the foramina is quite important as it will facilitate surgical procedures (6).

The healing process in sharps injuries or fractures depends on the arterial nutrition of the bone (2). During the healing process of bone fractures, bone nutrition plays a vital role in preventing complications that may develop. Therefore, the nutrient artery is important in fracture healing (7). Some studies also indicate that problems related to the union in fractures of the forearm bones may be caused by NF (8, 9).

When the studies in the literature are examined, there are few studies regarding the NF of the radius diaphysis, and the number of parameters evaluated is limited. This study aimed to evaluate the presence, number, direction, localization, and topography of the NF of the radius because of its clinical importance.

MATERIALS and METHODS

In this cross-sectional study, a total of 133 radii (66 right, 67 left) from adult human skeletons of unknown age, sex, and race found at the Department of Anatomy, İstanbul University, İstanbul Faculty of Medicine, were used. None of the radii had any pathology that would affect the measurements. Ethical approval was obtained from the Clinical Research Ethical Committee of İstanbul University İstanbul Faculty of Medicine (Date: 25/06/2021, No: 13). The following parameters related to the NF of the radius were analyzed with the naked eye:

The number and patency of the NFs were noted.

The direction and localization of the NFs were recorded.

To determine the NFs' patency and direction, an acupuncture needle with dimensions of 0.25X30 mm was used. Any openings smaller than the size of the mentioned acupuncture needle were not evaluated.

The localization of the NF was determined, i.e., on which of the three margins (anterior, interosseus, and posterior margins) and three surfaces (anterior, medial, and lateral surfaces) of the radius was the NF located.

Afterward, the following measurements were also performed on the radius with a digital caliper accurate to 0.01 mm (INSIZE Co., Ltd., Taiwan):

Total length (TL): The shortest distance between the most proximal and distal points of the radius (Figure 1A).

Distance to proximal end (DPE): The shortest distance of the NF to the most proximal point of the radius (Figure 1A).

Transverse diameter (TD): The transverse diameter of the radius at the level of the NF is shown in Figure 2.

Distance to dorsal tubercle (DDT): The shortest distance of the NF to the most prominent point of the dorsal tubercle (Figure 1B).

Additionally, the topography of the NFs was evaluated as it was located on the proximal 1/3, middle 1/3, and distal 1/3 of the total length of the radius. Calculations were made using the foraminal index (FI) formula defined by Hughes (10) to determine the topography of the NFs. The formula defined by Hughes is as follows: FI = (DPE/TL) x 100.

Two independent researchers performed the morphometric measurements, and the mean value per parameter was recorded. Both measurements were repeated if there was more than a 10% difference between the two measurements. The digital caliper was calibrated before each measurement to provide accurate calculations. The

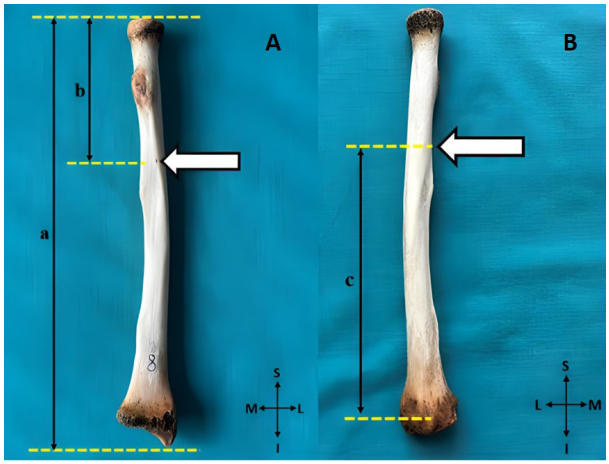

Figure 1: Some morphometric measurements. A. Representation of the measurement of TL and DPE of the radius B. Representation of the measurement of DDT of the radius. a: Total length (TL), b: Distance to proximal end (DPE), c: Distance to dorsal tubercle (DDT), NF: Nutrient foramen, S: Superior, I: Inferior, M: Medial, L: Lateral. The white arrow shows the nutrient foramen.

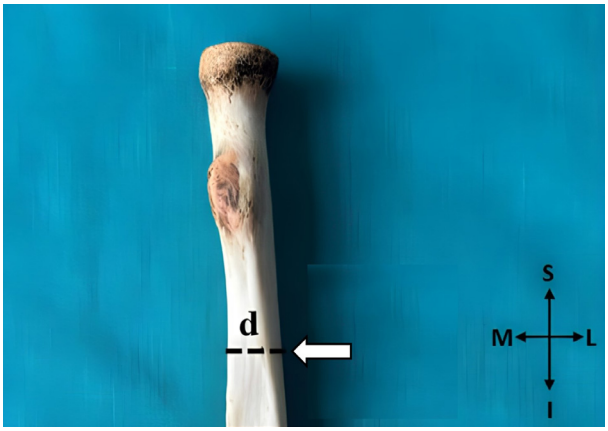

Figure 2: The transverse diameter of the radius at the level of the NF. d: Transverse diameter (TD), NF: Nutrient foramen, S: Superior, I: Inferior, M: Medial, L: Lateral. The white arrow shows the nutrient foramen.

mean and standard deviation of all morphometric parameters were calculated using SPSS 21.0 (IBM SPSS Corp., Armonk, NY, USA). Morphometric measurements of all evaluated parameters are shown in Figure 1 and Figure 2.

RESULTS

Of the 133 radii, 3 of them (1 right, 2 left) had no NF, whereas 130 had a single NF (Figure 3). The direction of all NFs was towards the elbow (Figure 3). The NFs were most frequently located on the anterior surface and least frequently on the anterior margin of the radius (Figure 3A). No NF existed on the posterior margin and lateral surface of the radius.

Localization of the NF on the radii is shown in Figure 3. In total, of the 130 NF, the TL, DPE, TD, and DDT values

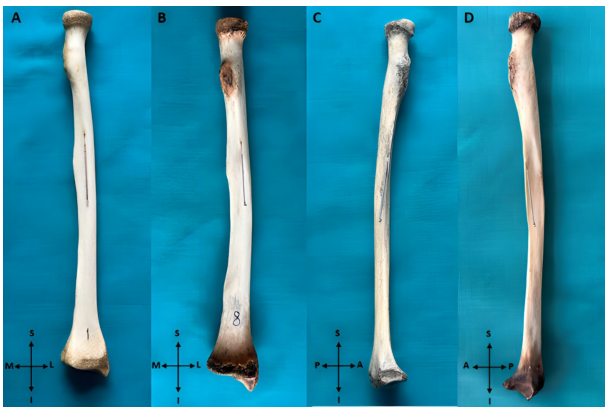

Figure 3: Localization of the NF of the radii. A. Radius with the NF on the anterior surface, B. Radius with the NF on the anterior margin, C. Radius with the NF on the posterior surface, D. Radius with the NF on the interosseus margin, NF: Nutrient foramen, S: Superior, I: Inferior, M: Medial, L: Lateral.

were 227.09 mm, 82.72 mm, 14.6 mm, and 129.99 mm, respectively. Of the total 130 foramina, 28 were located on the proximal 1/3 of the bone, and the rest (102) were located on the middle 1/3. In other words, no NF was observed on the distal 1/3. The mean FI was 35.6. All morphometric measurements regarding the NFs are detailed in Table 1 and Table 2.

Table 1: Number, topography, and localization of NF

Nutrient Foramen (NF)		Number of radii n (%)
Number of NF	0	3 (2.3)
	1	130 (97.7)
Localization of NF	Anterior surface	104 (80)
	Posterior surface	5 (3.9)
	Interosseus margin	15 (11.5)
	Anterior margin	6 (4.6)
Topography of NF	Proximal 1/3	28 (21.5)
	Middle 1/3	102 (78.5)
	Distal 1/3	-

DISCUSSION

The number and direction of nutrient foramina

A brief review of the literature regarding the number and direction of nutrient foramina is shown in Table 3 (8, 7, 11-17). In our study, NF was not found in 2.3% (3 bones), and 97.7% (130 bones) had a single NF out of a total of 133 radii. Nevertheless, we did not observe a radius with 2 NF. In previous studies, one conducted by Güner et al. and the other by Öztürk et al., the rate of the radius with 2 NF was reported as 2% (1 bone) and 12.3% (6 bones), respectively (15, 7). Most authors agree that a single nutrient foramen is in the radius (Table 3). Parmar et al. and Reddy et al. observed that the radius with a single NF was 96.6% (58 bones) and 96.3% (52 bones), respectively (8, 14). Our results regarding a single NF are compatible with the results of a single NF of these two previous studies.

Öztürk et al. assessed 49 radii and reported that 96.36% of NFs were towards the elbow, and 3.64% of NFs were towards the wrist (7). On the other hand, Patel et al. stated that all directions of NFs were toward the elbow in their study, with 40 radii (13). All of the 130 foramina evaluated in this study were towards the elbow.

It has been shown that radius fractures coinciding with the NF level may cause severe arterial nutrition loss, which may progress to bone ischemia (9). Since most of the radii we analyzed had a single NF, a fracture at the

Table 2: The morphometric data of 130 radii with single nutrient foramen

	Total length	Distance to proximal end	Transverse diameter	Distance to dorsal tubercle	F Index
Minimum	186.11 mm	61 mm	11 mm	90 mm	27.04
Maximum	266 mm	121 mm	21.96 mm	170.28 mm	49.59
Mean	227.09 mm	82.72 mm	14.6 mm	129.99 mm	35.6
Standard deviation	17.77 mm	11.4 mm	1.97 mm	15.41 mm	4.64

TL: Total length, DPE: Distance to proximal end, TD: Transverse diameter, DDT: Distance to dorsal tubercle

Table 3: The current review of the literature regarding the number and direction of nutrient foramina and our study

Study	Year	Number of radius	Number of NF			Direction of NF	Localization of NF						
			0	1	2		AS	PS	AB	IB	Proximal 1/3	Middle 1/3	Distal 1/3
Ukoha et al. (11)	2013	50	16 (32%)	34 (68%)	-	Elbow (except 1 NF)	16	3	11	5	20	15	-
Parmar et al. (8)	2014	60	-	58 (96.6%)	2 (3.4%)	Elbow	35	5	4	2	-	-	-
Solanke et al. (12)	2014	80	4 (5%)	74 (92.5%)	2 (2.5%)	-	53	4	6	17	-	-	-
Patel et al. (13)	2015	40	-	40 (100%)	-	-	35	5	-	-	-	-	-
Reddy et al. (14)	2016	54	-	52 (96.3%)	2 (3.7%)	-	49	1	-	4	-	-	-
Güner et al. (15)	2019	50	12 (24%)	37 (74%)	1 (2%)	-	33	1	2	3	-	-	-
Mishra et al. (16)	2019	38	-	-	-	Elbow	-	-	-	-	9	28	-
Challa et al. (17)	2019	50	-	50 (100%)	-	Elbow	35	-	-	15	13	37	-
Öztürk et al. (7)	2021	49	-	43 (87.7%)	6 (12.3%)	96.36% Elbow					25	30	-
Present study	2023	133	3 (2.3%)	130 (97.7%)	0	Elbow	104	5	6	15	28	102	-

AB: Anterior margin, AS: Anterior surface, IB: Interosseus margin, NF: Nutrient foramen, PS: Posterior surface

NF level may increase the risk of arterial nutritional loss. Besides, we think that knowledge that the direction of all NFs is towards the elbow may facilitate detection and imaging techniques and the application of interventional procedures of NFs.

Location of nutrient foramina

In this study, the most common location was on the anterior surface of the radius (104 NFs), followed by the interosseus margin (15 NFs) and anterior margin (6 NFs). The least common localization was on the posterior surface of

Table 4: The morphometric results of previous studies and our results

Study	Year	TL (mm)	DPE (mm)	TD (mm)	DDT (mm)	FI
Solanke et al. (12)	2014	229.4±21.5	-	13.03±1.68	-	-
Veeramuthu et al. (18)	2017	248.5+14	-		-	33.78±4.64
Güner et al. (15)	2019	227.6	81.5	-	-	35.9
Mishra et al. (16)	2019	226.7+14.66	-	-	-	-
Öztürk et al. (7)	2021	228.39±15.87	77.88±16.95	-	-	34.11±7.08
Present study	2023	227.09±17.77	82.72±11.4	14.6±1.97	129.99±15.41	35.6±4.64

TL: Total length, DPE: Distance to proximal end, TD: Transverse diameter, DDT: Distance to dorsal tubercle, FI: Foraminal Index

the radius (5 NFs). Our results are similar to the results of studies in the literature.

The anterior interosseus artery, the main artery providing endosteal and periosteal supply to the radius, is very important in transplantation and reconstruction surgery to reduce the incidence of pseudoarthrosis (5). The fact that the nutrient artery of the radius can also originate from the posterior interosseus artery can explain why some NFs are located on the posterior surface of the radius (5). To preserve nutrient arteries during surgery, it is important to know the course of the artery and the anatomical localization of the NF in the long bones (7).

Morphometric features and topography of nutrient foramina

In our study, we measured the total length (TL), distance to the proximal end (DPE), transverse diameter (TD), distance to dorsal tubercle (DDT), as well as the foraminal index (FI). We have reviewed the current literature about these parameters, as shown in Table 4 (7, 12, 15, 16, 18). In the present study, the mean TL and DPE were 227.09±17.77 mm and 82.72±11.4 mm, respectively. We also calculated the mean FI as 35.6±4.64. Our results are almost the same as those of the studies of Güner et al. (15).

The TD was 14.6±1.97 mm in this study. Solanke et al. obtained the value of 13.03±1.68 mm, which is very close to our TD value (12). Some studies have indicated that the transverse diameter of the radius is correlated with the anteroposterior diameter of the radius (19). With this information, the diameters of the radius are interpreted, and the length of the screw to be applied in distal radius fractures can be decided (19). The diameter data of the radius obtained in our study may also help practitioners.

The DDT value was 129.99±15.41 mm in our study. We could not find any studies that measured DDT value. In order to perform surgical procedures in a safe framework, some landmarks are utilized. For example, in forearm fractures, surgical planning concerns certain landmarks, such as the styloid process and radial tuberosity (20). In addition, these landmarks guide surgeons in imaging techniques (20). The dorsal tubercle is one of the palpable landmarks on the radius. We measured the distance of the NF to the radius's dorsal tubercle, which might be a good landmark for surgical application. We believe this value might be a helpful guide for surgeons in applications related to the NF. Furthermore, we think that having such information about the NF may reduce the development of the risk of complications related to NF surgery.

In their studies, Kızılkanat et al. pointed out that the majority of NFs were located on the proximal half of the radius (1). They also recorded that the NF was found between 22.2-46% of the total length of the radius (1). Murlimanju et al. reported that the NF was between 26-46% of the total length of the radius, and Campos et al. reported that it was between 25-50% (5, 21). We evaluated 130 NFs in this study and detected that 28 NFs were located on the proximal 1/3 and 102 NFs were on the middle 1/3 of the bones. We believe surgeons should focus on the latter location when planning operations with NFs. Thus, the planned surgical time related to NFs may be shortened, which may help prevent complications.

As a result, as new surgical techniques develop (such as microvascular bone transfer), the anatomical structure of the NF gains importance (1, 5, 12, 22). In this respect, knowing the morphometric values of the NF may be necessary to protect radius circulation.

The limitation of this study was the lack of age and gender information on the radii. We would have discussed more significant results if we accessed this information.

CONCLUSION

In this study, a total of 133 radii were examined morphometrically. Although many findings showed results similar to those of previous studies, unlike in previous studies, the distance of the nutrient foramen to the dorsal tubercle was measured. The current study's findings might contribute to the literature on clinical applications related to the nutrient foramen of the radius.

Ethics Committee Approval: The study has ethical approval from the İstanbul University İstanbul Faculty of Medicine (Date: 25.06.2021, No: 13).

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- E.T., L.S.; Data Acquisition- E.T., A.E.; Data Analysis/Interpretation- O.C., Ö.G.; Drafting Manuscript- E.T., L.S., O.C.; Critical Revision of Manuscript- O.C., A.E., Ö.G.; Final Approval and Accountability- E.T., L.S., O.C., A.E., Ö.G.

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PERITONEAL DIALYSIS IN NEWBORNS AND INFANTS IN THE LAST 20 YEARS: SINGLE CENTER EXPERIENCE

SON 20 YILDA YENİDOĞAN VE SÜT ÇOCUĞUNDA PERİTON DİYALİZİ: TEK MERKEZ DENEYİMİ

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ABSTRACT

Objective: To evaluate patients who underwent acute and chronic peritoneal dialysis (PD) under the age of one one in terms of etiology, complications, and prognosis over 20 years and to compare the results between the first and last 10 years of acute and chronic peritoneal dialysis.

Material and Method: Seventy-four peritoneal dialysis patients under the age of one in the Division of Pediatric Nephrology and Neonatal Intensive Care Unit of our hospital between January 2002 and December 2023 were evaluated retrospectively. The patients were divided into two groups: patients admitted in the 2002-2013 period (Group I) and patients admitted in the 2013-2023 period (Group II). Patients in Group I and Group II were compared in terms of acute and chronic peritoneal dialysis etiology, complications, and prognosis.

Result: Forty-four of the patients (60%) were newborns, and the remaining 30 were infants (40%). There were 39 patients in Group I and 35 patients in Group II. There was no difference between Group I and Group II for acute dialysis in terms of neonatal and infant diagnoses, infectious and non-infectious complications, and prognosis (p>0.05). There was no difference between Group I and Group II in terms of neonatal and infant diagnoses, infectious and non-infectious complications, and infant prognosis (p>0.05). There was no death in the newborns in Group II and patient survival was higher than in the newborns in Group I (p=0.019).

ÖZET

Amaç: Bir yaş altında akut ve kronik periton diyalizi (PD) uygulanan hastaları 20 yıllık süreçte etiyoloji, komplikasyon ve prognoz açısından değerlendirmek ve akut ve kronik periton diyalizinin ilk ve son on yıllık dönemleri arasındaki sonuçları karşılaştırmak.

Gereç ve Yöntem: Hastanemiz Çocuk Nefroloji ve Yenidoğan Yoğun Bakım Ünitesi'nde Ocak 2002 ile Aralık 2023 tarihleri arasında yatan bir yaş altı 74 periton diyalizi hastası retrospektif olarak değerlendirildi. Hastalar 2002-2013 döneminde başvuran hastalar (Grup I) ve 2013-2023 döneminde başvuran hastalar (Grup II) olmak üzere iki gruba ayrıldı. Grup I ve Grup II'deki hastalar akut ve kronik periton diyalizi hastalığının etiyolojisi, komplikasyonları ve prognozu açısından karşılaştırıldı.

Bulgular: Hastaların 44'ü (%60) yenidoğan, geri kalan 30'u sütçocuğu (%40) idi. Grup I'de 39 hasta, Grup II'de ise 35 hasta vardı. Akut diyaliz için Grup I ve Grup II arasında yenidoğan ve sütçocuğu tanıları, enfeksiyöz ve enfeksiyöz olmayan komplikasyonlar ve prognoz açısından fark yoktu (p>0,05). Kronik diyaliz için Grup I ve Grup II arasında yenidoğan ve sütçocuğu tanıları, enfeksiyöz ve enfeksiyöz olmayan komplikasyonlar ve sütçocuğu prognozu açısından fark yoktu (p>0,05). Grup II'deki yenidoğanlarda ölüm yoktu ve hasta sağ kalımı Grup I'deki yenidoğanlara göre daha yüksekti (p=0,019).

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Conclusion: Peritoneal dialysis is the most commonly used method for renal replacement therapy in children facing both acute and chronic renal failure. In the last decade, despite high-quality care in the neonatal care unit, positive technological developments and effective management of PD, the most common infectious complication was still peritonitis, and the non-infectious complication was dialysate leakage, as in the previous 10 years.

Keywords: Newborn, infant, peritoneal dialysis

Sonuç: Periton diyalizi, hem akut hem de kronik böbrek yetmezliği ile karşı karşıya olan çocuklarda renal replasman tedavisi için en sık kullanılan yöntemdir. Son on yılda, yenidoğan bakım ünitesindeki yüksek kaliteli bakıma, olumlu teknolojik gelişmelere ve PD'deki etkin yönetime rağmen, önceki 10 yılda olduğu gibi en sık görülen enfeksiyöz komplikasyon hala peritonit, enfeksiyöz olmayan komplikasyon ise diyalizat kaçağıydı.

Anahtar Kelimeler: Yenidoğan, sütçocuğu, periton diyalizi

INTRODUCTION

Peritoneal dialysis (PD) is a renal replacement treatment method that can be applied at all ages, including the neonatal age group. PD is based on water and solute transport via diffusion, ultrafiltration, and absorption through the peritoneal membrane, which separates the blood in the peritoneal capillaries and the dialysis solution in the peritoneal cavity. Peritoneal dialysis can be used in both acute and chronic treatment of renal failure (1, 2). It is the preferred treatment option, especially in hemodynamically unstable and newborn babies and infants (3-5). In addition to acute kidney injury (AKI) in the neonatal period, PD is an effective method for disorders that are unresponsive to medical treatment, such as electrolyte disorders, resistant acidosis, and hyperammonemia secondary to congenital metabolic diseases. PD applications are performed through single or double-felt, straight or curved PD catheters placed in the peritoneal cavity by percutaneous or open surgical methods (6). The primary objective of this study was to assess children who underwent acute and chronic peritoneal dialysis under the age of 1 within 20 years, with a focus on etiology, complications, and prognosis. The secondary objective aimed to compare the outcomes of acute and chronic peritoneal dialysis between the initial and later ten-year periods.

MATERIAL and METHODS

Seventy-four peritoneal dialysis patients under the age of one in the Division of Pediatric Nephrology and Neonatal Intensive Care Unit of our hospital between January 2002 and December 2023 were evaluated retrospectively. The dialysis indications of the cases were decided by the neonatology and nephrology teams, and the process was managed by these two teams. PD catheters were inserted percutaneously or via open surgery. Catheter exit site care and dressing were performed by peritoneal dialysis nurses at one-day intervals. Patients were evaluated daily in terms of PD complications.

Cell counts were performed daily in the peritoneal fluid to evaluate peritonitis. Peritonitis was defined as ≥100 leukocytes/mm^3 and >50% neutrophils in the peritoneal fluid or culture positivity (7, 8). Exit-site infection was defined as erythema around the site where the catheter exits from the skin or purulent drainage from the exit site or both. A tunnel infection was defined as erythema or tenderness or edema over the subcutaneous pathway of the catheter (9). Dialysate leakage, catheter dysfunction, hydrocele/hernia, bleeding at the catheter exit site, catheter displacement, and protrusion of the catheter cuff were considered non-infectious complications (10).

The patients were divided into two groups: patients admitted in the 2002-2013 period (Group I) and patients admitted in the 2013-2023 period (Group II). The etiology, complications, and prognosis of patients with acute and chronic PD were obtained from the patient files and recorded in the study form. Patients in the newborn and infant (<1 year of age) groups were compared in terms of acute and chronic PD etiology, complications, and prognosis. Additionally, Group I and Group II were compared in terms of acute and chronic dialysis. This study was approved by the Ethical Committee of İstanbul University İstanbul Faculty of Medicine (Date: 15.12.2023, No: 25).

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (IBM SPSS Corp., Armonk, NY, USA). For the presentation of quantitative data, mean, standard deviation, minimum, and maximum were given. Frequency and percentage values were used to present categorical variables (qualitative variables). Chi-Square and Fisher's exact tests were used to compare the rates between groups. During statistical analysis, the confidence interval $p<0.05$ was considered significant.

RESULTS

Out of the total 74 patients, forty-four (60%) were newborns, and the remaining 30 were infants (40%). Acute peritoneal dialysis was applied to 45 patients, while chronic peritoneal dialysis was administered to 29 patients. The boy/girl ratio was 1.4. Group I consisted of 39 patients from the 2002-2013 period, and Group II included 35 patients from the 2013-2023 period.

Acute peritoneal dialysis

Acute PD was administered to 45 patients (29 newborns, and 16 infants). The most common diagnoses for new-

borns were prematurity (45%) and sepsis (14%), while infants presented with metabolic diseases (25%) and after surgery (25%). The etiologies of patients who underwent acute PD are shown in Table 1. There were 24 girls and 21 boys. Group I included 27 patients, and Group II had 18 patients. Azotemia, oligoanuria, and hypervolemia were indications for acute PD in 40 patients (89%), hyperkalemia (≥6.5 mmol/L) in 21 patients (47%), and resistant acidosis in 26 patients (58%). The mean age of onset of acute PD was 8.0±9.4 days (1.0-39.0 days) in newborns and 128.1±118.8 days (31.0-388 days) in infants. The total duration of acute PD was 14.3±16.8 days (1.0-67.0) for newborns and 15.8±17.9 days (1.0-56.0 days) for infants. The most common complication was non-infectious complications in both groups. Dialysate leakage was present in 28 out of 45 patients. Nine patients (20%) had peritonitis, and 1 patient (2%) had a catheter exit site infection. Complications of acute PD are detailed in Table 2. The catheter was replaced in 28% of newborns and 19% of infants due to non-infectious complications. Mortality rates were 72.4% for newborns and 56.3% for infants.

Chronic peritoneal dialysis

Chronic PD was applied to 29 patients (15 newborns, and 14 infants). The most common diagnosis for newborns was congenital kidney and urinary tract anomalies (CAKUT) (87%), while infants had CAKUT (50%) and congenital nephrotic syndrome (21%). The etiologies of patients who underwent chronic PD are outlined in Table 1. There were 7 girls and 22 boys. Group I included 12 patients, and Group II had 17 patients. The mean age of onset of chronic PD was 15.3±17.6 days (2.0-62.0 days) for newborns and 34.2±49.0 months (2.0-148 months) for infants. The total duration of chronic PD was 27.1±24.8 months (3.3-71.5) for newborns and 32.3±23.4 days (5.0-72.0 months) for infants. The most common complication for newborns was non-infectious complications. Dialysate leakage (53%) and catheter dysfunction (27%) were the most common complications in newborns. Infectious complications were more common in infants. Thirteen patients (93%) had peritonitis, and six patients (43%) had a catheter exit site infection. Complications of chronic PD are listed in Table 3. Mortality rates were 27% in newborns and 43% in infants.

Comparison of patients in groups I and II according to dialysis modality

Acute peritoneal dialysis

The gender distribution of the patients was not different in the two groups (p>0.05). There was no difference between group I and group II in terms of neonatal and infant diagnoses, neonatal and infant infectious and non-infectious complications, and neonatal and infant prognosis (p>0.05) (Table 2).

Chronic peritoneal dialysis

The gender distribution of the patients was not different in the two groups (p>0.05). There was no difference between group I and group II in terms of neonatal and infant diagnoses, neonatal and infant infectious and non-infectious complications, and infant prognosis (p>0.05) (Table 3). A significant difference was found between group I and group II in terms of neonatal prognosis (p=0.019). There was no death and patient survival was higher in group II patients. Patients in group I and group II, who started chronic PD in the neonatal period, were similar in terms of gender, history of prematurity, and other parameters (p>0.05) (Table 3).

Table 1: Etiology in acute and chronic peritoneal dialysis patients

	Acute PD		Chronic PD	
	Newborns (n=29)	Infants (n=16)	Newborns (n=15)	Infants (n=14)
	n (%)	n (%)	n (%)	n (%)
CAKUT	4 (14)	3 (19)	13 (87)	7 (50)
ARPKD	2 (7)	-	1 (7)	2 (14)
Metabolic disease	2 (7)	4 (25)	-	-
Drug-induced acute kidney injury	1 (3)	-	-	-
Prematurity	13 (45)	-	-	-
Sepsis	4 (14)	3 (19)	-	-
Congenital heart disease	-	1 (6)	-	-
After surgery	-	4 (25)	-	-
Unknown	1 (3)	1 (6)	-	-
Hydrops fetalis	2 (7)	-	-	-
Congenital nephrotic syndrome	-	-	-	3 (21)
Bilateral renal vein thrombosis	-	-	1 (7)	-
Primary hyperoxaluria	-	-	-	1 (7)
Bilateral diffuse mesangial sclerosis	-	-	-	1 (7)

ARPKD: Autosomal recessive polycystic kidney disease, CAKUT: Congenital kidney and urinary tract anomalies in children, PD: Peritoneal dialysis

Table 2: Comparison of Group I and Group II in terms of acute dialysis

	Newborns			Infants		
	Group I (n=15)	Group II (n=14)	p	Group I (n=12)	Group II (n=4)	p
	n (%)	n (%)		n (%)	n (%)	
Gender			0.782			1.000
Boy	10 (67)	10 (71)		3 (25)	1 (25)	
Girl	5 (33)	4 (29)		9 (75)	3 (75)	
Diagnoses			0.208			0.114
CAKUT	2 (13)	2 (14)		1 (8)	2 (50)	
ARPKD	2 (13)	-		-	-	
Metabolic disease	2 (13)	-		4 (33)	-	
Drug-induced acute kidney injury	1 (7)	-		-	-	
Prematurity	5 (33)	8 (57)		-	-	
Sepsis	3 (20)	1 (7)		1 (8)	2 (50)	
Congenital heart disease	-	-		1 (8)	-	
After surgery	-	-		4 (33)	-	
Hydrops fetalis	-	2 (14)		-	-	
Unknown	-	1 (7)		1 (8)	-	
Non-infectious complications						
Dialysate leakage	11 (73)	12 (86)	0.411	3 (25)	2 (50)	0.547
Bleeding at the catheter exit site	3 (20)	-	-	3 (25)	-	-
Catheter dysfunction	4 (27)	1 (7)	0.164	1 (8)	2 (50)	0.136
Catheter displacement	3 (20)	-	-	-	-	-
Hydrocele/hernia	2 (13)	1 (7)	1.000	1 (8)	-	-
Infectious complications						
Peritonitis	3 (20)	2 (14)	0.684	3 (25)	2 (50)	0.547
Catheter exit site infection	-	-	-	-	1 (25)	-
Prognosis			0.682			0.521
Renal improvement	5 (33)	3 (21)		3 (25)	2 (50)	
Death	10 (67)	11 (79)		7 (58)	2 (50)	
Switching to HD	-	-		2 (17)	-	

ARPKD: Autosomal recessive polycystic kidney disease, CAKUT: congenital kidney and urinary tract anomalies in children, HD: Hemodialysis, PD: Peritoneal dialysis

Although the total PD duration was longer in group I than in group II (24.5 months vs 12.8 months), it was not statistically significant (p=0.694). The median age of onset PD was younger in group I than in group II (5.5 days vs 24.0 days; p=0.009). All four patients who died in group I were male and 75% of them were premature. The mean age of onset PD was 4.8±2.2 days (2.0-7.0 days). The mean total PD duration was 8.8±4.2 months (3.3-12.5 months).

DISCUSSION

Peritoneal dialysis is the most commonly used method for renal replacement therapy in children facing both acute and chronic renal failure (11). Its effectiveness is particularly noteworthy in newborns and infants, primarily due to the high ratio of peritoneal surface area to body surface area (12). This method is characterized by its technical simplicity and reliability in gradually removing both liquid and solute loads. Coagulation control and the absence of the need for vascular intervention are the reasons for its preference. In newborns and infants, it is mostly caused by many factors such as hypovolemia, hypotension, hypoxia, asphyxia, and septicemia. Acute PD is applied to remove metabolites in acute kidney injury and metabolic diseases (13, 14). In the literature, PD in the first two months of life has been most frequently applied to AKI (68.8%) followed by metabolic disorders (23.4%), and these rates are similar to our cases (15-17). It has been reported that the most common diagnosis of primary end-stage renal disease (ESRD) and therefore chronic PD in patients under 1 year of age is CAKUT (18). Similarly, in our study, the most common cause of ESRD in our patients under the age of 1 who underwent chronic PD was CAKUT (87% in newborns, 50% in infants). Additionally, when our patients in Group I and Group II were compared in terms of the reasons for starting acute and chronic dialysis, no difference was found between the 2 groups.

PD is recognized as an invasive procedure. The International Society of Peritoneal Dialysis (ISPD) recommends

Table 3: Comparison of Group I and Group II in terms of chronic dialysis

	Newborns			Infants		
	Group I (n=8)	Group II (n=7)	p	Group I (n=4)	Group II (n=10)	p
	n (%)	n (%)		n (%)	n (%)	
Gender			0.200			1.000
Boy	8 (100)	5 (71)		3 (75)	6 (60)	
Girl	-	2 (29)		1 (25)	4 (40)	
Prematurity			0.119			1.000
Yes	3 (38)	6 (86)		1 (25)	4 (40)	
No	5 (62)	1 (14)		3 (75)	6 (60)	
Diagnoses			0.364			0.163
CAKUT	6 (75)	7 (100)		1 (25)	6 (60)	
ARPKH	1 (13)	-		-	2 (20)	
Bilateral renal vein thrombosis	1 (13)	-		-	-	
Congenital nephrotic syndrome	-	-		2 (50)	1 (10)	
Primary hyperoxaluria	-	-		1 (25)	-	
Other	-	-		-	1 (10)	
Non-infectious complications						
Dialysate leakage	5 (63)	3 (43)	0.447	2 (50)	2 (20)	0.520
Bleeding at the catheter exit site	2 (25)	-	-	1 (25)	-	-
Catheter dysfunction	3 (38)	1 (14)	0.569	2 (50)	1 (10)	0.176
Catheter displacement	2 (25)	-	-	1 (25)	-	-
Hydrocele/hernia	3 (38)	1 (14)	0.569	1 (25)	1 (10)	0.505
Protrusion of catheter cuff	2 (25)	1 (14)	0.176	-	-	-
Infectious complications						
Peritonitis	6 (75)	6 (86)	1.000	4 (100)	9 (90)	1.000
Catheter exit site infection	3 (38)	2 (29)	0.714	2 (50)	4 (40)	1.000
Prognosis			**0.019**			0.286
Renal improvement	-	2 (29)		-	2 (20)	
Death	4 (50)	-		2 (50)	4 (40)	
Transplantation	4 (50)	1 (14)		1 (25)	-	
PD	-	3 (43)		-	3 (30)	
Switching to HD	-	1 (14)		1 (25)	1 (10)	

ARPKD: Autosomal recessive polycystic kidney disease, CAKUT: Congenital kidney and urinary tract anomalies in children, HD: Hemodialysis, PD: Peritoneal dialysis

starting peritoneal dialysis 10-15 days after catheter insertion to prevent dialysate leakage (5). Unfortunately, the performance of acute PD is associated with a higher incidence of catheter-related complications. This is attributed to the emergency placement of catheters and their immediate utilization upon insertion. Additionally, in newborns and infants, insufficient abdominal wall elasticity, dialysis peritoneal dialysis fluids around the catheter increase the possibility of leakage, and omentum adhesions may cause difficulties in fluid drainage (12). Dialysate leakage is particularly prevalent in low-birth-weight children, with reports indicating a threefold increase in occurrence among those weighing less than 12.4 kilograms (19). Studies have suggested that the risk of leakage is heightened in individuals with a short interval between the insertion of the PD catheter and its commencement of use (3, 4). Gozmen et al. conducted a study identifying the most common acute PD complications, including catheter-related leakage, catheter dysfunction, and, less frequently, hyperglycemia and peritonitis (17). Hakan et al., in their research, reported hyperglycemia (52.2%) as the most prevalent PD complication, with dialysate leakage occurring less frequently (19.4%) (15). In our cases, dialysate leakage around the catheter was detected as the most common complication of acute PD, especially in newborns (79%) and also in infants (31%).

Non-infectious complications, such as dialysate leakage, bleeding at the catheter exit site, catheter dysfunction, catheter displacement, hydrocele/hernia, and protrusion of the catheter cuff, are widely recognized as the primary causes of catheter revision. The PD catheter revision rate in children ranges from 13% to 34%. Revision is usually required within four weeks following the initial insertion of the catheter (5). In a study by Duzalka et al., mechanical

dysfunction (60%) emerged as the most common reason for PD catheter revision followed by peritonitis (16%), tunnel infection (12%), fluid retention, and leakage (6%) (5). Radtke et al. reported that children weighing less than 10 kilograms exhibit a higher frequency of revision (3). The one-year survival rate of the catheters in children under 6 months of age is 50%, while for children aged 6-24 months, it is noted as 83.7% (4,18). In our present study, catheter replacement due to non-infectious complications was required in 28% of newborns and 19% of infants. Notably, peritonitis is identified as the most prevalent cause of catheter revision beyond the initial year (5). It is stated that peritonitis is more common in the 0-2 age group compared to older children (4, 18).

The most common complications observed in pediatric patients undergoing chronic PD were non-infectious complications in newborns and infectious complications in infants within the content of our study. Our patients in Group I and Group II exhibited comparable occurrences of acute and chronic dialysis complications. However, despite technological advancements in PD application, peritonitis and catheter-associated within the scope of our study complications persist as the primary factors influencing patient morbidity (5).

Limited data are available regarding the mortality rates of newborns and infants undergoing PD. Mortality mostly depends on the underlying cause or developing complications (12, 13). No fatalities were attributed to peritonitis or other PD-related complications in our study. The causes of mortality in our study cohort were identified as sepsis in all newborns and cardiovascular complications in infants. In the literature, the mortality rate for children across various age groups undergoing acute PD was reported as 62% (35-95%) (15-17, 20).

For newborns undergoing chronic PD, the mortality rate within the first year of life was reported as 48% (21). Our study identified mortality rates of 72.4% for newborns 56.3% for infants in acute PD, and 27% for newborns and 43% for infants in chronic PD. Notably, despite no difference in acute dialysis outcomes, a more favorable prognosis was observed between 2013-2023, indicating a decline in mortality rates among children undergoing chronic dialysis when compared to the period from 2002 to 2013. Between 2002-2013, four children who started chronic PD in the first week of life during the neonatal period died at the end of a follow-up period of approximately nine months. There was no death between 2013-2023. It is not possible to interpret the reason for this difference with the data we obtained.

CONCLUSION

Peritoneal dialysis is the most commonly used method for renal replacement therapy in children facing both acute and chronic renal failure. Between the years 2002-2013 and 2013-2023, when acute and chronic peritoneal dialysis diagnoses were compared in terms of diagnoses, infectious and non-infectious complications, and prognosis, there was no difference in almost all factors between the two periods. In the last decade, positive developments were observed only in chronic PD deaths that started in the neonatal period. Despite high-quality care in the neonatal care unit, positive technological developments, and effective management in PD, the most common infectious complication was still peritonitis, and the non-infectious complication was dialysate leakage, as in the previous 10 years.

Ethics Committee Approval: The study has ethical approval from the İstanbul University İstanbul Faculty of Medicine (Date: 15.12.2023, No: 25).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

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DOPPLER INDICES AND PERINATAL OUTCOMES IN FETUSES WITH EBSTEIN'S ANOMALY

EBSTEİN ANOMALİLİ FETÜSLERDE DOPPLER İNDEKSLERİ VE PERİNATAL SONUÇLAR

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ABSTRACT

Objective: Ebstein's anomaly (EA) is a rare congenital malformation associated with high perinatal mortality. In this study, we aimed to assess perinatal outcomes and factors associated with mortality in fetuses with EA.

Material and Method: In this study, fetuses diagnosed with EA from 2016 to 2022 were included. Clinical information, ultrasonographic findings, and Doppler parameters were collected retrospectively.

Result: A total of 14 fetuses with EA were included. Twelve patients had isolated EA, while one had unilateral renal agenesis and the other had mega cisterna magna. Amniocentesis was performed in six cases and normal results were obtained. Nine fetuses reached term pregnancy. All fetuses survived to birth. Three cases died in the first week after birth. Survivors were found to have lower tricuspid valve annulus diameter z score when compared with non-survivors (4.81±3.05 vs 6.97±1.26, respectively, p=0.05). Reversal pulmonary artery flow (2/11 vs 4/4 in survivors and non-survivors, respectively, p=0.01) and pulmonary atresia (1/11 vs 4/4 in survivors and non-survivors, respectively, p<0.01) were significantly more frequent in non-survivors.

Conclusion: Perinatal mortality remains high in EA. Higher tricuspid valve annulus diameter z score, presence of reversal pulmonary artery flow, and pulmonary atresia during prenatal diagnosis are associated with poorer diagnosis. Future multicenter studies are warranted to identify risk factors and guide perinatal management.

Keywords: Doppler, echocardiography, ultrasonography, Ebstein's anomaly

ÖZET

Amaç: Ebstein anomalisi (EA) yüksek perinatal mortalite ile ilişkili nadir bir konjenital malformasyondur. Bu çalışmada, EA'lı fetüslerde perinatal sonuçları ve mortalite ile ilişkili faktörleri değerlendirme amaçlandı.

Gereç ve Yöntem: Bu çalışmaya, 2016-2022 yılları arasında EA tanısı alan fetüsler çalışmaya dahil edilmiştir. Klinik bilgiler, ultrasonografik bulgular ve Doppler parametreleri retrospektif olarak toplandı.

Bulgular: EA'lı toplam 14 fetüs çalışmaya dahil edildi. On iki hastada izole EA, birinde tek taraflı renal agenezi ve diğerinde mega sisterna magna vardı. Amniyosentez altı olguda yapıldı ve normal sonuçlar elde edildi. Dokuz fetüs term gebeliğe ulaştı. Tüm fetüsler doğuma kadar hayatta kaldı. Üç olgu doğumdan sonraki ilk hafta içinde kaybedildi. Hayatta kalanların triküspit kapak anulus çapı z skoru hayatta kalmayanlara göre daha düşük bulundu (sırasıyla 4,81±3,05 ve 6,97±1,26, p=0,05). Pulmoner arterde ters akım (hayatta kalanlarda ve hayatta kalmayanlarda sırasıyla 2/11 ve 4/4, p=0,01) ve pulmoner atrezi (hayatta kalanlarda ve hayatta kalmayanlarda sırasıyla 1/11 ve 4/4, p<0,01) hayatta kalmayanlarda anlamlı olarak daha sıktı.

Sonuç: EA'da perinatal mortalite hala yüksektir. Prenatal tanı sırasında daha yüksek triküspit kapak anulus çapı z skoru, pulmoner arterde ters akım ve pulmoner atrezi varlığı daha kötü prognoz ile ilişkilidir. Risk faktörlerini belirlemek ve perinatal dönemi yönetmek için gelecekte yapılacak çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Doppler, ekokardiyografi, ultrasonografi, Ebstein anomalisi

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INTRODUCTION

Ebstein's anomaly (EA) is a rare malformation of the tricuspid valve and right ventricle, characterized by apical displacement of the tricuspid valve (TV) (1). The incidence of EA is 0.12 per 1000 live births, accounting for <1% of all congenital heart diseases (2, 3). When present, severe tricuspid regurgitation leads to cardiomegaly, arrhythmia, and hydrops (4). In a large multicenter study, Freud et al., reported a 45% perinatal mortality. Gestational age at diagnosis, pulmonary regurgitation, larger TV, and pericardial effusion on fetal echocardiography were found to be the strongest predictors of mortality (5). Neonatal mortality remains high and ranges from 17% to 80% (6-9).

Efforts have been made to identify the prognostic value of hemodynamic factors, indices of cardiomegaly, and extracardiac Doppler indices in EA. The presence of pulmonary regurgitation and higher right atrial (RA) area index scores increased umbilical artery (UA) pulsatility index (PI) and decreased umbilical vein (UV) velocity have been associated with poor outcomes in fetuses with EA (5, 10-12).

The present study aims to report perinatal outcomes and investigate clinical and fetal Doppler predictors in fetuses with EA.

MATERIAL and METHODS

This was a single-center, retrospective cohort study of fetuses diagnosed with EA between January 2016 and September 2022 at Health Sciences University, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Istanbul, Türkiye. This study was approved by Zeynep Kamil Women and Children's Diseases Training and Research Hospital Ethics Committee (Date: 05.04.2023, No: 52).

All pregnant women referred to our center with suspicion of fetal anomaly or for routine second-trimester ultrasonographic examination and prenatally diagnosed with Ebstein anomaly were included in the study. Exclusion criteria were as follows: cases with incomplete clinical data and cases not confirmed by a pediatric cardiologist.

EA was defined as a primary defect in TV delamination with an inferior displacement from the atrioventricular valve annulus, which determined a TV and right ventricular dysplasia (Figure 1). Clinical information, ultrasonographic findings, and Doppler parameters, including maternal age, gestational age at diagnosis, delivery mode, birth weight, cardiothoracic ratio (CTR), RA area index, TV annulus diameter, tricuspid regurgitation, aortic maximum velocity, pulmonary artery (PA) flow, ductus venous (DV) flow, umbilical artery (UA) pulsatility index (PI) and middle cerebral artery (MCA) PI were reviewed.

The CTR was calculated as the epicardial circumference of the heart/internal thoracic circumference. RA area index was calculated by dividing the combined area of the RA and atrialized right ventricle by the combined areas of the functional right ventricle, left atrium, and left ventricle at end-diastole (13). Maximum tricuspid jet velocity was measured in systole. Measurement of DV, UA, and MCA flow velocities and indices were performed using a spectral waveform. All sonographic and Doppler examinations were performed by the same team, a collaborative group of experienced perinatologists. Voluson E6 system (GE Medical System, Milwaukee, WI, USA) was used in all examinations with a 2-8 MHz probe. Following birth, postnatal echocardiographic examinations were performed on all patients. These examinations were carried out by the same pediatric cardiologist. The purpose of postnatal assessments was to validate the fetal findings and provide a comprehensive characterization of the cardiac anatomy and function in the neonatal period.

Patients' characteristics and clinical features were summarized using standard descriptive statistics. Continuous Doppler measurements were expressed as mean ± and qualitative variables as numbers (%). Pearson's chi-squared test or Fischer's exact test were used to compare Doppler indices, where appropriate. All p-values were two-sided, and $p<0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS statistical software, version 21 (IBM, SPSS Corp., Armonk, NY, USA).

RESULTS

During the study period, 18 fetuses with EA were diagnosed. Two cases were excluded as parents chose termination of pregnancy. One case of EA with tetralogy of Fallot and another with congenitally corrected transposition of great arteries were excluded as echocardiographic predictors could not be applied. Finally, a total of 14 cases were included in the analysis (Figure 2). Maternal

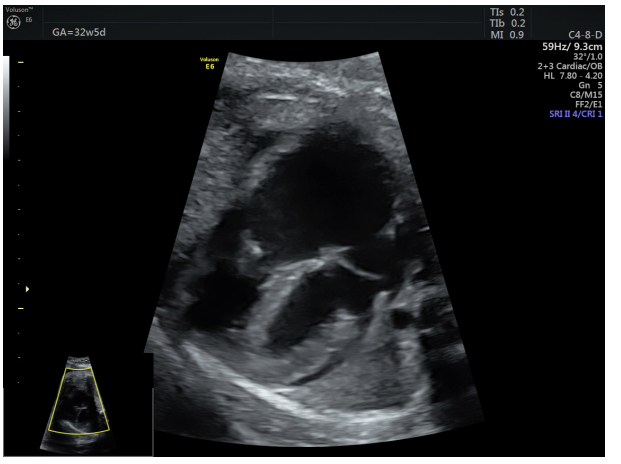

Figure 1: Fetal echocardiogram four-chamber image in a 32-week gestation fetus with Ebstein's anomaly

and fetal data for these patients are outlined in Table 1. The median maternal age was 30.5 years (range 22-39 years). Gestational age at the time of diagnosis ranged from 16 to 34 weeks (median 26 weeks). Twelve patients were grouped as isolated EA, two cases had an additional finding of unilateral renal agenesis, and three cases had mega cisterna magna. Amniocentesis was performed in six cases and normal results were obtained in all. Amniocentesis, comprising analysis through both karyotype and array-CGH, was performed in six cases, and normal results were obtained in all.

Among 14 patients, four developed hydrops, and nine cases reached term pregnancy (64.2%). All fetuses survived to birth. Six cases were delivered vaginally (42.9%), while eight underwent cesarean section. Gestational age at delivery ranged from 28.3 to 40 weeks (median 37.6 weeks). The indications for preterm birth and cesarean section in our study cohort were diverse. Three cases were due to fetal distress, one case was attributed to a low-lying placenta and anhydramnios, two cases were associated with breech presentation and preterm rupture of membranes, and two cases resulted from previous cesarean section and preterm labor. The mean birth weight was 2767.8±406.2 g. Eleven cases (78.5%) survived to three months of age. All neonatal deaths occurred witin the seven days after birth.

Table 2 compares Doppler indices between the survivors and non-survivors. TV annulus diameter z-score was significantly lower in survivors compared with non-survivors (4.81±3.05 vs 6.97±1.26, respectively, p=0.05). Reversal PA flow (2/11 vs 4/4 in survivors and non-survivors, respectively, p=0.01) and pulmonary atresia (1/11 vs 4/4 in survivors and non-survivors, respectively, p<0.01) were significantly more common in non-survivors. None of the other Doppler parameters differed between groups.

DISCUSSION

In this single-center series of EA, the perinatal mortality was 21%, similar to previous single-center experiences (8, 14). However, in prior multi-center studies of EA, a perinatal mortality of 45% was reported (4, 15).

Identifying high-risk fetuses with EA is important in several aspects. It allows the scanning of additional anomalies

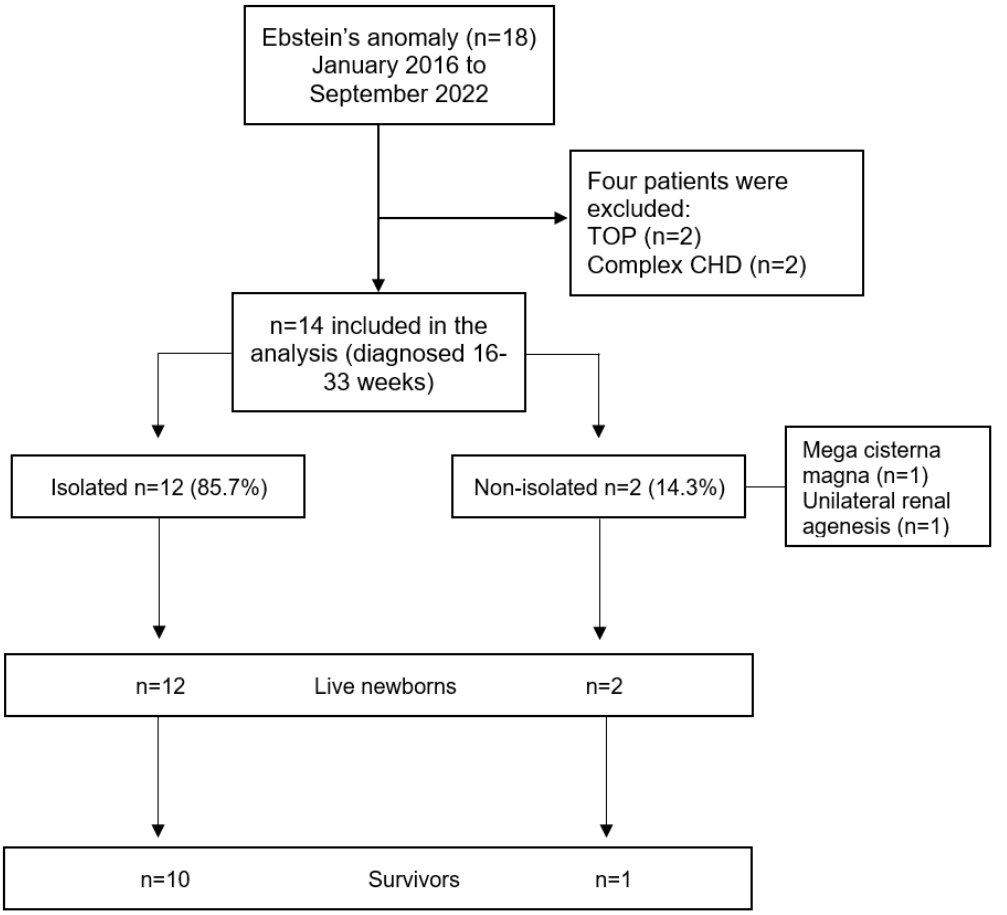

Figure 2: The flowchart of the study group
CHD: Congenital heart disease, TOP: Termination of pregnancy

Table 1: Maternal and fetal characteristics

Case No	Maternal age (years)	GA at diagnosis (weeks)	Additional findings	Amniocentesis	Complication	Delivery	Birth weight (grams)	Outcome
1	31	28		NP		CS	2680	
2	24	33	Unilateral renal agenesis	NP	Hydrops	V	3020	
3	22	22	Mega cisterna magna	Normal	Hydrops	CS	2690	ND
4	25	29		Normal		CS	2130	ND
5	29	26		Normal		V	3000	
6	23	26		NP		CS	3110	
7	36	30		Normal		CS	2880	
8	26	31		NP	Hydrops	V	2700	
9	33	34		NP		CS	3570	
10	33	21		NP		V	2980	
11	34	25		Normal	Arrhythmia, hydrops	CS	1890	ND
12	39	16		NP		V	2700	
13	38	23		NP		V	2720	
14	30	26		Normal		CS	2680	

CS: Cesarean section, GA: Gestational age, ND: Neonatal death, NP: Not performed, V: Vaginal birth

Table 2: Doppler indices at the time Ebstein's anomaly was diagnosed

Doppler indices	Survivors (n=11)	Non-survivors (n=3)	p
Isolated EA, n	10	1	0.51
CTR	0.62±0.06	0.60±0.03	0.89
RA area index	0.59±0.14	0.62±0.21	0.30
TV annulus diameter z-score	4.81±3.05	6.97±1.26	**0.05**
Tricuspid regurgitation			
Maximum velocity, cm/s	201.1±89.31	208.1±30.30	0.34
Aortic maximum velocity, cm/s	98.7±14.40	99.1±8.51	0.85
Reversal PA flow, n (%)	2 (18.1)	4 (100)	**0.01**
Pulmonary insufficiency, n (%)	3 (27.2)	1 (33.3)	1.00
Pulmonary atresia	1 (9.1)	4 (100)	**<0.01**
Abnormal DV flow, n (%)	0	0	1.00
Absent/reversal UA flow, n (%)	0	0	1.00
UA pulsatility index	0.85±0.28	0.86±0.16	0.25
MCA pulsatility index	1.5±0.26	1.6±0.15	0.72

EA: Ebstein's anomaly, CTR: Cardiothoracic ratio, DV: Ductus venosus, MCA: Middle cerebral artery, PA: Pulmonary artery, RA: Right atrium, TV: Tricuspid valve, UA: Uterine artery

and may lead to genetic testing, which can assist the family's decision-making process. In our series, amniocentesis was performed in 43% of the patients (6/14) and all results were normal. However, in a study by Wertaschnigg et al., genetic anomalies were 11% and associated with a significantly increased mortality rate (16). Detecting risky fetuses with EA also allows for closer follow-up in the third trimester, where these fetuses may rapidly decompensate (5). Taking both points into consideration, possible predictors of mortality have been investigated in several studies. Increased CTR, RA area index, TV annulus diameter, severe tricuspid regurgitation, reversal PA flow, and presence of pulmonary regurgitation were shown to be associated with poor prognosis (5, 11, 15-17). Similarly, in the present study, the non-survivor group had significantly higher TV annulus diameter z-score, reversal PA

flow, and pulmonary atresia. Other Doppler parameters did not differ between groups. This may be explained by the small number of patients in our study.

The optimal timing for delivery of the fetus with EA remains a challenge. Worse neonatal outcome was reported with premature delivery in EA (5, 16). Our clinical strategy is to avoid preterm deliveries unless there is an increased risk of fetal death. In our study, five of 14 patients had premature birth.

A small number of patients and retrospective design are the main limitations of this study. In addition, we could not reach and present long-term postpartum data of the included patients. On the other hand, the same perinatology team managed all the patients. Follow-up data for all patients from diagnosis were present.

CONCLUSION

In conclusion, EA remains a cause of increased perinatal mortality. Increased TV annulus diameter, reversal PA flow, and pulmonary atresia at diagnosis may help determine high-risk cases. As EA is a rare condition, larger multicenter series are required to determine the prognostic factors and identify the ideal prenatal management and delivery time.

Ethics Committee Approval: The study has ethical approval from the Zeynep Kamil Women and Children's Diseases Training and Research Hospital Ethics Committee (Date: 05.04.2023, No: 52).

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RESEARCH / ARAŞTIRMA
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EFFICACY OF EXTRACORPOREAL ELECTROMAGNETIC STIMULATION FOR THE TREATMENT OF URINARY INCONTINENCE AND THE PREDICTIVE FACTORS FOR SATISFACTION

EKSTRAKORPOREAL ELEKTROMANYETİK STİMÜLASYONUN ÜRİNER İNKONTİNANS TEDAVİSİNDE ETKİNLİĞİ VE BAŞARIYI ETKİLEYEN FAKTÖRLERİN ANALİZİ

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ABSTRACT

Objective: Extracorporeal electromagnetic stimulation (ExMS) has been used widely to treat Urinary Incontinance (UI). We aim to analyze the subjective and objective outcomes of ExMS treatment and evaluate factors that could predict satisfaction.

Material and Method: Patients who underwent ExMS treatment for UI were evaluated. ExMS was performed twice weekly with 20-minute sessions for six-eight weeks. Subjective satisfaction and objective improvement were evaluated before and three months after treatment with a bladder diary, pad test, and pelvic floor muscle strength assessment. King's Health Questionnaire was used to evaluate quality of life.

Result: Eighty-one patients were included. The mean age was 50.4±9.7 (30-76). Fourty four (54.3%) patients suffered from mixed UI, and 19 (23.5%) and 18 (22.2%) suffered from stress UI and urge UI, respectively. Six patients were cured, 64 (79.1%) were better than before, and the rest noticed no change. After treatment, there were significant improvements in bladder diary, pelvic floor muscle strength, pad test, and King's Health Questionnaire. There was a significant correlation between the type of UI and satisfaction after treatment; women suffering from stress UI were less satisfied when compared to urge or mixed UI. No correlations were found between treatment satisfaction and age, pretreatment pelvic floor muscle strength, 1-hour pad test,

ÖZET

Amaç: Elektromanyetik dalgalarla tedavi (ExMS) üriner inkontinansın tedavisinde sıklıkla kullanılmaktadır. Bu çalışmada, Üriner inkontinansın (İÜ) şikayetleri olan hastalarda EXMS tedavisinin etkinliğinin değerlendirilmesi ve tedavi memnuniyetini etkileyen faktörlerin analiz edilmesi amaçlanmıştır.

Gereç ve Yöntem: Üriner inkontinans nedeniyle ExMS tedavisi uygulanan hastalar retrospektif olarak değerlendirilmiştir. ExMS, manyetik stimülasyon sandalyesi kullanılarak, haftada üç seans ve her seans 20 dakika olmak üzere altı-sekiz hafta boyunca uygulanmıştır. Subjektif memnuniyet, tedavi öncesi ve sonrasında ürojinekolojik semptomlar, bir saatlik ped testi, dört günlük üriner günlük, pelvik taban kas gücü ve King Sağlık Anketi değerlendirilmiştir.

Bulgular: Seksen bir hasta çalışmaya dahil edilmiştir. Ortalama yaş 50,4±9,7'dir (30-76). Kırkdört (%54,3) hasta mikst Üİ, 19 hasta (%23,5) stres Üİ ve 18 hasta (%22,2) acil Üİ tanısı almıştır. ExMS tedavisinden memnuniyet değerlendirildiğinde, altı hasta tamamen iyileştiklerini, 64 hasta (%79,1) daha iyi olduklarını, geri kalan hastalar değişiklik olmadığını belirtmiştir. Tedavi sonrası üriner günlük, pelvik taban kas gücü, bir saatlik ped testi ve King Sağlık Anketi sonuçlarında anlamlı düzelme görülmüştür. Üriner inkontinans tipi ile memnuniyet arasında anlamlı ilişki bulunmuştur. Stres Üİ şikayeti olan kadınlarda memnuniyet urge veya mikst

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or mean number of leakage and urgency episodes. No complications developed.

Conclusion: ExMS is an effective treatment for UI with almost 80% subjective satisfaction. Quality of life, pad test, bladder diary, and pelvic floor muscle strength were improved significantly. The UI type (urge or mixed UI) was a significant predictive factor for treatment satisfaction.

Keywords: Electromagnetic stimulation, mixed urinary incontinence, overactive bladder syndrome, quality of life, stress urinary incontinence, urinary incontinence

Üİ olanlara göre daha düşük bulunmuştur. Bunun dışında yaş, ped testi, pelvik taban kas gücü ve ortalama kaçak ve aciliyet sayısı ile memnuniyet arasında anlamlı ilişki bulunamamıştır. Tedavi esnasında veya sonrasında herhangi bir komplikasyon gelişmemiştir.

Sonuç: ExMS, Üİ şikayeti olan kadınlarda etkin bir tedavidir. Subjektif tatmin oranları %80'e varmaktadır. Objektif olarak ped testi, pelvik taban kas gücü, üriner günlük ve hayat kalitesinde anlamlı düzelmeye neden olmaktadır. Üriner inkontinans tipi (urge veya mikst Üİ) tedavi memnuniyeti etkileyen bir faktördür.

Anahtar Kelimeler: Elektromanyetik stimülasyon, üriner inkontinans, mikst üriner inkontinans, stres üriner inkontinans, aşırı aktif mesane, hayat kalitesi

INTRODUCTION

Urinary incontinence (UI), the involuntary leakage of urine, is a frequent problem among women with an adverse effect on quality of life (1). The first-line treatment for UI is conservative, with several treatment options, such as behavioral modification and pharmacotherapy with anticholinergic medications (2). In addition, physical therapies, including vaginal cones, biofeedback, electrical stimulation or peripheral or sacral neuromodulation methods, and extracorporeal magnetic stimulation (ExMS) may be used for the treatment of UI (2).

ExMS is commonly used in the world and our country. ExMS achieves nerve stimulation and neuromodulation by generating an electrical activity that penetrates tissues without alteration and induces controlled depolarization of the nerves. Therefore, a greater effect can be achieved on deeper neural tissue with minimal discomfort at the application point (3). ExMS treatment stimulates the pelvis's central and peripheral nerve pathways and induces pelvic floor muscle contraction (4, 5). The main advantages of ExMS include its non-invasive and relatively painless nature, the lack of internal electrodes, and the ability to be fully clothed during treatment.

In this study, we aimed to analyze the subjective satisfaction and objective results of ExMS in the treatment of UI. The primary outcome was subjective improvement in UI and satisfaction. Secondary outcomes were objective improvement rates in bladder diary, pad test, quality of life, pelvic floor muscle strength, and defining factors that could affect the outcome of ExMS treatment.

MATERIAL and METHODS

One hundred twenty-five patients suffering from UI and treated with ExMS were included. The inclusion criteria for ExMS treatment were a history of UI of at least six months, written informed consent for the treatment and the presence of detailed history and urogynecology evaluation.

Exclusion criteria for ExMS treatment were the presence of a cardiac pacemaker or other implantable devices, pregnancy, and active urinary tract infection. Exclusion criteria for the study needed to include data during pretreatment evaluation and follow-up. Ethical approval was obtained from İstanbul Faculty of Medicine, Clinical Research Ethics Committee (Date: 02.04.2021, No: 08). All patients signed the informed consent form.

Before treatment, all patients were evaluated, including medical history, dipstick urine test, and urine culture, stress test, pelvic organ prolapse evaluation using POP-Q system, Q-tip test, pelvic floor muscle strength using digital palpation and perineometer, four-day bladder diary, one-hour pad test, and urodynamics. Urodynamics, including cystometry and uroflowmetry, were performed using the MMS UD 2000 Urodynamics System (*MMS UD-2000*, Medical Measurement System, Enschede, The Netherlands). All women completed the Turkish-validated version of King's Health Questionnaire for the quality of life assessment (6).

ExMS was performed in hospital settings using a MAGTHER E-6000 magnetic stimulation chair for pelvic rehabilitation. All patients were treated every three days for six-eight weeks. The duration of each session was 20 minutes, made up of two episodes of 10 minutes with a resting interval of 10 minutes. As suggested in previous studies, 50 Hz frequency was used for patients suffering from stress UI, and 10 Hz frequency was used for patients suffering from urge UI (7). Patients with mixed UI were treated for 10 minutes with 50 Hz and 10 minutes with 10 Hz.

Two months after completing the treatment program, medical history, pelvic floor muscle strength, pad test, four-day bladder diary, and King's Health Questionnaire were performed. The patients either received biofeedback or were educated regarding pelvic floor muscle exercises depending on their muscle strength after the treatment.

The primary outcome was subjective improvement in UI: women who suggested that they were either completely dry or that their UI was improved. Subjective evaluation by the patients was reported as 'cure,' 'better than before,' 'no change at all,' and 'worse than before.'

Secondary outcomes included improved quality of life, pad test, four-day bladder diary, pelvic floor muscle strength, and defining predictive factors that could affect satisfaction after ExMS treatment.

Statistical analysis

Statistical analysis was performed with the computer program IBM Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM SPSS Corp., Armonk, NY, USA). Descriptive tests were used to describe patients' characteristics. Data were expressed as mean ± standard deviation. Because the Kolmogorov-Smirnov test indicated that data distribution deviated significantly from normality, the Wilcoxon signed-rank test was used for pre-treatment and post-treatment comparison. Spearman's correlation test was used to determine any association between type of UI, age, 1-hour pad test, pelvic floor muscle strength, bladder diary, and satisfaction. A p-value <0.05 was considered statistically significant.

RESULTS

One hundred twenty-five women received ExMS for treatment of UI. Forty-four women were excluded because of missing data during follow-up regarding either measurement of pelvic muscle strength, bladder diary, or 1-hour pad test. Total number of women included was 81.

The demographic variables of the patients are summarized in Table 1. The mean age of the patients was 50.4±9.7 (30-76). Forty-six patients were in the postmenopausal period. The mean body mass index was 29.9±5.4 kg/m^2. Mean number of deliveries was 2.3±1.4 (0-5); six patients were nulliparous, 64 patients delivered vaginally, three patients had a history of vacuum extraction, and eight patients had a history of cesarean section. Six patients had diabetes, five patients had depression, and two patients suffered from disc hernia. Two patients had undergone an anti-incontinence surgery before. Four patients had a history of total abdominal hysterectomy, and three patients underwent vaginal hysterectomy. Forty-four patients suffered from mixed UI (54.3%), and 19 patients (23.5%) and 18 patients (22.2%) suffered from stress UI and urge UI, respectively. Sixteen patients suffered from coital incontinence. Fifty-six (69.1%) patients were using pads for UI every day.

Table 1: Demographic variables of the women included in the study

	n=81
Age	50.4±9.7 (30-76)
Menopause n (%)	46 (56.7%)
Body mass index (kg/m^2)	29.9±5.4
Number of deliveries	2.3±1.4 (0-5)
Anti-incontinence surgery n (%)	2 (2.4%)
Type of UI	
Stress UI n (%)	19 (23.5%)
Urge UI n (%)	18 (22.2%)
Mixed UI n (%)	44 (54.3%)

UI: Urinary incontinence

All patients completed the treatment program, and no adverse events developed during treatment. Self-reported satisfaction related to ExMS treatment was as follows: Six patients suggested that they were cured, 64 patients (79.1%) suggested that they were better than before, and 11 patients (13.6%) noticed no change.

Four-day bladder diary results before and after treatment are summarized in Table 2. The mean number of voiding and urgency episodes before treatment was 8.6±3.5 and 2.2±3.8, respectively. The mean number of leakage episodes was 2.2±3.7 before treatment. Mean number of nocturia was 0.9±0.9. There was significant improvement after treatment in all these parameters. The mean number of voiding episodes was 6.4±1.7, the mean number of urgency episodes was 0.83±1.6, the mean number of leakage episodes was 0.6±1.4, and the mean number of nocturia was 0.5±0.8 after treatment.

There were significant changes in pelvic floor muscle strength and 1-hour pad test results after treatment (Table 2). The mean pelvic floor muscle strength was 18.7±9.5 cmH2O and 23.7±11.9 cmH2O before and after treatment. The mean pad tests were 26.8±43.4 gr and 1.2±2.5 gr before and after treatment. The distribution of the pad weight results of the women are summarized in Table 3. Forty patients (49.4%) had a negative pad test before treatment, whereas 70 patients (86.4%) had a negative pad test after treatment. Twelve patients (14.8%) had a pad test above 50 gr before treatment, but none had a pad test above 45 gr after treatment; four patients (4.9%) had a pad test between 10 gr and 45 gr.

There were significant changes in all domains and total scores of the King's Health Questionnaire except for personal relationships and symptom severity domains when the pretreatment and posttreatment results were compared. The pretreatment and posttreatment total scores of the King's Health Questionnaire were 422.4±205.5 and 297.9±212.5, respectively. The results are summarized in Table 4.

A significant correlation was found between the type of UI and satisfaction related to ExMS treatment (r=0.16,

Table 2: The 4-day bladder diary, pelvic floor muscle strength measured by a perineometer, and 1-hour pad test results before and after treatment

	Pretreatment	Posttreatment	P value
The mean number of voiding episodes	8.6±3.5 (5-25)	6.4±1.7 (5-15)	0.001
The mean number of urgency episodes	2.2±3.8 (0-13)	0.83±1.6 (0-8)	0.001
The mean number of leakages	2.2±3.7 (0-20)	0.6±1.4 (0-10)	0.001
The mean number of nocturia	0.9±0.9 (0-9)	0.5±0.8 (0-5)	0.001
Pelvic floor muscle strength measured by perineometer (cmH_2O)	18.7±9.5 (1-45)	23.7±11.9 (1-54)	0.01
1-hour pad test (gr)	26.8±43.4 (0-200)	1.2±2.5 (0-45)	0.001

Wilcoxon signed rank test was used

Table 3: Distribution of the 1-hour pad test results of the women before and after treatment

	Pretreatment n (%)	Posttreatment n (%)
<2 gr	40 (49.4%)	70 (86.4%)
2≤10 gr	15 (18.5%)	7 (8.6%)
10≤ 50 gr	14 (17.3%)	4 (4.9%)
≥50 gr	12 (14.8%)	0

Table 4: Results of the King's Health Questionnaire before and after treatment

	Pretreatment	Posttreatment	P value
General health perceptions	48.8±20.3	40.9±19.7	0.04
Incontinence impact	68.5±35.6	46.9±40.7	0.03
Role limitations	53.2±34.9	40.1±35.5	0.03
Physical limitations	54.6±36.7	37.9±37.1	0.04
Social limitations	40.4±32.7	23.2±28.5	0.003
Personal relationships	19.4±26.0	11.4±23.2	0.25
Emotions	49.1±31.9	30.8±32.2	0.003
Sleep/ energy	36.1±28.0	24.9±26.1	0.03
Symptom severity	50.2±23.2	38.9±32.9	0.10
Total score	422.4±205.5	297.9±212.5	0.003

Wilcoxon signed rank test was used

p=0.037). Women suffering from stress UI had a lower rate of satisfaction (47.3%±36.0%) when compared to women suffering from urge UI (59.9%±28.4%) or mixed UI (62.0%±29.5%). No significant correlations were observed between age (r=0.13, p=0.08), pretreatment pelvic floor muscle strength (r=0.04, p=0.609), 1-hour pad test (r=0.01, p=0.99), and a mean number of pretreatment leakage (r=-0.064, p= 0.398) or urgency episodes (r=0.01, p=0.86).

No pain or adverse effects developed during ExMS. No complications were observed during the treatment or posttreatment periods.

DISCUSSION

ExMS is a recent technique used for the treatment of UI. ExMS uses Faraday's law of magnetic induction; membrane depolarization of adjacent nerves occurs, leading to subsequent muscle contraction (8). The targets of ExMS treatment are sacral S2-S4 nerve roots, which are the primary autonomic and somatic innervation of the urethra and bladder. ExMS stimulates pelvic floor muscles, urethral sphincter, and pudendal nerve afferents, which results in detrusor inhibition (3).

As the study's primary outcome, we have shown that ExMS led to greater than 60% improvement in women suffering from UI with no pain or adverse effects during or after treatment. In our study, there were significant changes in pad test, bladder diary, pelvic floor muscle strength, and quality of life in patients suffering from stress, urge, and mixed UI. The decreases in the mean leakage, urgency, and voiding episodes show that ExMS effectively treats urge UI.

Success rates regarding ExMS treatment vary between studies. In a prospective multicenter study, Galloway et al., reported cure and improvement rates of 34% and 66%, respectively, in 83 patients with stress UI (9). In this study, 50 women had longer than three months of follow-up. In addition, they showed a reduction in pad usage and pad weight. Detrusor instability was found in five women before treatment and was present in a single patient during follow-up. Yamanishi et al., reported that 86% of patients with stress UI and 75% of patients with

urge UI had significant improvements in quality of life, maximum urethral closure pressure, and urgency after treatment (10). Chandi et al. reported objective improvements in 58% of patients treated for urge and mixed UI (11). Significant clinical improvement was seen only in patients with urge UI. They showed no significant change in urodynamic parameters after treatment. Groenendijk et al. evaluated the clinical effects and urodynamic changes in 16 women suffering from stress, urge, and mixed UI treated with ExMS (12). There were no significant differences in bladder diary, pad test, and visual analog scale before and after treatment; however, detrusor overactivity and urethral instability disappeared in 60% and 66% of the patients, respectively, in posttreatment urodynamics. Voorham-van der Zalm et al. evaluated the effect of ExMS on pelvic floor function (8). The authors found no significant difference in the quality of life using KHQ except for role limitations, bladder diary, and pad test. The authors suggested that ExMS may increase awareness of pelvic floor muscles and should be combined with active exercises to strengthen the effect.

On the other hand, Yokoyama et al., reported 53% improvement that lasted until 24 weeks after last treatment in 17 of the 20 patients suffering from urge UI (13). Almedia et al. evaluated the effects of ExMS on 91 women suffering from UI with a follow-up of 1 year (14). Immediately after treatment, quality of life improved by 35%, the number of pads used daily decreased by 40%, and the number of leakage episodes decreased by 54%, with a cure rate of 37%. A 24.3% average increase in leak point pressure and detrusor overactivity disappeared in 77% of the patients. However, at 1-year follow-up, 94% of patients who became dry had a recurrence. Possible reasons for these controversial results among studies are small sample sizes, inclusion of male and female patients, differences in the stimulation protocol, duration of stimulation, and duration of follow-up after treatment.

There are controversial results in studies comparing ExMS with other stimulation methods and sham stimulation. However, But et al. compared the efficacy and safety of ExMS with placebo in the treatment of UI (15). Fifty-five women with UI were randomly assigned to an active treatment group or placebo group. A 56.3% improvement was observed in the active treatment group versus a 26.3% improvement in the placebo group. Compared with placebo, the number of pads used, and pad weight were significantly lower, and the duration and strength of pelvic floor muscle contractions were significantly improved. Bolukbas et al. compared the effectiveness of vaginal electrical stimulation and ExMS in 22 women suffering from UI (16). They found significant improvement in pelvic floor muscle strength and pad test results; however, the improvement in bladder diary was greater in the electrical stimulation group. Fujishiro et al. reported a beneficial effect of ExMS for patients with stress UI over sham stimulation (17). The stimulation group had a 74% improvement, whereas the sham group had a 32% improvement, with improved bladder diary and quality of life results. Gilling et al., in their double-blind, randomized controlled trial, found significant improvements in quality of life and pad test results in the active stimulation group compared to the sham stimulation group; however, these improvements did not reach statistical significance (18).

Lim et al., reported the efficacy of ExMS for treating stress UI with a 1-year follow-up in their multicenter randomized study (19). Seventy five percent of the patients in the active stimulation group responded versus 21.7% in the sham stimulation group. Yamanishi et al. evaluated the effects of ExMS on urodynamic stress UI resistant to pelvic floor muscle training in their randomized sham-controlled study (20). Quality of life scores, severity of UI, and abdominal leak point pressures significantly improved in the active stimulation group. Lim et al., in their systematic review evaluating the efficacy of ExMS for UI, evaluated eight studies, including 494 patients. Two hundred eighty-five underwent active stimulation, whereas 209 received sham treatment (21). The most extended follow-up was six months. The active stimulation group improved incontinence (2.3 times) compared to sham stimulation. The systematic review was weak due to varying inclusion criteria, varying follow-up, and poor reporting. There were controversial results regarding the effects on quality of life.

Main strengths of our study include the adequate sample size and detailed pretreatment and post-treatment evaluation including subjective and objective measures of success. Main limitations of the study are the short follow-up period, lack of sham stimulation as a control group, and lack of correlation with urodynamic findings. In addition, blinding of the patients during treatment assignment was not possible due to the nature of the interventions.

CONCLUSION

In conclusion, ExMS is an effective treatment option for patients suffering from UI, with almost 80% subjective satisfaction and significant improvement in quality of life, pad test, bladder diary, and pelvic floor muscle strength. Further prospective studies are needed for the evaluation of the long-term effects of ExMS and comparison with sham stimulation.

Ethics Committee Approval: The study has ethical approval from the İstanbul Faculty of Medicine, Clinical Research Ethics Committee (Date: 02.04.2021, No: 08).

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ALTERATIONS IN CATALASE, SUPEROXIDE DISMUTASE, GLUTATHIONE PEROXIDASE AND MALONDIALDEHYDE LEVELS IN SERUM AND LIVER TISSUE UNDER STRESS CONDITIONS

STRES KOŞULLARINDA SERUM VE KARACİĞER DOKUSUNDAKİ KATALAZ, SÜPEROKSİT DİSMUTAZ, GLUTATYON PEROKSİDAZ VE MALONDİALDEHİT DÜZEYLERİNİN DEĞİŞİMİ

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ABSTRACT

Objective: Chronic stress is a factor that affects organs/tissues and disrupts homeostasis. This condition can lead to increased oxidative stress, which damages cellular components. Antioxidants attempt to prevent this damage by neutralizing free radicals. Our study aimed to investigate the effect of chronic mild stress on the levels of Catalase (CAT), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Malondialdehyde (MDA) in serum and liver tissue.

Material and Method: In our study, 16 Wistar albino rats were divided into control and experimental groups. The chronic unpredictable mild stress (CUMS) model protocol was employed. The levels of CAT, SOD, GPx, and MDA in serum and liver tissue were measured using the Enzyme-Linked Immunosorbent Assay method.

Result: Upon comparison of serum CAT, SOD, GPx, and MDA levels, no statistically significant difference was observed between the control and stress groups ($p>0.05$). However, when comparing CAT, SOD, GPx, and MDA levels in the liver tissue, a significant increase in the levels of antioxidant enzymes was noted in the stress group ($p<0.05$).

Conclusion: Under chronic stress, liver tissue's antioxidant levels appear to increase. We believe our study may contribute to understanding the connection between stress, free radicals, and antioxidants.

Keywords: Antioxidant, chronic stress, oxidative stress

ÖZET

Amaç: Kronik stres, organ/dokuları etkileyen ve homeostazisi bozan bir faktördür. Bu durum, hücresel bileşenlere zarar veren oksidatif stresin artmasına neden olabilir. Antioksidanlar ise serbest radikalleri notralize ederek bu zararı önlemeye çalışır. Çalışmamızın amacı, kronik hafif stresin serum ve karaciğer dokusundaki Katalaz (CAT), Süperoksit Dismutaz (SOD), Glutatyon Peroksidaz (GPx) ve Malondialdehit (MDA) seviyeleri üzerindeki etkisini araştırmaktır.

Gereç ve Yöntem: Çalışmamızda 16 Wistar albino sıçan kontrol ve deney gruplarına ayrılmıştır. Kronik öngörülemeyen hafif stres model protokolü uygulandı. Serum/karaciğer CAT, SOD, GPx ve MDA düzeyleri Enzyme Linked Immunosorbent Assay metodu ile ölçüldü.

Bulgular: CAT, SOD, GPx ve MDA serum düzeyleri karşılaştırıldığında kontrol ve stres grupları arasında istatistiksel olarak anlamlı fark belirlenmedi ($p>0,05$). Buna karşın, karaciğer dokularındaki CAT, SOD, GPx ve MDA seviyeleri karşılaştırıldığında, stres grubunda antioksidan enzim seviyelerinde anlamlı yükseliş belirlenmiştir ($p<0,05$).

Sonuç: Kronik stres altında, antioksidan enzim seviyelerinin karaciğer dokusunda arttığı görülmektedir. Çalışmamızın stres, serbest radikaller ve antioksidanlar arasındaki bağlantıya yönelik bir katkı sunabileceği kanısındayız.

Anahtar Kelimeler: Antioksidan, kronik stres, oksidatif stres

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INTRODUCTION

Chronic psychological stress has become an inevitable part of modern life, negatively impacting both physical and mental health. It is considered a factor that affects nearly all organs/tissues and disrupts homeostasis (1). Furthermore, it is a subject of current research that chronic stress may elevate oxidative stress at the cellular level, potentially contributing to the development of various diseases (2, 3).

Oxidative stress is a biological imbalance from accumulating reactive molecules, known as free radicals, within cells (4). The accumulation of free radicals within cells and resultant oxidative damage from oxidative stress can prompt a spectrum of morphological alterations in tissues. Such changes can affect the structure and functionality of cells, leading to potential harm across various organs. The liver, which has an important function in detoxification processes, is primarily affected by this process (1). Also, chronic psychological stress can increase cortisol levels and cause oxidative stress (5). Chronic stress can also impact the immune system, producing heightened inflammatory responses. In such cases, there is an increase in the secretion of pro-inflammatory cytokines, which may contribute to the formation of free radicals (6).

Moreover, chronic psychological stress can negatively affect mitochondrial function. Under the influence of stress, dysfunctions in mitochondria may arise, potentially contributing to an increase in oxygen radicals (2, 7). Additionally, chronic stress can impact antioxidant defense systems, reducing their effectiveness (4).

The organism responds to the harmful effects of oxidative stress with the antioxidant defense system. This defense system tries to prevent oxidative damage by neutralizing free oxygen radicals in cells (8). The biological system that prevents the progression of oxidation/peroxidation by reacting with oxygen radicals is defined as 'Antioxidant defense' (9). The primary members of the cellular antioxidant defense mechanism are Catalase (CAT), Superoxide Dismutase (SOD), and Glutathione Peroxidase (GPx). These enzymes trigger a series of biological activities that facilitate the removal of oxidative stress factors, which could disrupt the homeostatic balance of the cell (10).

Catalase is an important enzyme that plays a fundamental role in protecting cells from the harmful effects of hydrogen peroxide in almost all aerobic organisms (11). CAT serves as an efficient catalyst, facilitating the breakdown of hydrogen peroxide into water and molecular oxygen. This compound is generated as a byproduct during diverse cellular activities. The fundamental significance of the CAT enzyme lies in its role as a potent antioxidant agent within the biological system. Iron ions in CAT catalyze hydrogen peroxide oxidation (2). Hydrogen peroxide forms a compound that, as a reactive oxygen species, can damage cellular components, lipids, proteins, and genetic material (7). CAT, which also plays a role in detoxification, is found mainly in liver tissue (12).

Superoxide dismutase is a critical enzyme that provides an effective antioxidant defense mechanism against reactive oxygen species (ROS), especially superoxide anion radicals (13). SOD facilitates reactions that convert superoxide radicals into oxygen molecules and transform other superoxide radicals into hydrogen peroxide, which is a less reactive compound. This process enables cells to shield themselves effectively from oxidative harm induced by superoxide anions and ROS (14). SOD is an antioxidant enzyme that plays an important role in maintaining cellular homeostasis and is considered a key component in combating oxidative stress (10).

Glutathione peroxidase is an antioxidant enzyme that has important functions in maintaining the cellular redox balance. It also plays an important role in preventing lipid peroxidation, which can cause cellular damage (8). GPx reduces cellular peroxide compounds and organic hydroperoxide and turns them into harmless ones. This increases the resistance of cells to oxidative damage (9). GPx functionally interacts with GSH 'γ-glutamyl-cysteinyl-glycine,' enabling the formation of the reduced form of GSH and thereby counteracting the effects of oxidative stress (15). GPx plays a crucial role in reducing the oxidation of polyunsaturated fatty acids within cell membranes, thereby preserving cellular integrity through maintaining membrane structure. GPx constitutes a significant component of the cellular antioxidant defense system (16). It works together with other antioxidant enzymes, SOD and CAT, to provide an effective defense of cells against reactive oxygen radicals (17).

Malondialdehyde is generated through the interaction of oxygen molecules and free radicals with polyunsaturated fatty acids in the cell membrane. MDA is a common biomarker for evaluating the levels of oxidative stress in cells and tissues (18). Monitoring MDA levels can provide insights into the extent of oxidative stress and potential cellular damage. Elevated MDA levels indicate increased oxidative damage to cell membranes and lipids (10, 19).

Within this framework, the primary objective of our investigation is to ascertain the concentrations of antioxidant enzymes in the serum and liver tissues subjected to chronic stress. Our goal is to assess the impact of chronic mild stress on cellular oxidative stress by juxtaposing potential alterations in enzyme levels against those of the control group. This research will enhance the comprehension of the mechanisms by which chronic psychological stress may influence oxidative stress and potential cellular injury.

MATERIALS and METHODS

Animals and standard procedures

In the study, 4-month-old 190-200 gr female Wistar albinos (n=16) were used. We divided the rats into two groups in standard cages two weeks before the study process started and provided the standard room conditions. The menstrual cycles of rats were considered and analyzed. Rats in the same menstrual phase were included in the study. During anesthesia, a combination of ketamine hydrochloride (90 mg/kg; Ketalar, Parke-Davis) and xylazine hydrochloride (12 mg/kg, 2%; Rompun, Bayer) was administered intraperitoneally to rats. The anesthesia process of the rats was started approximately 15 minutes before. Muscle movements and reactions to pain were tested and processed. Euthanasia was performed by cervical dislocation after intracardiac blood collection. The principles of "Guidelines for the Care and Use of Laboratory Animals" were applied. Ethical approval of the study was obtained from the Kocaeli University Animal Experiments Local Ethics Committee (Date: 26.07.2023, No: 6/4-2023).

Stress model and groups

In our study, the chronic unpredictable mild stress (CUMS) protocol which was previously defined in the literature, was used as a stress model (20). Using the CUMS model, rats are prevented from learning stressors, which consequently inhibits their ability to develop resilience to the stress model. A total of 8 different stressors were identified, and the order of the stressors was previously determined (Box 1). At the end of the experiment, anhedonia behaviors, considered an indicator of the depression status of the animals, were closely monitored and measured.

Box 1: Stressors applied in Chronic Unpredictable Mild Stress (CUMS) model

1. Cage inclination, 45 °C/24 hours
2. Hanging from the tail, 1 minute
3. Buoyancy in cold water 4 °C/5 minutes
4. Buoyancy in hot water 45 °C/5 minutes
5. Changing day-night cycle
6. Cage shaking, 10 minutes
7. Cage wetting 200 mL/24 hours
8. Exchanging sawdust between cages

In our study, two groups were formed: experimental and control groups. Then, we applied the stressors to the experimental group for 28 days. Before the start of the experiment, the order in the application protocol was determined randomly.

Tissue lysis procedures

To prevent possible blood contamination, tissues were washed with a saline solution containing 0.09% NaCl. Subsequently, the tissues were weighed and homogenized in a 1/10 ratio of phosphate-buffered saline with a pH of 7.4. The homogenization was carried out at 24,000 revolutions per minute using a T25 Basic Ultra Turrax homogenizer (IKA Werke Deutschland/Germany). Following homogenization, the samples were centrifuged at 10,000 times the force of gravity for 15 minutes at a temperature of 4°C. The resulting homogenate was then divided into smaller tubes and preserved for further analysis based on tissue-specific measurements. The modified Lowry method determined the protein content (21). The total protein concentration of the liver tissue was equalized before the ELISA process.

Enzyme-linked immunosorbent Assay (ELISA) method and biochemical procedures

Blood samples (3 mL) were taken from the left ventricle. Blood specimens were allowed to clot for two hours at room conditions and centrifuged for 15 minutes at 1000g force at 4-8 °C. Serum samples were stored at -40°C. The supernatants were collected and diluted 1/10 before the assay. Serum and tissue GPx, CAT, and SOD levels were determined with ELISA (ELISA; BT Lab, Zhejiang, China) kits and measured with ‹Alisei Quality System Seac Radim Company analyzer› (Italy/Rome)-ELISA reader based on the manufacturer›s instructions (GPx-1, Code E1172Ra; CAT, Code E0869Ra; SOD-1, Code E1444Ra). Serum and tissue MDA levels were determined using a colorimetric MDA assay (BT Lab, Zhejiang, China) and measured with UV-1280 UV-VIS Spectrophotometer (Shimadzu, Kyoto, Japan) based on the manufacturer›s instructions (MDA, Code SH 0020). The dilution coefficient was multiplied by the results, and their concentrations were calculated according to the kit›s standards.

Data analysis and statistics

The Kolmogorov-Smirnov analysis was performed for the normal distribution suitability test in the statistical evaluation of our results. An Independent T-test was applied for the values that correspond to normal distribution. 'The Mann Whitney U' statistic method was used for the values that do not comply with the normal distribution. P values of 0.05 or less were considered statistically significant. The Statistical analysis SPSS 22.0 (IBM, SPSS Corp., Armonk, NY, USA) was used. The GraphPad Prism 8 package program was used for graphics design.

RESULTS

The mean serum CAT level and standard error were recorded as 0.4354±0.00002 pg/mL for the control group and 0.4357±0.00008 pg/mL for the stress group. Upon comparison of serum CAT levels, no statistically significant difference was observed between the control and stress

groups (p>0.05). The liver tissue CAT mean level and standard error were 75.1530±2.6575 pg/mg for the control group and 97.2244±4.3709 pg/mg for the stress group. Upon comparison of the CAT levels in liver tissue, a significant difference was noted between the stress and control groups (p=0.001). CAT levels were increased in the liver tissues of the rats belonging to the stress group (Figure 1).

When the SOD serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). The serum SOD mean level and standard error mean; 0.3153±0.0004 ng/mL for the control group, 0.3155±0.0005 ng/mL for the stress group. However, when the liver tissue SOD levels were compared, a significant difference was observed between the stress and control groups (p=0.002). The mean SOD level in liver tissue and the associated standard error were 53.4895±1.9065 ng/mg for the control group and 69.7734±3.4213 ng/mg for the stress group. Elevated SOD levels were observed in the liver tissues of rats subjected to stress (Figure 2).

The Glutathione peroxidase serum mean level and standard error were 0.1464±0.0001 ng/mL for the control group and 0.1465±0.0001 ng/mL for the stress group. When GPx serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). The liver tissue GPx mean level and standard error mean were 24.9962±0.8778 ng/mg for the control group and 32.3813±1.4753 ng/mg for the stress group. Upon comparing GPx levels in liver tissue, a significant difference was found between the stress and control groups (p=0.001). There was a significant increase in GPx levels in the liver tissues of the rats in the stress group (Figure 3).

When MDA serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). Serum MDA mean level and mean standard error: 2.4091±0.0612 ng/mL for the control group and 2.5675±0.0798 ng/mL for the stress group. Upon comparison of MDA levels in liver tissue, a significant difference was found between the stress and control groups (p=0.001). The mean MDA level in liver tissue and the mean standard error were 721.6182±26.6123 ng/mg for the control group and 924.2219±40.3367 ng/mg for the stress group. MDA levels were elevated in the liver tissues of the rats in the stress group (Figure 4).

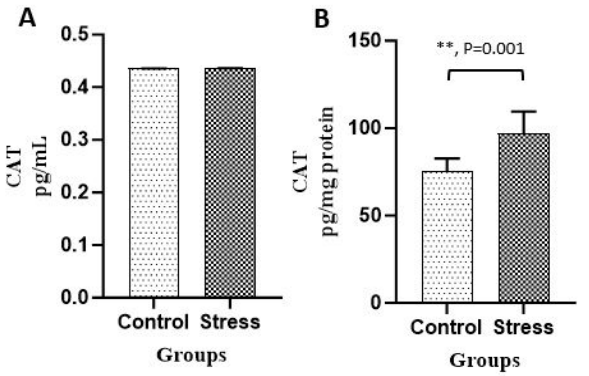

Figure 1: Mean Catalase (CAT) levels between groups: A) Serum CAT (pg/mL) level, B) Liver tissue CAT (pg/mg) level

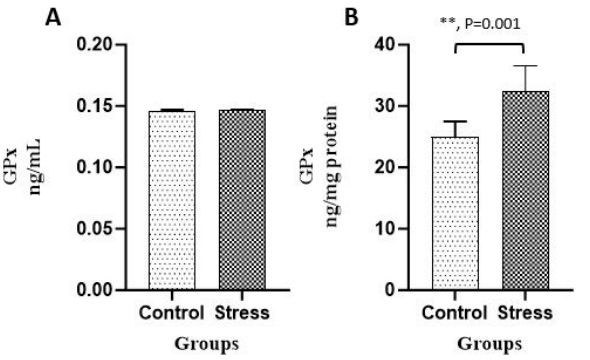

Figure 3: Mean Glutathione Peroxidase (GPx) levels between groups: A) Serum GPx (ng/mL) level, B) Liver tissue GPx (ng/mg) level

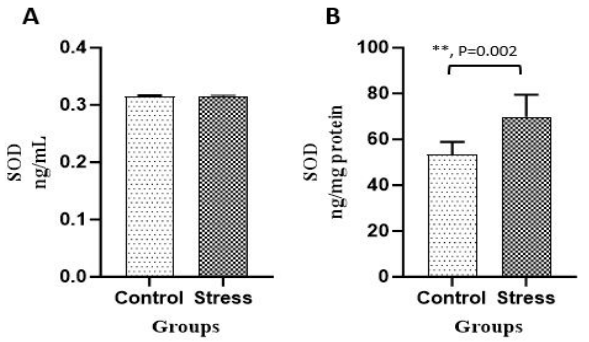

Figure 2: Mean Superoxide Dismutase (SOD) levels between groups: A) Serum SOD (ng/mL) level, B) Liver tissue SOD (ng/mg) level

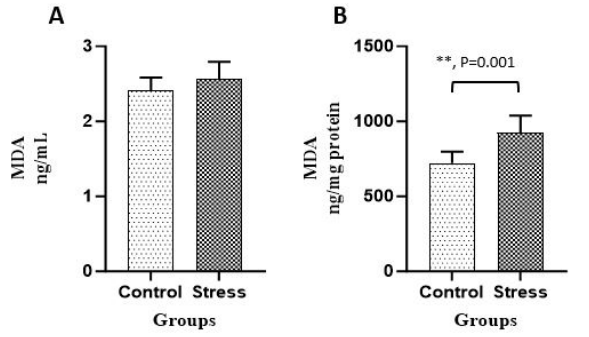

Figure 4: Mean Malondialdehyde (MDA) levels between groups: A) Serum MDA (ng/mL) level, B) Liver tissue MDA (ng/mg) level

DISCUSSION

Chronic psychological stress is increasingly recognized as a significant health issue in contemporary society, adversely impacting both the physical and mental well-being of individuals (22). At the core of this interaction lies the potential for stress to enhance oxidative stress at the cellular level (2). Homeostasis is the organism's ability to regulate and maintain its cellular balance against environmental factors. Stress is considered a factor that disrupts homeostasis (23). Oxidative stress factors cause changes in various intercellular reflex communication pathways in the organisms (24). Free radicals interact with proteins within the cell, changing their structure and disrupting their functions. In particular, the activities of enzymes can be affected in this way, leading to abnormalities in cellular processes (2). Moreover, it can cause cellular balance disorders by interacting with cell membranes, lipids, and genetic material (7). Depending on this biological change, cardiovascular pathologies, metabolic diseases, neurodegenerative changes, and related functional disorders may occur (3, 6).

Chronic psychological stress is recognized for its association with increased cortisol levels in the body. This elevation in cortisol has been identified as a factor that can intensify oxidative stress at the cellular level. Elevated cortisol can enhance the generation of free radicals and simultaneously impair the cellular antioxidant defense systems (5, 24). Cortisol binds to intracellular glucocorticoid receptors (GR), triggering a conformational change that facilitates the translocation of the resulting bio-complex into the nucleus. Within the nucleus, the GR-cortisol complex interacts with specific glucocorticoid response elements, modulating the transcriptional activity of certain genes (25). This modulation affects protein synthesis and cellular functions, producing the cortisol's anti-inflammatory, immunosuppressive, metabolic, and neurological effects.

Additionally, cortisol regulates its secretion through negative feedback by affecting the hypothalamus and pituitary gland (1). The study investigating the effects of acute, subacute, and chronic stress on oxidative radicals showed that chronic stress causes both oxidative stress and increased antioxidant biomolecules in the brain (22). In addition, the effects of various stressors on oxidation and antioxidant levels have been investigated. As a result, significant increases in plasma corticosterone levels and lipid and protein oxidations were observed. Nevertheless, increases in antioxidant enzyme levels have also been reported (26). Our study determined an increase in antioxidant biomolecules in the liver tissues of rats exposed to chronic mild stress. Increased oxidative stress at the cellular level can damage cell components, proteins, and genetic material, disrupting the normal functions of cells and causing various pathological conditions. In this process, excessive accumulation of free radicals and weakening of antioxidant defense mechanisms play a critical role (10).

Catalase enzyme constitutes one of the critical antioxidant mechanisms that combat oxidative stress at the cellular level. Its primary function is to convert hydrogen peroxide molecules accumulated in cells into water and molecular oxygen compounds (11). This reaction prevents oxidative damage by reducing reactive oxygen species within the cell and contributes to maintaining cellular homeostasis (4). Cells under stress accelerate detoxification processes through the CAT enzyme to cope with oxidative stress (2). CAT is found in high concentrations, especially in the liver tissue, where detoxification processes are intense in cases where oxidative stress increases and free radicals and reactive oxygen species can cause damage by changing (12, 24).

The CAT enzyme helps preserve the structure and functionality of cells by neutralizing these harmful compounds. This biochemical reaction is catalyzed through changes in the oxidation state of iron ions in the prosthetic groups of the enzyme (11). Under stress conditions, binding the cortisol hormone to cell surface receptors triggers cellular signaling pathways and subsequent modifications. This mechanism is particularly critical in prolonged oxidative stress resulting from chronic psychological stress (5, 25). Chronic stress can induce oxidative stress through elevated cortisol levels. In this case, the enzyme CAT plays a crucial role in the cellular defense mechanism by mitigating oxidative damage (9). Thus, the CAT enzyme has a central role in combating cellular oxidative stress, and the activity of this enzyme is critically important in protecting cells against oxidative damage caused by chronic psychological stress (15). The increased CAT level may be an adaptive response that helps cope with oxidative stress by contributing to cellular detoxification. Although our research did not show a significant difference in serum CAT levels between groups, it revealed a remarkable distinction in liver tissue. A significant increase was observed, especially CAT levels, in the liver tissue of rats under stress conditions. This finding highlights the vital role of CAT in cellular protection and reveals the importance of cellular defense mechanisms against oxidative damage caused by chronic psychological stress.

Superoxide dismutase enzyme is critical in detoxifying reactive oxygen species produced within cells (10). This metalloprotein contains copper, zinc, or manganese and forms a critical part of the cellular defense mechanism against oxidative damage (13). Neutralization of the superoxide radical leads to hydrogen peroxide and oxygen molecules forming. Hydrogen peroxide is converted into water and oxygen by CAT or GPx enzymes and is

rendered harmless (26). SOD, which exists in three different isoforms in the cell, is localized in the mitochondrial matrix, cytosol, and extracellular matrix and regulates intracellular and extracellular ROS accumulation (7). Liver and serum levels of SOD can fluctuate based on metabolic activity, inflammation, and the presence of oxidative stress.

Given that the liver is abundant in antioxidant enzymes, the activity of SOD is vital for safeguarding this organ from oxidative harm (12, 13). Serum SOD levels are commonly indicative of the body's antioxidant defense status and are utilized as markers for various disease states and stress. Under conditions of stress, the level of cellular SOD generally increases (27). This situation aims to increase the cells' capacity to cope with oxidative stress, thereby preserving cellular integrity and functionality (28). While this increase is observed as a rapid adaptive response in acute stress situations, a continuous rise in SOD activity during chronic stress can lead to the depletion of intracellular antioxidant defense systems and potentially to an increase in oxidative damage (29).

Superoxide dismutase enzyme prevents cellular oxidative damage by biochemically detoxifying superoxide radicals. This enzyme is found in various localizations inside and outside the cell, and its cellular levels increase in cases of oxidative stress (14). The levels of SOD in the liver and serum reflect the antioxidant status in the body, providing information about various biological and pathological conditions (12). In a study investigating the effects of stressors such as cold application and immobilization on oxidative stress, it has been shown that there is a significant increase in SOD levels parallel to the increase in lipid/protein oxidation (26). In the study carried out on patients with traumatic stress due to spinal fractures, researchers detected a significant elevation in serum SOD and MDA levels when compared to the control group. However, there was no observed change in GPx levels within the same group of patients (30). Under stress conditions, changes in the levels of cellular SOD signify the cells' adjustment and defensive response to oxidative stress (29). In our study, while there is no significant difference between serum SOD values in the stress group, there is an increase in liver tissue levels in the stress group.

Glutathione peroxidase is a family of enzymes that contain selenocysteine and protect cellular membranes and other cellular components from oxidative damage by reducing hydrogen peroxide or organic hydroperoxides (17). This enzyme contributes to the antioxidant defense mechanism, especially through GSH-dependent reactions (15). GPx uses hydrogen peroxide as a substrate and converts it into water and oxygen molecules while producing the oxidized form of glutathione. This reaction occurs to maintain intracellular redox balance and provide defense against oxidative stress (4).

The glutathione peroxidase enzyme complex is especially abundant in tissues with intense oxygen metabolism, such as the liver, kidneys, and lungs (17, 31). Because these tissues constantly produce free radicals and reactive oxygen species, high levels of GPx and other antioxidant enzymes are critical for maintaining cellular integrity. GPx levels increase in situations of increased oxidative stress. This indicates the cell is strengthening its antioxidant defenses to deal with ROS and free radicals (29). GPx mainly interacts with GSH, selenium, and other cofactors. While GSH is a substrate for the GPx enzyme, selenium is a critical component at the enzyme's active site (17). The association between psychological stress and GPx activity can be attributed to elevated cellular oxidative stress levels by cortisol and other stress hormones, which modulate GPx enzyme activity. Chronic psychological stress may result in prolonged cortisol secretion and heightened oxidative stress (5,25). This condition enhances the production and activity of antioxidant enzymes such as GPx, protecting the cell against oxidative damage. However, under consistently high levels of oxidative stress, GPx and other antioxidant defense mechanisms can be depleted, potentially leading to cellular damage and various diseases (16). A study has shown that while mild stress does not change GPx levels, there is a dramatic increase in severe stress levels (28). In our study, it was found that while the CUMS model did not change serum GPx levels, there was a significant increase in liver tissue levels.

Malondialdehyde is generated through lipid peroxidation, representing a form of reactive aldehyde. Lipid peroxidation occurs due to free radicals oxidizing polyunsaturated fatty acids in the cell membrane. MDA is an end product of this process and can indicate oxidative stress in the cell (18). MDA is a marker of oxidative stress, and because it arises from the peroxidation of lipids in cell membranes, it tends to be higher in tissues rich in lipids, such as the liver, brain, heart, and kidneys. Elevated MDA levels indicate increased oxidative stress and lipid peroxidation within these tissues (32). MDA is a by-product of the lipid peroxidation of polyunsaturated fatty acids and serves as a reliable indicator of oxidative stress. Its accumulation can occur as a result of an increase in free radicals and ROS within cells. To form adducts, MDA can react with proteins, genetic material, glycoproteins, and other cellular components. These interactions can lead to cellular structure and function disruptions, contribute to cellular aging, and are implicated in the pathogenesis of various diseases due to the damage they cause to essential biomolecules (3, 19). It has been stated that various acute and chronic stress models, such as Restraint, immobilization, cold, and psychological stressors, cause an

increase in MDA levels (31, 32). There are studies where no change was observed depending on the stress model. For instance, in rats subjected to acute footshock stress, no change in MDA/Thiobarbituric acid reactivity was noted (28). The link between oxidative stress and idiopathic chronic fatigue has been investigated. While ROS and MDA increased significantly, antioxidant parameters, including total antioxidant activity and CAT, increased significantly (29). It was also found that levels in patients with inflammatory diseases and cancer were higher than in healthy controls (18, 19). In our study, although there was no change in the serum of the rats in the group in which the CUMS model was applied, a significant increase was detected in liver tissue levels. Chronic psychological stress can trigger the continuous release of stress hormones, raising cellular levels of ROS. This elevation stimulates lipid peroxidation and, consequently, MDA production. High levels of MDA indicate oxidative damage within cells and can reflect the damage caused by stress at the cellular level (29).

CONCLUSION

Chronic stress has the potential to modulate oxidative stress in the liver and activate antioxidant enzymes. This suggests that the antioxidant response may function as a potential adaptive mechanism to reduce the adverse effects of stress at the cellular level.

When comparing the levels of serum CAT, SOD, GPx, and MDA, no statistically significant difference was found between the control and stress groups ($P>0.05$). However, when comparing the liver tissue levels of CAT, SOD, GPx, and MDA, a significant difference was observed between the stress and control groups. CAT, SOD, GPx, and MDA levels were found to be increased in the liver tissues of rats belonging to the stress group.

Considering the widespread and profound effects of chronic psychological stress on the body, it is clear that this condition reduces the quality of life. Particularly, the increase in oxidative stress at the cellular level that it causes can pave the way for the development of various diseases. The study results could assist in better understanding the complex interactions between stress, free radicals, and antioxidants.

Ethics Committee Approval: The study has ethical approval from the Kocaeli University Animal Experiments Local Ethics Committee (Date: 26.07.2023, No: 6/4-2023)

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Author Contributions: Conception/Design of Study- M.D.Y., T.Ç.; Data Acquisition- Ö.D.Ö., F.C.E.; Data Analysis/Interpretation- M.D.Y., Ö.D.Ö.; Drafting Manuscript- M.D.Y., Ö.D.Ö.; Critical Revision of Manuscript- M.D.Y., T.Ç., Ö.D.Ö., F.C.E.; Final Approval and Accountability- M.D.Y., T.Ç., Ö.D.Ö., F.C.E.

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RESEARCH / ARAŞTIRMA
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ASSESSMENT OF INDIVIDUAL, BEHAVIORAL, AND ENVIRONMENTAL FACTORS INFLUENCING OVERWEIGHT/ OBESITY DEVELOPMENT IN CHILDREN AGED 10–14 YEARS*

10-14 YAŞ ARALIĞINDAKİ ÇOCUKLARDA FAZLA KİLO/OBEZİTE GELİŞİMİNİ ETKİLEYEN BİREYSEL, DAVRANIŞSAL VE ÇEVRESEL FAKTÖRLERİN DEĞERLENDİRİLMESİ

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ABSTRACT

Objective: Childhood obesity has emerged as a pressing global public health issue. This study aims to examine the influence of individual, behavioral, and environmental factors on student body mass index (BMI), thereby contributing to a deeper understanding of the multifaceted determinants of obesity among children.

Material and Method: This study employed a cross-sectional survey using a structured questionnaire to collect sociodemographic, physical activity, and dietary behavior data of students. In addition, the study administered a school information form to evaluate the physical condition of school buildings and quality of school canteen services.

Result: Among the students, 24% and 13% were in the overweight and obese categories, respectively. Mean student age was 12.41±1.13 years. The mean ages of students with obesity were significantly lower than those of students who were underweight or had normal weight. The distribution of student BMI according to obesity status among family members was statistically highly significant. Among students with obesity, the families of 30.1% were obese, whereas this percentage was 8.9% in families of students without obesity. The relationship between gender, age, family history of obesity, time spent watching TV,

ÖZET

Amaç: Çocukluk çağı obezitesi önemli bir küresel halk sağlığı sorunu haline gelmiştir. Bu çalışma, öğrencilerin vücut kitle indeksi (VKİ) düzeylerini etkileyen çeşitli bireysel, davranışsal ve çevresel faktörlerin etkisini incelemeyi amaçlamaktadır. Bu şekilde, çocuklardaki obezitenin çok yönlü belirleyicilerinin daha derinlemesine anlaşılmasına katkıda bulunmayı hedeflemektedir.

Gereç ve Yöntem: Kesitsel tipteki bu çalışmada, öğrencilerin sosyo-demografik, fiziksel aktivite ve beslenme davranışları hakkında bilgi sağlayan yapılandırılmış bir anket formu, okulların fiziki durumunu ve okul kantinlerini değerlendirmek için de okul bilgi formu uygulanarak veriler toplanmıştır.

Bulgular: Çalışmadaki öğrencilerde fazla kilolu oranı %24, obezite oranı ise %13 saptanmıştır. Ortalama yaş, tüm öğrenciler için 12,41±1,13 olarak belirlendi. Obez öğrencilerin yaş ortalamaları, zayıf/normal kilolu öğrencilerinkinden önemli ölçüde daha düşüktü. Öğrencilerin VKİ'lerinin aile bireyleri arasındaki obezite durumuna göre dağılımı istatistiksel olarak ileri derecede anlamlı bulunmuştur. Obez öğrencilerin %30,1'inin aileleri obezdi, bu oran obez olmayan öğrencilerin ailelerinde %8,9'du. Cinsiyet, yaş, ailede obezite öyküsü, TV seyrederek geçirilen zaman, fiziksel aktivite süresi, kantinden alışveriş yapmak sıklığı ile VKİ dağılımı arasındaki ilişki anlamlıydı. Zayıf/normal kilolu grupta,

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physical activity duration, canteen shopping frequency, and BMI distributions was significant. Mean distance between school and home was longer in the underweight/normal weight group than the other two groups. However, this difference did not reach statistical significance (p>0.05).

Conclusion: Addressing childhood obesity requires a holistic approach encompassing various interventions targeting individual behaviors, environmental influences, and societal norms. By promoting physical activity, regulating food environments, and providing education on healthy diets, we can work together to combat the epidemic of childhood obesity, and promote the health and wellbeing of future generations.

Keywords: Childhood obesity, overweight, public health, school, primary health care

okul ile ev arasındaki ortalama mesafe diğer iki gruptan daha yüksekti. Ancak bu fark istatistiksel olarak anlamlı değildi (p>0,05).

Sonuç: Çocukluk obezitesi ile başa çıkmak için bütünsel bir yaklaşım gereklidir ki bu, bireysel davranışları, çevresel etkileri ve toplumsal normları hedef alan çeşitli müdahaleleri içermelidir. Fiziksel aktiviteyi teşvik ederek, besin ortamlarını düzenleyerek ve sağlıklı beslenme konusunda eğitim vererek, çocukluk obezitesi salgınıyla mücadele edebilir ve böylelikle gelecek nesillerin sağlığını ve refahını artırabiliriz.

Anahtar Kelimeler: Çocukluk çağı obezitesi, fazla kilololuk, halk sağlığı, okul, birinci basamak sağlık hizmeti

INTRODUCTION

Obesity has become a severe health issue worldwide, a root cause of many life-threatening diseases in high-income countries. However, overweight and obesity have become a burgeoning crisis in low and middle-income countries, especially in urban environments. The global prevalence of obesity has increased nearly threefold between 1975 and 2016 (1).

Although increased childhood obesity has hereditary, metabolic, and hormonal causes (polygenic obesity), the most consequential reason for increased childhood obesity is high-calorie food intake. However, physicians should not overlook the existence of genetic and hormonal effects on weight gain, though such cases are limited (2). A rapid increase in obesity rates worldwide cannot be explained only by genetics, albeit a significant risk factor. It requires analysis of different environmental, behavioral, and social dimensions of obesity employing innovative methodologies. Researchers have discovered correlations between unhealthy eating, sedentary lifestyles, and obesity from an environmental perspective. Most researchers believe that "genetics loads the gun, but the environment pulls the trigger" (3, 4). Although individual decisions have little impact on human health, many microenvironments (home, school, restaurant, etc.) can directly influence behavioral choices (5). The availability of calorie-rich foods at home, family budgets, and routine meals can affect obesity in children. Children can affect the food environment at home over time, but the environment around the home can significantly influence them (3). Children tend to eat foods that are proportional to what is served. For example, having fruits and vegetables at home can lead to increased consumption in teenagers. Additionally, easily accessible unhealthy foods and drinks cheaper than healthy food items are among the most critical factors for obesity (6).

An increase in screen time reduces the frequency of outdoor activities, leading to weight gain and obesity in children (7). The widespread advertising in media also enhances the consumption of junk food (3). A study of preschool and early adolescence children in Framingham showed that long-term TV viewing caused excessive body fat compared to low-level activity or a high-fat diet (8).

The school is another microenvironment affecting obesity, because children and adolescents spend one-third of the day at school. Therefore, schools provide critical microenvironments for developing diet and exercise habits until adulthood (9, 10).

In recent years, various concerns have been raised about the obesogenic nature of the school environment, including increased competition in food and beverage sales and reduced opportunities for physical activity during the school day (11). International literature suggests that when food is available for sale within a school, and the sale of food is a revenue stream, the food for sale is likely to be less healthy (3). Opportunities of physical activity for students include walking to and from school, physical education classes, and activities during break. However, rapid urban sprawl, road network discontinuity, increased road traffic, steep slopes, and longer distances from the school have reduced the opportunity to walk, and many children use different modes of transportation to reach schools (12, 13). According to the Centers for Disease Control and Prevention, the proportion of students living ≤800 m to school decreased from 90% in 1969 to 31% in 2008 (12). The possibility of walking to school increases if the distance is <800 m (5).

A rapid increase in childhood obesity rates leads to severe social and economic consequences, including an increase in health complications, increased cost of healthcare services, and a decrease in economic growth. In addition, it can reduce child participation in educational and physical activities (14).

Therefore, childhood obesity is seen as a priority public health issue due to its short- and long-term adverse effects

(15). Without proper preventive measures, the detrimental impacts of obesity will reduce individual health and quality of life and overburden the health system and economy. Therefore, more empirical studies must find the links between environmental factors and the prevalence of obesity among children. In this context, this study was conducted to determine the prevalence of overweight and obesity in students and identify the risk factors for obesity.

MATERIALS and METHODS

The study was conducted using a descriptive design.

Population and sampling

This study utilized a cross-sectional field survey technique, collecting data between April 2019 and February 2020, after obtaining necessary approvals from the "National Education Directorates of Karabük and Safranbolu" and Non-Interventional Clinical Research Ethics Committee (Date: 10.03.2019, No: 3/12).

In cluster sampling, samples are carefully chosen from homogeneous subgroups, considering their proportional size and statistical power within the population. For instance, in 2019, Karabük and Safranbolu had 47 middle schools with 9,780 students. The sample size was calculated with a 99% confidence interval and a 5% margin of error using OpenEpi software, resulting in a minimum sample size of 622. The research was conducted in 14/47 randomly selected schools in the region, employing a cluster sampling method. The student sample was chosen systematically using a systematic random process, and the study was completed with 907 students.

Data collection and evaluation

A survey form based on relevant literature and student self-reporting was prepared to assess factors influencing obesity. The questionnaire form included questions about sociodemographic information, eating habits, screen time, and physical activity. The assessment forms were developed utilizing the "Audit Form for School Canteens' Food Offerings and Hygiene Standards of Food Establishments in Educational Institutions," prepared by the "Workplace Health and Safety Unit of the Ministry of National Education Support Services Directorate," aimed at assessing the school environment and opportunities for physical activity. With the assumption that students need to gain full knowledge of legal regulations and the physical and environmental facilities of the school, the evaluation of the physical and environmental conditions of the school and canteen was not included in the student survey. The researcher conducted the evaluation of schools and canteens personally with the school administration's permission.

The researchers measured the heights (in cm) and weights (in kg) of the students who answered the surveys, using the same instruments for everyone. Student heights and weights were measured after removing shoes and outerwear.IBM SPSS statistical software, version 28 (IBM, SPSS Corp., Armonk, NY, USA) and Microsoft Office Excel programs were used for statistical analysis. The cutoff values for obesity were interpreted according to reference z-score values of body mass index (BMI) for age and gender provided by the World Health Organization (WHO) for BMI categories. For data analysis, the chi-square (χ^2) test was used to compare the descriptive characteristics of the students and the categorical features related to their eating habits. Normality tests were conducted using histogram graphs and skewness or kurtosis values. The values of kurtosis and skewness are considered normally distributed when they are between −2.0 and +2.0 (16). analysis of variance (ANOVA) test was used for multiple comparisons that showed normal distribution. $P<0.05$ was considered statistically significant.

RESULTS

According to the analysis, 54.6% of the participants were female, and 45.4% were male students. The average age of the students participating was 12.41±1.13 years. The age distribution was determined to be very close according to gender. The comparison of age distribution of students according to their BMI categories was conducted using one-way ANOVA. Descriptive analyses revealed that 62.62% (n=568) of the students were underweight/normal, 24.15% (n=219) were overweight, and 13.23% (n=120) were obese. Examination of the boxplot graphs indicated the absence of outlier values in the dataset and normality of data distribution across all independent variable categories, as evidenced by kurtosis and skewness ranging from −1 to +1. Levene's test confirmed the homogeneity of group variances (p=0.264). The analysis results indicated a statistically significant difference among the groups, with an observed *F*-statistic of 5.564 and a p-value of 0.004. Effect size (η^2) was 0.12, indicating a moderate effect. Following Bonferroni's *post hoc* analysis, the significance level of 0.05 was adjusted by dividing it with the number of comparisons (0.05/3=0.0166), resulting in a new adjusted significance level of 0.0166. Consequently, mean age was significantly lower for students with obesity than students who were underweight or had normal weight (p=0.004). *Post hoc* analysis did not reveal statistically significant differences among the age averages of other group comparisons (Table 1).

The findings indicated that 13% of the students examined were classified as obese and 24% were identified as overweight. The prevalence of obesity was higher among males (17.7%) than females (9.96%), and this difference was statistically significant. Furthermore, 20.5% of the students reported having family members with obesity, and the prevalence of obesity was notably elevated in student who had family members with obesity (Table 2).

Table 1: Relationship between distribution of mean age and BMI

	n	Min–Max (Year)	Yaş ortalaması±SD (Year)	Skewness	Kurtosis
Age distribution	907	9.83–15.33	12.41±1.13	0.002	−0.980
BMI			**Yaş ortalaması±SD (Year)**	**F**	**p**
Normal/underweight	568		12.49±1.14	5.564**	0.004*
Overweight	219		12.37±1.06		
Obese	120		12.12±1.16		

*: p<0.05, F = One-way ANOVA, **: Bonferroni = normal/underweight >obese, SD: Standard deviation, P: Probability, BMI: Body Mass Index

Table 2: BMI status according to demographic characteristics of students

		Normal/ underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	p
Gender	Girl	328 (66.3)	119 (24)	48 (9.7)	495 (100)	0.002
	Boy	240 (58.3)	100 (24.3)	72 (17.5)	412 (100)	
Child order	1.	238 (61.3)	95 (24.5)	55 (14.2)	383 (100)	0.901
	2.	217 (63.1)	82 (23.8)	45 (13.1)	345 (100)	
	3.	85 (65.4)	29 (22.3)	16 (12.3)	130 (100)	
	4.	22 (62.9)	11 (31.4)	2 (20.0)	36 (100)	
	5.	6 (60.0)	2 (20.0)	2 (20.0)	10 (100)	
Grades	Weak	24 (60.0)	15 (37.5)	1 (2.5)	40 (100)	0.091
	Moderate	53 (68.8)	14 (18.2)	10 (13.0)	77 (100)	
	Good	167 (62.8)	57 (21.4)	42 (15.8)	266 (100)	
	Very Good	324 (61.8)	133 (25.4)	67 (12.8)	524 (100)	
Mother's education level	Illiterate	7 (53.8)	4 (30.8)	2 (15.4)	13 (100)	0.831
	Primary school	150 (62.2)	55 (22.8)	36 (14.9)	241 (100)	
	Secondary school	127 (63.8)	46 (23.1)	26 (13.1)	199 (100)	
	High School	175 (59.9)	79 (27.1)	38 (13.0)	292 (100)	
	University	109 (67.3)	35 (21.6)	18 (11.1)	162 (100)	
Father's education level	Illiterate	2 (40.0)	2 (40.0)	1 (20.0)	5 (100)	0.402
	Primary school	86 (68.3)	25 (19.8)	15 (11.9)	126 (100)	
	Secondary school	107 (65.2)	33 (20.1)	24 (14.6)	164 (100)	
	High School	199 (57.8)	99 (28.8)	46 (13.4)	344 (100)	
	University	174 (64.9)	60 (22.4)	34 (12.7)	268 (100)	
Chronic illness in the student	No	543 (62.3)	213 (24.4)	116 (12.8)	872 (100)	0.542
	Yes	25 (71.4)	6 (17.1)	4 (11.4)	35 (100)	
Presence of obese individuals in the family	No	479 (66.4)	178 (24.7)	64 (8.9)	721 (100)	0.000
	Yes	89 (47.8)	41 (22.0)	56 (30.1)	186 (100)	
Number of meals	2 meals	96 (57.1)	46 (27.4)	26 (15.5)	168 (100)	0.421
	3 meals	370 (62.0)	144 (24.1)	83 (13.9)	597 (100)	
	4 meals	73 (68.2)	24 (22.4)	10 (9.3)	107 (100)	
	≥5 meals	30 (83.3)	5 (14.3)	1 (2.9)	36 (100)	

Table 2: Continue

		Normal/ underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	p
Regularly consumed main meals at home	Breakfast is eaten	410 (63.5)	154 (23.8)	82 (12.7)	646 (100)	0.660
	Breakfast is not eaten	158 (60.5)	65 (24.9)	38 (14.6)	261 (100)	
	Lunch is eaten	227 (63.9)	93 (26.2)	35 (9.9)	355 (100)	0.045
	Lunch is not eaten	341 (61.8)	126 (22.8)	85 (15.4)	552 (100)	
	Dinner is eaten	557 (62.5)	216 (24.2)	118 (13.2)	891 (100)	0.860
	Dinner is not eaten	11 (68.8)	3 (18.8)	2 (12.5)	16 (100)	
Duration of exercise	<1 h per week	113 (54.3)	55 (26.4)	40 (19.2)	208 (100)	0.009
	1–2 h per week	204 (62.0)	80 (24.3)	45 (13.7)	329 (100)	
	3–4 h per week	134 (64.1)	53 (25.4)	22 (10.5)	209 (100)	
	>4 h per week	117 (72.7)	31 (19.3)	13 (8.1)	161 (100)	
Duration of sleep	< 6 h	3 (50.0)	2 (33.3)	1 (16.7)	6 (100)	0.963
	6–8 h	275 (62.2)	108 (24.4)	59 (13.3)	442 (100)	
	9–10 h	268 (63.5)	99 (23.5)	55 (13.0)	442 (100)	
	>10 h	22 (59.5)	7 (27.0)	5 (13.5)	37 (100)	
Time spent watching TV	0–30 min.	89 (69.5)	26 (20.3)	13 (10.2)	128 (100)	0.034
	31–60 min.	139 (70.2)	44 (22.2)	15 (7.6)	198 (100)	
	61–120 min.	180 (57.5)	84 (26.8)	49 (15.7)	313 (100)	
	121–180 min.	84 (61.8)	32 (23.5)	20 (14.7)	136 (100)	
	181–240 min.	31 (67.4)	10 (21.7)	5 (10.9)	46 (100)	
	>240 min.	45 (52.3)	23 (26.7)	18 (20.9)	86 (100)	
Computer playtime	0–30 min.	124 (70.1)	40 (22.6)	13 (7.3)	177 (100)	0.220
	31–60 min.	89 (15.7)	28 (12.8)	19 (15.8)	136 (100)	
	61–120 min.	131 (60.1)	51 (23.4)	36 (16.5)	218 (100)	
	121–180 min.	87 (58.4)	38 (25.5)	24 (16.1)	149 (100)	
	181–240 min.	56 (63.6)	21 (23.9)	11 (12.5)	88 (100)	
	>240 min.	81 (58.3)	41 (29.5)	17 (12.2)	139 (100)	
Type of school-home transportation	Walking	322 (63.6)	116 (23.0)	66 (13.1)	506 (100)	0.624
	Vehicle	246 (61.0)	103 (25.6)	54 (13.4)	401 (100)	

P: Probability, BMI: Body Mass Index

There was no significant link between student sleep time and BMI distribution. However, duration of physical activity showed meaningful correlation to BMI distribution. Obesity rate was 19.2% for students with <1 h of exercise per week, compared with 8.1% for those >4 h per week. Table 2 shows a significant correlation between student TV viewing times and BMI. Watching TV for >240 min daily correlated with higher obesity and overweight rates.

The study did not find a significant link between student mode of transportation to school and BMI distribution. For students who walked, walking distance was 58–1,500 m. Although students with obesity had a slightly shorter average walking length, this difference was insignificant (Table 3).

The types of beverages and foods most students purchased from the school canteen are shown in Figure 1. Bagels, pastries (70.2%), wafers (60.1%), and toast (49.8%) were the most purchased foods, whereas nuts (3%) and soup varieties (1.3%) were the least purchased foods from the school canteen.

Examination of BMI distributions according to food and beverage preference showed that overweight and obe-

sity rates were higher in students who consumed raw meatballs, ice cream, chicken doner, meatball sandwiches, schnitzel soup, from the canteen than those who did not. This difference was found to be statistically significant (Table 4).

Although the difference between purchasing frequency from the school canteen and BMI distribution was not statistically significant, noteworthy patterns emerged. Students who never made purchases had 0.0% obesity rate, whereas the rate was 22% for consistent buyers (Table 5).

Table 3: Relationship between the distance between home and school (in m) and BMI

	n	Min–Max (Meter)	$\bar{x}$±SD (Meter)	Skewness	Kurtosis
Distance between home and school	504	58–1500	516±268	0.695	0.360
BMI	**n**		**$\bar{x}$±SD (Meter)**	**F**	**p**
Normal/Underweight	322		519.14±272.41	0.244	0.783
Overweight	116		520.07±257.68		
Obese	66		494.64±267.05		

F = One-way ANOVA, SD: Standard deviation, n: Number, p: Probability, BMI: Body Mass Index

Table 4: BMI distribution according to student food and beverage preferences from the school canteen or external sources

	Purchase Status	Normal/underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	p
Bagel-pastry	Not purchasing	171 (63.3)	62 (23)	37 (13.7)	270 (100)	0.851
	Purchasing	397 (62.3)	157 (24.6)	83 (13)	637 (100)	
Waffle-chocolate varieties	Not purchasing	219 (60.5)	94 (26)	49 (13.5)	362 (100)	0.527
	Purchasing	349 (64)	125 (22.9)	71 (13)	545 (100)	
Ice cream	Not purchasing	525 (63.9)	192 (23.4)	105 (12.8)	822 (100)	0.047
	Purchasing	43 (50.6)	27 (31.8)	15 (17.6)	85 (100)	
Chewing gum	Not purchasing	461 (63)	178 (24.3)	93 (12.7)	732 (100)	0.646
	Purchasing	107 (61.1)	41 (23.4)	27 (15.4)	175 (100)	
Biscuit-cake	Not purchasing	350 (59.4)	155 (26.3)	84 (14.3)	589 (100)	0.024
	Purchasing	218 (68.6)	64 (20.1)	36 (11.3)	318 (100)	
Chips	Not purchasing	516 (63.1)	194 (23.7)	108 (13.2)	818 (100)	0.626
	Purchasing	52 (58.4)	25 (28.1)	12 (13.5)	89 (100)	
Popcorn	Not purchasing	543 (62.7)	210 (24.2)	113 (13)	866 (100)	0.747
	Purchasing	25 (61)	9 (522)	7 (17.1)	41 (100)	
Nuts	Not purchasing	552 (62.7)	212 (24.1)	116 (13.2)	880 (100)	0.921
	Purchasing	16 (59.3)	7 (25.9)	4 (14.8)	27 (100)	
Color candy	Not purchasing	548 (62.7)	211 (24.1)	115 (13.2)	874 (100)	0.967
	Purchasing	20 (60.6)	8 (24.2)	5 (15.2)	33 (100)	
Meatball sandwich	Not purchasing	518 (64.8)	192 (24)	89 (11.1)	799 (100)	0.000
	Purchasing	50 (46.3)	27 (25)	31 (28.7)	108 (100)	
Chicken doner	Not purchasing	413 (69.9)	136 (23)	42 (7.1)	591 (100)	0.000
	Purchasing	155 (49.1)	83 (26.3)	78 (24.7)	316 (100)	
Schnitzel	Not purchasing	558 (63.3)	215 (24.4)	108 (12.3)	881 (100)	0.000
	Purchasing	10 (38.5)	4 (15.4)	12 (46.2)	26 (100)	

Table 4: Continue

	Purchase Status	Normal/underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	p
Hamburger	Not purchasing	449 (62.4)	178 (24.7)	93 (12.9)	720 (100)	0.673
	Purchasing	119 (63.6)	41 (21.9)	27 (14.4)	187 (100)	
Toast	Not purchasing	281 (61.8)	116 (25.5)	58 (12.7)	455 (100)	0.610
	Purchasing	287 (63.5)	103 (22.8)	62 (13.7)	452 (100)	
Pizza	Not purchasing	553 (63.2)	208 (23.8)	114 (13)	875 (100)	0.168
	Purchasing	15 (46.9)	11 (34.4)	6 (18.8)	32 (100)	
Raw meatball	Not purchasing	472 (64)	177 (24)	89 (12.1)	738 (100)	0.072
	Purchasing	96 (56.8)	42 (24.9)	31 (18.3)	169 (100)	
Soup	Not purchasing	566 (63.2)	214 (23.9)	115 (12.8)	895 (100)	0.003
	Purchasing	2 (16.7)	5 (41.7)	5 (41.7)	12 (100)	
Milk	Not purchasing	511 (63.3)	197 (24.4)	99 (12.3)	807 (100)	0.55
	Purchasing	57 (57)	22 (22)	21 (21)	100 (100)	
Buttermilk	Not purchasing	526 (64.6)	199 (24.4)	92 (11.3)	817 (100)	0.000
	Purchasing	42 (46.7)	20 (22.2)	28 (31.1)	90 (100)	
Coke	Not purchasing	491 (62.8)	190 (24.3)	101 (12.9)	782 (100)	0.796
	Purchasing	77 (61.6)	29 (23.2)	19 (15.2)	125 (100)	
Fruit juice	Not purchasing	271 (63.3)	107 (25)	50 (11.7)	428 (100)	0.415
	Purchasing	297 (62)	112 (23.4)	70 (14.6)	479 (100)	
Fruit-flavored soda	Not purchasing	511 (62.9)	197 (24.2)	105 (12.9)	813 (100)	0.727
	Purchasing	57 (60.6)	22 (23.4)	15 (16)	94 (100)	

P: Probability, BMI: Body Mass Index

Table 5: Relationship between frequency of purchase from the canteen, place where lunch is eaten, and student BMI

	Normal/underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	P
Frequency of purchases from the canteen					
Never	15 (71.4)	6 (28.3)	0 (0.0)	21 (100)	0.132
Rarely	115 (64.6)	46 (25.8)	17 (9.6)	178 (100)	
Occasionally	284 (64.3)	101 (22.9)	57 (12.9)	442 (100)	
Often	109 (59.2)	47 (25.5)	28 (15.2)	184 (100)	
Always	45 (54.9)	19 (23.2)	18 (22.0)	82 (100)	
Lunch in					
Yes	17 (56.7)	9 (30.0)	4 (13.3)	17 (56.7)	0.736
No	551 (62.8)	210 (23.9)	116 (13.2)	551 (62.8)	
Where lunch is eaten					
Walking home and eating at home	150 (64.4)	67 (28.8)	16 (6.9)	233 (100)	0.000
Taking a bus home and eating at home	40 (65.6)	14 (23.0)	7 (11.5)	61 (100)	
Bringing from home and eating at school	48 (67.6)	14 (19.7)	8 (12.7)	71 (100)	

Table 5: Continue

	Normal/underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	P
Eating at the canteen	155 (67.1)	53 (22.9)	23 (10.0)	231 (100)	0.000
Eating at the restaurant	42 (52.5)	18 (22.5)	20 (25.0)	80 (100)	
Sometimes canteen or restaurant	75 (51.0)	37 (25.2)	35 (23.8)	147 (100)	
Occasionally walking home for lunch or dining at the canteen	35 (81.4)	6 (14.0)	2 (4.7)	43 (100)	
Sometimes walking home and eating or dining at a restaurant	23 (56.1)	10 (24.4)	8 (19.5)	41 (100)	

n: Number, P: Probability

Table 5 presents the relationship between the frequency of purchases from the canteen, the location where lunch is eaten, and student BMI. Regarding the frequency of canteen purchases, no statistically significant differences were observed in the distribution of BMI categories (normal/underweight, overweight, and obese) (p=0.132). However, significant associations were found between where lunch is eaten and BMI categories (p<0.001). Notably, a higher percentage of students who walked home had normal/underweight BMI. Students who ate at the canteen, restaurant, or both canteen and restaurant showed varying distributions across BMI categories. Further analysis indicates a potential correlation between lunch location and student BMI status.

Within the study's parameters, four schools held a Nutrition-Friendly School Certification (with an average obesity rate of 12.62%), whereas thirteen had a canteen supervision committee. Of these, thirteen school canteens were operated by private businesses, and one was managed by the school administration. None of the schools had vending machines, energy drinks, flavored drink powders, syrups, or water. In total, one canteen sold coke; four sold hamburgers; and three sold chips, French fries (with ketchup), and nugget sandwiches.

The distribution of student BMI according to some characteristics of the schools is given in Table 6. According to this table, the rate of obese and overweight students was

Table 6: Distribution of student BMI according to defining characteristics of schools

		Normal or underweight n (%)	Overweight n (%)	Obese n (%)	Total n (%)	P
Basketball court	Yes	527 (62.4)	203 (24.0)	115 (13.6)	845 (100)	0.478
	No	41 (66.1)	16 (25.8)	5 (8.1)	62 (100)	
Soccer field	Yes	520 (63.5)	190 (23.2)	109 (13.3)	819 (100)	0.126
	No	48 (54.5)	29 (33.0)	11 (12.5)	88 (100)	
Volleyball court	Yes	504 (63.8)	192 (24.3)	94 (11.9)	790 (100)	0.008
	No	64 (54.7)	27 (23.1)	26 (22.2)	117 (100)	
Table tennis	Yes	434 (63.4)	167 (24.4)	84 (12.3)	685 (100)	0.323
	No	134 (60.4)	52 (23.4)	36 (16.2)	222 (100)	
Indoor sports hall	Yes	103 (60.2)	39 (22.8)	29 (17.0)	171 (100)	0.278
	No	465 (63.2)	180 (24.5)	91 (12.4)	736 (100)	
Canteen supervision committee	Yes	524 (62.5)	201 (24.0)	114 (13.6)	839 (100)	0.553
	No	44 (64.7)	18 (26.5)	6 (8.8)	68 (100)	
Area per student >5 m^2	Yes	416 (63.8)	153 (23.5)	83 (12.7)	652 (100)	0.489
	No	152 (59.6)	66 (25.9)	37 (14.5)	255 (100)	

n: Number, P: Probability

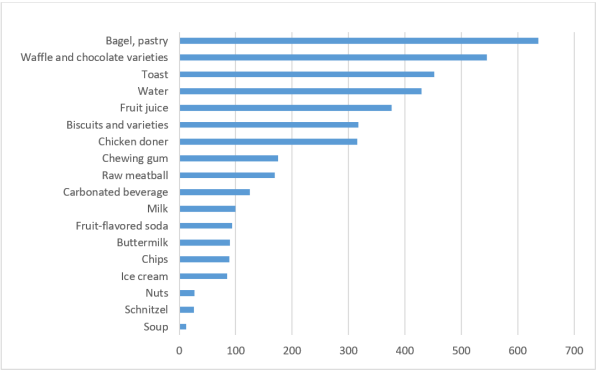

Figure 1: Frequency of food and beverage purchase from the school canteen by students

higher in schools without a volleyball court than schools with a volleyball court.

DISCUSSION

According to WHO data, the obesity rate among children aged 10–19 in 2016 was 20.7% in the US, 11.4% in Canada, 9% in Brazil, 6.9% in France, 16.7% in Saudi Arabia, and 2.5% in Japan. In Türkiye, the obesity rate in the same age group in the same year was 9.8% (girls: 9.4%, boys: 10.2%) (1).

Our findings revealed that 24% of the students were overweight and 13% were obese. When comparing these values with international and national literature, the obesity rates in our study are lower than those in the US, Canada, and Saudi Arabia, but higher than those in Brazil, France, Austria, and Japan (15, 17, 18). When looking at the results of studies in different regions of Türkiye, it can be seen that the overweight and obesity rates in our study are higher than in most areas (7, 19, 20). This situation can be due to differences in age distribution in study groups, references used to determine BMI values, or regional differences.

According to the study, the overweight and obesity rate in the 10–14 age groups was significantly higher in boys than in girls. Similar results have been found in studies conducted in different countries and other regions of Türkiye, where the overweight and obesity rates were either significantly higher in both groups or only boys (11, 18). However, studies have shown that obesity is higher in girls than boys (21, 22).

In some studies conducted in Türkiye and other countries, breast milk did not protect against obesity (23, 24). Breast milk can focus on the hypothesis that it will protect against obesity in the future by reducing weight gain during infancy compared to formula milk, as it contains lower protein and energy (25). Many systematic reviews and meta-analyses of observational studies have investigated the relationship between breastfeeding and obesity risk (26). Some studies have shown that breast milk provides a protective effect against obesity in childhood (27-29). In our study, no significant relationship existed between the number of siblings, order of siblings, and student BMI (Table 1). Consistently, Nabavi et al. and Uskun et al. did not find a significant difference between the number of siblings and order of siblings and obesity (23, 30). In our study, there was no statistically significant difference between school achievement and obesity. Our results showed similarities with some domestic studies (30, 31) but differed from others (19, 20).

In studies conducted on primary school students in Yemen and Kastamonu in Türkiye, a positive relationship was found between the education level of parents and the prevalence of overweight/obesity (32, 33). By contrast, similar studies conducted in Germany, China, and İzmir in Türkiye found a negative relationship between the education level of parents and prevalence of overweight/obesity (18, 34, 35). Although this difference was not statistically significant in our study, there are similar studies in terms of results. In some domestic and international studies, there was no statistically significant relationship between the education level of parents and prevalence of obesity, which is identical to this study (13, 23, 30, 36). Our study had no statistically significant relationship between chronic illnesses and BMI changes. Some studies in the literature support our results (7, 20, 37).

Many studies show that there is a strong connection between obesity and genetics. Individuals with a family history of obesity are more likely to become obese (8, 38). Studies have found that if both parents are obese, the likelihood of their children becoming obese is 80%. If only one parent is obese, the rate is 50%, and if neither parent is obese, the rate is 9% (39). In a study conducted by Tchicaya and Lorentz in Luxembourg, the likelihood of a child becoming overweight or obese was 6.51-fold higher if at least one of the parents was obese, compared with children with both parents at a normal weight (40). In addition to genetic and hereditary factors, parent attitudes toward life, physical activity, and eating habits can influence a child's eating and behavior choices. If a parent has poor eating habits, children can continue these habits. According to a study by Wardle et al., in a taste test, children from obese/overweight families preferred fatty foods more, liked vegetables less, and had a more "excessive eating" type of meal style (41). In our study, obesity rate was 30.1% in children whose parents were overweight or obese and 8.9% in children whose parents were not obese. Our study results were similar to those from other studies conducted domestically and abroad (18, 23, 31, 42), and a positive relationship was found between the obesity status of the parents and the obesity distributions of the children. The difference in our study

results could be due to differences in the amount of energy and types of food consumed by the students in one meal. Overweight and obesity rate was higher for students who did not eat breakfast, but the difference was not statistically significant. Students who frequently or consistently purchased food and drinks from the school cafeteria had a higher rate of overweight and obesity than those who rarely or never bought food. However, the difference was not statistically significant.

Li et al. showed a weak relationship between pocket money and obesity in schools that banned the sale of unhealthy food (43). In our study, obesity rate was significantly higher among students who had lunch outside of school at restaurants, including fast-food restaurants, than others. Thus, dining at restaurants is a contributing factor to obesity. Walking to school provides significant potential in maintaining the daily physical activity required for children, and thus, fighting obesity. The safety of the streets for walking between home and school is critical (44). Regarding public health, walking to school has a significant physical activity potential for children (45).

Our study found that the rate of overweight and obesity among students who accessed the school by car was higher, although statistically insignificant, than those who walked. There was no statistically significant relationship between the student's mode of transportation between home and school and their BMI distribution in our study. However, some studies have obtained similar results (13, 20, 30, 37).

Studies have suggested that sleep, a sedentary lifestyle, and physical activity status can affect weight through sleep deprivation on appetite, physical activity, and thermoregulation (18). A systematic review by Patel and Hu of cross-sectional and cohort studies in 1966–2007 found that short sleep duration in children is strongly and consistently associated with concurrent and future obesity (46). In a study conducted in China, Xiaoqing et al. showed that less sleep caused overweight and obesity in children and more sleep was a protective factor against obesity (18). According to the results of our study regarding the relationship between sleep duration and changes in BMI, the rates of overweight/obesity among students who slept for <6 h were high, although not statistically significant. Some of the results of the studies are similar to our results (20, 37), whereas others are different (7, 18). To better define the causal impact of sleep deprivation on obesity, more research is needed using objective measurements of sleep duration, repeated evaluations of sleep and weight, and experimental study designs that manipulate sleep (46). The shift from outdoor play to indoor entertainment, watching television, spending time on Internet, and playing computer games (47), has rapidly increased childhood obesity. Watching television contributes to obesity in children by reducing physical activity and encouraging people to consume more snacks while watching TV, as well as through the impact of advertisements on unhealthy food and beverage choices (48). A longitudinal observational study by Wiecha et al. showed that increasing daily TV viewing by 1 h caused teens to consume an additional 160 calories daily (49). Most international and national studies have found a positive correlation between TV viewing and obesity (18, 30, 39, 50).

According to our research, students who spent ≤30 min playing computer games or on Internet had a lower obesity rate (7.3%) than those who spent >30 min. However, this difference was not statistically significant. By contrast, students who spent >240 min had a higher obesity rate (29.5%) than those who spent less time, but this difference was not statistically significant. According to Siddarth, computer game time and obesity had a statistically significant positive relationship (50). Although our study did not find a meaningful relationship between time spent at the computer and BMI distribution, some studies support our results (20, 23, 36).

Our study found that people who exercise <1 h per week have a higher rate of overweight and obesity than other groups, which was statistically significant. This result is consistent with other studies (13, 30, 31, 36, 37).

CONCLUSIONS

In addition to the multifaceted approach needed to address childhood obesity, our study underscores the critical role of physical activity in promoting healthy lifestyles among children. Encouraging regular participation in sports and physical activities from an early age can help mitigate obesity risk by promoting cardiovascular health, improving muscle strength, and enhancing overall well-being. Initiatives aimed at creating safe and accessible spaces for recreational activities within schools and communities are essential for fostering a culture of active living among children.

Our findings highlight the importance of implementing policies that restrict the availability of high-calorie foods and beverages in school canteens. By prohibiting the sale of unhealthy snacks and promoting nutritious options, such as fruits, vegetables, and whole grains, schools can create an environment that supports healthy eating habits and contributes to the prevention of childhood obesity. Collaborative efforts between educational institutions, policymakers, and food suppliers are crucial for effectively implementing and enforcing such policies.

Our study underscores the need for comprehensive education on healthy diets and nutrition for students and their families. Educational programs can empower indi-

viduals to make informed decisions about their dietary habits and lifestyles by providing evidence-based information on balanced nutrition, portion control, and the importance of diverse food choices. Moreover, initiatives promoting cooking skills, meal planning, and grocery shopping strategies can further support families in adopting healthier eating habits and reducing the risk of childhood obesity.

In conclusion, addressing childhood obesity requires a holistic approach, encompassing various interventions targeting individual behaviors, environmental influences, and societal norms. By promoting physical activity, regulating food environments, and providing education about healthy diets, we can work together to combat the epidemic of childhood obesity and promote the health and wellbeing of future generations.

Ethics Committee Approval: The study has ethical approval from the National Education Directorates of Karabük and Safranbolu" and Non-Interventional Clinical Research Ethics Committee (Date: 10.03.2019, No: 3/12).

Informed Consent: Written consent was obtained from the families of all participants.

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EVALUATION OF BALNEOLOGICAL TREATMENT ON PAIN, FUNCTION, AND QUALITY OF LIFE IN KNEE OSTEOARTHRITIS: A RANDOMIZED, CONTROLLED, SINGLE-BLINDED TRIAL

DİZ OSTEOARTRİTİNDE BALNEOLOJİK TEDAVİNİN AĞRI, FONKSİYON VE YAŞAM KALİTESİNE ETKİSİNİN DEĞERLENDİRİLMESİ: RANDOMİZE, KONTROLLÜ, TEK KÖR BİR ÇALIŞMA

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ABSTRACT

Objective: The study aimed to evaluate the efficacy of balneological treatment in patients with knee osteoarthritis using clinical scales and to determine its effect on pain, function, and quality of life.

Material and Method: Thirty-two patients with knee osteoarthritis were divided into two randomization groups. The patients in the study group were given a full bath for 20 min in the hydrotherapy pool at 38°C. Then, medical mud was applied to both knees at 43°C. The second group was not given any specific treatment and continued to receive routine treatment (control group). Patients completed the clinical scales with the blinded physician before treatment/day 1 (baseline), at the end of treatment/day 12, and 3 months.

Result: At the end of treatment, WOMAC total, VAS pain, and global assessment scores of patients and physicians were statistically significant improved compared with baseline and third-month controls in the study group. A statistically significant improvement occurred in the 12-d and 3-month Lequesne knee index scores compared with the baseline in the study group. A statistically significant improvement was observed in Nottingham Health Profile pain, emotional reactions, physical move-

ÖZET

Amaç: Bu çalışmada balneolojik tedavinin diz osteoartritli hastalarda etkinliğinin klinik ölçeklerle değerlendirilmesi ve ağrı, fonksiyon ve yaşam kalitesi üzerine etkisinin belirlenmesi amaçlandı.

Gereç ve Yöntem: Diz osteoartriti tanısı almış 32 hasta, randomizasyonla iki gruba ayrıldı. Çalışma grubundaki hastalara, hidroterapi havuzunda 38°C'de 20 dakika tam banyo uygulandı, ardından tıbbi çamur her iki dize de 43°C'de uygulandı. İkinci grup özel bir tedavi almadı ve rutin tedavilerine devam etti (kontrol grubu). Hastalar, tedavi öncesi/1. gün, tedavi sonu/12. gün ve 3. ayda kör bir hekimle klinik ölçekleri tamamladı.

Bulgular: Çalışma grubunda WOMAC toplam, VAS ağrı, hasta ve hekim global değerlendirme skorlarında, başlangıca göre, tedavi sonu ve üçüncü ay kontrollerinde istatistiksel olarak anlamlı bir iyileşme gözlendi. Çalışma grubunda Lequesne Diz İndeksi başlangıca göre 12. gün ve üçüncü ay skorlarında istatistiksel olarak anlamlı bir iyileşme gözlendi. Nottingham Sağlık Profili ağrı, duygusal reaksiyonlar, fiziksel hareket ve enerji skorlarında, çalışma grubunda 12. günde başlangıca istatistiksel olarak anlamlı bir iyileşme gözlendi ve bu anlamlı fark üçüncü ayda da

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ment, and energy scores in the study group on day 12 compared with baseline, and this significant difference continued in the third month for all scores, excluding the energy score. No change was observed in the control group.

Conclusion: The positive effects of balneological treatment on pain, functional status, and quality of life in knee osteoarthritis have been demonstrated.

Keywords: Hydrotherapy, peloidotherapy, knee osteoarthritis, balneotherapy

enerji skoru dışında devam etti. Kontrol grubunda herhangi bir değişiklik gözlemlenmedi.

Sonuç: Balneolojik tedavinin diz osteoartritinde ağrı, fonksiyonel durum ve yaşam kalitesi üzerinde olumlu etkileri gösterilmiştir.

Anahtar Kelimeler: Hidroterapi, peloidoterapi, diz osteoartriti, balneoterapi

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease characterized by progressive cartilage destruction and osteophyte formation, especially in load-bearing joints. The incidence of OA increases with age. OA can affect all joint structures, including the cartilage, bone and synovium, and surrounding muscles (1, 2). OA is the most common form of arthritis and a leading cause of disability in >65 year old individuals (3). Pain is the most common clinical symptom and is associated with joint use. The medial tibiofemoral and patellofemoral joints are the most affected areas in the knee (4).

Definitive treatment for OA are lacking. Evidence-based approaches to the nonsurgical treatment of knee OA include a combination of pharmacological and nonpharmacological treatment methods to relieve pain, improve joint function, and change risk factors for disease progression. Balneological treatment modalities are nonpharmacological treatment methods commonly used to treat OA, because they are well-tolerated and have positive effects on pain relief, stiffness, and function (5).

Balneological treatment utilizes natural resources, such as thermal mineral-rich waters, peloids (muds), and gases, which are administered to patients through bathing, drinking, inhalation treatments, etc. (6). Hydrotherapy is a type of balneological treatment method that uses tap water. Hydrotherapy includes the external application of water using the physical characteristics of water, such as temperature, hydrostatic pressure, buoyancy, and viscosity (7). However, peloid therapy improves blood flow, connective tissue flexibility, and plasma level of β-endorphins. Peloid therapy affects the neuro–immune–endocrine system and has anti-inflammatory properties. Among the most popular treatments within the field of spa therapy, balneotherapy, hydrotherapy, and peloid therapy are usually employed in musculoskeletal conditions (8, 9). Balneological treatment modalities are a clinically effective treatment option for many low-grade inflammations, especially rheumatic conditions, due to their anti-inflammatory, antioxidant, and chondroprotective properties (10).

Our study aimed to evaluate the effects of hydrotherapy and peloid package application in hospital settings on pain, function, and quality of life in patients with knee OA via clinical scales.

MATERIAL and METHODS

Participants and Sample

Patients with knee OA who met our research criteria and were followed up in the Leucomotor System Diseases outpatient clinic of Istanbul University, Istanbul Faculty of Medicine, Department of Medical Ecology and Hydroclimatology, were included in the study. Sample size calculation on powerandsamplesize.com revealed that type 1 error was 5%, type 2 error was 20%, and power (power) was 80%. A minimal sample size of 26 patients was targeted for each group, with a difference of 15 units and a standard deviation of 20 units between the two groups. Sample size was calculated according to Fioravanti et al. (11). The files of 368 patients who applied to the Department of Medical Ecology and Hydroclimatology with complaints of knee pain were scanned and evaluated for suitability (Figure 1). Patients who were followed up in our hospital with knee OA, who met the inclusion criteria, and agreed to participate in the study, were randomly divided into two groups. Each patient was given information about the study.

Inclusion criteria: The study included patients 40–80 years of age, who were diagnosed with knee OA according to American College of Rheumatology criteria after physical examination and radiological evaluation and who scored two or three on the Kellgren and Lawrence scale.

Exclusion criteria: Patients who had decompensated organ failure, malignant disease, systemic inflammatory diseases, infectious diseases; received balneotherapy in the last year; changed their medication in the last two months; and had a history of intramuscular injection, arthroplasty, or prosthetic surgery in the knee joint in the last six months were excluded from the study.

Permissions

The study is a randomized, controlled, single-masked study according to the guidelines of the Declaration of Helsinki. The study protocol was approved by İstanbul Faculty of Medicine Clinical Research Ethics Committee, İstanbul University (Date: 21.08.2020, No: 19).

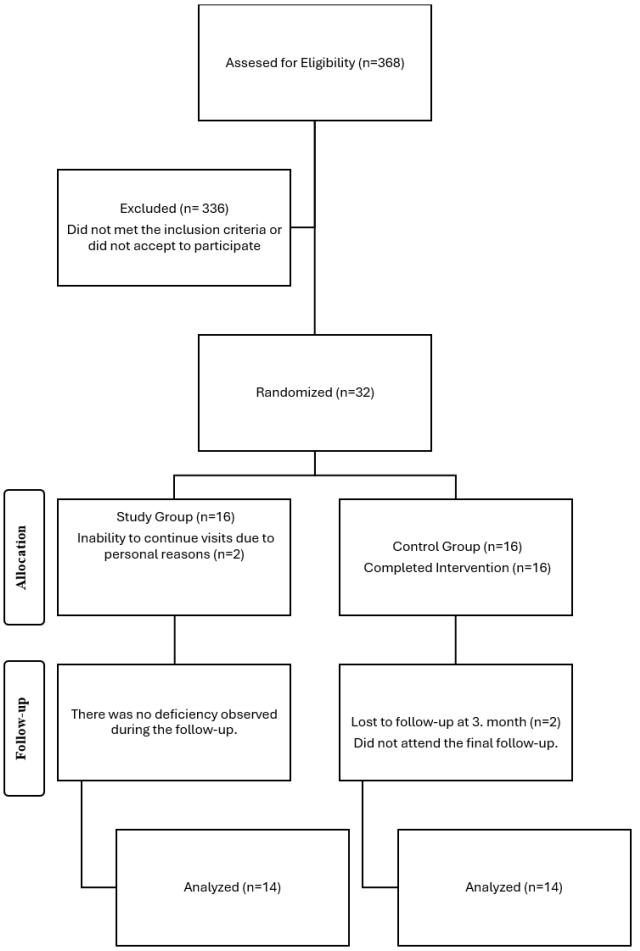

Figure 1: Flow diagram of the patients

Intervention

The patients who accepted to participate were divided into two groups, study and control, by randomization according to the computer-generated random numbers table.

Patients in the study group were given a full bath (up to shoulder level) in a hydrotherapy pool with water temperature 38°C for 20 min, once a day, five days a week, (in total 10 times in two weeks). Following the bath, the peloid was applied directly on the skin of both knee areas with a thickness of approximately 1 cm at 43°C for 20 min (Figure 2). To maintain the application temperature, the top of the peloid was first wrapped with a stretch film and then a towel. The peloid (palomino) used in the application was obtained by mixing natural substances containing 90% magnesite and 10% sepiolite with salt and mineral water. During peloidotherapy, the patients sat comfortably or lay on their backs/prone. In the hydrotherapy pool, patients sat without exercising. The dimensions of the pool were 2.25–1.30 m^2. Pool temperature was normal and was not increased for operation.

Figure 2: Peloid package application

Patients in the control group were not given balneological treatment. They were allowed to take oral paracetamol if needed (maximum 2 g/d).

In both groups, in the beginning, at the end of the treatment (day 12), and in month 3 after treatment, the visual

analog scale (VAS), which is one of the clinical scale forms, pain, general evaluation of the patient, general evaluation of the physician, Western Ontario and McMaster Universities knee index (WOMAC), Lequesne knee index, and Nottingham Health Profile (NHP) forms were filled in by the blind physician. The forms were filled by a physician blinded to the treatments and treatment groups. Blood samples were taken at baseline, after treatment, and 3 months after treatment to detect serum levels of C-reactive protein (CRP). Both groups continued their treatments for comorbidities.

Data collection tools

Patient Global Assessment-VAS: This assessment questions the patient's general well-being. The patient is asked to evaluate the effect of the disease and mark the point that is most appropriate for their condition.

Physician Global Assessment-VAS: The doctor evaluates the patient's general well-being on the same scale.

Pain Assessment-VAS: The patient assesses their pain between "no pain: 0" and "very severe pain: 10" and marks the current situation on this line.

WOMAC: This consists of 24 questions: 5, 2, and 17 in the pain, stiffness, and function sections, respectively.

Lequesne Knee Index: This is an index used in patients with knee OA. It questions pain, stiffness, and functionality. The form consists of 10 questions, including three separate titles.

NHP: This assesses the quality of life.

Laboratory: Blood samples were taken from all patients for the hemogram, erythrocyte sedimentation rate, total cholesterol, low-density lipoprotein, uric acid, creatinine, aspartate aminotransferase, alanine aminotransferase, and CRP at each control, and evaluated at the Clinical Biochemistry Laboratory of Istanbul University Faculty of Medicine on the same day.

Blinding: The clinical evaluations of the patients were made by a physician who was blinded to treatment and groups. Another physician who was blinded to treatment and groups was responsible for treatments. A biostatistician who was blinded to the study analyzed the results.

Statistical analysis

Independent sample t-test and Mann–Whitney U test were used to analyze continuous independent data. The Wilcoxon test was used to analyze dependent continuous data. The chi-square test or Fisher's exact test was used to analyze categorical independent data. SPSS program version 27.0 (IBM SPSS Corp., Armonk, NY, USA) was used for analysis.

RESULTS

Flow diagram

Because our patient population mainly consisted of older patients, 32 patients (16 each in the study and control groups) were studied study due to restrictions during the coronavirus disease 2019 (COVID-19) pandemic. The study was completed with 28 patients, 14 in the study group and 14 in the control group. In total, 11 patients received 10 sessions, two patients received 9 sessions, and one patient received 8 sessions. During treatment, no side effects were observed.

Sociodemographic data

There was no difference between the study and control groups in terms of age, body mass index, employment status, smoking and alcohol use, and comorbidity. The mean age of patients was 61.7±6.8 years in the study group and 56.6±9.7 years in the control group. The rate of female patients in the control group was significantly higher than the rate of male patients in the study group (Table 1).

Clinical evaluation criteria results

Patient VAS global assessment, physician VAS global assessment, and VAS Pain scores in the study group significantly decreased on day 12 and month 3 after treatment, compared with baseline ($p<0.005$). By contrast, VAS scores in the control group did not change significantly on day 12 and month 3 after treatment, compared with baseline ($p=0.202$) (Table 2).

In the study group, on day 12, third-month WOMAC total and Lequesne knee index score decreased significantly ($p<0.05$) compared with pretreatment. In the control group, WOMAC total and Lequesne knee index score did not significantly change compared with pretreatment on day 12 and month 3 (Table 3) (Figure 1).

In the study and control groups, CRP levels were 7.7±12.3 and 2.6±1.9 mg/L before treatment, respectively. After 3 months of treatment, CRP levels were 4.3±2.9 and 3.3±3.3 mg/L in the study and control groups, respectively. There was no significant difference in CRP value change on day 12 and month 3 in the study and control groups.

In the study group, day-12 and month-3 NHP pain score, Nottingham emotional reaction score, and Nottingham physical activity score decreased significantly ($p<0.05$) compared with pretreatment. In the study group, day-12 and month-3 Nottingham sleep score, Nottingham social isolation score, and NHP part 2 score did not change significantly ($p>0.05$) compared with pretreatment level. The Nottingham energy score on day 12 decreased significantly ($p<0.05$) in the study group, whereas that on month 3 did not change significantly ($p>0.05$) in the study group compared with pretreatment. In the control group, day-12 and month-3 Nottingham scores did not

Table 1: Comparison of the sociodemographic data of the groups

		Study group (n:16)	Control group (n:16)	p
		Mean±SD (Median) or N (%)	Mean±SD (Median) or N (%)	
Age, years		61.7±6.8 (61.5)	56.6±9.7	0.098 [t]
Sex	Female	10 (62.5)	15 (93.8)	**0.033** [X²]
	Male	6 (37.5)	1 (6.2)	
BMI, kg/m^2		32.3±4.3	30.6±5.5	0.331 [t]
Working Status	Not working	8 (%50.0)	12 (75.0)	0.144 [X²]
	Working	3 (18.8)	3 (18.8)	
	Retired	5 (31.3)	1 (6.3)	
Smoking	(-)	14 (87.5)	11 (68.8)	0.200 [X²]
	(+)	2 (12.5)	5 (31.3)	
Alcohol Use	(-)	16 (100)	13 (81.3)	0.226 [X²]
	(+)	0 (0)	3 (18.8)	
Comorbidity	(-)	5 (31.3)	10 (62.5)	0.077 [X²]
	(+)	11 (68.7)	6 (37.5)	
Hypertension		8 (%50.0)	3 (18.8)	0.063 [X²]
Hypothyroidism		5 (31.3)	2 (12.5)	0.200 [X²]
Hypercholesterolemia		2 (12.5)	1 (6.3)	1.000 [X²]
DM		4 (25.0)	3 (18.8)	0.669 [X²]
Heart disease		1 (6.3)	0 (0)	1.000 [X²]
Asthma		2 (12.5)	1 (6.3)	1.000 [X²]
Depression		2 (12.5)	0 (0)	0.484 [X²]

[X²]: Pearson Ki-Square, [t]:Student's t-test, SD: Standard deviation, BMI: Body mass index, N: Count, DM: Diabetes Mellitus

change significantly (p>0.05) compared with pretreatment (Table 4).

The changes in the parameters evaluated in the study and control groups in month 3 are shown in Figure 2. A decrease was observed in the study group in all parameters. Although there was an increase in some parameters in the control group, the rate in the parameters with a decrease was higher in the study group.

DISCUSSION

Nonpharmacological interventions form the basis of OA management. Balneological treatments-one of the nonpharmacological treatments-have been a treatment option for knee OA for years (12). Balneotherapy can be a good alternative for patients who cannot tolerate pharmacological treatments or as an adjunct to pharmacological treatment for knee OA (13). Balneotherapy and physical therapy were more effective than physical therapy alone in patients with knee OA (14).

In a study comparing the effectiveness of balneotherapy with pharmacological treatment in patients with advanced knee OA, balneotherapy was superior in reducing pain and improving functional capacity in the short and medium term. Consistently, our study found the superiority of the balneological treatment group compared with the control group on day 12 and at the 3-month follow-up (15).

Another study showed that balneological treatment could be an alternative option without medication; consecutive and intermittent balneological treatment regimens were effective in patients with knee OA (16). In a study evaluating the duration of thermal spring treatment, group 1 received treatment for three weeks, and group 2 received treatment for two weeks. Patients were evaluated using VAS, WOMAC, and NHP before, after, and at 1-month follow-up. Measurements showed significant improvements in both groups compared with baseline measurements, except for the social isolation subgroup of the Nottingham Health Profile, which is consistent with our study (17). In our study, statistically significant improvements were

Table 2: General wellness in the study and control groups at the beginning, end of treatment, and month 3

	Study group (n:14) Mean±SD (Median)	Control group (n:14) Mean±SD (Median)	p
VAS global patient assessment			
Before treatment	49.4±17.4 (50.0)	52.6±20.0 (50.0)	0.890 [m]
Day 12	39.9±25.1 (47.5)	50.0±24.9 (51.0)	0.114 [m]
Month 3	32.1±24.9 (22.0)	43.9±20.6 (50.0)	0.227 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.028**[w] 19.28% ↓ Cohen d:0.43	0.780[w] 4.88% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.013**[w] 35.03% ↓ Cohen d:0.80	0.202[w] 16.43%↓	
VAS pain			
Before treatment	52.8±16.8 (50.0)	48.3±23.1 (50.0)	0.908 [m]
Day 12	41.3±21.8 (44.0)	51.8±25.4 (51.0)	0.116 [m]
Month 3	29.5± 24.9 (28.0)	43.4±21.1 (50.0)	0.195 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.037**[w] 21.83% ↓ Cohen d:0.59	0.409[w] 7.24%↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.010**[w] 44.21% ↓ Cohen d:1.09	0.443[w] 10.26% ↓	
VAS global physician assessment			
Before treatment	51.5±15.5 (50.0)	50.8±20.7 (50.0)	0.938 [m]
Day 12	39.2±22.9 (42.5)	49.8±24.0 (51.0)	0.065 [m]
Month 3	31.2±24.3 (25.0)	43.1±21.0 (50.0)	0.257 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.022**[w] 23.86% ↓ Cohen d:0.62	0.916[w] 1.85% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.01**[w] 39.51% ↓ Cohen d:0.99	0.161[w] 14.99% ↓	

[m] Mann–Whitney U test / [w] Wilcoxon test, SD: Standard deviation, VAS: Visual analog scale

observed in the study group regarding VAS pain and patient and physician global assessment scores compared with baseline at the end of treatment and 3-month follow-up. A statistically significant reduction was observed in WOMAC subgroups and WOMAC-total scores, except for stiffness, in the study group at the 3-month follow-up compared with baseline. Significant improvement was observed in the study group after treatment compared with before treatment in NHP, except for the social isolation and sleep subgroups.

In a meta-analysis evaluating the effects of balneotherapy using WOMAC scores, balneotherapy was found to be clinically effective in relieving pain and stiffness and improving functional status compared with controls, similar to our study (18). Consistently, a meta-demonstrated the beneficial effects of balneotherapy and mud therapy on pain, stiffness, and functional status in patients with knee OA (19). In a meta-analysis evaluating thermal modalities, such as balneotherapy, mud therapy, and thermal spring treatment, thermal modalities were effective in the short-term prognosis of patients with OA (20). The effects of balneotherapy are probably related to the temperature and physicochemical and microbial properties of natural mineral water. This type of therapy triggers a set of biological, physiological, and perceptional responses involved in a neuroendocrine reaction that increases serum levels of opioid peptides, such as endorphins, and changes the circulating levels of prostaglandins, leukotrienes, and metalloproteinases (21).

Studies on the long-term clinical efficacy of thermal spring treatment in knee OA are lacking. In a study to determine the clinical efficacy of thermal spring treat-

Table 3: Osteoarthritis assessment measurements at baseline, end of treatment, and month 3 in study and control groups

	Study group (n:14) Mean±SD (Median)	Control group (n:14) Mean±SD (Median)	p
WOMAC Total			
Before treatment	41.8±17.0 (46.0)	42.3±18.3 (33.0)	0.910 [m]
Day 12	35.1±21.3 (35.0)	42.1±20.3 (31.5)	0.360 [m]
Month 3	30.9±22.9 (31.0)	39.1±13.7 (29.5)	0.254 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.041**[w] 15.95% ↓ Cohen d:0.34	0.938[w] 0.3% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.039**[w] 26.04% ↓ Cohen d:0.54	0.969[w] 7.35% ↓	
Lequesne Knee Index			
Before treatment	11.3±3.5 (11.8)	11.4 ±4.6 (12.3)	0.636 [m]
Day 12	8.2±3.5 (9.0)	11.3±4.1 (11.5)	**0.021**[m] Cohen d:0.81
Month 3	7.9±4.7 (9.5)	10.7±2.8 (10.5)	0.187 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.002**[w] 27.3% ↓ Cohen d:0.88	0.959[w] 0.82% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.003**[w] 29.57% ↓ Cohen d:0.82	0.729[w] 6.38% ↓	

[m] Mann–Whitney U test/[w] Wilcoxon test, SD: Standard deviation, WOMAC: Western Ontario and McMaster Universities multifunctional index

ment in the long-term prognosis of patients with bilateral knee OA, the treatment group received a combination of peloidotherapy and balneotherapy. The control group continued routine medical treatment. Follow-up was performed two weeks after treatment and at 3, 6, 9, and 12 months. VAS and WOMAC scores, which were also used in our study as primary outcome measures, were used. Consistent with our study, significant improvements were observed in the VAS and WOMAC scores of the treatment group, which continued at the 3-month follow-up. However, no significant changes were observed in the control group. Unlike our study, longer-term follow-up was performed, and the significant difference between the two groups continued until month 9 (22).

Table 4: Quality-of-life measurements at baseline, end of treatment, and at month 3 in study and control groups

Nottingham health profile	Study group (n:14)		Control group (n:14)		p
	Mean ± Sd	Median	Mean ± Sd	Median	
Pain					
Before treatment	67.10±31.17 16	74.15	58.73±24.4	54.41 16	0.34 [m]
Day 12	49.33±29.11 14	53.79	57.57±27.9 16	59.4	0.36 [m]
Month 3	45.25±28.15 14	48.91	59.74±16.77	59.4 14	0.25 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.01**[w] 26.48% ↓ Cohen d:0.59		0.78[w] 1.98% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.02**[w] 32.56% ↓ Cohen d:0.73		0.58[w] 1.72% ↑		

Table 4: Continue

Emotional reactions					
Before treatment	48.49±33.21	56.28	47.94±28.15	48.87	0.84 [m]
Day 12	30.17±32.76	13.95	41.81±27.44	40.88	0.23 [m]
Month 3	35.65±31.62	29.54	54.42±37.44	60.07	0.16 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.02**[w] 37.78% ↓ Cohen d:0.55		0.43[w] 12.79% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.04**[w] 26.46% ↓ Cohen d:0.39		0.48[w] 13.53% ↑		
Sleep					
Before treatment	36.27±26.52	39.89	42.30±19.09	43.36	0.45 [m]
Day 12	27.97±25.16	22.47	48.33±29.7	49.65	0.07 [m]
Month 3	31.94±24.81	28.67	38.66±23.75	43.36	0.39 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	0.14[w] 22.88% ↓		0.67[w] 14.25% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	0.41[w] 11.94% ↓		0.64[w] 8.63% ↓		
Physical movement					
Before treatment	49.48±15.5	53.4	43.54±16.75	41.61	0.19 [m]
Day 12	43.51±18.1	44.17	47.34±24.4	54.96	0.63 [m]
Month 3	34.65±18.7	33.53	47.94±20.2	43.15	0.11 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.03**[w] 12.07% ↓ Cohen d:0.35		0.82[w] 8.73% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.001**[w] 29.97% ↓ Cohen d:0.86		0.36[w] 10.11% ↑		
Energy scores					
Before treatment	67.10±38.52	76	65.50±40.71	81.6	1 [m]
Day 12	44.40±38.96	36.8	62.50±39.52	63.2	0.19 [m]
Month 3	61.17±32.97	60.8	66.00±37.63	69.6	0.5 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.02**[w] 33.83% ↓ Cohen d:0.58		0.55[w] 4.58% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	0.53[w] 8.84% ↓		0.58[w] 0.76% ↑		
Social isolation					
Before treatment	32.65±41.39	7.99	41.44±33.71	41.76	0.4 [m]
Day 12	29.00±36.57	7.99	35.59±36.16	22.01	0.45 [m]
Month 3	19.05±29.54	0	41.85±41.89	41.26	0.16 [m]

Table 4: Continue

Social isolation					
Before treatment and day 12 intragroup exchange p-value and percent change	0.72[w] 11.18% ↓		0.4[w] 14.12% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	0.34[w] 41.66% ↓		0.53[w] 0.99% ↑		
Nottingham health profile part 2					
Before treatment	1.9±2.1	1.5	1.4±1.4	1.5	0.627 [m]
Day 12	2.1±2.2	1.5	2.5±2.5	3.0	0.830 [m]
Month 3	0.9±1.8	0.0	1.6±1.4	2.0	0.109 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	0.573[w] 10.60% ↑		0.106[w] 73.91% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	0.37[w] 52.36% ↑		0.491[w] 14.29% ↓		

[m]: Mann–Whitney U Test / [w]: Wilcoxon Test, SD: Standard deviation

In another study involving long-term follow-up in patients with OA, group A received peloidotherapy and balneotherapy in three cycles for one year. By contrast, group B did not receive additional treatment. The mean value reported in VAS pain assessments was significantly lower in group A than group B. After treatment, the mean scores of the Lequesne knee index in group A were lower than those of patients in group B, who did not receive therapy (23). Our study group observed statistically significant improvement in VAS pain and patient and physician global assessment scores at the end of treatment and at 3-month follow-up compared with baseline. No change was observed in the control group who did not receive treatment.

Similarly, in our treatment group (hydrotherapy + peloidotherapy), a significant decrease in the Lequesne knee index score was observed on day 12 and month 3 compared with before treatment. In the control group who did not receive treatment, there was no significant change in the Lequesne knee index score on day 12 and month 3 compared with before treatment. The decrease in the Lequesne knee index score on day 12 and month 3 was significantly higher in the study group than the control group.

In patients with knee OA, chronic pain and functional impairment significantly decrease quality of life (related to difficulty in performing daily life activities). Therefore, a systematic meta-analysis was conducted to evaluate the effects of balneotherapy and spa treatment on the quality of life of patients with knee OA. Balneotherapy and spa treatment significantly improved the quality of life of patients with knee OA, as well as reduced medication consumption and improved algofunctional indices (5). In our study group, statistically significant improvement was observed in NHP pain, emotional reactions, physical movement, and energy scores on day 12 compared with baseline, and this significant difference continued, except for the energy score in month 3. In our control group, there was no statistically significant change in scores on day 12 and month 3 compared with baseline. Our study results show that balneological treatments improve the quality of life in patients with knee OA.

Recent studies have shown that some biomarkers may be useful in predicting OA prognosis and evaluating therapeutic response. After balneological treatment, levels of proinflammatory molecules, such as tumor necrosis factor-alpha, interleukin-1 beta, prostaglandin E2, leukotriene B4, and CRP, decreased and levels of anti-inflammatory molecules, such as insulin-like growth factor 1, increased in the serum (24). Another study investigated serum human glycoprotein of cartilage (YKL-40) and hsCRP levels in patients with knee OA after mud therapy. Mean serum YKL-40 and hsCRP levels were higher in patients than healthy controls. However, no significant change was observed in hsCRP levels throughout follow-up (25). The findings show that an anti-inflammatory effect may mediate the clinical benefits of balneotherapy in patients with musculoskeletal disease. A decrease in circulating interleukin-6 levels and improvements in pain mitigation and patient functionality were observed. Circulating levels of CRP were observed after balneotherapy, with no statistically significant difference (26). In our study, no statistically significant changes were observed in CRP values in the study and control groups during follow-up.

The main limitation of this study was that we could not reach target sample size due to COVID. Another limitation was the short duration of follow-up after treatment. However, our study has several strengths. It was a prospective study with a control group during the pandemic.

CONCLUSION

Our study found that balneological treatment effectively improved pain, function, and quality of life in patients with knee OA and persisted over at least 3 months. Our results indicate benefits in all the dimensions assessed produced in the patients who underwent balneotherapy intervention both in response to the intervention and concerning control patients. Our outpatient treatment approach allowed patients to receive treatment for <1 h per day without disrupting their daily routines or requiring a change in environment. This approach enabled us to observe the effectiveness of balneological treatment in isolation, without the confounding effects of other factors, such as rest, vacation, and climatic factors. Further investigations must broaden the application of this therapeutic intervention in patients with OA, elucidate its mechanism of action, and delineate its clinical outcomes with greater clarity.

Ethics Committee Approval: The study has ethical approval from the İstanbul Faculty of Medicine Clinical Research Ethics Committee, İstanbul University (Date: 21.08.2020, No: 19)

Informed Consent: All patients signed the informed consent form.

Peer Review: Externally peer-reviewed.

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CASE REPORT / OLGU SUNUMU
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İst Tıp Fak Derg 2024 / J Ist Faculty Med 2024

A RARE CASE OF LOCALIZED PULMONARY NOCARDIOSIS CAUSED BY *NOCARDIA FARCINICA* IN A PATIENT WITH A BRAIN TUMOR

BEYİN TÜMÖRÜ OLAN HASTADA *NOCARDIA FARCINICA*'NIN NEDEN OLDUĞU NADİR BİR LOKALİZE PULMONER NOKARDİYOZ OLGUSU

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ABSTRACT

Nocardia farcinica is rarely isolated from clinical specimens, and it is a more virulent strain than other types of *Nocardia*. In this report, we evaluated a rare case of pleural empyema and pneumonia caused by *Nocardia farcinica* in a patient who had risk factors such as long-term use of corticosteroids, chronic respiratory disease, and a brain tumor. The distinction of *N. farcinica* from other Nocardia species is important because *N. farcinica* is more virulent and highly resistant, especially to broad-spectrum cephalosporins, which can make treatment difficult. In conclusion, in the presence of nonspecific physical examination and radiographic findings in patients using immunosuppressives and having comorbid diseases, atypical causative agents such as *Nocardia infection* should be considered in the differential diagnosis.

Keywords: Nocardiosis, *Nocardia farcinica*, pleural effusion, antibiotic susceptibility test, immunocompromised patients

ÖZET

Nocardia farcinica klinik örneklerden nadiren izole edilir ve diğer *Nocardia* türlerine göre daha virülan bir türdür. Bu makalede uzun süreli kortikosteroid kullanımı, kronik solunum yolu hastalığı ve beyin tümörü gibi risk faktörlerine sahip bir hastada *Nocardia farcinica*'nın neden olduğu nadir bir plevral ampiyem ve pnömoni olgusu değerlendirildi. *N. farcinica*'nın diğer Nocardia türlerinden ayrılması önemlidir, çünkü *N. farcinica* daha virülandır ve özellikle geniş spektrumlu sefalosporinlere yüksek derecede dirençlidir ve bu da tedaviyi zorlaştırabilir. Sonuç olarak, immünsüpresif ilaç kullanan ve eşlik eden hastalıkları olan hastalarda nonspesifik fizik muayene ve radyografik bulguların varlığında ayırıcı tanıda *Nocardia* enfeksiyonu gibi atipik etkenlerin akılda tutulması gerekmektedir.

Anahtar Kelimeler: Nokardiyoz, *Nocardia farcinica*, plevral efüzyon, antibiyotik duyarlılık testi, bağışıklığı zayıflamış hastalar

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INTRODUCTION

The *Nocardia* species is a Gram-positive, partially acid-fast, aerobic, filamentous genus of *Actinomycetes* commonly found in decaying matter, soil, and water (1). *Nocardia* is usually transmitted by inhalation (2). Pulmonary nocardiosis is the most common clinical presentation; the most common symptoms are shortness of breath and coughing (2, 3). Although *Nocardia farcinica* is rarely isolated, it is more virulent than other *Nocardia* species (4). It mainly causes infections in immunocompromised patients who have risk factors such as long-term corticosteroid therapy, use of immunosuppressive drugs, organ transplantation, malignancy, human immunodeficiency virus (HIV) infection, diabetes, chronic obstructive pulmonary disease (COPD), or alcoholism (2, 5, 6). Although it is rarely isolated from local and systemic infections in healthy individuals, it can also cause opportunistic infections in immunocompromised patients (7). Pleural involvement in *N. farcinica* infections is rare; few studies have been reported in the literature (4, 8).

In this case report, pleural empyema and pulmonary nocardiosis caused by *N. farcinica*, which developed in a patient with long-term corticosteroid use, COPD, and malignancy, are evaluated.

CASE PRESENTATION

A 70-year-old male patient was admitted to the emergency department with complaints of shortness of breath. The patient was diagnosed with hypertension, COPD, ischemic heart disease, and diabetes mellitus and was waiting for surgery, with the preliminary diagnosis of a brain tumor. The patient's vital signs were TA: 147/88 mmHg, pulse: 110/min, and O_2 saturation: 86-88 (while oxygen was administered). During physical examination, costal movements were restricted on the right side, and respiratory findings decreased with auscultation. Right total pneumothorax was detected on posteroanterior chest radiography and thorax computed tomography (Figure 1). A thoracostomy tube was placed at the right 4th intercostal level. The patient was transferred to the intensive care unit. C-reactive protein: 190 mg/L, sedimentation: 119 mm/hour, and glucose: 516 mg/dL were revealed in laboratory tests. Other biochemical parameters and hemogram results were within normal limits. The patient was discharged with full recovery on the 10th day after admission.

One month later, the patient was admitted again to the emergency department with findings such as shortness of breath, subcutaneous emphysema, and discharge from the drain site and was transferred to the thoracic surgery clinic. Radiological examinations revealed a minimal expansion defect of the right lung, atelectasis at the base of the right hemithorax, and secondary minimal pleural effusion and bilateral cavitary lesions (Figure 2). Considering the patient's newly developing cavitary lesions and possible brain tumor metastases, positron emission tomography/computed tomography (PET/CT) was planned. Thoracentesis was performed from the right hemithorax. Pleural fluid was purulent and sent to the bacteriology laboratory for further analysis. The pleural fluid sample was inoculated on 5% sheep blood agar, eosin-methylene blue agar, and chocolate agar. Direct Gram staining was performed from the sample. Gram-positive bacilli with branching structures and polymorph nuclear inflammatory cells were detected. After two days of incubation, non-hemolytic, small, irregular colonies appeared on sheep blood agar. Microscopic examination of the grown colonies revealed Gram-positive bacilli with branching structures (Figure 3). The bacteria were identified as *N. farcinica* by Mass Spectrometry (VITEK MS, bioMérieux, Marcy l'Etoile, France). Antimicrobial susceptibility tests (AST) were evaluated according to the Clinical and Lab-

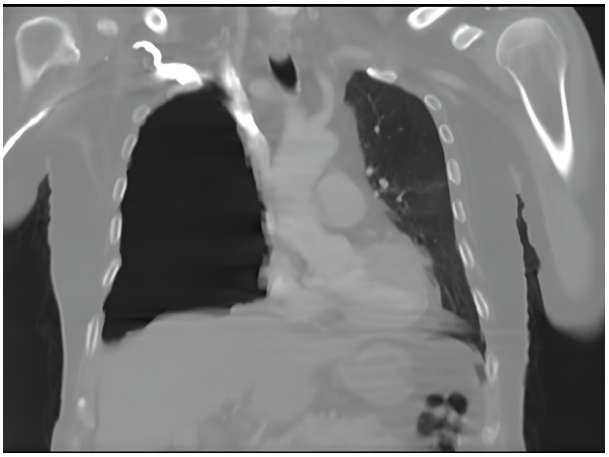

Figure 1: Admission thoracic tomography (June 15, 2022)

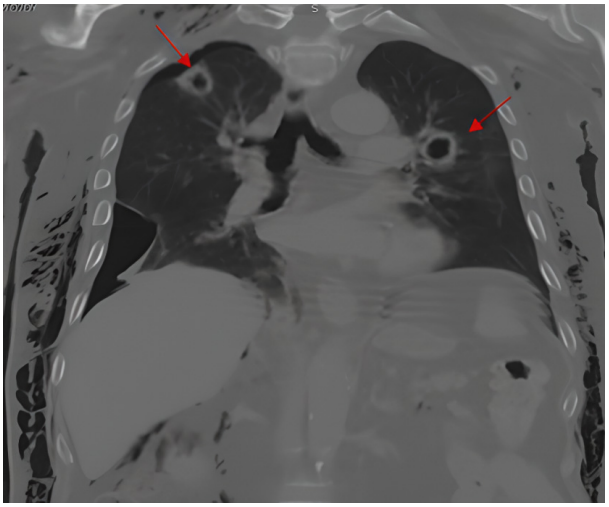

Figure 2: Bilateral cavitary lesions on coronal computed tomography (July 14, 2022)

oratory Standards Institute (CLSI) (9). The isolate was susceptible to increased doses of imipenem, amikacin, ciprofloxacin, and gentamicin. It was resistant to amoxicillin plus clavulanic acid.

Progression in the number and size of bilateral cavitary lesions were determined on PET/CT. The lesions were compatible with infective processes (Figure 4). The patient received ampicillin/sulbactam treatment for five days, and his treatment was revised after the causative agent was reported as *N. farcinica*. Trimethoprim-sulfamethoxazole (4x3 400/80 mg I.V.) and linezolid (2x600 mg I.V.) treatment was administered. During the patient's follow-up and treatment continued in the ward, the patient's health deteriorated. The patient, who developed sepsis in the intensive care unit, died on the 5th day of his admission to the intensive care unit.

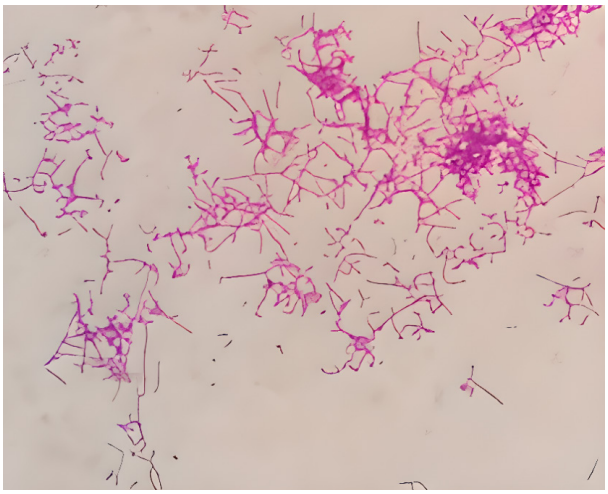

Figure 3: Gram-positive branching bacillus on microbiological staining of the pleural fluid specimen

DISCUSSION

Nocardia species can cause opportunistic infections in patients with predisposing factors such as malignancy, chemotherapeutic agents and/or steroid use, and COPD (2, 4). According to the study conducted by Torres et al., almost all of the 53 patients with *N. farcinica* infection had predisposing factors (5). *N. farcinica* can cause serious infections such as pneumonia and sepsis (2). Pulmonary and pleural infections, brain abscesses, and skin infections are the main clinical manifestations of *N. farcinica* infections (5). Although the onset of symptoms is subacute or chronic, it is difficult to recognize clinically because it occurs with nonspecific symptoms such as coughing, fever, shortness of breath, weight loss, fatigue, chest pain, hemoptysis, and night sweats (10). *N. farcinica* should be considered in pneumonia in the presence of radiological nodules, airspace consolidations, pleural effusion, and cavitary lesions (Figure 2, Figure 4) (11). As in this case, cavitary lesions are generally seen in immunocompromised patients and progress rapidly (2). In a review of 18 cases of pleural infection caused by *N. farcinica*, mortality was found to be more than 30% (4).

The diagnosis of nocardiosis is achieved by isolating the bacteria from clinical samples such as sputum, bronchoalveolar lavage fluid, pleural fluid, and abscess aspiration within 2-7 days (6). 16S rRNA sequence analysis is the gold standard for the identification of *Nocardia* species (12). However, the mass spectrometry method has promising results and is used successfully in rapid diagnosis (13).

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) is still working to determine AST

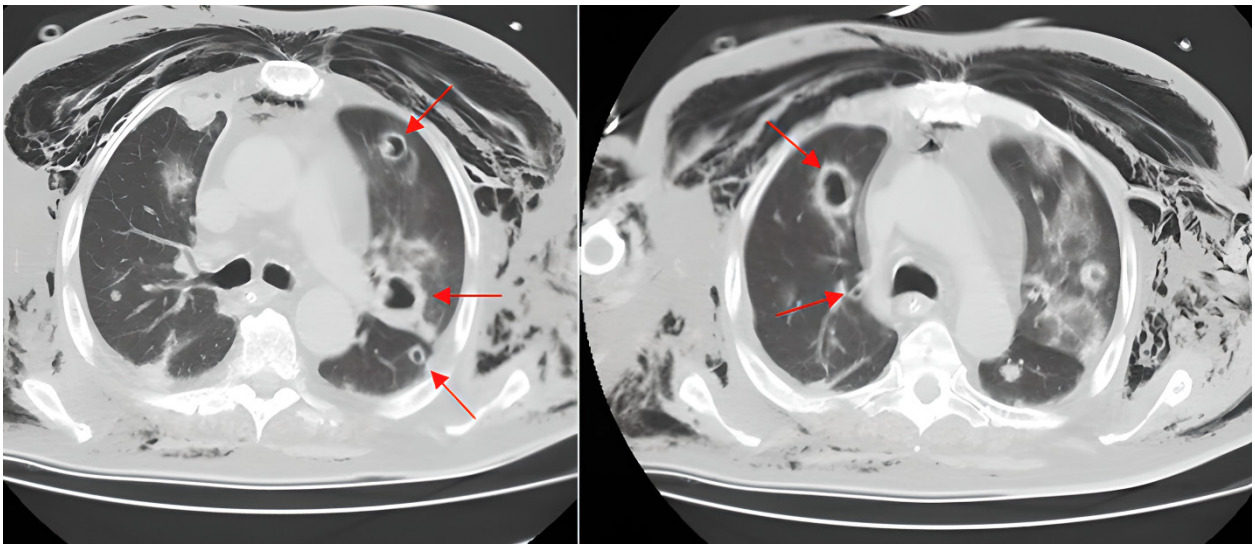

Figure 4: Rapidly progressing cavitary lesions (July 28, 2022)

breakpoints for *Nocardia* species (12). For this reason, the CLSI guideline is still used for AST (12). According to CLSI guidelines, broth microdilution is recommended for AST of *Nocardia* (12). Gradient strip tests and disk diffusion methods can also be used (8, 14). The results obtained in all AST methods should be interpreted carefully (15).

Trimethoprim-sulfamethoxazole has been the basis of nocardiosis treatment for the last 70 years (12). However, very high resistance rates have been reported for *N. farcinica* in some studies (8). All *Nocardia* species are generally susceptible to linezolid, amikacin, and trimethoprim-sulfamethoxazole in vitro (12). However, the susceptible profiles of other antibiotics vary greatly among *Nocardia* species (12).

In pneumonia caused by *Nocardia*, the combination of trimethoprim-sulfamethoxazole and carbapenem is recommended as initial treatment (4). In more severe cases, aminoglycoside can be added to this combination, and oral monotherapy can be switched after clinical improvement following 3 to 4 weeks of parenteral treatment (4). The treatment period may last 6-12 months (10). In addition to antibiotic treatment, interventional methods such as tube thoracostomy or therapeutic thoracentesis can be considered (4).

CONCLUSION

In conclusion, *Nocardia* infection should be considered in differential diagnosis in immunocompromised patients. Rapid identification of the microorganism can be life-saving, as identification at the species level is important in initiating the appropriate antimicrobial therapy. Considering the increasing resistance rates, antimicrobial susceptibility testing is of vital importance.

Informed Consent: Written informed consent was obtained from the patient and their legal guardians.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- S.V., T.D.; Data Acquisition- S.V., S.B.; Data Analysis/Interpretation- S.V., T.D.; Drafting Manuscript- S.V., T.D., S.B.; Critical Revision of Manuscript- S.V., T.D., S.B., Ö.A., M.K.; Final Approval and Accountability- S.V., T.D., S.B., Ö.A., M.K.

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

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CASE REPORT / OLGU SUNUMU
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INVESTIGATION OF DEATH AFTER VIDEO-ASSISTED THORACOSCOPIC SURGERY IN TERMS OF MEDICAL MALPRACTICE: AN AUTOPSY CASE REPORT

VİDEO YARDIMLI TORAKOSKOPİK CERRAHİ İŞLEMİNDEN SONRA MEYDANA GELEN ÖLÜM OLAYININ TIBBİ MALPRAKTİS AÇISINDAN İNCELENMESİ: OTOPSİ OLGUSU

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ABSTRACT

Video-assisted thoracoscopic surgery (VATS) is considered a safe method and is commonly performed in recent years. However, as with other invasive medical procedures, some complications may be encountered during and after this procedure. Of late, medical malpractice cases have become a prominent issue in the healthcare field. The case under discussion was sent to us for autopsy because of an allegation of medical malpractice. The cause of death was claimed to be an invasive procedure, namely pulmonary wedge resection with level 5 lymph node biopsy and VATS. We contribute to the literature by sharing, discussing, and evaluating our autopsy findings with forensic and medical documents. The possible complications of the procedure in question are generally known to be rare, nonfatal, minor traumas.

Keywords: Video-assisted thoracoscopic surgery, medical malpractice, autopsy

ÖZET

Video yardımlı torakoskopik cerrahi (VATS) son yıllarda sıklıkla kullanılmakta olan güvenli bir yöntem olarak kabul edilmektedir. Ancak diğer invaziv tıbbi işlemlerde olduğu gibi bu işlem sonrasında ve sırasında da bazı komplikasyonlarla karşılaşılabilir. Tıbbi uygulama hatası davaları son yıllarda sağlık alanında öne çıkan konulardan biri haline geldi. Olgumuz tıbbi uygulama hatası iddiası nedeniyle otopsi için tarafımıza gönderilmişti. Ölüm nedeninin Seviye 5 lenf bezi biyopsisi ve VATS ile pulmoner kama rezeksiyonu gibi invaziv bir prosedür olduğu iddia ediliyordu. Otopsi bulgularını adli ve tıbbi belgelerle birlikte paylaşarak, tartışarak ve değerlendirerek literatüre katkıda bulunmayı amaçladık. Zira söz konusu işlemin olası komplikasyonları genellikle nadir görülen, ölümcül olmayan küçük travmalar olduğu bilinmektedir.

Anahtar Kelimeler: Video yardımlı torakoskopik cerrahi, tıbbi malpraktis, otopsi

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INTRODUCTION

Video-assisted thoracoscopic surgery (VATS), usually pulmonary wedge resection, is commonly used to diagnose and treat several pulmonary diseases (1). In the literature, certain complications, such as pneumothorax, chylothorax, pneumonia, acute renal failure, liver failure, pulmonary embolism, postoperative delirium, stroke, atrial fibrillation, and postoperative death, related to this procedure have been reported. However, no case of intraoperative death has so far been encountered. VATS is a reliable and safe approach for the diagnosis and treatment of lung diseases (1-3). We contribute to the literature by evaluating the autopsy findings and all medical and forensic documents in detail.

CASE PRESENTATION

Our patient was a 58-year-old man with a diagnosis of asthma, hypertension, and chronic obstructive pulmonary disease. The medical reports stated that the patient had multiple pulmonary hypermetabolic nodular structures of different sizes, which were prominent in the lower lobe of the left lung. Primary pulmonary malignancy and lymphatic metastases were considered. Using VATS, a biopsy of the level 5 lymph node and wedge resection of the left lung lower lobe were performed. According to medical documents pertaining to the procedure under consideration, 25–30 minutes postoperatively, shortness of breath developed suddenly in the recovery unit. Portal lung radiography was performed considering intrathoracic organ damage, and bleeding was interpreted as normal. The patient was intubated and taken into surgery again. As per the surgery notes, an emergency left thoracotomy was performed on the patient. There was no bleeding in the biopsy area or in the thorax, but massive bleeding that accumulated in the abdomen was observed, and a lesion was seen on the left hemidiaphragm. The medical documents did not specify the exact location of the lesion on the diaphragm. The documents further stated that general surgery and cardiovascular surgery specialists were also called for the surgery. General surgeons detected 3–4 L of fluid in the abdomen, a 3–4 cm laceration on the anterior side of the spleen, and bleeding in the form of leakage in the tail of the pancreas. Splenectomy and suturing were performed in the tail of the pancreas. Cardiovascular surgeons examined the aorta and its surroundings, but no pathology was detected. The patient, who was intubated and under follow-up and treatment in the intensive care unit, died on the same day. Histopathological examination of the acquired samples revealed that non-small-cell carcinoma had metastasized to the lung and lymph nodes. In addition, predominant extramedullary hematopoietic cell infiltration and iron deposition from young cells of the myeloid series were observed in the splenectomy material.

The corpse was taken to the autopsy table for external examination, and the classical autopsy procedure was applied. Suture materials and bleeding areas resulted from medical procedures performed under the skin of the chest and abdomen, and wound trajectories resulted from medical procedures extending from the left midaxillary line. The ninth intercostal space in the chest was observed. Widespread ecchymotic areas were noted on both sides of the left dome of the diaphragm, and a sutured lesion was present in the anterior part of the left dome (Figure 1). A smooth-edged medical procedure-related (wedge resection) lesion on the distal left lower pulmonary lobe, suture materials, and bleeding areas were detected in the pancreatic tail and the outer surface of the stomach (Figure 2). The spleen was not perceived in its place (splenectomy), and hemorrhagic areas were spotted in the spleen lodge. The abdominal aorta and kidneys were in their natural morphology, and no signs of injury were discerned.

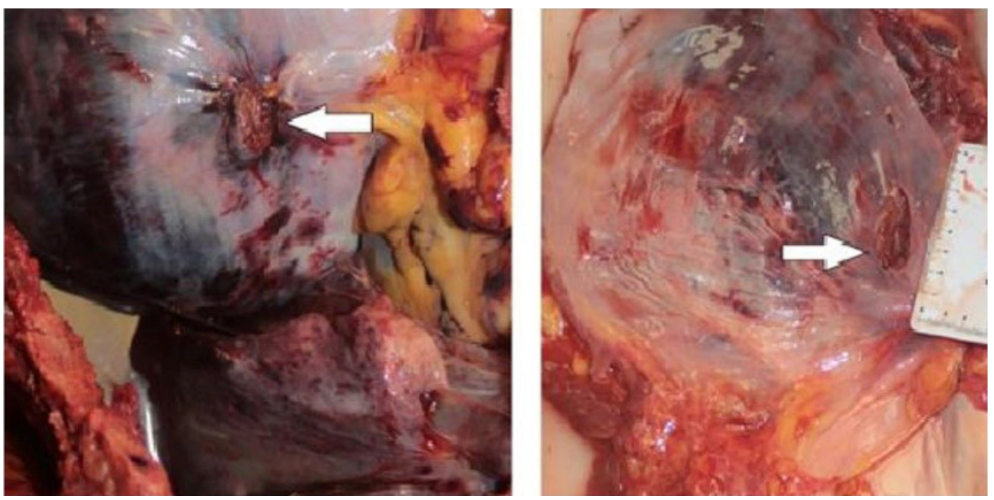

Figure 1: A: Sutured diaphragm lesion before organ dissection at autopsy. B: Sutured diaphragm lesion after organ dissection.

In lung and lymph node samples, which were examined at the macroscopic and microscopic levels, a congested atelectatic lung with malignant tumor infiltration and a hilar lymph node with malignant tumor metastasis were witnessed (Figure 3 A-B). The autopsy was performed as a team, and efforts were made to consult different medical specialties, as required. In toxicological examinations, drug levels were found at the treatment doses.

Medical documents play an essential role in the diagnosis and treatment of the patient and serve as evidences in the event of legal disputes. Therefore, these documents must be prepared accurately and completely (7). Although several medical procedures were performed in the case under study, medical documents were not maintained adequately and carefully.

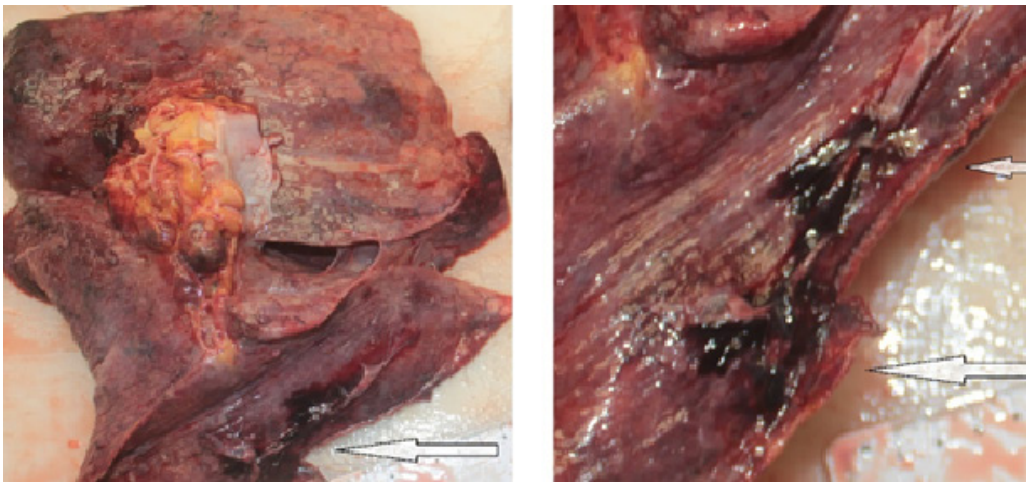

Figure 2: The region of wedge resection performed using the video-assisted thoracoscopic surgery method.

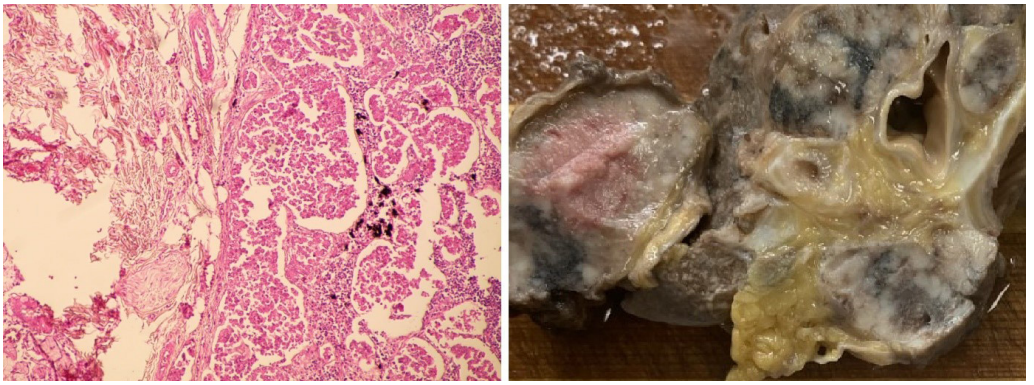

Figure 3: A: Samples of lungs for microscopic examination. B: Macroscopic appearance of a lung sample embedded in formaldehyde.

DISCUSSION

Harm to the patient owing to the physician's recklessness, negligence, or inexperience is termed medical malpractice (4). In the literature, surgical malpractices are classified as intraoperative wrong decisions, operative complications, and operative mistakes (5). Of late, the concept of malpractice has become one of the most frequently discussed topics in the healthcare field. Although the prevalence and size of malpractice litigations are unknown, there has been an increase in the number of accusations on all healthcare professionals, especially those on physicians, in recent years (6).

Lung cancer is one of the most common cancers worldwide, the frequency of which is increasing day by day, and it is the most common cause of cancer-related death (8). Cell blocks, cytological samples, resections, endobronchial biopsies, core biopsies, and fine-needle aspirations are conducted to diagnose lung cancer. These procedures should be performed safely and less invasively (9). In imaging studies performed in this study, hypermetabolic nodular structures were detected in the left lung, and primary pulmonary malignancy and lymphatic metastases were considered. Wedge resection of the lower lobe was performed.

VATS has now become a reliable approach that is commonly used in the diagnosis and treatment of lung diseases. This procedure is used for various purposes, such as pulmonary wedge resection, pleural and mediastinal biopsy, pleurectomy, and pneumothorax treatment (1). The literature has reported that complications occur at a rate of 7%–8.6% after this procedure. Pneumothorax, chylothorax, pneumonia, acute renal failure, liver failure, pulmonary embolism, postoperative delirium, stroke, and atrial fibrillation are the important and common complications. No case of intraoperative death has been reported in the literature. Postoperative mortality varies between 0.6% and 2% (1-3, 10). Vascular injury and intrathoracic bleeding have often been described in several studies (10-12). In a similar study in the literature, spleen injury was detected on computed tomography in a patient who was hypotensive and had low hematocrit values during postprocedure follow-up, and splenectomy was performed. These are some of the complications associated with the procedure (10).

Contrary to the complications commonly described in the literature, intraabdominal hemorrhage and spleen rupture were detected during the intraoperative and postoperative periods in our patient. In the autopsy, no traumatic lesion was detected either in the chest or in the abdomen, except for the surgical lesions. Contrary to the claims, the kidney and abdominal aorta were intact during the autopsy. The lesions observed on the diaphragm, pancreas, and stomach were determined to be surgical incisions. In this case, an opinion was also requested from the First Specialized Department of the Istanbul Forensic Medicine Institute by the relevant judicial body. The death of the patient was attributed to lymph cancer that had spread to other organs and the complications resulting from it (spleen rupture). Although splenic rupture and intraabdominal bleeding are not among the common complications of VATS, these have rarely been reported in the literature (10). We have emphasized this situation, which is quite rare, in our study. Another noteworthy point in this case is that patients and their relatives should be properly informed to prevent malpractice claims.

Although deficiencies prevailed in the medical documentation and in the stages of informing the patient's relatives, the complication was quickly evaluated. Radiological imaging, laboratory tests, and consultations were performed rapidly, the patient was immediately taken into surgery, and interventions were made to protect the patient's life as a team with the participation of relevant surgeons. Hence, it was concluded that the medical procedure was performed in accordance with the rules of scientific medicine and that the medical personnel did not have any legal responsibility.

CONCLUSION

Before VATS or similar medical interventions, patients and their relatives should be carefully and properly informed in detail by the physician who performs the procedure. Furthermore, physicians performing this procedure must have sufficient anatomical knowledge and the required technical equipment. The physicians must have adequate knowledge and experience regarding possible complications that may arise during the procedure and the necessary interventions.

Medical documents should be prepared elaborately and completely in case of legal disputes between the patient and the doctor after the procedure as these may also provide some evidence. Furthermore, facilities provided by the autopsy should be considered in medical malpractice cases to clarify the case and determine the truth. However, the duration of final decision and workload of the Council of Forensic Medicine are also important factors. Legal regulations should be formulated to enable appropriate consultations from relevant specialties at the place where the autopsy is initially performed.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer Review: Externally peer-reviewed.

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