

Grand Journal of UROLOGY

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Aims and Scope

Grand Journal of Urology (Grand J Urol) is an open access, peer-reviewed journal publishing original scientific articles in the field of urology. It aims to issue scientific publications on Andrology (Male Sexual Disfunction, Infertility), Endourology, Female Urology, Functional Urology, General Urology, Genitourinary Radiology, History of Urology, Laparoscopic and Robotic Surgery, Minimally Invasive Urology, Neurourology, New Technology and Techniques, Pediatric Urology, Reconstructive Urology, Renal Transplantation, Urolithiasis, and Urological Oncology. It is published electronically three times a year (January, May, September), and the language of publication is English.

The target audience of the journal includes, urology specialists, residents in urology and other specialists who are interested in the field of urology. The journal aims to publish original scientific articles, clinical research, reviews, case reports, clinical images, editorial comments, and letters to the editor that are prepared in accordance with the ethical guidelines. Mini reviews, clinical updates, surgical techniques, and a guideline of guidelines that are in the scope of the journal are considered for publication and/or invited by the editor. All manuscripts must be submitted via the online submission system at <u>www.grandjournalofurology.com</u>. The journal guidelines, technical information, and the required forms are available on the journal's web page.

Only articles that have not been published elsewhere or are not reviewed for publication may be submitted. Grand J Urol does not accept multiple submission and duplicate submission even though the previous one was published in a different language. The journal's publication policy is based on independent and unbiased double-blinded peerreviewed principles. Following the online article submission, the journal's fast publishing process is an important policy, with our members of the Advisory Board and referees, peerreviewes are conducted to the highest standards and feedbacks are provided in the shortest time possible. The journal reserves the right to request any research material related to the article.

Mission

The mission of the Grand J Urol (GJU) is to distribute urological medical data to the World as well as create a supportive and vibrant scientific platform to connect and explore ideas by publishing articles related to all fields of urology. The GJU aims to address current urological issues at both national and international levels, start debates, and exert an influence on decision-makers all over the world by integrating science in everyday life.

The Grand Journal of Urology encourages and enables academicians, researchers, and specialists to publish their valuable research in urology branch.

Basic Publication Rules

The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications in the World. The Grand Journal of Urology's editorial policy (evaluation and publication processes) is shaped according to the guidelines of international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the US National Library of Medicine (NLM), the World Medical Association (WMA), the US Office of Research Integrity (ORI), the European Association of Science Editors (EASE), and the International Society of Managing and Technical Editors (ISMTE), and National Information Standards Organization (NISO). The journal also is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (https://doaj.org/apply/transparency/).

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- Turkish (if the article is sent from Turkey) and English short title of the article, not exceeding 50 characters.

- Authors' names, institutions and ORCID IDs.

- Name, institution, e-mail, mobile phone and address of the corresponding author.

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- Manuscript must be written and sent on the Microsoft Word program.

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- Line breaks must be double spaced type.

- At least 2.5 cm margins must be left on all sides of each page.

- If there is, figure should be sent separately, it should not be in the main text.

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- When referring to a drug, product, hardware, or software program, product information, including the name of the product, the manufacturer of the product, and the city of the company (including the state in the USA) and country, should be specified in parentheses.

- The limitations of the original articles should be declared in the Discussion section before the conclusion paragraph.

- There should be no information that could indicate a person or organization to ensure a blind assessment process.

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The main text should contain the following sections in order:

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Original articles and review articles should be a maximum of 300 words and structured (Objective, Methods, Results, Conclusion). Case reports should have a maximum of 200 words and be unstructured. If the article is sent from Turkey, Turkish abstract should be sent (Amac, Gerecler ve Yöntemler, Bulgular, Sonuc).

Keywords

4 to 6 keywords, can be used for indexing purposes should be provided. Keywords should be selected from Medical Subject Headings (MeSH) databases prepared by the National Library of Medicine (NLM).

What is Medical Subject Headings (MeSH)? <u>http://</u><u>www.nlm.nih.gov/mesh/MBrowser.html</u> is a wide range of medical-biological terms list used for the classification of articles in main international article search directories and databases, aimed to standardize medical-biological terminology and updated continuously, from which keywords of English articles can be chosen.



Manuscript

Original Article: It is the most crucial article type since it provides new data based on original research. The main text should be structured with the subtitles of Introduction, Materials and Methods, Results, Discussion, and Conclusion.

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Restrictions by Article Type

Article Type	Number of Authors	Font Word	Summary of Word	Source	Table
Research	12	4000	450	30	5
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Case Report	8	1500	250	15	1
Clinical Image	5	500	N/A	10	0
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All participants who do not meet the authorship criteria (ICMJE: authorship and contributorship) and conflict of interest and financial statement, must be submitted under this subheading.

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Ethics committee approval is required in accordance with the National Ulakbim TR Index criteria for research/ original article studies using patients' data, even if they are retrospective, and this approval document should be attached when submitting the article (For more information: https://grandjournalofurology.com/static.php?id=32).

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[1], [3-5], [6,9], [8-12,16].

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[1] Guner E, Seker KG, Arikan Y, Huseynov C, Sam E, Ozdal OL. Aktuelle Urol. 2020; 51: 285-289. https:// doi.org/10.1055/a-1117-2776.

- Article with more than six authors

[2] Karabulut D, Karabulut U, Caglar FN, Ekşi M, Yenice MG, Guner E, et al. The association between CHA2DS2-VASc score and erectile dysfunction: a cross-sectional study. Int Braz J Urol. 2019; 45: 1204-1208. https://doi.org/10.1590 / S1677-5538. IBJU.2019.0058.

- Book

[3] Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.

- Book chapter

[4] McKenna K. Ejaculation. In: Knobil E, Neil J, editors. Encyclopedia of Reproduction, New York: Academic Press; 1999, p. 1002-8.

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Editorial

Dear colleagues,

I am honored to share with you the third issue of 2023 (volume 3, issue 3) of the Grand Journal of Urology (Grand J Urol) with the contributions of many respected researchers and authors.

Grand Journal of Urology (GJU) aims to carry written and visual scientific urology studies to academic platforms and to make significant contributions to the science of urology.

Our journal has been abstracted/indexed in Tubitak Ulakbim TR Index, DOAJ, EBSCOhost, J-Gate, Index Copernicus International, EuroPub, SciLit, ResearchGate, ScienceGate and Google Scholar international databases. As of these achievements, the Grand Journal of Urology (GJU) has taken its place among the journals indexed by national and international databases.

In this issue of our journal, there are many valuable articles under the subheadings of Andrology, Urological Oncology, Endourology, Urolithiasis, Pediatric Urology, Functional Urology and General Urology. I hope that these carefully prepared articles will make important contributions to valuable readers, researchers and the urology literature.

On this occasion, I would like to express my heartfelt gratitude to our authors who have contributed to our journal with their articles, to our reviewers who have meticulously evaluate the articles.

Respectfully yours September 2023 Assoc. Prof. Ekrem GUNER, MD Editor-in-Chief



The Effectiveness of Manual Detorsion Applied in the Emergency Department in Testicular Torsion: A Single - Center Experience of 13 Years Acil Serviste Uygulanan Manuel Detorsiyonun Testis Torsiyonunda Etkinliği: 13 Yıllık Tek Merkez Deneyimi

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Abstract

Objective: As a urological emergency, testicular torsion is one of the causes of acute scrotum in all age groups. This study aimed to evaluate the effectiveness of manual detorsion performed before surgical intervention.

Materials and Methods: Retrospective data analysis of the patients with acute scrotum who applied to the emergency department of a 3rd level hospital between the years January 2010 and January 2023 with the complaint acute unbearable pain within the first 12 hours of its onset was performed. Patients were grouped according to whether or not manual detorsion was performed in the emergency department. Successful manual detorsion was defined as post-procedural normal color Doppler ultrasound findings and complete resolution of pain. All patients had undergone surgical exploration. Age, laterality of the torsioned testis, manual testicular detorsion attempt (if any), and surgical conditions resulting in testis preservation or orchiectomy were the patient data analyzed.

Results: Sixty patients were included in the study. Manual detorsion was performed in 29 (48.3%) patients in the emergency department (Group 1). Scrotal exploration was performed in 31 (51.7%) patients without applying manual detorsion (Group 2). In Group 1, testicular preservation was achieved in 26 (89.7%) patients. In Group 1, in 3 patients (10.3%) testicular necrosis occurred due to failure to achieve adequate blood supply, while orchiectomy was performed in 11 (35.5%) patients in Group 2. Lower rates of orchiectomy were observed in Group 1 compared to Group 2 (p=0.021). We also observed that manual detorsion decreased the rate of orchiectomy (rho- 0.297, p=0.021), and the probability of undergoing orchiectomy increased with increasing age (rho 0.512, p<0.001).

Conclusion: Manual testicular detorsion is a noninvasive method that can be safely applied to all patients diagnosed with testicular torsion. We think that it will shorten the duration of testicular ischemia in the emergency department and contribute to testicular salvage.

Keywords: testicular torsion, manual detorsion, emergency, orchiectomy

Öz

Amaç: Ürolojik bir acil durum olarak testis torsiyonu tüm yaş gruplarında akut skrotum nedenlerinden biridir. Bu çalışmada cerrahi müdahale öncesi yapılan manuel detorsiyonun etkinliğinin değerlendirilmesi amaçlandı.

Gereçler ve Yöntemler: Ocak 2010-Ocak 2023 tarihleri arasında 3. basamak bir hastanenin acil servisine ilk 12 saat içerisinde akut dayanılmaz ağrı şikayeti ile başvuran akut skrotumlu hastaların retrospektif veri analizi yapıldı. Hastalar acil serviste manuel detorsiyon yapılıp yapılmadığına göre gruplandırıldı. Başarılı manuel detorsiyon, işlem sonrası normal renkli Doppler ultrason bulguları ve ağrının tamamen çözülmesi olarak tanımlandı. Tüm hastalara cerrahi eksplorasyon uygulandı. Yaş, torsiyonlu testisin lateralitesi, manuel testiküler detorsiyon girişimi ve testisin korunması veya orşiektomi ile sonuçlanan cerrahi durumlarlar analiz edilen hasta verileri oldu.

Bulgular: Çalışmaya 60 hasta dahil edildi. Acil serviste 29 (%48,3) hastaya (Grup 1) manuel detorsiyon uygulandı. 31 (%51,7) hastaya manuel detorsiyon uygulanmadan skrotal eksplorasyon yapıldı (Grup 2). Grup 1'de testis korunan hasta sayısı 26 (%89.7) olarak belirlendi. Grup 1' de 3 hastada (%10.3) yeterli kanlanma sağlanamaması nedeniyle testis nekrozu izlenmesi üzerine orşiektomi uygulanırken Grup 2' de 11 (%35.5) hastaya orşiektomi uygulandı. Grup 1'de Grup 2'ye göre daha düşük orşiektomi oranları gözlendi (p=0,021). Ayrıca manuel detorsiyonun orşiektomi oranını azalttığını (rho- 0.297, p=0.021), yaş arttıkça orşiektomi geçirme olasılığının arttığını (rho 0.512, p<0.001) gözlemledik.

Sonuç: Manuel testis detorsiyonu, testis torsiyonu tanısı alan tüm hastalara güvenle uygulanabilen noninvaziv bir yöntemdir. Acil serviste testiküler iskemi süresini kısaltacağını ve testisin kurtarılmasına katkı sağlayacağını düşünüyoruz.

Anahtar kelimeler: testis torsiyonu, manuel detorsiyon, acil, orşiektomi

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© Copyright 2023 by GJU. @ 2023 The Effectiveness of Manual Detorsion Applied in the Emergency Department in Testicular Torsion: A Single- Center Experience of 13 Years by Kursat Kucuker is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License which permits unrestricted non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Testicular torsion is defined as twisting of the testis along the spermatic cord resulting in venous congestion and poor arterial supply eventually leading to ischemia [1]. As a urological emergency, it is one of the causes of acute scrotum in all age groups. The overall incidence of testicular torsion in males is 2.02 to 21.76 per 100,000 population [2,3]. Differentiation of testicular torsion from other acute scrotal emergencies is important in terms of fertility and organ preservation. It is most often confused with epididymitis. An abnormal (horizontal) position of the testis is more common in testicular torsion than in epididymitis [4]. Searching for the absence of cremasteric reflex is a simple diagnostic test for testicular torsion with 100% sensitivity and 66% specificity [5,6]. Elevation of the scrotum (testes) may reduce symptoms in epididymitis, but not in testicular torsion. Determining the cause of acute scrotum based on history and physical examination alone is not easy [7]. Although scrotal color Doppler ultrasonography (CDU) is helpful in diagnosis, the possibility of false negatives and variable CDU findings pose a problem in clinical practice [8].

In case of suspected testicular torsion, manual detorsion of the testis is performed without anesthesia and should be attempted in all patients if possible [9]. As long as the pain does not increase or there is no obvious resistance, it should initially be done by turning the testicles outward as if opening a book. Success is defined as the immediate resolution of all symptoms and disappearance of abnormal findings on physical examination [10]. In case of failed attempts at detorsion, emergency surgical treatment is required. Although success rates related to manual testicular detorsion ranging between 61.5%, and 91% have been reported in the literature, residual torsion has been demonstrated in 27-32% of the patients who had undergone manual detorsion [11-13]. With this study, as a contribution to the literature, we aimed to investigate the effectiveness and success rates of manual detorsion in the light of our clinical experience.

Materials and Methods

Study Design and Ethics Approval

This study was designed as a cross-sectional retrospective study. The study protocol was reviewed and approved by the Institutional Review Board of Pamukkale University School of Medicine Ethics Committee (ethics committee approval date and number: 04.04.2023/353797).

Study Population and Data Collection

The medical files of 71 patients who were admitted to the emergency department of Pamukkale University School of Medicine with the complaint of the acute onset of scrotal pain and diagnosed with testicular torsion between the years January 2010 and January 2023 were retrospectively analyzed. Although discrepancies in postoperative outcomes of orchiectomies performed have been reported in the literature, it has been stated that the rates of testicular salvage decrease significantly if intervened 12 hours after onset of pain [13,14]. Therefore, the cases that applied within the first 12 hours after the onset of complaints were included in the study. All patients were diagnosed with testicular torsion by physical examination and CDU. Scrotal exploration was performed in all patients. Testicular fixation was performed in cases with testicular detorsion detected in scrotal exploration, while surgical detorsion and fixation were performed in cases without detorsion. These patients were noted as cases with preserved testis. Orchiectomy was performed in cases with impaired blood supply and testicular necrosis detected during scrotal exploration. Retrospectively, patients who had, and had not undergone manual detorsion in the emergency department were included in Groups 1 and 2, respectively. Successful manual detorsion was defined based on the cessation of pain and the demonstration of adequate testicular blood flow by CDU. The patients' age and laterality of torsioned testis were recorded.

Statistical Analysis

Statistical analyses were performed using the SPSS version 22 software. The fitness of variables to normal distribution was tested using the Shapiro-Wilk test. Descriptive statistics were expressed as mean and standard deviation for variables with normal distribution, median, minimum and maximum values for ordered ordinal data, and numbers and percentages for categorical variables. In the evaluation of numerical data between the groups, the parameters with normal distribution were evaluated with Student t-test, ordinal data with Mann-Whitney U test, and categorical data with chi-square test. The correlations between the orchiectomy and application of manual detorsion, age, laterality of torsioned testis were analyzed using the Spearman correlation coefficients. The model fit was analyzed using the required residual and fit statistics. The cases with a type-1 error level below 0.5% were statistically interpreted.



Figure 1. Appearance after surgical detorsion



Figure 2. Appearance before surgical detorsion



Figure 3. Necrotic testis appearance before orchiectomy

Table 1. The characteristics of the groups

		Group 1 (Manual detorsion +) n=29	Group 2 (Manual detorsion -) n=31	Р
Age (years) (mean±	SD)	22.79±5.41	24.06±8.71	0.994
Latarality	Right testis n (%)	14 (48.3)	17 (54.8)	0.611
Lateratity	Left testis n (%)	15 (51.7)	14 (45.2)	0.011
Service evolution	Testicular preservation (No testicular loss) n (%)	26 (89.7)	20 (64.5)	0.021
Scrotal exploration	Orchiectomy (There is testicular loss) n (%)	3 (10.3)	11 (35.5)	0.021

Results

Sixty patients admitted to the emergency department with the diagnosis of testicular torsion within the first 12 hours of onset of acute scrotum in the last 13 years were included in the study. The mean age of 60 patients was 23.45 ± 7.27 years. Right testicular torsion was observed in 31 (51.7%), and left testicular torsion in 29 (48.3%) patients. Orchiectomy was performed in 14 (23.3%) patients. Twenty-nine (48.3%) patients had undergone manual detorsion in the emergency department (Group 1), and scrotal exploration had been performed in 31 (51.7%) patients without manual detorsion (Group 2). Testicular fixation was performed in 19 (65.5%) of 29 patients in Group 1, whose testicular blood flow was normal during scrotal exploration (Figure 1). In 7 (24.1%) patients in Group 1, manual detorsion was not found to be sufficiently effective during exploration, and surgical detorsion together with testicular fixation was applied (Figure 2). Testicular preservation was achieved in a total of 26 (89.7%) patients. In Group 1, 3 patients (10.3%) had testicular necrosis and since testicular blood supply did not improve, orchiectomy was performed, while in Group 2, 11 (35.5%) patients underwent orchiectomy (Figure 3). The characteristics of the groups are shown in Table 1.

There was no difference between the groups in terms of age and laterality of testicular torsion (p=0.994 and p=0.611, respectively). Patients who underwent manual detorsion in the emergency department (Group 1) were less likely to undergo orchiectomy than those who did not (Group 2) (p=0.021).

In the correlation analysis between the application of orchiectomy and age at orchiectomy, laterality of testicular torsion, and manual detorsion; we observed that manual detorsion decreased the orchiectomy rates (rho-0.297, p=0.021), and the probability of undergoing orchiectomy increased with increasing age (rho 0.512, p<0.001).

Discussion

Testicular torsion is an emergency that requires urgent surgical treatment. It is the second most common cause of acute scrotum in children and adolescents [12]. The two most important determinants of early testicular salvage rate are the time elapsed between symptom onset and detorsion and the degree of torsion [15]. Apart from these, in studies conducted in Ireland and Korea, age (infancy and advanced age), lack of private insurance, place of residence far away from healthcare facilities and transfer from another hospital were associated with increased rates of orchiectomy [2,3]. In our study, a positive correlation was found between increasing age and rates of orchiectomy, although the neonatal group was not fully evaluated since it was not the group in which we intervened. Rates of testicular salvage after testicular torsion were reported as 75.22-76% in South Korea [2,16], 84% in Ireland [3], 58-68% in the USA [17-19], and 74% in Taiwan [20]. In our study, in consistent with the literature data, rates of testicular salvage were 89.7%, and 64.5% in those who had, and had not undergone manual detorsion, respectively with an overall testicular salvage rate of 76.7%. In a study the success rate of manual detorsion reported based on evaluation of scrotal color Doppler ultrasound scan results was reported as 61.5%, which was lower than our testicular salvage rates [11]. In their study, S. Vasconcelos-Castro et al. reported results similar to ours. In other words, testicular preservation was achieved in 91% of the patients who had, and in 56% of them who had not undergone manual detorsion [12].

Manual detorsion is a known noninvasive and effective maneuver since it was first described by Nash in 1893 who reported its advantage in testicular preservation [9,10,21-25]. Manual detorsion is always recommended in patients diagnosed with testicular torsion clinically and/or with CDU so as to restore testicular blood flow as soon as possible and to refrain from orchiectomy [12]. With the patient overload of the emergency system and the delay in consultation, surprisingly we observed that manual detorsion was not applied in the emergency departments. Testicular torsion should be suspected in patients presenting with an acute scrotum until proven otherwise. The potential risk of other possible causes causing testicular torsion in a patient presenting with an acute scrotum is theoretically possible but very unlikely, and has been never previously reported [26]. In addition, any attempt to rotate a testicle without testicular torsion, even if suspected, or manual detorsion in the wrong direction causes or increases pain [10,27]. It has been stated that manual detorsion to be applied in the emergency department will reduce testicular loss [9]. Manivel et al. [28] stated that it is important to teach and apply manual detorsion to general practitioners who intervene in the acute scrotum. We think that manual detorsion will be beneficial for the preservation

of testicles during the referral of patients who cannot undergo urology consultation and/or CDU in the emergency department.

This study has some limitations such as the pediatric age group was not included in the study, the patients were intervened within at most 1 hour after onset of their symptoms, and duration of testicular torsion could not be exactly determined due to the missing retrospective data. In addition, the lack of longterm follow-up results, and inability to differentiate between intravaginal / extravaginal testicular torsion can be stated as a limitation of the study.

Conclusion

Manual detorsion is a noninvasive method that can be safely applied to all patients diagnosed with testicular torsion. We think that manual detorsion will reduce the longevity of testicular ischemia and contribute to testicular salvage, both in the waiting period for consultation in the emergency department and in patients who will be referred to an advanced medical center.

Ethics Committee Approval: The study protocol was reviewed and approved by the Institutional Review Board of Pamukkale University School of Medicine Ethics Committee (ethics committee approval date and number: 04.04.2023/353797).

Informed Consent: An informed consent was obtained from all the patients.

Publication: The results of the study were not published in full or in part in form of abstracts.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – H.Y.B., K.K.; Design – H.Y.B., K.K.; Supervision – H.Y.B., K.K.; Resources – H.Y.B., K.K.; Materials – H.Y.B., K.K.; Data Collection and/or Processing – H.Y.B., K.K.; Analysis and/ or Interpretation – H.Y.B., K.K.; Literature Search – H.Y.B., K.K.; Writing Manuscript – H.Y.B., K.K.; Critical Review – H.Y.B., K.K.

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

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Absolute White Blood Cell Count and Neutrophil-Lymphocyte Ratio May Predict the Need for Double- J Stent Insertion in Ureteral Stones in Children: A Comparative Study

Çocuklarda Mutlak Beyaz Kan Hücresi Sayısı ve Nötrofil-Lenfosit Oranı, Üreter Taşlarında Double- J Kateter Yerleştirilmesi İhtiyacını Öngörebilir: Karşılaştırmalı Bir Çalışma

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Abstract

Objective: Our goal was to determine whether or not a double-J (DJ) stent insertion is required in cases of ureteral stones based on the absolute white blood cell (WBC) counts, neutrophil-lymphocyte ratio (NLR), absolute monocyte counts, and other laboratory markers.

Materials and Methods: The patients were divided into two groups as those who did (Group 1), and did not (Group 2) need DJ stent insertion. The age, symptoms, diagnosis, hemogram parameters, and treatment results of the patients were evaluated.

Results: Forty-nine percent (n=44) of the patients were female and 51% (n=46) were male. The groups did not differ in terms of age and gender (p>0.05). A higher incidence of hematuria was observed in Group 1 (p<0.05). WBC (p<0.05), NLR (p<0.05), and monocyte counts (p<0.05) were found to be higher in Group 1. In the ROC analysis; WBC and NLR were found to be two predictive markers for the need for DJ stent insertion. At a cut-off value of 12.6 x 10⁹/L, WBC had 37% sensitivity, and 81% specificity (AUC: 0.67; 95% CI: 0.54-0.80), and at a cut-off value of 3.8, NLR had 65% sensitivity, and 76% specificity (AUC: 0.70; 95% CI: 0.57-0.82) in predicting the need for a DJ stent insertion. Reoperation was not required in any case.

Conclusion: In cases of ureteral stones, the absolute WBC count and NLR may help determine the requirement (if any) for a DJ stent insertion.

Keywords: double-J catheter, neutrophil-lymphocyte ratio, ureteral stone, white blood cell count

Öz

Amaç: Amacımız, mutlak beyaz kan hücresi (WBC) sayısı, nötrofil-lenfosit oranı (NLO), mutlak monosit sayıları ve diğer laboratuvar belirteçlerine dayalı olarak üreter taşı vakalarında double-J (DJ) kateter yerleştirilmesinin gerekli olup olmadığını belirlemektir.

Gereçler ve Yöntemler: Hastalar DJ stent takılanlar (Grup 1) ve takılmayanlar (Grup 2) olarak iki gruba ayrıldı. Hastaların yaşı, semptomları, tanıları, hemogram parametreleri ve tedavi sonuçları değerlendirildi.

Bulgular: Hastaların %49'u (n=44) kadın, %51'i (n=46) erkekti. Gruplar yaş ve cinsiyet açısından farklılık göstermedi (p>0,05). Grup 1'de daha yüksek hematüri insidansı gözlendi (p<0,05). WBC (p<0,05), NLO (p<0,05) ve monosit sayısı (p<0,05) Grup 1'de yüksek bulundu. ROC analizinde; WBC ve NLO'nun DJ kateter yerleştirilmesi ihtiyacını öngören iki prediktif belirteç olduğu saptandı. DJ stent yerleştirme ihtiyacını tahmin etmede 12,6 x 10⁹/L eşik değerinde WBC %37 duyarlılığa ve %81 özgüllüğe (EAA: 0,67; %95 GA: 0,54-0,80), 3,8 eşik değerinde NLR %65 duyarlılık ve %76 özgüllük değerine (AUC: 0.70; %95CI: 0.57-0.82) sahipti. Hiçbir durumda reoperasyon gerekmedi.

Sonuç: Üreter taşı vakalarında, mutlak WBC sayısı ve NLO, double-J kateter yerleştirilmesinin gerekli olup olmadığını belirlemeye yardımcı olabilir. Anahtar kelimeler: double-J kateter, nötrofil-lenfosit oranı, üreter taşı, beyaz kan hücre sayımı

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Introduction

The incidence of urolithiasis in children has increased, ranging from 0.1 to 5% [1]. There are a variety of metabolic, environmental, and dietary variables that may lead to the formation of urinary stones in children [2,3]. While hematuria, dysuria, and discomfort are the usual symptoms of urolithiasis in older children, younger children may have nonspecific symptoms including irritability [3].

Often the best treatment alternative for urolithiasis is chosen depending on the size, location, composition of the stone and anatomy of the urinary system. Along with the advancement of endoscopic technology, the primary surgical approach for the management of urinary stones has also changed over time, moving from open surgery to less invasive techniques [4,5]. In extracorporeal shock wave lithotripsy (ESWL), external shock waves are focused directly on the stone. Both kidney and ureteral stones may be treated using this approach. On the other hand, many ureterorenoscopy-guided (URS) contact lithotripsy methods, including laser, ultrasound, and pneumatic lithotripsy may be used for this purpose. When imaging fails to facilitate the procedure or cannot be done during ESWL in children with stones larger than 4 mm, DJ stent insertion is primarily employed [6,7].

The use of DJ stents after URS therapy is still debatable. In this research, we have aimed to investigate whether the absolute WBC, neutrophil-lymphocyte ratio (NLR), absolute monocyte counts, and other laboratory markers may help determine the need for double-J stent insertion in cases of ureteral stones.

Materials and Methods

Patients and Groups

The patients who were diagnosed and treated in our clinic between January 1, 2018 and December 30, 2022 were included in the study. Patients (total n=90) who did (n =50), and did not need, (n = 40) a DJ stent insertion were included in the study. The data of the patients were retrospectively scanned. The patients were divided into two groups as those that did (Group 1) and did not (Group 2) need DJ stent insertion. The age, symptoms, diagnoses, hemogram parameters, and treatment results of the patients were evaluated. Ethical approval was obtained from the local ethics committee of Dicle University Medical Faculty (approval date and number: 28.02.2023/60).

Surgical Procedure

All patients who presented to the emergency department with flank pain underwent physical, ultrasonographic, and radiological examinations, and their CRP values and hemogram parameters were evaluated. Among them, patients with ureteral stones were hospitalized. After adequate hydration, patients with persistent stones detected in the control ultrasonography underwent URS. After URS, DJ stent was inserted in patients with proper indications (patients who developed edema or excessive edema due to large stones). No additional procedure was applied to the patients who did not need DJ stent insertion.

Inclusion Criteria

Among patients aged 0-18 years with complete retrospective medical data and diagnosed, and treated in our clinic, those who had undergone surgery for ureteral stones were included in the study.

Exclusion Criteria

Patients aged >18 years with comorbidity and/or urinary extravasation and inconsistent retrospective data were excluded from the study.

Statistical Analysis

Statistical analyzes including descriptive statistics. frequencies, and other statistical methods were performed for all patient data. Continuous data were expressed as mean \pm standard deviation. Continuous variables were analyzed with the Shapiro-Wilk and Kolmogorov-Smirnov tests to determine whether the data had a normal distribution. Continuous and normally distributed variables were compared using Student's T-test. Nonparametric tests were used for the data that did not fit the normal distribution. In case of need, categorical variables were evaluated with a chi-square test and some other data with Fisher's exact test. Correlation between data was checked with Pearson and Spearman correlation tests. Binary logistic regression tests were used for the analysis of risk factors and indications for DJ-stent insertion. Analyzes were performed using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Forty-nine percent (n=44) of the patients were female and 51% (n=46) were male. The mean ages of the patients were 5.8±3.4 years in Group 1 and 5.5±4.7 years in Group 2. Age and gender of the patients did not differ significantly between both groups (p>0.05). Twenty-seven percent (n=27) of the patients had hematuria at presentation. The average duration of symptoms was approximately 36±12.7 hrs in Group 1, and 39±11.3 hrs in Group 2 (p>0.05). In addition to symptom duration, we also examined the presence of comorbidities in both groups. Remarkably, the average comorbidity score was found to be 1 for both groups. Again, the computed p-value exceeded 0.05, signifying that the difference in comorbidity scores between the two groups lacks statistical significance. A higher incidence of hematuria was observed in Group 1 (p<0.05). Two patients had an acute renal failure at admission (p>0.05). While there was no difference between the groups in terms of laterality of the stone (p>0.05), the mean stone size, WBC, NLR, and monocyte counts were significantly higher in Group 1 (for all p<0.05) (Table 1).

In the ROC analysis; WBC and NLR were found to be the predictive markers for the need for DJ stent insertion (Figure 1). At a cut-off value of 12.6×10^{9} /L WBC had 37% sensitivity, and 81% specificity (AUC: 0.67; 95% CI: 0.54-0.80), and a cut-off value of 3.8, NLR had 65% sensitivity, and 76% specificity (AUC: 0.70; 95%CI: 0.57-0.82) in foreseeing the need for DJ stent insertion (Table 2).

Any correlation could not be found between stone size and NLR or WBC (p>0.05). Reoperation was not required in any case.

Table 1. Analysis of the pa	atients and	characteristics
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	Group 1 (n=50)	Group 2 (n=40)	P value
Age (Mean±SD, year)	5.8±3.4	5.5±4.7	>0.05
Gender Male	33	13	>0.05
Female	27	17	
Hematuria	20	4	<0.05
Symptom duration (hour)	36±12.7	39±11.3	>0.05
Comorbidity	1	1	>0.05
Acute renal failure	1	1	>0.05
Stone size (Mean±SD, mm)	11.83±5.07	9.42±3.01	<0.05
Stone side Right	33	14	>0.05
Left	27	16	
Reoperation	0	0	>0.05
WBC	14.67±2.87	11.22±2.91	<0.05
NEU	8.48±2.18	7.35±2.96	>0.05
LYM	2.63±1.37	2.51±1.49	>0.05
MONO	1.01±1.31	0.61±0.28	<0.05
PLT	382.6±122.1	351.8±88.6	>0.05
CRP	1.31±2.05	1.27±3.9	>0.05
UREA	27.11±8.57	29.53±11.13	>0.05
CRE	0.78±0.37	0.73±0.51	>0.05
NLR	4.34±0.87	3.2±1.42	<0.05



Figure 1. ROC analysis

Discussion

Hematological parameters including NLR, plateletlymphocyte ratio (PLR), and absolute monocyte counts (AMCs) have gained prominence in recent years because of their strong diagnostic predictive values, particularly in inflammatory conditions like acute appendicitis [8]. Similar studies have been conducted on NLR, monocyte-lymphocyte ratio (MLR), PLR, red blood cell distribution width (RDW), monocyte counts, and pentraxin-3 as predictors of survival in various cancers [9-12]. The use and usefulness of monocytes and WBC in youngsters have been restricted despite all investigations favoring their predictive values.

Inflammatory responses have been recently linked to kidney and ureter stones. Biomarkers for inflammatory diseases include C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR). Immune cells play an important role in the inflammatory process throughout the human body. Multiple studies have pointed to the NLR as a significant indicator of kidney stone formation. The spontaneous passage of a ureteral stone was correlated negatively with both NLR and PLR. However a recent research disproved the hypothesis suggesting that inflammatory biomarkers like NLR and PLR are linked to the spontaneous passage of ureteral stones [13].

As is shown in various research studies, diseases progressing with inflammation had higher total WBC, NEU, and monocyte

Table 2. Suggested cut-off values and diagnostic value

Variable	Suggested cut-off value	AUC	P value	95% CI Lower bound	95% CI Upper bound	Sensitivity	Specificity
WBC	12.6	0.67	0.009	0.54	0.80	37%	81%
Monocyte	3.8	0.70	0.003	0.57	0.82	65%	76%

counts [14]. According to Halaseh et al., NLR, LMR, and monocyte counts should be taken into consideration as diagnostic parameters in patients with suspected complex appendicitis [15]. According to Kriplani et al., NLR, PLR, and LMR may be independent, accessible, and cheap predictors for early detection of SIRS/sepsis following percutaneous nephrolithotomy (PNL) [16].

Considering the literature data cited so far, predictive value of the NLR and the absolute WBC count for the need for DJ stent insertion in pediatric patients with urolithiasis has been investigated for the first time in our study.

In the present study, we have found higher WBC (p<0.05) and monocyte counts (p<0.05) in Group 1. However, any correlation could not be found between stone size and NLR or WBC (p>0.05). As a result; in the ROC analysis; WBC and NLR were found to be two predictive markers for the need for a DJ stent insertion after URS in pediatric patients. For WBC, a cut-off value of 12.6 x 10⁹/L had 37% sensitivity, and 81% specificity (AUC: 0.67; 95% CI: 0.54-0.80), and for NLR, a cut-off value of 3.8 had 65% sensitivity, and 76% specificity, (AUC: 0.70; 95% CI: 0.57-0.82) as predictive markers for the need for a DJ stent insertion after ureterolithotomy in pediatric patients.

Limited number of patients included in our study, and retrospective analysis of only the data of the patients who applied to the pediatric surgery service of Dicle University Medical Faculty Hospital were the most important limitations of our study.

Conclusion

In cases of ureteral stones, the absolute WBC count and NLR may help determine whether or not a DJ stent should be inserted.

Ethics Committee Approval: The study protocol was reviewed and approved by the Institutional Review Board of Dicle University Medical Faculty (approval date and number: 28.02.2023/60).

Informed Consent: An informed consent was obtained from all the patients.

Publication: The results of the study were not published in full or in part in form of abstracts.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – S.A., M.A., T.O.K.; Design – S.A., M.A., T.O.K.; Supervision – S.A., M.A., T.O.K.; Resources – E.B., B.A., M.H.O., M.K.; Materials – E.B., B.A., M.H.O., M.K.; Data Collection and/or Processing – E.B., B.A., M.H.O., M.K.; Analysis and/or Interpretation – S.A., M.A., T.O.K.; Literature Search – E.B., B.A., M.H.O., M.K.; Writing Manuscript – S.A., M.A., T.O.K.; Critical Review – S.A., M.A., A.Ö.

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Management of Non-Deflating Foley Catheter Balloons in Emergency and Urology Clinics: A 5-Year Retrospective Study

Acil Servis ve Üroloji Kliniklerinde Sönmeyen Foley Kateter Balonlarının Yönetimi: 5 Yıllık Retrospektif Bir Çalışma

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Abstract

Objective: This study aims to discuss the techniques for safely, quickly, and successfully removing transurethral (TU) foley catheter balloons in patients who present to the emergency and urology clinics due to the inability to remove the catheter through normal means, and to contribute options and insights to the literature. **Materials and Methods:** This retrospective study included patients who presented to the emergency department for the inability to remove the TU foley catheter, patients referred to the urology clinic, or patients consulted from other clinics, between January 2017 and September 2022. The treatment methods applied by the urologist in this patient group, hospitalization durations, voiding status, and any developed complications were recorded based on patient files.

Results: A total of 22 patients who had a transurethral (TU) catheter inserted for various reasons and were unable to remove it were included in our study. It was found that 7 of the patients had permanent TU catheters due to comorbidities, while the remaining 15 had TU catheters inserted after acute urinary retention. Among them, 2 cases had the catheter removed by cutting the inflation channel, 1 case with the assistance of a guidewire, 2 cases by puncturing the balloon with a needle under transrectal ultrasound guidance, 10 cases by puncturing the catheter balloon with a needle under suprapubic ultrasound guidance, and 7 cases had their catheters removed by laser under anesthesia. Only 1 patient who had the balloon punctured by a needle under transrectal ultrasound guidance developed fever after the procedure and had a total of 5 days of hospitalization, while the others were discharged either immediately after the procedure or 1 day later.

Conclusion: Patients with indwelling foley catheters that cannot be removed rarely present to us; however, these patients often come to us in an agitated state after multiple unsuccessful attempts to remove the catheter. Therefore, it is important to know which technique should be applied to this patient group in a faster, appropriate, and reliable manner as soon as possible.

Keywords: balloon, catheter, foley, transurethal

Öz

Amaç: Çeşitli nedenlerle, hastalara takılan transüretral (TU) sondaların normal yolla çıkmaması sonucu acil servise ve üroloji polikliniğine başvuran ve yönlendirilen hastaların kataterini güvenli, hızlı ve başarılı bir şekilde çıkartan teknikleri tartışarak literatüre seçenek ve katkı sunmak.

Gereçler ve Yöntemler: Retrospektif olarak dizayn edilen bu çalışma; Ocak 2017- Eylül 2022 tarihleri arasında acil servise sonda çıkmaması üzerine başvuru yapılan, üroloji kliniğine başvuran veya diğer kliniklerden konsülte edilen hastaları içermektedir. Bu hasta grubunda üroloji hekimi tarafından uygulanan tedavi yöntemleri sonrasında hastane yatış süreleri, idrar yapıp-yapmama durumları, eğer gelişmişse gelişen komplikasyonlar hasta dosyalarından alınarak kaydedildi.

Bulgular: Çeşitli nedenlerle TU kateter takılan ve çıkarılamayan toplam 22 hasta çalışmamıza dahil edildi. 22 hastanın 7'sinin komorbiditeler nedeniyle TU kateterlerin kalıcı olduğu, geri kalan 15'inin ise akut üriner retansiyon sonrası TU kateter takıldığı öğrenildi. Bunların 2'si sadece şişirme kanalı kesilerek, 1'i kılavuz tel yardımı ile, 2'si transrektal usg eşliğinde iğne ile balonu patlatılarak, 10'u suprapubik usg eşliğinde iğne ile sonda balonunun patlatılarak, 7 hastanın ise anestezi altında laser ile sondasının patlatılarak sondasının çıkarıldığı kaydedildi. Sadece transrektal usg eşliğinde iğne ile balonu patlatılara işlem sonrası ateş olduğu ve toplam 5 gün yatış olduğu diğerlerinin ise işlem sonrası veya 1 gün sonra externe edildiği görüldü.

Sonuç: TU sondası çıkmayan hastalar nadir olarak karşımıza çıkmakla beraber bu hastalar bize ulaşana kadar birçok sonda çıkarma denemesinden geçtikleri için ajitasyon ile karşımıza çıkmaktadırlar. Bu bakımdan bu hasta grubuna hangi tekniğin daha hızlı, uygun ve güvenilir bir biçimde bir an önce uygulanması gerektiğinin bilinmesi kanaatindeyiz.

Anahtar kelimeler: balon, katater, foley, transüretral

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Introduction

Indwelling Foley catheters, filled with approximately 10 cc of isotonic saline solution, are commonly used in patients for various reasons. To remove these catheters, the saline solution in the balloon needs to be drained. However, in rare cases, it may not be possible to deflate the balloon, which is a known complication of Foley catheterization.

It is estimated that 15% to 20% of patients in the hospital have a TU catheter [1]. The failure of a Foley catheter balloon to deflate can be caused by a faulty valve mechanism, blockage of the inflation channel, or crystallization of the fluid inside the balloon [2]. After multiple unsuccessful attempts, patients usually seek assistance from urologists in an agitated state. Over the years, various techniques and methods have been reported to address this issue, including over-inflation of the balloon, injection of ether or chloroform into the inflation channel, and insertion of a guidewire into the inflation channel [3-5]. Additionally, there are techniques such as needle puncture of the balloon under ultrasound guidance [4,6-8].

When the balloon does not deflate, the initial approach often involves over-inflating the balloon until it bursts. However, a study has shown that in 83% of cases where the balloon burst, significant fragments were left behind [9]. Chemical agents like ether and chloroform are no longer used to deflate the balloon as they can cause damage to the bladder mucosa.

Another method that can be used in a patient with an indwelling catheter that cannot be removed, is to cut off the path to the balloon. In these cases, the deflation of the balloon is expected through the backflow of the saline. If this method is not successful, that means a problem in the valve part of the balloon, it is necessary to consider invasive procedures, such as needle puncture of the balloon under suprapubic/transrectal ultrasound guidance or laser puncture of the balloon under cystoscopy.

The goal of successful management is to remove the catheter in a safe manner as soon as possible, alleviate patient agitation, and minimize complications. The aim of our study is

to contribute to the literature by identifying the most reliable and least complication-prone techniques for managing patients who have indwelling catheters that cannot be removed, and have undergone various attempted methods.

Materials and Methods

This study is a retrospective study conducted between January 2017 and September 2022 at the Erzurum Regional Training and Research Hospital, involving patients who presented to the Emergency Department and Urology Clinic with non-deflating TU foley catheters. The study was approved by the Local Ethics Committee of Health Sciences University Erzurum City Hospital (Approval date and number: 2022/17-168). All procedures performed in this study involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. An informed consent was obtained from all the patients.

The medical records of the patients were obtained from the hospital archives, and it was found that 16(73%) patients were referred to the Urology Clinic through the Emergency Department or other clinics, while 6 (27%) patients directly sought the Urology Clinic for catheter removal or replacement. All patients were male. The age range of this patient group varied between 55 and 89 years, and the length of hospital stay ranged from 0 to 5 days. Upon reviewing the treatment methods applied to these patients, it was observed that non-invasive techniques such as over-inflation and bursting of the catheter balloon, cutting the inflation channel, and sending a guide wire through the inflation channel were used. In addition, invasive procedures such as needle puncture of the catheter balloon with the assistance of suprapubic ultrasonography (USG), needle puncture with the assistance of transrectal ultrasonography (TRUS), and endoscopic laser balloon puncture under anesthesia were performed.

Method	Number of patients applied (n)	Number of success removal (n)
Cutting inflation channel	22 (100%)	2 (9%)
Bursting with a guidewire applied through inflation channel	20 (90%)	1 (4%)
Using a needle under the guidance of suprapubic USG	11 (50%)	10 (46%)
Using a needle under the guidance of TRUS	3 (13%)	2 (9%)
Endoscopic laser intervention	7 (32%)	7 (32%)

Table 1. Removal methods for non-deflating TU foley catheter ballons

TRUS: transrectal ultrasound; USG: ultrasonography

Results

The medical records obtained from the hospital archives were reviewed, and it was observed that all of these patients were male. The age range of the patients was between 55 and 89, with an average age of 72 ± 5 years. Among the 22 patients, 7 (31%) were under permanent catheterization, while 15 (69%) had temporary catheterization due to acute urinary retention. The average age of patients under permanent catheterization was found to be 75±3 years, while it was 64±6 years for patients with temporary catheterization. It was determined that all patients under permanent catheterization had at least one neurological, cardiac, or endocrinological condition, while the group of patients with catheterization due to acute urinary retention did not have any additional diseases recorded. All of these patients were initially subjected to the method of cutting the inflation channel of the Foley catheter and waiting for a certain period. It was found that only 2 (9%) patients had the Foley catheter come out without any additional procedures after the deflation of the balloon. Subsequently, for the remaining patients, a guide wire was passed through the cut inflation channel. It was recorded that in only 1 (4%) patient, the Foley catheter came out by bursting the balloon with the help of the guide wire.

Among the patients who failed the previous procedures, it was observed that 11 (50%) of them did not undergo general anesthesia and opted for local anesthesia. For these patients, the primary plan was to perform a minimally invasive procedure using a needle under the guidance of suprapubic ultrasonography (USG) (46%) to burst the balloon of the Foley catheter. It was recorded that all except 1 patient had the Foley catheter come out after this procedure. In the case where this procedure failed, TRUS was used, and a prostate biopsy needle was inserted to burst the balloon of the catheter. 2 patients had wounds and infections in the suprapubic region, and an attempt was made to burst the balloon using a TRUS-guided needle (9%). It was successful in one patient but unsuccessful in another due to patient non-compliance. Both this patient and the remaining 6 patients underwent endoscopic laser intervention (32%) under general anesthesia to burst the balloon of the catheter. The applied methods and results are summarized in Table 1.

For the 7 patients who were followed with a permanent Foley catheter, the catheter was reinserted and externalized. For all patients who underwent non-invasive procedures, the catheter was externalized after the procedure. For patients who underwent invasive procedures, they were followed for one day and then the catheter was externalized. It was found that only one patient who had their catheter removed using a transrectal USG-guided needle developed fever after the procedure and was externalized on the 5th day after antibiotic therapy.

Discussion

Indeed, it is known that transurethral (TU) catheters are not only used for urological patients but also for various other patients, particularly during hospital stays in intensive care units and clinics for monitoring purposes. Although the insertion and removal of TU catheters are minimally invasive procedures, sometimes the removal of the catheter is not straightforward due to crystallization of the fluid in the catheter balloon or a malfunctioning valve channel. In such cases, patients undergo multiple maneuvers and methods in other clinics in an attempt to remove the catheter, but when these attempts fail, they become agitated and seek consultation with a urologist. It is necessary to resolve their problem promptly and effectively in a rational, practical, and efficient manner in order to alleviate their agitation.

Various techniques have been applied to patients with a retained catheter from the past to the present. One of the primary techniques involves overinflating and bursting the catheter balloon, where the bladder is first filled with 200 cc of isotonic solution to minimize bladder injury [10]. However, the main complication of this technique is the risk of catheter balloon fragments remaining inside and the potential for bladder rupture, which has led to the abandonment of this method [1,11]. Similarly, the injection of chemical substances (such as ether, toluene, benzene, chloroform, etc.) into the balloon has also been abandoned due to the risk of bladder cystitis. Some authors suggest that performing bladder lavage after balloon dissolution can minimize the risk of developing cystitis [12]. These methods are not widely preferred in today's practice. It is possible to cut the inflation channel of TU foley catheter and wait for the balloon to deflate spontaneously after a certain period. However, this method is not highly favored by both patients and doctors due to the need for patients to wait for a certain period, the continuation of their agitation and low success rates as shown in our study. If the balloon still does not deflate after these methods, another approach is to insert a guidewire through the catheter inflation channel valve and attempt to burst the balloon. In a study, the use of a hydrophilic guidewire with a rigid tip was employed to deflate the catheter balloon, and it was observed that the balloon deflated immediately or within a few minutes after the removal of the guidewire [9,13]. However, complications and failure of this procedure may arise due to the risk of crystallization of the water inside the catheter balloon and potential injury to the bladder and urethra caused by the rigid tip of the guidewire. All of these procedures, although considered non-invasive for patients, are generally evaluated to have a low success rate.

If the catheter still hasn't been removed using the previous methods, it is necessary to consider more minimally invasive procedures. To alleviate the patient's agitation and increasing anxiety as quickly as possible, the least invasive and fastest method should be chosen. The first option is to use a needle to deflate the catheter balloon under the guidance of suprapubic ultrasound, with the application of local anesthesia [8,14] (Figure 1). In this technique, after visualizing the catheter balloon under USG guidance, the plan is to enter the suprapubic area with a needle to deflate the balloon. It is important to note that the mobility of the catheter balloon within the bladder can be a disadvantage during the procedure. To prevent this, the catheter can be gently pulled back from the urethral meatus to ensure that the balloon remains fixed at the bladder neck. In rare cases, it is also possible to deflate the catheter balloon using a needle through a TRUS probe (Figure 2). With the guidance of TRUS, an 18 G Tru-cut needle is directed towards the catheter balloon through the prostate in an attempt to deflate the balloon [15]. In this technique, despite the potential disadvantages of the catheter balloon being mobile and a higher risk of intestinal and bladder injury compared to other procedures, as well as the possibility of infection and the risk of bleeding in patients with coagulation disorders, the success



Figure 1. Imaging of the catheter balloon with suprupubic USG



Figure 2. Imaging of the catheter balloon with transrectal USG

rate of these methods is high. The disadvantages of this technique include patient non-compliance, lack of equipment (TRUS), the minimal invasiveness of the procedure, and the subsequent risk of developing an infection requiring antibiotic therapy. Despite all these methods, if there is patient non-compliance or if the patient requests the procedure under general anesthesia, a final approach can be performed using cystoscopy. Through the side of the indwelling catheter, instruments such as a thin rigid URS or flexible cystoscope can be used to enter and deflate the catheter balloon using a laser [16]. However, it should be noted that for this technique, the conditions of an operating room and the risks and complications of general anesthesia must be taken into consideration.

Conclusion

Patients presenting with an indwelling catheter that cannot be removed have typically undergone various manipulations in primary care or emergency departments, leading to agitation and anxiety. However, we can solve this problem quickly, efficiently, and without complications by applying the above-mentioned techniques.

Ethics Committee Approval: The study protocol was approved by the Local Ethics Committee of Health Sciences University Erzurum City Hospital (Approval date and number: 2022/17-168). **Informed Consent:** An informed consent was obtained from all the patients.

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Comparison of Intrarenal Retrograde Surgery Results Between Different Age Groups Farklı Yaş Gruplarında İntrarenal Retrograde Cerrahi Sonuçlarının Karşılaştırılması

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Abstract

Objective: In this study, we aimed to investigate whether there is a difference in the reliability and efficacy of the method according to age in patients divided into 3 different age groups who underwent retrograde intra renal surgery (RIRS) due to kidney stones.

Materials and Methods: Patients who underwent RIRS for kidney or ureteral stone disease at the Urology Clinic of Health Sciences University Umraniye Health Application and Research Hospital between May 2017 and January 2021 were retrospectively screened, and those aged 20-80 years were included in the study. The demographic and clinical data of the patients and stone-related data were recorded. Patients aged 20-40 years were classified as Group 1, those aged 41-60 years as Group 2, and those aged 61-80 years as Group 3.

Results: After the inclusion and exclusion criteria were applied, the sample consisted of a total of 320 patients, of whom 121 (37.8%) were in Group 1, 133 (41.5%) were in Group 2, and 66 (20.6%) were in Group 3. The mean operative times and stone-free rates were similar between the groups. However, the mean hospital stay was significantly longer in Groups 3 compared to Groups 1 and 2. The minor complication rates were 2.4% in Group 1, 3% in Group 2, and 13.6% in Group 3, indicating a significantly higher value in Group 3 compared to the remaining two groups (p=0.03). The major complication rates of Groups 1, 2, and 3 were 0.8%, 0.7%, and 7.5%, respectively. Accordingly, Group 3 had a significantly higher rate than Groups 1 and 2 (p=0.04). **Conclusion:** RIRS can be performed on the elderly with success rates comparable to other age groups. However, the elderly, who represent a higher-risk patient population with more comorbidities, have increased rates of minor and major complications both in the perioperative and postoperative periods. **Keywords:** retrograde intra-renal surgery, age, geriatric, complications

Öz

Amaç: Bu çalışmada böbrek taşı nedeniyle retrograde intrarenal cerrahi (RIRS) uygulanan 3 farklı yaş grubuna ayrılmış hastalarda yöntemin güvenilirliği ve etkinliğinde yaşa göre farklılık olup olmadığını araştırmayı amaçladık.

Gereçler ve Yöntemler: Mayıs 2017-Ocak 2021 yılları arasında Sağlık Bilimleri Üniversitesi Ümraniye Sağlık Uygulama ve Araştırma Hastanesi Üroloji Kliniği'nde böbrek ya da üreteral taş hastalığı sebebiyle RIRS uygulanan hastalar geriye dönük olarak tarandı. Çalışmaya 20-80 yaş aralığında hastalar dahil edildi. Hastalara ait demografik, klinik verilerin yanı sıra taşa ait veriler kaydedildi. 20-40 yaş aralığındaki hastalar Grup 1, 41-60 yaş aralığındaki hastalar Grup 2, 61-80 yaş aralığındaki hastalar Grup 3 olarak sınıflandırıldı.

Bulgular: Dahil edilme ve hariç tutulma kriterleri uygulandıktan sonra Grup 1'de 121 (%37.8), Grup 2'de 133 (%41.5) ve Grup 3'te 66 (%20.6) olmak üzere toplam 320 hasta çalışmaya dahil edildi. Ortalama ameliyat süreleri ve taşsızlık oranları gruplar arasında benzerdi. Ancak ortalama hastanede kalış süresi Grup 3'te Grup 1 ve Grup 2'ye göre anlamlı olarak daha uzundu. Minör komplikasyon oranları Grup 1'de %2.4, Grup 2'de %3 ve Grup 3'te %13.6 oranında tespit edildi ve Grup 3'te Grup 1 ve 2'ye oranla anlamlı olarak yüksek saptandı (p=0.03). Major komplikasyon oranları Grup 1'de %0.8, Grup 2'de %0.7 ve Grup 3'te %7.5 oranında saptandı. Buna göre Grup 3, Grup 1 ve 2'de anlamlı olarak daha yüksek bir orana sahipti (p=0,04).

Sonuç: İleri yaş grubunda RIRS diğer yaş gruplarındaki hastalarla benzer başarı oranları ile uygulanabilmektedir. Bununla birlikte, daha fazla komorbiditesi olan daha yüksek riskli bir hasta popülasyonunu temsil eden yaşlılar hem perioperatif hem de postoperatif dönemlerde artmış minör ve majör komplikasyon oranlarına sahiptir.

Anahtar kelimeler: retrograde intrarenal cerrahi, yaş, cerrahi, komplikasyon

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Introduction

The world population is aging, and it is estimated that the number of people over 60 years will exceed 2 billion in the next 30 years [1]. Age-related cardiovascular, respiratory, and nervous system changes, coupled with comorbidities, can lead to an increased incidence of surgical complications and medical problems [2,3]. This complicates the treatment of urinary system stone disease in the elderly patient population. Considering that the lifetime risk of urinary system stone disease is 10%, it seems that safe and effective methods with low complication rates will increasingly gain popularity in the geriatric population with the increasing human lifespan [4].

Retrograde intrarenal surgery (RIRS), an alternative method to shock wave lithotripsy (SWL) and percutaneous nephrolithotomy (PNL) in the treatment of stones located in the renal pelvis and kidney, offers better lithotripsy efficacy and shorter operation times with the advances in technology. Because of its advantages, RIRS is considered an effective and safe method for the elderly patient population [5]. This method results in a lower pain score and shorter recovery time without the need for an incision; therefore, it seems to be a suitable option for elderly and risky patient populations.

In this study, we divided patients with kidney stones who underwent RIRS into three different age categories to investigate whether there was a difference in the safety and efficacy of this method according to age.

Materials and Methods

Following the approval of the local ethics committee (approval date and no: 22.12.2022/416), patients who underwent RIRS for the treatment of kidney or ureteral stone disease at the Urology Clinic of Health Sciences University Umraniye Health Application and Research Hospital between May 2017 and January 2021 were retrospectively screened, and those aged 20-80 years were included in the study. Patients with solitary kidneys or chronic renal failure, cases in which fragmentation with semi-rigid ureteroscopy was performed or the treatment could not be completed with RIRS, patients with ureteral or renal abnormalities, and those with calvceal diverticula were not included in the study. Pregnant women and patients with bleeding diathesis, neurogenic lower urinary tract dysfunction, or a history of immunosuppressive disease were also excluded. Patients with a positive urine culture test in the preoperative period were treated with appropriate antibiotic therapy for at least seven days according to susceptibility tests. The treatment of these patients was continued until a sterile urine culture was obtained. Further excluded from the sample were patients who had a history of nephrostomy/double-J catheterization due to acute pyelonephritis in the preoperative period, those who underwent surgery under anti-biotherapy due to the inability to sterilize urine cultures, and those with incomplete data.

The patient's demographic and clinical data [age, gender, and body mass index (BMI), American Society of Anesthesiologists (ASA) score, stone side, the presence of shock wave lithotripsy (SWL) history and the number of SWL sessions applied, and preoperative stent requirement], and stone characteristics, such as localization, number, and density, were recorded. Contrastenhanced computed tomography (CT) was performed on all patients preoperatively.

All operations were performed by endourologists who had completed the RIRS learning curve. As the surgical technique, the patient was placed in the lithotomy position under general anesthesia. At the beginning of the operation, a single dose of intravenous prophylactic antibiotic therapy (cefazolin 1 g, intravenous) was administered to all patients. A 0.038-inch hydrophilic guide wire was inserted into the renal pelvis under rigid ureterorenoscopy (standard 8.0/9.8F Karl Storz). A ureteral access sheath (UAS) (Cook Medical Inc., USA) was inserted over the guide wire, and a flexible ureterorenoscopy (Storz Flex-X2, Tuttlingen, Germany) was placed over the UAS. Lithotripsy was undertaken using a 200-mm Holmium: YAG laser (Coherent Power Suite, 60 watts, Lumenis, Israel) with an energy level of 0.6-1 J and a frequency range of 5-10 Hz. Ureteral double-J (DJ) catheters were routinely placed postoperatively.

Direct urinary system radiography was performed on the first postoperative day to evaluate the presence of residual stones or the placement of the double-J catheter. Stone-free status, defined as the absence of any calculus or the absence of calculus over 2 mm, was assessed using non-contrast CT performed during the first month postoperatively. In patients with stone-free status, the ureteral catheters were withdrawn at one month postoperatively.

The complications were evaluated according to the Clavien-Dindo classification. Patients aged 20-40 were classified as Group 1, those aged 41-60 years as Group 2, and those aged 61-80 years as Group 3.

Statistical Analysis

The three age groups were compared in terms of demographic data, stone characteristics, and operative and postoperative data. Normally distributed numerical data were presented as mean and standard deviation. Categorical variables were expressed as frequency (percentage). Normally distributed numerical data were compared using the one-way analysis of variance test. The Bonferroni correction was used for post-hoc analyses. The chi-square test was conducted to compare categorical variables. A p-value of <0.05 was considered statistically significant.

Results

After the inclusion and exclusion criteria were applied, the sample consisted of a total of 320 patients, of whom 121 (37.8%) were in Group 1, 133 (41.5%) were in Group 2, and 66 (20.6%) were in Group 3. There was no significant difference between the three groups in terms of gender distribution or body mass index (BMI). However, significant differences were observed between the mean ASA scores and comorbidities of the three groups (p=0.01) (**Table 1**).

The presence of SWL history and stone characteristics (size, side, localization, and density) did not significantly differ between the three groups. The mean operation times and stone-free rates were also similar. However, the mean hospital stay was found to be significantly longer in Group 3 compared to Group 1 and Group 2 (**Table 2**).

Complications were observed in a total of 23 (7.1%) patients. The rates of minor complication were 2.4% in Group 1, 3% in Group

2, and 13.6% in Group 3, and the major complication rates were determined to be 0.8%, 0.7%, and 7.5%, respectively. Accordingly, Group 3 had significantly higher rates of both minor (p=0.03) and major (p=0.04) complications compared to Groups 1 and 2.

Patients who developed hematuria, mucosal injury, and perirenal hematoma were followed up conservatively, those who developed a fever in the postoperative period were treated with appropriate antibiotic therapy, and those with hematuria and decreased hemoglobin due to perirenal hematoma were treated with erythrocyte replacement therapy. Patients presenting with ureteral stenosis during the long-term follow-up underwent double-J catheterization, followed by ureteroureterostomy in the case of failure. Patients who developed urosepsis, acute coronary syndrome, or pulmonary embolism were managed according to the results of consultation with appropriate branches. Mortality was observed at a rate of 1.5% in Group 3 (**Table 3**).

Parameters	Group 1 (n=121)	Group 2 (n=133)	Group 3 (n=66)	р
Age (year)	29.1 ± 5.5	47.2 ± 4.4	67.3 ± 7	-
Gender Male Female	70 (57.8) 51 (42.1)	73 (54.8) 60 (45.1)	35 (53) 31 (46.9)	0.533
BMI (kg/m ²)	28.1 ± 3.9	29.1 ± 4.3	28.9 ± 5.5	0.232
ASA	1.6 ± 0.4	2.1 ± 0.3	2.6 ± 0.2	0.01 1 vs 2 vs 3
Comorbidities				p<0.001
DM	8 (6.1)	15 (11.2)	30 (45.4)	1 vs 2 vs 3
HT	12 (9.9)	22 (16.5)	38 (57.5)	1 vs 2 vs 3
IHD	2 (1.6)	6 (4.5)	8 (12.1)	1-2 vs 3
COPD	0 (0)	1 (0.7)	3 (4.5)	similar
Antiaggregant use	1 (0.8)	3 (2.2)	21 (31.8)	1-2 vs 3

BMI: body mass index; ASA: American Society of Anaesthesiologists; DM: diabetes mellitus; HT: hypertension; IHD: ischemic heart disease; COPD: chronic obstructive pulmonary disease

Table 2. Stone characteristics and intraoperative and postoperative datas

Parameters	Group 1 (n=121)	Group 2 (n=133)	Group 3 (n=66)	р
Previous SWL (n; %)	64 (52.8)	71 (53.3)	30 (45.4)	0.121
Stone size (mm)	17.1 ± 3.2	18.2 ± 4.5	18 ± 3.8	0.339
Stone Side Right Left	65 (53.1) 56 (46.2)	70 (52.6) 63 (47.3)	30 (45.4) 36 (54.5)	0.07
Stone location Pelvis Lower pole Middle pole Multicaliceal	74 (61.1) 22 (18.1) 15 (12.3) 10 (8.2)	70 (51.6) 30 (22.5) 21 (15.7) 12 (9)	41 (62.1) 13 (19.6) 7 (10.6) 5 (7.5)	0.103
Stone density (HU)	1071 ± 87.1	1129 ± 100.2	1055.2 ± 96	0.132
Operation time	80.1 ± 10.2	83.2 ± 13.2	79.8 ± 9.8	0.497
Stone free rate	103 (85.1)	111 (83.4)	54 (81.1)	0.232
Length of stay (hour)	21.4 ± 2.5	23.9 ± 5.4	36.2 ± 7.2	0.04 1-2 vs 3

SWL: shock wave lithotripsy; HU: Hounsfield unite

Table 3. Complications chart

Complications	Group 1 (n=121)	Group 2 (n=133)	Group 3 (n=66)	р
Minor	3 (2.4%)	4 (3%)	9 (13.6%)	0.03
Grade 1				1/2 vs 3
Hematuria	0 (0)	1 (1%)	2 (3%)	
Mucosal injury	1 (0.8%)	1 (1%)	2 (3%)	
Perirenal hematoma	0 (0)	1 (1%)	1 (1.5%)	
Grade 2			, í	
Fever	2 (1.6%)	1 (1%)	3 (4.5%)	
ERT	0 (0)	0(0)	1 (1.5%)	
Major	1 (0.8%)	1 (0.7%)	5 (7.5%)	0.04
Grade 3	, , ,	× ,	l í í í	1/2 vs 3
Stricture	0 (0)	1 (0.7%)	1 (1.5%)	
Grade 4		× ,	l í í í	
Urosepsis	1 (0.8%)	0 (0)	1 (1.5%)	
ACS	0 (0)	0 (0)	1 (1.5%)	
Pulmonary emboli	0 (0)	0 (0)	1 (1.5%)	
Grade 5				
Death	0 (0)	0 (0)	1 (1.5%)	

ERT: erytrocyte replacement therapy; ACS: acute coronary syndrome

Discussion

In the literature, there are ongoing discussions concerning urinary system stone disease in the advanced age group. In the geriatric population, age-related changes in kidney functions, cardiopulmonary system capacity, and the effects of medications used due to comorbidities can predispose these patients to surgical complications and result in changes in their medical conditions [2,6]. Since comorbidities such as diabetes mellitus, coronary artery disease, and hypertension are more common in this patient group compared to the younger patient population, the treatment modality to be applied must be more minimally invasive and effective [5].

The current treatment options that are accepted as minimally invasive in the treatment of large kidney stones include SWL, PNL, and RIRS [7]. Although PNL is accepted as safe and effective, it can result in serious complications, such as blood loss and organ injuries [2,6,8]. In a study evaluating over 1,000 patients, Unsal et al., reported that the mean complication rate was 29.3%, and the success rate was 83.7%. It has been determined that postoperative complications are associated with older age and the presence of comorbidities [8]. In another study, Resorlu et al., reported the surgical complication rate to be 25% and the medical complication rate to be 13% after PNL in the geriatric patient group [2]. The authors of both studies concluded that elderly high-risk patients should be informed about RIRS and follow-up options due to their relatively high surgical and medical complication rates. In another study conducted by Gulpinar et al., the surgical complication rate was determined to be 6.4% and the medical complication rate to be 1% among the RIRS operations performed in the elderly patient group [5]. In the current study, the rates of minor and major complications were 13.6% and 7.5%, respectively, in our oldest age group (61-80 years). We found the overall complication rate in this group to be 21.2%. In our opinion, the high rate of complications in the advanced age group prolongs the length of stay in the hospital, while at the same time increasing the cost, it also poses a risk in terms of nosocomial infections.

The effects of SWL treatment on the geriatric patient population remain controversial. Although SWL has been reported to be effective and safe in this patient population [9], stone fragmentation has been reported to provide less favorable results than in younger patients [10]. With its higher success rate than SWL and lower morbidity rate than PNL, RIRS seems to be a preferable method in the geriatric patient population [11].

The main limitation of our study concerns its retrospective nature. In addition, the exclusion of patients with a history of renal surgery and those with renal abnormalities to obtain homogeneous groups limits the generalizability of our findings. In addition, the small number of patients is an additional limitation. There is a need for prospective randomized studies on this subject.

Conclusion

RIRS can be performed on the elderly with success rates comparable to other age groups. However, the elderly, who represent a higher-risk patient population with more comorbidities, have increased rates of minor and major complications both in the perioperative and postoperative periods.

Ethics Committee Approval: The study protocol was reviewed and approved by the University of Health Sciences, Umraniye Training and Research Hospital (Approval date and number: 22.12.2022/416).

Informed Consent: An informed consent was obtained from all the patients.

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The Relationship of Urological and Psychological Problems with Circumcision – A Cross-sectional Study

Ürolojik ve Psikolojik Problemlerin Sünnetle İlişkisi – Kesitsel Bir Çalışma

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Abstract

Objective: Circumcision is one of the most common surgical procedures in the world which is performed for various reasons. The aim is to investigate whether people's satisfaction with circumcision, their perspectives on circumcision, and whether there is a connection between circumcision and psychological/urological problems.

Materials and Methods: Between 21 March 2023- 10 April 2023, 1009 men aged between 18-50 who volunteered to participate in the survey were included in the study. Demographic structures of the people (age, education, income status), age of circumcision, by whom, where and with what type of anesthesia; problems during circumcision, satisfaction with circumcision, any sexual and psychological problems and the relationship of this problem with circumcision were investigated.

Results: Mean age of 1009 participants was 32.02 ± 9.15 and mean age of circumcision was 6.18 ± 3.10 . 269 (26.7%) men stated that they experienced circumcision complications and 145 (14.4%) stated that they were not satisfied with circumcision. 267 men (26.5%) had sexual or urological problems, and 274 (27.2%) had psychological problems, but the relationship of both problems with circumcision was not significant. Both sexual/urological problems and psychological problems were found to be significantly higher in the group satisfied with circumcision (both p:0.000, p<0.05). The relationships between the characteristics of the circumcision performed (circumcision age, anesthesia method, circumcision site and the person performing it) and urological/sexual problems were found to be significant (all p<0.05).

Conclusion: This cross-sectional study supports the hypothesis that circumcision has no relationship with urological/andrological or psychological problems. However, although circumcision is a relatively simple and frequently performed surgical procedure, characteristics such as the age at which the circumcision was performed, the type of anesthesia, the place where it was performed, and the person performing the circumcision are important in order to avoid future urological/sexual problems.

Keywords: circumcision, psychology, complication, andrology

Öz

Amaç: Sünnet, dünya üzerinde en sık yapılan cerrahi girişimlerden biridir. Dini, geleneksel ve tıbbi nedenler ile yapılmaktadır. Çalışmamızda kişilerin sünnet memnuniyeti, sünnete bakış açıları ve sünnet ile psikolojik ve ürolojik sorunların hastalara göre bağlantısı olup olmadığı araştırıldı.

Gereçler ve Yöntemler: 21 Mart 2023- 10 Nisan 2023 tarihleri arasında ankete katılmaya gönüllü olan 18-50 yaş arası 1009 erkek çalışmaya dahil edildi. Hastalara hazırlanan 15 soruluk anket doldurtuldu. Anket sorularında, kişilerin demografik yapıları (yaş, eğitim, gelir durumu), sünnet olduğu yaş, sünnetinin kim tarafından, nerede ve hangi anestezi şekliyle yapıldığı; sünnet sırasında herhangi bir problem yaşanıp yaşanmadığı, sünnetinden memnun olup olmadığı; herhangi bir cinsel ve psikolojik probleminin olup olmadığı ve bu problemin sünnet ile ilişkisi sorgulandı.

Bulgular: 1009 katılımcıda ortalama yaş 32.02±9.15 ve ortalama sünnet yaşı 6.18±3.10 idi. Katılımcıların 269 tanesi (%26.7) sünnet komplikasyonu yaşadığını ve 145 tanesi (%14.4) sünnetten memnun olmadığını belirtti. Katılımcıların 267 tanesinde (%26.5) cinsel veya ürolojik problem, 274 tanesinde (%27.2) psikolojik problem olduğu tespit edildi ancak iki problemin de sünnetle ilişkisi anlamlılık göstermemekteydi. Sünnetten memnun olan grupta hem cinsel/ ürolojik problemler, hem de psikolojik problemler anlamlı oranda daha yüksek bulundu (her iki p:0.000, p<0.05). Yapılan sünnetin özellikleri ile (sünnet yaşı, anestezi metodu, sünnet yeri ve yapan kişi) ürolojik/cinsel problemler arasındaki ilişkiler anlamlı olarak tespit edildi (tüm p<0.05).

Sonuç: Bu kesitsel çalışma, sünnetin, ürolojik/androlojik veya psikolojik problemlerle bir ilgisinin olmadığı savını desteklemektedir. Ancak sünnet, her ne kadar görece basit ve çokça yapılan bir cerrahi prosedür olsa da, sünnetin yapıldığı yaş, anestezi tipi, yapıldığı yer ve yapan kişi gibi özellikleri, ileride yaşabilecek ürolojik/cinsel problemlerle karşılaşmamak açısından önem göstermektedir.

Anahtar kelimeler: sünnet, psikoloji, komplikasyon, androloji

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Introduction

Circumcision is the most common surgical procedure in the world, which has been practiced since ancient times, both traditionally and religiously in various societies, and also has medical indications [1]. The World Health Organization (WHO) reported that 30% of men worldwide are circumcised [2]. The positive and negative psychological effects of such a frequently performed surgical procedure on patients and some urological complications have been the subject of discussion in the literature for many years.

Psychologically, the social anxiety of being uncircumcised in a mostly circumcised society can affect men. In this respect, circumcision can be seen as a procedure that can provide positive psychological contributions such as reinforcing the feeling of "being a man", improving body image, and being accepted in society [3,4]. On the other hand, the fact that this age group's ability to decide on its own body is debatable, as it is a procedure that is mostly applied in infancy and childhood, and that parents are often decisive instead of the child, increases the ethical debates about circumcision [5,6].

On the urological aspect, it is an undeniable fact that the circumcision procedure reduces the frequency of urinary tract infections and sexually transmitted infections. In addition, it reduces the risk of cervical cancer in partner women by reducing

Figure 1. Ouestionnaire of 15 questions prepared for the patients

- 1) Age?
- 2) **Income Status?**
 - Below 2000TL a.
 - 2001-5000TL b.
 - 5001-10000TL с
 - d. 10001TL and above

Educational Status? 3)

- Illiterate а
- b. Literate
- Primary School c.
- d. Middle School
- High School e.
- f. University/College

How old were you circumcised? 4)

Who performed the circumcision? 5)

- Traditional circumciser/Health worker a.
- b. General practitioner
- c. Specialist
- Was any type of anesthesia done during circumcision? 6)
 - Local anesthesia a.
 - h General anesthesia

Where was the circumcision done? 7)

- a. House
- Health center b.
- c. Hospital
- d. Mass circumcision events
- 8) Have you encountered any kind of problem during or after circumcision?
 - No а b.
 - Bleeding Infection c.
 - Recircumcision d

the incidence of penile human papillomavirus (HPV) [7,8]. In addition, it significantly reduces the risk of penile cancer and eliminates preputial pathologies such as phimosis [9]. However, the sexual effects of circumcision are a popular topic of discussion in the literature.

The aim of this study is to evaluate people's perspectives on their circumcision, to measure their satisfaction, and to investigate whether there is a connection with circumcision if they have psychological and/or urological problems.

Materials and Methods

This observational cross-sectional survey study was approved by the Haydarpasa Numune Training and Research Hospital Clinical Research Ethics Committee on 20.03.2023 with the decision number HNEAH-KAEK 2023/40. Between 21 March 2023 and 10 April 2023, 1009 men between the ages of 18-50 who volunteered to participate in the survey were included in the study. A non-validated, semi-structured questionnaire of 15 questions prepared for the patients was filled out (Figure 1). In the survey questions, demographic structures of the people (age, education, income status), age at which circumcision was performed, by whom, where and with what type of anesthesia; whether there were any problems during circumcision, whether he was satisfied with his circumcision; whether he had any sexual

- 9) Are you satisfied with your circumcision?
 - Yes a.
 - No h
- 10) Do you have any sexual / urological problems?
 - а No
 - Erectile Dysfunction b.
 - Premature Ejaculation C.
 - Penile Curvature d.
 - Difficulty in voiding / Stricture at meatus e.
 - f. Other (specify.....)
- 11) Do you think that this problem is related to circumcision?
 - Yes a. No
 - b
- 12) Do you have any psychological problems?
 - No a.
 - Mild depression b.
 - Difficulty in communication c.
 - Low self-esteem d.
 - Aggressive behaviors e.
 - f. Anxiety
 - Other (specify.....) g.
- 13) Do you think that this problem is related to circumcision?
 - a. Yes
 - b. No
- 14) Who would you like your child to be circumcised by?
 - Traditional circumciser a.
 - b. General practitioner
 - Specialist c.

15) Where would you like your child to be circumcised by?

- House a.
 - Health center b.
 - Hospital c.
 - Mass circumcision events d
| Table 1. | Demographic | data of the | participants |
|----------|-------------|-------------|--------------|
|----------|-------------|-------------|--------------|

	Mean ± SD	N (%)
Age (y)	32.02±9.153	
Age of circumcision (y)	6.18±3.109	
<7		555 (55)
7-12		436 (43.2)
>12		18 (1.8)
Income status (TL)		
<2000		253 (25.1)
2001-5000		395 (39.1)
5001-10000		285 (28.2)
>10001		76 (7.5)
Educational level		
Illiterate		60 (5.9)
Literate		88 (8.7)
Elementary school		134 (13.3)
Middle school		172 (17)
High school		325 (32.2)
University or above		230 (22.8)
Person performing circumcision		
Traditional circumciser / health worker		614 (60,9)
General practitioner		143 (14,2)
Specialist		252 (25)
Anesthesia		
None		329 (32,6)
Local		539 (53,4)
General		141 (14)
Place of circumcision		
House		528 (52.3)
General health center		107 (10.6)
Hospital		270 (26.8)
Mass circumcision events		104 (10.3)
Total		1009 (100)

SD: standard deviation; y: years; TL: Turkish Lira; N: number

and psychological problems and the relationship of this problem with circumcision were questioned. The study was carried out in accordance with the principles of the Declaration of Helsinki, no personal information was included in the questionnaire and the data was collected completely anonymously.

Statistical Analysis

After the data in the questionnaires were collected, the results were reported as mean, standard deviation and percentage (%). Distribution normality was evaluated with the Shapiro-Wilks test. Chi-Square, Mann-Whitney U or Kruskal-Wallis tests were used to determine statistical differences according to the type and distribution of variables. Bonferroni-corrected Dunn's test was used as a post-hoc analysis to determine which group was significant in multiple groups that were significant. Statistical significance was taken as p < 0.05.

Results

The mean age of 1009 participants were 32.02 ± 9.15 and the mean age of circumcision was 6.18 ± 3.10 . Demographic information of the participants is given in **Table 1**.

Table 2. General satisfaction and problems	
encountered concerning circumcision	

Complication of	n (9/.)	Circumsision	n (9/.)	
circumcision	II (70)	satisfaction	II (70)	
No	740 (73.3)	Satisfied	864 (85.6)	
Bleeding	145 (14.4)	Not Satisfied	145 (14.4)	
Infection	69 (6.8)			
Recircumcision	55 (5.5)			
Sexual / Urological problems	<i>></i>	Is it related to circumcision?		р
No	742 (73.5)	Yes	101 (10)	0,376
Erectile dysfunction	59 (5.8)	No	166 (16.5)	
Premature ejaculation	69 (6.8)	Unanswered	742 (73.5)	
Penile curvature	76 (7.5)			
Lower urinary tract symptoms	53 (5.3)			
Other	10(1)			
Psychological problems	÷	Is it related to circumcision?		р
No	735 (72.8)	Yes	117 (11.6)	0,983
Mild depression	73 (7.2)	No	157 (15.6)	
Communication difficulties	55 (5.5)	Unanswered	735 (72.8)	
Low self-esteem	64 (6.3)			
Aggressive behaviours	46 (4.6)			
Anxiety	26 (2.6)			
Other	10(1)			
To whom do you want your child to be circumsized?		Where?		
Traditional circumsizer	194 (19.2)	House	158 (15.7)	
General practitioaner	84 (8.3)	General health center	93 (9.2)	
Specialist	731 (72.4)	Hospital	667 (66.1)	
		Mass circumcision events	91 (9)	
Total	1009 (100)		1009 (100)	

Chi-Square test; Bold*: indicating statistical significance; N: number

Of the participants, 269 (26.7%) stated that they experienced circumcision complications and 145 (14.4%) stated that they were not satisfied with circumcision. 267 of the participants (26.5%) declared that they had sexual or urological problems and 274 (27.2%) of them had psychological problems, but the relationship of both problems with circumcision was not significant (p=0.376 and 0.983, respectively). Data on general circumcision satisfaction, problems experienced and their relationship with circumcision are given in Table 2.

Considering the participants who had sexual/urological or psychological problems, those who were satisfied with circumcision were statistically significantly higher than those who were not (p=0.000 and p=0.000). There was no significant difference between sexual, urological or psychological problem subtypes in terms of circumcision satisfaction. Data on the relationship between circumcision satisfaction and problems are given in **Table 3**.

When the relationship between the characteristics of circumcision performed on the participants and urological

problems was examined, it was seen that circumcision age (p=0.000), anesthesia type (p=0.000), circumcision site (p=0.000) and circumcised person (p=0.001) were statistically significant in the occurrence of urological problems. Circumcision age >12, circumcision under general anesthesia, mass circumcision ceremonies or circumcision performed by general practitioners in the health center and circumcision performed by general practitioners have been found to be stastistically significantly related with urological problems. The relationship between circumcision features and urological problems is summarized in Table 4.

Discussion

Circumcision, which is a surgical procedure applied to almost every man, especially in Muslim and Jewish societies, is also on the agenda in other societies, both for medical indications and for its protection from possible medical consequences. The

			Satisfied with ci Yes	rcumcision? No	р
	Erectile	n	42	17	
	dysfunction	%	71,2%	28,8%	
	Premature ejaculation	n	41	28	
Served (uncleasing) problems		%	59,4%	40,6%]
Sexual / urological problemis	Penile curvature	n	40	36]
		%	52,6%	47,4%	0,064
	Lower urinary tract symptoms	n	38	15	
		%	71,7%	28,3%	
Total	n	161	96		
%			62,6%	37,4%	
			p: 0,00)0*	

Yes No			Satisfied with Ci	rcumcision?	р
	Mild depression	n	47	26	
	wind depression	%	64,4%	35,6%	
	Communication	n	37	18	
Darrah ala zi azl zwahlazwa	difficulties	%	67,3%	32,7%	
r sychological problems	Low self-esteem Aggressive behaviours	n	44	20	
		%	68,8%	31,3%	0.823
		n	27	19	
		%	58,7%	41,3%	
	Anxiety	n	18	8	
		%	69,2%	30,8%	
Total		n	173	91	
		%	65,5%	34,5%	
b			p: 0,00	0*	

Chi-Square and Mann-Whityney U test; Bold*: indicates statistical significance

			Urological Problem		р
			Yes	No	
	~7	n	435	120	
	</td <td>%</td> <td>78,4%</td> <td>21,6%</td> <td></td>	%	78,4%	21,6%	
Age of	7.10	n	298	138	
circumcision	/-12	%	68,3%	31,7%	0.000*
	> 12	n	9	9	0.000*
	>12	%	50,0%	50,0%	
	None	n	277	52	
	None	%	84,2%	15,8%	
A	Level	n	383	156	
Anestnesia	Local	%	71,1%	28,9%	0.000*
	General	n	82	59	
		%	58,2%	41,8%	
	House	n	424	104	
		%	80,3%	19,7%	
	General health center	n	64	43	
		%	59,8%	40,2%	
Location		n	199	71	0.000*
	Hospital	%	73,7%	26,3%	
	Mass	n	55	49	
	events	%	52,9%	47,1%	
	Traditional	n	471	143	
	circumciser	%	76,7%	23,3%	
Person	General	n	88	55	0.001*
Circumcision	practitioner	%	61,5%	38,5%	0.001*
	Specialist	n	183	69	
		%	72,6%	27,4%	

Table 4. The relationship between circumcisionfeatures and urological problems

Kruskal Wallis test; Bold*: indicates statistical significance

fact that it is such a frequently performed surgery has led to the fact that the psychological and urological/andrological effects of circumcision are frequently the subject of research in the literature [6,10].

When the answers given by the participants in our study are examined, it is seen that the rate of participants who are not satisfied with circumcision in general is 14%. When the literature is examined, although there is no long-term feedback study on individuals' own circumcision, it was seen in the study conducted by Özen and Eroğlu in 2019 that parents were not satisfied with the circumcision of their children at a rate of 41.2% [11]. In this study, although the parents' satisfaction with circumcision changes significantly with age, it was observed that the lowest dissatisfaction rate (2.1%) was observed in the first month of neonatal period. Although the overall dissatisfaction rate was 14% in our study, this rate reached 37.4% in those with urological or sexual problems and 34.5% in those with psychological problems. This relationship with circumcision is statistically insignificant; possibly due to the vast majority of participants leaving this question unanswered. In addition, when only the respondents were considered, 38-42% reported that these problems could be related to circumcision.

In European and American communities where circumcision is not common, the psychological effects of circumcision, especially on children, have been discussed for years. It has been suggested that the feeling of "difference" caused by circumcision in a mostly uncircumcised society and the trauma to the body and "masculinity" perception caused by the intervention to the male genital organ during circumcision may cause psychosomatic symptoms of future depression, anxiety, and posttraumatic stress disorder [12,13]. On the contrary, it is obvious that being uncircumcised can lead to feelings of exclusion, not being accepted in society, shame and similar feelings in generally circumcised societies. However, the psychological effects of a surgical procedure performed on the genital area in childhood are important, and therefore, providing effective analgesia and anesthesia during the circumcision procedure is extremely important in order to avoid possible psychological effects [14,15]. However, in general terms, it is very unlikely that psychological problems in adulthood, which may be highly multifactorial, are attributed to circumcision performed in childhood.

In our study, it was seen that urological problems increase significantly as the age of circumcision increases. In published guidelines and studies, it is shown that circumcision performed especially in the neonatal period has a more effective and faster recovery period compared to other age groups and can be performed with fewer complications [16,17]. In addition, the sense of awareness that develops with advancing age increases the risk of complications, especially in circumcision procedures performed without anesthesia or with local anesthesia [18]. Although there is no data with a high level of evidence, most experts do not recommend circumcision in the age range of 3-6 years, which is called the "phallic" period, when children gain their sexual identity, for fear of sterilization and to avoid psychosexual effects that may occur in the future [19]. In their 2013 publication, Armağan et al. argue that circumcisions performed during the phallic period do not actually cause any sexual or depressive side effects, and that this is nothing more than an anecdote [20].

Unexpectedly, it was found to be significantly higher in the general anesthesia group when the relationship between the type of anesthesia and the urological problem was investigated. There are reports in the literature such as methemoglobinemia due to local anesthetic agents, necrosis of the glans or penis due to vasoconstriction [21-23]. However, there is no study in the literature comparing short or long-term urological complications after circumcision according to anesthesia type, and this study is the first data in the literature on this subject. However, a cause-effect relationship could not be established within the framework of logic on this subject, and it is obvious that there is a need for comprehensive studies on this subject.

In our study, it was observed that the circumcision site and the person performing the circumcision had a significant effect on urological problems. It has been observed that circumcisions performed in places such as general health centers or mass circumcision ceremonies are more open to the risk of urological complications, and circumcisions performed by general practitioners have a higher rate of urological problems. Although circumcision is often seen as a minor surgery, it is a surgery after all and the importance of care and experience cannot be denied. These results are in line with the data found in studies conducted in Nigeria and Turkey comparing medical and non-medical circumcised individuals [24,25]. In addition, it was shown in Özdemir's study that the complication risk rate is higher in mass circumcision ceremonies [26].

When our data were examined, it was seen that the majority of circumcised men were circumcised by a traditional circumciser, the majority of them were circumcised without anesthesia or with local anesthesia, and again, the majority of them were circumcised under household conditions. However, when these participants were questioned about where and by whom they wanted their children to be circumcised; most of them stated that they wanted the procedure to be performed by a specialist doctor and most of them in the hospital. It can be thought that this finding is a useful increase in awareness in order to reduce the urological and psychological complications that circumcision may bring in a constantly developing and changing world. In order to reduce the urological and psychological complications of circumcision, it is of great importance that it is performed preferably in the neonatal period or in infancy, accompanied by any anesthesia and in experienced health institutions.

As being an observational cross-sectional study, a definite judgment from the results obtained is difficult to sustain a causal inference and the association is difficult to interpret. Also, these kinds of studies are known to be susceptible to nonresponse and recall biases. Even though the study is done with a high number of participants, short-time interval and unanswered questions detract the scientific effect of this study. The questionnaire being a semi-structured, non-validated survey also contributes to the limitations of this study. All in all, as defining the key role important factors and features of circumcision that tend to effect possible urological/psychological complications, we believe that this study can shed light on new validation studies of the current questionnaire and also bring new horizons with multicenter collaborative studies with larger sample sizes.

Conclusion

Our study supports the argument that circumcision is not associated with urological/andrological or psychological problems in adulthood. However, although circumcision is a relatively simple and frequently performed surgical procedure, features such as the age at which the circumcision was performed, the type of anesthesia, the place where it was performed, and the person performing the circumcision may be deemed important in order to avoid future urological/sexual problems.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences, Haydarpasa Numune Training and Research Hospital Clinical Research Ethics Committee on 20.03.2023 with the decision number HNEAH-KAEK 2023/40. Informed Consent: An informed consent was obtained from all the patients. **Publication:** The results of the study were not published in full or in part in form of abstracts.

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Effect of Preoperative Kegel Exercises on Continence Rates After Open Radical Prostatectomy

Ameliyat Öncesi Kegel Egzersizlerinin Açık Radikal Prostatektomi Sonrası Kontinans Oranlarına Etkisi

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Abstract

Objective: To reveal the effect of preoperative Kegel exercises on early period continence rates after open radical prostatectomy

Materials and Methods: Data of patients with open radical prostatectomy between January 2019 and July 2022, in a tertiary academic health center were retrospectively reviewed. Patient' characteristics, perioperative parameters and postoperative follow-up results were recorded. Patients were divided into two groups as those who did Kegel exercises in the preoperative period and those who did not, and groups were compared.

Results: There were 38 patients in the Kegel exercise group and 40 patients in the other group. Postoperative 1st month and postoperative 3rd month incontinence rates were similar between the groups (p=0.406, and p=0.387). At 6th months postoperatively, the rate of incontinence in the Kegel group was 7.9%, while it was 25.0% in the other group (p=0.043). Similarly, the rate of incontinence at 1st year postoperatively was significantly lower in the Kegel group (5.3% vs 20.0%, p=0.001). At 6 months postoperatively, the QoL score in the Kegel positive group was 86, while it was 65 in the other group (p=0.001). In the postoperative 1st year controls, the quality of life (QoL) score was statistically significantly higher in patients with preoperative Kegel exercise (p=0.001).

Conclusion: Our study demonstrated that preoperative Kegel exercises had a significant positive effect on continence rate after radical prostatectomy in the postoperative 6th month and in the first year follow-up, and preoperative Kegel exercises were significantly associated with higher quality of life scores at 6th months and 1st year follow-up.

Keywords: Kegel exercise, incontinence, prostate cancer, radical prostatectomy

Öz

Amaç: Preoperatif Kegel egzersizlerinin açık radikal prostatektomi sonrası erken dönem kontinans oranlarına etkisini ortaya koymak.

Gereçler ve Yöntemler: Üçüncü basamak bir akademik sağlık merkezinde Ocak 2019 ile Temmuz 2022 arasında açık radikal prostatektomi yapılan hastaların verileri retrospektif olarak incelendi. Hastaların özellikleri, perioperatif parametreler ve postoperatif takip sonuçları kaydedildi. Hastalar ameliyat öncesi dönemde Kegel egzersizleri yapanlar ve yapmayanlar olarak iki gruba ayrıldı ve gruplar karşılaştırıldı.

Bulgular: Kegel egzersiz grubunda 38, diğer grupta 40 hasta vardı. Postoperatif 1. ay ve postoperatif 3. ay inkontinans oranları gruplar arasında benzerdi (p=0.406 ve p=0.387). Postoperatif 6. ayda inkontinans oranı Kegel grubunda %7.9 iken diğer grupta %25.0 idi (p=0.043). Benzer şekilde ameliyat sonrası 1. yılda inkontinans oranı Kegel grubunda anlamlı olarak daha düşüktü (%5.3'e karşı %20.0, p=0.001). Postoperatif 6. ayda Kegel pozitif grupta QoL skoru 86 iken diğer grupta 65 idi (p=0.001). Ameliyat sonrası 1. yıl kontrollerinde ameliyat öncesi Kegel egzersizi yapan hastalarda yaşam kalitesi (QoL) skoru istatistiksel olarak anlamlı derecede yüksekti (p=0.001).

Sonuç: Çalışmamız, ameliyat öncesi Kegel egzersizlerinin, radikal prostatektomi sonrası postoperatif 6. ay ve 1. yıl takibinde kontinans oranı üzerinde anlamlı pozitif etkiye sahip ve daha yüksek yaşam kalitesi skorları ile anlamlı şekilde ilişkili olduğunu gösterdi. **Anahtar kelimeler:** Kegel egzersizi, idrar kaçırma, prostat kanseri, radikal prostatektomi

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Introduction

Prostate cancer is the most diagnosed cancer in men, and surgery has a pivotal role in the treatment of prostate cancer. Although radical prostatectomy surgery has satisfactory oncological results, the possibility of encountering problems such as urethral stricture, erectile dysfunction and urinary incontinence in the postoperative period causes patients to be suspicious of the surgery [1]. Since the definition of urinary incontinence after radical prostatectomy is not the same in different clinics, the rates of urinary incontinence after radical prostatectomy have been found in a wide range in studies [2]. Even, Peyromaure et al. found that postoperative urinary incontinence rates could reach 30% [3]. Previous studies have shown that urinary incontinence after radical prostatectomy may cause more hospital admissions, more drug use, increased costs in the healthcare system, and social isolation of patients in the postoperative period [4].

Kegel exercises are defined to strengthen the muscles of pelvic floor, involving rapid and sustained voluntary contractions of the pelvic floor muscles to improve sexual function and urinary incontinence [5]. Studies examining the effect of Kegel exercises on urinary incontinence after radical prostatectomy have obtained conflicting results. Lilli and colleagues analyzed 90 patients' data who underwent radical prostatectomy, and authors concluded that pelvis floor muscles exercises did not significantly improve urinary incontinence recovery following radical prostatectomy [6]. In contrast, Ribeiro et al. found that Kegel exercises associated with significant improvements in urinary incontinence severity after radical prostatectomy [7].

Although previous studies have examined the effect of postoperative pelvic floor exercises on post-radical incontinence, the number of studies examining the effect of preoperative Kegel exercises on continence after radical prostatectomy is limited. In this study, we aimed to reveal the effect of preoperative Kegel exercises on early period continence rates after open radical prostatectomy.

Materials and Methods

In this study, data of patients with open radical prostatectomy between January 2019 and July 2022, in a tertiary academic health center were retrospectively reviewed. Patients from this group with at least 1 year follow-up were included in the study. Before the study was planned, permission was obtained from the Haseki Training and Research Hospital local ethics committee with registration number 2023-12. All patients included in the study were informed in detail about prostate cancer and all treatments to be applied in prostate cancer. In addition, possible complications that may occur after prostate cancer surgery and the follow-up process were explained in detail to all patients. Informed consent for radical prostatectomy was signed by each patient 24 hours before surgery.

Patient' characteristics such as age, body mass index (BMI), smoking status, comorbidities, Prostate Specific Antigen (PSA) level, and tumor-related parameters were noted. In addition, perioperative parameters and postoperative follow-up results were recorded for each patient. Patients who underwent salvage radical prostatectomy surgery, patients who received prior pelvic radiotherapy, and patients with previous nerve or muscle disease affecting the pelvic floor muscles (Parkinson's disease, stroke, multiple sclerosis, spinal disorders etc.) were excluded from the study. Other exclusion criteria were undergoing laparoscopic or robotic radical prostatectomy, had transurethral resection of the prostate (TURP) before radical prostatectomy, and failed to complete the one-year follow-up period.

Preoperative Kegel Exercises, Radical Prostatectomy Procedure, and Follow up Procedure

Kegel exercises were started after the patient was diagnosed with prostate cancer pathologically and the patient chose prostate cancer surgery among the treatment options. The time from the diagnosis of prostate cancer to the operation of all patients was between 1-2 months. Kegel exercises were explained to all patients in detail by a professional health worker without any time limit. In addition, to avoid possible misunderstandings, all patients were provided with written and visual resources describing how to do Kegel exercises. All patients were taught to tighten their pelvic floor muscles and keep them tight until they counted one to five, and when patients relax their pelvic floor muscles, they have finished one Kegel exercise. Patients were advised to do 15- 20 Kegel exercises three to four times each day. In radical prostatectomy, the classical method described by Walsh et al. was used as a standard technique [8]. All operations were performed by the same team experienced in open radical prostatectomy. In the post-operative period, Kegel exercises were recommended to the patients for one year, the same as in the preoperative period.

In order to demonstrate the effect of Kegel exercise performed in the preoperative period on continence after radical prostatectomy, the patients were divided into two groups as those who did Kegel exercises in the preoperative period and those who did not. Patients who did and did not perform Kegel exercises in the preoperative period were compared in terms of preoperative demographic characteristics, operative parameters, postoperative patients' life quality and postoperative continence status.

Statistical Analysis

Statistical analysis was done with 'Statistical Package for the Social Sciences' (SPSS) 27 program. The normality assessment of data distribution was analyzed with the Shapiro-Wilk test and Q-Q plots. Independent Samples t-test was used for continuous variables. Quantitative data were presented as mean \pm standard deviation. Chi-square test was used to compare qualitative data. The data were analyzed at 95% confidence level and the values with p<0.05 were noted statistically significant.

Results

Demographic data of patients are compared between groups in **Table 1**. There were 38 patients in the Kegel exercise group and 40 patients in the other group. While the mean age was 63.5 years in the Kegel group, it was 61.8 in the other group (p=0.196). There was no difference between the groups in terms of BMI, PSA, and prostate volume (p=0.144, p=0.557, and p=0.147; respectively). Comorbidities and smoking rates were similar between the groups. Radical prostatectomy pathologies were compared according to International Society of Urological Pathology (ISUP) degrees, and no significant difference was observed between the groups (p=0.876).

Comparison of patients' incontinence status between groups is given in **Table 2**. Postoperative 1st month and postoperative 3rd month incontinence rates were similar between the groups (p=0.406, and p=0.387; respectively). At 6th months postoperatively, the rate of incontinence in the Kegel group was 7.9%, while it was 25.0% in the other group (p=0.043). Similarly, the rate of incontinence at 1st year postoperatively was significantly lower in the Kegel group (5.3% vs 20.0%, p=0.001).

The patients' life quality at the postoperative 1st month and 3^{rd} month were statistically similar between the groups. At 6 months postoperatively, the QoL score in the Kegel positive group was 86, while it was 65 in the other group (p=0.001). In the postoperative 1st year controls, the quality of life (QoL) score was statistically significantly higher in patients with preoperative Kegel exercise (p=0.001) (**Figure 1**).

Discussion

Prostate cancer is a common disease all over the world and radical prostatectomy is an effective and safe treatment method in prostate cancer [9]. However, urinary incontinence occurring after radical prostatectomy adversely affects the general health of the patient and studies to prevent this situation continue [10]. On the other hand, there is strong evidence that Kegel exercises are effective in preventing incontinence by strengthening the pelvic floor muscles, and many centers recommend that patients do Kegel exercises after radical prostate surgery [4,11]. In this study, we aimed to investigate the effect of preoperative Kegel exercises on continence after radical prostatectomy, and our findings revealed that preoperative Kegel exercises had a significant positive effect on continence after radical prostatectomy in the postoperative 6th month and in the first year follow-up. In addition, preparative Kegel exercises were significantly associated with higher quality of life scores at 6th months and 1st year follow-up.

Urinary incontinence is not life-threating but disturbing complication of radical prostatectomy. Hodges and colleagues performed literature analyses to define relation between pelvic muscle training and post-prostatectomy continence, and authors stated the importance of pelvic floor muscle training to prevent and treat incontinence after radical prostatectomy [12]. In different study, Overgard et al. recommended that patients with radical prostatectomy perform pelvic floor exercises under the guidance of a specialist physiotherapist, and those who accepted this offer had a significantly lower rate of incontinence at firstyear follow-up than those who did not. However, Overgard et al found that pelvic floor work did not affect continence rates at 3rd, 6th, and 9th month follow-ups [13]. In their meta-analysis, Levy et al. determined that pelvic endurance was important in early incontinence after radical prostatectomy and stated that pelvic floor exercises increased pelvic endurance and significantly decreased continence at the 3rd month postoperatively [14]. In present study, we found that preoperative Kegel exercises had a significant positive effect on continence after radical

Table 1. Comparison of preoperative demographic data and postoperative pathology results between groups

	Kegel +	Kegel -	Р
	(n:38)	(n:40)	value
Age (years)*	63.5±5.8	61.8±5.7	0.196
BMI (kg/m ²)*	26.9±3.0	26.7±2.7	0.144
PSA (ng/ml)*	7.1±2.5	6.8±2.6	0.557
Prostate volume (cc)*	54.7±24.6	62.6±22.9	0.147
Comorbidities, n (%)			
Hypertension	7 (18.4%)	10 (25.0%)	0.482
Diabetes Mellitus	9 (23.7%)	9 (22.5%)	0.901
CAD	7 (18.4%)	8 (20.0%)	0.860
COPD	4 (10.5%)	5 (12.5%)	0.785
СКД	2 (5.3%)	2 (5.0%)	0.958
Smoking status, n (%)	18 (47.4%)	17 (42.5%)	0.666
Final Pathology, n (%)			
ISUP Grade 1	12 (31.6%)	14 (35.0%)	
ISUP Grade 2	9 (23.7%)	8 (20.0%)	0.976
ISUP Grade 3	8 (21.0%)	9 (22.5%)	0.870
ISUP Grade 4	7 (18.4%)	6 (15.0%)	
ISUP Grade 5	2 (5.3%)	3 (7.5%)	

*mean ± standard deviation; BMI: body mass index; PSA: prostate specific antigen; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; ISUP: International Society of Urological Pathology

 Table 2. Comparison between incontinence groups at different postoperative periods

	Kegel + (n:38)	Kegel - (n:40)	P value
Stress incontinence, n (%)			
Postoperatively 1st month	10 (26.3%)	14 (35.0%)	0.406
Postoperatively 3rd month	8 (23.7%)	13 (32.5%)	0.387
Postoperatively 6th month	3 (7.9%)	10 (25.0%)	0.043
Postoperatively 1st year	2 (5.3%)	8 (20.0%)	0.042





prostatectomy in the postoperative 6th month and in the first year follow-up. Because of these results, we recommend that all patients undergoing radical prostatectomy perform Kegel exercises before surgery.

Previous reports demonstrated relation between urinary incontinence and embarrassment, social isolation and deterioration of quality of life. Bernardes and colleagues investigated the life quality of patients undergoing radical prostatectomy, and authors determined that urinary incontinence is one of the most important factors that impair the quality of life after surgery [15]. In another study, Nyarangi-Dix recommended to perform bladder neck preservation during radical prostatectomy to achieve higher urinary incontinence rate and higher patient satisfaction [16]. In this study, we found higher patients' life quality with radical prostatectomy at the 6th month and 1st year follow-up, we think that this result is associated with a significant decrease in incontinence rates in the same period.

Present study included small patient number, which accepted as study limitation. Moreover, this study only focused on short term results of preoperative Kegel exercises on post radical prostatectomy continence, and we believe that effect of Kegel exercises on long-term incontinence after radical prostatectomy may be the subject of a different study. Finally, we accepted on the basis of patient statements whether the patients did the Kegel exercises or did them correctly. In addition, the fact that the study was single-centered and the peroperative data were not taken into account can be shown as other limitations.

Conclusion

Our study demonstrated that preoperative Kegel exercises had a significant positive effect on continence rate after radical prostatectomy in the postoperative 6th month and in the first year follow-up, and preparative Kegel exercises were significantly associated with higher quality of life scores at 6th months and 1st year follow-up. Kegel exercises should be offered to patients who will be scheduled for radical prostatectomy operation, starting before the procedure.

Ethics Committee Approval: This study was approved by the local institutional review board (University of Health Sciences, Haseki Training and Research Hospital, approval date and number: 05.06.2023-12).

Informed Consent: An informed consent was obtained from all the patients.

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The Effect of Curcumin on Penile Fibrotic Plaque in Rats with Experimental Peyronie's Disease

Deneysel Peyronie Hastalığı Oluşturulan Ratlarda Kurkuminin Penil Fibrotik Plak Üzerine Etkisi

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Abstract

Objective: No effective medical approach for the treatment of Peyronie's disease (PD) has to date been described. This study was intended to evaluate the antifibrotic, antioxidant, and anti-inflammatory effects of curcumin on fibrotic tissue in the tunica albuginea (TA) in a rat model of PD.

Materials and Methods: Twenty-four male Sprague Dawley rats aged 10 months were randomized into three groups (n = 8 in each). No PD model was induced in the control group. The PD+saline (PD+Ps) group received fibrin injection, followed two weeks later by saline administration by oral gavage for 14 days. The PD+Curcumin (PD+Cur) group received fibrin injection into the TA followed two weeks later by curcumin administration by oral gavage for 14 days. At the end of the experiment, fibrotic activity was evaluated using stereological and histopathological methods. Transforming growth factor- β 1 (TGF- β 1), one of the most fibrogenic cytokines, was evaluated using immunohistochemistry with an anti-TGF- β 1 rabbit monoclonal antibody.

Results: Stereological analysis revealed significantly greater Peyronie-like plaque areas in the TA in the PD+Ps group than in the control and PD+Cur groups (p<0.0001). No significant difference was observed between the control and PD+Cur groups (p=0.35). The PD+Ps group exhibited strong TGFβ1 immunoreactivity with increased expression in the collagenous connective tissues and fibroblasts around the TA.

Conclusion: Curcumin reduced fibrotic tissue in the TA and may represent a novel therapeutic option in the treatment of PD.

Keywords: Peyronie's disease, curcumin, fibrin, antioxidant

Öz

Amaç: Bugüne kadar Peyronie hastalığı'nın (PH) tedavisi için etkili bir medikal tedavi tanımlanmamıştır. Bu çalışmada, deneysel olarak PH modeli oluşturulan ratların tunika albuginealarında (TA) oluşan fibrotik doku üzerine kurkuminin antiinflamatuar, antifibrotik ve antioksidan etkilerinin değerlendirmesi amaçlanmıştır.

Gereçler ve Yöntemler: On aylık 24 adet erkek Sprague Dawley cinsi rat, eşit bir şekilde üç gruba randomize edildi. Kontrol grubuna deneysel PH modeli uygulanmadı. PH+salin (PD+Ps) grubuna fibrin enjeksiyonu yapıldı ve ardından iki hafta sonra 14 gün boyunca oral gavaj ile salin verildi. PH+Kurkumin (PH+Kur) grubuna TA'ya fibrin enjeksiyonu yapılarak PH modeli oluşturuldu ve ardından iki hafta sonra 14 gün boyunca oral gavaj ile kurkumin verildi. Deneyin sonunda fibrotik aktivite stereolojik ve histopatolojik yöntemler kullanılarak değerlendirildi. En fibrojenik sitokinlerden biri olan Transforming büyüme faktörü-β1 (TGF-β1), tavşan monoklonal antikoru olan anti-TGF-β1 kullanılarak immünohistokimyasal olarak ölçüldü.

Bulgular: Stereolojik analizde PH+Ps grubunda, kontrol ve PH+Kur gruplarına göre anlamlı olarak TA'da daha fazla Peyronie benzeri plakların ortaya çıktığı görüldü (p<0,0001). Kontrol ve PH+Kur grupları arasında anlamlı fark izlenmedi (p=0,35). PH+Ps grubunda TA çevresindeki kollajenöz bağ dokularda ve fibroblastlarda güçlü TGF-β1 immün reaktivitesi izlendi.

Sonuç: Çalışmamızda kurkuminin TA'daki fibrotik dokuyu azalttığı görülmüştür. Bu nedenle kurkumin PH tedavisinde yeni bir terapötik seçenek olabilir. Anahtar kelimeler: Peyroni hastalığı, kurkumin, fibrin, antioksidan

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Introduction

Pevronie's disease (PD) is a condition that progresses with fibrosis in the tunica albuginea (TA) layer of the penis and therefore causes penile pain, curvature, and sexual dysfunction. Despite being frequently seen, its aetiology and pathophysiology are not yet fully understood [1,2]. Factors such as trauma, frequency of sexual intercourse, diabetes mellitus, Dupuytren's contracture, family history, gout, plantar facial contracture, radical prostatectomy, tympanosclerosis, Paget's disease, beta-blocker use, advancing age, genetic predisposition, smoking, hypertension, and tissue ischemia may play a role in the aetiology [1,3,4]. The most widely accepted theory involves abnormal collagen and glycosaminoglycan deposition in the TA after inflammation and fibroblast proliferation caused by repetitive microtraumas. Abnormal extracellular matrix production also occurs through increased myofibroblast activity and upregulation of tissue inhibitors of matrix metalloproteinases [2]. The prevalence of PD ranges from 3.2% to 8.9%, with patients being typically aged 50-60 years [5].

PD includes two phases, acute (inflammatory) and chronic (stable). The acute inflammatory phase usually lasts 6-18 months and is characterized by painful erections, the formation of a palpable nodule or plaque in the tunica of the penis and penile curvature. When the lesions stabilize, the chronic phase begins and the penile deformity stabilizes, inflammation decreases, pain improves, and erectile dysfunction symptoms develop [2]. Research has reported that the course of the disease remains stable in 47% of patients and resolves spontaneously in 13%. However, the manifestation worsens in 40% of patients, and these require active treatment [6].

Despite the many alternative treatments (antifibrotic, antiinflammatory, antioxidant drugs, various vitamins, amino acids, etc.) available in addition to surgical treatment since Francois de la Peyronie's definition of PD in 1743, no entirely satisfactory therapeutic option has still been discovered [1]. Curcumin is a yellow-orange substance obtained from the roots of the plant turmeric. It has occupied an important place in Asia for thousands of years, especially in Indian medicine, and has been the focus of scientific studies for the last 20 years. Studies have shown that curcumin possesses strong antioxidant, anti-inflammatory, antiapoptotic and antidiabetic properties. In addition to its antifibrotic property, it has also been reported to exhibit an antiproliferative effect on fibroblasts. Studies have also observed the protective effects of curcumin on pulmonary, cardiac, and renal fibrosis [7]. Considering that PD is associated with diabetes mellitus at a rate of 18-33%, the antidiabetic effect of curcumin suggests that it may be an important substance in terms of the treatment of the disease [4].

In light of this information, curcumin is worthy of note as a potential therapeutic agent capable of use in the treatment of PD. The purpose of this study was aimed to examine the efficacy of curcumin against abnormal fibrous tissue production in the TA using stereological, histopathological, and immunohistochemical methods. We think that the results obtained will be useful for the development of novel medical methods for the reduction or prevention of penile fibromatosis. This is the first experimental study in the literature to investigate the effects of curcumin in an experimental rat PD model.

Material and Methods

Animals

The experimental protocol adopted in the current study was approved by the Ondokuz Mayıs University, Animal Care and Ethics Committee (HADYEK no. 2018-29-dated 25.05.2018). The animals were obtained from the Experimental Animals Surgical Research and Application Centre of Ondokuz Mayıs University, Samsun, Turkey. Twenty-four male Sprague Dawley rats (weighing 250-300 g, aged 10 months) were divided into three equal groups. The rats were housed instainless-steel cages under a 12-h light/12-h dark cycle at a room temperature of 22±2°C with humidity of 50%±10 in the laboratory. Free access was allowed to food and water. The rats were cared for as specified by the guidelines related to the care and use of laboratory animals issued by the U.S. National institutes of Health (NIH Publication No. 85-23, revised 2011) [8]. This study was also conducted in conformity with the ARRIVE animal experiments guideline [9].

Peyronie's Disease Model

Physiological saline solution was injected into the TA of the rats in the control group. In the PD+saline (PD+Ps) group, 30 µL of fibrin (TISSEELVH Sealer; Baxter, Glendale, CA, USA; 30 uL each of human fibrin and thrombin solution) was injected into the TA in order to induce the formation of Peyronie-like fibrous plaques of rats, two weeks after which, saline solution was administered for 14 days by oral gavage [10]. In the PD+Curcumin (PD+Cur) group, 30 µL of fibrin was injected into the TA, two weeks after which curcumin was administered by oral gavage for 14 days [11]. Curcumin was obtained from Sigma-Aldrich Company (Sigma Aldrich, USA, Catalog number: BD9137). Curcumin was given as 30 mg/kg per day, similar to study of Huyut et al., which investigating the effects of curcumin on liver fibrosis [12]. The bioavailability of curcumin is poor due to its rapid metabolism. It has therefore been used by dissolving it in olive oil to increase oral and gastrointestinal absorption and to reduce clearance from the body in previous research [13]. At the end of the experimental procedure, all rats were anesthetized with intramuscular ketamine (50 mg/kg)/ xylazine (10 mg/kg) and subjected to transcardiac perfusion. The penile tissues were removed and examined using stereological, histopathological, and immunohistochemical methods.

Tissue Preparation

Tissue samples were subjected to routine histological tissue processing and embedded in paraffin for stereological and immunohistochemical analysis. The penile tissue of one rat from each group was embedded in resin blocks for electron microscopic analysis.

Stereology

For stereological analysis, sections 5 μ m in thickness were taken using the systematic random sampling method and stained with Masson's trichrome to determine histometric changes.

Images were captured at 40x magnification under a microscope with a camera attachment for the analysis of plaque areas in the TA. The fibrous plaque surface areas were estimated using the planimetry method of the Cavalieri principle on Image J (Image Processing and Analysis in Java, NIH, USA) software. Coefficient of error (CE) and coefficient of variation (CV) values were calculated to determine whether the number of animals per group and sampling intervals were appropriate for each animal.

Histopathology

Semi-thin sections (500 nm) were taken from the resin blocks for light microscopic examination and stained with 1 % toluidine blue. Images were captured at 10x, 40x and 100x magnification for histopathological evaluation. Thin (70 nm) sections were also taken from the resin blocks for electron microscopic examination and stained with 0.5 % uranyl acetate and 3% lead citrate (Leica Ultrostain II). After staining, the sections were examined ultrastructurally under a transmission electron microscope (JEOLJSM-7001F, Japan).

Immunohistochemistry

For immunohistochemical evaluation, 5 µm-thick sections from each group were placed onto positively charged slides. Sections were immunestained for transforming growth factor- β 1 (TGF- β 1) to determine whether fibrin injection induced TGF- β 1 expression and formed a Peyronie-like fibrous plaque in the TA. TGF- β 1 was evaluated by immunohistochemical analysis with an anti-TGF- β 1 rabbit monoclonal antibody (1:100; Abcam). Sections were cross-stained with Mayer's hematoxylin. Immunohistochemical staining was performed by the Department of Pathology at Ondokuz Mayıs University.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism version 9.0 software (GraphPad, CA, USA). All data are presented as mean \pm standard error of the mean. The data were found to be normally distribution using the Shapiro-Wilk normality test. A p values less than 0.05 were considered statistically significant and all groups were analyzed using One-way ANOVA.

Results

Stereology

When all three groups had been evaluated in terms of Peyronie-like plaque areas in the TA, the plaque area in the PD+Ps group was significantly higher than those in the Control and PD+Cur groups (p<0.0001). However, no significant difference was observed between the Control and PD+Cur groups (p=0.35) (Figure 1).

Histopathology

Light microscopic images taken from semi-thin (500 nm) sections were evaluated to determine morphological changes between groups. The histological structure of the tissue was

Fibrous Plaque Area



Figure 1. A statistical comparison of fibrous plaque areas induced by fibrin injection in TA between three study groups. Plaque areas were expressed as mean±standard deviation. Significant differences at the level of p <0.0001 between the groups are indicated by (****)



Figure 2. Light microscopic images of semi-thin sections from all groups. The TA and corpus cavernosum parts of the penile tissue are seen at small magnification (x10). The histological structure of the tissue is normal in the control group. Plaque structures were remarkable in the high magnification (x40 and x100) images of the TA in the PD+Ps group. Morphology is similar to that of the control group can be seen in the images from the PD+Cur group. Sections were stained with toluidine blue. Asterix (*); plaque.



Figure 3. Electron microscopic images of the penis taken from three groups that are the Cont, PD+Ps and PD+Cur groups were seen. Tunica albuginea of the Cont group has a normal structure in that collagen fibres (Col) are organised as parallel and compact in the fascicules. In the PD+Ps group, the uniformity of collagen bundles in the tunica albuginea region was seriously impaired. In most of the areas, there are no collagen fibres in the dashed line (*) or a very weak arrangement is observed. In the PD+Cur group, although some regions have a non-collagenous area (*), most places in the tunica albuginea have a well-organised collagen (Col) fibres.

normal in the Control and PD+Cur groups, whereas abundant Peyronie-like fibrous plaques were observed in the PD+Ps group (**Figure 2**).

Electron Microscopy

Thin sections of penis tissues from the animals, the Control, the PD+Ps, and the PD+Cur groups were examined by electron microscopy. The collagen fibres in TA of the Control group have a well-organised arrangement; there is no interruption of the fibres in their tunica. In the PD+Ps group, most area in the TA lost its collagen fibres, for this reason many of area in the tissue are observed as white area i.e. plaque structures. In this group, it is hard to see fasciculation of collagen fibres in the TA since pronounced collagen degeneration and formation of plaque structures. In the PD+Cur group, collagen fibres of TA are well protected after curcumin treatment except few areas in the tissue and these areas would be evaluated as plaque structures. Protective effects of curcumin in this group were observed since parallel arrangement of collagen fibres are found in the tissue (**Figure 3**).



Figure 4. Immunohistochemical staining for TGF- β 1 in all groups. In the control group, opposed arrows indicate the presence of nonsevere staining. In the PD+Ps group, severe TGF- β 1 expression was observed in Peyronie-like plaques extending over a wide area in the TA. Very slight staining can be seen in the areas at the ends of the arrows in the PD+Cur group. Sections were cross-stained with Mayer's hematoxylin. Arrows; TGF- β 1 expression.

Immunohistochemistry

Sections were immunostained for TGF- β 1 expression in the TA. Positive areas for TGF- β 1 were negligible in the Control and PD+Cur groups, but severe staining was observed in the PD+Ps group (**Figure 4**).

Discussion

PD was once considered a rare entity but is now known to be more common. Although the etiology of the disease is not fully understood, it is thought to be related to trauma resulting in abnormal wound healing [1].

Various different therapeutic modalities are recommended for PD, including both conservative (oral, topical, and intralesional treatments) and invasive (surgical) measures [1]. Surgical repair is usually performed in the form of penile plication, penile prosthesis, penile plate incision, or excision in men with significant stable penile curvature after the failure of conservative treatment approaches. Risk factors for these procedures typically include penile shortening, erectile dysfunction, and penile numbness. If the primary goal in the treatment of the disease is to correct the curvature, surgery continues to represent the gold standard [1,13]. Surgery should be avoided in the acute inflammatory phase of PD due to the risk of disease progression and recurrence of the curvature [3,14].

Conservative approaches in the treatment of PD include oral agents such as vitamin E, tamoxifen, colchicine, procarbazine, omega-3 fatty acids, potassium para-aminobenzoate (potaba), nonsteroidal anti-inflammatory drugs, L-carnitine, phosphodiesterase type 5 inhibitors, and pentoxifylline. Topical therapies include extracorporeal shockwave treatment (ESWT), topical verapamil, H-100 gel and intralesional treatments such as verapamil, nicardipine, interferon α 2B, collagenase clostridium histolyticum (CCH), and hyaluronic acid and botulinum toxin. However, except for intralesional CCH, none has demonstrated a reliable and definitive clinical benefit [1].

CCH is the first Food and Drug Administration (FDA)approved injectable drug and can be considered a reasonable alternative for patients who are unwilling to undergo surgical treatment [15]. Intralesional collagenase injection has been reported to significantly reduce plaque size and penile curvature. However, there is no evidence that it improves penile pain or erectile dysfunction. Side effects reported in the literature include ecchymosis, swelling, corporal rupture and hematoma related to the use of collagenase [16].

Stem cell and platelet-rich plasma applications are recently developed non-invasive therapeutic options, and promising results have been reported. However, despite their promising potential, their clinical efficacy has not yet been proven. Numerous randomized clinical studies investigating their long-term effects are therefore needed [17-19].

Plant-derived products have become increasingly popular in recent years as an alternative to traditional medicines. Phytochemicals isolated from plants are characterized by numerous biological activities, primarily anti-inflammatory in nature. Curcumin, also known as diferuloylmethane, is a lipophilic polyphenol derived from the roots of Curcuma longa (turmeric). It has been widely used in traditional Asian medicine for thousands of years for its anti-inflammatory and wound-healing properties [20]. Curcumin is a compound considered "generally safe" by the FDA. The source of the pharmacological effects of turmeric is mainly bioactive curcuminoids, which include curcumin, demetoxycurcumin, and bisdemethoxycurcumin [21,22].

Curcumin is known to exhibit numerous properties, such as antioxidant, anti-inflammatory, anti-diabetic, anti-apoptotic and antifibrotic activities. Recent studies suggest that curcumin modulates different molecular pathways by acting on various cytokines, transcription factors, growth factors and their associated receptors, thus playing a protective role against cardiac fibrosis [7,23,24]. Curcumin treatment has been reported to reduce inflammatory cells and improve collagen deposition in animal models [25,26]. It has also been observed to be capable of ameliorating pulmonary fibrosis, characterized by infiltration of inflammatory cells, fibrotic tissue deposition and increased collagen content [27].

The normal histological structure of the TA surrounding the penile corpora cavernosa consists of an inner circular and an

outer longitudinally arranged elastin and collagen network. In the pathophysiology of PD, tissue healing is impaired leading to scarring through collagen deposition and decreased elastin, possibly due to acute or repetitive penile trauma [1,28]. In the healing process of impaired tissue, repetitive traumas to the TA cause an increase in pro-fibrotic factors such as TGF- β 1 and platelet-derived growth factor and a decrease in anti-fibrotic factors [29]. TGF- β 1 plays a role in soft tissue fibrosis and erectile dysfunction. It is synthesized as an inactive peptide by various cell types including platelets, macrophages, and fibroblasts. When activated, it binds to specific cell surface receptors, resulting in increased connective tissue synthesis and inhibition of collagenases [29,30].

Stereological analyses in the present study revealed that the numerical data for fibrous plaque areas in the control and PD+Cur groups were close to one another, although there was a significant difference between them and the PD+Ps group. Electron microscopic evaluation of the tissues taken from the groups supported the stereological analysis, since few number of plaque structures in the PD+Cur group in comparison of the PD+Ps group. Immunohistochemical analyses revealed intense TGF- β 1 expression in the PD+Ps group. In contrast, a small amount of positive staining was observed in the TA in the PD+Cur group. In light of all these data, it may be concluded that curcumin may play a potential role in the treatment of PD by exhibiting anti-fibrotic activity.

Conclusion

Pharmacotherapeutic approaches are not yet effective or widely accepted in the treatment of PD. Surgical removal of plaque or the installation of penile prostheses continues to be considered the mainstay of treatment. Curcumin, a plant-derived compound, reverses the effect of pro-fibrotic factors by affecting the expression and activation of various intracellular molecules. Curcumin treatment in this study reduced TA fibrosis in an experimentally induced rat PD model. Our results suggest that curcumin may represent a new oral therapeutic option in the treatment of PD. Although our findings are promising and suggest a possible oral medical treatment for PD, further studies are needed on the subject.

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Ethics Committee Approval: The experimental protocol adopted in the current study was approved by the Ondokuz Mayıs University, Animal Care and Ethics Committee (HADYEK no. 2018-29-dated 25.05.2018).

Informed Consent: An informed consent was obtained from all the patients.

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– M.U., A.K.; Literature Search – A.A.K., K.K.T., E.A.; Writing Manuscript – M.U., A.K.; Critical Review – M.U., S.K.

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Investigation of the Relationship between Prostate Weight and Clinical Outcomes in Retzius-Sparing Robot-Assisted Radical Prostatectomy

Retzius Koruyucu Robot Yardımlı Radikal Prostatektomide Prostat Ağırlığı ile Klinik Sonuçlar Arasındaki İlişkinin Araştırılması

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Abstract

Objective: To examine the relationship between prostate weight and oncological and functional outcomes of Retzius-sparing robot-assisted radical prostatectomy (RS-RARP).

Materials and Methods: Data of the patients who underwent RS-RARP in our clinic between December 2018 and December 2020 were evaluated retrospectively. A total of 106 patients with 12-month postoperative follow-up data were included in the study. The patients were separated into 2 groups according to the weights of the pathology specimens as Group 1 (n=53, prostate weight less than 50 g), and Group 2 (n=53, prostate weight more than 50 g). Postoperative oncological and functional data were analyzed. At the end of the 12th month, continence was regarded as requirement of no pad or 1 pad per day. Potency was considered as the ability to have sexual intercourse. Prostate-specific antigen (PSA) above 0.2 ng/ml in the follow-up period was considered as biochemical recurrence.

Results: Preoperative PSA levels were comparable between groups (9.78+7.84 ng/ml vs. 11.87+8.38 ng/ml). There was no difference in clinical cancer stages and The International Society of Urological Pathology (ISUP) scores between the groups. Median vesicourethral anastomosis time (30 minvs.33 min) and median operative time (240 min vs. 240 min) were comparable in both groups (p>0.05). There was no difference in localized disease and locally advanced disease rates between the groups (pT2: 58.5% vs. 67.9%, pT3: 41.5% vs. 32.0%). Surgical margin positivity (SMP) ([16.9% (n=9) vs 9.4% (n=5]), and 12th month biochemical recurrence rates (11.32% vs 3.77%) were similar in groups 1 and 2 (p>0.05). Postoperative urinary continence rates at 12 months were 89% and 90% in Groups 1 and 2, respectively (p>0.05). Continence status was not different between the groups. Potency rates at 12 months were comparable between the groups.

Conclusion: RS-RARP can be applied in patients with any size of prostates with comparable functional and oncological outcomes.

Keywords: Retzius-sparing, prostate weight, robotic, prostatectomy, potency, urinary continence

Öz

Amaç: Retzius koruyucu robot yardımlı radikal prostatektominin (RS-RARP) onkolojik ve fonksiyonel sonuçları ile prostat ağırlığı arasındaki ilişkiyi araştırmak.

Gereçler ve Yöntemler: Aralık 2018 ile Aralık 2020 tarihleri arasında kliniğimizde RS-RARP uygulanan hastaların verileri retrospektif olarak değerlendirildi. Ameliyat sonrası 12 aylık takip verileri toplanan 106 hasta çalışmaya dahil edildi. Hastalar patoloji örneklerinin ağırlığına göre 2 gruba ayrıldı (Grup 1, n=53, prostat ağırlığı 50 gramdan az ve Grup 2, n=53, prostat ağırlığı 50 gramdan fazla). Ameliyat sonrası onkolojik ve fonksiyonel veriler analiz edildi. 12. ayın sonunda kontinans hiç ped kullanmama veya günde 1 ped kullanma olarak kabul edildi. Potens cinsel ilişkiye girebilme yeteneği olarak kabul edildi. Takip döneminde prostat spesifik antijen (PSA)'nın 0.2 ng/ml'nin üzerinde olması biyokimyasal nüks olarak kabul edildi.

Bulgular: Ameliyat öncesi PSA düzeyleri gruplar arasında benzerdi (9.78+7.84 ng/ml ve 11.87+8.38 ng/ml). Gruplar arasında klinik kanser evreleri ve Uluslararası Ürolojik Patoloji Derneği (ISUP) skorları açısından fark yoktu. Median vezikoüretral anastomoz süresi (30 ve 33 dk) ve ameliyat süresi her iki grupta da benzerdi (240 ve 240 min, p>0.05). Gruplar arasında lokalize hastalık ve lokal ileri hastalık oranları açısından fark yoktu (pT2: %58.5'e karşı %67.9, pT3: %41.5'e karşı %32.0). Cerrahi sınır pozitifliği (SMP) oranları Grup 1 ve 2 için sırasıyla %16.9 (n=9) ve %9.4 (n=5), 12. ay biyokimyasal nüks oranları ise %11.32 ve %3.77 idi (p>0.05). Ameliyat sonrası 12. ayda idrar kontinansı Grup1 ve Grup 2'de sırasıyla %89 ve %90 idi (p>0.05). Kontinans durumu gruplar arasında farklı değildi. Gruplar arasında 12. aydaki potens oranları benzerdi.

Sonuç: RS-RARP, benzer fonksiyonel ve onkolojik sonuçlarla her boyutta prostatı olan hastalarda uygulanabilir.

Anahtar kelimeler: Retzius koruyucu, prostat ağırlığı, robotik, prostatektomi, potens, üriner kontinans

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© Copyright 2023 by GJU. @222 Investigation of the relationship between prostate weight and clinical outcomes in Retzius sparing robotic assisted radical prostatectomy by Sahin Kilic is licensed under a <u>Creative Commons Attribution-NonCommercial 4.0 International License</u> which permits unrestricted non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Prostate cancer is a prevalent disease among men, and surgical intervention is often recommended for its management [1]. One of the surgical techniques gaining popularity is Retziussparing robot-assisted radical prostatectomy (RS-RARP). This approach aims to minimize damage to the surrounding structures and improve functional postoperative outcomes [2].

RS-RARP is a technique that involves the robot-assisted removal of the prostate gland while preserving the Retzius space. This approach aims to minimize damage to the surrounding nerves and tissues, leading to improved functional outcomes [3,4].

Prostate size is a special condition that requires surgical experience during the removal of the prostate in patients who underwent RARP [5]. There are limited studies on the impact of prostate size on post-RS-RARP oncological and functional outcomes. In this study, we aimed to examine the influence of prostate weight on post-RS-RARP oncological and functional outcomes [6,7].

Materials and Methods

After obtaining the local ethics committee approval (Antalya Training and Research Hospital Ethics Committee (2023/07-17), we retrospectively included 106 patients who underwent RS-RARP between December 2018 and December 2020 in our study. Clinical data, perioperative variables, and postoperative follow-up data were collected for analysis. All surgeries were applied using the da Vinci[®] Robotic Surgical System (Xi, USA). RS-RARP was conducted via the transperitoneal approach.

The patients were separated into 2 groups according to the weight of the pathology specimens. Group 1 included patients with prostate specimens weighing less than 50 grams. Group 2 comprised of patients with prostate specimens weighing more than 50 grams.

Erectile function and continence status were evaluated at the end of the 12th month. No pad or only one pad usage per day was considered as continence. An erection sufficient for sexual intercourse was considered as potency. A prostate-specific antigen (PSA) value above 0.2 ng/ml in follow-up period was regarded as biochemical recurrence.

Statistical Analysis

SPSS version 22.0 for Windows software (SPSS, Chicago, IL, USA) program was used. The Shapiro-Wilk test was performed to determine normality of distributions for continuous variables. Normally distributed continuous variables were compared with the Student's t-test and non-normally distributed variables with the Mann-Whitney U test. Pearson's chi-square or Fisher's exact test was used for the analysis of categorical data. Normally distributed continuous variables were expressed as mean plus standard deviation (SD) and non-normally distributed variables as median. Categorical variables were expressed as numbers and percentages. P<0.05 was accepted as the the level of statistical significance.

Results

Table 1. Preoperative characteristics of the patients

		Group 1 (n=53)	Group 2 (n=53)	Р
Age (years)		65.72 <u>+</u> 5.32 (51-75)	66.45 <u>+</u> 6.35 (49-79)	>0.05
BMI (kg/m2)		26.12 <u>+</u> 3.51	27.18 <u>+</u> 3.52	>0.05
Preperative PSA (ng/ml)		9.78 <u>+</u> 7.84 (2.4-55)	11.87 <u>+</u> 8.38 (1.15-48)	0.084
Clinic cancer stage (n, %)	T1	41 (77.3)	47 (88.6)	0.121
	T2	12 (22.6)	6 (11.3)	0.121
Potent patients ratio at preoperatif period (n, %)	1	35 (66.0)	37 (69.8)	0.676
Prostate biopsy ISUP score (n, %)	1	25(47.1)	32 (60.3)	
	2	16 (30.1)	12 (22.6)	
	3	7 (13.2)	1 (1.9)	0.131
	4	3 (5.7)	6 (11.3)	
	5	2 (3.8)	2 (3.8)	

BMI: body mass index; ISUP: international society of urological pathology

The median age of the patients was 65.72 ± 5.32 (51-75) years and 66.45 ± 6.35 (49-79) years for Groups 1 and 2, respectively. There was no significant difference between Groups 1 and 2 in terms of age, BMI, preoperative PSA levels, clinical T stages, ISUP scores, and potency rates. The preoperative characteristics of the patients are summarized in **Table 1**.

Surgical margin positivity (SMP) rates were found as 16.9% (n=9) and 9.4% (n=5) in Groups 1 and 2, respectively (p=0.390). The twelfth month biochemical recurrence rates were 11.32% and 3.77% for Groups 1 and 2, respectively without any statistically significant intergroup difference (p=0.270).

There was no significant difference between Groups 1 and 2 in terms of pathological T stage, ISUP scores, lymphadenectomy, and lymph node positivity rates. Main oncological results are summarized in **Table 2**. At 12 months, there was no significant difference between Groups 1 and 2 in terms of potency and continence rates (**Table 3**).

Discussion

In this study, we aimed to invesigate the influence of RS-RARP on postoperative oncological and functional outcomes. There are few studies on this topic in the literature. Oncological outcomes, such as SMP and biochemical recurrence, are crucial in assessing the long-term success of RS-RARP. Several studies

		Group1 (n=53)	Group 2 (n=53)	Р
12th month PSA (n	ng/ml)	0.026 <u>+</u> 0.06	0.018 <u>+</u> 0.04	0.034
Patological T	T2	31(58.5)	36(67.9)	0.214
stage (n, %)	Т3	22 (41.5)	17 (32.0)	0.314
	1	14(26.4)	28 (52.8)	
Specimen ISUP score (n, %)	2	22 (41.5)	18 (33.9)	
	3	7 (13.2)	2 (3.8)	0 046
	4	5 (9.4)	2 (3.8)	0.040
	5	5 (9.4)	3 (5.7)	
Lymphadenectomy (n, %)		23 (43.3)	16 (30.1)	0.159
Lymph node positivity (n, %)		7 (13.2)	3 (5.7)	0.480

ISUP: international society of urological pathology

Table 3. Functional	l results of the patients
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	Group 1 (n=53)	Group 2 (n=53)	Р
Urinary continency at 12th month (n, %)	47 (88.6)	48 (90.6)	0.750
Potent patients ratio at postoperative 12th month (n, %)	15 (28.3)	14 (26.4)	0.172

have explored the impact of prostate volume on these outcomes.

Santok et al. analyzed 294 patients who underwent RS-RARP. They divided the patients into three groups based on estimated prostate volume by transrectal ultrasonography and compared surgical outcomes between the groups. They found that there was no significant difference in terms of biochemical recurrence rates among patients with different prostate volumes [8]. Similarly, Galfano et al., analyzed 750 patients undergoing RS-RARP in three groups according to post-RP prostate specimen weights (<40 g, 40-60 g, >60 g). They reported comparable surgical margin positivity rates in prostate cancer cases, regardless of prostate volume [9]. Our study design has also taken weights of pathology specimens of prostate into consideration. There was no significant difference in ISUP scores of patients categorized regarding the weights of pathology specimens of prostates as Groups 1 and 2.

In addition, pathologic T stages, SMP and biochemical

recurrence rates were comparable between Groups 1 and 2, regardless of prostate volume. However, in our study the mean of postoperative 12th-month control PSA levels were lower in the large prostate group. These findings indicate that prostate volume does not appear to have a significant influence on post-RS-RARP oncological outcomes.

Xu et al. conducted a comparative study between RS-RARP and conventional RARP. The study found that RS-RARP had better early continence recovery rates compared to conventional RARP. However, there were no significant differences between both groups in terms of continence rates during the followup period [10]. Zorn et al. reported no difference between continence rates regardless of prostate volume in patients who had undergone conventional RARP [11]. Although prostate volume seems to significantly affect perioperative surgical dynamics in RS-RARP studies, no effect of prostate weight on late-term continence rates was found in our study [12].

A multivariate analysis of prospective randomized controlled trials performed on 139 conventional RARP patients have shown that only smaller prostate volume was predictive of potency. In addition, lower prostate weight was the only factor found to be correlated with early return of potency [13]. Although, the relationship between prostate weight and early-term potency rates was not evaluated in our study population of RS-RARP patients, potency rates in the long-term did not differ between the groups.

The main limitations of our study were its retrospective and non-randomized design in addition to its small-scale patient population. In order to avoid bias in patient selection in our study, patients were included chronologically starting from the first date of RS-RARP surgery in our clinic to the present. In the future, a prospective study with a higher number of patients who underwent RS-RARP is planned as the second phase of the study.

Conclusion

RS-RARP can be performed regardless of prostate weight in patients with small- or large-sized prostates with similar oncological and functional outcomes.

Ethics Committee Approval: The study was approved by the Health Science University Antalya Training and Research Hospital Ethics Committee (Approval date and no: 25.05.2023/7-17)

Informed Consent: An informed consent was obtained from all the patients.

Publication: The results of the study were not published in full or in part in form of abstracts.

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Comparison of Fixed and Ramping Voltage Extracorporeal Shockwave Lithotripsy with Acute Kidney Injury Biomarkers: Prospective Randomized Clinical Study

Akut Böbrek Hasarı Biyobelirteçleri ile Sabit ve Artan Voltajlı Ekstrakorporeal Şok Dalga Litotripsinin Karşılaştırılması: Prospektif, Randomize Klinik Çalışma

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Abstract

Objective: To compare extracorporeal shock wave lithotripsy (ESWL) induced renal injury in patients undergoing different ESWL treatment protocols by measuring urinary tissue metalloproteinase-2 inhibitor (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7) excretion.

Materials and Methods: This prospective, randomized study was conducted between April 2016 and June 2016 in group 1 patients undergoing fixed voltage ESWL and group 2 patients undergoing ramping voltage ESWL. Urinary TIMP-2 and IGFBP7 levels were analyzed before ESWL and 2 hours after ESWL, and urinary beta-2-microglobulin (β 2-MG) and albumin were analyzed before ESWL and 1 week after ESWL to assess renal injury. The primary outcome was to compare the effect of ESWL on early renal injury with biochemical markers in the different treatment protocols, and the secondary outcome was to compare the two treatment protocols in terms of stone free rate and complications.

Results: There was no statistically significant difference between groups in terms of demographic and stone characteristics. There were statistically significant differences in serum creatinine and e-GFR at baseline and one week after treatment (p<0.05). There was no significant change in serum urea, urinary β 2-MG and albumin levels before and after ESWL. There was a statistically significant increase in urinary TIMP-2, IGFBP7 and TIMP-2 x IGFBP7/1000 levels in both groups compared to baseline (p<0.05). There was no statistically significant difference in the rates of stone free and complications between the groups (p<0.05).

Conclusion: In this prospective randomized study, we observed a significant increase in TIMP-2, IGFBP7 and combination levels after ESWL treatment in both groups, suggesting that these two biomarkers could be used to identify acute kidney injury due to ESWL. However, the comprehensive evaluation of clinical parameters and urinary markers did not differ in the rates of renal injury, success, and complications after ESWL in both protocols.

Keywords: extracorporeal shock wave lithotripsy, urolithiasis, acute kidney injury, biomarker

Öz

Amaç: Ekstrakorporeal şok dalga litotripsi (ESWL) ile indüklenen böbrek hasarını, üriner doku metalloproteinaz-2 inhibitörü (TIMP-2) ve insülin benzeri büyüme faktörü bağlayıcı protein 7 (IGFBP7) atılımını ölçerek farklı ESWL tedavi protokolleri uygulanan hastalarda karşılaştırmak.

Gereçler ve Yöntem: Bu prospektif randomize çalışmaya Nisan 2016 - Haziran 2016 tarihleri arasında sabit voltaj ile ESWL uygulanan hastalar Grup 1, artan voltaj ile ESWL uygulanan hastalar ise Grup 2 olmak üzere toplamda 88 hasta alındı. ESWL'den önce ve 1 hafta sonra üriner beta-2 mikroglobulin (β2-MG) ve albumin, ESWL'den önce ve 2 saat sonra üriner TIMP-2 ve IGFBP7 düzeyleri böbrek hasarını değerlendirmek için analiz edildi. Birincil sonlanım noktası farklı tedavi protokollerinde ESWL'nin erken dönem böbrek hasarına etkisinin biyokimyasal belirteçlerle karşılaştırılması, ikincil sonlanım noktası ise iki farklı tedavi protokolünün taşsızlık oranı ve komplikasyonlar açısından karşılaştırılması olarak belirlendi.

Bulgular: Gruplar arasında demografik özellikler ve taş karakteristikleri açısından istatistiksel olarak anlamlı fark saptanmadı. Grup 1'in başlangıç ile bir hafta sonraki serum kreatinin ve e-GFR değerleri arasında istatistiksel olarak anlamlı bir fark saptandı. (p<0.05). ESWL'den önce ve sonra serum üre, idrar β 2-MG ve albumin düzeylerinde anlamlı bir değişiklik izlenmedi. Her iki grupta da idrar TIMP-2, IGFBP7 ve TIMP-2 x IGFBP7/1000 düzeyleri başlangıça göre istatiksel olarak anlamlı bir artış gösterdi (p<0.05). Gruplar arasında taşsızlık ve komplikasyon oranları arasında istatiksel olarak anlamlı bir fark saptanmadı (p>0.05).

Sonuç: Bu prospektif, randomize çalışmada her iki grupta ESWL tedavisi sonrası TIMP- 2, IGFBP7 ve kombinasyon düzeylerinde anlamlı artış olduğunu izledik, bu durum ESWL'ye bağlı akut renal hasarın belirlenmesinde, bu iki biyobelirteçin kullanılabileceğini göstermiştir. Bununla birlikte klinik parametreler ve üriner belirteçlerin kapsamlı bir şekilde değerlendirilmesi, her iki protokolde ESWL sonrası böbrek hasarı, başarı ve komplikasyon oranlarında farklılık göstermemiştir. Anahtar kelimeler: ekstrakorporeal şok dalgası litotripsi, ürolitiyazis, akut böbrek hasarı, biyobelirteç

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Introduction

Extracorporeal shock wave lithotripsy (ESWL) has been used successfully for many years in the minimally invasive treatment of upper urinary tract stone disease. Although ESWL is considered a minimally invasive treatment, it has been shown to cause various short- and long-term structural and functional changes in the kidney. Short-term renal damage may be due to vascular or tubular mechanical trauma or oxidative stress due to free radical formation causing ischemia-reperfusion injury in the renal capillary system. ESWL may cause acute kidney injury (AKI) by causing peritubular vessel rupture, ischemia, hemorrhage, inflammation and hemodynamic disturbance [1,2].

Potential renal injury after ESWL has been studied using many biochemical parameters. Markers such as serum creatinine and lactate dehydrogenase have been studied in the blood, and markers such as microalbumin, albumin and β 2-microglobulin (β 2-MG) have been studied in the urine to indicate tubular damage [2]. However, there is no clear biomarker that can provide clinicians with an early and accurate indication of kidney injury following ESWL.

Recently, several new biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, interleukin-18 (IL-18), kidney injury molecule-1 (KIM-1) have been studied in the detection of kidney injury after ESWL. Some of these biomarkers are indeed superior to others for early diagnosis. However, follow-up studies have shown that most of them are not specific for AKI [2,3].

In recent years, new potential biomarkers for the early detection of AKI have been identified. The most prominent are tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulinlike growth factor binding protein 7 (IGFBP7). Both molecules have been shown to prevent renal tubular cell division in the G1 phase of the cell cycle by arresting the G1-S cell cycle in sepsis and ischemia. Because of all these proven effects, TIMP-2 and IGFBP7 are currently considered to be two promising biomarkers for the identification of AKI [3,4].

Several strategies with different treatment protocols have been used to improve the efficacy of ESWL in the treatment of urolithiasis and to minimise renal damage [5]. In porcine models, a stepwise increase in voltage has been shown to significantly reduce the size of renal parenchymal haemorrhagic lesions [6]. To date, clinical evidence in humans has only come from studies with small numbers of participants and/or suboptimal study design. Despite these negative factors, these studies suggest that stepwise ramping ESWL treatment is safe and may even provide a protective effect compared to conventional fixed voltage [7-9]. However, there are conflicting data regarding the effect of different voltage applications in ESWL treatment on clinical efficacy and complications [10-13].

In our study, urinary TIMP-2 and IGFBP7, which are used to determine AKI, are investigated for the first time in ESWL treatment. In our study, we aimed to compare the effect of ESWL treatment on AKI in patients undergoing ESWL in different treatment protocols using biomarkers of AKI and to compare these two treatment protocols in terms of success and complications.

Materials and Methods

Between April 2016 and June 2016, a total of 88 patients who underwent ESWL treatment for the first time with a diagnosis of kidney stones at Bakırköy Dr. Sadi Konuk Health Application and Research Centre were included in the study.

Patients were randomized into two groups: group 1: constant, conventional, fixed -voltage protocol and group 2: escalating, stepwise ramping voltage protocol using an online-based computer programme.

Inclusion criteria were: age older than 18 years, unilateral radiopaque kidney stones and no previous ESWL treatment. Exclusion criteria were: age younger than 18 years, bleeding tendency, positive urine culture, uncontrolled hypertension, use of nephrotoxic drugs, autoimmune disease, polycystic kidney disease, congenital renal malformations, musculoskeletal disorders, ureteral stent, or nephrostomy catheter. None of the patients in the study had obstruction below the level of the stone in the urinary tract, obstruction at the level of the stone or uremia.

After obtaining informed consent to participate in the study, complete blood count, biochemical parameters, coagulation test, serological tests and urine culture were prospectively evaluated for each patient before ESWL. All patients underwent radiological evaluation before and after ESWL by kidney ureter bladder (KUB) X-ray, urinary tract ultrasonography (USG) and non-contrast spiral computed tomography (CT). Stone size was calculated in millimeters based on the longest axis.

Routine biochemical tests including creatinine (mg/dL), urinary β 2-MG (mg/L) and albumin (mg/dL) before and one week after ESWL in all patients, urinary TIMP-2 (ng/mL) and IGFBP7 (ng/mL) levels before and two hours after ESWL were prospectively analyzed to assess kidney injury. Estimated glomerular filtration rate (e-GFR) was calculated from serum creatinine levels using the Modification of Diet in Renal Disease Study Equation (MDRD) [14].

The degree of stone fragmentation at 3 months after ESWL was categorized by CT: stone-free, <2 mm, 2-5 mm and >5 mm in 4 groups. Success was defined as complete stone-free. All radiographic images were evaluated by the same radiologist and urologist to minimize interobserver variability. Clavien-Dindo classification was used in the evaluation of complications [15].

Both groups were compared in terms of demographic data [age, gender, body mass index (BMI)], stone characteristics [size, localization, Hounsfield unit (HU), stone skin distance (SSD)], ESWL treatment data (success and complication rates) and changes in serum and urinary biomarkers.

The primary endpoint of the study was to compare the effect of ESWL on early renal damage in different treatment protocols using biochemical markers, and the secondary endpoint was to compare two different treatment protocols in terms of stone-free rate and complications.

Ethical committee approval number 2016-110 was obtained from Bakırköy Dr. Sadi Konuk Health Application and Research Centre, Ethical Committee. In addition, funding for this study was obtained from the Bakırköy Dr.Sadi Konuk Health Application and Research Centre Education Planning Board.

ESWL Protocol

Group 1 (constant, conventional, fixed) received 2000 shock

waves at 18 kilovolts (kV) energy, 1 Hz frequency, and group 2 (escalating, stepwise ramping) received a total of 2000 shock wave lithotripsy protocols at 1 Hz frequency, increased by 500 shock waves at 12-14-16-18 kV energy steps.

ESWL was performed in a single session in the supine position using a triple focus F3 ($3.5 \times 16 \text{ mm} / 4.0 \times 25 \text{ mm} / 6.0 \times 30 \text{ mm}$), piezoelectrolytic lithotripter, Wolf Piezolith- 3000 (Richard Wolf GmbH, Knittlingen, Germany). All ESWL treatments were performed by a single urologist. In most cases, a combination of ultrasound and fluoroscopy was used to target the stone.

Serum and Urine Analyses

Urine samples were immediately centrifuged at 2000 xg for 10 minutes. Aliquots of the urine supernatant were stored at -80°C for analysis. Urinary levels of TIMP-2 and IGFBP7 were assessed by ELISA. TIMP-2, IGFBP7 were analyzed using a human TIMP-2, IGFBP7 ELISA kit (YHB3004Hu, YHB3609 Hu, respectively) purchased from Shanghai Yehua Biological Technology (YHB, Shanghai, China) according to the manufacturer's instructions. Levels were expressed as ng/mL. The combination of TIMP-2 and IGFBP7 was expressed as TIMP-2 x IGFBP7/1000 and its level was expressed as ng²/mL². The intra-assay coefficient of variation of TIMP-2 and IGFBP7 was 10% and 12% respectively. Urine β 2-MG was analysed by particle-enhanced immunonephelometry using the BNII system. The upper limit of the reference range for urine is 0.2 mg/L.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software was used for statistical analyses. In addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum), the Student t test was used for between-group comparisons of normally distributed quantitative data, and the Mann-Whitney U test was used for comparisons of non-normally distributed variables. Paired-sample t-test was used for within-group comparisons of normally distributed parameters, and Wilcoxon signed-ranks test was used for within-group comparisons of non-normally distributed parameters. Pearson's chi-squared test, Fisher's Freeman-Halton test, Fisher's exact test and Yates' continuity correction test were used to compare qualitative data. Significance was assessed at the p<0.05 level.

Results

Of the 88 patients who participated in the study, 45.5% (n=40) were male and 54.5% (n=48) were female. The age of the patients ranged from 18 to 66 years with a mean age of 42.60 ± 11.71 years. There was no statistically significant difference between the groups for age, gender and BMI measurements (p>0.05). No statistically significant difference was found between the groups regarding side, location, multiple stone status, stone size, stone density, SSD (p>0.05). Demographic data and stone characteristics are shown in **Table 1**.

In group 1, a statistically significant difference was found between creatinine and e-GFR measurements before ESWL and creatinine and e-GFR measurements after ESWL (p=0.001, p=0.001, p<0.01, respectively). In group 1, no statistically significant difference was found between urea, β 2-MG and albumin measurements before ESWL and urea, β 2-MG and

 Table 1. Data on demographic characteristics and stone

 characteristics by groups

Creare		Group 1	Group 2	Р
Group		(n=44)	(n=44)	value
Age	Min-Max (Median)	18-66 (47)	20-66 (43)	ª0.257
(years)	Mean±SD	44.02±12.83	41.18±10.42	
	Male	21 (47.7)	19 (43.2)	
Condor	Female	23 (52.3)	25 (56.8)	
n (%)	Min-Max (Median)	19.1-44.4 (25.3)	19-27.8 (25.5)	^b 0.830
	Mean±SD	25.90±4.10	25.02±1.84	
Side; n	Left	24 (54.5)	22 (50.0)	h0 021
(%)	Right	20 (45.5)	22 (50.0)	0.831
	Pelvis	24 (54.5)	19 (43.2)	
Location;	Upper	7 (15.9)	6 (13.6)	c0 126
n (%)	Middle	8 (18.2)	15 (34.1)	0.420
	Lower	5 (11.4)	4 (9.1)	
Number	Single	40 (90.9)	35 (79.5)	^b 0.229
of stones; n (%)	Multiple	4 (9.1)	9 (20.5)	
	<5 mm	1 (2.3)	4 (9.1)	
Stone	5-10 mm	23 (52.3)	19 (43.2)	°O 484
(%)	10-20 mm	18 (40.9)	20 (45.5)	0.404
	>20 mm	2 (4.5)	1 (2.3)	
Stone	<1000 HU	27 (61.4)	23 (52.3)	
density; n (%)	>1000 HU	17 (38.6)	21 (47.7)	^b 0.519
SSD	Min-Max (Median)	4.4-14.4 (8.4)	6-15 (8.9)	^a 0.673
	Mean±SD	8.76±2.06	8.94±1.92	

^aStudent-t Test; ^bYates' continuity correction test; ^cFisher Freeman Halton test; SD: standart deviation; HU: Hounsfield unit; SSD: stone-to-skin distance

albumin measurements after ESWL (p=0.455, p=0.317, p=0.414, respectively). In group 2, no statistically significant difference was found between creatinine, e-GFR, urea, β 2-MG and albumin measurements before ESWL and creatinine, e-GFR, urea, β 2-MG and albumin measurements after ESWL (p=0.053, p=0.074, p=0.781, p=0.564, p=0.074, respectively p>0.05). Data on the measurement of laboratory markers of the groups are shown in **Table 2** and **Table 3**.

In group 1, the difference of 1.26 ± 2.49 units between IGFBP7 concentration measurements before ESWL and IGFBP7 concentration measurements after ESWL was statistically significant (p=0.001; p<0.01). In group 2, the difference of 1.07 ± 1.95 units between IGFBP7 concentration measurements before ESWL and IGFBP-7 concentration measurements after ESWL was statistically significant (p=0.001; p<0.01). In group 1, the difference of 12.89 ± 52.50 units between TIMP-2 concentration measurements before ESWL and TIMP-2

Table 2. Evaluations	related to	biochemical	measurements
according to groups			

	Group 1	Group 2	Р	
	(n=44)	(n=44)	value	
	Min-Max	Min-Max		
	(Median)	(Median)		
	Mean±SD	Mean±SD		
Creatinine before	0.4-1.1 (0.8)	0.5-1.1 (0.8)	a0 876	
ESWL	0.78±0.18	0.77±0.16	0.870	
Creatinine after	0.5-1.2 (0.8)	0.4-1.3 (0.8)	a0 188	
ESWL	0.85±0.19	0.80±0.19	0.100	
°р	0.001**	0.053		
Urea before	14-96.3 (28)	15-45.9 (25.9)	f0.075	
ESWL	29.82±12.98	25.66±6.29	0.075	
Uroo ofter ESWI	18-85 (29.5)	14.8-52.6 (25)	f0 011*	
Utea atter ESWL	30.38±10.91	25.64±7.54	0.011	
^g p	0.455	0.781		
	60.5-149.3	73-129.8		
e-GFK before	(102.1)	(108.9)	a0.232	
LOWL	103.70±17.30	107.68±13.41		
a CED after	51.9-146.8	7.9-135.8		
e-GFR alter	(98.8)	(106.6)	a0.194	
LOWL	97.51±19.50	103.11±20.61		
^e p	0.001**	0.074		
Albumin before	0.1-80 (4)	0-76.4 (2.1)	f0 400	
ESWL	9.85±16.89	8.12±14.99	0.409	
Albumin after	0.2-54.7 (2.3)	0.1-17.1 (2.5)	f0 445	
ESWL	7.56±12.23	4.20±4.53	0.443	
^g p	0.414	0.074		

^aStudent-t Test; ^ePaired Samples t Test; ^fMann-Whitney U Test; ^gWilcoxon Signed Rank test; *p<0,05; **p<0,01; ESWL: extracorporeal shock wave lithotripsy; e-GFR: estimated glomerular filtration rate

Table 3. Evaluation of Beta-2 microglobulin (β2-MG)

measurements according to groups

		Group 1 (n=44)	Group 2 (n=44)
		n (%)	n (%)
β2-MG before ESWL	<0.21	43 (97.7)	42 (95.5)
	>0.21	1 (2.3)	2 (4.5)
β2-MG after ESWL	<0.21	41 (93.2)	43 (97.7)
	>0.21	3 (6.8)	1 (2.3)
	^g p	0.317	0.564

^gWilcoxon Signed Rank test; β2-MG: β2-microglobulin; ESWL: extracorporeal shock wave lithotripsy

concentration measurements after ESWL was statistically significant ($p\leq0.05$). In group 2, the difference of 12.81 ± 43.03 units between TIMP-2 concentration measurements before ESWL and TIMP-2 concentration measurements after ESWL was statistically significant (p=0.019; p<0.05).

In group 1, the difference of 0.12 ± 0.31 units between TIMP-2xIGFBP7/1000 concentration measurements before ESWL and TIMP-2xIGFBP7/1000 concentration measurements after ESWL was statistically significant (p=0.001; p<0.01). In group 2, the difference of 0.15 ± 0.27 units between TIMP-2xIGFBP7/1000 concentration measurements before ESWL and TIMP-2xIGFBP7/1000 concentration measurements after ESWL was statistically significant (p=0.001; p<0.01) (**Figure 1**). The results of IGFBP7, TIMP-2 and TIMP-2xIGFBP7/1000 concentration measurements by group are shown in **Table 4**.

When the complication and success rates of both groups were evaluated, no statistically significant difference was found (p: 1.000 and p: 0.606, respectively). The success rate of ESWL treatment was 81.8% in group 1 and 84.1% in group 2. Patients with residual stones underwent additional intervention or surgery. Complications were renal colic (grade 1) in 3 patients, hematuria (grade 1) in 1 patient, pyelonephritis (grade 2) in 1 patient and perirenal hematoma (grade 3a) in 1 patient in group 1. Complications in group 2 were renal colic (grade 1) in 2 patients, hematuria (grade 1) in 2 patients and urinary tract infection (grade 2) in 1 patient. There were no major complications. All complications were managed conservatively (**Table 5**).

Discussion

The mechanism of renal injury after ESWL is still not fully understood. The effects of a transient decrease in renal blood flow, oxidative stress due to the formation of free oxygen radicals resulting from ischemic damage, thermal and cavitation effects, and vascular damage have been implicated as mechanisms [16]. The development of ESWL treatment strategies that reduce or prevent tissue damage and the practical use of sensitive biomarkers that can show the damage that has occurred will help to determine renal damage after ESWL [17].



Figure 1. Distribution of TIMP-2 x IGFBP7 concentration measurements by groups

Table 4. Evaluation of IGFBP-7, TIMP-2 and TIMP-2xIGFBP7/1000 concentration measurements accordingto groups

	Group1 (n=44)	Group 2 (n=44)	P value
	Min-Max (Median)	Min-Max (Median)	
	Mean±SD	Mean±SD	
IGFBP7 Concentration	0.2-10.8 (2.9)	0.4-12.1 (2.9)	^f 0.670
Defote ESWL	3.20±2.09	3.71±2.80	
IGFBP7 Concentration	0.4-9.3 (4.3)	0.5-12.8 (4.3)	^f 0.732
alter ESWL	4.46±2.10	4.78±2.64	
^g p	0.001**	0.001**	
TIMP-2 Concentration	0.8-211.8 (62.8)	0-168.8 (90.5)	^f 0.097
Defote ESWL	65.28±48.13	78.04±46.07	
TIMP-2 Concentration	0-203.2 (72.5)	8.5-189.4 (89.6)	^f 0.169
aller ESWL	78.18±48.64	90.85±48.33	
^g p	0.050*	0.019*	
TIMP-2 x IGFBP7	0-1.2 (0.2)	0-1.4 (0.3)	f0.313
/1000 Before ESWL	0.24 ± 0.26	0.31±0.31	
TIMP-2 x IGFBP7	0-0.9 (0.3)	0-1.3 (0.4)	f0.187
/1000 After ESWL	0.35±0.24	0.46±0.34	
^g p	0.001**	0.001**	

^fMann-Whitney U test; ^gWilcoxon Signed Rank test; *p≤0,05; **p<0,01; TIMP-2: Tissue inhibitor of metalloproteinase-2; IGFBP7: Insulin-like growth factor binding protein 7

Urinary biomarkers have been widely used to assess kidney injury in various clinical settings and can provide earlier and more sensitive detection of kidney injury with good correlation to clinical outcomes. Recently, data have been reported from multicentre studies of the (TIMP2) x (IGFBP7)/1000 combination in critically ill patients. This combination has been validated for risk stratification of moderate to severe AKI associated with cell cycle arrest [18,19] A urine (TIMP2) x (IGFBP7) value >0.3 (ng/ mL) $^{2}/1000$ was found to have >90% sensitivity in predicting the development of moderate to severe AKI within 12 hours [19]. Unlike other new AKI biomarkers that reflect renal cell damage or impaired renal function, these markers are thought to reflect the renal tubular epithelial response [18,20]. (TIMP2) x (IGFBP7) compared to other markers such as NGAL, KIM-1, cystatin C and IL-18, it has been associated with superior results for AKI risk stratification [18]. Similar results were found in a study of patients undergoing cardiopulmonary bypass. Measurement of (TIMP-2) x (IGFBP-7) in urine proved to be a highly sensitive marker of AKI in cardiac surgery patients [21]. In contrast to all these positive data, in another study, in urine samples collected from 94 intensive care unit patients, these biomarkers did not

Table 5. Data on complications and success results

Group 1 (n=44)		Group 2 (n=44)		P value
Complication; n (%)	None	38 (86.4)	39 (88.6)	^b 1.000
	Yes	6 (13.6)	5 (11.4)	
Rest stone size; n (%)	None	36 (81.8)	37 (84.1)	
	<2 mm	1 (2.3)	0 (0)	°0.605
	2-5 mm	6 (13.6)	4 (9.1)	
	>5mm	1 (2.3)	3 (6.8)	

^bYates' Continuity Correction test;

°Fisher Freeman Halton test

differ between patients with and without AKI [22]. In a metaanalysis performed to evaluate the diagnostic accuracy of the urinary (TIMP-2) x (IGFBP7) combination for AKI in adult patients, it was concluded that the urinary (TIMP-2) x (IGFBP7) combination may be a reliable biomarker for the early detection of AKI [23]. In our study, we evaluated these two biomarkers and their combination in the assessment of AKI after ESWL at two hours after ESWL. According to our results, TIMP-2, IGFBP7 and their combination were statistically significantly increased in both groups after ESWL. Based on the data obtained, we believe that these biomarkers can be used to assess AKI after ESWL.

In addition to these new biomarkers, the study evaluated and confirmed the utility of known indicators of kidney function. The basic markers of serum creatinine, urea and e-GFR and urinary albuminuria, another way of assessing kidney damage, were assessed [2]. Serum creatinine and e-GFR levels were statistically significantly higher in group 1 than at baseline. However, it is well known that markers such as urea and creatinine used to monitor kidney function are not reliable enough to detect early kidney damage. However, all these methods are mainly useful for assessing chronic renal failure and show low sensitivity in acute injury processes. There are many studies in the literature evaluating e-GFR and serum creatinine levels before and after ESWL, and most of these studies did not find significant changes in GFR and serum creatinine levels.

In determining tubular damage after ESWL, the increase in urinary low-molecular-weight proteins and renal tubular enzymes other than albumin has also been studied. As β 2-MG is one of the low molecular weight proteins and is completely filtered from the glomeruli, increased urinary excretion is observed in cases of proximal tubule dysfunction [24]. In their study investigating the effect of ESWL on renal tubular damage, Nasseh et al. reported that urinary β 2-MG increased significantly immediately after ESWL. They also highlighted that the likelihood of this damage was higher in patients with hypertension and a history of previous ESWL compared to others [25]. Skuginna et al. found evidence that urinary β 2-MG levels 24 hours after constant and stepwise voltage ramping ESWL were higher in the constant group than in the stepwise voltage ramping group, but the difference between

the changes was not statistically significant (p=0.06) [12]. Lambert et al. found no statistically significant difference between urinary biomarkers before and after treatment in the fixed and escalating voltage ESWL groups. However, they found a significant increase in β 2-MG and microalbumin 1 week after ESWL and suggested that there may be less renal damage in the escalating voltage ESWL group [8]. In our study, no statistically significant difference was found between β 2-MG levels in the two groups.

Although the safety and efficacy of ESWL have been demonstrated in large series studies, serious side effects and complications associated with ESWL can occur. Complications related to ESWL can be seen in acute and chronic periods. When the mechanism of complications is analyzed, they are directly related to shock waves, stone fragmentation, and the effects of stone fragments as they pass through the urinary system. Several studies have shown that ESWL causes acute or chronic renal damage [26]. Most of our knowledge about ESWL damage to the kidney is based on animal studies using invasive methods to assess tissue damage. This damage can take the form of vascular renal injury ranging from self-limited hematuria to perinephric/nephric hematomas. Numerous studies have described various complications including intraparenchymal, subcapsular and perirenal hemorrhage. There is evidence that even short-term exposure to shock waves can cause changes in the renal microvasculature. In addition, hemorrhage can trigger an inflammatory response that can lead to scarring with permanent loss of functional renal volume. In the long term, human and animal studies suggest that these acute hemorrhagic lesions may progress to scarring and complete atrophy of the renal papillae [2]. Complications were renal colic (grade 1) in 3 patients, hematuria (grade 1) in 1 patient, pyelonephritis (grade 2) in 1 patient and perirenal hematoma (grade 3a) in 1 patient in group 1. In group 2, renal colic (grade 1) in 2 patients, hematuria (grade 1) in 2 patients and urinary tract infection (grade 2) in 1 patient. There were no major complications. All complications were treated conservatively. According to the results of our study, there was no statistically significant difference in complications between the two groups.

Treatment protocols have been tried in many animal studies to minimize renal damage in ESWL treatment. Ramp and pause protocols have been observed to reduce damage. Many treatment protocols have been proposed to minimize renal injury. Stepwise voltage ESWL was effective in the treatment of urinary calculi in 31 children with acceptable success rates without morbidity [27]. In another study in humans, no statistically significant difference was found between treatment protocols [10]. The latest metaanalysis in the literature reported that escalating voltage ESWL offers comparable safety and efficacy to constant voltage ESWL [28]. In their prospective randomized study of 150 patients, Rabah et al. Compared constant, escalating and reduction energy ESWL protocols for renal stones. Although the stone-free rate was higher in the constant energy group, no statistically significant difference was found between the groups. In addition, no difference was found between the 3 groups in terms of complications [11]. Similarly, Skuginna et al. reported in their clinical study that a stepwise voltage ramping during ESWL was associated with a lower risk of renal damage compared with a constant maximal voltage without compromising treatment efficacy [12]. In a prospective randomized study of 40 patients, they found no

statistically significant difference in stone fragmentation (75% vs. 72%, respectively) comparing stepwise and constant voltage strategy [13]. Skuginna et al. reached the same result in their study with 418 patients in two groups (stepwise and fixed) and reported this rate as 72.2% versus 74.5% [12]. Demirci et al. compared the results of the two treatment methods 8 weeks after the first treatment and found that the success rate in the stepwise ESWL group was statistically significantly higher than in the conventional group (stone free rate 96% (24/25) and 72% (18/25), p<0.05) [7]. In another study, Lambert et al. Compared stepwise and fixed protocol ESWL treatment in 45 patients and found a statistically significant difference in favour of the stepwise method in terms of both stone fragmentation and less renal tissue damage (81% versus 48%, p=0.03) [8]. In our study, we found no statistically significant difference between the two ESWL treatment protocols in terms of primary and secondary outcomes. In terms of stone free rate, we achieved a stone free rate comparable to other randomized trials and even higher.

Our study has some limitations. These include not comparing TIMP-2 and IGFPB7 levels with GFR and creatinine clearance, and not analyzing long-term outcomes. Another limiting factor is that early renal damage, especially renal perfusion, was not correlated with radiological examination in our study. Larger, prospective, case-controlled studies to further identify patients at risk of renal injury after ESWL may help to confirm our results.

Conclusion

In this prospective, randomized study, a significant increase in TIMP-2, IGFBP7 and combination levels was observed after ESWL treatment with two different protocols. This showed that these two biomarkers can be used to determine acute renal injury in patients undergoing ESWL. In contrast, a statistically significant effect of a stepwise voltage ramping on renal injury compared to a constant maximal voltage was not detected by evaluating urinary TIMP-2 and IGFBP7. Furthermore, no significant difference in treatment efficacy was observed between the two ESWL protocols. More detailed studies including long-term follow-up are needed to determine these early changes in renal physiology due to ESWL with shock waves and the long-term results.

Ethics Committee Approval: The study was approved by the Ethics Committee of Bakırköy Dr. Sadi Konuk Health Application and Research Centre (Approval date, and registration number: 2016-110).

Informed Consent: An informed consent was obtained from all the patients.

Publication: The results of the study were not published in full or in part in form of abstracts.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – K.G.S., F.A.A.; Design – K.G.S., F.A.A.; Supervision – K.G.S., E.G., S.S., V.T.; Resources – A.K., R.T., M.G.Y., E.G.; Materials – A.K., R.T., M.G.Y., E.G.; Data Collection and/or Processing – A.K., R.T., M.G.Y., E.G.; Analysis and/or Interpretation – A.K., R.T., M.G.Y., E.G.; Literature Search – A.K., R.T., M.G.Y., E.G.; Writing Manuscript – K.G.S., F.A.A.; Critical Review – K.G.S., V.T., A.I.T. **Conflict of Interest:** The authors declare that they have no conflicts of interest.

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The Synergistic Effect of Trazodone on the Development of Priapism in the Background of Chronic Myeloid Leukemia

Trazodonun Kronik Miyeloid Lösemi Zemininde Priapizm Gelişimi Üzerindeki Sinerjistik Etkisi

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A 50-year-old male patient was admitted to our emergency department with the complaint of prolonged erection lasting for about three hours without sexual stimulation. As understood from the patient's anamnesis and medical file, he applied to the emergency department with the complaints of fever, lassitude, and fatigability in 2015. His hemogram parameters on admission were: WBC:18.2 x10⁹/L, Hgb: 12.9 g/dl, Htc: 39%, PLT: 379 x10³ K/µL. Besides, his lactate dehydrogenase (LDH) and uric acid values were elevated were found to be high, and he was referred to the hematology clinic with a preliminary diagnosis of leukemia. In the physical examination, any remarkable finding other than splenomegaly was not detected. Microscopic examination of his peripheral blood smear revealed the presence of platelet deformities, megakaryocyte fragments, normocytic normochromic erythrocytes, all cells of myeloid series, markedly increased number of basophils and eosinophils, myelocytes, metamyelocytes, rods and fragmented neutrophils.

It was learned from his medical documents that the patient received the diagnosis of "CML in chronic phase" based on the histopathologic examination reports of the bone marrow aspiration and biopsy specimens obtained for definitive diagnosis, Karyotype analysis revealed the presence of Philadelphia (Ph*) chromosome, and BCR/ABL chimeric gene was detected using PCR and FISH techniques. The patient diagnosed with CML received initial treatment with single daily oral doses of a first-generation tyrosine kinase inhibitor (imatinib 400 mg cap.) and allopurinol (300 mg tb) and he was called for outpatient control. The patient, who claimed that severe muscle and bone pain developed during the imatinib treatment stopped taking the drug by his own decision, so hematology physician started to give him

second generation tyrosine kinase inhibitors in turn (nilotinib and dasatinib). However, it was observed that these drugs also caused severe pancytopenia, and treatment with single daily oral doses of 400 mg imatinib was started again. Still, it was noted that the patient used the drug irregularly, stopped using the drug from time to time and did not routinely attend the hematology outpatient clinics for control.

The patient stated that he had been prescribed trazodone HCl (50 mg/d PO) in another center due to the anxiety he had experienced and had taken the first dose the previous evening. The patient said that he had never experienced a spontaneously prolonged erection before and thought that the cause of the problem developed was related to trazodone tablet he had used for the first time the previous evening. From the anamnesis of the patient, it was learned that he did not use any drugs containing phosphodiesterase-5 (PDE-5) inhibitors. The results of the hemogram test performed when the patient applied to our emergency department were as follows; WBC: 22.2 x10⁹/L, Hgb: 10.9 g/dl, Htc: 30%, and PLT: 579 x10³ K/µL. The patient was admitted to the urology clinic for examination and treatment because of the sustained rigid erection. As the first intervention performed in the urology clinic, an 18G butterfly needle was inserted laterally into both penile corpora cavernosa of the patient to aspirate cavernosal blood. When the erection persisted despite aspiration, intracavernosal irrigation with 0.90% w/v saline was performed, but when detumescence could not be achieved, intracavernosal injection of 2 ml 1/100,000 adrenaline was performed. After the procedure, detumescence was ensured, a CobanTM self-adherent bandage was wrapped around the penis to prevent development of hematoma. The patient was

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Figure 1. Top: Flask penis, Bottom: Erect penis

Corporeal relaxation exerts external pressure on the emissary veins emerging from the tunica albuginea, causing blood to remain in the penis resulting in an erection. https://storymd.com/journal/mpq5pdku6j-penis/page/elqozasy75pq-penis

monitorized for 4 hours, and then discharged. Priapism did not occur again during the follow-up period.

Chronic Myeloid Leukemia (CML) is a stem cell disease manifested by abnormal clonal proliferation of myeloid precursor cells and accounts for 15% of adult leukemias. Its incidence is 1-2/100,000. It is more common in men (male/ female: 1.3/1) and its incidence increases between the ages of 40-60. CML was the first disease in humans to be associated with a specific chromosomal abnormality. In more than 90% of CML cases, the Philadelphia (Ph*) chromosome is detected by cytogenetic analysis [1,2].

Symptoms associated with anemia (such as weakness, fatigue, effort intolerance, decreased functional capacity), splenomegaly (abdominal swelling and pain, rapid satiety due to pressure of enlarged spleen on the stomach) hypermetabolic state (fever, anorexia, weight loss, gout), platelet dysfunction (hemorrhage, ecchymosis, hematoma, thromboembolic events, retinal hemorrhage), hyperleukocytosis and hyperviscosity-related findings (tinnitus, stupor, visual impairment, dyspnea, priapism and cerebrovacular events), thrombocytosis, hypereosinophilia, increase in basophil counts, anemia, elevated LDH and uric acid levels can be seen in CML. Physical examination reveals the presence of splenomegaly in 50-90%, and hepatomegaly in 10-20% of CML patients [1,2].

Priapism is an uncontrolled, prolonged, and sustained erection developing without sexual stimulation and cannot be terminated by ejaculation, (Figure 1). This is a true urological emergency and early intervention is crucial for functional recovery. It has ischemic, non-ischemic and intermittent subtypes. Although often idiopathic priapism is seen, many etiologic factors of priapism are known including hematological diseases (ie. sickle cell anemia, thalassemia, leukemia, multiple myeloma), toxins (ie. scorpion, spider, malaria), metabolic diseases (ie. Fabry disease, amyloidosis), neurogenic diseases (ie. brain tumors, cerebrovascular diseases, spinal cord injury), metastatic or local invasion of tumors (ie. prostate, urethra, testis, lung) and drugs (PDE-5 inhibitors, vasoactive erectile agents such as papaverine, alpha adrenergic receptor agonists, heparin, warfarin, antidepressants, antipsychotics, antihypertensives, testosterone, alcohol, and cocaine) [3].

Imatinib mesylate is the first selective tyrosine kinase inhibitor (TKI) to target the BCR-ABL protein. While nilotinib and dasatinib are second generation tyrosine kinase inhibitors used in the treatment of imatinib-resistant CML. Muscle cramps, joint, muscle or bone pain, which are common imatinib-related side effects, may also occur during imatinib treatment or after its discontinuation [4].

Trazodone HCl is an antidepressant used in the treatment of

symptoms caused by anxiety and depression such as anxiety, appetite disorder, insomnia, and attention deficit. Serotonin reuptake inhibitors (SSRIs) belong to the drug group and its most basic feature is that their effects start to improve symptoms within a short period of about a week.

In addition to common side effects such as blurred vision, headache, dizziness, and severe fatigue, long-term painful erection (not associated with sexual activity) may also occur in men when using trazodone HCl [5]. Although the relevant mechanism is not fully understood, its high affinity for the αl and $\alpha 2$ receptors that trazodone antagonizes is blamed in the pathophysiology [6]. This antagonism causes an increase in blood flow due to arteriolar dilation followed by a decrease in venous flow and obstruction of the emissary veins. In addition, αl blockade may trigger nitric oxide release in nerves innervating arterioles and corpora cavernosa [7]. This whole process results in an erection.

CML is one of the etiologies of priapism and there are multiple relevant case reports in the literature [8,9]. Herein, it has been accepted that priapism develops due to stasis associated with leukocyte aggregation in the corpora cavernosa and penile dorsal vein due to hyperleukocytosis. Another contributing factor to venous occlusion is the mechanical effect of pressure from the abdominal veins draining the spleen. In addition, infiltration into the sacral nerves or central nervous system by leukemia cells is thought to contribute to the process [9].

In our case, remission of the disease could not be achieved because the patient did not regularly use tyrosine kinase inhibitor (TKI) drugs that regulate the leukocyte level of the patient. Despite hyperleukocytosis and hyperviscosity in the bloodstream, which are considered to be the causes of priapism in CML, the patient did not develop priapism. However, priapism, which cannot develop on the basis of CML alone, has been predicted to develop due to the synergistic effect of antidepressant agent trazodone HCL in the pathogenesis.

Keywords: trazodone, chronic myeloid leukemia, priapism, adrenergic effect, alpha adrenergic receptor

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Anuria in a Child Secondary to Rupture due to Ureteropelvic Junction Obstruction in a Solitary Functioning Kidney Following Trivial Trauma: An Incidental Finding

Önemsiz Bir Travma Sonrası Soliter Çalışan Bir Böbrekte Üreteropelvik Bileşim Obstrüksiyonuna Bağlı Rüptüre Sekonder Bir Çocukta Gelişen Anüri: Rastlantısal Bir Bulgu

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Pediatric kidneys are more susceptible to trauma due to poor protective mechanisms due to immature and more pliable thoracic cage, weak abdominal wall musculature and inadequate perirenal fat. Ureteropelvic junction obstruction (UPJO) is one of the most frequently found renal anomaly, and pelvicalyceal (PCS) rupture is a rare presentation whose diagnosis may be delayed due to lack of hematuria and unnoticed trauma. We present a case of child with PCS rupture in solitary functioning right kidney following trivial trauma.

A 6 -year- old male child was referred with complaint of abdominal pain with anuria for 2 days after a small fight with a close friend. Physical examination findings were as follows: abdominal distension with fullness in the right renal fossa, stable vitals, and lack of any urine output on catherization, while he had lower hemoglobin (11.6 mg/dl), and higher serum creatinine (1.8 mg/dl) levels. Whole abdominal ultrasound demonstrated grossly hydronephrotic right kidney with large perinephric fluid collection, absence of left kidney, and empty bladder. Contrast Enhanced Computed Tomography (CECT) of the whole abdomen demonstrated right PCS rupture: grossly dilated right PCS with large perinephric fluid collection extending to the pelvis, absence of the left kidney (Figure 1). Right side USG-guided percutaneous nephrostomy (PCN) was performed under general anesthesia and immediately after 500 ml clear urine was drained. While 24 hrurine output reached up to 1000ml, and serum creatinine levels normalized 3 days later. After 6 weeks, repeat CT urography revealed the diagnosis of right UPJO. Then the patient underwent open Anderson-Hynes dismembered pyeloplasty (Figure 2).

Most children with grade IV/V renal injury following blunt trauma can be managed nonoperatively [1]. Kidneys are affected in 8-10% of the cases exposed to blunt abdominal trauma which is seen twice more commonly in children. Trivial trauma leading to PCS rupture is a rare presentation. This is more common in children with hydronephrotic kidney mostly due to UPJO. High level of suspicion is required as occasionally it manifests minimal symptoms so its diagnosis is delayed. Our patient presented as a case of emergency within 2 days after the traumatic incident due to solitary functioning kidney with anuria. DJ stenting



Figure 1. A-B: Abdominal CECT during initial presentation just after trauma

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Figure 2. C-D: Follow- up CT urography 6 weeks after trauma E: Intraoperative picture of ureteropelvic junction

and PCN insertion are appropriate options for these patients in emergency situation. Sometimes these patients may present with hemodynamic instability requiring immediate exploration. Judicious and early use of minimally invasive interventions, instead of persisting with nonoperative management improve functional outcomes [2].

Conclusion

Symptoms of PCS ruptures are not specific and can mimic several other conditions. So, early recognition with USG and CT scan imaging is a must for diagnosis. PCN insertion or double-J stenting helps restore the normal excretory functions of the urinary tract and resolves urinary extravasation.

Keywords: trauma, ureteropelvic junction obstruction, anuria, percutaneous nephrostomy, pyeloplasty

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