# VENI UROLOJI DERGISI

### The New Journal of Urology



Sezal Z, Tekden BC, Ersöz C, Çoban G. Mixed epithelial and stromal tumor in a young male case with hydronephrotic nonfunctional kidney: Comparison with literature findings. The New Journal of Urology 2022; 17(1):52-57.

### The effect of intracavernosal alprostadil use in erectile dysfunction second line treatment on sexual functions

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### Dear Colleagues,

We are pleased to have published the first issue of The New Journal of Urology for 2022. This issue includes 7 original articles and 2 case reports. Published articles consist of andrology, endourology, transplantation, general urology, pediatric urology and urooncology. We believe that all the current articles will be read with interest and these articles are expected to contribute to the literature and serve as a reference for future studies.

The New Urology Journal has been indexed in the TUBİTAK-ULAKBİM TR Index since the first issue of 2011. The indexing process of our journal in ESCI, Pubmed and EMBASE continues. Our goal is to increase the visibility of our journal both nationally and internationally with articles of high scientific quality and to become one of the most read urology journals. We would like to inform you that as of 2021 only articles in English will be considered for publication.

The editorial team is very grateful to all the authors and reviewers who have contributed to this issue. We are aware that this is a painstaking effort, and we cannot thank you enough for it.

We request that you submit your articles to The New Journal of Urology, take timely and rigorous action as a referee, and read the articles published in the journal and cite them where appropriate.

Respectfully yours.

Ali İhsan TAŞÇI Editor-in-Chief Fatih YANARAL Editor

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Original Research / Özgün Araştırma

# The effect of intracavernosal alprostadil use in erectile dysfunction second line treatment on sexual functions

Erektil disfonksiyon 2.basamak tedavide intrakavernozal alprostadil kullanımının cinsel fonksiyonlar üzerine etkisi

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### Özet

Amaç: Bu çalışmada erektil disfonksiyon nedeniyle ikinci basamak tedavide intrakavernozal alprostadil uygulanarak tedavi edilen hastalarda tedavinin 15 soruluk Uluslararası Erektil Fonksiyon Endeksi (IIEF-15) anketi ile ölçülen cinsel fonksiyonlar üzerine etkisi araştırılmıştır.

Gereç ve Yöntemler: Haziran 2018 - Ekim 2019 arasında erektil disfonksiyon nedeniyle tedavi gören, birinci basamak tedavi modalitelerinden yetersiz yanıt alınan, ikinci basamak tedavide intrakavernozal alprostadil uygulanan ve 12 haftadan daha uzun süre tedaviye devam eden hastaların verileri retrospektif olarak incelenerek 21 hasta çalışmaya dahil edildi. Hastaların yaşları, ek hastalıkları, ilaç kullanım süreleri, ilaca bağlı yan etkiler, uygulama öncesi penil Doppler ultrasonografi (USG) parametreleri ve ilaç kullanımı öncesi ve 12 hafta sonrası ereksiyon fonksiyonları IIEF-15 formu ile değerlendirildi. İntrakavernozal alprostadile 5 µg dozdan başlandıktan sonra doz titrasyonu neticesinde 10 µg dozunda devam edildi.

**Bulgular:** Tedavi öncesi yapılan penil Doppler USG de hastaların ortalama peak sistolik akım hızı (PS) değeri 24,4  $\pm$ 15,1 cm/sn, ortalama end diastolik akım hızı (ED) değeri 4,3 $\pm$ 4,5 cm/sn olarak ölçüldü. IIEF skorları 12. haftada ölçülmesine rağmen ortalama ilaç kullanım süreleri 21,9 $\pm$ 16,6 hafta olarak ölçüldü. Erektil Fonksiyon Skoru uygulama öncesi 9.2 $\pm$ 5.3 iken uygulama sonrası 20.33 $\pm$ 6.2 olarak tespit edildi. Orgazmik İşlev Skoru uygulama öncesi 3,2 $\pm$ 2,5, uygulama sonrası

### Abstract

**Objective:** In patients treated through the application of intracavernosal alprostadil in second-line treatment due to erectile dysfunction, the effect of the treatment on sexual functions measured with a 15-question International Index of Erectile Function (IIEF-15) questionnaire was investigated in this study.

Material and Methods: Twenty-one patients treated due to erectile dysfunction between June 2018-October 2019, taking inadequate response from first-line treatment modalities, were applied intracavernosal alprostadil in second-line treatment and continued it for more than 12 weeks were included in the study, retrospectively. Ages, comorbid diseases, drug usage duration, drug-related side effects, penile Doppler ultrasonography (USG) parameters before application and the erection functions before and 12 weeks after drug use were evaluated with IIEF-15 form for the patients. Intracavernosal alprostadil was started with a dose of 5 µg and was continued with a dose of 10 µg as the result of dose titration.

**Results:** The mean peak systolic blood flow velocity (PS) value of the patients was  $24.4 \pm 15.1$  cm/sec, and the mean end-diastolic flow velocity (ED) value was measured as  $4.3\pm4.5$  cm/sec based on the pre-treatment penile Doppler USG. Although the IIEF scores were measured in the 12th week, mean drug usage durations were measured as  $21.9\pm16.6$  weeks. Erectile Function Score was  $9.2\pm5.3$  before application; it was detected as  $20.33\pm6.2$  after the application. Orgasmic Function Score was  $3.2\pm2.5$  before application; it was

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The study was approved by Ethical Committee of Necmettin Erbakan University Meram Faculty of Medicine (Approval No: 2020/2494). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants. ise 7,5±2,4 olarak tespit edildi. Cinsel İstek Skoru uygulama öncesi 3,72±1,48, uygulama sonrası 8,9±1,4 olarak tespit edildi. Cinsel Memnuniyet Skoru uygulama öncesi 3,7±2,8, uygulama sonrası ise 9,1±2,7 olarak tespit edildi. Genel Memnuniyet Skoru uygulama öncesi 4±1.7 iken uygulama sonrası 8.1±1.7 olarak tespit edildi (Tüm parametreler p<0,001).

**Sonuç:** Erektil disfonksiyon ikinci basamak tedavisinde kullanılan intrakavernozal alprostadil tedavisi IIEF-15 parametreleri ile ölçülebilen cinsel parametrelerde düzelme sağlayan, tolere edilebilir yan etki profiline sahip, kostefektif ve etkin bir tedavi yöntemidir.

Anahtar Kelimeler: Alprostadil, erektil disfonksiyon, intrakavernozal tedavi.

### INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to acquire penile hardness necessary for successful sexual intercourse and continue it even if it is acquired (1).

Different therapeutic agents were developed for ED treatment, and their effect mechanism depends on the understanding of erection physiology. Lifestyle changes and phosphodiesterase type 5 inhibitors (PDE5 inhibitors) as first-line treatment options may be used in ED treatment. PDE5 inhibitors are non-invasive, are generally well-tolerated and efficient in most males. Intracavernosal injections (ICUs) such as alprostadil and Papaverine can be used in 25-50% of patients who are recalcitrant to the treatment and contraindicate PDE5 inhibitors (2-4).

In patients inadequately responding to first-line treatment modalities in erectile dysfunction treatment and targeted to take early rehabilitation after prostatectomy, intracavernosal alprostadil can be used in second-line treatment (2,3). It was observed to be effective in more than 70% of the patients in the general ED population, 94% of the patients could have sexual intercourse after injection, and approximately 90% of the partners were satisfied due to the drug (4,5). International Index of Erectile Function (IIEF-15) questionnaire is a standard questioning form is used to evaluate functions including erectile function, orgasm function, sexual desire, sexual intercourse adequacy, and general satisfaction (2-4).

The effect of treatment on sexual functions measured with IIEF-15 was investigated in patients evaluated for erectile dysfunction, did not benefit from detected as 7.5±2.4 after the application. Sexual Desire Score was 3.72±1.48 before application; it was detected as 8.9±1.4 after the application. Intercourse Satisfaction Score was 3.7±2.8 before application; it was detected as 9.1±2.7 after the application. Overall Satisfaction Score was 4±1.7 before application; it was detected as 8.1±1.7 after the application (All parameters p<0.001).

**Conclusion:** Intracavernosal alprostadil treatment used in erectile dysfunction second-line treatment is a cost-effective and efficient treatment method with a tolerable side effect profile and provides recovery in sexual parameters that can be measured with IIEF-15 parameters.

Keywords: Alprostadil, erectile dysfunction, intracavernosal treatment.

first-line treatment methods, and was treated through intracavernosal alprostadil application in second-line treatment.

### **MATERIAL AND METHODS**

Patients treated in the Urology department of a university hospital due to erectile dysfunction between June 2018 and October 2019 had an inadequate response from first-line treatment modalities and were applied intracavernosal alprostadil in second-line treatment were retrospectively examined. Twenty-one patients who continued the treatment for more than 12 weeks were included in the study. The glucose-lipid and hormone profiles were evaluated. Patients with vascular ED demonstrated by penile Doppler ultrasonography (USG) were included in the study. None of the patients had hormonal ED.

Failure to respond to Tadalafil 5 mg daily for at least 12 weeks was defined as oral therapy failure.

Ages, comorbid diseases, drug usage duration, drug-related side effects, penile Doppler USG parameters before application, and the erection functions before and 12 weeks after drug use were evaluated with IIEF-15 form for the patients.

Doppler USG was performed on all patients with 60 mg Papaverine Hcl. The drug was applied by intracavernosal injection from the 1/3 zone of the penis proximally with a 26-gauge and 2-ml injector. Then, in the fifth, tenth, fifteenth, and twentieth minutes, arterial and venous penis flows were evaluated. Measurements were made with Siemens Acuson S2000, 9 Mhz linear probes.

### **Treatment Protocol**

Alprostadil (Jectera<sup>\*</sup>, Vem Pharmaceuticals, İstanbul, Turkey) application was applied using a 0.5 inch, 27 to 30 gauge needle, avoiding visible veins and injecting in the dorsolateral direction of the proximal third of the penis. alprostadil was started with a dose of 5  $\mu$ g and was continued with a dose of 10  $\mu$ g as the result of dose titration in all patients. IIEF-15 scores before and after the application were compared.

### **Statistical Analysis**

Statistical analysis was performed with SPSS v.23.0 statistical software (SPSS, Inc., Chicago, IL, USA). Quantitative data were given as mean  $\pm$  SD. The Wilcoxon signed Rank Test was used to analyze the relationship between IIEF-15 scores before and after treatment. Kolmogorov-Smirnov test was used to evaluate the normal distribution of the data. The p-value below 0.05 was considered statistically significant.

### RESULTS

The mean age of 21 patients included in the study was 53.8  $\pm$ 11.6 years. Twelve patients (57.1%) had a story of diabetes mellitus (DM), and 4 (19%) had pelvic organ cancer surgery stories. Two patients had a story of radical prostatectomy, one patient had rectum surgery, and one had a radical cystectomy story. Five patients (23.8%) did not have any comorbidities.

Fasting Glucose levels were 91.6±20.3 mg/dL. Total

Table 1. General details of the patients

Testosterone levels were 471.2 $\pm$ 127.5 ng/dl. The Follicle-stimulating hormone (FSH) levels were 8.2 $\pm$ 3.6 mIU/mL, while the Luteinizing hormone (LH) levels were 6.2 $\pm$ 2.4 mIU/mL.

The mean peak systolic blood flow velocity (PS) of the patients was measured as  $24.4 \pm 15.1$  cm/sec, and the mean end-diastolic flow velocity (ED) was measured as  $4.3\pm4.5$  cm/sec based on the pre-treatment penile Doppler USG.

Although the IIEF-15 sub-scores were measured in the 12th week, mean drug usage durations were measured as 21.9±16.6 weeks. General parameters of the patients are available in Table 1.

Two out of 21 patients (9.5%) had penile pain in the application zone, and 2 had (9.5%) priapism after application, and 17 patients (81%) did not have any side effects.

Erectile Function Score was  $9.2\pm5.3$  before application; it was detected as  $20.33\pm6.2$  after the application. Orgasmic Function Score was  $3.2\pm2.5$  before application; it was detected as  $7.5\pm2.4$  after the application. Sexual Desire Score was  $3.72\pm1.48$  before application; it was detected as  $8.9\pm1.4$  after the application. Intercourse Satisfaction Score was  $3.7\pm2.8$  before application; it was detected as  $9.1\pm2.7$  after the application. Overall Satisfaction Score was  $4\pm1.7$  before application. It was detected as  $8.1\pm1.7$  after the application (All parameters p<0.001). Scores of IIEF-15 sub-parameters are available in Table 2.

Tuble 1. General details of the patients	
Number (n)	21
Age (years) (mean±SD)	53.8 ±11.6
Comorbidity n (%)	
DM	12 (57.1%)
Pelvic Organ Surgery	4 (19%)
Fasting Glucose Levels (mg/dL) (mean ± SD)	91.6±20.3
Total Testosterone (ng/dl) (mean ± SD)	471.2±127.5
FSH (mIU/mL) (mean $\pm$ SD)	8.2±3.6
LH (mIU/mL) (mean ± SD)	6.2±2.4
Penile Doppler USG (cm/sec)	
Peak systolic velocity (PS)	24.4 ±15.1
End diastolic velocity (ED)	4.3±4.5
Side Effect (%)	
Penile Pain	2 (9.5%)
Priapism	2 (9.5%)
Alprostadil Usage Duration (weeks)	21.9±16.6

	Pre-Treatment	Post- Treatment	р
Erectile Function Score (IIEF-15)	9.2±5.3	20.33±6.2	p<0.001
Orgasmic Function Score (IIEF-15)	3.2±2.5	7.5±2.4	p<0.001
Sexual Desire Score (IIEF-15)	3.72±1.48	8.9±1.4	p<0.001
Intercourse Satisfaction Score (IIEF-15)	3.7±2.8	9.1±2.7	p<0.001
Overall Satisfaction Score (IIEF-15)	4±1.7	8.1±1.7	p<0.001

Table 2. Pre-treatment and post-treatment IIEF-15 parameters

### DISCUSSION

Alprostadil is a synthetic form of prostaglandin E1 binding to the specific receptors on flat muscle cells and causing tissue relaxation through the second messenger system by activating intracellular adenylate cyclase (6).

In patients with an inadequate response to oral treatment in erectile dysfunction treatment, it can be applied with a success ratio reaching 80% in erectile dysfunction caused by neurogenic, vasculogenic, and psychogenic causes in second-line treatment (5,7).

Its use is contraindicated in patients with psychological disease, priapism story, severe coagulopathy or unstable cardiovascular disease story, decreased hand skill although the partner is trainable in injection technique and use monoamine oxidase inhibitors (8). We included patients without a condition forming contraindication for intracavernosal alprostadil use in our study.

Alprostadil provides complete erection in 70-80% of ED patients at doses between 10 and 20  $\mu$ g (9). Erection was provided in all patients in our study after starting alprostadil with a dose of 5  $\mu$ g and continuing with 10  $\mu$ g following the clinic and dose titration application, and this dose was continued.

Approved questionnaires are suggested to evaluate the disease severity, measure treatment efficiency, and future lead treatment in patients with erectile dysfunction (10). We evaluated our patients with the International Index of Erectile Functions (IIEF-15) before and after the treatment in our study. In the study by Linet et al., 87% of the males and 86% of their partners were satisfied with their sexual activity after intracavernosal alprostadil injection. Similar to this data, we detected a statistically significant recovery in all IIEF parameters in all our patients after the treatment. Treatment's most common side effects are a pain in the injection zone in 11%, hematoma in 1.5%, and lengthened erection or priapism in 1-5% (5). During the mean drug usage duration of  $21.9\pm16.6$  weeks, penile pain was detected in the injection zone in 9.5%, and priapism was observed in 9.5% of the patients in our study. These values are parallel to literature.

The advantages of alprostadil compared to other intracavernosal applied agents are lengthened erection, lower systemic side effects, and penile fibrosis incidence. To our patients not benefiting from first-line treatment in our study, we recommended alprostadil treatment due to its low side effect profile and high efficiency. We acquired a statistically significant response in all sexual function parameters in all patients at the end of 12-week treatment. Penile pain and priapism were the most common side effects in our patients. The monthly treatment cost is approximately 26 dollars.

In addition, it was also observed that the treatment lasted up to 21 weeks in patients using intracavernosal alprostadil. This condition shows that the drug is tolerable.

As a result, intracavernosal alprostadil treatment is a tolerable, cost-effective, and efficient treatment method in second-line treatment.

### CONCLUSION

Intracavernosal alprostadil treatment used in erectile dysfunction second line treatment is a cost-effective and efficient treatment method with a tolerable side effect profile and provides a recovery in sexual parameters with can be measured with IIEF-15 parameters.

### **Conflict of interest**

The authors declare to have no conflicts of interest.

### **Financial Disclosure**

The authors declared that this study has received no financial support.

### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

### **Ethical Approval**

The study was approved by Ethical Committee of Necmettin Erbakan University Meram Faculty of Medicine (Approval Number: 2020/2494) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

### **Author Contributions**

Conception and design; HT, MGS, MTK, Data acquisition; HT, MGS, MTK, NA, AA, MB, Data analysis and interpretation; HT, MGS, MTK, NA, AA, MB, Drafting the manuscript; HT, MGS, MTK, Critical revision of the manuscript for scientific and factual content; HT, MGS, MTK, NA, AA, MB, Statistical analysis; MGS, Supervision; HT.

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### Hawk® JAWS versus Lumenis® VersaCut prostate morcellation devices: A comparative study and comprehensive literature review

Hawk® JAWS ve Lumenis® VersaCut prostat morselasyon cihazları: Karşılaştırmalı bir çalışma ve kapsamlı literatür incelemesi

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### Özet

Amaç: Morselasyon, prostatın holmium lazer ile enükleasyonunun (HoLEP) standart bir prosedürü olmasına rağmen, kullanılan morselatorlerle ilgili çalışmalar sınırlı sayıdadır. HoLEP'de kullanılan, benzer amaçlara sahip ancak çalışma prensipleri farklılıkları olan iki farklı doku morselatörünü verimlilik ve güvenlik açısından karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Aralık 2018 ile Aralık 2019 arasında HoLEP uygulanan 130 hastanın verileri retrospektif olarak incelendi. Lumenis<sup>®</sup> Versacut (Lumenis Inc., Santa Clara, CA, ABD) morselatorün kullanıldığı 65 hasta, Hawk<sup>®</sup> JAWS (Hawk, Minitech Co., China) morselatorün kullanıldığı 65 hasta çalışmada yer aldı. Morselasyon etkinliği (g / dk), morselasyon süresi (dk), toplam operasyon süresi (dk), enükleasyon süresi (dk), enükle edilen doku ağırlığı (g), enükleasyon etkinliği, çıkarılan prostat dokusu yoğunluğu, perioperatif komplikasyonlar kaydedildi.

**Bulgular:** İki grup arasında toplam operasyon süresi (dk), enükleasyon süresi (dk), enükleasyon etkinliği (g / dk) morselasyon etkinliği (g / dk), morselasyon süresi (dk) açısından anlamlı bir fark yoktu (p> 0.05). Versacut grubunda 3 hastada (%4) mesane mukoza hasarı meydana gelirken, Hawk\* JAWS grubunda mesane mukozal hasarı hiçbir hastada gözlenmedi (p = 0.08).

### Abstract

**Objective:** Although morcellation is a standard procedure of Holmium Laser Enucleation of the Prostate (HoLEP), studies on the morcellators used are limited in number. We aimed to compare two different tissue morcellators used in HoLEP, which have similar objectives but differences in efficiency and safety in working principles.

Material and Methods: The data of 130 patients who underwent HoLEP between December 2018 and December 2019 were retrospectively reviewed. Sixty-five patients received Lumenis<sup>®</sup> Versacut (Lumenis Inc., Santa Clara, CA, USA) morcellator and 65 patients received Hawk<sup>®</sup> JAWS (Hawk, Minitech Co., China) morcellator after enucleation were included in the study. The efficiency of morcellation (g/min), morcellation time (min), total operation time (min), enucleation time (min), enucleated tissue weight (g), the efficiency of enucleation, densities of the removed prostate tissues, perioperative complications associated with the use of a morcellator were recorded perioperatively.

**Results:** There was no significant difference in total operation time (min), enucleation time (min), enucleated tissue weight (g), and efficiency of enucleation (g/min) efficiency of morcellation, morcellation time (min) between the two groups. Bladder mucosal damage occurred in 3 patients (4%) in the Versacut group, while mucosal bladder

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This study was approved by the local ethics committee of University Gazi University Faculty of Medicine (Approval number: 2020-04). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

**Sonuç:** Hawk\* JAWS ve Lumenis\* VersaCut morselatorleri, verimlilikleri ve güvenlik profilleri açısından karşılaştırılabilir sonuçlara sahiptir.

Anahtar Kelimeler: Hawk, HoLEP, morselasyon, morselator, Versacut.

### INTRODUCTION

Endoscopic enucleation of the prostate by using laser has become popular in recent years in the surgical treatment of benign prostatic obstruction (BPO). Holmium Laser Enucleation of the Prostate (HoLEP) method employing enucleation and mechanical morcellator was first described by Gilling and Fraundorfer in 1998 (1). It has been demonstrated in randomized studies with long follow-up periods that HoLEP, performed using Holmium laser, could also be performed in large prostates >100 g (2). HoLEP has come into prominence as an alternative minimally invasive prostate surgery in terms of efficiency, safety, and complications to TUR P and open prostatectomy (3-5). HoLEP is now among the top options in the guidelines for the surgical treatment of BPO as a result of the satisfactory results obtained in studies conducted with large series (6, 7).

HoLEP surgery has two basic steps: Enucleation and morcellation (8,9). HoLEP studies in the literature mostly focus on enucleation and its techniques. Although morcellation is a standard procedure of Ho-LEP and the step that entails the highest risk of complications, studies on morcellation and morcellators used are limited in number (8, 10, 11). The importance of morcellation has become evident as it is a variable that directly affects the duration of surgery and, thus, anaesthesia, especially in patients with a large prostate. Accordingly, studies have started for fast and safe morcellators, and different types of morcellators from many brands have been introduced to the market. Research and development studies on this subject are still ongoing.

This study aimed to compare two different tissue morcellators used in HoLEP surgery, which have similar objectives but differences in efficiency and safety in working principles. damage was not observed in any patient in the Hawk\* JAWS group (p = 0.08).

**Conclusion:** Hawk\* JAWS and Lumenis\* VersaCut morcellators were comparable in their efficiency and safety.

Keywords: Hawk, HoLEP, morcellation, morcellator, Versacut.

### MATERIAL AND METHODS

The approval was obtained by the Institutional Review Board of Gazi University Faculty of Medicine (No: 2020-04). Informed consent was obtained from all men. This study was conducted following the Helsinki Declaration. The data of 130 patients who underwent HoLEP between December 2018- December 2019 were retrospectively reviewed. Age, body mass index (BMI) (kg/m2), hemoglobin (Hb), prostate-specific antigen (PSA) levels, prostate volume measured by transabdominal ultrasonography were obtained. International Prostate Symptom Score total (IPSS-T), IPSS storage (IPSS- S) and voiding (IPSS- V), mean maximal urinary flow rate (Qmax), postvoiding residual volume (PVR) were recorded. All patients received alpha-blocker medication for at least 6 months before surgery. Inclusion criteria for HoLEP surgery were; failure of medical treatment, Qmax≤ 15 ml/s, IPSS-T≥ 8, PVR $\geq$  50 ml. Patients with a history of previous BPO surgical treatment, prostate or bladder cancer, neurogenic bladder, urethral strictures, and patients with a history of using 5-alpha reductase inhibitor were excluded from the study.

The efficiency of morcellation (enucleated prostate weight/morcellation time, morcellation time (min), total operation time (min), enucleation time (min), enucleated tissue weight (g), the efficiency of enucleation (enucleated prostate weight/enucleation time) (g/min), densities of the removed prostate tissues and perioperative complications associated with the use of a morcellator were recorded perioperatively. The technique for prostatic tissue density measurement has been previously described (12). Catheterization time (hours) and hospitalization time (hours) were recorded postoperatively.

### **Surgical Technique**

A 26-Fr continuous flow laser resectoscope for each patient, a laser-fibre stabilizing bridge, a 120 W holmium laser (VersaPulse; Lumenis Ltd., Israel), a 550- $\mu$ m end-firing laser fibre (SlimLine; Lumenis Ltd.), and a 26-Fr nephroscope was used. For the morcellation step, 65 patients received Lumenis<sup>®</sup> Versacut (Lumenis Inc., Santa Clara, CA, USA) morcellator and 65 patients received Hawk<sup>®</sup> JAWS (Hawk, Minitech Co., China) morcellator after enucleation were included in the study (Suppl- 1). The blade system of the morcellators was renewed after each 100 gr tissue morcellation.

All patients were operated on using the "Omega Sign" technique, a HoLEP technique described earlier (13). The operations were performed by a single surgeon (LT) with HoLEP experience of over 500 cases (14). During the morcellation phase, the continuous flow was provided with 4 units of 3-liter physiological saline solutions, and bladder distension was achieved by closing the drain. In addition, an assistant doctor stood by the patient and constantly checked the bladder fullness until the end of the procedure.

### **Statistical Analysis**

The Statistical Package for Social Sciences 23.0 software (SPSS 23.0, Chicago, USA) was used for the statistical analysis. The Kolmogorov-Smirnov, Kurtosis, and Skewness Tests were used to assess the data normality. The clinical characteristics of the two groups were compared with Mann-Whitney U or Student t-test for continuous variables and with the Fisher's Exact or Pearson Chi-Square test for categorical variables. All statistical tests were two-sided, and the p < 0.05 value was considered statistically significant.

### RESULTS

Table 1 presents main preoperative characteristics of the patients. Preoperative parameters including patient age (years), PSA (ng/mL), BMI (kg/m2), Hb level (g/dL), prostate volume (mL), IPSS pre-V, IPSS pre-S, IPSS–Total, Qmax (ml/s) and PVR (mL) were similar between two groups.

Table 2 presents the postoperative surgical results of the patients. No significant difference was found in postoperative Hb levels, prostatic tissue density (g/mL), Hb decrease (g/dL), catheterization time (hours), and hospitalization time(hours) between the two groups.

Table 3 presents the perioperative results. There was no statistically significant difference in total operation time (min), enucleation time (min), enucleated tissue weight (g), and efficiency of enucleation (g/min) efficiency of morcellation, morcellation time (min) between the two groups.

Table 4 presents the comparison of perioperative complications due to morcellator use between groups. Intraperitoneal or extraperitoneal bladder perforation did not occur in any patient in either group. Bladder mucosal damage occurred in 3 patients (4%) in the Versacut group, while mucosal bladder damage was not observed in any patient in the JAWS group, and the difference was not statistically significant (p= 0.08).

Table 1. Baseline characteristics and preoperative data of the patients	\$
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Variables	Lumenis <sup>®</sup> Versacut (N:65)	Hawk <sup>*</sup> JAWS (N: 65)	P Value
Patient age (year)	65 ± 6.53	$64 \pm 6.86$	0.41
PSA (ng/mL)	$2.53 \pm 11.62$	$2.4 \pm 11.92$	0.28
BMI	$24.8 \pm 2.77$	$24.6 \pm 3.04$	0.9
Hb level (g/dL)*	$14.6 \pm 1.11$	$14.6 \pm 1.08$	0.41
Prostate Volume (mL)	84.71 ± 41.54	$65.01 \pm 37.46$	0.6
IPSS pre-Voiding	15 ± 3.22	15± 3.72	0.6
IPSS pre-Storage	$11 \pm 1.67$	$11 \pm 1.66$	0.54
IPSS Total	26 ± 3.36	$27 \pm 4.1$	0.66
Qmax(ml/s)*	$7.8 \pm 3.03$	$7.9 \pm 2.48$	0.38
PVR (ml)	139 ± 78.06	$134\pm73.06$	0.96

*N*: number of patients; *SD*: Standart Deviation; *PSA*: Prostat Spesific Antigen; *Hb*: hemoglobin; *BMI*: Body mass index; *IPSS*: International ProstateSymptom Score; *Qmax*: maximum velocity at voiding; *PVR*: Post Voiding Residue; *S*: second. \* Statistically analyzed with Student t test; others analyzed with Mann Whitney U test

	Lumenis <sup>®</sup> Versacut (N:65)	Hawk <sup>®</sup> JAWS (N:65)	P Value
Prostatic tissue density*(g /mL)	$1.03 \pm 0.07$	$1.04 \pm 0.11$	0.44
Postop Hb (g/dL)	$14.15 \pm 1.17$	$14.15\pm1.07$	0.31
Hb-decrease (g/dL)	$0.5 \pm 0.29$	$0.5 \pm 0.27$	0.93
Catheterization time (hour)	19 ± 3.53	$20 \pm 4.86$	0.26
Hospitalization time (hour)	23 ± 3.32	$23 \pm 4.27$	0.26

Table 2. Comparison of the postoperative outcomes of the patients

N: number of patients; SD: Standart Deviation; Hb: hemoglobin.

\* Statistically analyzed with Student t-test others analyzed with Mann Whitney U test.

	Lumenis <sup>®</sup> Versacut (N: 65)	Hawk <sup>®</sup> JAWS (N: 65)	P Value
Enuclated tissue weight (g)	45.31 ± 27.28	47.28 ± 30.25	0.59
Efficiency of enucleation	$1.23\pm0.19$	$1.23\pm0.22$	0.95
Efficiency of morcellation	$4.1\pm0.69$	$4.25\pm2.53$	0.1
Enucleation time (min)	$52.2 \pm 28.62$	$43.34 \pm 25.37$	0.85
Morcelation time (min)	$10.63 \pm 6.59$	$9.85\pm6.44$	0.34
Total operation time (min)	$70.7 \pm 32.8$	$61.07 \pm 28.44$	0.55

Table 3. Comparison of perioperative outcomes between groups

\* Statistically analyzed with Mann Whitney U test

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Complications	Lumenis <sup>®</sup> Versacut n(%) (N:65)	Hawk <sup>®</sup> JAWS n(%) (N:65)	P Value
Device Problem	1 (1.5)	0	1
Mucosa damage*	3 (4)	0	0.08

\*Statistically analyzed with Pearson Chi-Square test; others analyzed with Fisher's Exact test

Patients with mucosal damage were discharged with a catheter (it did not affect hospitalization time), and their catheters were kept for 3 days. Device problem was observed in 1 patient (1.5%) only in Group 1, and there was no statistically significant difference between groups.

### DISCUSSION

Prostate enucleation techniques have been developed and modified with the introduction of HoLEP in urology practice (15). The morcellation step is common in all of the HoLEP techniques described so far, and the basic principle is the same in all techniques except for the morcellators used. According to our literature review, no studies are comparing Hawk<sup>®</sup> JAWS and Lumenis<sup>®</sup> VersaCut morcellators in terms of efficiency and safety profile in HoLEP. In that respect, our study is the first in the literature.

Morcellation can be defined as dividing a large tissue sample into smaller pieces to facilitate tissue extraction as a result of surgery (16). In the morcellation step, the last step of HoLEP, free prostate tissue pushed into the bladder following enucleation is taken out in small pieces. The tissue morcellators used in this process are designed to perform suction (aspiration) and tissue cutting (8, 17). The suction removes the morcellated tissues out of the bladder while keeping the tissue close to the blade, and the movable blade of the morcellator breaks the prostatic adenoma tissue into small fragments. The efficiency of the morcellator and possible complications depend on suction pressure and cutting mechanism. The bladder should be kept constantly distended to avoid possible bladder injuries during the morcellation process. We aimed to minimize possible complications during the procedure by performing bladder control during morcellation with the help of a bedside assistant doctor.

Today, there are three popular prostate tissue morcellators commonly used following prostate enucleation. These include VersaCut (Lumenis Inc., Santa Clara, USA), Piranha (Richard Wolf Inc., Knittlingen, Germany), and DrillCut (Karl Storz Inc., Tuttlingen, Germany) morcellators (18, 19). The differences between morcellators are mainly related to blade movements of the morcellator (reciprocating vs. oscillating) and the presence of teeth on the blade (non-toothed vs. toothed) (8, 10). The oscillating system has a rotating morcellator with a disposable jagged blade that oscillates alongside. The tip of the oscillating morcellator is blunt, and this tip does not move. Morcellator's blade is connected to a motor handle and connected to a generator, a suction pump, and a disposable tubing set (20). In the reciprocating system, the blade reaches beyond the end of the device while moving back and forth. This system works with a motor arm and a disposable tube attached to a cylinder pump to provide suction and does not require much effort for installation (20).

Piranha and DrillCut morcellators are oscillating and toothed, while VersaCut is a non-toothed and reciprocating morcellator (18, 19). Hawk<sup>®</sup> morcellators used in the present study are toothed and oscillating morcellators. Most studies on morcellators in the literature are about Piranha and VersaCut morcellators. In a retrospective study, morcellation time with Piranha morcellator was found to be shorter, and morcellation efficiency was almost twice that of VersaCut (8.6 g/min vs. 3.8 g/min; p< 0.0001) (20). Elshal et al. similarly showed that the morcellation efficiency of the Piranha morcellator was higher than that of the VersaCut morcellator (8). Rivera et al. also demonstrated that the morcellator efficiency of Piranha was higher than that of VersaCut (4.4 vs. 7.0 g/min, p< 0.01) (21). In a randomized prospective study by El Tayeb et al., the morcellation efficiency of Piranha was higher than that of VersaCut; however, the difference was not statistically significant (22). In contrast to these studies, VersaCut had a shorter morcellation time (9.8 min vs. 14.5 min) and higher morcellation efficiency than Piranha (8.4 g/ min vs. 4.7 g/min) in another study (17). In a study comparing the efficiency and reliability of DrillCut and VersaCut morcellators, there was no significant difference between their morcellation times; however, it was found that the efficiency of VersaCut morcellator was significantly higher (3.6 vs. 4.9 g/min; p= 0.03) (20).

The number of studies in the literature reporting the efficiency of Hawk morcellator is limited. In a study conducted by He et al., HoLEP was performed in 63 patients, and a Hawk morcellator was used for morcellation. Similar to our results, morcellation efficiency was  $5.4\pm2.9$  g/min, and morcellation time was  $11.2\pm3.9$ min in that study (23). Morcellation time has been previously shown to positively correlate with prostatic tissue density ( $\rho$ = 0.272, p= 0.0005) (12). As there is no difference between the prostate densities between the groups, we believe it provides more accurate comparisons of morcellation efficiency and morcellation time in our study.

Bladder injury is the most likely and important complication during morcellator use. Injuries may occur if the bladder is not sufficiently full during morcellation or if the endoscopic view during the operation is suboptimal (17). While superficial injuries can be managed by leaving the urethral catheter for a longer time, deeper and full-thickness bladder perforations may require open surgical repair (24). Bladder mucosal injury during HoLEP has been reported at a rate of 0.7–5.7% and bladder perforation at a rate of 0.1–1.5% (8, 22, 25) in the literature. Ibrahim et al. observed no significant difference between DrillCut and VersaCut morcellators regarding complication rates, although the rate was higher for VersaCut (2.4% vs. 7.3%; p= 0.1) (19). While mucosal bladder injury occurred in 2 (4.8%) patients during the use of VersaCut and in 1 (2.4%) patient during the use of DrillCut, only one patient had bladder perforation requiring open surgical repair after the use of VersaCut (19). Intraperitoneal or extraperitoneal bladder perforation did not occur in any patient in either group in the present study.

Maheshwari et al. compared Piranha and VersaCut morcellators, and no patient in the Piranha group had perforation including the bladder muscle, whereas in the VersaCut group, three patients had deep bladder muscle injury, and none of the patients had bladder rupture (17). The incidences of bladder mucosal injury, deep muscle injury and bleeding requiring electrocoagulation were statistically significantly lower in the Piranha group (17). In another study, no bladder perforation occurred in Piranha or VersaCut groups, while one patient in the VersaCut group had superficial bladder mucosal injury (20). Elshal et al. observed bladder mucosa injury at a rate of 9% with VersaCut, while bladder mucosal injury or perforation was not observed with Piranha, and the difference was statistically significant (p=0.01) (8). In a study that Zhang et al. performed diode laser prostatic enucleation and used Hawk morcellator, no perioperative bladder injury occurred in any patient (26). In a study by He et al. comparing HoLEP and diode laser enucleation, a Hawk morcellator was used in all patient groups, and no bladder injury, perforation, or injury in the urethral orifices were observed in any groups (23). In a more recent study in which Hawk morcellator was used after prostatic enucleation, no bladder injury occurred in any patient (27). In a study in which Thulium laser enucleation of the prostate and resection were compared, and Hawk morcellator was used, mucosal bladder injury was observed in 3 patients (1.6%) in the enucleation group in which a morcellator was used; however, no statistically significant difference was found between groups (p=0.065). In the present study, bladder mucosa damage occurred in 3 patients (4%) in the VersaCut group, while it was not observed in any patient in the Hawk group, and the difference was not statistically significant (p=0.08). In studies in the literature, the morbidity associated with VersaCut has ranged from 0 to 9.1%, while morbidity with Piranha is at a rate of 0–2.4% (8, 18, 20, 22). In the present study, complications were observed at a rate of 5.5% in the Versacut group. Surgeons' experience, dual water use, and bladder distension control may be the factors that led to the low complication rate in the present study.

During the use of a morcellator, mechanical failures related to the morcellator may also occur. Ibrahim et al. reported that DrillCut morcellator failure occurred in 9.7% of the cases (19). In the literature, it was observed that VersaCut morcellator failed at a rate of 0-9.1%, while Piranha morcellator failed in 0-2.7% of the cases (8, 19, 20, 22). In the present study, morcellator failure occurred in 1 patient (1.5%) in the VersaCut group, while no failure occurred in the Hawk group, and no statistically significant difference was found between groups.

Our study has certain limitations to be stated. First, the number of patients in study groups is small, and the study is retrospective in nature. Secondly, the fact that morcellators have not been compared in terms of cost analysis. Thirdly, the learning curves of the morcellators have not been analyzed, and this may be considered one of the limitations of the present study.

### CONCLUSION

Morcellation is an important step in HoLEP surgery and should be considered regarding complications. We showed that Hawk<sup>®</sup> JAWS and Lumenis<sup>®</sup> VersaCut morcellators were comparable in their efficiency and safety. The present study will contribute to the literature since scientific data about the morcellation step and morcellator equipment are limited.

### **Conflict of interest**

The authors declare to have no conflicts of interest.

### **Financial Disclosure**

The authors declared that this study has received no financial support.

### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

### **Ethical Approval**

The study was approved by the Institutional Review Board of Gazi University Faculty of Medicine (No: 2020-04) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

### **Supplementary Material**

Accompanying video can be found on YouTube (Clip: Morcellation with Versacut and Hawk devices https://youtu.be/tQvJ7gOB1Co) and also be accessed by scanning QR code in below:



Suppl-1: Morcellation with Versacut and Hawk devices

### **Author Contributions**

Conception and design; HÇA, SY, LT, Data acquisition; MY, SY, EK, OA, Data analysis and interpretation; HÇA, MY, SY, EK, OA, LT, Drafting the manuscript; HÇA, MY, EK, Critical revision of the manuscript for scientific and factual content; HÇA, MY, SY, EG, EK, SY, OA, Statistical analysis; HÇA, EG, Supervision; SY, LT.

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# Simultaneous native nephrectomy with renal transplantation: Our experience and a brief literature review

## Renal transplantasyonla eş zamanlı nativ nefrektomi: Deneyimlerimiz ve kısa bir literatür derlemesi

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### Özet

Amaç: Renal transplant cerrahisinin güvenliğini arttırmak veya postoperatif fonksiyonları iyileştirmek adına, bazı durumlarda nativ böbrek nefrektomisi gereksinimi söz konusu olmaktadır. Prosedürün ise zamanlaması halen tartışmalıdır. Bu yazımızda, transplant ile eş zamanlı gerçekleştirdiğimiz nativ nefrektomi prosedürlerimizi literatür eşliğinde sunmayı amaçladık.

Gereç ve Yöntemler: Eylül 2011 ve Şubat 2020 tarihleri arasında Son Dönem Böbrek Yetmezliği (SDBY) nedeniyle renal transplantasyon gerçekleştirilen 245 hastanın verileri retrospektif olarak incelendi. Transplantasyon ile eşzamanlı tek taraflı veya bilateral nefrektomi gerçekleştirilen hastalar dahil edildi. Hastaların demografik özellikleri, preoperatif ve postoperatif laboratuar verileri, primer hastalığı, komorbid hastalık varlığı, diyaliz süreleri, vasküler anastomoz süreleri, cerrahi ve klinik komplikasyonları, hastaneye yatış süreleri ve greft fonksiyonları kaydedildi.

**Bulgular:** Renal transplantasyona eş zamanlı ipsilateral veya bilateral nativ nefrektomi gerçekleştirilen toplam 12 hasta mevcuttu. Hastaların SDBY'ye yol açan primer hastalıkları şu şekildeydi; 6 (50%) hasta Polikistik Böbrek Hastalığı (PBH), 5 (41,6%) hasta vezikoüretral reflü (VUR), bir (8,3%) hasta ise böbrek taşı. Üç hastada postoperatif ateş, üç hastada eritrosit replasman tedavisi, bir hastada ürosepsis ve lenfosel nedenli perkutan drenaj kateteri gereksinimi kaydedildi. İki hastada hümoral rejeksiyon ve iki hastada BK virüs nefropatisi gelişti.

### Abstract

**Objective:** There is a need for native kidney nephrectomy to increase renal transplant surgery's safety or improve postoperative function in some cases. The timing of the procedure is still controversial. This study aimed to present our native nephrectomy procedures performed simultaneously with the transplantation in light of the literature.

Material and Methods: A retrospective analysis was performed on the data of 245 patients who underwent renal transplantation due to end-stage renal failure (ESRD) between September 2011 and February 2020. Patients who underwent unilateral or bilateral nephrectomy simultaneously with transplantation were included. Demographic characteristics of the patients, preoperative and postoperative laboratory data, primary disease, presence of comorbid diseases, duration of dialysis, duration of vascular anastomosis, surgical and clinical complications, duration of hospital stay, and graft functions were recorded.

**Results:** 12 patients underwent ipsilateral or bilateral native nephrectomy simultaneously with renal transplantation. The primary diseases of the patients leading to ESRD were as follows; 6 (50%) patients with Polycystic Kidney Disease (PKD), 5 (41.6%) patients with vesicoureteral reflux (VUR), one (8.3%) patient with kidney stones. Postoperative fever in three patients, erythrocyte replacement therapy in three patients, urosepsis and urinary drainage catheter requirement in one patient due to lymphocele was recorded. Two patients developed humoral rejection, and two patients developed BK virus nephropathy.

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The study was approved by Ethical Committee of Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences (Approval Number: 2021/191). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants. **Sonuç:** Uygun endikasyon varlığında renal transplantasyon hazırlığındaki hastalarda eş zamanlı nativ nefrektomi güvenli ve efektif bir yöntemdir. Yeterli deneyim ve donanımı olan merkezlerde, nativ nefrektominin renal transplantasyon ile eş zamanlı gerçekleştirilmesi tercih edilebilir.

Anahtar Kelimeler: Böbrek nakli, nefrektomi, bilateral nefrektomi, polikistik böbrek hastalığı, komplikasyonlar. **Conclusion:** In the presence of appropriate indications, simultaneous native nephrectomy is a safe and effective method in patients preparing for renal transplantation. In centers with sufficient experience and equipment, it may be preferable to perform native nephrectomy simultaneously with renal transplantation.

**Keywords:** Kidney transplantation, nephrectomy, bilateral nephrectomy, polycystic kidney disease, complications.

### INTRODUCTION

The gold standard treatment method for end-stage renal failure (ESRD) is renal transplantation (1). In some cases, to increase the safety of transplant surgery or improve postoperative functions, native nephrectomy may be necessary. The most common indications include symptomatic Autosomal Dominant Polycystic Kidney Disease (PKD), reflux nephropathy, staghorn stones, Goodpasture Syndrome, massive proteinuria, and uncontrolled hypertension (2). On the other hand, it is still debated whether the nephrectomy procedure should be planned before or after the transplantation or simultaneously (1, 2).

In the 1970s, bilateral nephrectomy was performed before renal transplantation when indicated. However, this method has gradually lost its popularity due to complications such as fluid overload in the anephric phase, congestive heart failure, uremia, anemia due to erythropoietin deficiency, and renal osteodystrophy caused by 1,25-dihydroxycholecalciferol deficiency (3). In the 1980s, prolonged anephric phase complications and multiple surgical interventions were avoided by performing native nephrectomy simultaneously with transplantation. However, it is widely believed that this method increases post-transplant complications (4).

In our clinic, we preferred to perform the nephrectomy procedure simultaneously with the transplantation in patients who required ipsilateral or bilateral native nephrectomy during transplantation preparation. This article aimed to present our simultaneous native nephrectomy experiences in our center, which has a kidney transplant history of nearly ten years.

### **MATERIAL AND METHODS**

Following the approval (2021/191) obtained from the Ethical Committee of Dr. Sadi Konuk Training and Research Hospital, the data of 245 patients, who underwent renal transplantation due to ESRD between September 2011 and February 2020, were retrospectively analyzed. Patients who underwent unilateral or bilateral nephrectomy simultaneously with transplantation were included. Demographic characteristics of the patients, preoperative and postoperative laboratory data, primary diseases leading to ESRD, presence of comorbid diseases, duration of dialysis, duration of vascular anastomosis, surgical and clinical complications, duration of hospitalization, and graft functions were recorded.

Routine biochemical and microbiological tests were performed in all patients before the operation. In patients whose primary disease was vesicoureteral reflux (VUR), the severity of reflux was evaluated by preoperative voiding cystourethrography (VCUG). Methylprednisolone or anti-thymocyte globulin was used in induction; mycophenolic acid, tacrolimus, and prednisolone were used for maintenance as immunosuppression protocols in patients. The patients were called for a monthly follow-up in the first year in the postoperative period.

The standard transabdominal method with a midline incision was performed in all patients with bilateral nephroureterectomy. After completion of nephrectomies, the transplanted kidney was placed in the iliac fossa, and then the vein and the artery were continuously anastomosed to the external iliac artery and vein using standard methods. The peritoneum was sutured and closed on the transplanted kidney, thus preventing the connection of the kidney with the intraperitoneal space. In patients who underwent ipsilateral nephrectomy, the right iliac fossa was reached by making an extraperitoneal curvilinear incision (Gibson), which we use as a standard in kidney transplantation. Then, the incision was extended caudally to reach the native kidney, and an ipsilateral nephrectomy was performed. Subsequently, vascular anastomosis was performed, as we mentioned. A conventional transabdominal method with a midline incision was performed in two patients who have undergone cyst aspiration or decortication in the left kidney concomitant with a right nephrectomy. Ureteroneocystostomy was performed in all patients using the modified Lich-Gregoir technique by placing a routine double-J stent.

### RESULTS

There were 12 patients who underwent ipsilateral or bilateral native nephrectomy simultaneously with renal transplantation. The demographic and perioperative data of the patients are presented in Table 1. The mean age of the patients was  $43.5 \pm 12.2$  years, and the mean body mass index (BMI) was calculated as 25.7  $\pm$  5 kg/m 2. There were 8 male (66.7%) and 4 female (33.3%) patients. Preemptive renal transplantation was performed in 8 (66.7%) of the patients. Renal transplantations were performed using open techniques in all patients, and donor nephrectomy procedures were performed from living donors using laparoscopic techniques. All transplanted grafts had single arteries. The primary diseases of the patients leading to ESRD were as follows; 6 (50%) patients with Polycystic Kidney Disease (PKD), 5 (41.6%) patients with vesicoureteral reflux (VUR), one (8.3%) patient with kidney stones. Except for hypertension in two patients, none of the patients had additional comorbidities.

Perioperative complications of the patients, postoperative graft status, changes in preoperative and postoperative creatinine levels up to the first year are presented in Table 2. Bilateral native nephroureterectomy was performed simultaneously with transplantation in all patients with VUR in the etiology. Severe VUR decision in these patients was made with the detection of grade 4-5 reflux in VCUG. The aim of native nephrectomies in these patients was to prevent recurrent urinary tract infections and eliminate potential infection sources. Simultaneous right native nephrectomy was performed in patients whose primary disease was PKD. The aim was to reduce the risk of complications such as recurrent urinary tract infections and bleeding, reduce increased intra-abdominal pressure due to the size of the native kidney, and make room for the graft kidney. At the same time, hemorrhagic cyst aspiration was performed in the left native kidney in one of these patients, and cyst decortication was performed in the left native kidney in another one. In cases with relatively large cysts, we aspirated the cysts. Simultaneous right native nephrectomy was performed in the patient whose etiology was urolithiasis due to recurrent urinary tract infections and the presence of a 6 mm calculus in the lower pole. The mean duration of operation was 269.1  $\pm$  37.1 minutes, the mean amount of bleeding was 233.3  $\pm$  83.8 ml, the mean duration of arterial anastomosis was  $10.9 \pm 3$  minutes, and the mean duration of venous anastomosis was  $15.4 \pm 5.4$  minutes. The mean duration of hospital stay was  $9.5 \pm 6.1$  days.

Erythrocyte replacement therapy (ERT) was required during the postoperative follow-up of the three patients who underwent concurrent right nephrectomy due to PKD. In one of these patients (Patient 4), coronary angiography due to acute coronary syndrome was performed on the third postoperative day, and a cardiac stent was placed. None of the ERTs were performed due to acute gross hemoglobin decrease in the early postoperative period, and their indication was to treat the postoperative anemia. Postoperative fever developed in two patients who underwent bilateral nephroureterectomy and one patient who underwent right nephrectomy. In one of these patients (Patient 10), the infective process progressed to urosepsis, and the clinical condition was controlled with supportive and antibiotic therapy. However, in the imaging performed in this patient, a lymphocele was detected with a diameter of 10 cm adjacent to the graft kidney, and a drainage catheter was required to be placed by interventional radiology. At the same time, the development of humoral rejection was also noted in this patient.

In one of the patients (Patient 5), creatinine increased, hematuria developed in the early postoperative period, and the biopsy resulted in humoral rejection. The creatinine level decreased with plasmapheresis treatment. In two patients (Patients 3 and 4), graft biopsies, which were performed due to increased creatinine in the late period, resulted in BK virus nephropathy, intravenous immunoglobulin therapies were administered to these patients due to the development of side effects against cidofovir.

None of the patients developed wound infections and long-term incisional hernia. The native kidney nephrectomy pathologies of all patients were benign.

Patient	Age	Gender	BMI	Etiology	Operation	Duration	Incision	Bleeding Amount	Arterial Anastomosis	Vein Anastomosis
						(min)		(ml)	Time (min)	Time (min)
1	48	М	24,2	PKD	Right nephrectomy Left cyst aspiration	345	Midline	120	15	17
2	49	F	23,4	PKD	Right nephrectomy	235	Gibson	160	14	15
3	56	F	26,7	PKD	Right nephrectomy	265	Gibson	250	10	16
4	59	М	25,7	PKD	Right nephrectomy	270	Gibson	340	9	12
5	56	F	25,2	PKD	Right nephrectomy	270	Gibson	350	8	15
6	37	М	25,4	VUR	Bilateral nephroureterectomy	210	Midline	120	12	17
7	29	М	17,9	VUR	Bilateral nephroureterectomy	270	Midline	250	13	13
8	29	М	29,4	VUR	Bilateral nephroureterectomy	310	Midline	200	12	28
9	29	F	19,7	VUR	Bilateral nephroureterectomy	235	Midline	350	9	10
10	29	М	21,1	VUR	Bilateral nephroureterectomy	300	Midline	250	15	22
				Urolithiasis	Right					
11	56	М	26,7	Chronic Pyelonephritis	nephrectomy	280	Gibson	160	6	8
12	45	М	23,6	PKD	Right nephrectomy Left cyst decortication	240	Midline	250	8	12

 Table 1. Preoperative and intraoperative data

BMI: Body mass index PKD: Polycystic Kidney Disease VUR: Vesicoureteral reflux

lable 2.	Perioperative compli	cations and	creaunine levels						
Patient	Dialysis status (duration, months	Co- morbidity	<b>Perioperative</b> Complication	Rejection	Duration of Hospitalization (days)	Preop. Cr (mg/dl)	Postop. 1. Day Cr (mg/dl)	Postop 1. Week Cr (mg/dl)	Postop 1. Year Cr (mg/dl)
-	Preemptive	HT	None	None	7	6,9	3,3	1	1,2
2	Preemptive	HT	None	None	4	7,3	1,4	0,8	0,9
3	Preemptive	None	None	Graft biopsy due to increased creatinine: BK virus nephropathy	8	4,1	1,5	0,6	1,2
4	Preemptive	None	ERT, Coronary angiography and stenting for ACS on the 3rd postoperative day	Graft biopsy due to increased creatinine: BK virus nephropathy	16	6,6	4,5	1,5	1,8
ß	Emptive (6)	None	ERT	Creatinine increase and hematuria in the early postoperative period. Graft biopsy: Humoral rejection	13	4,1	3	2,7	1,2
6	Preemptive	None	None	None	7	7,8	4,2	1,1	1,2
7	Emptive (1)	None	None	Graft biopsy due to creatinine remaining at the level of 2 mg / dl: borderline	12	5,7	2,5	2,1	2,3
8	Emptive (6)	None	None	None	5	8,2	5,7	1,4	1,2
6	Emptive (24)	None	Fever	None	6	6,4	3,4	1,2	1,3
10	Preemptive	None	Urosepsis, percutaneous drainage from infected lymphocele	Humoral rejection	25	8,3	2,6	5,1	2,3
11	Preemptive	HT	None	None	5	7,1	3,1	1,1	1,4
12	Preemptive	None	ERT, Fever	None	6	6,5	3,4	1	1,3

creatining landle -4 • ŕ ¢ Table Cr: creatinine, HT: hypertension, ERT: erythrocyte replacement therapy, ACS: acute coronary syndrome

### DISCUSSION

Native nephrectomy is one of the most frequently used auxiliary surgical procedures in patients scheduled for renal transplantation (5). The most common indication for nephrectomy in these patients is PKD (4). PKD is an inherited and progressive kidney disease in which renal functions are impaired by compression of the normal parenchyma by multiple bilateral cysts, resulting in ESRD by 50% during adulthood. In 5-10% of all ESRD, the primary disease is PKD (6). Cystic kidneys cause symptoms such as abdominal pain, abdominal swelling, and early satiety with the effect of local compression. They can lead to complications such as cyst rupture, hemorrhage, and urinary tract infections as far as sepsis. The management of symptoms and other abdominal complications of PKD is complex, and its surgery poses technical challenges. Controversy continues about the indications for surgery, surgical approach, and timing (7). The reasons for nephrectomy in this disease include urinary tract infections, hematuria, flank pain, cancer risk, respiratory problems due to excessively enlarged kidneys, gastroesophageal reflux, signs of increased intra-abdominal pressure, and the need to provide more space for the graft kidney (1, 4, 8). In half of our patients, who underwent concurrent native nephrectomy, the primary cause was PKD, and ipsilateral nephrectomy was performed mostly with the indication of providing space for the graft.

Studies on patients with PKD have demonstrated that concurrent native nephrectomy improves the quality of life in patients without increasing mortality and morbidity (1, 9). Drognitz et al. argued that ipsilateral nephrectomy could be performed safely with a Gibson incision within the retroperitoneal approach without impairing patient and graft functions (1). On the contrary, in the study by Dinckan et al., more complications were observed in patients who underwent bilateral nephrectomy for PKD than patients who underwent nephrectomy due to other reasons (8). In this study, transplantation and simultaneous nephrectomy procedures were performed using a transabdominal approach. This change in complication rates may have stemmed from the differences in the surgical approach, such as the retroperitoneal approach with the Gibson incision or the transabdominal approach. The complication rate increases significantly with the transabdominal approach. With the transabdominal method using midline incision may cause delays in the recovery of postoperative enteral dysfunctions (10).

Interestingly, in the study of Dinkcan et al., fewer complications developed in patients without PKD who underwent bilateral nephrectomy with the transabdominal method, compared to the patients with PKD, although the same surgical technique was used (8). The authors attribute this result to the larger dissection requirement due to the larger size of the cystic kidneys, adhesions to surrounding organs, and the rupture of infected cysts. This finding was also confirmed in the study conducted by Song et al. (11). Longer durations of operation, more frequent need for blood transfusions, and neighboring organ injuries were reported in patients who underwent concomitant bilateral native nephrectomy, compared to the patients who did not undergo native nephrectomy. Nonetheless, better blood pressure control was achieved in the long term in these patients, and the possibility of recurrent infections was reduced. Fuller et al. also supported this and reported that concurrent native nephrectomy was safe and effective and did not affect the graft results in their study in which they compared the results of pre-, simultaneous and post-transplant native nephrectomy in PKD patients (12).

Renal transplantation and other concurrent native nephrectomy indications include uncontrolled hypertension, Goodpasture syndrome, chronic pyelonephritis, urolithiasis, heavy proteinuria, structural abnormalities in the urinary tract that increase susceptibility to infections, and severe VUR (1, 2). VUR may cause problems in transplantation candidates such as post-transplant recurrent infections and bleed; therefore, it requires ureteral reimplantation and nephroureterectomy (13). We performed simultaneous bilateral nephroureterectomy in five patients due to VUR.

The timing of the procedure is still controversial. Today, instead of performing native nephrectomy before transplantation, the simultaneous procedure comes to the fore due to complications such as hyperkalemia, congestive heart failure, osteodystrophy, and anemia in the anephric period (14, 15). Patients undergoing nephrectomy simultaneously with transplantation have significantly higher hemoglobin levels at the time of transplant due to erythropoietin produced from native kidneys, compared to patients who have previously undergone nephrectomy (15). In addition, the fact that these patients have residual diuresis makes the fluid restriction process more manageable in patients undergoing dialysis treatment (15). Moreover, in the case of a native nephrectomy before transplantation, a blood transfusion may be required during or after the nephrectomy procedure, which may cause sensitization that may complicate the scheduled transplantation (16).

The sandwich technique and unilateral nephrectomy were tested in the past to prevent the risk of an anephric phase. Nephrectomy was performed before transplantation to the kidney, which was more damaged, and nephrectomy of the contralateral kidney was performed after the transplantation; hence, there was no need for intraperitoneal access and additional simultaneous operations (17, 18). Nonetheless, the most important disadvantage of this technique was the morbidity brought by the three consecutive surgical requirements (10).

Simultaneous native nephrectomy does not appear to cause an additional burden in terms of surgical complications or allograft function (8, 15, 19-21). However, the situation is slightly different for bilateral nephrectomy. Simultaneous bilateral nephrectomy is beneficial in PKD for reasons such as bleeding, recurrent infection, and cancer after the transplantation. Nonetheless, simultaneous bilateral native nephrectomy is associated with a higher rate of perioperative complications compared to renal transplantation alone, albeit being a tolerable procedure with good patient satisfaction (2, 8, 21). Routine nephrectomy before the transplantation is no longer recommended unless there is a clear indication of bleeding, infection, or suspected malignancy (20, 22, 23).

The most important limitation of our study was that the number of cases was too small to make an inference, and there were no comparison groups. In addition, another important limitation was its retrospective design.

### CONCLUSION

In the presence of appropriate indications, simultaneous native nephrectomy is a safe and effective method in patients preparing for renal transplantation. Simultaneous native nephrectomy procedures performed in our clinic resulted in acceptable rates of complication. In centers with sufficient experience and equipment, it may be preferable to perform native nephrectomy simultaneously with renal transplantation.

### **Conflict of interest**

The authors declare to have no conflicts of interest.

### **Financial Disclosure**

The authors declared that this study has received no financial support.

### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

### **Ethical Approval**

The study was approved by Ethical Committee of Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences (Approval Number: 2021/191) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

### **Author Contributions**

Conception and design; SK, TK, ME, DNÖ, Data acquisition; HP, İE, OÖ, Data analysis and interpretation; SK, AFG, AH, ME, DNÖ, Drafting the manuscript; SK, TK, AH, İE, DNÖ, OÖ, Critical revision of the manuscript for scientific and factual content; AFG, AH, DNÖ, Statistical analysis; AFG, HP, ME, Supervision; SK, TK, İE, DNÖ, OÖ.

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# Preventive effect of pomegranate juice on ESWL-related renal damage in patients with kidney stones

### Böbrek taşı hastalarda ESWL' ye bağlı renal hasar üzerine nar suyunun önleyici etkisi

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### Özet

Amaç: Böbrek taşı tanısı nedeni ile ekstrakorporeal şok dalga litotripsi (ESWL) tedavisi uygulanan hastalarda, ESWL'nin neden olduğu oksidatif stresin yarattığı böbrek hasarının; nar suyunun (NS) antioksidan etkisiyle tedaviye bağlı böbrek hasarına karşı koruyucu etkisi olup olmadığını göstermeyi amaçladık.

Gereç ve Yöntemler: Böbrek taşı nedeniyle ESWL uygulanacak 90 hasta çalışmaya dahil edildi ve 30 kişiden oluşan 3 gruba ayrıldı. Grup 1'deki (kontrol grubu) hastalara sadece ESWL tedavisi uygulandı. Grup 2'deki (çalışma grubu) hastalara ESWL'den 2 gün önce 30 ml/kg/gün hazırlanan nar suyu karışımı 2 gün oral alınması önerildi. Grup 3'teki (plasebo grubu) hastalara ESWL'den 2 gün önce 30 mg/kg/gün su oral alınması önerildi. Hastalara 18-24 kV aralığında 2000-2500 atış yapıldı. Oksidatif stres, DNA lezyonunu gösteren lipid peroksidasyonun belirteçleri ve ESWL'den sonra tübüler hasar göstermek amacı ile her üç gruptaki hastalardan ESWL'den 3 gün önce ve hemen sonra 24 saatlik idrar toplandı ve spot idrar numunesi alındı.

**Bulgular:** Grup 1'de tedavi sonrası 8-Hydroxy deoxyguanosine (8-OHdG) düzeylerinde ortalama 52,39± 10,49 düzeyinde artış gözlendi (p<0,01). Grup 2'de tedavi sonrası 8-OHdG düzeylerinde ortalama 13,16±7,71 düzeyinde artış gözlendi (p<0,01).

Grup 1'de tedavi sonrası N-acetyl-beta-D-glucosaminidase (NAG) düzeylerinde görülen ortalama 19,20±5,21 düzeyinde artış göz-

### Abstract

**Objective:** We aimed to show whether the antioxidant properties of pomegranate juice (PJ) show a protective effect against renal damage associated with oxidative stress caused by Extracorporeal Shock Wave Lithotripsy (ESWL) in patients who have undergone ESWL for kidney stones.

Material and Methods: Ninety patients who were to undergo ESWL for kidney stones were included in the study and were divided into 3 groups with 30 patients each ESWL. Group 1 (control group) patients received only ESWL treatment. Group 2 (study group) patients were recommended to take 30 ml/kg/day pomegranate juice mixture orally for 2 days before ESWL. Group 3 (placebo group) patients were recommended to take 30 mg/kg/day water orally for 2 days before ESWL. All ESWL-treated patients received 2000 to 2500 shock waves at 18 to 24 in order to measure lipid peroxidation markers showing the DNA lesion associated with oxidative stress and to show tubular damage after ESWL,

**Results:** There was a statistically significant mean increase of  $52.39\pm10.49$  in 8-Hydroxy deoxyguanosine (8-OHdG) levels after treatment compared to pre-treatment levels in Group 1 (p<0.01). There was a statistically significant mean increase of  $13.16\pm7.71$  and  $33.24\pm12.82$  in Groups 2 and 3, respectively (p<0.01; p<0.01, respectively)

There was a statistically significant mean increase of 19.20±5.21 in N-acetyl-beta-D-glucosaminidase (NAG) levels after treatment compared to pre-treatment levels in Group 1 (p<0.01).

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The study was approved by the University of Health Sciences, Bakırköy Dr.Sadi Konuk Training and Research Hospital (Approval Number: 2009/78, 18.06.2009). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants. lendi (p<0,01).Grup 2'de tedavi sonrası NAG düzeylerinde ortalama 3,44±5,21 düzeyinde artış gözlendi(p<0,01).

**Sonuç:** Çalışmamızda NS'nin ESWL'ye bağlı böbrek hasarı üzerine koruyucu etkisi olduğunu gösterdik.

Anahtar Kelimeler: Antioksidan, böbrek taşı, taş kırma, nar suyu.

### INTRODUCTION

Extracorporeal Shock Wave Lithotripsy (ESWL) is an effective non-invasive method for treating urinary stones (1). However, it has damaging effects on the renal parenchyma and surrounding tissues. There are poorly understood mechanisms underlying ESWL-induced renal damage (2). ESWL-induced renal damage has poorly understood underlying mechanisms, including thermal and impact effects, the transient decline in renal perfusion, and the generation of free radicals due to ischemic cell damage and oxidative stress (3). There is a striking similarity between ESWL-related histopathological changes and ischemia-related findings in the kidney (4).

There are high N-acetyl-beta-D-glucosaminidase (NAG) levels, especially in lysosomes in renal proximal tubule cells. An increase in NAG levels in the urine indicates renal tubular dysfunction. A marked increase in diuresis and NAG excretion and a transient decrease in osmolality have been demonstrated after ESWL. These are indicators of tubular dysfunction caused by ESWL (5,6).

8-Hydroxy deoxyguanosine (8-OHdG) is a molecule that arises from oxidative stress, causes cellular injury by interfering with the structure of biological macromolecules

such as lipids, proteins, and DNA. Measurement of 8-OHdG levels is accepted as a direct marker of oxidative damage in DNA, which is the most commonly used method to determine the levels of oxidative DNA damage (7,8).

ESWL causes a transient increase in EPO levels independent of hemoglobin levels. This increase is attributed to intrarenal microcirculatory disorders resulting in tissue hypoxia (9). There was a statistically significant mean increase of  $3.44\pm5.21$  and  $13.07\pm5.50$  in Groups 2 and 3, respectively (p<0.01; p<0.01, respectively).

**Conclusion:** Our study concluded that pomegranate juice (PJ) has protective effects against ESWL-related renal damage.

Keywords: Antioxidant, kidney stones, lithotripsy, pomegranate juice.

Pomegranate juice is rich in polyphenol antioxidants. Polyphenols are the most abundant dietary antioxidants. These polyphenols include tannins and anthocyanins. These antioxidants are stronger than vitamin E, vitamin C, Qenzim10, and similar antioxidants (10). Pomegranate juice has been shown to have antioxidant effects against lipid peroxidation. Polyphenols are protective against reactive oxygen species produced intracellularly and extracellularly. The polyphenol content of pomegranate juice is between 0.2-1%, which varies between species. Pomegranate juice has a strong antioxidant effect, which further potentiates the biological effects of nitric oxide synthesis (eNO) (11,12).

Faria et al. reported that PJ has a protective role against hepatic protein and DNA oxidation, and systemic oxidative stress (13). Kaur et al. reported that pomegranate extract could scavenge superoxide (O(2) up to 53.3%, H2O2 up to 30%, 'OH radicals up to 37% and nitric oxide (NO) up to 74.5% and reduce hepatic lipid oxidation caused by 'OH radicals (14). Rosenblat et al. showed that pomegranate juice reduces the severity of atherosclerosis with its strong antioxidant effects (11).

This study measured NAG and 8-OHdG levels as an indicator of oxidative stress after ESWL, erythropoietin (EPO) levels to indicate an intrarenal microcirculatory disorder, and creatinine clearance and blood creatinine levels to indicate an alteration in renal function. It was aimed to show whether pomegranate juice has a protective effect against ESWL-induced renal damage.

### **MATERIAL AND METHODS**

The pomegranate juice used in our study was prepared in accordance with the food regulations in the laboratories of Istanbul Technical University, Faculty of Chemistry and Metallurgy, Department of Food Engineering. After washing the fresh pomegranates, their inner and outer skins and seeds were squeezed in a press. It was treated with pectinase enzyme to facilitate the filtration process and prevent pectin gel formation. It was then filtered, posturized, and dried. An extract of 400 g was obtained from approximately 1 kg of pomegranate. Subsequently, 10 g of pomegranate extract was diluted with 90 ml of drinking water and centrifuged at 3000 rpm for 20 minutes. This prepared concentration contained 10 g of pomegranate juice in every 100 ml (15, 16).

We divided patients to undergo ESWL due to renal calculus into three groups containing 30 participants. All patients received 2000 to 2500 shock waves in the range of 18-24 kV (mean 20 with PCK Stonelith-V5 Lithotripter). In the pre-ESWL evaluation, after careful history taking and physical examination, the calculi's number, size, and localization were determined. Any obstruction distal to or any dilatation proximal to the calculi was evaluated with IVP and/or USG. It was ensured that the radiological examinations were performed shortly before the ESWL. Vital signs (pulse, fever, and blood pressure) were evaluated. Preoperatively, we determined BUN and creatinine levels and performed complete blood count and coagulation tests in all patients. The patients were informed about the procedure and its complications. Smokers, patients with hypertension, diabetes, malignancy, and urinary tract infection, patients who had previously undergone ESWL or were operated on for renal calculi, patients who did not accept treatment, and those who had contraindications were excluded from the study.

All patients followed a diet low in vegetables and fruits for 1 week before ESWL. Group 1 (control group) patients received only ESWL treatment. Group 2 (study group) patients were recommended to take 30 ml/kg/day pomegranate juice mixture orally for 2 days before ESWL. Group 3 (placebo group) patients were recommended to take 30 mg/kg/day water orally for 2 days before ESWL. In order to measure lipid peroxidation markers showing the DNA lesion associated with oxidative stress and to show tubular damage after ESWL, 24-hour and spot urine samples were collected 3 days before and just after ESWL from patients in three groups. NAG ( 12889 Gregg curt Poway CA 92064, USA ), 8-OHdG (Vancouver, WA 98662 product NWK-0HDG01), creatinine, sodium, volume, and osmolality levels were measured by complete and 24-hour urine analysis. Venous blood samples were collected from all patients following a 12-hour fasting period 2 days before and 3 hours after ESWL. A 3 ml sample was taken from peripheral venous blood into a dry tube, and the levels of urea, creatinine, and EPO (according to IVDD 98/79/EC MDSS Burckhardstrasse 1 30163 Hannover, Germany) were measured in the biochemistry laboratory in our hospital on the same day. Creatinine clearance (mg/min) was calculated using the formula: (urine creatinine (mg/dL) x urine volume (mL/24 h)(serum creatinine (mg/dL) x 1440.

### **Statistical Analysis**

NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical Software (Utah, USA) package was used for statistical analysis of the results. Descriptive statistical methods (mean, standard deviation) were used to evaluate data. In addition, in comparing quantitative data, the Kruskal Wallis test was used for intergroup comparisons of non-normally distributed parameters, and the Mann-Whitney U test was used to determine the groups responsible for the difference. Paired sample t-test was used for in-group comparisons of normally distributed parameters. The level of statistical significance was set as p<0.05.

### RESULT

There was a statistically significant mean increase of  $52.39 \pm 10.49$  in 8-OHdG levels after treatment compared to pre-treatment levels in Group 1 (p<0.01).

There was a statistically significant mean increase of  $13.16\pm7.71$  and  $33.24\pm12.82$  in Groups 2 and 3, respectively (p<0.01; p<0.01, respectively)

There was a statistically significant difference between the percentage changes of 8-OHdG levels of the groups. Therefore, pairwise comparisons were made to determine the group responsible for the difference. The percentage change was statistically significantly higher in Group 1 compared to Groups 2 and 3 (p<0.01; p<0.01, respectively) and in group 2 compared to group 3 (p=0.01; p<0.01, respectively). Paired sample t-test p<0.05.

	Control	Pomegranate Juice	Water	Р
	Mean±SD	Mean±SD	Mean±SD	
8-OndG	(Median)	(Median)	(Median)	
Pre-Treatment	31.32±8.72	31.23±10.24	32.21±10.38	
Post-Treatment	83.71±16.17	44.40±13.13	65.45±19.12	
р	0.001	0.001	0.001	
0/ shange	178.25±55.91	47.85±39.45	110.52±43.66	0.001
% change	(166.54)	(38.77)	(111.1)	0.001

### Table 1. Reviews of 8-OHdG

*Kruskal–Wallis test p<0.01* 

In our study, the increase in 8-OHdG, which indicates DNA damage, was the least in group 2. We established that pomegranate juice protects against oxidative stress. We showed that it provides hydration and protects it from oxidative damage during ESWL.



**Figure 1.** Distribution of 8-OHdG levels between groups before and after treatment



**Figure 2.** Distribution of NAG levels between groups before and after treatment

Table 2. Increase in NAG levels between	en groups
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	Control	Pomegranate Juice	Water	Р
	Mean±SD	Mean±SD	Mean±SD	
NAG	(Median)	(Median)	(Median)	
Pre-Treatment	4.92±3.0	6.995±5.64	4.69±3.79	
Post-Treatment	24.12±5.78	$10.40 \pm 4.58$	19.56±6.75	
р	0.001	0.001	0.001	
0/ sharras	956.85±1540.66	158.39±216.47	444.38±631.67	0.001
% change	(349.75)	(59.05)	(201.8)	0.001

Kruskal-Wallis test p<0.01

There was a statistically significant mean increase of  $19.20\pm5.21$  in NAG levels after treatment compared to pre-treatment levels in Group 1 (p<0.01).

There was a statistically significant mean increase of 3.44±5.21 and 13.07±5.50 in Groups 2 and 3, respectively (p<0.01; p<0.01, respectively).

There was a statistically significant difference between the percentage changes in the NAG levels of the groups. Pairwise comparisons showed that the percentage change was statistically significantly higher in Group 1 compared to Groups 2 and 3 (p<0.01; p<0.01, respectively) and in Group 3 compared to Group 2 (p<0.01; p<0.01, respectively). Paired sample t-test p<0.05. We determined that pomegranate juice significantly reduced tubular dysfunction due to ESWL.

	Control	Pomegranate Juice	Water	Р
	Mean±SD	Mean±SD	Mean±SD	
EPO	(Median)	(Median)	(Median)	
Pre-Treatment	36,6744.95	39,0349.26	35.7547.13	
Post-Treatment	74.04410.51	75.61148.52	75.69413.01	
p	0.001	0.001	0.001	
0/ shanga	106.13443.19	98.52451.62	120.67464.56	- 0 1 1 5
70 change	(102.95)	(84.41)	(118.79)	0.115

Table 3. Increase in EPO levels between groups

Kruskal–Wallis test p<0.01

There was a statistically significant mean increase of  $37.37 \pm 11.99$  in EPO levels after treatment compared to pre-treatment levels in Group 1 (p<0.01).

There was a statistically significant mean increase of  $36.57\pm16.14$  and  $37.37\pm11.99$  in Groups 2 and 3, respectively (p<0.01; p<0.01, respectively). We established that pomegranate juice is protective in intrarenal microcirculatory disorder due to ESWL.

There was a statistically significant difference between the percentage changes of EPO levels of the groups.

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Table 4.	Changes in	Clearance	by Groups
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	Control	Pomegranate Juice	Water	Р
	Mean±SD	Mean±SD	Mean±SD	
Clearance	(Median)	(Median)	(Median)	
Pre-Treatment	175.5±1.85	175.5±1.85	175.8±1.60	
Post-Treatment	172.53±1.71	172.53±1.71	173.16±1.64	
р	0.001	0.001	0.001	
0/ sharras	$-1.68 \pm 0.63$	-1.68±0.63	$-1.49 \pm 0.52$	0.166
% change	(-1.16)	(-1.16)	(-1.14)	0.166

Kruskal-Wallis test p<0.01

There was a statistically significant mean decrease of  $32.96 \pm 1.12$  in clearance levels after treatment compared to pre-treatment levels in Group 1 (p<0.01).

There was a statistically significant mean decrease of  $2.96 \pm 1.12$  and  $2.63 \pm 0.92$  in Groups 2 and 3 (p<0.01; p<0.01, respectively). Paired sample t-test p<0.05.

### DISCUSSION

ESWL has been accepted as an effective non-invasive treatment of urinary tract stones. There is a striking similarity between ESWL-related histopathological changes and ischemia-related findings in the kidney. It has been accepted that there is an ischemia formation in the renal parenchyma distal to the lesion associated with damage to the intrarenal vessels (17, 18). After ischemia, the tissue is exposed to hypoxia, resulting in hypoxic tissue damage. Prolonged ischemia leads to loss of integrity of cells and even cellular death. The production of free oxygen radicals (FOR) is a normal physiological phenomenon. However, the increase in the synthesis of FORs leads to oxidation and DNA damage in cells (19, 20).

Free radical inhibitors are effective in most of the total damage caused by the reperfusion component. For a successful timing of the prevention of lipid peroxidation, it is important to administer antioxidants before or at the time of reperfusion (21). In our study, PJ with antioxidant properties was started to be given 2 days before ESWL.

It has been reported that oxidative stress can cause DNA damage such as base modifications and strand breaks. Among the base modifications induced by ROS, 8-OHdG is one of the DNA products with the highest oxidative properties. Hirano et al. reported that urinary and leukocytic 8-OHdG levels were higher in patients with non-insulin-dependent diabetes mellitus (NIDDM) with complications than in patients without complication. They stated that increased oxidative stress induced by hyperglycemia plays a role in the emergence of diabetic complications (7). In our study, we showed that 8-OHdG levels were statistically significantly increased in the urine of all groups after ESWL (p<0.01). This has been attributed to increased oxidative DNA damage as a result of lipid peroxidation after ESWL. We found a statistically significant difference between the groups (p<0.01). There was the lowest increase in Group II (PJ) (p<0.01). We also showed that when PJ is used as an antioxidant, it protects from oxidative DNA damage, and there was a statistically significant difference between Groups 1 and 3 (p<0.01). Moreover, we found that hydration before ESWL reduces oxidative DNA damage (p<0.01).

Hinokio et al. showed increased urinary NAG levels after ESWL compared to pretreatment levels. They attributed this increase to the damage on the proximal tubule after ESWL (22). In an animal study, Biri et al examined the effects of the combination of antioxidant vitamins C and E in the renal tissues of rabbits after ESWL. They showed a lower increase in NAG and malodialdehyde (MDA) levels in the antioxidant group (23). In an animal study, Özguner et al. used caffeic acid phentanyl ester (CAPE) as an antioxidant to prevent oxidative stress-induced renal tubular damage after ESWL. They divided the rabbits into two groups and administered CAPE in one group. They measured urinary NAG and malodialdehyde (MDA) levels before and after ESWL in both groups. They showed a higher increase in the ESWL group than in the CAPE group. They showed that ESWL causes damage to renal tubules due to oxidative stress, which can be prevented by antioxidants (24). In our study, a diet low in green vegetables and fruits was followed for 1 week in order to prevent any antioxidant intake in all groups .Two days before ESWL, PJ was started orally as an antioxidant at a dose of 2mg/kg/day. There was an increase in urinary NAG levels after ESWL in all groups (p<0.01). We interpreted that the increase in NAG levels is associated with renal tubular damage due to oxidative stress after ESWL. There was a statistically significant difference in the increase between the groups (p<0.01). The control group had the highest increase in urinary NAG levels (p<0.01). We showed a lower increase in group 2 compared to the other groups (p<0.01). We showed that oxidative stress after ESWL can be reduced with PJ used as an antioxidant. We showed that the difference between groups 1 and 3 was due to the reducing effect of pre-ESWL hydration on renal tubular injury (p<0.01).

Eterović et al. showed that ESWL caused a transient increase in EPO levels independent of hemoglobin levels. This increase is attributed to intrarenal microcirculatory disorders resulting in tissue hypoxia (25). In an animal study on pigs, Willis et al established 3 groups: ESWL only (Group 1); ESWL after verapamil (Group 2); and sham (Group 3). In their study, GFR and RPF were measured for both kidneys. In group 1, there was a decrease in GFR and RPF after 1 hour in the kidney that was subjected to ESWL. In the other kidney, there was no change in GFR, but there was a decrease in RPF. These changes showed an improvement after 24 hours. In the verapamil group, there was a decrease in GFR and RPF after 1 hour in the kidney subjected to ESWL, but there was an increase in GFR and RPF in the other kidney. This has been attributed to vasoconstriction during ESWL (26).

We showed that PJ, used as an antioxidant, had no effect on the increase of EPO and the decrease of GFR. We attributed the increase in EPO and decrease in GFR 3 hours after ESWL to vasoconstriction in the renal parenchyma and intrarenal microcirculatory disorders.

### CONCLUSION

ESWL-induced kidney damage leads to ischemia-reperfusion imbalance, vasoconstriction by direct action, and ultimately to oxidative stress as a result of intrarenal microcirculation disorder. We have shown that PJ is protective against oxidative stress when given before ESWL. We have shown that providing adequate hydration also protects against ESWL-induced oxidative damage. Therefore, high fluid intake may help protect against oxidative stress caused by ESWL. In this study, we showed that PJ can be used as an antioxidant.

### **Conflict of interest**

The authors declare to have no conflicts of interest.

### **Financial Disclosure**

The authors declared that this study has received no financial support.

### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

### **Ethical Approval**

The study was approved by the University of Health Sciences, Bakırköy Dr.Sadi Konuk Training and Research Hospital (Approval Number: 2009/78, Approval Date: 18.06.2009) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

### **Author Contributions**

Conception and design; ST, VT, Data acquisition; ST, SŞ, SK, Data analysis and interpretation; ST, VT, Drafting the manuscript; ST, Critical revision of the manuscript for scientific and factual content; ST, VT, Statistical analysis; ST, VT, Supervision; VT.

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### An analysis of YouTube videos on female genital mutilation as a global issue

Küresel bir sorun olarak kadın sünneti üzerine YouTube videolarının bir analizi

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### Özet

Amaç: Kadın sünneti, tüm dünyada yaygın olarak uygulanan, tıbbi olmayan nedenlerle kadın genital organının çıkarılmasıdır. Kadın sünneti genellikle kapalı toplumlarda uygulandığından bilim dünyası için karanlık bir konudur. Bu çalışmada kadın sünnetinin önlenmesinde YouTube videolarının rolünü değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu kesitsel çalışmada YouTube.com web sayfasında 1 Mayıs 2021 tarihinde "female genital mutilation" ve "female circumcision" anahtar kelimeleri kullanılarak net önbellek ve son güncellemeler içeren bir web tarayıcısında internet araması yapılmıştır. Arama sonuçları, yükleyicilerin demografik özellikleri, videoların kalitesi ve güvenilirliği açısından değerlendirildi.

**Bulgular:** Videoların çoğu kadınlar tarafından paylaşıldı. Kadınların ve sağlık çalışanlarının paylaştığı videolar, erkekler ve din görevlileri tarafından yüklenen videolara göre daha kaliteli ve daha güvenilirdi.

Sonuç: YouTube.com videoları kadın sünnetinin önlenmesi için faydalı olabilir ancak özellikle sağlık çalışanları tarafından bu konuya daha fazla dikkat edilmeli ve daha güvenilir ve daha kaliteli videolar paylaşılmalıdır.

Anahtar Kelimeler: Sirkümsizyon, kadın, genitalya.

### Abstract

**Objective:** Female genital mutilation is the removal of female genital organs for non-medical reasons, which is widely practiced worldwide. Female genital mutilation is a dark subject for the scientific world since it is often practiced in closed societies. In this study, we aimed to evaluate the role of YouTube videos in the prevention of female genital mutilation.

Material and Methods: In this cross-sectional study, an internet search was conducted on YouTube.com on May 1, 2021, using the keywords «female genital mutilation» and «female circumcision» on a web browser with a clear cache and latest updates. Search results were evaluated in terms of the demographic characteristics of uploaders and the quality and reliability of the videos.

**Results:** Most of the videos were shared by women. The videos shared by women and healthcare professionals were higher quality and more reliable compared to videos uploaded by men and religious personnel.

**Conclusion:** YouTube.com videos may be beneficial for the prevention of female genital mutilation, but more attention should be paid to this issue, particularly by healthcare professionals, and more reliable videos with the higher quality should be shared.

Keywords: Circumcision, female, genitalia.

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The study was conducted retrospectively. All research was performed in accordance with relevant guidelines/regulations.
# INTRODUCTION

Female genital mutilation (FGM), also known as female circumcision, is the partial or complete removal of female genital organs for non-medical reasons (1). This method is mostly applied for sociocultural and religious reasons and is widely performed in many countries globally, though considered infrequent. Although it is more common in West African countries, it is also administered in 28 other African countries and several Middle and Far Eastern countries. It is estimated that there are 115-130 million women with FGM globally and that around 3 million girls or women will be exposed to it every year (2-4). For these reasons, FGM can be accepted as a global problem.

In countries where FGM is implemented, the lack of governmental efforts to prevent FGM makes mass media, particularly social media, an important public education tool (5). Of these, YouTube.com is a popular social media platform and the world's largest video-sharing platform, with millions of subscribers and billions of views every day. Therefore, YouTube.com has a substantial social impact (6). A previous study examining YouTube.com videos on early childhood sexual abuse concluded that the videos were useful in preventing abuse (7).

In this study, we aimed to investigate whether You-Tube.com videos about FGM could be useful for preventing FGM. To our knowledge, this is the first study in the literature to examine YouTube.com videos about FGM.

# MATERIAL AND METHODS

# Study Design

In this cross-sectional study, an internet search was conducted on YouTube.com on May 1, 2021, using the keywords "female genital mutilation" and "female circumcision" by two independent physicians, including one urologist and one pediatric surgeon (MD, VA, respectively). The search was conducted using a web browser with a clear cache and the latest updates. Search results were listed according to their relevance, and then the Uniform Resource Locator (URL) of the first 200 videos were recorded. Videos that were non-English, silent, and did not share any relevant information were excluded from the study. The interaction level of the 156 videos' likes, dislikes, comments, views, and total durations was recorded for assessment. Subsequently, both physicians evaluated the videos separately in terms of content. The sources of the videos were recorded as news agencies, individual users, religious personnel, and healthcare provider, and the target audiences were recorded as healthcare professionals and the general public. The videos were evaluated in terms of quality and reliability according to the Global Quality Scale (GQS) and the DISCERN instrument. Interrater reliability was tested using the Kappa statistic. All discussions were continued until a consensus position was reached for all videos.

# **Global Quality Scale and DISCERN**

Our study used the Global Quality Scale and Brief DISCERN questionnaires (Appendix). Global Quality Scale is a scale developed by Bernard et al. for measuring the utility, flow, and quality of videos and is widely preferred by patients and healthcare professionals due to its ease of use (8).

DISCERN is a brief online questionnaire providing internet users with a valid, impartial, and reliable way of assessing the quality of consumer health information. The questionnaire consists of 16 questions (graded 1-5). The DISCERN score has been shown compatible with the quality of health information (9-11). The Brief DISCERN, which consists of 5 questions, was developed at a later period, and its results were found to be highly compatible with those of the original DIS-CERN (9,12)

# **Statistical Analysis**

Data were analyzed using SPSS for Windows version 21.0 (Armonk, NY: IBM Corp.). Continuous variables were expressed as mean, standard deviation (SD), and minimum-maximum values. Categorical variables were expressed as frequencies (n) and percentages (%). Group means were compared using the One-Way ANOVA test for continuous variables, followed by Duncan's Multiple Range Test (DMRT). Correlations were determined using Pearson's Correlation Coefficient. Relationships between categorical variables were assessed using the Chi-square test. A p-value of <0.05 was considered significant.

# Appendix:

GQS and Brief DISCERN Instrument

	Global Quality Scale					
1	Poor quality, poor flow of the site, most information missing, not at all useful for patients					
2	Generally poor quality and poor flow, some information listed but many important topics missing, of very limited use to patients					
3	Moderate quality, suboptimal flow, some important information is adequately discussed but others poorly discussed, somewhat useful for patients					
4	Good quality and generally good flow, most of the relevant information is listed, but some topics not covered, useful for patients					
5	Excellent quality and excellent flow, very useful for patients					
	Brief DISCERN Instrument					
1	Are the explanations given in the video clear and understandable?					
2	Are useful reference sources given?					
3	Is the information in the video balanced and neutral?					
4	Are additional sources of information given from which the viewer can benefit?					
5	Does the video evaluate areas that are controversial or uncertain?					
	Brief DISCERN Scoring					
4-5	Good quality, involving highly useful information					
3	Moderate quality, involving partially useful information					
1-2	Poor quality, involving little or no useful information					

# RESULTS

The results indicated that most of the 156 videos were uploaded by women (n=129; 82.6%). Of these, 130 (83.3%) videos were defending FGM, while 26 (16.6%) of them were against FGM, of which 20 (74.1%) videos were uploaded by men and 6 (4.7%) videos were uploaded by women (p<0.001). News agencies were the most common sources of the videos (n=64), followed by individual users (n=63), religious personnel (n=20), and healthcare personnel (n=9). All the videos uploaded by news agencies and healthcare personnel were against FGM, while 9 (14.3%) videos uploaded by individuals and 17 (85%) videos uploaded by religious personnel defended FGM (p<0.001).

As for the audience, all the videos addressed the general public. The average number of likes was 2,153.9, the average number of dislikes was 19.2, the average

number of comments was 2,266.5, the mean duration of the videos was 580.3 seconds, the meantime from the upload date was 70.2 months, and the mean number of views was 170,196.6. In terms of duration, the videos uploaded by religious personnel were significantly longer compared to other videos (p=0.03), while no significant difference was found among the videos uploaded by other sources (Table 1).

According to quality and reliability, both GQS and DISCERN scores were significantly higher in the videos presented by females compared to men ( $p \le 0.001$ ), in the videos uploaded by healthcare professionals compared to other sources ( $p \le 0.001$ ), and in the videos against FGM compared to the videos defending FGM ( $p \le 0.001$ ) (Table 2,3). The kappa coefficient for interrater reliability was 0.85.

Parameter	News agency	Individual users	Religious	Healthcare	р
			personner	professional	
Likes (n)	2182.53	1900.60	189.50	8089.00	0.26
Dislikes (n)	188.83	136.08	45.05	191.11	0.45
Comments (n)	5229.19	263.94	39.95	165.89	0.67
Duration of video (sec)	596.50	541.30	541.30	646.65	0.92
Views (n)	269658.19	122790.78	17317.90	134485.56	0.19
Time from upload date (months)	71.3	61.02	90.8	81.8	0.03

Table 1. Characteristics of the videos according to their uploaders

(In terms of duration, the videos uploaded by religious personnel were significantly longer compared to other videos (p=0.03), while no significant difference was found among the videos uploaded by other sources) (One-Way ANOVA)

		1	2	3	4	5	Total	р
Candan	Male	20	7	0	0	0	27	<0.001
Gender	Female	7	92	13	13	4	129	<0.001
	News agency	5	50	6	3	0	64	
Tralaadaa	Individual users	4	47	5	6	1	63	<0.001
Oploader	Religious personnel	18	2	0	0	0	20	<0.001
	Healthcare professional	0	0	2	4	3	9	
A 4414 1 .	For	25	1	0	0	0	26	-0.001
Attitude	Against	2	98	13	13	4	129	<0.001

# Table 2. DISCERN Scores

The DISCERN scores were significantly higher in the videos presented by females compared to men ( $p \le 0.001$ ), in the videos uploaded by healthcare professionals compared to other sources ( $p \le 0.001$ ), and in the videos against FGM compared to the videos defending FGM ( $p \le 0.001$ ) (Chi-square test)

# Table 3. GQS scores

		1	2	3	4	5	Total	р
Condon	Male	16	10	0	0	1	27	<0.001
Gender	Female	6	77	30	12	4	129	<0.001
	News agency	1	44	15	3	1	64	
Unloadan	Individual users	7	35	14	6	1	63	<0.001
Oploader	Religious personnel	14	6	0	0	0	20	<0.001
	Healthcare professional	0	2	1	3	3	9	
Attitude	For	19	7	0	0	0	26	<0.001
	Against	3	80	30	12	5	130	<0.001

The GQS scores were significantly higher in the videos presented by females compared to men ( $p \le 0.001$ ), in the videos uploaded by healthcare professionals compared to other sources ( $p \le 0.001$ ), and in the videos against FGM compared to the videos defending FGM ( $p \le 0.001$ ) (Chi-square test)

# DISCUSSION

The physical and psychological effects of female genital mutilation have been demonstrated in the literature (13,14). A study conducted in Mali and Burkina Faso showed that women with FGM had a lower sense of trust and a higher prevalence of psychological trauma and relationship problems. The study also indicated that these women had less pleasure from sex, reached orgasm relatively later, and also had a higher prevalence of complications such as urethral and anal rupture or urination problems due to urethral stricture, difficulty in sexual intercourse due to frequent urinary tract infections and vaginal narrowing, and painful sexual intercourse (15,16). Despite the presence of many studies on FGM reporting on these complications, our study indicated that the number of videos uploaded by healthcare professionals was highly limited, which implicates that healthcare professionals do not pay enough attention to this issue. Nonetheless, the high quality and reliability scores of the videos uploaded by healthcare professionals show that these professionals have mastered the subject matter. Accordingly, we suggest that the awareness of healthcare professionals on this issue should be increased.

In our study, the videos were mostly uploaded by individual users and news agencies, which shows that women suffering from FGM share their grievances on YouTube and that the mass media is relatively more interested in the subject matter. Nevertheless, considering the insufficient quality and reliability of the videos analyzed in our study, it can be asserted that even the women suffering from FGM do not have enough information about the complications of FGM or do not care enough about this subject matter.

The influence of religion on society, particularly in African and Middle Eastern countries, is undeniable, and religious leaders' opinions are highly valued (17,18). However, the FGM videos shared by religious personnel in our study were not only full of misinformation but also harmful because they promoted FGM, which provides an idea about the role of religious personnel in the widespread implementation of FGM in these countries. In countries where FGM is commonly practiced, most men seem to dream of a female partner with FGM. One of the reasons for this is that the vagina narrowed by some FGM techniques is considered to provide the male partner greater pleasure during sexual intercourse, while another reason is the moral, cultural, and honor values attributed to FGM through the reduction of sexuality of women (19). In a study conducted in 13 countries in Africa, it was reported that women with FGM had a 40% higher chance of getting married (20). The relatively lower number of videos shared by men in our study and the lower quality and reliability of the videos implicate that men are not interested in and are less knowledgeable about this subject matter when compared to women.

In many countries, FGM is practiced even before girls reach puberty. Moreover, it is known that 90% of FGMs in Egypt are performed between the ages of 5-13, with the intention of suppressing their sexual desires that emerge with the hormonal changes occurring during puberty. In addition, it has been reported that FGM is mostly performed in the first two months of life in Yemen and that the average age of FGM is gradually decreasing in countries such as Burkina Faso, Kenya, and Mali (21,22). Children in this age range are under the control of their families and do not have an individual say, and thus it is not possible for them to take a stand against FGM. In our study, almost all the women who uploaded the videos were against FGM. Therefore, we suggest that even if FGM cannot be prevented, it should be delayed until the women gain their voice.

The limitation of our study was that it only included English-language videos and did not evaluate the videos produced in the local languages of Africa, where FGM is frequently applied. In addition to this limitation, the strength of our study is that the first study on this subject was conducted prospectively.

# CONCLUSION

YouTube.com videos may be beneficial for the prevention of FGM, but more attention should be paid to this issue, particularly by healthcare professionals, and more reliable videos with the higher quality should be shared. However, it is necessary to be aware of the videos supporting FGM and take steps to prevent them.

# **Conflict of interest**

The authors declare to have no conflicts of interest.

# **Financial Disclosure**

The authors declared that this study has received no financial support.

# **Informed Consent**

Patient data did not use in the study.

# **Ethical Approval**

In this study, ethical approval did not obtain because it did not use patient data. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

# **Author Contributions**

MD; conceptualized the project, designed the study questionnaire in its final form, analyzed the collected data, and wrote the entire manuscript. VA; helped in the data collection, did the statistical analysis of the collected data, and made sense of it. MD; helped in data collection, proofreading, revising, and drafting of tables & figures of the final version of the manuscript. VA; helped in data collection, proofreading, revising the final version of the manuscript.

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# How effective is the duration of breastfeeding on monosymptomatic enuresis nocturna?

# Anne sütü süresi monosemptomatik enürezis nokturnada ne kadar etkili?

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# Özet

**Amaç:** Bu çalışmada, monosemptomatik enurezis nokturna üzerine anne sütü alımının süresi ve ilişkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Temmuz 2020- Eylül 2020 tarihleri arası üroloji kliniğimize başvuran 78 enürezis nokturna tanısı alan, 72 si kontrol grubu olan 150 çocuk çalışmaya dahil edildi. Anne sütünün süresi, evdeki çocuk sayısı, formül mama ile beslenme, ebeveyn eğitimi ve pasif sigara içiciliği soruldu.

**Bulgular:** Çalışmaya dahil edilen 150 hastanın yaş ortalaması 7,6 (5-10 yıl) idi. Enürezis grubunu 36 kız, 42 erkek oluştururken, kontrol grubunu 36 kız, 36 erkek oluşturdu. Evdeki çocuk sayısı enürezis grubunda 7(3-10) iken, kontrol grubunda 5(4-8) idi. Her iki grup arasında anlamlı fark mevcuttu (p=0,008). Anne sütü ile beslenme süresi değerlendirildiğinde enürezis grubu ile kontrol grubu arasındaki anlamlı fark 18 ay olarak bulundu (p=0,016). Formül mama ile beslenme enürezis grubu ve kontrol grubu arasında fark yoktu (p=0,599). Pasif sigara içiciliği ve ebeveynlerin eğitimi açısından her iki grup arasında fark yoktu.

**Sonuç:** Çocukluk çağında sık görülen rahatsızlıklardan birisi de enürezis nokturnadır. Yaşla birlikte devam etmesi çocuk da olumsuz birçok etki ortaya çıkarmaktadır. Çalışmamızda 18 aydan fazla emzirmeye devam edilirse enurezis nokturna görülme sıklığının azaldığı saptanmıştır. Ulaşılabilirliği kolay olan emzirmenin, çocukluk gelişiminin birçok yönü üzerindeki etkisine benzer şekilde, enürezis nokturna üzerinde olumlu bir etkisi vardır.

Anahtar Kelimeler: Enürezis nokturna, anne sütü, beslenme.

# Abstract

**Objective:** This study aimed to evaluate the relationship and duration of breastfeeding in monosymptomatic enuresis nocturna.

**Material and Methods:** 150 children, 78 of whom were diagnosed with enuresis nocturna and 72 of whom were in the control group, who applied to our urology clinic between July 2020 and September 2020, were included in the study. The duration of breastfeeding, the number of children at home, formula feeding, parent education, and passive smoking were asked.

Results: The mean age of 150 patients included in the study was 7.6 (5-10 years). The enuresis group consisted of 36 girls and 42 boys, while the control group consisted of 36 girls and 36 boys. In comparison, the number of household members was 7(3-10) in the enuresis group, 5(4-8) in the control group. There was a significant difference between both groups (p=0.008). When the duration of breastfeeding was evaluated, the significant difference between the enuresis group and the control group was found to be 18 months (p=0.016). There was no difference between the formula and feeding enuresis group and the control group (p=0.599). There was no difference between the two groups in terms of passive smoking and parental education.

**Conclusion:** One of the most common disorders in childhood is enuresis nocturna. Continuing with age has many negative effects on the child. Our study observed that the incidence of enuresis decreased if breastfeeding was continued for more than 18 months. Readily available breastfeeding positively affects enuresis nocturna, similar to its effect on many aspects of childhood development.

Keywords: Enuresis nocturna, breastfeeding, nutrition.

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The study was approved by Clinical Research Ethics Committee of Harran University, Turkey (Approval Number: 11/20, Approval Date: 15.06.2020). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

# INTRODUCTION

Monosymptomatic enuresis nocturna (MEN) is characterized by urinary incontinence that occurs only at night in children aged >5 years without any pathology in the urinary system (1). Although prevalence rates of 5%–15% have been reported for MEN, its prevalence in Turkey has been reported 20%–30% in schoolage children (2).

There is no definite consensus for the etiology of MEN; however, many factors, such as central nervous system development disorders, psychological and environmental factors, sleep disorders, genetic factors, passive smoking, the abnormal release of anti-diuretic hormone, some diseases of the urinary system (infections and anomalies), and other causes (polyuria, renal tubular diseases, neurological disorders, and parasites), may play a role in its etiology (3,4). Thus, these factors indicate that neurological development is associated with MEN (5).

There is ample evidence that breast milk is very important for neurological development (6). As the nutrients required for neurological development are present in sufficient amounts in breast milk, adequate breast milk intake positively affects the mental and intellectual development of the infant (7). The role of polyunsaturated fatty acids in brain development function is important. Without a dietary source, infants must synthesize large amounts of docosahexaenoic acid and arachidonic acid to keep up with the needs of the developing brain. Without a dietary source, infants must synthesize large amounts of docosahexaenoic acid and arachidonic acid to keep up with the needs of the developing brain. (8).

Therefore, we aimed to evaluate the effect of breastfeeding duration on enuresis frequency in children with MEN and its relationship with other factors.

# **MATERIAL AND METHODS**

Seventy-eight patients diagnosed with primary MEN, aged 5–18 years, whose parents were not divorced, and who applied to the urology outpatient clinic between July 2020 and September 2020 with the complaint of nocturnal urinary incontinence were in-

cluded in the study. Participants were informed about the study, and written consent was obtained from their parents. All data were reviewed retrospectively. A total of 72 healthy children who applied to the urology outpatient clinic for circumcision were included in the control group in the study. Patients with urinary tract infection, day and night voiding symptoms, hormonal disorders (diabetes insipidus, diabetes mellitus), and psychiatric diseases (attention deficit hyperactivity disorder, autism spectrum disorder, conduct disorder, anxiety, and mood disturbance) were excluded from the study. After detailed anamnesis and physical examination, patients were asked about their height, weight, number of children at home, how many months they had breastfed, whether they were fed with formula, history of passive smoking, and family education status. Those who had a history of being fed with a formula for any period in the first two years of life were classified as formula (+), and those who did not were classified as formula (-).

Data were analyzed with SPSS software version 25.0 for Windows (SPSS Inc, Chicago, Illinois). The Kolmogorov-Smirnov test was used to verify that continuous variables were normally distributed. Normally distributed variables were expressed as mean  $\pm$  standard deviation (SD), while non-normally distributed variables were expressed as median (minimum, maximum). The categorical variables are presented as percentages. Differences between the two groups were evaluated with students' unpaired t-test or the Mann–Whitney U test for normal or non-normal distribution parameters. The frequencies of nominal variables were compared using the Fisher's exact test or chi-square test.

# RESULTS

The mean age of 150 patients included in the study was 7,6±1.8 (5–10 years). The mean age of the enuresis group was 7,4±1.8 years, and the mean age of the control group was 7.9±1.8 years. No significant difference was found between the groups regarding age (p=0.203) (Table 1). The enuresis group consisted of 36 girls and 42 boys, whereas the control group consisted of 36 girls and 36 boys. There was no significant difference between the groups in terms of gender (p=0.819). The mean body mass index (BMI) was 15,1 kg/m2 in the enuresis group, 15.2 kg/m2 in the control group. BMI was similar between the patient group and the control group (p=0.970). The median number of children at home was 7 (3–10) in the enuresis group, whereas it was 5 (4–8) in the control group; there was a signifi-

cant difference between the groups (p=0.008). When the duration of breastfeeding was evaluated, a significant difference of 18 months was found between the enuresis and control groups (p=0.016). There was no difference between the two groups regarding being fed formula (p=0.599) nor in terms of passive smoking and parental education (Table 1).

	All groups	Enuresis Noctu	ırna, %(n)	Р
		(+)	(-)	
Household members	6 (3, 10)	7 (3, 10)	5 (4, 8)	0.008*
Breast feeding				0.016*
< 18 months	58.7 (88)	71.8 (56)	44.4 (32)	
> 18 months	41.3 (62)	28.2 (22)	55.6 (40)	
Formula feeding				0.599
Formula feeding +	58.7 (88)	61.5 (48)	55.6 (40)	
Formula feeding -	41.3 (62)	38.5 (30)	44.4 (32)	
Pasive smoker				0.525
Pasive smoker +	57.3 (86)	53.8 (42)	61.1 (44)	
Pasive smoker -	42.7 (64)	46.2 (36)	38.9 (28)	
Maternal Education				0.416
Educated	50.7 (76)	46.2 (36)	55.6 (40)	
Uneducated	49.3 (74)	53.8 (42)	44.4 (32)	

Table 1	. Com	parison	of	patients	and	control	groups
							D

# DISCUSSION

Breastfeeding has many benefits for the mother and infant. Breast milk is the best food for the infant as it contains all the nutrients needed for healthy growth and development (9). Breastfeeding supports the child's neurological development because of the lipid structure in the constituents of milk. Breastfeeding not only serves the purpose of feeding but is also a special psychophysical stimulant for the mother and infant. During breastfeeding, the mother provides the infant with a feeling of warmth, security, and protection. If emotional bonds are established securely in childhood, undesirable behaviors, such as addiction and involvement in crime, can be prevented (10). Girard et al. found that difficulties in establishing emotional bonds and attention deficits were more common in breastfed children for <12 months (11). Kwok et al. reported that breastfeeding for <3 months was associated with worse behavior and lower self-esteem. Psychogenic factors play a role in the etiology of MEN in a manner similar to stress (12). Furthermore, neurodevelopmental delays were observed in children with MEN (13). In the literature, the relationship between MEN and breastfeeding is still unclear. In a cross-sectional study by Gümüş et al., different clinical factors that played a role in childhood bedwetting were evaluated, and no difference was found between patients with and without enuresis, with reference to breastfeeding rates in the first four months after birth (14). In a study conducted on 1212 school-age children, Sristava et al. reported that enuresis nocturna was significantly more common in children who were not exclusively breastfed until the age of 6 months (15). Barone et al. compared children with enuresis with a control group and demonstrated that breastfed for >3 months had a protective effect against bedwetting (16). In a recent observational case-control study involving 200 subjects (children and adolescents) aged 6 to 14 years, Oliviera et al. reported that a breastfeeding duration of <4 months was strongly associated with MEN (17). In the present study, when breastfeeding durations were compared, a duration of 18 months was found to be significant. The prevalence of enuresis was found to be significantly higher in those who were breastfed for <18 months compared with that in those who were breastfed for >18 months (p<0.05). In terms of child development, the World Health Organization recommends breastfeeding for 24 months (18). In line with this recommendation and the results of the present study, we believe that the prevalence of MEN can be reduced by prolonging the duration of breastfeeding.

Passive smoking in children is an extremely important public health problem directly associated with many childhood diseases (19). Previous studies have shown that passive smoking leads to impaired respiratory symptoms, allergic diseases, and sleep quality in children (20). Studies on adult female patients with secondary enuresis nocturna reported that smoking negatively affects bladder function and that smoking was identified as a risk factor for enuresis nocturna (21). A recent study on children with MEN demonstrated that the response to desmopressin treatment was lower in those exposed to cigarette smoke (22). Although there is scientific evidence on the relationship between MEN and exposure to cigarette smoke, no difference was found between the enuresis and control groups in terms of passive smoking in the present study.

MEN may be associated with nocturnal urine production due to insufficient vasopressin hormone formation during sleep (23). Breastfeeding increases early neuronal maturation and visual acuity, which may be important in driving the normal circadian rhythm and establishing normal neuronal pathways (24). Kalo et al. showed that breastfeeding increases the development of nocturnal continence and reduces this possibility as an incidental finding (25). We also obtained similar results in the present study. Many studies in the literature demonstrate that familial factors, such as low socioeconomic status, low educational level of parents, family size, and birth order are associated with MEN (26). On the other hand, Spee-van der Wekke et al. reported that the parents' education level was not associated with the prevalence of MEN (27). In the present study, we were unable to find a relationship between parental education level and MEN.

Studies are reporting that the prevalence of enuresis nocturna increases in extended families (28). The present study found that the prevalence of enuresis nocturna increased in families with many children at home.

The most important limitation of the present study was the large time difference between breastfeeding, the onset of enuresis, and when the survey was conducted. The data used in the study were based on the parents' statements, and those who had difficulty remembering and those who could not completely remember necessary details were excluded from the study.

# CONCLUSION

MEN is an important public health problem common in childhood and causes considerable distress for children and their parents. The present study found that the prevalence of MEN decreased in children who were breastfed for >18 months. Like many of its effects on childhood development, breastfeeding, an easy and convenient feeding method for mothers, also positively affects MEN. There is a need for further prospective multicenter studies on this subject with larger patient series.

# **Conflict of interest**

The authors declare to have no conflicts of interest.

# **Financial Disclosure**

The authors declared that this study has received no financial support.

# **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

# **Ethical Approval**

The study was approved by Clinical Research Ethics Committee of Harran University (Approval Number: 11/20, Approval Date: 15.06.2020) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

# **Author Contributions**

Conception and design; KG, Data acquisition; KG, Data analysis and interpretation; TK, HFÖ, Drafting the manuscript; KG, Critical revision of the manuscript for scientific and factual content; TK, HFÖ, Statistical analysis; KG, Supervision; TK, HFÖ.

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# The approach of emergency physicians to patients with acute renal colic

Acil servis doktorlarının akut renal kolikli hastaya yaklaşımı

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# Özet

**Amaç:** Çalışmamızda acil servise başvuran ve akut renal kolik tanısı alan hastalarda acil tıp uzmanı ve asistanların tanı ve tedavi stratejilerini belirlemeyi amaçladık.

Gereç ve Yöntemler: Bu çalışmada acil tıp doktorlarına internet tabanlı kesitsel bir anket yapıldı. Ankette katılımcılara ait demografik verileri, acil serviste çalışma süreleri ve acil tıp uzmanı veya asistanı oldukları soruldu. Katılımcılara acil servise başvuran akut renal kolik hastalarında ilk tercih görüntüleme yöntemleri, tetkikler, hangi durumlarda üroloji konsültasyonu istedikleri, analjezik ve tedavi tercihleri soruldu.

Bulgular: Çalışmaya katılan 108 gönüllünün yaş ortancası 31 (27 - 34,8) yıl olarak hesaplandı. Katılımcıların %60,2'i (n=65) acil tıp asistanı, %39,8'i (n=43) acil tıp uzmanı olan çalışma grubunun acil serviste çalıştığı sürenin yıl cinsinden ortancası 4 (2-8) yıl olarak hesaplandı. Acil tıp uzmanı ve asistanlarının renal kolik ön tanısı ile acil servise başvuran hastalardaki yaklaşımları ile ilgili değişkenler açısından farkları incelendi. Non-steroidal antienflamatuvar ilaç (NSAID) verilmesi planlanan hastalarda seçilecek ilk ilaç, diklofenak ve diğer NSAID olarak dikotomize edildiğinde, uzmanların 34 (%79,1)'nün, asistanların ise 60 (%92,3)'ının ilk tercih olarak diklofenak seçtiği görülmüş ve gruplar arasında istatistiksel anlamlı fark saptandı.

# Abstract

**Objective:** This study was conducted to describe the current diagnosis and treatment strategies of patients admitted to the emergency department and diagnosed with acute renal colic.

Material and Methods: In this study, an internet-based cross-sectional survey was administered to emergency medicine physicians. In addition to the participants' demographic data, such as age and gender, years of experience in the emergency medicine department, and whether they were a specialist or resident, the survey also inquired about their choices of imaging methods, laboratory tests, analgesic medications, and intravenous fluids, and tendency to refer patients to a urologist for a consultation.

**Results:** The median age of the 108 volunteers participating in the study was calculated as 31 (27 - 34.8) years and their years of experience as 4 (2-8) years. More than half (60.2%, n=65) of the participants were emergency medicine residents, while the remaining 39.8% (n=43) were emergency medicine specialists. The emergency medicine specialists and residents were compared in terms of the variables related to their approaches to patients presenting to the emergency department with a preliminary diagnosis of renal colic. The first choice of analgesic drugs was dichotomised as diclofenac and other non-steroidal anti-inflammatory drugs, with 34 (79.1%) of the specialists and

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This study was approved by the Ethics Committe of Health Sciences University, Bakırköy Training and Research Hospital (No: 2021-20/479, Date: October 18, 2021). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

**Sonuç:** Çalışmamızda acil tıp uzmanı ve asistanı arasında renal kolik görüntüleme yöntemi açısından benzer tercihler yapmasına rağmen birinci basamak tedavide acil tıp asistanları, acil tıp uzmanlarına kıyasla daha çok Diklofenalćı tercih etmiştir.

Anahtar Kelimeler: Akut renal kolik, acil tıp, böbrek taşı.

60 (92.3%) of the residents reporting diclofenac as their first choice, and there was a statistically significant difference between the two groups.

**Conclusion:** In this study, the emergency medicine residents preferred diclofenac more than the emergency medicine specialists in primary care, although they had similar renal colic imaging methods preferences.

Keywords: Acute renal colic, emergency medicine, kidney stone.

# INTRODUCTION

Hospital admissions for renal colic account for approximately 1% of all emergency presentations each year, and emergency department physicians provide care for this patient population at least once a day (1, 2). Renal colic is a common urologic emergency in hospital emergency departments, caused by stones in the urinary system and associated with severe flank pain (3,4). Costovertebral angle tenderness, abdominal pain, and haematuria are the main symptoms used to diagnose acute renal colic (5).

The emergency physician's role is to initiate appropriate treatment if the diagnosis is correct and refer the patients for consultation (2). The physician should intervene appropriately to relieve pain in treated patients and prevent complications associated with the etiological factor causing renal colic (1,6). Emergency medicine specialists and residents may have different approaches to patients presenting to the emergency department. However, to our knowledge, no study compared emergency medicine specialists and residents in terms of their approach to patients with renal colic presenting to the emergency department.

This study aimed to define the diagnosis and treatment strategies of the emergency medicine specialist and residents in managing patients who presented to the emergency department and were diagnosed with acute renal colic.

# MATERIAL AND METHODS

The study included 121 emergency medicine specialists. Six did not complete the questionnaire, and seven were excluded because they were not emergency medicine residents or specialists. As a result, the study was completed with 108 participants.

We used the Google Forms platform for this cross-sectional study and designed an online survey with 11 questions. The study was designed according to the Checklist Rules for Reporting Results of Electronic Surveys on the Internet (CHERRIES) (7). Participants who completed the survey between October 1, 2021, and October 15, 2021, were included in the study and divided into two groups as emergency medicine residents and specialists (Ethics committee approval number: 2021-479).

A web-based cross-sectional survey was administered to emergency medicine physicians in this study. The participants were informed about the study's aims with a brief presentation, and their electronic informed consent was obtained before the study began. They were also informed that they could withdraw from the survey without giving any reason, and in that case, their data would not be used. No personal information was collected during the survey to allow participants to be identified. The survey took approximately 5 minutes to complete and included questions related to demographic data, such as the participant's age and gender, years of experience in the emergency medicine department, and whether they had an emergency medicine specialist or resident. The participants were also asked about the first-choice imaging modality in patients presenting to the emergency department with acute renal colic, laboratory tests they requested at the time of admission, indications they used to refer patients for urological consultation, analgesics they preferred,

and whether and how often they administered saline to patients. The findings obtained from the survey were compared between the groups. Due to the survey's design, the participants needed to answer all the questions to ensure successful participation.

# **Statistical Analysis**

SPSS (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) was used for data analyses. The conformity of continuous data to the normal distribution was analyzed using the Shapiro-Wilk test. Continuous data that did not conform to the normal distribution were expressed as median (25%-75% quartile) values and categorical data as frequency and percentages. Paired-group comparisons were performed using the Mann-Whitney U test for continuous data that did not conform to the normal distribution. Group comparisons for categorical data were undertaken using the chi-square test, with Fisher's exact test conducted when necessary. The statistically significant level was accepted as p < 0.05.

# RESULTS

The mean age of the 108 volunteers who participated in the study was 31 (27-34.8) years. In the study group, 60.2% (n = 65) of the participants were emergency medicine residents, and 39.8% (n = 43) were emergency medicine specialists. The median length of service in the emergency department was calculated as

4 (2-8) years. The primary demographic characteristics of the participants and their responses to the survey questions are summarized in Table 1.

The emergency medicine specialists and their residents were compared in terms of variables related to their approach to patients presenting to the emergency department with a pre-diagnosis of renal colic. The first choice of analgesic drugs was dichotomised as diclofenac and other non-steroidal anti-inflammatory drugs (NSAIDs), with 34 (79.1%) of the specialists and 60 (92.3%) of the residents reporting diclofenac as the first choice, and there was a statistically significant difference between the two groups (p = 0.045).

When comparing the frequency of C-reactive protein (CRP) requests between the two groups, it was found that 21 of the specialists (48.8%) and 48 of the residents (73.8%) requested this test, and the difference was statistically significant (p = 0.008). There was a statistically significant difference between the two groups in relation to the frequency of blood gas requests, [3 (7%) among the specialists and 18 (27.7%) among the residents] (p = 0.008). The frequency of albumin requests also statistically significantly differed between the specialists (0%) and residents (n = 7, 10.8%) (p =0.025). There was no statistically significant difference between the two groups concerning the remaining variables. The primary outcome measures are summarized in Table 2.

Table 1. Baseline characteristics of the sample

n = 108	Median (25-75% quartile)/n (%)
Age	31 (27-34.8)
Gender (male)	67 (62)
Title	
Emergency medicine resident	65 (60.2)
Emergency medicine specialist	43 (39.8)
Years of experience	4 (2-8)
Emergency medical residents	2 (1-3.5)
Emergency medical specialists	9 (6-11)

What is the first imaging method you would request in patients with suspected renal colic?	
X-ray	13 (12)
Abdominal CT	46 (42.6)
Ultrasonography	49 (45.4)
Which laboratory tests would you request?	
Complete urinalysis	107 (99.1%)
Complete blood count	80 (74.1%)
Creatinine	89 (82.4%)
Urea	84 (77.8%)
CRP	72 (66.7%)
Blood electrolytes	53 (49.1%)
Blood gas analysis	21 (19.4%)
Albumin	4 (3.7%)
What would be the first analgesic treatment protocol you would choose?	
NSAID	43 (39.8%)
NSAID + opioid	65 (60.2%)
If you were to give the patient an NSAID, what would be your first choice?	
Diclofenac	94 (87%)
Etodolac	2 (1.9%)
Ketorolac	4 (3.7%)
Ibuprofen	3 (2.8%)
Other	5 (4.6%)
If you were to give the patient opioids, what would be your first choice?	
Fentanyl	40 (37%)
Morphine	6 (5.6%)
Tramadol	62 (57.4%)
Do you prefer to use an isotonic solution?	
Never	1 (0.9%)
Rarely	20 (18.5%)
Sometimes	35 (32.4%)
Often	37 (34.3%)
Always	15 (13.9%)
In which situations would you request a urology consultation?	
Resistant flank pain	46 (42.6%)
Decreased urine output	93 (86.1%)
Presence of fever	52 (48.1%)
Newly diagnosed renal colic	2 (1.9%)

CT: computed tomography, CRP: C-reactive protein, NSAID: non-steroidal anti-inflammatory drug

	Emergency medicine resident, n (%)	Emergency medicine specialist, n (%)	p-value
What is the first imaging method you would request in patients with suspected renal colic?			
X-ray	8 (12.3)	5 (11.6)	0.980
Abdominal CT	28 (43.1)	18 (41.9)	
Ultrasonography	29 (44.6)	20 (46.5)	
What would be the first analgesic treatment protocol you would choose?			
NSAID	27 (41.5)	16 (37.2)	0.653
NSAID + opioid	38 (58.5)	27 (62.8)	
If you were to give the patient an NSAID, what would be your first choice?			
Diclofenac	60 (92.3)	34 (79.1)	0.045
Other NSAIDS	5 (7.7)	9 (20.9)	
If you were to give the patient opioids, what would be your first choice?			
Fentanyl	27 (41.5)	13 (30.2)	0.060
Morphine	1 (1.5)	5 (11.6)	
Tramadol	37 (56.9)	25 (58.1)	
Do you prefer to use an isotonic solution?			
Rarely	12 (18.5)	9 (20.9)	0.247
Sometimes	25 (38.5)	10 (23.3)	
Often	28 (43.1)	24 (55.8)	
In which situations would you request a urology consultation?			
Resistant flank pain	29 (44.6%)	17 (39.5%)	0.601
Decreased urine output	54 (83.1%)	39 (90.7%)	0.262
Presence of fever	30 (46.2%)	22 (51.2%)	0.610
Newly diagnosed renal colic	2 (3.1%)	0 (0%)	0.516
Which laboratory tests would you request?			
Complete blood count	49 (75.4%)	31 (72.1%)	0.702
CRP	48 (73.8%)	21 (48.8%)	0.008
Blood urea nitrogen	51 (78.5%)	33 (76.7%)	0.834
Creatinine	52 (80%)	37 (86%)	0.419
Blood electrolytes	36 (55.4%)	17 (39.5%)	0.107
Complete urinalysis	65 (100%)	42 (97.7%)	0.398
Blood gas analysis	18 (27.7%)	3 (7%)	0.008
Albumin	7 (10.8%)	0 (0%)	0.025

Table 2. Comparison of the approaches of the emergency medicine residents and specialists to patients presenting with renal colic

CT: computed tomography, CRP: C-reactive protein, NSAID: non-steroidal anti-inflammatory drug

# DISCUSSION

This national survey study aimed to determine the differences in the approaches of emergency medicine specialists and residents in patients with renal colic. The results revealed that the emergency medicine residents and emergency medicine specialists differed in their approaches to diagnosing and managing patients with renal colic. There is no other study in Turkey that questioned the approach of emergency department physicians to patients with renal colic and determined the differences in these approaches between specialists and residents considering many articles published in Turkish and other languages, to our knowledge.

Renal colic due to obstruction caused by a stone places a significant burden on health systems and emergency services worldwide (8,9). Two percent of adult patients admitted to the emergency department constitute those with suspected renal colic. The incidence of these patients has doubled in the last two decades (10). Essential steps in managing patients with renal colic are to diagnose a complete obstructive stone, relieve severe pain leading to nausea and vomiting, decide on intervention by establishing the negative findings of the clinical picture, and safely discharge the patient by demonstrating adequate urine flow (8,9). Renal colic caused by an obstructive stone is usually manifested by the sudden onset of severe and sharp, local or radiating pain, often accompanied by nausea, vomiting, and urinary symptoms (8).

After a general examination of these patients, imaging techniques are essential in diagnosis (10). The European Association of Urology (EAU) guidelines state that the first imaging procedure should be ultrasonography (US) if urolithiasis is suspected. However, for patients with treatment-resistant pain and in cases where another diagnosis is suspected, abdominal computed tomography (CT) without contrast enhancement is recommended (11). In a study by Smith et al., it was found that the rates of complications, serious adverse events, readmission to the emergency department, and hospitalization were similar between the groups in which US or CT was performed as the first imaging modality among the patients presenting to the emergency department (12). Our study found that the preferred imaging modalities in patients admitted to the emergency department were US, CT, and X-ray of the urinary system in order of frequency. We also determined no significant difference between the residents and specialists regarding their preference for these imaging modalities.

In renal colic, reducing severe acute pain is one of the main steps in managing the patient. Essential factors in deciding on the first choice of analgesic therapy include the safety, efficacy, cost, and availability of a drug in addition to the patient and clinician preferences (13). NSAIDs with proven efficacy in treating renal colic, acting through inhibition of prostaglandin synthesis, constitute the first-line therapy (14). Although the efficacy of NSAIDs has been proven, many clinicians now prefer opioids as the first step in pain management. The use of opioids is common today due to their advantages of dose titration and avoiding the possible risks of renal failure and gastrointestinal bleeding of NSAIDs (13). In our study, 39.8% of the emergency medicine physicians preferred NSAIDs alone, while 60.2% preferred NSAIDs and opioids together. It was determined that the emergency medicine residents and specialists had similar preferences in first-line treatment, but they preferred diclofenac more as an NSAID. However, studies have shown that high-dose dipyrone (2 g) is more effective than diclofenac (15). Although there are differences in the usage or preference rates, NSAIDs can reduce pain as much as opioids (13).

There are several situations where discharge or a conservative approach is not warranted, and the patient's immediate referral to a urology clinic for consultation is required due to complete or incomplete ureteral obstruction. Urology clinic consultation should be performed in patients with solitary or transplanted kidneys, pyelonephritis or sepsis, and general condition disorder, which may endanger the patient's life or cause irreversible damage to the kidney (8). Our study determined that urology consultation was requested in patients presenting with renal colic in cases of decreased urine output, accompanying fever, persistent flank pain, and newly diagnosed renal colic. There was no difference between the emergency medicine residents and specialists regarding clinical behavior patterns.

Biochemical evaluation is similar for all patients with stones. The EAU guidelines recommend C-reactive protein (CRP), electrolyte, complete blood count, and creatinine evaluation in patients presenting to the emergency department with renal colic (11). CRP, a non-specific acute phase reactant, is considered a good marker for emergency urinary diversion and surgical intervention in patients admitted to the emergency department (16, 17). This study determined that patients who presented to the emergency department with renal colic were evaluated for complete urinalysis, creatinine, urea, hemogram, CRP, blood electrolytes, blood gas, and albumin in order of frequency. A CRP test was requested by 73.8% of the emergency medicine residents and 48.8% of the emergency medicine specialists as the first application. In addition, the rates of blood gas and albumin request rates as laboratory tests were higher among the emergency medicine residents than among the specialists. While 10.8% of the emergency medicine residents requested an albumin test, none of the specialists used albumin as a diagnostic test in patients presenting with renal colic. Although various guidelines define diagnostic tests requested in patients presenting with renal colic, the lack of consensus on this issue leads to different management styles. However, the use of complete blood count, creatinine, and blood electrolytes when necessary can provide the necessary information concerning the clinical status of patients (8).

Our study has certain limitations, including the relatively small number of participants, stratification of residents by years of education, and data is based on the participants' self-reports.

# CONCLUSION

In this study, we obtained data from the emergency medicine specialist and residents working in reference centres to which patients present with acute renal colic. We determined that the emergency medicine residents and emergency medicine specialists had different approaches to diagnosing and treating patients with renal colic. We determined that the imaging method preferences of the two groups were similar. However, the emergency medicine specialists had a different approach than the residents in terms of using NSAIDs as first-line treatment. In addition, there were differences between the two groups concerning the laboratory tests performed on patients with renal colic. There is a need for multicentre prospective clinical studies to provide extensive and more precise data.

# **Conflict of interest**

The authors declare to have no conflicts of interest.

# **Financial Disclosure**

The authors declared that this study has received no financial support.

# **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

# **Ethical Approval**

The study was approved by the Ethics Committe of Health Sciences University, Bakırköy Training and Research Hospital (No: 2021-20/479, Date: October 18, 2021) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

# **Author Contributions**

Conception and design; ÖB, YOD, Data acquisition; ÖB, MMİ, Data analysis and interpretation; ÖB, MMİ, Drafting the manuscript; ÖB, YOD, MMİ, Critical revision of the manuscript for scientific and factual content; ÖB, YOD, MMİ, Statistical analysis; ÖB, MMİ, Supervision; ÖB, YOD, MMİ.

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Case Report / Olgu Sunumu

# Mixed epithelial and stromal tumor in a young male case with hydronephrotic nonfunctional kidney: Comparison with literature findings

Hidronefrotik fonksiyon göstermeyen böbrekli genç erkek olguda mikst epitelyal stromal tümör: Literatür bulguları ile karşılaştırma

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# Özet

Mikst epiteliyal stromal tümör (MEST) ailesi, kistik komponenti baskın olan erişkin kistik nefroma ve solid komponent baskın MEST'ten oluşmaktadır. MEST, epitelyal ve stromal komponente sahip böbreğin nadir görülen benign, bifazik tümörüdür. Karın ağrısı ile başvuran 24 yaşında erkek olgunun tetkiklerinde grade 4 hidronefroz saptandı. Nefrektomi piyesinin mikroskobik incelemesinde, ovaryan stroma içerisinde değişken çaplarda küboidal epitel ile döşeli tubul yapıları mevcuttu. Olguya, morfolojik ve immunohistokimyasal bulgular ile MEST tanısı verildi. Genç erkeklerde sınırlı sayıda saptanan ve daha önce fonksiyon göstermeyen böbrek ile birlikteliği bildirilmeyen MEST tanısı verdiğimiz olgumuzun klinik ve histopatolojik özelliklerini literatür verileri ile karşılaştırmayı amaçladık.

Anahtar Kelimeler: Mikst epitelyal stromal tümör, böbrek, erkek.

### Abstract

The mixed epithelial and stromal tumor (MEST) family is comprised of adult cystic nephroma with a dominant cystic component and MEST with a dominant solid component. MEST is the rarely observed benign, biphasic tumor of the kidney with a mixed epithelial and stromal component. In the examinations of a 24-yearold male patient who presented with abdominal pain, grade-4 hydronephrosis was detected. In the microscopic examination of his nephrectomy specimen, there were tubular structures with cuboidal epithelium in different diameters within the ovarian stroma. The patient was diagnosed with MEST via morphological and immunohistochemical findings. We aimed at comparing the clinical and histopathological characteristics of our case, which we diagnosed with MEST, which is encountered in limited numbers in young men and has never been reported together with a nonfunctional kidney before, to the literature data.

**Keywords:** Mixed epithelial and stromal tumor, nonfunctional kidney, male.

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# INTRODUCTION

The mixed epithelial and stromal tumor (MEST) family is comprised of the adult cystic nephroma and mixed epithelial and stromal tumor. Adult cystic nephroma (ACN) had been classified together with pediatric cystic nephroma, independently from MEST, before (1). Later, ACN was included in the MEST family through clinical and genetic findings. MEST was first defined by Michal and Syrucek in 1998 and named as renal pelvis hamartoma, adult mesoblastic nephroma, cystic nephroma, mature nephroblastic tumor, or cystic partially differentiated nephroblastoma, respectively (2). ACN and MEST are benign kidney tumors with similar clinical, morphological, and immunohistochemical characteristics (1). The major morphological difference between the two groups is that cystic nephroma has a structure consisting of thin-walled cysts. On the contrary, MEST has cysts with thicker walls and solid areas. Ovary-like stroma is an important finding for MEST (3).

The mixed epithelial and stromal tumor mostly appears in perimenopausal women. The most common localization area is the pelvis; however, it can also be seen in the renal cortex (3). Macroscopically, it is a well-bordered tumor with a solid and cystic component, often growing towards the pelvis (4). Microscopically, hypocellular fibrous stroma and cellular spindle cell stroma are the most common types of stroma. It contains cystic structures in different diameters within the stroma. The cyst epithelium is cuboidal and likely to have the appearance of a tack (5). Immunohistochemically, stromal cells express the smooth muscle markers, Estrogen, and Progesterone while the epithelial component expresses GATA3 and PAX 8 (4). 22 cases have been reported in male patients, so far. This paper presents the MEST case detected incidentally with localization in the nonfunctional kidney in a young male case in company with clinical and pathological findings.

# **CASE REPORT**

Our male case was 24 years old and presented to our hospital with abdominal pain. No characteristics were found in his laboratory examination. The patient did not have any comorbidity or family history, and grade-4 hydronephrosis was observed in the left kidney in abdominal US examination; the renal pelvis diameter was measured as 16 mm, which was considered stricture in the ureteropelvic junction. Clear findings conforming to hydronephrosis were found in the left kidney in the static kidney scintigraphy. Activity involvement had decreased in favor of the parenchymal injury in the kidney parenchyma. In the dynamic kidney scintigraphy, the size of the left kidney was increased, and there were blood-filling, concentration, and severe reduction expression functions. The patient underwent a left nephrectomy with a pre-diagnosis of an atrophic kidney.

In the macroscopic evaluation of the nephrectomy specimen, the pelvis and calyces had expanded. In the area, rim-shaped residual kidney parenchyma was observed. No solid focal points were observed in the pelvis, which had a cystic expanded appearance (Figure 1).

In the samples of the cystic areas, a 1.2 cm irregular tumor focus was observed in the pelvis. The tumor contained ductus structures in different diameters in the microscopic sections (Figure 2A). The ductus is lined with a single row of cuboidal epithelium and has nuclei with a tack appearance (Figure 2B). In the epithelium, subnuclear vacuolization was seen locally (Figure 2C). The presence of dystrophic calcification in the tumor attracted attention (Figure 2D). In the areas around the tumor, sclerotic glomeruli, atrophy in tubules, fibrosis in the interstitium, and slight mononuclear inflammatory cell infiltration were observed.

Strong staining was obtained with Estrogen (ER), progesterone (PR), Actin, and negative staining with CD10 in stromal cells in immunohistochemical studies on the tumor. In epithelial cells, on the other hand, strong staining was observed with PAX8 and GATA3 (Figure 3).

Based on the present findings, the patient was diagnosed with a mixed epithelial-stromal tumor. It was explained to the patient that studies such as mRNA gene expression profiles, Insulin-like growth factor 2, Carbonic anhydrase 2 gene, and translocation t(1;19) could be done.



Figure 1. Gross appearance of the kidney



**Figure 2.** Ductus structure of different diameters in the pelvis (A, H&Ex40), ductus lined with cuboidal epithelium (B, H&Ex100), subnuclear vacuolization of the epithelium (C, H&Ex200), calcification in the tumor (D, H&Ex100)



**Figure 3.** Positive staining with PAX8 and GATA3 in the epithelial component (A, B, x100), positive staining with Estrogen and Progesterone in tumor stroma (C, D, x100)

# DISCUSSION

Mixed epithelial and stromal tumors are rare benign, biphasic tumors. They are generally seen in perimenopausal women (3). Male cases are often in advanced ages and receive hormonotherapy (6). The number of cases reported in young men is limited in the literature. Most cases are incidentally detected, and dysuria, hematuria, and abdominal pain may be observed. Although they are well-bordered, solid, and cystic masses, the tumor in our case was irregular. They are often protruded to the renal pelvis. Histologically, they consist of stromal and epithelial elements. Hypocellular fibrous stroma and cellular spindle cell stroma are the most common types of stroma. Another common stroma type is the ovary-like stroma. It is a prevalent change, smooth muscle differentiation. In the female and male cases reported, there was no clear difference between the stromas (4, 5). Edematous fibrous stroma and fat tissue are other types of stroma (3, 5).

Moreover, calcification, ossification, chronic inflammation, and even necrosis can be observed. The epithelial component may have an appearance of branching tubules, which have tightly come together. The epithelium is cuboidal in those with a small tubular appearance. They may contain eosinophilic material resembling thyroid follicles. Complex papillary structures and a tack appearance are the other findings. Our case shows that there can be focal subnuclear vacuolization and oxyphilic cytoplasm. Immunohistopathologically, the stromal component is stained positively with the smooth muscle markers (smooth muscle actin, desmin, caldesmon), estrogen, progesterone, and CD10, and the epithelial component is stained positively with PAX8 and GATA3 (4).

In our literature review, we observed that 15 more male cases and 7 male cases reported by Anna et al. (4) were diagnosed with MEST. No findings could be reached about the seven cases. The average age of diagnosis of the fifteen cases was 42.4 (12-71) years. Two cases had abdominal pain, and 6 had hematuria and dysuria (7-11, 12). In six cases, tumors were detected incidentally (2, 6, 13, 16, 17). There were 8 cases with localization in the right kidney and 4 cases with localization in the left kidney. The tumor diameter of these

	~ ~						rothers Known Renal										
	Family history	ои	ou	no	No	No	Two B With I Cystic Diseas	No	No	No	None	None	No	No	No	No	no
EST cases described in the literature	Hormonal history	Hormonal therapy within 5 months	None	None	None	None	ė	1	None	ou	None	None	None	ou	DES, Lupron	ou	no
	Other tumors	Prostate cancer	None	None	None	None	left renal cyst, and nephrolithiasis	оц	no	ои	Hydro- nephrosis	ои	1	Angiomyolipoma	Prostate carcinoma	оп	no
	recurrence	Follow up for 22 months, no metastasis or recurrence	Local recurrence and metastasis after 9 months	Follow up for 9 months, no metastasis or recurrence	Follow up for 48 months, no metastasis or recurrence	follow up for 18 months, no metastasis or recurrence	Follow up for 2 years, no metastasis or recurrence	по	Follow up for 6 months, no metastasis or recurrence	Follow up for 23 months, no metastasis or recurrence		Follow up for 3 months, no metastasis or recurrence	Follow up for 10 months, no metastasis or recurrence	Follow up for 2 years, no metastasis or recurrence		Follow up for 8 months, no metastasis or recurrence	Being followed-up
	Pathology	S: CD99, Bcl2, Vimentin (+), SMA, CK(-) E: CK, Vimentin, ER, PR (+)	S: Vimentin, CD99, Bcl2 (+), CK, Desmin, SMA, S100, ER, PR (-) E: CK, EMA (+)	S: ER, PR, SMA (+)	E: EMA, CK (+) S: Actin, Desmin, Vimentin, HHF35, CD34, CD57, ER (+)	S: ER, PR, Desmin (+)		S: Desmin, Vimentin, ER, PR (+), E: CK(+)	Positive for CK, PR, SMA, desmin, and vimentin	S: CD10, ER, PR, vimentin and desmin (+), Melan-A and HMB-45 (-)	E and S: AMACR, CK 7, p53, ER, PR inhibin, calretinin, pax2, pax8, and p63 (+)	S: actin, desmin, vimentin, and ER and PR E: AE1/AE3, vimentin	E: CK7, HMWC, PAX8 (+) S: Vimentin, Actin (+) CD20, CD34, desmin, ER and PR (-)			S: vimentin, ER, PR, Desmin, CD34 (+) S100, HMB45, CD117, Chromogranin, Synaptophysin (-) E: CK (+)	S: Actin, ER, PR, CD10 (+) E: DAYR CATA3 (+)
	Surgery	Radical nephrectomy	Radical nephrectomy	Partial nephrectomy	Partial nephrectomy	Radical nephrectomy	Radical nephrectomy	Partial nephrectomy	Radical nephrectomy	Radical nephrectomy	Radical nephrectomy	Radical nephrectomy	Radical nephrectomy	Radical nephrectomy		Partial nephrectomy	Radical
	Size (cm)	3.5 cm	28 cm	2 cm	5 cm	7 cm	30 cm	N/A	1	ı	10 cm	5.7 cm	6 cm	11 cm	11.5 cm	4 cm	1.2 cm
	Location	Right kidney, lower pole	Right kidney, upper pole	Right kidney, lower pole	Left kidney, upper pole	Right kidney anteromedial	Left kidney, whole	Left kidney	1	1	Left kidney	Right kidney	Right kidney, lower pole	Right kidney		Right kidney	Left kidney
	Clinical presentation	In prostate cancer screening	Abdominal discomfort	Microscopic hematuria	Gross hematuria	Nausea trauma hematuria	Abdominal pain, nausea, vomiting	N/A	Incidental	Incidental	Incidental	Macroscopic hematuria (30 days)	Macroscopic hematuria (16 days), fever, weight loss, dysuria	Dysuria and a palpable mass in the right kidney area	Incidental, during a work-up for prostatic carcinoma treated	Incidental	Abdominal pain
fale M	Age	67	19	14	12	14	65	44	60	58	68	26	44	16	71	58	24
Table 1. M	Case	Suzuki et al. (6)	Zou et al. (7)	Choy et al. (8)	Teklali et al. (9)	Gibson et al. (10)	Moses et al. (11)	D. Jevremovic et al. (3)	Wang et al. (2)	Wang et al. (2)	Horsanali et al. (13)	Pegas et al. (12)	Wang Y et al. (14)	Lang et al. (15)	Adsay et al. (16)	Colombo et al. (17)	present

# New J Urol. 2021;17(1):52-57. DOI: 10.33719/yud.2022;17-1-936184

15 cases was 10.3 cm. As the operational procedure, 11 cases underwent nephrectomy and 4 partial nephrectomies. Only in 1 case reported by Zou et al. (7), out of the cases followed up for recurrence and metastasis, local recurrence and metastasis were found after 9 months. When we looked at their backgrounds, Suzuki et al. (6) and Adsay et al. (16) reported 2 cases in which hormone was used due to prostate cancer. Moses et al. (11) reported a case with a family history, and two brothers of the case also had cystic renal disease (Table 1). All the cases had similar histopathological and immunohistochemical findings.

Our case is young and male contrary to the expectations in MESTs. The tumor was detected incidentally in a nephrectomy performed for hydronephrosis. Because of these rare findings, we believe that our case report will contribute to the literature.

# **Conflict of Interest**

All authors declared that there is no conflict of interest.

# **Financial Disclosure**

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# **Author Contributions**

Conception and design; ZS, BCT, CE, GÇ, Data acquisition; BCT, Data analysis and interpretation; ZS, BCT, GÇ, Drafting the manuscript; ZS, GÇ, Critical revision of the manuscript for scientific and factual content; CE, GÇ, Statistical analysis; CE, GÇ, Supervision; CE.

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Case Report / Olgu Sunumu

# Renal abscess in childhood: a case report 6 years girl

Çocukluk çağında renal apse; 6 yaş kız hasta vaka sunumu

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# Özet

Renal apseler çocukluk yaş grubunda nadir görülürler. Tanıda gecikmeler böbrek kaybına neden olabilir. Tedavi yöntemi de halen tartışmalıdır. Ek hastalığı olmayan geniş spektrumlu antibiyoterapi ile regrese olmayan, organize oldugu için perkütan drenajla drene olmadığı için opere ettiğimiz büyük renal apseli hasta literatür eşliğinde değerlendirildi.

**Anahtar Kelimeler:** Renal apse, çocukluk çağı, açık cerrahi, perkütan drenaj.

# Abstract

Renal abscesses are rarely seen in the childhood period. Delays in diagnosis may cause kidney loss. The treatment method is still controversial. The patient with a large renal abscess, which we operated on because it did not regress with broad-spectrum antibiotic therapy and was not drained with percutaneous drainage because it was organized, was evaluated in the light of the literature.

Keywords: Renal abscess, childhood, open surgery, percutaneous drainage.

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# INTRODUCTION

Renal abscesses are rare in children who do not have an underlying predisposing factor, and very few cases have been reported in this regard (1,2). The rare occurrence of renal abscesses causes a delay in diagnosis, which leads to kidney damage and late initiation of treatment (3). Imaging methods such as ultrasonography (USG), Computed Tomography (CT), and Magnetic Resonance (MR) are used in diagnosis (1,4). The source usually spreads in an ascending manner, but there is a hematogenous spread in rare cases. While the agent in ascendant dissemination is E. Coli, the agent is Staph. aureus in a hematogenous spread. Urine analysis may give normal results in 70% of the patients, and the treatment method is still controversial. There is not enough information in the literature regarding children; thus, adult cases are often utilized. Although broad-spectrum antibiotic therapy alone may be sufficient for initial treatment, surgical intervention may also be required, especially in large-sized abscesses. Delays in diagnosis can lead to kidney damage, especially in children (5,6).

In our case, an underlying predisposing factor was not found, the diagnosis was delayed, and percutaneous drainage could not be applied because the abscess was organized, and surgery had to be performed because it did not improve with long-term antibiotic therapy.

# **CASE REPORT**

A 6-year-old female patient presented with sudden onset of fever and left flank pain, while investigating the etiology of high fever in the center where she applied, WBC: 14500 (reference range: 4000-12000 /uL), CRP: 12 (reference range: 0-5 mg/dl), there were 22 leukocytes in urine microscopy and 100,000 cfu/ml of E. Coli in urine culture. Ultrasonography (USG) revealed a 6 cm abscess in the left renal region. It was stated that the CT result was compatible with the abscess but could not be clearly separated from the mass due to its excessive density, and it was stated that it was not suitable for percutaneous drainage, and the material could not be drained. During the patient's follow-up, a pigtail catheter was inserted into the left thorax due to pleural effusion in the left hemithorax. Due to the absence of anything in the drainage on the day, she was

referred to our clinic with pre-diagnoses of Renal Abscess and Renal Mass.

There was no specificity in her history, except for receiving outpatient medical treatment for inflammation two years ago. A pigtail catheter was present in the left thorax, and the other systemic examination gave normal results in physical examination. In laboratory tests; CRP: 12 mg/dl (reference range: 0-5 mg/dl), sedimentation value; 69 (reference range: 1-10 mm / hour), and other biochemical values were within normal limits. There was no feature in the urine test, and there was no growth in the urine culture. Tuberculosis and mycobacterial examinations of the patient gave negative results, and immunological and tumor markers were normal. There was no feature in the fluid cytology sent from the thorax tube.

In the Abdomen USG, an abscess with an approximate size of 40x50 mm extending towards the renal sinus in the upper pole cortex of the left kidney and a dense pleural effusion with a depth of 2 cm in the left hemithorax were observed. Abdomen MRI showed an exophytic collection at the level of the upper pole of the left kidney, 73x48x30 mm in size, at air-fluid level, compatible with an abscess that contrasted the thick wall in contrast examination (Figure-1a-1b, Figure 2). Thorax CT resulted in a septal subpulmonic pleural effusion with a depth of 14 mm in the left hemithorax (Figure-3). The thorax drain was removed on the 7th day when the patient's clinical condition improved, nothing was not coming from the drain, and the PA chest radiography was normal. Antibiotic treatment was decided by the Committee of Infection, Nephrology, Radiology, and Pediatric Surgery. Since there was no growth in the urine culture and the urine culture antibiogram result with external growth was not reached, Ciprofloxacin (Ciproxin) 3x230 mg iv (10 mg/ kg/dose), Amikacin (Amijeksin) 3x125 mg iv (15 mg/ kg/day), Vancomycin (Vankopol) 4x230 mg iv (10 mg/ kg/dose) antibiotics were continued to be given. Percutaneous Drainage was repeated for the patient whose abscess size did not regress in the third week of treatment.

Trucut biopsy of the patient, who had no apparent improvement in drainage, showed abscess formation and pyelonephritis findings. After the USG was performed in the first month of medication treatment, there was no significant change in abscess size, the decision for surgery was taken in the council. Transperitoneal laparoscopy revealed that the kidney was opened to the perirenal fascia and gerota, and the upper pole was more prominent. Still, there was no extrarenal mass or abscess formation. Pus appeared in the laparoscopic puncture performed on the upper pole. The incision was enlarged up to 1 cm. It was washed with physiological saline solution until nothing came to the cavity, and the procedure was terminated after placing two perirenal drains in the abscess cavity. There was no growth in the abscess culture taken during the procedure. The perirenal drain was removed on the 10th day, and the cavity drain on the 12th day since the patient was improving and nothing was coming to the drains. However, when the patient had fever on the postoperative 14th day, her antibiotherapy was revised as Meropenem (Merosid) 3\*800 mg (120 mg/kg/day), Amikacin (Amijeksin) 1X400 mg (20 mg/kg/day), Teicoplanin (Tekosit) 1\*200 mg (10 mg/kg/dose) (vanco-



Figure 1a-1b. First Arrival Coronal and axial post-contrast T1A series

mycin allergy developed), and antifungal Fluconazole (Flukopol) 1x200mg (10mg/kg/day) was added. It was seen that the abscess persisted with a size of 38 mm in the postoperative examination and MRI results of the patient (Figure-4). As the patient's fever continued, a decision was made for another surgery on the postoperative 16th day. In the laparotomy performed on the left Lombotomy incision, the kidney was normal, but the extrarenal abscess structure in the upper pole of the kidney was approximately 1 cm in diameter, with an organized predominantly fibrinous character. No intrarenal or perirenal abscess was detected in the intraoperative USG. In the follow-up, the patient's general condition was good and vital signs were stable, and the control USG examination performed on the postoperative 3rd day was evaluated as normal. The patient was discharged after completing antibiotherapy and antifungal therapy. Urination cystourethrography performed 1 month after discharge was evaluated as normal.



Figure 2. Significant diffusion restriction is observed in the abscess site in simultaneous diffusion-weighted examinations.



**Figure 3.** Thorax CT, atelectatic changes in the basal segment of the lower lobe of the left lung, and a loculated collection compatible with abscess with air densities in the upper pole of the left kidney.



**Figure 4.** PO16 in coronal T2 series. Regressed abscess with a thick wall and air signals in it, according to previous reviews, under antibiotherapy on the 1st day.

# DISCUSSION

Renal abscesses are kidney infections rarely seen in pediatric patients who do not have an underlying predisposing factor (5). Suppurative material in the renal abscess is located in the cortical or corticomedullary area (4).

The frequency of renal abscesses in children is still unknown (7). It can be seen at any age, but it is more common in the young population. It is seen to three times more frequently in men compared to women. It is seen unilaterally in 77-90% and mainly in the right kidney, with 63%. (6) In our patient, there was an abscess in the left renal region. A renal abscess is rare, and studies on children are limited.

The largest pediatric series is the series of Cheng et al., in which 45 patients were retrospectively evaluated over 10 years between 1997 and 2016. This series's most common clinical symptoms were nonspecific symptoms such as fever, nausea/vomiting, and abdominal or flank pain. It has been found that the average time taken for CT confirmation of renal abscess after the onset of symptoms is nine days. Therefore, a careful history and suspicion are essential in diagnosing renal abscesses (3).

In our case, there were nonspecific symptoms such as sudden fever and left flank pain, and tomography was performed on the 10th day of medical treatment. Laboratory tests for renal abscesses are not specific for diagnosis. Leukocytosis and elevation of inflammatory markers are common in the laboratory, and no changes may occur. There may be pyuria and leukocyturia in urinalysis, which may be complicated with pyelonephritis (3,5). Conversely, urine tests may be normal if a renal or perinephric abscess develops due to hematogenous spread and does not communicate with the collecting system or if they are performed after antibiotic treatment has been initiated. It should be considered that less than half of the patients may have positive urine and blood cultures (1-2). Gram (-) bacteria are the most common cause of infections, especially E. Coli ascendancy. Staph. aureus is a common factor in the hematogenous spread and perinephric abscesses (10).

Abdominal USG, CT, and MR are cornerstones in the diagnosis of renal and perirenal abscesses. In recent

years, morbidity and mortality, which was 40-50%, has decreased to 1.5% -15% with imaging techniques (3).

Abdomen USG is the first choice because it is noninvasive and easy to apply. It has a high diagnosis rate of 70-86%. On USG, the renal abscess is seen as a hypoechoic mass. The specificity and sensitivity of CT are higher (90-100%). Better detection of abscess size is important in detecting the kidney status, additional pathologies, and treatment follow-up. On CT, the abscess wall is seen as a low-density mass in the postcentral series (4). Although the sensitivity is high, it should not be preferred except for the obligatory cases due to increased exposure to radiation.

On the other hand, MR sensitivity is higher than CT. However, general anesthesia is required for MRI in young children and babies. Since our patient was old enough, general anesthesia was not required for MRI.

Treatment of renal and perirenal abscess is medical broad spectrum antibiotherapy (including anaerobes), percutaneous drainage, open surgery, and nephrectomy.

There are publications regarding complete cure with broad-spectrum antibiotherapy and percutaneous drainage in treatment (1,4). Fernandez achieved a 92% cure rate, successful treatment in 24 of 26 cases with percutaneous drainage of kidney abscesses in adults, and intravenous antibiotics (9). Siegel et al. classified abscesses in adults as small (<3 cm), medium (3-5 cm), and large (> 5 cm). A 73% cure rate has been reported for large and medium kidney abscesses in adults when treated with parenteral antibiotics and percutaneous drainage, and it was concluded that percutaneous drainage is as adequate as open surgery. Abscesses smaller than 3 cm healed with 4-6 weeks of medical antibiotherapy alone (10).

Reported rates of kidney loss in children continue to be significant, 16–25% (1,2). Although a full cure is provided with broad-spectrum antibiotic therapy alone in adults, there is no information supporting this treatment modality in children. We think these patients should be treated as quickly as possible with percutaneous or open drainage to reduce the risk of kidney damage or loss (8).

Our patient was a healthy girl who had no known illness before. There were nonspecific symptoms such

as left flank pain and fever. Her laboratory showed ESR and CRP elevation, pyuria in the first urinalysis, and E.Coli growth in the urine culture. Therefore, renal abscess due to spreading from ascending was considered. No change in blood and urine was detected in the examinations during follow-up. Although there are some protocols in treating adult renal abscesses, there is no clear information in the literature on this issue in children. Antibiotic therapy was initially applied to the patient with the council decision, but the surgery had to be performed when treatment was impossible. Percutaneous drainage failed because the abscess was organized. After surgery, the patient's clinic improved. We think that the organized fibrinous structure, which persisted with 3 cm after the first surgery, which did not regress despite antibiotherapy, was located in the extrarenal and was considered an abscess with the imaging methods, leaks around the drain in the renal abscess lodge. As the abscess was large, early surgery could have been performed as in adult protocols so that the hospital stay could have been shorter.

# CONCLUSION

A renal abscess is an extremely rare pathology in children. Early diagnosis is very important in its treatment. Since there is no clear protocol for treatment, adult protocols can be used for effective treatment and early response to treatment. Early laparoscopic or open surgery can be performed if renal abscesses with a diameter of > 3 cm do not allow drainage.

# **Conflict of Interest**

All authors declared that there is no conflict of interest.

# **Financial Disclosure**

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# **Author Contributions**

Conception and design; FTG, Data acquisition; FTG, Data analysis and interpretation; FTG, ES, SK, Drafting the manuscript; FTG, Critical revision of the manuscript for scientific and factual content; FTG, BE, Zİ, Statistical analysis; FTG, Supervision; FTG, Zİ.

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# **PREPARATION OF MANUSCRIPT**

All pages of the manuscript should be numbered at the bottom center, except for the title page. Papers should include the necessary number of tables and figures to provide better understanding.

Limitations for each manuscript type; Type of Text Abstract References Table Figure Article (Word) Original 250 3000 30 6 5 Article Structured

Review 250 4000 50 6 5 Article Unstructured 250 Case 2000 10 1 3 Unstructured Reports Letter to No 1000 5 1 1 the Editor abstract

Original Research Articles should include subheadings below;

- Title (both Turkish and English)
- Abstract (both Turkish and English)
- Keywords (both Turkish and English)
- Introduction
- Material and Methods
- Results
- Discussion
- Conclusions
- Figures and Tables Legend
- References

Case Reports should include subheadings below;

- Title (both Turkish and English)
- Abstract (unstructured, both Turkish and English)
- Keywords (both Turkish and English)
- Introduction
- Case Presentation
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- Figures and Tables Legend
- References

Review Article should include subheadings below;

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- Conclusion
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- References

For systematic reviews, authors must adhere to the PRISMA guidelines.

Letters to Editor should include subheadings below; • Title

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- Main text
- Figures and Table Legend
- References

# **Figures and Tables**

Figures, graphics, and photographs should be submitted as separate files (in JPEG format) through the submission system.

The files should not be embedded in a Word file of the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system.

Images should be numbered by Arabic numbers to indicate figure subunits.

Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends.

The minimum resolution of each submitted figure should be 300 DPI.

Figures or illustrations must not permit the identification of patients and written informed consent for publication must be sought for any photograph.

Figure legends should be listed at the end of the main document.

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## **PREPARATION OF MANUSCRIPT**

### References

While citing publications, preference should be given to the latest, most up-to-date publications. Authors should avoid using references that are older than ten years. All the references should be written according to the Vancouver reference style. The references used in the article must be written in parenthesis, at the end of the sentences. References should be numbered in the order they appear in the text and listed in the same order in which they are cited in the text. Be consistent with your referencing style across the document.

References must contain surnames and initials of all authors, article title, name of the journal, the year and the first and last page numbers. If there are more than 6 authors, an abbreviation of "et al." should be used for the authors out of the first three. Journal titles should be abbreviated according to Index Medicus.

You must add the DOI (Digital object identifier) at end of each reference.

#### For Examples;

<u>Article in journal:</u> Tasci A, Tugcu V, Ozbay B, et al. Stone formation in prostatic urethra after potassium-titanyl-phosphate laser ablation of the prostate for benign prostatic hyperplasia. J Endourol. 2009;23:1879-1881.

<u>For Books:</u> Günalp İ. Modern Üroloji. Ankara: Yargıçoğlu Matbaası, 1975.

Chapters in books: Anderson JL, Muhlestein JB. Extra corporeal ureteric stenting during laparoscopic pyeloplasty. Philadelphia: W.B. Saunders, 2003; p. 288-307.

<u>For website</u>; Gaudin S. How moon landing changed technology history [serial online]. 2009 [cited 2014 June 15]. Available from: http://www.computerworlduk. com/in-depth/it-business/2387/how-moon-landing-changed-technology-history/

<u>For conference proceeding</u>; Anderson JC. Current status of chorion villus biopsy. Paper presented at: APSB 1986. Proceedings of the 4th Congress of the Australian Perinatal Society, Mothers and Babies; 1986 Sep 8-10; Queensland, Australian. Berlin: Springer; 1986. p. 182-191. <u>For Thesis</u>; Ercan S. Venöz yetmezlikli hastalarda kalf kası egzersizlerinin venöz fonksiyona ve kas gücüne etkisi. Süleyman Demirel Üniversitesi Tıp Fakültesi Spor Hekimliği Anabilim Dalı Uzmanlık Tezi. Isparta: Süleyman Demirel Üniversitesi; 2016.

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Manuscript Retraction: For any other reason authors may withdraw their manuscript from the journal with a written declaration.

## Revisions

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be canceled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial period is over.

#### AFTER ACCEPTANCE

Accepted manuscripts are copy-edited for grammar, punctuation, and format. A PDF proof of the accepted manuscript is sent to the corresponding author and their publication approval is requested. The journal owner and the editorial board are authorized to decide in which volume of the accepted article will be printed. Authors may publish their articles on their personal or corporate websites by linking them to the appropriate cite and library rules.

# $\ddot{U} R O L_{D E R G I S I}^{Y E N I} O J I$

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# PEER REVIEW PROCESS

# The Double-Blind Peer Review Process 1. Submission of Paper

The corresponding author submits the paper via Dergipark online system to the journal (http://dergipark.gov.tr/journal/1455/submission/start).

# 2. Editorial Office Assessment

Editorial Office checks the paper's composition and arrangement against the journal's Author Guidelines to make sure it includes the required sections and stylizations. The quality of the paper is not assessed at this point.

# 3. Appraisal by the Editor-in-Chief

The Editor-in-Chief assigns submission to Section Editor to see through the editorial process. Section Editor checks that the paper is appropriate for the journal and is sufficiently original and interesting. If not, the paper may be rejected without being reviewed any further.

## 4. Invitation to Reviewers

The Section Editor sends invitations to individuals he or she believes would be appropriate reviewers. As responses are received, further invitations are issued, if necessary, until the required number of acceptances is obtained – commonly this is 2.

## 5. Response to Invitations

Potential reviewers consider the invitation as anonymous against their own expertise, conflicts of interest and availability. They then accept or decline. If possible, when declining, they might also suggest alternative reviewers.

## 6. Review is Conducted

The reviewer sets time aside to read the paper several times. The first read is used to form an initial impression of the work. If major problems are found at this stage, the reviewer may feel comfortable rejecting the paper with-out further work. Otherwise they will read the paper several more times, taking notes so as to build a detailed point-by-point review. The review is then submitted to the journal, with a recommendation to accept or reject it – or else with a request for revision (usually flagged as either major or minor) before it is reconsidered.

# 7. Journal Evaluates the Reviews

The Section Editor considers all the returned reviews before making an overall decision. If the reviews differ widely, the editor may invite an additional reviewer so as to get an extra opinion before making a decision.

# 8. The Decision is Communicated

The Section Editor sends a decision email to the author including any relevant reviewer comments as anonymous.

## 9. Next Steps

If accepted, the paper is sent to language Editor. If the article is rejected or sent back for either major or minor revision, the Section Editor should include constructive comments from the reviewers to help the author improve the article. At this point, reviewers should also be sent an email or letter letting them know the outcome of their review. If the paper was sent back for revision, the reviewers should expect to receive a new version, unless they have opted out of further participation. However, where only minor changes were requested this follow-up re-view might be done by the Section Editor.

- After these;
- Copyedit submission
- Layout
- Corrections
- Publishing the submissions on the web page as early print
- Creating issues
- Organize Table of Contents
- Publishing the issue on the web page and printing hardcopy.

We are applying the same steps on The Double-Blind Peer Review Process when we got the inhouse submission.



