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Persistent Urine Culture Positivity Increases Hospital Stay Without Raising Sepsis Risk After Ureteroscopy

Persistan İdrar Kültürü Pozitifliği, Üreteroskopi Sonrası Hastanede Kalış Süresini Artırıyor Fakat Sepsis Riskini Yükseltmiyor

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Abstract

Objective: We aimed to investigate whether ureteroscopy can be safely performed during antibiotherapy period in patients with urinary tract stones who have persistent positive or contaminated urine cultures preoperatively.
Materials and Methods: A total of 325 patients who underwent ureteroscopy at our clinic between January 2019 and May 2024 were included in the study. Patients who had symptomatic infections, malignancy or hematological diseases were excluded from the study. Based on preoperative urine culture results, patients were divided into two groups: Group 1 (negative urine culture) and Group 2 (recurrent positive or contaminated urine cultures). Demographic, clinical, radiological and surgical data were retrospectively collected and statistically analyzed.
Results: Among 325 patients, Group 1 consisted of 268 patients (82.5%), while Group 2 consisted of 57 patients (17.5%). The median age of patients in Group 2 was significantly higher ($p = 0.021$). The proportion of female patients was higher in Group 2 (52.6%) compared to Group 1 (25.4%) ($p < 0.001$). Diabetes mellitus, hypertension and chronic kidney disease were significantly more prevalent in Group 2 ($p < 0.05$). The frequency of postoperative fever and duration of hospital stay were significantly higher in Group 2 ($p < 0.001$). No cases of urosepsis or more severe than Clavien-Dindo grade 2 complications were observed in any patient.
Conclusion: Our study showed that ureteroscopy may be performed safely under antibiotic treatment in patients with persistently positive urine cultures without causing serious complications. Thus, delaying surgery solely for urine sterilization may not be necessary under appropriate antibiotic treatment.

Keywords: complication, fever, ureteroscopy, urine culture, urinary stones

Özet

Amaç: Bu çalışmanın amacı, üriner sistem taşları olan ve preoperatif dönemde dirençli pozitif veya kontamine idrar kültürleri bulunan hastalarda, üreteroskopinin antibiyoterapi baskısı altında güvenli bir şekilde yapılıp yapılamayacağını araştırmaktır.
Gereçler ve Yöntemler: Ocak 2019 ile Mayıs 2024 arasında kliniğimizde üreteroskopi operasyonu uygulana toplam 325 hasta çalışmaya dahil edilmiştir. Semptomatik enfeksiyonu, malignite veya hematolojik hastalığı olan hastalar çalışmadan çıkarılmıştır. Preoperatif idrar kültürü sonuçlarına göre hastalar iki gruba ayrılmıştır: Grup 1 (negatif idrar kültürü) ve Grup 2 (tekrarlayan pozitif veya kontamine idrar kültürleri). Demografik, klinik, radyolojik ve cerrahi veriler retrospektif olarak toplanmış ve istatistiksel olarak analiz edilmiştir.
Bulgular: Toplam 325 hasta arasında, Grup 1 268 hasta (%82.5) içerirken, Grup 2 57 hasta (%17.5) içermektedir. Grup 2'deki hastaların ortanca yaşı anlamlı şekilde daha yüksekti ($p = 0.021$). Kadın hasta oranı Grup 2'de (%52.6) Grup 1'e (%25.4) göre daha yüksekti ($p < 0.001$). Diyabet mellitus, hipertansiyon ve kronik böbrek hastalığı Grup 2'de anlamlı şekilde daha yaygındı ($p < 0.05$). Postoperatif ateş sıklığı ve hastanede kalış süresi Grup 2'de anlamlı şekilde daha yüksekti ($p < 0.001$). Hiçbir hastada ürosepsis veya Clavien-Dindo sınıflamasına göre derece 2'den daha ciddi komplikasyon vakası gözlemlenmemiştir.
Sonuç: Çalışmamız, dirençli pozitif idrar kültürlerine sahip hastalarda ciddi komplikasyonlar oluşturmadan antibiyotik tedavisi altında üreteroskopi yapılabileceğini göstermiştir. Bu nedenle, yalnızca idrar sterilizasyonu için cerrahinin ertelenmesi uygun antibiyotik tedavisi altında gerekli olmayabilir.

Anahtar kelimeler: komplikasyon, ateş, üreteroskopi, idrar kültürü, üriner sistem taşları

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Introduction

Urolithiasis is one of the most common conditions encountered in urological practice, with its prevalence ranging from 1% to 20%, depending on geographical, ethnic, dietary, and genetic factors [1]. The high frequency of both newly diagnosed and recurrent stone disease causes a significant psychosocial and economic burden on patients, healthcare providers, and the healthcare system, which cannot be overlooked [2]. Untreated urinary tract stone disease significantly increases the risk of acute and chronic renal failure, urinary tract infections, and other complications associated with stones. A considerable number of these stones necessitate active intervention [3,4].

Surgical treatment options include ureteroscopy (URS), shock wave lithotripsy (SWL) and percutaneous nephrolithotomy (PCNL) for most of the patients. It is known that among these treatment options, URS has lower complication rates compared to PCNL and higher stone-free rates compared to SWL [5]. With technological advancements and the development of endoscopic devices in more practical forms, ureteroscopy has gained increasing application even in >2 cm diameter stones. Due to its high treatment success and low morbidity, it is becoming an increasingly preferred treatment option for the management of ureteral and kidney stones [6].

Although a substantial proportion of complications following URS are minor and do not require further intervention, the overall complication rate can reach up to 25% [5,7]. Among these, infectious complications such as postoperative fever, urinary tract infections, systemic inflammatory response syndrome (SIRS), and urosepsis are particularly concerning [7-10]. Preoperative bacteriuria is a known risk factor for such complications, especially in patients with additional risk factors including female gender, chronic diseases, higher American Society of Anesthesiologists (ASA) physical status classification system score, hydronephrosis, or infectious stones [11,12]. While prophylactic antibiotics and careful perioperative management can help reduce these risks [13] a positive preoperative urine culture remains a significant predictor of postoperative infection and should be managed accordingly [14]. However, in patients with urinary tract stone disease, achieving sterile urine cultures may not always be possible due to persistent or recurrent bacteriuria and contamination [15]. The belief that persistent urine culture positivity increases the risk of surgical complications may heighten anxiety for both the patient and the urologist. This concern often leads to repeated antibiotic use, which contributes to bacterial resistance and may increase patient's morbidity [16]. Additionally, delaying surgery in pursuit of urine sterilization prolongs hospitalization, raises healthcare costs, and may result in irreversible renal damage due to ongoing obstruction [17]. Despite these challenges, there is currently no clear consensus on whether URS should be delayed until urine cultures are sterile or whether it can be performed safely under targeted antibiotic therapy [18].

In this single-center, retrospective study, we hypothesized that URS can be performed safely in patients with persistent positive or contaminated urine cultures, provided that appropriate antibiotic treatment is administered. Therefore, we aimed to compare the surgical outcomes of patients with sterile preoperative urine cultures and those with persistent non-sterile cultures.

Materials and Methods

Patients and Study Design

After obtaining approval from the local ethics committee (Date and decision number: 29.11.2024/128), patients who underwent ureteroscopy due to ureteral or renal stones were reviewed between January 2019 and May 2024 at our clinic. After excluding patients with a history of symptomatic infection, hematological diseases and malignancies, a total of 325 patients were included in the study. Patients were categorized into two groups based on their preoperative urine culture results. Patients with sterile preoperative urine cultures were classified as Group 1, while those with recurrent positive or contaminated urine cultures who underwent surgery under appropriate antibiotic treatment were designated as Group 2 (**Figure 1**).

A positive urine culture was defined as the isolation of a single uropathogenic organism at a concentration of ≥10□ colony-forming units per milliliter (CFU/mL). Contaminated cultures were characterized by mixed bacterial growth or the presence of non-uropathogenic organisms. Due to their similar clinical impact in terms of delaying treatment, both groups were pooled together and analyzed as a single cohort (Group 2).

Demographic, laboratory, imaging, and surgical data were retrieved from the hospital database and reviewed retrospectively. For the assessment of complications, the Modified Clavien classification system (MCCS), previously introduced by Mandal et al. for URS, was used [9]. Stone-free status was evaluated 6-8 weeks after surgery using ultrasound, X-ray, and/or computerized tomography (CT). In the late follow-up period, if the patient had no additional complaints, monitoring was conducted using ultrasound only. The groups were compared statistically in terms of postoperative complications, hospital stay, and stone-free rates.

Surgical Technique

Ureteroscopy was performed using semirigid ureteroscopes (8 Fr and 9.5 Fr, Karl Storz®, Tuttlingen, Germany) and single-use flexible ureteroscopes (9 Fr, Redpine®, Guangzhou). Flexible ureteroscopy procedure was performed using an aspirated access sheath (Clear-Petra®). Lithotripsy was performed using

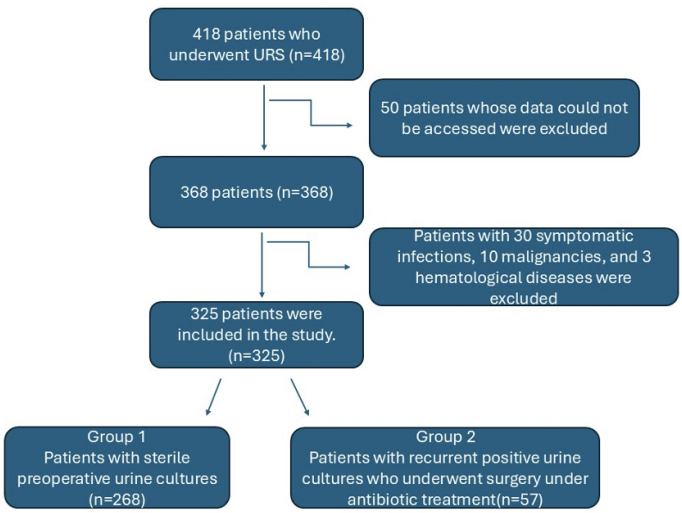

Figure 1. Flow chart of the patient's selection

a holmium: YAG laser system (272 µm). None of the patients exhibited purulent urine in the collecting system during the procedure. At the end of the procedure, some patients did not require ureteral catheterization, while in those who did, either a 5 Fr ureteral catheter or a 4.8 Fr double J ureteral stent was placed.

Statistical Analysis

The continuous variables were presented as medians, along with counts and percentages when applicable. Data analyzed using statistical software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Mann Whitney U test was used in cross-group comparisons of variables that did not show normal distribution. Pearson Chi-Square test and Fisher's Exact test were used to compare qualitative data. Statistical significance was set at $p<0.05$ level in outcome analysis.

Results

Demographic, radiological and surgical data of the patients were shown in **Table 1**. The median follow-up duration was 42 (4–56) months. Preoperative persistent urine culture growth was present in 57 (17.5%) patients. Postoperative fever was observed in 14 (4.3%) patients and postoperative pain was observed in 60 (18.5%) patients. The median duration of surgery for all patients was 60 (45–80) minutes. No recurrence of urinary system stones was observed in 310 (95.4%) patients during follow-up. No cases of urosepsis or any complications more severe than Clavien-Dindo grade 2 were observed in any patient.

Among 325 patients, Group 1 consisted of 268 patients (82.5%), while Group 2 consisted of 57 patients (17.5%). There was no statistically significant difference between the two groups regarding surgical procedure and duration, stone location and size, preoperative hydronephrosis status, systemic inflammatory response indices (SIRI-SII), type of catheterization, and postoperative pain ($p > 0.05$). The median age of patients in group 2 was significantly higher ($p = 0.021$). The proportion of female patients was 52.6% in group 2, whereas it was 25.4% in group 1, indicating that nearly half of the patients with positive urine cultures were female. In contrast, the proportion of female patients was significantly lower in the culture-negative group ($p < 0.001$). Additionally, the frequency of postoperative fever and length of hospital stay were significantly higher in group 2 ($p < 0.001$). Comparison of the groups is shown in **Table 2**.

Diabetes mellitus, hypertension, and chronic kidney disease were significantly more prevalent in group 2 ($p < 0.05$). In contrast, no statistically significant difference was observed between the groups regarding coronary artery disease, smoking, and alcohol consumption ($p > 0.05$). Relevant data are shown in **Table 3**.

Discussion

Recurrent urine culture positivity in patients with urinary system stone disease often leads to delays in surgical intervention due to the surgeon's concern about postoperative septic complications [19]. However, delaying these procedures may increase the risk of chronic kidney disease due to stone-induced obstruction [20]. In our study, we hypothesized that

Table 1. Demographic and clinical characteristics of the patients

Variables		Median (IQR)	n, %
Age (years)		48 (39 – 60)	
Gender	- Male		227 (69.8%)
	- Female		98 (30.2%)
BMI (kg/m²)		27.10 (24.61 – 30.47)	
Stone location	- Ureter		271 (83.4%)
	- Kidney		54 (16.6%)
MET use	- No		176 (54.2%)
	- Yes		149 (45.8%)
Preoperative ESWL	- No		202 (62.2%)
	- Yes		123 (37.8%)
SII		578.93 (396.59 – 901.46)	
SIRI		1.21 (0.76 – 1.83)	
Preoperative urine culture	- No Growth		268 (82.5%)
	- Growth		57 (17.5%)
Operation type	- Rigid URS		254 (78.2%)
	- Flexible URS		71 (21.8%)
Postoperative ureteral catheter	- None		20 (6.2%)
	- DJ Stent		268 (82.5%)
	- Ureteral Catheter		37 (11.4%)
Postoperative fever	- No		311 (95.7%)
	- Yes		14 (4.3%)
Postoperative pain	- No		265 (81.5%)
	- Yes		60 (18.5%)

IQR: interquartile range; BMI: body mass index; MET: medical expulsive therapy; ESWL: extracorporeal shock wave lithotripsy, SII: systemic immune-inflammation index; SIRI: systemic ınflammation response index; URS: ureterorenoscopy

Table 2. Comparison of groups in terms of clinical and surgical characteristics

Variables		Group-1	Group-2	P-value
		n=268, 82.5%	**n=57, 17.5%**	
Age (years)		47 (38 – 59)	54 (40 – 66)	**0.021**
Gender	- Male	200 (74.6%)	27 (47.4%)	**<0.001***
	- Female	68 (25.4%)	30 (52.6%)	
BMI (kg/m²)		26.87 (24.61 – 30.09)	28.20 (24.69 – 31.20)	0.281
Stone location	- Ureter	226 (84.3%)	45 (78.9%)	0.322
	- Kidney	42 (15.7%)	12 (21.1%)	
Stone size (mm)		10 (3 – 48)	10 (5 – 30)	0.378
Preoperative hydronephrosis	- None	74 (27.6%)	21 (36.8%)	0.317
	- Grade-1	85 (31.7%)	19 (33.3%)	
	- Grade-2	93 (34.7%)	13 (22.8%)	
	- Grade-3	16 (6.0%)	4 (7.0%)	
MET use	- No	141 (52.6%)	35 (61.4%)	0.226
	- Yes	127 (47.4%)	22 (38.6%)	
MET Duration (days)		0 (0 – 15)	0 (0 – 15)	0.281
Preoperative ESWL	- No	163 (60.8%)	39 (68.4%)	0.283
	- Yes	105 (39.2%)	18 (31.6%)	
	ESWL Sessions	0 (0 – 2)	0 (0 – 1)	0.180
SII		566.55 (396.80 – 898.40)	624.55 (385.22 – 924.38)	0.724
SIRI		1.18 (0.76 – 1.84)	1.36 (0.67 – 1.81)	0.690
Operation type	- Rigid URS	212 (79.1%)	42 (73.7%)	0.368
	- Flexible URS	56 (20.9%)	15 (26.3%)	
Operation Duration (min)		60 (45 – 80)	60 (49 – 80)	0.532
Postoperative ureteral catheter	- None	17 (6.3%)	3 (5.3%)	0.477
	- DJ Stent	218 (81.3%)	50 (87.7%)	
	- Ureteral Catheter	33 (12.3%)	4 (7.0%)	
Postoperative fever	- No	264 (98.5%)	47 (82.5%)	**<0.001***
	- Yes	4 (1.5%)	10 (17.5%)	
Postoperative pain	- No	223 (83.2%)	42 (73.7%)	0.092
	- Yes	45 (16.8%)	15 (26.3%)	
Hospital stay (days)		1 (1 – 1)	1 (1 – 2)	**<0.001***
Follow-up (months)		42 (7 – 56)	44 (8 – 58)	0.543
Stone recurrence	- No	258 (96.3%)	52 (91.2%)	0.100
	- Yes	10 (3.7%)	5 (8.8%)	

*p<0.05; ^a^ Mann-Whitney U test; ^b^ Pearson Chi-Square test; ^c^ Fisher's Exact test; BMI: body mass index; MET: medical expulsive therapy; ESWL: extracorporeal shock wave lithotripsy; SII: systemic immune-inflammation index; SIRI: systemic ınflammation response index; URS: ureterorenoscopy

urinary calculi patients with recurrent growths in preoperative urine culture can be safely operated without delay by giving appropriate antibiotics under antibiogram guidance. Our study showed that no major postoperative complications were observed in these patients when operated under antibiotic treatment, and postoperative fever and hospital stay were prolonged.

Despite significant technological advances in endoscopic stone surgery, complications associated with these procedures can still occur in clinical practice. Complication rates in the literature vary considerably, ranging from conditions that do not require additional intervention, such as ureteral stent discomfort or ureteral mucosal injury, to conditions with high mortality rates, such as urosepsis and even ureteral avulsion [21]. Early postoperative complications following URS or Retrograde intrarenal surgery such as fever, urinary tract infection, and progression to urosepsis, are frequently reported as major complications in the literature [21,22]. Fever and urinary tract infection after URS occur in 0.2% to 15% of cases [7-9]. Rarely, these conditions may progress to pyelonephritis and urosepsis due to inadequate treatment or underlying comorbidities. In a

multicenter prospective study published in 2015 by Daels et al., which included more than 10,000 patients and investigated the risk factors for URS complications, it was found that the prevalence of diabetes mellitus and hypertension increased with age and that the probability of postoperative complications was higher in patients with diabetes, cardiovascular disease, obesity or receiving anticoagulant therapy [23]. In our study, hypertension, diabetes mellitus and chronic kidney disease were statistically significantly more common in group 2, and therefore the hospital stay in this patient group was longer.

In a retrospective study by Uchida et al. involving 469 patients who underwent URS , risk factors for the development of postoperative systemic SIRS were evaluated [24]. A positive urine culture was detected in 12.4% of the patients before the procedure and the procedure was performed during antibiotic treatment. However, SIRS was significantly more common after URS in patients with a positive urine culture before surgery. The article emphasizes that SIRS increases the length of hospital stay and the economic and social burden for both the patient and the healthcare system, while it is also stated that no fatal SIRS cases developed. In our study, a positive urine culture was detected in 17.5% of the patients before surgery. Although the length of hospital stays and postoperative fever rates were higher in these patients compared to patients with sterile cultures, SIRS or urosepsis was not observed in any patient. In the aforementioned study, 21.3% of the patients had a history of obstructive pyelonephritis and approximately 5% of the patients underwent bilateral stone surgery. We believe that this situation has an impact on the SIRS result. In addition, none of the patients in our study had a history of obstructive pyelonephritis and we would like to emphasize that the period from diagnosis to treatment should not be prolonged under appropriate conditions. In addition, although the female gender was found to be statistically significant in terms of SIRS development in the study in question, no difference was observed between the two genders in terms of postoperative fever and hospital stay in our study. In our study, the median age and female gender ratio were found to be statistically significantly higher in Group 2 and therefore the hospital stay was found to be significantly longer in this group.

Rao et al. [25] identified preoperative bacteriuria as a significant risk factor for urosepsis, while Matlaga et al. [26] suggested that urinary tract infection could be considered a contraindication for URS due to the potential risk of urosepsis. However, a positive urine culture alone may not be indicative in patients with stones who lack clinical symptoms. Consequently, one study proposed that it is more informative to correlate urine microscopy with culture and symptoms [27]. In our study, urine microscopy data were not assessed; however, none of the patients with positive urine culture results or contamination exhibited symptomatic urinary tract infections.

In a retrospective study of 170 patients by Sahin et al., patients who underwent URS after receiving appropriate antibiotics and had preoperative positive urine cultures were compared with patients with negative urine cultures [28]. This study particularly emphasized that there was no statistically significant difference in infectious complication rates (such as fever and septic findings), length of hospital stays or readmission rates between patients who had positive urine cultures and who underwent URS without a control urine culture after a maximum of 10 days of antibiotic therapy and patients with negative urine cultures. Similarly, in our study, patients with positive urine cultures received appropriate treatments and were operated on under antibiotic treatment. However, in this study, it is understood that the positive cultures were not repeated but the first culture results. In our study, the number of patients was approximately twice the number of patients in the aforementioned study, and patients with contaminated or repeated positive urine cultures were evaluated; the length of hospital stay and postoperative fever were found to be significantly higher in this group. The higher median age of patients in group 2 and the presence of additional diseases may have also been effective in this situation. There is no statistically significant difference in terms of age and comorbidities between the two groups compared in the relevant study.

Table 3. Comparison of groups in terms of comorbidities

Comorbidities		Group-1	Group-2	P-value
		n=268, 82.5%	**n=57, 17.5%**	
Diabetes mellitus	- Yes	218 (81.3%)	38 (66.7%)	**0.014***
	- No	50 (18.7%)	19 (33.3%)	
Hypertension	- Yes	204 (76.1%)	34 (59.6%)	**0.011***
	- No	64 (23.9%)	23 (40.4%)	
Chronic kidney disease	- Yes	258 (96.3%)	51 (89.5%)	**0.043***
	- No	10 (3.7%)	6 (10.5%)	
Coronary artery disease	- Yes	233 (86.9%)	46 (80.7%)	0.220
	- No	35 (13.1%)	11 (19.3%)	
Smoking	- Yes	115 (42.9%)	26 (45.6%)	0.708
	- No	153 (57.1%)	31 (54.4%)	
Alcohol consumption	- Yes	241 (89.9%)	55 (96.5%)	0.114
	- No	27 (10.1%)	2 (3.5%)	

*p<0.05; ^a^ Pearson Chi-Square test; ^b^ Fisher's Exact test

Delay in the treatment of urinary stone disease, especially in patients with positive urine culture, can lead to serious consequences on renal function. Studies have shown that persistent obstruction due to stones increases intrarenal pressure, leading to ischemic damage, nephron loss, and ultimately chronic kidney disease [29]. When infection is present, the risk of pyonephrosis and sepsis further worsens renal damage, requiring urgent intervention [30]. Long-term untreated obstruction can lead to irreversible renal function deterioration, emphasizing the importance of early diagnosis and appropriate treatment. Therefore, timely drainage and definitive stone treatment in infected cases are critical to preserve renal function and prevent long-term complications [29].

The present study demonstrated that the patients who received appropriate and sufficient antimicrobial treatment, i.e., those who underwent surgery with antibiotic coverage, preoperative positive urine culture was associated with lower-grade complications such as fever and extended hospital stay, but did not lead to severe complications like urosepsis. We can conclude that repeated positive urine cultures, both from the patient and the physician's perspective, pose a high risk in terms of surgery and may increase anxiety for both parties. Thus, patients with no urinary infection findings but resistant urine culture growth can be operated on without delay after being

informed in detail. Keeping the time from diagnosis to surgical treatment short will also minimize the risk of renal function loss, which can reduce both patient morbidity and surgeon anxiety.

The inclusion of patients with recurrent positive or contaminated urine cultures adds both novelty and real-world relevance to our study, highlighting that surgical intervention can be safely performed under appropriate antibiotic coverage in this challenging patient population. Although the retrospective design of the study represents a limitation, the use of a prospectively maintained institutional database enhances data quality and integrity. Furthermore, the relatively large sample size supports the external validity and generalizability of our findings. Despite its strengths, this study has several limitations that should be acknowledged. First, urine microscopy data were not available, limiting the ability to correlate culture results with microscopic evidence of infection. Second, the distinction between contaminated and truly positive cultures was based on standard microbiology reporting without a universally accepted or validated definition, which may introduce classification bias. Third, the study was conducted at a single center with small sample size, which may limit the generalizability of the findings to other settings with different patient populations or surgical practices. Lastly, variations in surgeon experience and intraoperative decision-making were not controlled for, which could have influenced complication rates and clinical outcomes.

Conclusion

Our study has shown that when URS is performed without delay in patients with recurrent urine culture growth under appropriate antibiotic treatment, postoperative fever and hospital stay are prolonged, but the risk of sepsis is not increased. These findings may be a driving force for the implementation of the operation in this type of patient group without prolonging the period from diagnosis to treatment and, in this context, for the implementation of the operation without increasing the risk of sepsis, especially in order to reduce the risk of chronic kidney disease. However, caution should still be exercised when performing URS in patients with infected urine cultures, as the risk of sepsis, although not observed in our cohort, remains a recognized complication in the general literature.

Ethics Committee Approval: Ethical approval for this study was obtained from Istanbul Training and Research Hospital Local Ethics Committee (Approval number: 2024/128)
Informed Consent: An informed consent was obtained from all the patients.
Publication: The results of the study were not published in full or in part in form of abstracts.
Peer-review: Externally peer-reviewed.
Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – M.H.E.A., Y.Ş.; Design – M.H.E.A., Y.Ş.; Supervision– H.A.A., M.H.E.A., Y.Ş., U.Y.; Resources – H.A.A., Y.Ş.; Materials – H.A.A., M.H.E.A., Y.Ş.; Data Collection and/or Processing – H.A.A., M.H.E.A., Y.Ş.; Analysis and/or Interpretation – H.A.A., M.H.E.A., Y.Ş., U.Y.; Literature Search – M.H.E.A., Y.Ş.; Writing Manuscript – H.A.A., M.H.E.A., Y.Ş.; Critical Review – H.A.A., M.H.E.A., Y.Ş., U.Y.

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