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The Role of Sterile Pyuria in Febrile Urinary Tract Infections After Retrograde Intrarenal Surgery: A Single Center Retrospective Study

Retrograd İntrarenal Cerrahi Sonrası Ateşli İdrar Yolu Enfeksiyonlarında Steril Piyürinin Rolü: Tek Merkezli Retrospektif Çalışma

Abdullah Hızır YAVUZSAN[a], Ahmet Tevfik ALBAYRAK[a], Kadir Cem GÜNAY[a], Semih TÜRK[a], Kerem BURSALI[a], İbrahim Halil BALOĞLU[a], Cemil KUTSAL[a], Sinan Levent KİREÇÇİ[a], Kaya HORASANLI[a]

[a]Department of Urology, University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, TURKEY

ABSTRACT Objective: We aimed to investigate sterile pyuria as a risk factor of the postoperative febrile urinary tract infection (UTI) following retrograde intrarenal surgery (RIRS). **Material and Methods:** The data of 195 patients who underwent RIRS for kidney stones were reviewed retrospectively. The patients were separated into two groups: Those with sterile pyuria were Group 1, and those without pyuria were Group 2. Age, sex, body mass index, concomitant chronic diseases, duration of the operation, ureteral stent placement, stone characteristics, preoperative urine culture, and stone-free status were compared between the two groups. **Results:** The patients in Group 1 had more concomitant chronic diseases. However, only chronic obstructive pulmonary disease rates were statistically higher in Group 1 (8.26% vs. 0%) (p=0.014). Hydronephrosis was statistically significantly higher in Group 1 than in Group 2 (p=0.008). However, there was no statistically significant difference between the groups in terms of stone characteristics such as stone size (mm), volume (mm^3), density, and location (p=0.495, p=0.281, p=0.871, and p=0.081, respectively). Furthermore, the overall number of complications was higher in Group 1; however, this difference was not statistically significant between both groups (p=0.706). **Conclusion:** Our results suggest that pyuria was not associated with postoperative UTI in RIRS operations with a sterile preoperative urine culture.

Keywords: Kidney calculi; pyuria; retrograde intrarenal surgery; urinary tract infections

ÖZET Amaç: Bu çalışmamızda, retrograd intrarenal cerrahi (RIRC) sonrası postoperatif ateşli idrar yolu enfeksiyonu (İYE) için bir risk faktörü olarak steril piyüriyi araştırmayı amaçladık. **Gereç ve Yöntemler:** Böbrek taşı nedeniyle RIRC uygulanan 195 hastanın verileri retrospektif olarak incelendi. Hastalar steril piyüri olanlar Grup 1, piyüri olmayanlar Grup 2 olmak üzere 2 gruba ayrıldı. Yaş, cinsiyet, beden kitle indeksi, eşlik eden kronik hastalıkları, ameliyat süresi, üreter stent hikâyesi, taş özellikleri, ameliyat öncesi idrar kültürleri ve taşsızlık durumu 2 grup arasında karşılaştırıldı. **Bulgular:** Grup 1'deki hastalarda eşlik eden kronik hastalık sayısı Grup 2'ye göre daha fazla idi. Ancak sadece kronik obstrüktif akciğer hastalığı oranları Grup 1'de istatistiksel olarak daha yüksekti (%8,26'ya karşı %0) (p=0,014). Hidronefroz Grup 1'de Grup 2'ye göre istatistiksel olarak anlamlı derecede yüksekti (p=0,008). Ancak taş boyutu (mm), hacmi (mm^3), yoğunluğu ve yeri gibi taş özellikleri açısından gruplar arasında istatistiksel olarak anlamlı fark yoktu (sırasıyla p=0,495, p=0,281, p=0,871 ve p=0,081). Ek olarak, toplam komplikasyon sayısı Grup 1'de daha yüksekti; ancak bu fark her 2 grup arasında istatistiksel olarak anlamlı değildi (p=0,706). **Sonuç:** Sonuçlarımız, steril preoperatif idrar kültürü olan hastalarda piyürinin postoperatif İYE ile ilişkili olmadığını göstermektedir.

Anahtar Kelimeler: Böbrek taşı; piyüri; retrograde intrarenal cerahi; üriner sistem enfeksiyonu

Retrograde intrarenal surgery (RIRS) is suggested as the optimal treatment method for stones smaller than 20 mm which are placed in kidney.[1] This procedure allows approaching renal stones without parenchymal contact.[2] With advancing technology and experience, it has become competitive with percutaneous nephrolithotomy (PCNL) in terms of results and success.[2] Furthermore, its efficacy and safety made it an indispensable tool for renal stone surgery.[3]

Correspondence: Ahmet Tevfik ALBAYRAK
Department of Urology, University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, TURKEY/TÜRKİYE
E-mail: atevfikalbayrak@gmail.com

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Although RIRS is a modern and minimally invasive procedure, it has got some drawbacks. Limited field of view, expensive tools, maintenance, and the steep learning curve can be counted as its main drawbacks.[4,5] Despite these drawbacks, it is generally accepted as a safe procedure.[4] Fever, hematuria, and infection are the most common complications.[5] However, obstruction and urosepsis can occur as severe complications in some cases.

Various studies were conducted to evaluate the perioperative complications of RIRS. However, few studies can be found in the literature, which evaluated the febrile urinary tract infection (UTI) which occur postoperatively.[6-8] Therefore, we conducted a study to evaluate sterile pyuria as a risk factor of the postoperative febrile UTI following RIRS.

MATERIAL AND METHODS

Ethical approval of the study was obtained from the Şişli Hamidiye Etfal Ethical Review Committee (08.06.2021/1924). The study was conducted according to the Decleration of Helsinki principles. Informed consent was obtained from all individual participants included in the study. The data of the RIRS procedures between January 2018 and March 2021 were retrospectively evaluated. The patients with a history of ipsilateral open or endoscopic urinary surgery in the last three months, a history of tumor or known stenosis in the ureter, a history of diseases that may cause sterile pyuria (urinary tuberculosis, mycoplasma and candida infections, and glomerulonephritis), patients with a previous double-J (DJ) stent, and the patients whose preoperative laboratory or radiological data could not be obtained were excluded from the study and consequently 195 patients were enrolled in the study. The patients with a persistent fever above 38 °C for 48 hours following RIRS operation were considered postoperative UTI. Age, sex, body mass index (BMI), and concomitant diseases such as diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), and chronic obstructive pulmonary disease (COPD) were analyzed. Preoperative pyuria, bacteriuria, and antibiotic use were investigated. All patients were separated into two groups due to the presence of pyuria preoperatively. Group 1 was defined as pyuria, and Group 2 was defined as a non-pyuria group. More than 5 white blood cells (WBCs) per high power field on urinalysis was described as pyuria.[9] The size, location, density, multiplicity of the stones, and stone-free rates were evaluated. Furthermore, postoperative complications were categorized according to the Clavien-Dindo classification system.[10]

All patients had sterile urine cultures before the operation. All operations were performed in the standard lithotomy position under general anesthesia. After a safety wire was placed in the ureter, a semi-rigid ureteroscope was used to check whether there was a possible stone, tumor, or stenosis in the ureter. After a second working wire was placed through the semirigid ureteroscope, a 12/14 F ureteral access sheath (UAS) was placed into the ureter. A 9.5/11.5F UAS was placed in patients who could not be placed with a 12/14 F UAS. Lithotripsy was performed by inserting a flexible ureteroscope (Storz-X2® 7.5 F, Karl Storz, Tuttlingen, Germany) through the UAS. Fluid irrigation with saline was done at 60 cm above the patients, and lithotripsy was not performed in any patient for more than 60 minutes. A 6F DJ stent was placed in the ipsilateral ureter after lithotripsy. The DJ stent was removed 2-4 weeks postoperatively.

STATISTICAL ANALYSIS

SPSS v.23 (IBM, Armonk, NY) was used for statistical analysis. The normal distribution of the variables was measured with the Kolmogorov-Smirnov test. Continuous variables showing normal distribution were expressed with mean±standard deviation (SD), and comparative analysis was applied with Student's t-test. Continuous variables that did not show normal distribution were expressed with median and IQR (interquartile range, 1st and 3rd, respectively), and were analyzed with the Mann-Whitney U test. Categorical variables were expressed with number (n) and percentage (%). Chi-square test or Fischer's exact test was used to analyze categorical variables. The level of significance was set at $p<0.05$.

RESULTS

The data of 195 patients were evaluated retrospectively. The patient's mean age and BMI were found to be 47.5±14.2 years, 26.5±3.6 kg/m^2, respectively. The

median stone size was 18.3 (14.2-22.9) mm. The median stone volume and mean stone density were 1223 (501-2786) mm^3 and 1003±313 HU, respectively. Patient and their stone characteristics were shown in Table 1. It was observed that the patients in Group 1 had more concomitant chronic diseases such as DM, HT, CAD, COPD. However, only COPD rates were significantly higher in Group 1 (8.26% vs. 0%) (p=0.014). Median hydronephrosis was statistically higher in Group 1 than in Group 2 (1 [0-2] vs. 0 [0-1], respectively) (p=0.008). However, stone characteristics, such as stone size (mm), volume (mm3), density, location, and also stone-free rates, were not significant between the groups (p=0.495, p=0.281, p=0.871, p=0.081, and p=0.111, respectively).

The postoperative complications between the groups were shown in Table 2. The overall complications were higher in Group 1, without any statistically significance (p=0.706). The most common complication was postoperative fever, which was treatable with antipyretics. Moreover, antibiotic treatment was applied in two patients in both groups due to postoperative fever and positive urine culture. Computed tomography was performed in a patient in Group 2 because of severe early postoperative lumbar pain. The perirenal fluid collection was observed, and DJ stents were protruded beyond the renal parenchyma. Therefore, the DJ stent was replaced. Broad-spectrum antibiotics were applied. The patient's hemogram was stable, therefore was

TABLE 1: Patient and stone characteristics.

Variable	Group 1 (n=121)	Group 2 (n=74)	Total (n=195)	p value
Age (y), mean (SD)	47.2 (14)	48.0 (14.7)	47.5 (14.2)	0.712[t]
Gender				0.096[χ]
Male, n (%)	68 (56.19)	51 (68.91)	119 (61.03)	
Female, n (%)	53 (43.80)	23 (31.)	76 (38.97)	
BMI (kg/m^2), mean (SD)	26.7 (3.5)	26.2 (3.7)	26.5 (3.6)	0.327[t]
Comorbidity				
DM, n (%)	17 (14.04)	9 (12.16)	26 (13.33)	0.829[χ]
HT, n (%)	34 (28.09)	15 (20.27)	49 (25.12)	0.239[χ]
CAD, n (%)	13 (10.74)	6 (8.10)	19 (9.74)	0.626[χ]
COPD, n (%)	10 (8.26)	0 (0)	10 (5.12)	0.014[f]
Complaints				
None (incidental), n (%)	11 (9.09)	5 (6.75)	16 (8.20)	0.606[χ]
Pain, n (%)	102 (84.29)	66 (89.18)	168 (86.15)	0.397[χ]
Hematuria, n (%)	17 (14.04)	10 (13.51)	27 (13.84)	1.000[χ]
Dysuria, n (%)	8 (6.61)	6 (8.10)	14 (7.17)	0.777[χ]
Urine density, mean (SD)	1016 (6.7)	1015 (8.6)	1016 (7.5)	0.425[t]
Urine pH, median (IQR)	6 (5.5-6.1)	6 (5.5-6)	6 (5.5-6)	0.637[m]
Hydronephrosis, median (IQR)	1 (0-2)	0 (0-1)	1 (0-2)	0.008[m]
Laterality of operation				0.301[χ]
Right, n (%)	61 (50.41)	31 (41.90)	92 (47.18)	
Left, n (%)	60 (49.59)	43 (58.10)	103 (52.82)	
Number of stones, median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)	0.888[m]
Stone size (mm), median (IQR)	18.9 (14.3-22.8)	17.6 (13.5-23.1)	18.3 (14.2-22.9)	0.495[m]
Stone volume (mm^3), median (IQR)	1375 (548-2832)	986 (407-2605)	1223 (501-2786)	0.281[m]
Stone density (HU), mean (SD)	1006 (311)	999 (318)	1003 (313)	0.871[t]
Stone location				0.081[χ]
Renal pelvis, n (%)	20 (16.53)	15 (20.27)	35 (17.95)	
Calyx, n (%)	33 (27.27)	10 (13.51)	43 (22.05)	
Renal pelvis + calyx, n (%)	68 (56.20)	49 (66.22)	117 (60.00)	
Stone free rates, n (%)	89 (73.55)	46 (62.16)	135 (69.23)	0.111[χ]

SD: Standard deviation; BMI: Body mass index; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; IQR: Interquartile range; DM: Diabetes mellitus; HT: Hypertension; HU: Hounsfield unit; UTI: Urinary tract infection; [t]Student t-test; [m]Mann-Whitney U test; [χ]Chi-square test.

TABLE 2: Comparison of postoperative complications between the groups.

Variable	Group 1 (n=121)	Group 2 (n=74)	Total (n=195)	p value
Complications according to Clavien-Dindo classification				0.706[f]
Grade I, n (%)	6 (4.95)	2 (2.70)	8 (4.10)	
Postoperative fever treated with antipyretics, n (%)	5 (4.13)	1 (1.35)		
Gross hematuria, n (%)	1 (0.82)	1 (1.35)		
Grade II	2 (1.65)	2 (2.70)	4 (2.05)	
Postoperative fever treated with broad-spectrum antibiotics, n (%)	2 (1.65)	2 (2.70)		
Grade IIIb	0 (0)	1 (1.35)	1 (0.51)	
Double-J stent replacement, n (%)	0 (0)	1 (1.35)		
Grade IVa, n (%)	2 (1.65)	1 (1.35)	3 (1.53)	
Septicemia, n (%)	1 (0.82)	1 (1.35)		
Cardiac complication, n (%)	1 (0.82)	0		

[f]Fischer's exact test.

discharged after 10 days from the operation. One patient in both groups with postoperative hypotension and fever was followed up with the diagnosis of sepsis in the intensive care unit with appropriate antibiotics and supportive treatments. One patient in Group 1 with known CAD was followed for three days in the intensive care unit due to postoperative cardiac arrhythmia. Only postoperative infectious complications such as UTI and sepsis were seen in 8 (6.61%) patients in Group 1 and 4 (5.40%) patients in Group 2. In terms of these rates, no statistically significant difference was observed in both groups (p=1.000).

DISCUSSION

RIRS and PCNL together are widespread procedures for the treatment of renal stones.[4] They both are considered as safe. The most common complication of the RIRS procedure is UTI.[11] Although it is usually mild, it can cause febrile UTI and even sepsis.[12] In this study, we retrospectively evaluated pyuria as a risk factor of the febrile UTI following RIRS.

In our study, twelve patients (6.15%) had postoperative febrile UTI following RIRS. Our result is similar to the literature, which suggested a range of 7.6-13.4%.[6,7] Furthermore, we think that our rates are lower than these rates because all patients had postoperative sterile urine cultures, and the duration of lithotripsy did not exceed one hour. The European Association of Urology Guidelines also recommends using prophylaxis of antibiotics to minimize the risk of the development of symptomatic UTI after endoscopic stone surgery.[13] In our study, we gave antibiotics to all patients on the day of surgery, regardless of the groups.

As we mentioned before, we evaluated pyuria as a risk factor for febrile UTI following RIRS. Our results showed that if the preoperative urine culture was sterile, pyuria is not a risk factor. Various risk factors suggest that infection which develops following RIRS may be associated with preoperative factors in the literature. The results of various studies suggested that the long duration of the operation, female sex, and infectious stones are the most common risk factors for febrile UTI.[14-16] Moreover, pyuria has been shown to predispose postoperative UTI in some studies.[7,17] Furthermore, Kim et al. proved that pyuria was a risk factor for the postoperative UTI following RIRS.[17]

In this study, two patients in both groups had postoperative positive urine cultures, although their urine cultures were sterile preoperatively. However, there are many reports that stone culture might be the reason for postoperative UTI following RIRS.[11,18] In our study, it may be that there is also bacterial growth in the stone, and this colonization may have passed into the urine because of the disintegration of the stone, causing the postoperative urine culture positive.

We observed a significantly higher rate of COPD in the pyuria group; however, we think that this result was detected incidentally in our study population. Furthermore, sterile pyuria can be developed as a result of increased inflammation in the urinary system. Stones, hydronephrosis, tuberculosis, and glomerulonephritis can be given as examples of pathologies that cause this.[19] We think that the higher incidence of hydronephrosis in the pyuria group is increased urinary inflammation due to increased urinary stasis.

Our strong point in this study is consistency. The irrigation fluid was administered at the height of 1m above the patient to prevent excessive irrigation pressure in the renal pelvis.[20] Furthermore, we were consistent with the literature about the safe decontamination methods to keep the flexible ureteroscope clean.[21] Therefore, we could be focused on patient and stone-related factors more. Moreover, we have some limitations. The retrospective nature of the study, small sample size, and one-center study are the main limitations.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Abdullah Hızır Yavuzsan, Ahmet Tevfik Albayrak, Kerem Bursalı;* ***Design:*** *Abdullah Hızır Yavuzsan, Sinan Levent Kireççi;* ***Control/Supervision:*** *Sinan Levent Kireççi, Kaya Horasanlı, Cemil Kutsal;* ***Data Collection and/or Processing:*** *Semih Türk, Kerem Bursalı, İbrahim Halil Baloğlu;* ***Analysis and/or Interpretation:*** *Ahmet Tevfik Albayrak, Kadir Cem Günay, Abdullah Hızır Yavuzsan;* ***Literature Review:*** *Kadir Cem Günay, Semih Türk, İbrahim Halil Baloğlu;* ***Writing the Article:*** *Ahmet Tevfik Albayrak, Abdullah Hızır Yavuzsan;* ***Critical Review:*** *Sinan Levent Kireççi, Kaya Horasanlı, Cemil Kutsal.*

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