The significance of stone culture in the incidence of sepsis: Results from a prospective, multicenter study on Infections post Flexible UreteroreNescopy (I-FUN) and laser lithotripsy for renal stones

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TITLE PAGE

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ABSTRACT

Objective

Sepsis is the most serious complication of flexible ureteroscopy (F-URS) and laser lithotripsy. We assessed the influence of positive stone culture (SC) on major infectious complications (sepsis, septic shock).

Methods

This prospective study enrolled adult patients deemed suitable for F-URS and laser lithotripsy from 9 centers (January 2022-August 2023). Inclusion criteria: kidney stone(s); preoperative mid-stream urine culture (MSU); stone(s) assessed at CT scan; SC. Exclusion criteria: bilateral procedures; ureteral stones; children. Group 1: patients with sterile SC. Group 2: patients with positive SC. Data are presented as median (interquartile range). A multivariable logistic regression analysis was performed to evaluate factors associated with having a positive SC.

Results

293 were included. Median age was 51.0 (24) years. There were 167 (57.0%) males. Group 2 included 32 (2.5%) patients. Group 2 patients were significantly older [75.0 (14) vs 51.0 (23) years, p=0.02]. Stone features were similar. Major infectious complications were higher in Group 2 (15.6% vs 0.4%). One patient died due to sepsis in Group 2. 2/6 (33.3%) of patients with major infectious complications had the same pathogen in MSUC and SC. At multivariable regression analysis, diabetes (OR 3.23), symptomatic urinary infections within 3 months before surgery (OR 4.82), and preoperative stent/nephrostomy (OR 2.92) were factors significantly associated with higher odds of positive SC.

Conclusions

Patients with positive SC have a higher incidence of major infectious complications following F-URS lithotripsy. SC should be performed whenever feasible being a poor pathogen correlation between MSUC and SC.

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MAIN TEXT

1. Introduction

Flexible ureteroscopy (F-URS) with laser lithotripsy has gained popularity in the treatment of kidney stones worldwide[1], being among the first-line options for stones up to 2 cm in diameter[2,3]. By virtue of technological advancements, the utilization of F-URS is gaining momentum as a choice even for large stone burden[4]. However, F-URS is not devoid of serious complications such as sepsis, septic shock, and even sepsis-related death[5–7]. The sepsis rate varies in the literature between 0.5% and 11.1%, while the rate of septic shock ranges from 0.3% to 4.6%[6].

It is common practice to obtain a preoperative midstream urine culture (MSUC) before any stone surgical intervention and adequately treat preoperative infections if present. Nevertheless, MSUC is a poor predictor for major postoperative infectious complications after both ureteral and percutaneous lithotripsy[8]. To the best of our knowledge, there is only one prospective study assessing the correlation between stone culture (SC) and sepsis and this included a series of patients undergoing either percutaneous or ureteral lithotripsy[9].

This study aimed to evaluate the influence of a positive SC obtained by laser lithotripsy during F-URS for kidney stones on the occurrence of postoperative sepsis. The secondary outcome was to assess predictors of having a positive SC.

2. Materials and Methods

2.1 Study design

All consecutive patients with renal stone(s) scheduled for F-URS and laser lithotripsy were prospectively assessed from January 2022 to August 2023and eventually included in the study across 9 centers. Inclusion criteria were ≥18 years, renal stone(s) judged suitable for F-URS by the treating physician, a computed tomography (CT) scan performed within 3 months of surgery, an MSUC performed within 10 days of surgery and an SC collected during surgery. Exclusion criteria were concomitant ureteral stone, bilateral procedures, unavailable preoperative CT scan, MSUC, and SC.

We collected the following data: gender, age, comorbidity, body mass index, American Society of Anesthesiology score, age-adjusted Charlson comorbidity index, presence of symptomatic urinary infections 3 months before surgery, stone features at CT scan (i.e. stone size and location, Hounsfield units), presence of indwelling catheters at surgery (i.e. ureteral stent, nephrostomy, urethral, suprapubic), previous stone surgery on the affected kidney, and MSUC. Stone volume was assessed at CT scan by measuring the stone diameter in three axes and using the ellipsoid formula (length*width*depth*π*0.167)[2].

In instances of symptomatic infection or asymptomatic bacteriuria detected during preoperative MSUC, patients received a 6-day course of antibiotics based on susceptibility profiles. There was no repetition of MSUC before the surgical procedure. Intraoperative and perioperative data were also gathered: use and size of ureteral access sheath, type of irrigation, lasing and total surgical time (from cystoscopy to bladder catheter positioning), exit strategy, SC results, and post-operative complications. Antiplatelets/anticoagulants were discontinued 3-7 days before surgery as per practices followed at each center. The SC was conducted by crushing the largest stone fragments in saline with a sterile mortar and pestle and subsequently streaking it on agar plates[10]. Bacterial growth on the agar plates was then examined after 24 to 48 hours.

Complications were characterized as any adverse events occurring within the first 30 days post-surgery and their severity was assessed based on the Clavien classification system. Infectious complications were divided into minor (steadily or intermittently 38°C body temperature for a minimum of 24 hours) and major (sepsis, septic shock, and death related to sepsis). The definitions of sepsis and septic shock adhered to the guidelines outlined in the Third International Consensus Definitions (sepsis-3) by the presence of at least two clinical criteria that constitute the quick SOFA score[11].

The study was approved by the ethical board of the leading center (Comitato Etico Regione Marche, #378/2021) and other centers obtained approval from their institutional review board. All patients signed an informed consent form.

2.2 Surgical procedure

All patients received antibiotic prophylaxis 30 minutes before anesthesia with II-III generation cephalosporins, penicillin, or aminoglycosides, guided by local guidelines and resistance patterns. There were no specific criteria for performing F-URS, and the surgery adhered to the standard of care and surgical practices of each participant center. Laser lithotripsy was performed using either holmium or Thulium fiber laser, depending on the availability and preference of each center.

2.3 Statistical analysis

Patients were divided into two groups according to the growth of pathogens at SC. Group 1 included patients with sterile culture, whilst Group 2 patients who had a positive SC.

Continuous variables are presented as median and (interquartile range). Categorical variables are reported as absolute frequency and percentage. Chi-square test was employed to evaluate differences in categorical variables between the two groups. Mann-Whitney U-test was used for continuous variables. A multivariable logistic regression analysis was performed to evaluate factors associated with having a positive SC. Variables that have been suggested in previous literature to impact sepsis following F-URS were entered into the model to assess their significance as independent predictors [6,8]. Data are presented as odds ratio (OR), 95% confidence interval (CI), and p-value. Statistical significance was set at a 2-tailed p-value <0.05. All statistical tests were conducted using SPSS software package version 25.0 (IBM Corp., Armonk, NY).

3. Results

During the study period, 737 patients underwent F-URS and laser lithotripsy for kidney stone(s) only. SC was non-performed in 444 of them, leaving 293 patients for the analysis. Table 1 shows patient baseline characteristics. Median age was 51.0 (24) years. There were 167 (57.0%) males. Among the included patients, 32 (2.5%) had a positive SC (Group 2). Group 2 patients were significantly older [median age 75.0 (14) years] than Group 1 patients [median age 51.0 (23) years, p=0.02]. There was a significantly higher proportion of diabetic, ischemic heart disease, and hypertension patients in Group 2. Median age-adjusted Charlson comorbidity index was significantly higher in Group 2 [4 (3) vs 1 (2), p=0.002]. There was also a significantly higher proportion of patients having a nephrostomy tube/ureteral stent in Group 2 (75.1%) compared to Group 1 (48.7%, p=0.003). There was a significantly higher proportion of patients having symptomatic urine infections within 3 months before surgery in Group 2 [40.6% vs 10.3%, p=<0.001]. Overall, 65 (69.9%) patients had a positive MSUC, and *Escherichia coli* was the most common isolated pathogen (Table 2). There was a significantly higher proportion of patients having asymptomatic bacteriuria or symptomatic infection at preoperative MSUC in Group 2 (p=0.025).

Lasing time, use, and caliber of ureteral access sheath, placement of postoperative ureteral stent, and stone composition were similar among the Groups (Table 3). Median total surgical time was significantly longer in Group 2 [90.0 (50) minutes vs 65 (35) minutes, p=0.032]. There was also a significant difference in the type of irrigation, where intermittent flushing with a syringe was more prevalent in Group 2 (12.7% vs 2.7%), whilst Traxer's flow was in Group 1 (27.2% vs 12.5%). *Escherichia coli* and *Enterococcus faecalis* were the most prevalent isolated pathogens in SC (2.1% for each one) (Table 4).

Nineteen patients out of 228 (8.3%) with negative preoperative MSUC had a positive SC, whilst 52 patients out of 65 (80%) with positive MSUC had a negative SC (Table 5). Among 13 patients who had both positive cultures, only 6 patients were harboring the same pathogen, namely *Escherichia coli* (n=2), *Pseudomonas aeruginosa* (n=2), *Enterococcus faecalis,* and *Proteus mirabilis*.

Regarding complications, there was a significant difference among the groups where only 34.4% of Group 2 patients had no complications as compared to 79.7% in Group 1 (p<0.001).

Concerning infectious complications, there was a significantly higher incidence in Group 2 (p<0.001) with 5.4% cases of prolonged fever requiring antibiotics (Clavien grade 2) in Group 1 and 34.4% in Group 2. The sepsis rate was 0.4% in Group 1 vs 3.1% in Group 2 (Clavien grade 4b). Septic shock rate was 9.4% (Clavien grade 4b) in Group 2, where there was also one sepsis-related death (3.1%) (Clavien grade 5). No cases of septic shock and death occurred in Group 1. Only two patients out of the six patients with major infectious complications had the same pathogen in MSUC and SC (i.e. *Escherichia coli*). The patient who died harbored *Escherichia coli* in MSUCC and Kluyveromyces spp in SC. This difference in complication rate converted to a significantly longer postoperative stay in Group 2 [3.0 (4) days vs 1 (2) days, p<0.001].

At multivariable regression analysis, diabetes (OR 3.23 95% CI 1.2-8.66, p=0.02), symptomatic urinary infections within 3 months before surgery (OR 4.82 95% CI 1.89-12.23, p=0.001), and preoperative stent/nephrostomy (OR 2.92 95% CI 1.16-7.34, p=0.03) were factors significantly associated with higher odds of having a positive SC (Table 6).

4. Discussion

Despite being a current practice worldwide, MSUC showed to have a poor correlation with the occurrence of systemic inflammatory response syndrome post endourological stone procedures, while SC demonstrated a better diagnostic accuracy[8]. However, there was in the past a misconception and overemphasis on inflammation with the misleading hypothesis that there is a continuum from systemic inflammatory response syndrome through severe sepsis to shock[11]. Therefore, in modern era, only sepsis should be considered as the endpoint in clinical trials for postoperative major infections.

In the present study, we evaluated the importance of performing an SC collected during F-URS lithotripsy. Our results pointed out several important findings.

Firstly, we found that patients harboring SC pathogens had a significantly higher incidence of major postoperative infectious events compared with those with negative SC. This highlights the importance of performing an SC in every patient undergoing F-URS whenever possible. Nevertheless, lack of stone for culture is a common limitation often seen when lasers are preferentially used for dusting and perhaps surgeons attempted dusting in most cases in our study. Indeed, SC was feasible in only 39.8% of patients in our series. This could also be related to the fact that dusting, fragmenting and extraction or their combination can be applied during F-URS with similar outcomes in terms of efficacy and safety[12].

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Additionally, SC could undoubtedly play a crucial role in selecting postoperative antibiotics, especially in cases of sepsis and this is particularly important in patients with negative MSUC. The need to change antibiotics based on SC results varied widely after endourological procedures, ranging from 1.3% to 64%[8]. To reinforce this, several studies also found that the pathogens identified in blood cultures of patients with sepsis following were concordant with those isolated from SC[13–15].

As shown by a recent systematic review[8], MSUC showed discordance between pathogens detected by MSUC and SC, supporting the feeling that relying on MSUC alone is a remarkably inadequate predictor for postoperative major infectious events. As an example, De Lorenzis and al. evaluated the concordance of pathogens isolated in MSUC, pelvic urine culture, and SC in a series of 107 patients undergoing F-URS or percutaneous nephrolithotripsy[16]. They found that the concordance between MSUC and SC and between pelvic urine culture and SC was 54.5% and 65.4%, respectively. Notably, the concordance increased to 94.1% between SC and urine culture derived from stone fragmentation. In our study too there was a low concordance of isolated pathogens in MSUC and SC, with only 6/13 (46.2%) patients harboring the same pathogen. Therefore, a pelvic urine culture collected during lithotripsy is a practical and reasonable compromise in daily practice when a stone sample is inadequate for culture.

Another important finding is the reflection that pathogens can be present around the stone even when the MSUC is negative and appropriate preoperative antibiotic treatment has been administered. This could particularly be the case in the presence of obstruction or an indwelling ureteral stent/nephrostomy tube due to colonization. This hypothesis is reinforced by the results of our regression analysis where a preoperative stent/nephrostomy tube was associated with almost threefold odds of having a positive SC. To support this, several studies are showing the increased risk of postoperative sepsis in patients undergoing ureteroscopy with a ureteral stent inserted before surgery, particularly when dwelling time exceeds 30 days[6]. Unfortunately, we did not gather this data and were not able to confirm a correlation between stent dwelling time and positive SC.

Additionally, renal stone itself can serve as a potential source of infection. Pathogens may reside inside stones as demonstrated by the presence of 16S rRNA gene sequencing of multiple bacteria in stones, not only struvite but also calcium oxalate and calcium phosphate stones[17]. Pathogens can be released during lithotripsy, with the possibility of entering the bloodstream due to high intrarenal pressure during F-URS and consequent pyelo-venous and pyelo-lymphatic backflow. This assumption could be another reason why Group 2 patients had a higher incidence of major infectious events in our series. In Group 2 there was a significantly higher use of flush manual irrigation with syringe that was demonstrated to be associated with the highest rise in pressure in an ex vivo model compared with other irrigation systems[18] and this could have had a role in the higher incidence of sepsis in Group 2 patients.

Of note, microbiological characteristics of isolated pathogens in our study reveal that the

most frequent pathogens identified in MSUC were Gram-positive, whereas Gram-positive and uncommon urinary pathogens were the most common agents isolated in SC. This finding is in line with previous reports[9,19] and is another supporting reason to routinely perform SC.

A further important finding of our study is that diabetic patients had a threefold risk of having a positive SC. It is well-known that diabetes mellitus is associated with a higher risk of infections. A recent meta-analysis based on 345 studies demonstrated that diabetes was associated with an increased risk of multiple types of infections and a stronger association with urinary infections (OR 2.59) was observed in case-control studies[20]. The elevated risk of urinary tract infections in diabetic patients may be attributed to several unique mechanisms. Increased susceptibility in diabetic patients is positively associated with increased duration and severity of diabetes[21]. This in part explains why patients were significantly older in Group 2 and there was a significantly higher incidence of diabetic patients in Group 2 (31.3% vs 9.9%). Moreover, elevated glucose concentrations in urine[22] and renal parenchyma[23] among diabetic individuals can create an environment conducive to the growth of pathogens, which might convert into the colonization of kidney stones. In addition, chronic hyperglycemia raises the risk of developing kidney stone disease[24] making a vicious circle in diabetic patients between stone formations, pathogens colonization of stones, and urinary infections.

Lastly, we found that symptomatic urinary infections within 3 months of surgery were associated with the highest risk of positive SC. This observation is supported by the evidence that patients suffering from renal stones frequently present with recurrent urinary tract infections and surgical clearance of stones often results in the resolution of infections[25]. However, we are still far from fully clarifying the correlation between kidney stone disease and urinary tract infections, and the “chicken and egg dilemma” still exists.

The present study has some limitations. Firstly, we were not able to assess why SC was not performed in all cases despite being a common practice in the involved centers. However, we argue that this was mostly related to insufficient samples. Secondly, we did not gather data on stent/nephrostomy tube-dwelling time and long-term would potentially influence positive SC. Thirdly, stone composition was not performed in more than half of patients making it difficult to evaluate its influence on positive SC. Yet, 45.4% of included patients had a previous treatment in the affected kidney and this might also influence stone colonization. Moreover, total surgical time was significantly longer in Group 2 patients and there was a significant difference in the type of irrigation employed between the groups with a potentially higher intrarenal pressure using intermittent irrigation with a syringe that was employed more commonly in Group 2 patients. These differences could have had a role in post-operative sepsis incidence in Group 2 patients. Finally, we acknowledge that we did not have blood cultures of our patients with sepsis and positive SC to make further correlations.

5. Conclusion

Our study shows that patients with a positive SC have a significantly higher incidence of sepsis following F-URS lithotripsy. Yet, we demonstrated a poor pathogen concordance between preoperative MSUC and SC highlighting the need to perform the latter in all patients whenever feasible.

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ABBREVIATIONS USED

F-URS: flexible ureteroscopy

MSUC: midstream urine culture

SC: stone culture

CT: computed tomography

OR: odds ratio

CI: confidence interval

Table 1. Patient baseline characteristics

	Overall population (n=293)	Negative stone culture (n=261)	Positive stone culture (n=32)	P value
Age, years, median (IQR)	51.0 (24)	51.0 (23)	75.0 (14)	**0.001**
Gender				0.22
Male, n (%)	167 (57.0)	152 (58.2)	15 (46.9)	
Female, n (%)	126 (43.0)	109 (41.8)	17 (53.1)	
BMI, median (IQR)	26.8 (5)	26.4 (15.8)	26.3 (6.4)	0.875
Age adjusted Charlson comorbidity index, median (IQR)	1 (2)	1 (2)	4 (3)	**0.008**
Motility, n (%)				0.496
Normal	282 (96.2)	250 (95.8)	32 (100)	
Wheelchair bound	9 (3.1)	9 (3.4)	0	
Bed bound	2 (0.7)	2 (0.8)	0	
Neurogenic bladder, n (%)	7 (2.4)	7 (2.7)	0	0.348
Multiple sclerosis, n (%)	3 (0.9)	3 (1.5)	0	0.542
Ischemic heart disease, n (%)	20 (6.8)	12 (4.6)	8 (25.0)	**<0.001**

Hypertension, n (%)	98 (33.4)	78 (29.9)	20 (62.5)	**<0.001**
COPD, n (%)	11 (3.8)	8 (3.1)	3 (9.4)	0.076
Indwelling bladder catheter, n (%)				0.900
Urethral	12 (4.1)	11 (4.2)	1 (3.1)	
Suprapubic	1 (0.3)	1 (0.4)	0	
Diabetes, n (%)				**0.002**
Type 1	7 (2.4)	5 (1.9)	2 (6.3)	
Type 2	29 (9.9)	21 (8.0)	8 (25.0)	
ASA score, n (%)				**0.013**
1	88 (30.0)	86 (33.0)	2 (6.3)	
2	143 (48.8)	124 (47.5)	19 (59.3)	
3	58 (19.8)	48 (18.4)	10 (31.3)	
4	4 (1.4)	3 (1.1)	1 (3.1)	
Symptomatic urinary infections within 3 months prior to surgery, n (%)	40 (13.7)	27 (10.3)	13 (40.6)	**<0.001**

Preoperative urine culture, n (%)				**0.025**
Sterile	228 (77.8)	209 (80.1)	19 (59.4)	
Asymptomatic bacteriuria	48 (16.4)	39 (14.9)	9 (28.1)	
Infection	17 (5.8)	13 (5.0)	4 (12.5)	
Affected kidney, n (%)				0.728
Left	155 (52.9)	139 (53.3)	16 (50.0)	
Right	138 (47.1)	122 (46.7)	16 (50.0)	
Stone volume, mm^3, median (IQR)	629.0 (725.5)	629 (836)	835 (1373)	0.095
HU, median (IQR)	997.0 (424)	950 (400)	1013 (280)	0.266
Stone(s) location, n (%)				0.503
Pelvis	110 (37.6)	100 (38.3)	10 (31.3)	
Lower pole	69 (23.5)	61 (23.4)	8 (25.0)	
Interpolar	32 (10.9)	30 (11.5)	2 (6.2)	
Upper pole	30 (10.2)	27 (10.3)	3 (9.4)	
Multiple sites	52 (17.8)	43 (16.5)	9 (28.1)	
Multiple stones, n (%)	116 (39.6)	103 (39.5)	13 (40.6)	0.899

Number of stones, n (%)				0.435
1	177 (60.4)	158 (60.6)	19 (59.4)	
2	73 (24.9)	65 (24.9)	8 (25.0)	
3	20 (6.8)	16 (6.1)	4 (12.5)	
4	17 (5.8)	17 (6.5)	0	
5	2 (0.7)	2 (0.8)	0	
6	4 (1.4)	3 (1.1)	1 (3.1)	
Hydronephrosis, n (%)				0.624
No	183 (62.5)	163 (62.5)	20 (62.5)	
Mild	74 (25.3)	66 (25.3)	8 (25.0)	
Moderate	26 (8.9)	22 (8.4)	4 (12.5)	
Severe	10 (3.3)	10 (3.8)	0	
Preoperative stent or nephrostomy, n (%)	151 (51.5)	127 (48.7)	24 (75.1)	**0.005**
Previous treatment for stone in the same kidney, n (%)				0.057
None	160 (54.6)	140 (53.6)	20 (62.5)	

SWL	48 (16.4)	42 (16.1)	6 (18.7)	
RIRS	73 (24.9)	70 (26.8)	3 (9.4)	
PCNL	6 (2.0)	5 (1.9)	1 (3.1)	
Open surgery	2 (0.7)	2 (0.8)	0	
More than one	4 (1.4)	2 (0.8)	2 (6.3)	
Anomalous kidney, n (%)*		25 (9.6)	1 (3.1)	0.226
Duplex system	1 (0.3)	1 (0.4)	0	
Uretero-pelvic junction obstruction	20 (6.8)	20 (7.7)	0	
Horseshoe kidney	1 (0.3)	1 (0.4)	0	
Malrotated kidney	5 (1.7)	4 (1.5)	1 (100)	
Ectopic kidney	2 (0.7)	2 (0.8)	0	

*more than one possible

Mann- Whitney U-test per continuous variables

Chi square for categorical variables

Table 2. Isolated bacteria in preoperative urine culture in 63 out of 293 patients

	N=293
Negative	230 (78.5)
E. coli	18 (6.3)
Contaminated	13 (4.5)
Klebsiella pneumoniae	7 (2.4)
Enterococcus faecalis	5 (1.8)
Proteus mirabilis	5 (1.8)
Pseudomonas aeruginosa	4 (1.4)
Staphylococcus epidermidis	3 (0.7)
Polymicrobic	2 (0.7)
E.coli ESBL	2 (0.7)
Candida albicans	1 (0.3)
Klebsiella aerogens	1 (0.3)
Stenotrophomonas maltophilia	1 (0.3)
Klebsiella ozaenae	1 (03)

Data are presented as absolute number (%)

Table 3. Intraoperative and postoperative outcomes.

	Overall population (n=293)	Negative stone culture (n=261)	Positive stone culture (n=32)	**P value**
Total surgical time, minutes, median (IQR)	65.0 (39)	65 (35)	90.0 (50)	**0.032**
Lasing time, minutes, median (IQR)	20.0 (20)	20 (20)	30.0 (22)	0.513
Postoperative stay, days, median (IQR)	1 (2)	1 (2)	3.0 (4)	**<0.001**
Type of irrigation during lithotripsy, n (%)				**<0.001**
Gravity	0	0	0	
Pump	205 (70.0)	183 (70.1)	22 (68.8)	
Intermittent with syringe	13 (4.4)	7 (2.7)	6 (12.7)	
Traxer's flow	75 (25.6)	71 (27.2)	4 (12.5)	
Use of UAS, n (%)				0.067
No	25 (8.5)	25 (9.6)	0	
Yes	268 (91.5)	236 (90.4)	32 (100)	

Caliber of UAS, n (%)				0.336
Sheathless	26 (8.9)	26 (10.0)	0	
9/11 Fr	3 (0.9)	3 (1.1)	0	
10/12 Fr	67 (22.9)	62 (23.8)	5 (15.7)	
9.5/11.5 Fr	6 (2.0)	5 (1.9)	1 (3.1)	
11/13 Fr	146 (49.8)	125 (47.9)	21(65.6)	
12/14 Fr	40 (13.8)	36 (13.8)	4 (12.5)	
12/14 Fr vacuum assisted	5 (1.7)	4 (1.5)	1 (3.1)	
Placement of a postoperative ureteral stent, n (%)	262 (89.4)	230 (88.1)	32 (100)	**0.039**
Stone biochemistry, n (%)				**0.007**
Not performed	163 (55.6)	135 (51.7)	28 (87.5)	
Calcium oxalate dihydrate,	53 (18.1)	53 (20.3)	0	
Calcium oxalate monohydrate	44 (15.0)	42 (19.0)	2 (6.3)	
Uric acid	9 (3.1)	8 (3.1)	1 (3.1)	
Struvite	1 (0.3)	1 (0.4)	0	
Calcium phosphate	23 (7.8)	22 (8.4)	1 (3.1)	

Postoperative complications§, n (%)				**<0.001**
None	219 (74.7)	208 (79.7)	11 (34.4)	
Clavien grade 1				
Loin/abdominal pain (pain killer)	16 (5.5)	15 (5.7)	1 (3.1)	
Clavien grade 2				
Acute urinary retention (catheterization)	1 (0.3)	1 (0.4)	0	
Hematuria (prolonged catheterization)	6 (2.1)	6 (2.3)	0	
Prolonged fever*/UTI (antibiotics)	25 (8.6)	14 (5.4)	9 (28.1)	
Post-discharge UTI (antibiotics)	17 (5.8)	5 (1.9)	12 (37.5)	
Clavien 3a				
Perirenal hematoma (embolization)	1 (0.3)	1 (0.4)	0	
Clavien 3b				
Stent displacement (stent repositioning)	6 (2.1)	6 (2.3)	0	
Stein Strasse (ureterolithotripsy)	1 (0.3)	1 (0.4)	0	
Clavien 4b				
Sepsis (antibiotics, fluids, noradrenaline)	4 (1.4)	1 (0.4)	3 (9.4)	
Septic shock (ICU admission)	1 (0.3)	0	1 (3.1)	

Clavien 5				
Death due to sepsis	1 (0.3)	0	1 (3.1)	
Type of postoperative infection, n (%)				**<0.001**
None	262 (89.5)	246 (94.3)	16 (50.0)	
Minor				
Fever* (Clavien 2)	25 (8.6)	14 (5.4)	11 (34.4)	
Major				
Sepsis (Clavien 4b)	2 (0.7)	1 (0.4)	1 (3.1)	
Septic shock with ICU admission (Clavien 4b)	3 (0.9)	0	3 (9.4)	
Death (Clavien 5)	1 (0.3)	0	1 (3.1)	

UAS: ureteral access sheath

***** Temperature above 38°C for a minimum of 24 hours (steadily or intermittently)

§ more than one possible

ICU: intensive care unit; **UTI:** urinary tract infection

Mann-Whitney U-test per continuous variables

Chi square for categorical variables

Table 4. Isolated bacteria in stone culture in 32 patients out of 293.

	N=293
Negative	261 (89.1)
Escherichia coli	6 (2.1)
Enterococcus faecalis	6 (2.1)
Polymicrobic	3 (1.2)
Candida albicans	2 (0.7)
Pseudomonas aeruginosa	2 (0.7)
Proteus mirabilis	2 (0.7)
Staphylococcus epidermidis	2 (0.7)
Serrattia marcescens	1 (0.3)
Acinetobacter baumannii	1 (0.3)
Klebsiella pneumoniae	1 (0.3)
Staphylococcus aureus	1 (0.3)
Kluyveromyces spp	1 (0.3)
Pseudomonas stutzeri	1 (0.3)
Trichosporon asahii	1 (0.3)
Enterococcus faecium MDR	1 (0.3)
Enterococcus faecium	1 (0.3)

Data are presented as absolute number (%)

MDR: multidrug resistant

Table 5. Results of preoperative mid-stream urine and stone cultures.

	Negative stone culture	**Positive stone culture**	*Total*
Negative urine culture	209	19	228
Positive urine culture	52	13	65
Total	261	32	293

Table 6. Multivariable analysis of predictive factors of having a positive stone culture.

	OR (95% CI)	*p-value*
Female gender	1.51 (0.66-3.47)	0.33
Diabetes	3.23 (1.2-8.66)	**0.02**
Symptomatic urinary infections within 3 months prior to surgery	4.82 (1.89-12.23)	**0.001**
Preoperative stent/nephrostomy	2.92 (1.16-7.34)	**0.03**
Preoperative positive urine culture	1.20 (0.47-3.10)	0.71