



## Postoperative urinary tract infection after ureteroscopic lithotripsy in patients with asymptomatic bacteriuria

### Postoperativna urinarna infekcija nakon ureterskopske litotripsije kod bolesnika sa asimptomatskom bakteriurijom

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#### Abstract

**Background/Aim.** Postoperative urinary tract infection (UTI) is one of the most common infective complications of ureteroscopic lithotripsy. Preoperative asymptomatic bacteriuria is not a contraindication for performing ureteroscopic lithotripsy but it can be a significant risk factor for occurrence of severe forms of postoperative urinary infection. **Methods.** From January 2010 until December 2014 at the Urology Clinic of the Military Medical Academy in Belgrade, 389 patients undergoing ureteroscopic lithotripsy were analyzed, and their postoperative infective complications were monitored. From the group, the incidence of postoperative urinary infection was analysed in 52 patients with preoperative asymptomatic bacteriuria. **Results.** Infective complications occurred in 18.7% of patients, and postoperative UTI in 10% of patients. Out of 52 patients with preoperative asymptomatic bacteriuria, 36.5% had postoperative urinary tract infection ( $\chi^2 = 46.773$ ;  $p < 0.001$ ). In these patients, we registered higher frequency of severe forms of postoperative UTI, systemic inflammatory response syndrome (SIRS) and sepsis. **Conclusion.** Preoperative asymptomatic bacteriuria represents a significant risk factor for developing postoperative UTI following ureteroscopic lithotripsy and is associated with increased risk for occurrence of severe forms of SIRS and sepsis. It is desirable that every patient with indicated ureteroscopic lithotripsy has sterile urine culture, and if this is impossible to achieve, a special caution and an adequate antibiotic therapy and prophylaxis are needed before and during the surgical procedure.

#### Key words:

bacteriuria; lithotripsy; ureteroscopy; postoperative complications; urinary tract infections.

#### Apstrakt

**Uvod/Cilj.** Postoperativna urinarna infekcija jedna je od najčešćih infektivnih komplikacija ureterskopske litotripsije. Asimptomatska preoperativna bakteriurija nije kontraindikacija za izvođenje ove metode, ali može biti značajan faktor rizika za nastanak teških oblika postoperativne urinarnе infekcije. **Metode.** Od januara 2010. do decembra 2014. godine, u Klinici za urologiju Vojnomedicinske akademije u Beogradu, analizirano je 389 bolesnika kod kojih je urađena ureterskopska litotripsija i praćene su postoperativne infektivne komplikacije. Kod 52 bolesnika iz ove grupe sa preoperativnom asimptomatskom bakteriurijom, analizirana je učestalost postoperativne urinarnе infekcije. **Rezultati.** Infektivne komplikacije javile su se kod 18,7% bolesnika, a postoperativnu urinarnu infekciju imalo je 10% bolesnika. Od 52 bolesnika sa asimptomatskom preoperativnom bakteriurijom, postoperativnu urinarnu infekciju imalo je njih 36,5% ( $\chi^2 = 46.773$ ;  $p < 0.001$ ). Kod ovih bolesnika zabeležena je veća učestalost teških oblika postoperativne urinarnе infekcije, sindroma sistemskog inflamatornog odgovora (SSIO) i sepse. **Zaključak.** Asimptomatska preoperativna bakteriurija predstavlja značajan faktor rizika za pojavu postoperativne urinarnе infekcije nakon ureterskopske litotripsije i udružena je sa povećanim rizikom za nastanak teških oblika SSIO i sepse. Poželjno je da svi bolesnici kod kojih je indikovana ureterskopska litotripsija imaju sterilnu urinokulturu, a ako je to nemoguće postići, potreban je poseban oprez i adekvatna antibiotska terapija i profilaksa pre i tokom operativne procedure.

#### Ključne reči:

bakteriurija; litotripsija; ureterskopija; postoperativne komplikacije; urinarni trakt, infekcije.

## Introduction

Ureteroscopic lithotripsy is one of the most common surgical methods for treating kidney and ureter stone<sup>1</sup>. The multicentric study of the Endourological Society (*Clinical Research Office of the Endourological Society – CROES*), which was done at 114 hospitals in 32 countries, with 11,885 patients, has found that the incidence of this procedure success, when the patients lose the stone (stone free rate – SFR) is 85.6%, and the incidence of postoperative complications is 3.5%<sup>2</sup>.

According to recent studies, the frequency of infective complications following ureteroscopic lithotripsy is between 1.7% and 18.8%<sup>3-5</sup>.

Patients with stone in the kidney or ureter often have asymptomatic bacteriuria with values from 10,000 to 100,000 colonies *per* millilitre, but without local and general signs of urinary tract infection (UTI). This condition is explained by existence of bacterial biofilm at the surface of the stone or at the previously placed ureteral JJ stent or at the nephrostomy catheter<sup>6, 7</sup>. Untreated preoperative UTI presents absolute contraindication for performing ureteroscopic lithotripsy<sup>1</sup>, while it can be done in patients with asymptomatic bacteriuria with the application of a short term preoperative antibiotic therapy recommended in order to mitigate risks for developing possible infective complications<sup>8</sup>.

The aim of this study was to analyze significance of preoperative asymptomatic bacteriuria as a risk factor for development of infective complications following ureteroscopic lithotripsy.

## Methods

The research was done at the Urology Clinic of the Military Medical Academy in Belgrade, Serbia through retrospective analysis of medical records of 389 patients, male and female, who had pneumatic and laser ureteroscopic lithotripsy in the ureter or kidney, by a semirigid and/or a flexible ureteroscope, in the period from January 2010 until December 2014. During preparations for ureteroscopic lithotripsy the detailed anamnesis was taken from all the patients, and physical examination and laboratory tests (erythrocyte sedimentation rate, complete blood analyses, biochemical analyses, microscope exam of the urine sediment and urine culture) were done.

In patients who developed infective complications, their gradation was done according to the Modified Clavien Classification System – MCCS. According to the MCCS all infective complications following ureteroscopic lithotripsy in this study were divided into 4 degrees: gradus I – temporary febrile condition not requiring additional treatment besides applying antipyretics; gradus II – postoperative urinary tract infection, non-obstructive pyelonephritis, systemic inflammatory response syndrome (SIRS) or sepsis requiring applying additional antibiotics, and sepsis requiring also inotropic drugs; gradus III – obstructive sepsis requiring applying additional endoscopic procedures and multi-pharmacological treatment, and gradus IV – severe sepsis (IVa) and septic

shock (IVb) requiring staying and treating patients in an intensive care unit<sup>9</sup>.

The criteria of the International Conference for Sepsis and Organ Collapsing and Guidelines for Using Innovative Therapies in Sepsis of the American College of Chest Physicians and the Society of Critical Care, established in 1992, where sepsis is defined as presence and verification of infection source and SIRS, were used in this study. The existence of two or more criteria is characteristic for SIRS: body temperature > 38 °C or < 36°C; heart rhythm > 90 beats/min; respiration rate number > 12/min or partial pressure of CO<sub>2</sub> < 32 mmHg; leukocytosis > 12,000/mm<sup>3</sup> or < 4,000/mm<sup>3</sup>. Organ dysfunction is characteristic for severe sepsis and acute circulatory collapse with persistent arterial hypotension is characteristic for septic shock<sup>10,11</sup>.

The examinees were classified into two groups: the first group – patients with preoperative asymptomatic bacteriuria subjected to the pneumatic or laser ureteroscopic lithotripsy, who did not have postoperative urinary infection, and the second group – patients with preoperative asymptomatic bacteriuria subjected to the pneumatic or laser ureteroscopic lithotripsy who had postoperative urinary infection.

All data in the study were processed in SPSS 20.0 (IBM corporation) software package. The chosen level of significance, i.e. possibility of the first type mistake was 0.05.

## Results

The study comprised 389 patients, 200 (51.4%) male and 189 (48.6%) female, with unilateral ureteral or kidney calculosis (one or more stones in clearly defined levels of the upper urinary tract in which the stone was located: kidney, upper ureter, middle ureter and lower ureter), subjected to ureteroscopic lithotripsy by a semirigid and/or a flexible instrument. Patients without preoperative urinary tract infection were analysed.

Average age of the patients in this study was 55. The youngest patient was 13 and the oldest one 92. Average body mass index (BMI) of the patients was 26 kg/m<sup>2</sup> (minimum 14 and maximum 37 kg/m<sup>2</sup>). Average size of stones was 13 mm, and in 94 (24.2%) patients lithotripsy was performed in the kidney and in 295 (75.8%) patients in the ureter. Laser lithotripsy was performed in 237 (60.9%) patients, and breaking by a pneumatic probe in 152 (39.0%) patients. Average duration of surgery was 40 minutes, the shortest one lasted 5 minutes, the longest one 185 minutes. A semirigid ureteroscope was used in 357 (91.7%) patients, a flexible one in 28 (7.2%), and in 4 (1.1%) patients the both types of ureteroscope were used.

Infective complications in this study developed in 73 (18.7%) patients, and postoperative urinary tract infection in 39 (10%) patients. Temporary febrile condition not requiring additional treatment besides applying antipyretics occurred in 34 (8.7%) patients.

Postoperative urinary tract infection, according to definitions of the Section of Infection in Urology of the European Association of Urology<sup>11</sup> and the International Conference for Sepsis and Organ Collapsing and the Guidelines for

Using Innovative Therapies in Sepsis of the American Chest Physicians and the Society of Critical Care <sup>10</sup>, had 39 (10%) patients. In these patients the treatment implied using antipyretics, additional antibiotic therapy, additional infusion of inotropic and supportive therapy, and in 2 (0.4%) patients additional procedures were performed – placing JJ stent and percutaneous nephrostomy catheter. In Table 1 the incidence of infective complications and postoperative urinary infections and the treatment method are shown.

Out of total number of patients, 52 (13.4%) were with preoperative asymptomatic bacteriuria, while 337 (86.6%) patients had sterile urine culture. In the group of patients without postoperative urinary infection, in 33 (63.5%), asymptomatic bacteriuria was verified before the surgery, and in the group of patients with postoperative urinary infection, 19 (36.5%) had asymptomatic bacteriuria before the surgery. These data were analysed by  $\chi^2$  test which confirmed that there was a statistically highly significant difference between the groups ( $\chi^2 = 46.773$ ;  $p < 0.001$ ).

In 19 patients with postoperative urinary infection, the most common bacterium present in preoperative urine cultures was *Escherichia coli* (52.6%), the second most common one was *Pseudomonas aeruginosa* (21.0%), then mixed bacterial flora with *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Enterococcus faecalis* (10.5%), *Pseudomonas aeruginosa* and *Enterococcus faecalis* (5.3%), *Proteus mirabilis* (5.3%) and *Enterococcus faecalis* (5.3%). In postoperative urine cultures of these patients the following bacteria were isolated: *Escherichia coli* (43.7%), *Klebsiella species* (17.8%), *Pseudomonas aeruginosa* (15.0%), *Enterococcus faecalis* (13.2%) and *Proteus mirabilis* (10.3%).

Out of 7 patients with sepsis in this study, 5 (1.4%) patients were treated at the Urology Department. Out of these 5 patients, 3 (0.9%) patients received antibiotic therapy, infusion solutions and drugs for regulating circulatory collapse

and cardiorespiratory dysfunction, but it was not necessary to keep them in the Intensive Care Unit. In all three patients the *Staphylococcus coag. (-)* bacterium was isolated in the hemoculture. In the rest 2 (0.5%) patients treated at the Urology Department, postoperative obstructive pyelonephritis and sepsis were verified and it was necessary to place a JJ stent in one case and a percutaneous nephrostomy catheter in another case besides applying antibiotic therapy.

In 2 (0.4%) patients (out of 7 patients with sepsis), the treatment required monitoring and their staying in the Intensive Care Unit because of circulatory collapse and cardiorespiratory dysfunction, under diagnosis of severe sepsis and septic shock, with intubation and putting on respiratory device and applying several antibiotics, inotropic drugs and infusion of colloid solutions and nutritive solutions simultaneously. In both patients *Escherichia coli* was isolated from the hemoculture, and the same bacterium was found in the preoperative asymptomatic bacteriuria results.

## Discussion

The impact of preoperative asymptomatic bacteriuria on development of urinary tract infection in patients following ureteroscopic lithotripsy was analyzed in this study. Infective complications following ureteroscopic lithotripsy are the most common complications occurring after this procedure <sup>2</sup>, which is why it is important to identify patients with a risk for their developing following the procedure. Reasons for secondary postoperative urinary tract infection may also be dissemination of bacteria from the lower to the upper urinary tract in the course of the procedure, also performing the procedure on an infectious stone and using irrigation solution under high pressure which generates bacteremia <sup>9</sup>. Preoperative antibiotic therapy mitigates the risk of postoperative urinary infection <sup>8</sup>.

**Table 1**

**Incidence of infective complications and postoperative urinary infections and the treatment method**

Complication	Patients n (%)	Treatment
Gradus I		
Temporary febrile condition	34 (8.7)	Antipyretics
Gradus II		
SIRS	32 (8.3)	Antibiotic therapy
Sepsis	3(0.9)	Antibiotic therapy Parenteral solution infusion Inotropic drugs
Gradus III		
Obstructive sepsis pyelonephritis	2 (0.4)	Endoscopic intervention Placement of JJ stent or percutaneous nephrostomy catheter
Gradus IVa		
Severe sepsis	1 (0.2)	Intensive Care Unit management
Gradus IVb		
Septic shock	1 (0.2)	Intensive Care Unit management

**SIRS – systemic inflammatory response syndrome.**

Infective complications following ureteroscopic lithotripsy comprises: temporary febrile condition not requiring applying additional antibiotic therapy, postoperative urinary tract infection, SIRS and sepsis<sup>8, 12, 13</sup>. Temporary febrile condition requires applying only antipyretics and usually passes spontaneously in 24–48 hours, but postoperative urinary tract infections which comprise also severe forms of postoperative urinary infection – SIRS and sepsis, are complications extending time of a patient's hospitalizing, requiring expensive antibiotics therapy, requiring sometimes even additional procedure, significantly rising the price of treatment, and in the case of organ dysfunction are life threatening complications<sup>5, 14</sup>. Even with abiding basic principles in the preoperative preparation of a patient and applying antibiotic prophylaxis in line with recommendations of the Guidelines on Urological Infections – EAU Guidelines, patients frequently get unpredictable severe forms of postoperative urinary tract infections.

The incidence of postoperative urinary infection following ureteroscopic lithotripsy in the study was 10%, and the frequency of all infective complications, taking into account also temporary febrile condition was 18.7%. This incidence in our study is in line with the Japanese authors<sup>12</sup> that analyzed factors associated with occurrence of postoperative febrile urinary tract infection following ureteroscopic stone breaking in 153 patients. In their study, the incidence of all infective complications was 18.3%, and the incidence of postoperative infective complications requiring additional antibiotics and supportive therapy or endoscopic procedures was 7.8%<sup>12</sup>. However, other authors reported lower incidence of infective complications following ureteroscopic procedures. Sohn et al.<sup>13</sup> analyzed 531 patients that were subjected to ureteroscopic procedures from 2002 to 2010, including also ureteroscopic lithotripsy. In that study, the incidence of infective complications was 3.8%. Higher frequency of infective complications in our study can be explained by differences between the groups of patients analyzed and also by different definitions of infective complications and postoperative urinary infections among studies. In our study we analyzed only patients subjected to ureteroscopic lithotripsy, and the Sohn et al.<sup>13</sup> study comprised also 154 (29.0%) patients that were subjected to diagnostic ureteroscopy. In the study of Bloom et al.<sup>14</sup>, the infective complications comprised only complications requiring additional antibiotics or other treatment (Gradus  $\geq$  II complications according to the MCCS). In our study, infective complications Gradus  $\geq$  II were defined as postoperative urinary infections and their frequency in the study was 10%. Also, the difference in frequency of infective complications between these two studies may be due to using different types of ureteroscopes<sup>15</sup>. The size of a stone could also have impact on developing postoperative infection, because the average stone size in our study in patients with postoperative urinary infections was 15 mm, which was more than in the studies dealing with complications following ureteroscopy and endourological procedures<sup>5, 16</sup>.

An absolute contraindication for performing ureteroscopic lithotripsy was untreated urinary tract infection. Preo-

perative asymptomatic bacteriuria with positive findings of bacteria in the urine culture, from 10.000 to 100.000 colonies *per* mL, but with no local, general and clinic signs of urinary infection, was not an excluding factor because in a number of patients, sterile urine culture could not be achieved, which is explained by increasing bacterial colonies at the stone surface or at the ureteral JJ stent and on the nephrostomic catheter which the patients had to wear before the surgery<sup>6, 7</sup>. Totally, 52 (13.4%) patients in our study had preoperative asymptomatic bacteriuria and in these patients an antibiotic therapy was applied 1–12 days preoperatively according to the antibiogram results. Most frequently, a third generation cephalosporin, ceftriaxon was used – in 17 (32.7%) patients. In these patients, the most frequently isolated bacterium in preoperative urine cultures was *Escherichia coli* (40.4%). Among 52 patients with preoperative asymptomatic bacteriuria, a postoperative urinary tract infection had 19 (36.5%) of them. In these patients, the most commonly preoperatively used antibiotics were aminoglycosides (amikacin, gentamycin), ie. they were applied in 6 (31.6%) patients, and the most frequently isolated bacterium in preoperative urine cultures was also *Escherichia coli* (52.6%). In our study we found statistically significant difference between the group without and the group with postoperative urinary infection following ureteroscopic lithotripsy in comparison to patients that had asymptomatic bacteriuria and patients with sterile urine culture ( $p < 0.001$ ). Moses et al.<sup>8</sup> in their study examined 16.5% patients that had preoperatively positive urine cultures and received antibiotic therapy 3–7 days preoperatively. Preoperative bacteriuria was examined in other studies as a risk factor following ureteroscopic lithotripsy. Uchida et al.<sup>17</sup> proved, by using multivariate analysis, that positive preoperative findings of urine cultures in patients that were subjected to ureteroscopic laser lithotripsy, were associated with higher risk of postoperative SIRS. In that study, 12.4% patients, subjected to ureteroscopic laser lithotripsy, had positive preoperative findings of urine cultures, but with no signs of urinary tract infection. In those patients, an adequate antibiotic therapy was applied in duration prescribed by an urologist, but the study did not bring forward the therapy duration. It was proved in the study, through a multivariate logistic regression analyses, that positive preoperative urine culture, was a significant risk factor for occurrence of SIRS following laser ureteroscopic lithotripsy ( $p = 0.005$ ). The patients with preoperative asymptomatic bacteriuria, subjected to ureteroscopic lithotripsy, were also analyzed by Sohn et al.<sup>13</sup>. They examined 20.9% patients with preoperative bacteriuria, and 10.8% of these patients had infective complications ( $p = 0.000$ ). Matsumoto et al.<sup>18</sup>, in their study also have concluded that preoperative bacteriuria is a statistically significant risk factor for occurrence of infective complications following urologic procedures in the upper urinary tract. Blackmur et al.<sup>15</sup>, in their analysis of risk factors for developing sepsis following ureteroscopic lithotripsy, which was done in 462 patients, found that 34 (7.4%) patients had sepsis and that positive preoperative findings of urine cultures were associated with occurrence of postoperative urosepsis, although an ade-

quate antibiotic preoperative therapy was applied ( $p < 0.001$ ). All these studies showed results in line with our analysis. The study proving the opposite was not found in the existing literature.

Out of 19 patients that preoperatively had asymptomatic bacteriuria and developed infective complications following ureteroscopic lithotripsy, 7 (1.8%) patients were treated for severe postoperative urinary infections with signs of sepsis. All these patients preoperatively received an adequate antibiotic prophylaxis. Sepsis following ureteroscopic lithotripsy is one of the most severe complications. In other studies that analyzed risk factor for developing postoperative urinary infection, the frequency of sepsis was also between 1%–3%. Mitsuzuka et al.<sup>12</sup> reported 1.3% patients with sepsis developed after ureteroscopic lithotripsy. In the existing literature only few studies analyzed the frequency of sepsis following ureteroscopic lithotripsy. Geavlete et al.<sup>19</sup> brought forward the data of 1.13% out of 2,735 patients with sepsis occurred following ureteroscopic lithotripsy made by a semirigid ureteroscope. Eswara et al.<sup>20</sup> analyzed 328 patients that were subjected to endourological procedures, out of which 11 (3.0%) had sepsis. However, Blackmur et al.<sup>15</sup> in their analysis of risk factors for developing sepsis after ureteroscopic lithotripsy, in which they examined 462 patients, published data on 34 (7.4%) patients with sepsis. This somewhat larger number of patients with sepsis developed following ureteroscopic lithotripsy in that study was explained by the fact that the study comprised patients with both sides ureteroscopic lithotripsy also and a great number of patients with associated cardiovascular diseases and diabetes, high the American Society of Anesthesiology (ASA) score and larger stones.

Out of 19 patients in our study that had asymptomatic bacteriuria preoperatively and developed postoperative infective complications, the rest 12 (3.1%) patients had postoperative urinary infection and SIRS. Their treatment required applying additional antibiotic therapy according to findings of urine cultures, but not infusion of solutions and supportive therapy, nor additional endoscopic procedures.

From the above mentioned results it can be concluded that patients with asymptomatic bacteriuria preoperatively had also higher frequency of severe forms of urinary infections postoperatively.

Use of standardized system for infective complications classification (MCCS) enabled easier and more precised comparison with the referent studies. This study provided initial results of infective complications following ureteroscopic lithotripsy. A prospective multicenter study should be conducted that would analyze, in addition to preoperative bacteriuria, other risk factors for development of infective complications following ureteroscopic lithotripsy, in order to find ways to prevent these complications.

### Conclusion

In our study, out of all patients with preoperative asymptomatic bacteriuria, 36.5% of the patients had postoperative urinary infection which presented a statistically significant number. It was found a statistically significant difference between the group without and the group with postoperative urinary infection developed following ureteroscopic lithotripsy compared to patients who had asymptomatic bacteriuria and patients who had sterile findings of urine culture. This result proves that asymptomatic preoperative bacteriuria is a significant risk factor for developing postoperative urinary infection following ureteroscopic lithotripsy and is associated with higher risk for developing severe forms of SIRS and sepsis. This great risk must be taken into account in an observant preoperative preparation of patients for ureteroscopic lithotripsy. It is desirable that all patients indicated with ureteroscopic lithotripsy have sterile urine culture, but if this is impossible to achieve, a special caution and an adequate antibiotic therapy and prophylaxis are necessary in these patients before and in the course of the operative procedure. Immediate postoperative monitoring is also very important in order to timely prevent severe infective complications.

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