# *Sepsis after elective ureteroscopy*

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BLOOM J, FOX C, FULLERTON S, MATTHEWS G, PHILLIPS J. Sepsis after elective ureteroscopy. *Can J Urol* 2017;24(5):9017-9023.

***Introduction:*** *We sought to determine our rate of postoperative sepsis after ureteroscopy as well as identifying associative factors, common antibiotic practices along with culture data.*

***Materials and methods:*** *Records of all patients who underwent elective ureteroscopy from 2010 to 2015 at an urban tertiary care facility were retrospectively reviewed. Factors thought to be associated with infection were collected, along with comorbidities depicted as Charlson Age-Adjusted Comorbidity Index (CAACI) and American Society of Anesthesia (ASA) score. Each patient's course was reviewed to determine if they were treated for postoperative sepsis as defined by standardized criteria.*

***Results:*** *A total of 345 patients underwent elective ureteroscopy with 15 (4.3%) being treated for sepsis postoperatively. This resulted in an additional 5.33 ± 3.84 days of hospitalization per patient. The sepsis group grew three gram positive organisms and five multi-drug resistant (MDR) gram negatives while 7/15 (46.7%) had negative cultures. The most common preoperative antibiotics used in the sepsis group were cefazolin (60.0%), gentamicin (48.5%) and ciprofloxacin (20.0%). Univariate analysis showed prior endoscopic procedures, recent treatment for urinary tract infections (UTI), multiple comorbidities and longer operative times associated with sepsis. However, significant variables after multivariate analysis were treatment for UTI within the last month, (OR) 7.19 (2.25-22.99), p = 0.001.*

***Conclusions:*** *Patients with multiple comorbidities, prior endoscopic procedures, longer operative times and especially those recently treated for a urinary infection should be carefully monitored after ureteroscopy for signs of sepsis. Perioperative antibiotics in these patients should be selected to cover both MDR organisms and gram positives.*

**Key Words:** antibiotics, infection, sepsis, multi-drug resistance, ureteroscopy

## Introduction

Ureteroscopy remains the standard of care in the management of nephrolithiasis, upper urinary tract malignancies and other common urological conditions.[1,2] The advancements in this technology, along with the increasing incidence of nephrolithiasis, make ureteroscopy one of the most commonly performed procedures by practicing urologists.[3] Ureteroscopic procedures have been embraced by both junior and senior practitioners and is increasingly used in the management of complex urological conditions including the treatment of large stone burdens that were previously not possible while maintaining excellent stone free rates (SFR).[2,4,5]

Despite its low rate of complications, one of the most worrisome complications of ureteroscopy and other manipulations of the urinary tract is infection and sepsis. The risk of infection and sepsis after ureteroscopy is estimated to be between 3.4%-18.3%.[6-10] Sepsis has the potential for extended hospitalization, intensive care unit (ICU) stay, end-organ injury and even mortality.[11] These risks can be amplified in the elderly and immunocompromised patients who are most vulnerable to the effects of sepsis.

Standardized definitions of systemic inflammatory response syndrome (SIRS) and sepsis exist based on the degree of fever or hypothermia, white blood cell count, tachycardia, and respiratory rate.[12] However, the

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defining condition of sepsis occurs when a causative pathogen is identified.[12] Postoperative infection and sepsis cause significant morbidity for patients and places a burden on the healthcare system. These patients often require readmission and prolonged hospital stays. Infection and sepsis represent one of the most common reasons for readmission after surgery, including ureteroscopy.[13,14]

The prevalence of multi-drug resistant (MDR) bacteria has become a significant consideration in planning of urologic procedures. MDR bacteria have become increasingly common not only in simple urinary tract infections (UTI) but also as post-procedure infectious complications of common urological procedures such as percutaneous nephrolithomy (PCNL) and prostate biopsies.[15-17] Urology patients are often predisposed to harbor MDR bacteria due to prior antibiotic treatment, recurrent infection status, the presence of foreign bodies (stents and catheters) and the frequent need for multiple procedures.[17] Additionally, endoscopic stone surgery has inherent risks for bacteremia and sepsis. Stones may harbor bacteria and their endotoxins which when combined with positive-pressure irrigation may transit pyelovenous and pyelolymphatic channels into the general circulation and increase the risk of infection and sepsis.[18,19]

Previous studies of post-infectious complications after ureteroscopy have found associations between operative time, stone size, medical comorbidities and preoperative positive urine cultures.[6,7,18] As with other operative procedures, surgeon experience plays a key role in ureteroscopy in limiting complications, operating room time and SFR.[20] Studies of other urological procedures have additionally found that international travel, recent hospitalizations and recent treatment for UTIs were significant risk factors for the development of MDR infections and sepsis.[17] We sought to look for additional factors associated with sepsis along with perioperative antibiotic usage and culture data from patients who underwent elective ureteroscopy.

## Materials and methods

After IRB approval from our institution, a retrospective chart review was performed of all patients from 2010 to 2015 who underwent an elective ureteroscopy at a single tertiary care facility. We sought to capture only those patients without any confounding variables so patients were excluded if they were urgently admitted through the emergency department (ED) or were hospitalized for other reasons prior to the procedure.

In addition to medical evaluation by the patient's primary care doctor and any requested diagnostic work up, our standard preoperative planning for each patient consisted of checking either a urinalysis or urine culture in each patient within 30 days prior to the procedure. All urine cultures were considered positive with any Colony Forming Units (CFUs). If either urinalysis or culture were positive, the patient received a course of antibiotics based on provider preference, however not all patients received repeat urine studies to document resolution of bacteria. Any patient with multiple organisms with significant CFUs in preoperative urine cultures were treated for these organisms with the exception of urine that appeared to be contaminated or inappropriately collected. After preoperative work up, our standard perioperative course is for patients to receive intravenous antibiotics tailored to best cover any previous cultures prior to the start of the procedure. Stones that were endoscopically extracted during the procedure were not sent for culture.

Patient comorbidities were extracted and depicted as both Charlson Age Adjusted Comorbidity Index (CAACI) as well as by American Society of Anesthesia (ASA) Categorization. Additional patient factors were collected such as body mass index (BMI) and smoking status. We attempted to estimate which patients may have recent prior exposure to antibiotics or bacteriuria by noting those who underwent treatment of a urinary tract infection (UTI), based on clinical judgment, within the last 30 days, if the patient underwent an endoscopic procedure within the last 30 days, if the patient had ever undergone an endoscopic procedure, or if the patient currently had a ureteral stent in place. Operative factors such as the reason for the procedure, size, location and number of stones, whether a flexible or semi-rigid ureteroscope was used, ureteral access sheath use, ureteral stent placement at the end of procedure and operative time were noted.

Finally, preoperative and postoperative discharge antibiotics were collected. Preoperative and postoperative antibiotics were chosen by the providers based on prior urine cultures if available. Each patient's course was then reviewed to determine if they were treated for postoperative SIRS/sepsis as defined by two of the following criteria; heart rate > 90, temp above 38°C or white blood cell count > 12,000 $mm^3$. Blood and urine cultures were reviewed for any bacterial growth postoperatively to determine the criteria for sepsis. The sensitivities of these organisms were noted for each positive culture.

Pearson chi-square analysis was used for categorical variables while continuous variables were analyzed using Student's t-test. Logistic regression was then carried out on all categorical variables. Variables that were considered significant in univariate analysis underwent further testing using multivariate logistic regression. Statistical analysis was performed using Stata, version 12 (College Station, TX, USA).

## Results

A total of 345 patients met the inclusion criteria. Fifteen (4.3%) of these patients required subsequent treatment for sepsis, either immediately after surgery or within 24 hours. No mortalities occurred within this time frame. These patients were hospitalized for an additional 5.33 ± 3.84 days for treatment. Most of these patients, 64.9%, underwent flexible ureteroscopy compared with semi-rigid ureteroscopy, 35.1%. Baseline characteristics of all patients included in this study are listed in Table 1. The mean age of the sepsis group was 55.40 ± 10.94 years. A total of 269 (78%) had preoperative urine cultures. In the sepsis group, only 2 (13.3%) had positive preoperative cultures compared with 22 (6.7%) in the group without sepsis, p = 0.32. These cultures were treated with culture specific antibiotics but repeat urine culture was not documented. When compared to the group without sepsis, patients with sepsis were more likely to have an operative time greater than 60 minutes (86.7% versus 56.1%, p = 0.019), have a CAACI ≥ 1 (86.7% versus 59.4%, p = 0.04), have an ASA ≥ 3 (40.0% versus 18.5%, p = 0.04), and have had any prior endoscopic procedures (73.3% versus 43%, p = 0.021). Logistic regression was carried out on all variables as seen in Table 2. Multivariate logistic regression was then used on variables significant on univariate analysis as seen in Table 3. Receiving treatment for a UTI within the last 30 days remained statistically significant, odds ratio (OR) 7.19 (2.25-22.99), p = 0.001.

All preoperative and discharge antibiotics used in these patients are shown in Figure 1 and Figure 2, however no differences were significant. The most common preoperative antibiotics used in the sepsis and non-sepsis groups were cefazolin (60.0% versus 64.55%, p = 0.79), gentamicin (48.5% versus 60.0%, p = 0.36) and ciprofloxacin (20.0% versus 19.7%, p = 0.98). While the

TABLE 1. **Baseline characteristics of patients**

| | **No sepsis = 330 (95.7%)** | **Sepsis = 15 (4.3%)** | **p value** |
|---|---|---|---|
| Male | 169 (51.2%) | 4 (26.7%) | |
| Female | 161 (48.8%) | 11 (73.3%) | 0.063 |
| Age | 49.91 ± 14.84 | 55.40 ± 10.94 | 0.16 |
| Preop pos. Cx | 22 (6.7%) | 2 (13.3%) | 0.32 |
| Preop stent | 174 (52.7%) | 10 (66.6%) | 0.29 |
| Stent placed | 306 (92.7%) | 15 (100%) | 0.28 |
| Prior endoscopic procedures | 142 (43.0%) | 11 (73.3%) | 0.021* |
| Procedure within 30 days | 127 (37.6%) | 7 (46.7%) | 0.53 |
| Average stone size (mm) | 8.73 ± 5.37 | 9.89 ± 5.69 | 0.42 |
| Number of stones | 1.5 ± 0.95 | 1.89 ± 1.69 | 0.14 |
| Operative time (min) | 83.94 ± 44.24 | 90.07 ± 36.08 | 0.598 |
| Op time > 60 min | 185 (56.1%) | 13 (86.7%) | 0.019* |
| Op time > 90 min | 123 (37.3%) | 9 (60%) | 0.077 |
| Body mass index | 29.2 ± 5.55 | 29.21 ± 7.03 | 0.995 |
| Diabetes | 59 (17.9%) | 4 (26.7%) | 0.39 |
| Current or former smoker | 99 (30.0%) | 2 (13.3%) | 0.17 |
| Treated UTI w/in 30 days | 50 (15.2%) | 8 (53.3%) | < 0.001* |
| CAACI ≥ 1 | 196 (59.4%) | 13 (86.7%) | 0.035* |
| CAACI ≥ 2 | 126 (38.2%) | 9 (60.0%) | 0.09 |
| ASA ≥ 3 | 61 (18.5%) | 6 (40.0%) | 0.04* |

UTI = urinary tract infection; CACI = Charlson Age Adjusted Comorbidity Index; ASA = American Society of Anesthesia

TABLE 2. **Univariate logistic regression of all variables and multivariate logistic regression of significant variables on univariate analysis. P value < 0.05 considered statistically significant and denoted with ***

| | OR | CI | p value |
|---|---|---|---|
| **Logistic regression** | | | |
| Female gender | 2.10 | 0.70-6.28 | 0.178 |
| Preop positive urine culture | 2.08 | 0.43-10.11 | 0.363 |
| Preop stent/nephrostomy | 1.77 | 0.59-5.30 | 0.306 |
| Procedure within 30 days | 1.40 | 0.50-3.95 | 0.53 |
| Procedure within 60 days | 0.39 | 0.05-3.04 | 0.306 |
| Any prior endoscopic procedure | 3.64 | 1.14-11.67 | 0.03* |
| Operative time > 60 min | 5.09 | 1.13-22.94 | 0.034* |
| Operative time > 90 min | 2.52 | 0.88-7.26 | 0.086 |
| Diabetes mellitus | 1.67 | 0.51-5.43 | 0.393 |
| Smoking history | 0.36 | 0.08-1.62 | 0.183 |
| Urine infection within 30 days | 6.40 | 2.22-18.44 | 0.0006* |
| CAACI ≥ 1 | 2.43 | 0.84-6.99 | 0.1 |
| CAACI ≥ 2 | 1.59 | 0.53-4.79 | 0.41 |
| ASA ≥ 3 | 2.94 | 1.01-8.57 | 0.048* |
| **Multivariate logistic regression** | | | |
| Prior endoscopic procedure | 3.16 | 0.93-10.73 | 0.065 |
| Operative time over 60 min | 4.37 | 0.93-20.44 | 0.061 |
| Urine infection within 30 days | 7.19 | 2.25-22.99 | 0.001* |
| ASA ≥ 3 | 1.40 | 0.36-5.43 | 0.63 |
| CAACI > 1 | 2.49 | 0.65-9.58 | 0.19 |

CACI = Charlson Age Adjusted Comorbidity Index; ASA = American Society of Anesthesia

most common discharge antibiotics prescribed after surgery for these groups were ciprofloxacin (40.0% versus 60.61%, p = 0.11), cephalexin (20.0% versus 17.6%, p = 0.81) and trimethoprim/sulfamethoxazole (TMP/SMX) (13.3% versus 10.0%, p = 0.68).

Of the 15 patients who were treated for postoperative sepsis, a total of 8 (53.3%) had a positive culture with bacterial growth. Of these bacterial species 3/8 (37.5%) grew gram positive organisms while the remaining 5/8 (62.5%) grew MDR gram negatives. The cultures and sensitivities are seen in Table 4.

## Discussion

In this study of sepsis in an urban underserved population, our rate of sepsis was 4.3% which is similar to other studies.[10] This postoperative complication resulted in an average of over 5 days of additional hospitalization per patient. A novel risk factor we found was that being treated for a UTI or pyelonephritis within the last 30 days placed the patient at seven times higher risk of sepsis after ureteroscopy. We had some evidence that patients who underwent prior endoscopic procedures were more at risk for sepsis after ureteroscopy which also provides support that prior antibiotic exposure may lead to antibiotic resistance and greater risk of infectious complications following ureteroscopy. The patients in our study with multiple comorbidities and longer operative times seemed to be at greater risk for sepsis as well after surgery, however these relationships were not significant after multivariate analysis. This finding is similar to previous studies which have shown this to be an important factor.

Many of the isolated bacterial species we found were resistant to numerous antibiotics suggesting these patients had previous exposure to antibiotics and the healthcare system. However, in this study, undergoing recent endoscopic urological procedures

TABLE 3. **Isolated bacterial species of all postoperative ureteroscopy patients with sepsis**

| Species | Sensitive | Intermediate | Resistant |
|---|---|---|---|
| Staph epidermidis | Gent, Vanc, Tet | Rif | Pen, Oxa, Levo, Clinda |
| K. pneumoniae | Pip/Tazo, Imi, Cipro, Levo, Mero, Ami, Tet | Nitro | Amp, Amp/Sulb, Amox/Clav, Cefa, Ceft, Gent, Tobra, TMP/SMX, Cefu, Cefo, Azt |
| Coag neg. staph | Vanco, Tet, Rif | | Pen, Oxa, Levo, Ery, Clinda, TMP/SMX |
| E. coli | Pip/Tazo, Ceft, Cefe, Imi, Gent, Tobra, Cipro, Levo, Nitro, TMP/SMX, Cefu, Cefo, Azt, Mero, Ami, Tet | Amox/Clav | Amp, Ampi/Sul, Cefa |
| Coag neg. staph | Not reported | Not reported | Not reported |
| E. coli | Ceft, Cefe, Imi, Ami, Cefu, Cefo, Azt, Mero, Tet | Amox/Clav | Amp, Ampi/Sul, Cefa, Gent, Tobra, Cipro, Levo, TMP/SMX |
| E. coli | Ami, Gent, Macro, Tobra, Azt, Cefe, Cefo, Ceft, Imi, Mero, Pip/Tazo | Amox/Clav | Amp, Cefa, Tetra, Ampi/Sul, TMP/SMX, Levo, Cipro |
| P. aeruginosa | | | Cefe, Imi, Gent, Tobra, Cipro, Levo, Mero, Ami |

Ami = Amikacin; Amox/Clav = Amoxicillin/Clavulonic Acid; Amp = Ampicillin; Amp/Sulb = Ampicillin/Sulbactam; Azt = Aztreonam; Cef = Cefazolin; Cefe = Cefepime; Ceft = Ceftriaxone; Cefu = Cefuroxime; Cefo = Cefotaxime; Clinda = Clindamycin; Cip = Ciprofloxacin; Ery = Erythomycin; Gent = Gentamicin; Imi = Imipenem; Levo = Levofloxacin; Mero = Meropenem; Nitro = Nitrofurantoin; Oxa = Oxacillin; Pen = Penicillin; Pip/Tazo = Pipericillin/Tazobactam; Rif = Rifampin; Tet = Tetracyclin; TMP/SMX = Trimethoprim/Sulfamethoxazole; Tobra = Tobramycin; Vanco = Vancomycin

and the associated perioperative antibiotics, was not associated with an increased risk of sepsis after multivariate analysis.

Centers for Medicare and Medicaid Services (CMS) is intensely interested in readmissions due to the over $30 billion per year spent on hospital readmissions.[21] This increased scrutiny of readmission has resulted in the penalization of hospitals for higher than expected averages for certain conditions with the expectation that surgical procedures may have the same guidelines in the future.[22] Infectious concerns represent the most common reason for readmissions after surgery.[14,23] While not every readmission will be avoidable, every attempt should be made to prevent these infectious complications by careful preoperative planning in regards to preoperative sterile urine cultures, perioperative antibiotic use and close follow up of those most at risk. Surgical experience with other intraoperative factors such as limiting operative time while keeping intrarenal pressure low.

Those most at risk for sepsis should not only be carefully monitored after the procedure but have their perioperative antibiotics tailored to cover both gram positive and MDR organisms and every attempt made to limit operative time. Another strategy that has been employed, more routinely in PCNL procedures, is intraoperative stone cultures. Stone cultures have been proven to be more accurate in determining bacterial pathogens of infections and sepsis postoperatively in endourological procedures.[24] Another strategy routinely performed prior to PCNL is preoperative antibiotic prophylaxis which has been used for PCNL to decrease postoperative sepsis.[25]

One strength of this study is the nature of this hospital in that almost all patients treated there receive a majority of care at this institution and very few, if any, patients were treated at outside hospitals for complications and not captured. Limitations of this study are its retrospective design and limited sample size within one hospital center. Antibiotic resistance patterns are known to vary between not only regions but between hospitals and the culture patterns seen here are likely unique.[26] Another limitation of this

TABLE 4. **Isolated bacterial species of all postoperative ureteroscopy patients with sepsis**

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|---|---|---|---|
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| K. pneumoniae | Pip/Tazo, Imi, Cipro, Levo, Mero, Ami, Tet | Nitro | Amp, Amp/Sulb, Amox/Clav, Cefa, Ceft, Gent, Tobra, TMP/SMX, Cefu, Cefo, Azt |
| Coag neg. staph | Vanco, Tet, Rif | | Pen, Oxa, Levo, Ery, Clinda, TMP/SMX |
| E. coli | Pip/Tazo, Ceft, Cefe, Imi, Gent, Tobra, Cipro, Levo, Nitro, TMP/SMX, Cefu, Cefo, Azt, Mero, Ami, Tet | Amox/Clav | Amp, Ampi/Sul, Cefa |
| Coag neg. staph | Not reported | Not reported | Not reported |
| E. coli | Ceft, Cefe, Imi, Ami, Cefu, Cefo, Azt, Mero, Tet | Amox/Clav | Amp, Ampi/Sul, Cefa, Gent, Tobra, Cipro, Levo, TMP/SMX |
| E. coli | Ami, Gent, Macro, Tobra, Azt, Cefe, Cefo, Ceft, Imi, Mero, Pip/Tazo | Amox/Clav | Amp, Cefa, Tetra, Ampi/Sul, TMP/SMX, Levo, Cipro |
| P. aeruginosa | | | Cefe, Imi, Gent, Tobra, Cipro, Levo, Mero, Ami |

Ami = Amikacin; Amox/Clav = Amoxicillin/Clavulonic Acid; Amp = Ampicillin; Amp/Sulb = Ampicillin/Sulbactam; Azt = Aztreonam; Cef = Cefazolin; Cefe = Cefepime; Ceft = Ceftriaxone; Cefu = Cefuroxime; Cefo = Cefotaxime; Clinda = Clindamycin; Cip = Ciprofloxacin; Ery = Erythomycin; Gent = Gentamicin; Imi = Imipenem; Levo = Levofloxacin; Mero = Meropenem; Nitro = Nitrofurantoin; Oxa = Oxacillin; Pen = Penicillin; Pip/Tazo = Pipericillin/Tazobactam; Rif = Rifampin; Tet = Tetracyclin; TMP/SMX = Trimethoprim/Sulfamethoxazole; Tobra = Tobramycin; Vanco = Vancomycin

study is that antibiotic choices and duration were provider specific and standardized protocols do not exist. Preoperative urine cultures and any treatment of infection was also based on provider clinical judgment. Further studies are needed to determine if broad spectrum antibiotic coverage is possible to decrease the rate of postoperative sepsis or if simply the nature of the surgery and overall health status of the patient make some instances of postoperative sepsis inevitable. Other markers of sepsis such as procalitonin and C-reactive protein could be used in the future to differentiate between SIRS when treating postoperative patients and in future research studies.[27]

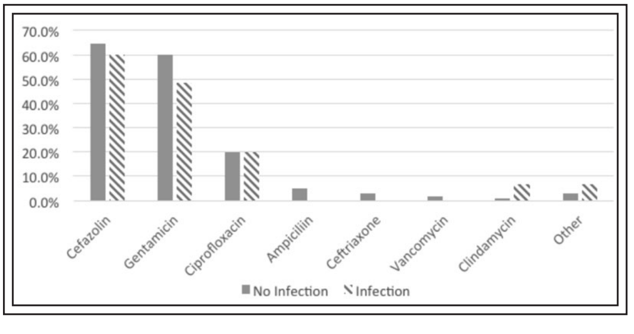


**Figure 1.** Preoperative antibiotics.

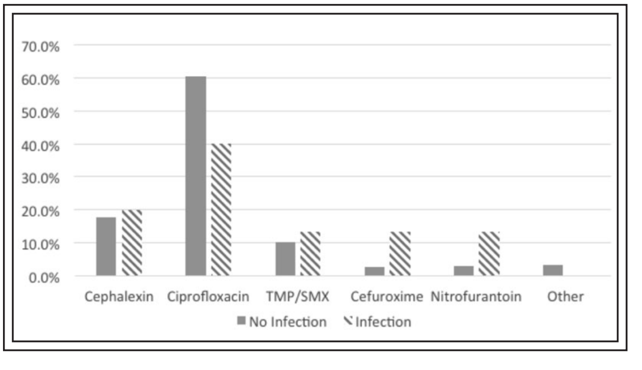


**Figure 2.** Discharge antibiotics.

## Conclusion

Severe infectious complications after ureteroscopy are rare and caused by both gram positive and MDR gram negative organisms. Clinicians should have a high index of suspicion for sepsis when performing long ureteroscopic procedures on patients with multiple comorbidities and a history of urinary tract infections. The use of broad spectrum perioperative antibiotics and consideration of multistage procedures to limit operative time is warranted to try to prevent the complications of sepsis. ☐

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