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Major Article

# Risk of infection in patients undergoing urologic surgery based on the presence of asymptomatic bacteriuria: A prospective study

Jorge A. Ramos-Castaneda MSc [a,*], Alberto Ruano-Ravina PharmD, MPH, PhD [b], L. Silvia Munoz-Price MD, PhD [c], Rodrigo Toro-Bermúdez MD [d], David Ruiz-Londoño MD [d], Angela M. Segura-Cardona PhD [a], Elkin V. Lemos-Luengas MD, MSc, PhD [e]

[a] *Public Health Observatory, Graduate School, Universidad CES, Medellín, Colombia*
[b] *Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Spain; Consortium for Biomedical Research in Epidemiology and Public Health, CIBERESP, Madrid, Spain*
[c] *Division of Infectious Diseases, The Medical College of Wisconsin, Milwaukee, WI, USA*
[d] *Department of Urology, Clínica CES; Universidad CES, Medellín, Colombia*
[e] *Public Health Observatory, Universidad CES, Medellín, Colombia*

*Key Words:*
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Urinary tract infection
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***Background:*** Treatment of asymptomatic bacteriuria (ASB) is recommended in pregnant women and prior to urologic procedures with anticipated mucosal disruption. However, there is still insufficient evidence of the usefulness of treating ASB prior to urologic procedures. Therefore, the aim of this study was to ascertain the risk of infections in patients undergoing urologic surgery based on the presence of ASB.

***Methods:*** We conducted a cohort study among patients undergoing urologic surgery at a single center located in Medellín, Colombia. All patients were screened for ASB prior to their procedures. Patients were evaluated for the development of any postoperative infectious complications for up to 30 days after the procedure.

***Results:*** A total of 149 patients were included in this cohort. Incidence of ASB was 14.8%. Thirteen patients (8.72%) developed infectious complications: 3 (13.64%) with ASB and 10 (7.87%) without ABS. Factors associated with postoperative infectious complications included urologic cancers (hazard ratio [HR], 5.26; 95% confidence intervals [CI], 1.24-22.37), urologic interventions in the preceding 3 months (HR, 3.72; 95% CI, 1.02-13.51), and use of antibiotics 3 months prior to surgery (HR, 3.83; 95% CI, 1.01-15.49). Presence of ASB was not associated with postsurgical infectious complications (HR, 1.02; 95% CI, 0.26-3.96).

***Conclusions:*** There was no association between ASB and postoperative infectious complications. There were other factors associated with infectious complications, such as urologic cancer, previous history of urologic manipulation, and antibiotic use.



The risk of infectious complications following urologic surgery is 2%-12%.[1] Urinary tract infections (UTIs) are the most frequent infectious complications in these patients (20%-30%),[2] followed by bacteremia, sepsis (6%-10%),[3] and surgical site infections (2.6%).[1] Annually, >1 million people in Europe develop infectious complications after urologic surgery,[4] increasing the costs associated with hospitalization.[5] Risk factors associated with infection after urologic surgery include smoking,[6,7] advance age, length of surgical procedures, high American Society Anesthesiologists (ASA) classification, poor patient nutrition,[1,8] and presence of asymptomatic bacteriuria (ASB).[9-12]

According to the Guidelines on Urological Infections,[10] ASB should not be treated, with the exception of 2 specific indications: (1) pregnant women and (2) prior to urologic procedures, with anticipated mucosal disruption.[10] The recommendation to treat ASB prior to urologic surgery is based on evidence obtained from 2 randomly selected clinical trials[13] performed in patients who underwent transurethral prostatic resection.[3] However, Cai et al[14] recently compared patients with and without ASB before surgical procedures and found that ASB was not associated with a higher risk of postoperative infectious complications.

* Address correspondence to Jorge A. Ramos-Castañeda, MSc, Graduate School, Universidad CES, Calle 10A # 22 - 04, Medellín, Colombia.
*E-mail address:* ramos.jorge@uces.edu.co (J.A. Ramos-Castaneda).
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Thus, there is still uncertainty if ASB is associated with infectious complications following urologic procedures.[13] We hypothesize that ASB is not associated with postoperative infectious complications. Additionally, other factors might be associated with higher risk of infection in urologic patients.

The aim of this study was to ascertain the association between postoperative infectious complications in patients undergoing urologic surgery based on the presence of ASB.

## METHODS

### *Type of study and study population*

We conducted a prospective cohort study among patients who underwent urologic surgery at a median- to high-complexity 200-bed hospital in Medellín, Colombia.

We included all consecutive patients undergoing urologic surgeries from May 2018 to October 2018 and who underwent ASB screening prior to the procedure. Urologic surgeries included in this study were: transurethral resection of the prostate (TURP), tumors of bladder or urethra, open prostatectomy (partial or radical), ureterolithotomy, nephrolithotomy, nephrectomy, and ureterorenoscopy. The exposure variable was the presence of ASB, which was defined as a positive urine culture ($>10^5$ colony-forming units/mL) in the absence of fever, costovertebral pain, urinary frequency, or bladder tenesmus.[15] The nonexposed cohort was made up of patients who had a negative urine culture prior to the urologic procedure.

Antibiotic regimens were ascertained from the time of ASB screening until 30 days postsurgery or development of the outcome variable, whichever happened first. All patients received preoperative prophylaxis within the 30-60 minutes before the procedure, as per institutional protocol. To ascertain the outcome, patients received a follow up phone call at day 15 and an additional follow-up call at day 30 postsurgery.

### *Dependent and independent variables*

The outcome variable was any postoperative infectious complications defined per the Centers for Disease Control and Prevention criteria.[15] Infectious complications were ascertained by an infectious diseases physician who was blinded to the exposure variable.

The independent variables were: presence of ASB, ASA level,[16] length of surgical procedure, gender, age, comorbidities (urologic cancers, arterial hypertension, diabetes mellitus, prostatic hyperplasia, nephrolithiasis), manipulation of the urinary tract (surgery or endoscopic procedure) in the preceding 3 months,[10,14] antibiotic use in the preceding 3 months, antibiotic treatment following the surgical procedure,[17] use of postoperative antibiotic, and type of urologic intervention.

All isolates were identified in the clinical microbiology laboratory using the Vitek 2 automated system (bioMérieux, Marcy l'Etoile, France), and susceptibility criteria were defined by the Clinical & Laboratory Standards Institute cut-off values.[18]

### *Statistical analysis*

Categorical variables were analyzed using the $X^2$ test, and in the case of numerical variables, the Kolmogorov Smirnov test was used to test for a normal distribution. Variables without normal distribution were analyzed using nonparametric tests, based on the median and interquartile range.

We ascertained the proportion and incidence rates of postsurgical infectious complications, and calculated the rates ratio according to presence of ASB. Survival curves were constructed using the Kaplan-Meier method to establish the average infection-free time. The initial time point was the date on which the urologic procedure was performed. Censored data included patients who were lost to follow-up, failed to develop postoperative infectious complications, or died owing to another cause. Events were patients who presented any postoperative infectious complications.

Significant differences in infection-free time by presence of ASB were determined using the Log Rank test. The contribution of ASB to infection-free time was established using a Cox proportional risks model. First, we performed a univariate analysis of main variables and after, a multivariate Cox analysis with those variables with statistical significance in the bivariate analysis and clinical importance. All data analyses were performed using the R Studio 3.5 software package.[19]

### *Ethical considerations*

The study was approved by the Universidad CES Research Ethics Committee (record no. 123, study 631), and classified as minimal risk, given that the data were collected prospectively. Informed verbal consent was obtained prior to the review of clinical histories.

## RESULTS

A total of 156 patients underwent urologic surgeries, of which 7 were excluded, given the presence of UTI prior to surgical procedures. Of the remaining 149 patients, a total of 22 (14.8%) had ASB. The most frequent organisms identified were: *Escherichia coli* (n = 14; 63.63%), *Proteus mirabilis* (n = 2; 9.10%), and *Serratia marcescens* (n = 2; 9.10%).

The ASB group had a higher proportion of female patients ($P < .01$), greater history of obstructive uropathy ($P = .03$), and urologic manipulation prior to their procedures ($P = .02$). No statistically significant differences were found regarding hospitalization and antibiotic use in the preceding 3 months among patients with or without ASB. Hydronephrosis was the most frequent trigger for urologic intervention ($P < .01$), and the length of surgical procedures was longer in patients with ASB ($P = .02$) (Table 1).

Use of postoperative antibiotic prophylaxis was indicated in 45.6% of urologic patients, with this being more frequent in patients with ASB (54.5% vs 44.1%, $P = .50$) (Table 1).

The proportion of incidence of postoperative infectious complications was 8.7%, and the infection rate was 3.1 per 1,000 patient days. Patients with ASB had a postoperative infectious complications incidence rate of 5.11 per 1,000 patient days (95% confidence intervals [CI], 1.05-14.9), and patients without ASB had a rate of 2.76 per 1,000 patient days (95% CI, 1.3-5.1) ($P = .36$), with a crude hazard ratio of 1.81 (95% CI, 0.50-6.59) (Fig 1).

Patients with postoperative infectious complications had a higher frequency of urologic cancer ($P < .01$), manipulation of the urinary tract in the preceding 3 months ($P < .01$), hospitalization ($P < .01$), and antibiotic use 3 months before surgery ($P < .01$). Use of postoperative antibiotics prophylaxis ($P = .74$) and presence of ASB ($P = .63$) showed no significant differences in infected patients (Table 2).

No significant difference was found in infection-free time among patients with or without ASB ($P = .4$), although after day 10 postsurgery, the cumulative risk of infection in patients with ASB doubled compared with patients without ASB.

The Cox proportional hazards analysis showed that after controlling for age, sex, history of urologic cancer, urologic manipulation, and antibiotic use in the preceding 3 months, ASB was not associated with postoperative infectious complications (hazard ratio [HR], 1.02; 95% CI, 0.26-3.96) (Table 3).

Factors associated with postoperative infectious complications were urologic cancers (HR, 5.26; 95% CI, 1.24-22.37), urologic interventions in the preceding 3 months (HR, 3.72; 95% CI, 1.02-13.51), and use of antibiotics 3 months prior to surgery (HR, 3.83; 95% CI, 1.01-15.49) (Table 3).

**Table 1**
Demographic characteristics of the urology patients based on the presence of ASB (N = 149)

| Characteristics | With ASB N = 22 | Without ASB N = 127 | *P* value* |
|---|---|---|---|
| Sex | | | |
| Male | 11 (50.0) | 106 (83.5) | <.01 |
| Age (y) | | | |
| Median (range) | 52.5 (24-73) | 55 (21-83) | .33† |
| Comorbidities | | | |
| Arterial hypertension | 4 (18.2) | 41 (32.2) | .28 |
| Diabetes mellitus | 4 (18.2) | 14 (11.0) | .55 |
| Urologic cancer | 1 (4.5) | 4 (3.1) | 1.0 |
| Nephrolithiasis | 14 (63.6) | 67 (52.7) | .47 |
| Benign prostatic hyperplasia | 5 (22.7) | 48 (37.8) | .26 |
| Obstructive uropathy | 5 (22.7) | 8 (6.3) | .03 |
| History of a urologic intervention | | | |
| Previous urologic intervention | 8 (36.4) | 17 (13.4) | .02 |
| Previous endoscopic intervention | 6 (27.3) | 14 (11.0) | .04 |
| Previous surgery | 2 (9.1) | 2 (1.5) | .04 |
| Permanent bladder catheter | 5 (22.7) | 0 | <.01 |
| Intermittent bladder catheter | 0 | 0 | NA |
| Double J catheter | 1 (4.5) | 12 (9.4) | .73 |
| Hospitalization in the last 3 mo | 3 (13.6) | 8 (6.3) | .44 |
| Antibiotics in the last 3 mo | 2 (9.1) | 9 (7.1) | 1.0 |
| Reason for urologic intervention | | | |
| Urologic cancer | 0 | 3 (2.4) | .60 |
| Hydronephrosis | 6 (27.3) | 5 (3.9) | <.01 |
| Benign prostatic hyperplasia | 5 (22.7) | 50 (39.4) | .13 |
| Nephrolithiasis | 11 (50.0) | 64 (50.4) | .97 |
| Tumor | 0 | 5 (3.9) | .90 |
| ASA level | | | |
| I | 1 (4.5) | 11 (8.7) | Ref. |
| II | 18 (81.8) | 99 (77.9) | .82 |
| III | 3 (13.6) | 17 (13.4) | 1.00 |
| Duration of surgery | | | |
| >75 percentile | 5 (22.7) | 22 (17.3) | .76 |
| Duration of surgery (min) median (range) | 105 (60-225) | 85 (30-330) | .02† |
| Risk of surgical site infections NNIS | | | |
| 0 | 0 | 89 (70.1) | Ref. |
| 1 | 15 (68.2) | 37 (29.1) | <.01 |
| 2 | 6 (27.3) | 1 (0.8) | <.01 |
| 3 | 1 (4.5) | 0 | <.01 |
| Use postoperative antibiotics prophylaxis | | | |
| Yes | 12 (54.5) | 56 (44.1) | .50 |

*ASB*, asymptomatic bacteriuria; *ASA*, American Society Anesthesiologists; *NA*, not applicable; *NNIS*, National Nosocomial Infections Surveillance System; Ref., reference.
*The $X^2$ test.
†The Wilcoxon rank test.

## DISCUSSION

In this prospective study, we found a low prevalence of ASB in a cohort of 149 patients who underwent urologic procedures. Most important, we found that ASB was not associated with postoperative infectious complications. There were other factors associated with postoperative infectious complications, such as urologic cancer, previous history of urologic manipulation, and antibiotic use in the last 3 months.

The prevalence of ASB in patients scheduled for urologic surgery is between 30%-32%,[14,20] and in this study prevalence of ASB was 14.8%. The low prevalence found was owing to there were few patients with factors associated to the colonization of bacteria in urine, such as previous urologic manipulation, use of urologic devices, hospitalization, or use of an antibiotic in the last 3 months.

Guidelines for the prevention of urologic infections recommend treating ASB prior to urologic procedures, with anticipated mucosal disruption.[9-11,21] This recommendation is based on evidence obtained from 2 randomly selected clinical trials performed several years ago (1984 and 1987).[22,23] Grabe et al[22] compared the effect of the cefotaxime in 192 patients with TURP. For patients who received preoperative antibiotic, the postoperative infectious complications were lower compared with the group without antibiotic. In the second clinical trial, Grabe et al[23] compared the efficacy of pre-operative ciprofloxacin in 222 patients with TURP by randomly allocating them to 3 groups: the first group received antibiotics the day of the surgery and continued until the bladder catheter was removed; the second group received antibiotics prior to surgery and for 5 days after the catheter was removed; and the control group did not receive any antibiotic treatment. The 2 groups who received preoperative antibiotics had lower ASB and infection complications compared with the control group. However, a recent prospective nonrandomly selected study conducted on patients who underwent different types of urological surgery found that the rate of symptomatic postoperative UTI was similar between patients with and without ASB (10.4% and 8.4%, respectively; OR, 0.77; 95% CI, 0.56- 1.05).[14] In our study, the rate of postoperative infectious complications was similar in patients with and without ASB. Similarly, other studies in nonurologic patients showed that ASB was not associated with postoperative infectious complications, including knee replacement,[24,25] cardiovascular[26] neurologic,[27] and transplant surgeries.[28,29]

We found the urologic cancer, urinary tract manipulation 3 months prior to the procedure, and use of antibiotics in the 3 months

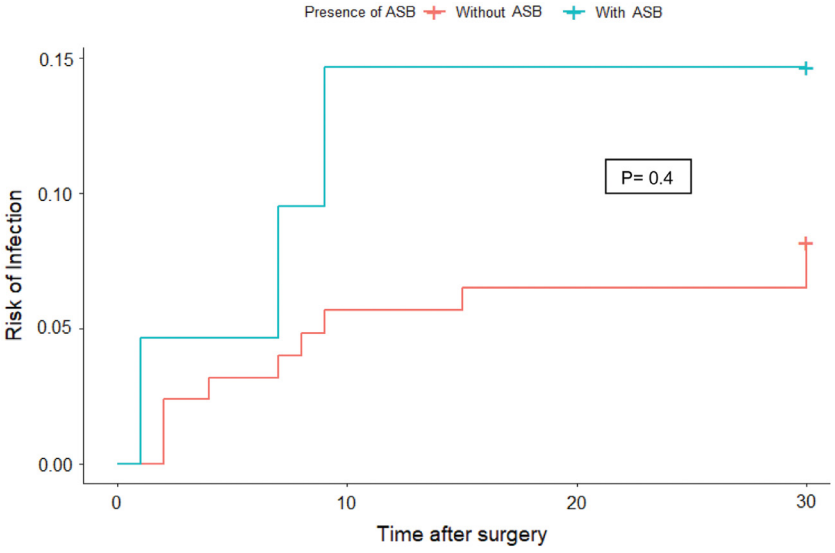


**Fig 1.** Risk of infection in patients undergoing urologic surgery based on the presence of asymptomatic bacteriuria. *ASB*, asymptomatic bacteriuria.

**Table 2**
Postoperative infectious complications in patients with urologic surgery (N = 149)

| Characteristics | Infectious complications N = 13 | No infectious complications N = 136 | *P* value |
|---|---|---|---|
| Sex | | | |
| Male | 9 (69.2) | 108 (79.4) | .62 |
| Age (y) | | | |
| Median (range) | 54.5 (22-73) | 55 (21-83) | .90 |
| Comorbidities | | | |
| Arterial hypertension | 4 (30.8) | 41 (30.1) | 1.0 |
| Diabetes mellitus | 3 (23.1) | 15 (11.0) | .41 |
| Urologic cancer | 3 (23.1) | 2 (1.5) | <.01 |
| Nephrolithiasis | 7 (53.8) | 74 (54.4) | 1.0 |
| Benign prostatic hyperplasia | 4 (30.8) | 49 (36.0) | .94 |
| Obstructive uropathy | 3 (23.1) | 10 (7.3) | .16 |
| History of a urologic intervention | | | |
| Previous urologic intervention | 7 (53.8) | 18 (13.2) | <.01 |
| Previous endoscopic intervention | 4 (30.8) | 16 (11.8) | .05 |
| Previous surgery | 3 (23.1) | 1 (0.7) | <.01 |
| Permanent bladder catheter | 2 (15.4) | 3 (2.2) | .09 |
| Double J catheter | 1 (7.7) | 12 (8.8) | 1.0 |
| Hospitalization in the last 3 mo | 6 (46.1) | 5 (3.7) | <.01 |
| Antibiotics in the last 3 mo | 4 (30.8) | 7 (5.1) | <.01 |
| Reason for urologic intervention | | | |
| Urologic cancer | 2 (15.4) | 1 (0.7) | <.01 |
| Hydronephrosis | 1 (7.7) | 10 (7.3) | .96 |
| Benign prostatic hyperplasia | 4 (30.8) | 51 (37.5) | .63 |
| Nephrolithiasis | 6 (46.1) | 69 (50.7) | .75 |
| Tumor | 0 | 5 (3.7) | 1.0 |
| ASA level | | | |
| I | 0 | 12 (8.82) | Ref. |
| II | 9 (69.23) | 108 (79.41) | .69 |
| III | 4 (30.77) | 16 (11.76) | .27 |
| Duration of surgery | | | |
| >75 percentile | 5 (38.5) | 22 (16.2) | .11 |
| Duration of surgery (min) median (range) | 120 (60 -330) | 90 (30-225) | .01 |
| Risk of surgical site infections NNIS | | | |
| 0 | 3 (23.1) | 86 (63.2) | Ref. |
| 1 | 9 (69.2) | 43 (31.6) | .01 |
| 2 | 0 | 7 (5.1) | 1.00 |
| 3 | 1 (7.7) | 0 | .02 |
| Use postoperative antibiotics prophylaxis | | | |
| Yes | 7 (53.8) | 61 (44.8) | .74 |
| ASB | | | |
| Yes | 3 (23.1) | 19 (14.0) | .63 |

*ASA*, American Society Anesthesiologists; *ASB*, asymptomatic bacteriuria; *NNIS*, National Nosocomial Infections Surveillance System; *Ref*., reference.

**Table 3**
Factors associated with infection in patients with urologic surgery (N = 149)

| Associated factors | Crude HR (95% CI) | Adjusted HR (95% CI)* | *P value* |
|---|---|---|---|
| ASB | 1.81 (0.50-6.59) | 1.02 (0.26-3.96) | .98 |
| Age | | | |
| *Y* | 1.00 (0.97-1.04) | 1.00 (0.96-1.04) | .95 |
| Sex | | | |
| Male | 0.60 (0.18-1.94) | 0.51 (0.13-2.04) | .34 |
| Urologic cancer | 9.45 (2.60-34.41) | 5.26 (1.24-22.37) | .02 |
| Urologic intervention in the last 3 mo | 6.72 (2.26-20.02) | 3.72 (1.02-13.51) | .04 |
| Antibiotics in the last 3 mo | 7.52 (2.31-24.49) | 3.83 (1.01-15.49) | .05 |

*ASB*, asymptomatic bacteriuria; *CI*, confidence interval; *HR*, hazard ratio.
*Adjusted HR according to presence of ASB, age, sex, urologic cancer, urologic intervention and antibiotics in the last 3 months.

immediately preceding the urologic procedure, were factors associated to postoperative infectious complications. Cai et al[14] found in a cohort of 2,201 patients with ASB that the comorbidities increased the risk of postoperative infectious complications (HR, 3.49; 95% CI, 1.67-3.11). Marshall[30] reported in a cohort of 156 patients with ASB that history of urinary tract manipulation was higher in patients with infectious complications. Finally, in a cohort of 550 patients, Cai et al[31] showed that inappropriate antibiotic use increased the risk of development UTI, especially with multidrug-resistant organisms. In the same way, our study found these factors to be associated with postoperative infectious complications.

This study, however, has some limitations. We could not conduct an analysis stratified by the microorganism identified or the procedure performed, owing to sample size and the low incidence of ASB. There were factors associated with the infectious complications that were not analyzed, such as smoking and nutritional status. The study may suffer from a referral center bias, since the patients analyzed were from a single institution, which could impair the generalizability of our results. We also believe that the study had several strengths, since selection bias was controlled by including all consecutive subjects who fulfilled the inclusion criteria. Another strength is the lack of loss to follow-up. Information biases were controlled because the outcome was assessed by reference to the CDC criteria[15,32] and subsequently validated by an infectious disease physician who was blinded to the exposure variable.

ASB does not appear to be not associated with postoperative infectious complications in patients undergoing urologic surgery. There are other factors that are associated with infectious complications, such as urologic cancer, previous history of urologic manipulation, and antibiotic use. Further studies should be done to evaluate the cost-effectiveness and consequences in terms of antibiotic resistance of the identification and treatment of ASB prior to urologic procedures. As some previous studies have suggested, antibiotic prophylaxis or a single dose of antibiotic treatment in the perioperative period may well suffice to cover the microorganisms present in the urine in patients with ASB.

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