

## Mini Review

# Impact of Asymptomatic Bacteriuria on Frequency of Urinary Tract Infection and Bladder Tumor Recurrences in Patients Undergoing Outpatient Surveillance Cystoscopy

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- Bladder tumors
- Papillary
- Low grade

## Abstract

**Objective:** We investigated the frequency of symptomatic urinary tract infection (UTI) and tumor recurrence in bacteriuric patients with low-grade papillary (TaLG) bladder tumors.

**Materials and methods:** We evaluated and followed 333 patients with multiple, recurrent TaLG bladder tumors with outpatient cystoscopy every 6 months for 3 years. At each cystoscopy, patients gave a urine culture, classified as no growth (uninfected) or  $>10^4$  CFU/ml. (infected). Antibiotics were not given before or after cystoscopy, and perioperative or adjuvant chemo-therapy was not used.

**Results:** Of the 333 patients, 92 (27.6%) had significant bacteriuria. Twelve patients (3.6%) developed a febrile UTI after undergoing a cystoscopy; 8 of 241 (3.3%) with sterile urine, and 4 of 92 (4.3%) who had asymptomatic bacteriuria (Odds ratio, 1.3 (95% CI, .39-4.5)  $P=.65$ ). With 3 year follow-up, 145 patients (44%) had one or more tumor recurrences; 120 of 241 (50%) uninfected patients vs 25 of 92 (27%) bacteriuric patients (Odds ratio, .38 (95% CI, .22-.64),  $P=.001$ ).

**Conclusion:** Symptomatic urinary infection after cystoscopy is rare in antibiotic-naïve bacteriuric patients. Asymptomatic bacteriuria appears to be associated with fewer tumor recurrences, raising the question whether resident uropathogens retard tumor growth by inflammation or local immunity.

## INTRODUCTION

Cystoscopy is the most common urologic procedure performed by urologists worldwide and is frequently repeated in patients with bladder tumors. Cystoscopy is safe and usually well tolerated, however it may cause acute urinary tract infection (UTI) in up to 10% of patients [1]. Asymptomatic bacteriuria is also common in bladder tumor patients, which persuades many urologists to administer antibiotics before, and sometimes after, cystoscopy. The downside of such practice is that overuse of antibiotics promotes multi-drug bacterial resistance [2].

We have shown that repeated outpatient flexible cystoscopy can be performed safely in antibiotic-naïve bladder tumor patients, even if they have bacteriuria [3]. We observe also that chronic bacteriuria is associated with fewer tumor recurrences [4], suggesting that bacterial inflammation may retard tumor growth by local immune or other mechanisms. This brief report summarizes our current experience in a selected cohort of patients with multiple and recurrent low-grade, noninvasive, papillary (TaLG) bladder tumors. We focus on TaLG tumors

because in our hands they are treated by transurethral surgery alone and more than half predictably recur by 3 years [5]. We aimed to determine the frequency of infectious complications and bladder tumor recurrences after cystoscopy in this subset of patients.

Since 2010, we performed repeated outpatient flexible cystoscopies in 333 high-risk patients with TaLG bladder tumors. Most patients had one or more risk factors for UTI, including elderly, current or prior smokers, prostatic obstruction, diabetes, and use of catheters [6]. None had current UTI, defined as fever associated with severe dysuria, and they were not taking antibiotics. Before each cystoscopy, patients submitted a voided urine specimen for culture, which was classified as no growth (including mixed flora) or significant bacteriuria ( $>10^4$  or  $>10^5$  CFU/ml with a single organism). Antibiotics were not given before or after cystoscopy.

Cystoscopy was performed with the patient in dorsolithotomy position. The genitalia were washed with povidine-iodine solution. In males, 10cc of 2% lidocaine jelly was instilled into

the urethra. A 15Fr flexible digital cystoscope was atraumatically inserted into the bladder. The procedure averaged about 5 minutes. Recurrent tumors were treated generally by cystoscopic fulguration, and no patient received intravesical chemotherapy. Cystoscopes were sterilized using the automated endoscopic reprocess or STERIS (SSIE) system [7].

After the procedure, patients were given a fact card with instructions to call if they had temperature 101°F or higher. A nurse called patients afterwards for infectious complications. End point was a febrile UTI within 30 days of cystoscopy, and included patients who received antibiotics from a local physician, for any reason. Patients underwent surveillance cystoscopy every six months for 36 months to detect recurrent tumors. The institutional review board approved the study.

Of the 333 patients, 92 (27.6%) had significant bacteriuria, mostly *E. coli*, *Enterococcus* or *Staphylo-coccus* species. Compared with uninfected patients, infected patients were older (median 66 vs 62 years) and female (39% vs 21%). Twelve patients (3.6%) developed a febrile UTI after undergoing a cystoscopy; 8 of 241 (3.3%) with sterile urine, and 4 of 92 (4.3%) who had asymptomatic bacteriuria (Odds ratio, 1.3 (95% CI, .39-4.5) P=.65). The majority of UTIs occurred a few days to a week after cystoscopy, responded to culture-sensitive oral antibiotics and no patient was admitted to hospital for bacterial sepsis.

With at least 3 year follow-up, 145 patients (44%) had one or more tumor recurrences; 120 of 241 (50%) uninfected patients vs 25 of 92 (27%) bacteriuric patients (Odds ratio, .38 (95% CI, .22-.64), P=.001, Pearson X<sup>2</sup>). Median time to tumor recurrence was 26 vs 31 months, respectively (P=.001, log rank). Median number of recurrent tumors in colonized patients was 2.3 vs 3.5 in uninfected patients (P=.05, Student's t-test).

Our experience suggests antibacterial therapy before outpatient flexible cystoscopy is unnecessary in patients who have no clinical signs or symptoms of acute urinary tract infection, including the presence of bacteriuria. Febrile UTIs after cystoscopy are rare in both infected and uninfected patients. Fewer than 5% of all patients developed a post-cystoscopy UTI, and the risk of infection was even less than that considering each patient underwent between 4 and 6 follow-up cystoscopies (only 2 patients had more than one UTI). For example, we reported a UTI rate of 1.9% in 3,108 individual patient cystoscopies, and slightly higher (3.7%) in bacteriuric patients [3].

A weakness of our experience is that we relied on patient self-reporting if they developed a UTI, were hospitalized elsewhere or received antibiotics from another physician, suggesting we

may have under-estimated the incidence of post-cystoscopy UTI. This is unlikely owing to close nursing monitoring of our patient population who return regularly for follow-up visits. However, our patients are evaluated using specific methods, equipment and procedure skills, which may not be generalizable to other urological settings.

Asymptomatic bacteriuria is common in bladder cancer patients undergoing cystoscopy. Routine antimicrobial prophylaxis appears to be unnecessary, even in patients with positive urine cultures, because subsequent UTIs are rare and easily treated. Such strategy avoids overuse of antibiotics and helps to reduce the emergence of resistant bacteria organisms [8,9]. Further, asymptomatic bacteriuria appears to be associated with fewer tumor recurrences and longer tumor-free survival times, raising the question whether endogenous bacteria may retard tumor growth by inflammatory or local immune mechanisms.

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