

# Perioperative Antimicrobial Prophylaxis for Preventing Infectious Complications After Transurethral Resection of the Bladder: To Use or Not to Use?

Michele Rizzo, MD,<sup>1</sup> Enrica Verzotti, MD,<sup>1</sup> Giacomo Di Cosmo, MD,<sup>1</sup> Tommaso Cai, MD,<sup>2</sup>  
Nicola Pavan, MD,<sup>1</sup> Gernot Bonkat, MD,<sup>3</sup> Paolo Umari, MD,<sup>4</sup> Andrea Cocci, MD,<sup>5</sup>  
Carlo Trombetta, MD,<sup>1</sup> and Giovanni Liguori, MD, PhD<sup>1</sup>

## Abstract

**Purpose:** Transurethral resection of the bladder (TURB) is a common endoscopic procedure. Perioperative antimicrobial prophylaxis (AMP) is used to reduce the risk of infectious complications. However, there is an absence of knowledge about both incidence of infectious complications after TURB and advantage of AMP in general. The objective of this study is to determinate the prevalence of postoperative infectious complications after routine TURB without AMP.

**Methods:** We retrospectively reviewed clinical data of all patients who underwent TURB in the same Academic Urologic Department between January 2011 and December 2013. We consider as relevant for analysis, patients that underwent TURB without receiving any AMP. Infection was defined as a body temperature  $>37.5^{\circ}\text{C}$  sustained for at least 24 hours. Sepsis was defined according to the third international consensus definition for sepsis and septic shock.

**Results:** In the period of the study, 223 TURBs were performed without use of AMP. Mean age was 70.3 years (standard deviation [SD] 11.3). Mean operative time was 25.14 minutes (SD 16). Median length of hospital stay was 3 days (interquartile range [IQR]: 2–4). Six (2.7%) patients developed postoperative infective complications. No case of sepsis was reported. Two (0.9%) patients received an antimicrobial therapy with fluor-quinolones despite absence of any signs of infection. Two hundred fifteen (96.4%) patients of TURBs did not receive any antimicrobial drugs and did not develop any infectious complications.

**Conclusion:** In our series, infectious complications after TURB occurred in  $<3\%$  of cases. In conclusion AMP should not be routinely used prior TURB.

**Keywords:** perioperative antimicrobial prophylaxis, infectious complications, bladder cancer, transurethral resection of bladder cancer, antimicrobial stewardship, antimicrobial resistance

## Introduction

THE AIM OF antimicrobial prophylaxis (AMP) is the prevention of infectious complications resulting from diagnostic and therapeutic procedures.<sup>1</sup> Transurethral resection of the bladder (TURB) is a common endoscopic procedure performed almost in all urologic departments for the treatment and staging of bladder tumors.<sup>2</sup> AMP is routinely given

to patients prior TURB. However, this practice is not supported by good quality evidence. There is an absence of knowledge about incidence of infectious complications after TURB and whether AMP is really advantageous. In our institution the management of AMP since 2009 is based on internal protocols developed by a multidisciplinary team composed by surgeons, kinesiologists, and microbiologists. According to this internal protocol, urine culture must be

<sup>1</sup>Department of Urology, Cattinara Hospital, University of Trieste, Trieste, Italy.

<sup>2</sup>Department of Urology, Santa Chiara Hospital, Trento, Italy.

<sup>3</sup>Alta Uro AG, Merian Iselin Klinik, Center of Biomechanics and Calorimetry (COB), University Basel, Basel, Switzerland.

<sup>4</sup>Division of Urology, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy.

<sup>5</sup>Department of Urology, University of Florence, Florence, Italy.

taken prior every elective urologic surgery. Patients with asymptomatic bacteriuria (AB) are treated with antibiotic therapy based on the antibiogram to reduce the bacterial load. Patients with negative urine culture or a previously treated AB do not receive any AMP prior TURB.

Patients are usually discharged after catheter removal with the clear instruction to refer to the institutional first aid in case of fever >38°C, hematuria, or severe abdominal pain. About 20 days after discharge all patients are reevaluated in the outpatient setting to schedule follow-up on the basis of the pathologic examinations. During this evaluation infections are routinely signaled in the report of the visit.

We report results of our clinical experience with the aim to determine the incidence of perioperative infection complications in a population of patients that underwent TURB without any AMP.

## Materials and Methods

### Study design and population

We retrospectively reviewed all clinical files connected to hospitalization and to the following first month after discharge of all patients who underwent TURB in our institution between January 2011 and December 2013.

### Inclusion and exclusion criteria

We included all patients undergoing TURB during the study period. All patients who received AMP were excluded. All TURB associated with other procedures, such as transurethral resection of the prostate, ureterorenoscopy, retrograde pyelogram, selective ureteral cytology, ureteral stenting, or urgent TURB for hematuria, as well as all nonoperative cystoscopies, were also excluded from the study.

### Data collection and microbiologic considerations

Following patient characteristics, perioperative and pathologic data were collected: demographic parameters, general health status evaluation according to the American Society of Anesthesiology (ASA) score, individual risk factor for urinary infection complications such as positive preoperative urine culture, presence of indwelling urethral catheter, lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia, diminished immune function, operative time, blood tests, length of the hospital stay, and

size, number, and histologic characteristics of the tumors. Postoperative complications were graded according to the Clavien-Dindo classification. All drugs administered during hospitalizations were analyzed with particular regard to antibiotics used.

### Definition of infectious complication and sepsis

We considered as infectious complications, all perioperative febrile status (body temperature higher than 37.5°C at two consecutive samples) that led to the clinical decision to give an antibiotic therapy. Sepsis was defined according to the third international consensus definitions for sepsis and septic shock.<sup>3</sup>

### Ethical considerations

The present study was designed in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was not required because all procedures were performed according to routine standards.

Considering the retrospective nature of the study and that avoiding AMP before TURB represents a practice promoted by guidelines, the study did not require approval by the local ethics committee.

### Statistic examinations

The statistical analysis was carried out using Student's *t*-test, Wilcoxon rank sum test, and Fisher's exact probability test according to the type and distribution of data. A *p*-value <0.05 was considered significant. Statistical analysis was performed using statistical package for the Social Sciences 23.0 software (SPSS, Inc., Chicago, IL).

## Results

Over the study period, a total of 352 consecutive TURBs were performed in our institutions. Every single TURB was considered as an independent event. Data were available for all patients.

According to the study design 80 patients were excluded because TURBs were performed in urgency or emergency timing for hematuria or TURBs were combined with other procedures. Further 49 patients were excluded because they underwent routine TURBs with AMP; in this subgroup one patient developed an infectious complication.

TABLE 1. BASELINE CHARACTERISTICS OF TWO HUNDRED TWENTY-THREE PATIENT-TURBS BY PRESENCE OR ABSENCE OF INFECTIOUS COMPLICATIONS

	<i>Absence of infectious complications</i>	<i>Presence of infectious complications</i>	<i>p-Value</i>
Patient TURBs, no. (%)	217 (97.3)	6 (2.7)	
Age, year, mean (SD)	70.22 (11.42)	73.67 (8.45)	0.46
ASA score, median (IQR)	2 (2–3)	2.5 (2–3.25)	0.09
BPH, no. (%)	34 (15)	1 (16.7)	0.95
Diabetes, no. (%)	42 (19.4)	1 (16.7)	0.87
Immunosuppressed (%)	8 (3.7)	0	0.63
Indwelling catheter (%)	1 (0.5)	0	0.87
Preoperative positive urine culture (%)	15 (6.9)	1 (16.7)	0.36

ASA = American Society of Anesthesiology; BPH = benign prostatic hyperplasia; IQR = interquartile range; TURB = transurethral resection of the bladder; SD = standard deviation.

TABLE 2. OPERATIVE AND PERIOPERATIVE PARAMETERS OF TWO HUNDRED TWENTY-THREE PATIENT-TURBS BY PRESENCE OR ABSENCE OF INFECTIOUS COMPLICATIONS

	<i>Absence of infectious complications</i>	<i>Presence of infectious complications</i>	<i>p-Value</i>
Mean operative time, minutes (SD)	25.24 (15.56)	21.5 (16.91)	0.56
Median in-hospital, days (IQR)	3 (2–4)	2.5 (2–6.25)	0.712
Dimensions			
Tumor size between 0 and 10 mm (%)	57 (25.6)	3 (1.3)	0.47
Tumor size between 10 and 30 mm (%)	114 (51.1)	3 (1.3)	
Tumor size between 30 and 50 mm (%)	43 (19.3)	0 (0)	
Tumor size >50 mm (%)	3 (1.3)	0 (0)	
Tumors that invade and exceed the tonaca muscolaris (Stage T2, T3, and T4) (%)	30 (13.5)	0 (0)	0.33
Tumors confined to the mucosa or submucosa (stage Ta, CIS, and T1) (%)	187 (83.9)	6 (2.7)	
Clavien Dindo, median (IQR)	1 (1–1)	2 (1–2.25)	<0.001

CIS = Carcinoma In Situ.

Two hundred twenty-three TURB patients met the criteria required and were consequently considered for analysis. Table 1 lists baseline demographic and clinical characteristics of the study population according to incidence of infectious complications. Study populations included 168 (75.3%) males and 55 (24.7%) females. Mean age was 70.3 years (standard deviation [SD] 11.3).

Of relevance to preexisting risk factors for infectious complications, 16 (7.2%) patients were found to have a significant bacteriuria in the preoperative urine culture. According to internal protocols all these patients received an antibiotic therapy based on drug susceptibility testing and underwent TURB without any AMP. Forty-three (19.3%) patients were diabetics but with glycemia not exceeding a level of 180 mg/dL at induction of anesthesia. Thirty-five (15.7%) patients were undergoing medical therapy for LUTS, and one patient had an indwelling bladder catheter for urinary obstruction. Eight (3%) patients had previously received an organ transplant or were taking corticosteroid-based therapies and were considered immunocompromised. Fifteen (6.7%) patients had Clavien-Dindo grade 2 complications, and only one patient (0.44%) observed to have a Clavien Dindo grade 3 complication was found in the population examined.

Table 2 lists the perioperative parameters. Mean operative time was 25.14 minutes (SD 16). None of the 223 TURB patients received a single dose of antibiotic drugs during the day of the surgery. Median and mean length of hospital stay were, respectively, 3 days (interquartile range [IQR]: 2–4) and 3.6 days (SD: 2.7). All patients were discharged after the removal of the bladder catheter with the single exception of the

man with the indwelling catheter. Six (2.7%) patients developed a febrile status in the perioperative period. In these subgroups, the median length of hospital stay was 3 days (IQR 2–4) for the noncomplicated group and 2.5 days (IQR 2–6.25) for the group with infectious complication ( $p=0.712$ ). All these patients were discharged after 2 days of apyrexia.<sup>4</sup>

Table 3 reports baseline features and perioperative parameters of the six patients who developed infectious complications. All received a fluoroquinolone-based antibiotic therapy.

Four patients (1.79%) had a perioperative febrile status, while one patient (0.44%) underwent TURB in October 2011 and repeated the treatment in February 2012 for a recurrence; on both occasions the patient developed an infectious complication.

This patient, evaluated as ASA 4, in February 2012 had a positive preoperative urine culture. The duration of resection was 15 minutes, 4 days later, and consequent to the onset of hematuria, he underwent cystoscopy for hemostatic purposes. After this second procedure the patient developed a febrile status and was treated with fluoroquinolones. Subsequently he received physical rehabilitation during the period of hospitalization. The patient was discharged 26 days after TURB.

Two patients that did not develop any febrile status received an antibiotic therapy with fluoroquinolones on the basis of a clinical decision.

No patients were readmitted for infectious complications until 1 month after their discharge, and no infectious complications were mentioned in the reports of their first outpatient reevaluation.

No case of sepsis or septic shock was reported.

TABLE 3. BASELINE CHARACTERISTICS AND OPERATIVE AND PERIOPERATIVE PARAMETERS OF THE PATIENTS THAT DEVELOPED INFECTIOUS COMPLICATIONS

<i>Patients with infectious complications</i>	<i>Age at surgery, years</i>	<i>Preoperative urine culture (isolated microbe)</i>	<i>ASA score</i>	<i>Operative time, minutes</i>	<i>In-hospital stay, days</i>	<i>Antibiotic treatment</i>
PT18	81	Negative	2	35	7	Fluoroquinolones
PT50	79	Negative	4	10	10	Fluoroquinolones
PT75	62	Negative	3	15	4	Fluoroquinolones
PT124	76	Negative	2	49	12	Fluoroquinolones
PT141	64	Negative	2	5	4	Fluoroquinolones
PT50	80	Positive ( <i>Escherichia coli</i> )	4	15	26	Fluoroquinolones

## Discussion

### Main findings

Use of AMP is a standard practice for many surgical procedures aiming to reduce the incidence of infectious complications. European Association of Urology and American Urological Association Guidelines suggest that AMP for TURB should be reserved only for patients with a high risk of infectious complications.<sup>4,5</sup> These recommendations are based on two relatively outdated trials and with a low number of patients. Delavierre and colleagues<sup>6</sup> published in 1993 a double blind randomized controlled trial comprising 61 patients. Twenty-nine patients received a single dose of pefloxacin, and 32 patients received placebo. At 2 weeks post TURB no statistically significant difference in terms of bacteriuria was reported, and no case of symptomatic urinary infection occurred in either group.<sup>6</sup> MacDermott and coworkers in 1988 compared incidence of bacteriuria in 91 patients divided into two groups (antibiotic prophylaxis vs placebo) without finding any significant difference.<sup>7</sup> Neither of these two studies presents a subgroup analysis according to the presence of risk factors for postoperative infection such as operative length and patient comorbidity.<sup>5</sup> Furthermore, MacDermott and associates<sup>7</sup> did not report incidence of urinary infection complications but only AB. Another prospective study, conducted in Japan, reported no differences in rate of infectious complications between the AMP vs the non-AMP group in a population of patients without significant risk factors.<sup>8</sup> Results reported in this study in terms of incidence of infective complications were similar to ours.

Considering that TURB is performed in almost all urologic departments we believe that better evidence is required for or against AMP.

To our knowledge this is the first study that reports the incidence of perioperative infectious complications after TURB considering risk factors such as general health status, comorbidity, surgical duration, and dimension of the tumors.

The most important finding of this analysis is that infectious complications occurred in the 2.7% of the TURB patients that did not receive any prophylaxis. Interestingly 215 (96.4%) patients underwent TURB without receiving a single dose of antibiotic drugs during the hospitalization.

As showed in Tables 1 and 2, we did not find any statistical associations between presence of risk factor for urinary infections and the incidence of infectious complications. Interestingly, in the subgroup of the 46 patients with tumors larger than 3 cm and in the subgroup of patients with a muscle invasive bladder cancer, no infectious complications were reported. These results suggest that tumor dimension does not seem to represent an indication for AMP.

No case of sepsis and septic shock was reported. According to this finding it appears that avoiding antibiotic therapy for elective TURBs the day of the procedure do not expose patients to life treating infections. The benefits of treating AB before surgical procedure remain uncertain; however, our results support the recommendation to treat AB with antibiotic therapy before endoscopic procedures.<sup>9</sup>

### Strengths and limitations of the present study

The study presents some elements of quality. According to the Joint Commission International, since 2008, our institu-

tion meets the international health care quality standards for patients' care and management. Therefore, data derived from documents produced during the in-stay can be considered of good quality and prospectively collected.

Usually, the primary outcomes evaluated in any study analyzing the usefulness of antibiotic prophylaxis before urologic procedures are urinary tract infections and not generic infectious complications.

Our analysis permits us to identify the presence of febrile status associated with elevated levels of inflammatory markers and eventual indications of organ failure, but we do not have enough data to distinguish urinary tract infections from other infectious complications.

It is reasonable to suggest that most infectious complications after urologic procedures are urinary tract infections. However, we believe that the chosen outcomes are appropriate for the purposes of the study.

The weakness of the present analysis came from the reliability of data concerning infection complications after patient discharge. Patients may have received an antibiotic therapy or may have been hospitalized elsewhere. These events may not have been reported in the early outpatients' evaluation; consequently, infectious complications could have been underestimated. However, mean length of the hospital stay was 3.6 days, and often infectious complications occur in the first days after surgery.

### Clinical implications

Remarkably in our institution there is a strict adherence to all nonantibiotic measures to reduce the risk of surgical site infections.<sup>10</sup> Operating theatres are routinely cleaned before every procedure, and the surgical team is trained to maintain asepsis. All members of the institutional urologic team are trained to routinely perform TURB autonomously. Given these considerations, it is reasonable that, following the correct surgical principle of asepsis, outcomes of the present study are reproducible elsewhere and probably could be improved.

Antimicrobial resistance is taking our health care system back to the preantibiotic era.<sup>11</sup> This slow-motion catastrophe represents a major world health problem and it is the responsibility of all health workers to follow the principle of antibiotic stewardship to avoid this disastrous scenario.<sup>12</sup>

Reducing the inappropriate use of antibiotics nowadays represents a major strategy toward preserving the effectiveness of these precious drugs.<sup>12</sup>

Despite practice guideline suggestions, many urologists continue to give a single antibiotic dose, or more, as prophylaxis to patients that undergo TURB.<sup>13-15</sup>

This practice is probably due to common habits but remarkably there is an absence of evidences in the literature demonstrating that avoiding antibiotic prophylaxis before routine TURB does not expose patients to infectious complications.

Our results are of importance because they clearly quantify the incidence of postoperative infectious complications and demonstrate that not using any antibiotic therapy on the day of surgery does not seem to expose patients to life-threatening infection.

Given the high incidence of bladder cancer, TURB is one of the most common urologic procedures. Not using antibiotic



prophylaxis prior TURB would spare thousands of doses of antibiotics every day. A randomized trial would produce better quality evidence but would expose many patients to unnecessary antibiotic therapy with the consequent risk of developing bacterial antibiotic resistance.

## Conclusion

The current literature lacks studies analyzing the incidence of infectious complications after TURB without any AMP. In our study, infectious complications occurred in <3% of patients that underwent TURB, and importantly, no cases of life-threatening infections were reported. According to these results we retain that AMP could be safely avoided prior routine TURB.

## Compliance with Ethical Standards

### *Research involving human participants*

The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

## Informed Consent

For this type of study, informed consent is not required.

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## Authors' Contribution

M.R.: Project development, article writing and editing, data analysis; E.V.: data collection; G.D.C.: Data collection; T.C.: Project development, review of the article; N.P.: Data analysis and review of the article; G.B.: Review of the article; P.U.: Data collection and review of the article; A.C.: Project development and review of the article; C.T.: Review of the article; and G.L.: Project development and review of the article.

## Author Disclosure Statement

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Address correspondence to:  
*Michele Rizzo, MD*  
*Department of Urology*  
*Cattinara Hospital*  
*University of Trieste*  
*Strada di Fiume 447*  
*Trieste 34149*  
*Italy*

*E-mail: mik.rizzo@gmail.com*

### Abbreviations Used

AB = asymptomatic bacteriuria  
AMP = antimicrobial prophylaxis  
ASA = American Society of Anesthesiology  
BPH = benign prostatic hyperplasia  
IQR = interquartile range  
LUTS = lower urinary tract symptoms  
SD = standard deviation  
TURB = transurethral resection of the bladder