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Role of Short-Term Antibiotic Therapy at the Moment of Catheter Removal after Laparoscopic Radical Prostatectomy

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Key Words
Antibiotic prophylaxis · Catheter-related infection · Urinary tract infection · Laparoscopic radical prostatectomy

Abstract
Objective: To assess the role of short-term antibiotic therapy (ABT) in preventing urinary tract infection (UTI) after catheter removal following laparoscopic radical prostatectomy (LRP). ***Methods:*** 729 consecutive patients underwent LRP by one of two surgeons. One surgeon systematically prescribed a 3-day course of ABT (ciprofloxacin) starting the day before catheter removal; the other surgeon did not. The groups were compared for the incidence of symptomatic UTI occurring within 6 weeks after catheter removal. ***Results:*** ABT was given to 261 of 713 patients (37%), while the remaining 452 patients (63%) did not receive ABT. After catheter removal, UTI was observed less frequently among patients receiving ABT: 3.1 vs. 7.3% in those not receiving ABT (p = 0.019). A number needed to treat to prevent 1 UTI is 24. Hospital readmission for febrile UTI was observed only in patients who did not receive ABT (n = 5, 1.1 vs. 0%, p = 0.16). One would need to prescribe ABT for 91 LRP patients to prevent 1 case of febrile UTI. ***Conclusions:*** ABT at the time of catheter removal reduced the risk of postoperative UTI after LRP. One would need to prescribe ABT to 24 patients to prevent 1 case of UTI.

Introduction

Postoperative urinary tract infection (UTI), especially occurring after prostate surgery, is a common cause of patient morbidity. UTI (including symptomatic UTI and asymptomatic bacteriuria) is the most frequent infectious complication encountered in the field of urology [1]. There are two critical times for the development of infectious complications following prostatic surgery: the perioperative period and the time of catheter removal [2, 3]. Short-term catheterization in radical prostatectomy ensures that the bladder remains empty during a period of anastomotic healing. The reported rate of bacteriuria in patients with short-term catheterization is 5–10% for each day the catheter is in place [4]. Catheter-associated bacteriuria is usually asymptomatic, uncomplicated, and

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resolves after the catheter is removed. However, up to 30% of patients may have genitourinary or systemic symptoms [4, 5].

Antibiotic prophylaxis during the perioperative period is widely accepted as a standard in open and laparoscopic radical prostatectomy (LRP), and it significantly reduces the rate of febrile UTI and surgical site infections [6, 7]. A recent randomized study in patients undergoing non-urological abdominal surgery shows a significant benefit of the use the antibiotic prophylaxis at the moment of the catheter removal [8]. However, there is currently no robust evidence in this population to advocate the use of antibiotics at the time of catheter removal [9, 10]. The present study was undertaken to assess if a short-term antibiotic therapy (ABT) starting the day before catheter removal decreases the incidence of subsequent symptomatic UTI in patients undergoing LRP.

Patients and Methods

From October 2004 to July 2007, 729 consecutive patients with clinically localized prostate cancer (cT1c-cT3b) underwent LRP at Memorial Sloan-Kettering Cancer Center by one of two surgeons (B.G. or K.T.). 16 patients who developed UTI before catheter removal or received antibiotics for other complications were excluded from the analysis; the final study cohort had 713 patients. Based on surgeon preference whether to administer antibiotics at the time of urinary catheter removal, the patients fell into two groups. One surgeon routinely prescribed a 3-day course of ABT (ciprofloxacin 500 mg twice daily) starting the day before catheter removal; the other surgeon prescribed no ABT at this time. Unless otherwise indicated, Foley catheter removal was at 11 days postoperatively for the surgeon who prescribed ABT and 7 days postoperatively for the surgeon who did not prescribe ABT. Urine culture was not obtained as a routine before catheter removal.

The perioperative management of both groups was similar. All patients were hospitalized the day of the surgery. Intravenous cefazolin (1 g) was administered half an hour before surgery plus two doses postoperatively. Patients were usually discharged 1–2 days after surgery. The drains were removed before discharge or when drain output was <50 ml/day. Follow-up included phone calls by a nurse; all patients with UTI symptoms (fever, dysuria, etc.) were assessed by a urologist at Memorial Sloan-Kettering Cancer Center or by a local treating physician. For patients treated for UTI at our institution, urine culture was obtained before commencing antibiotic treatment.

UTI was defined as every symptomatic UTI occurring within 6 weeks after catheter removal. However, patients who presented with clinical UTI before catheter removal and patients receiving antibiotic treatment for other, unrelated infectious complications were excluded from the analysis: 12/464 (2.6%) in the no-ABT group; 4/265 (1.5%) in the ABT group. Complications within 30 days of surgery were graded using the Clavien system: grade I – oral medication or bedside care; grade II – intravenous therapy or thoracostomy tube; grade III – intubation, interventional radiology, endoscopy, or reoperation; grade IV – major organ resection or chronic disability, and grade V – death [11].

The association between ABT use and UTI as a result of catheter removal was evaluated using Fisher's exact test. To test whether clinical characteristics (age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, prostate volume, and operative time) were associated with UTI as a result of catheter removal, we performed univariate logistic regression in the subset of patients not receiving ABT. We restricted the analysis to the no-ABT group to remove operating surgeon and ABT use as confounding factors. Age, BMI, prostate volume, and operative time were considered continuous variables, while ASA score was categorized as 1 or 2 vs. 3 or 4. All statistical analyses were conducted using Stata 10.0 (StataCorp LP, College Station, Tex., USA).

This retrospective analysis of prospectively collected data was approved by our institutional review board.

Results

Presurgery patient characteristics and perioperative characteristics and complications occurring within 30 days of surgery are given in table 1.

Of the 713 patients analyzed, ABT was given to 261 patients (37%). After catheter removal, UTI was observed significantly less frequently ($p = 0.019$) in patients who had received ABT (8/261, 3.1%) than in those without ABT (33/452, 7.3%). The absolute reduction in UTI risk associated with use of prophylaxis was 4.2%, resulting in a number needed to treat of 24. That is, one would need to prescribe ABT for 24 patients to prevent 1 case of UTI as a result of catheter removal.

Regarding symptomatology, lower urinary tract symptoms (LUTS) such as burning sensation, frequency, and urgency were the predominant symptoms of UTI in both groups (table 2). Fever was observed in 11 patients in the no-ABT group only (2.4 vs. 0% in the ABT group, $p = 0.009$). Five of the patients with fever required readmission because of the severity of the febrile UTI (1.1 vs. 0% in the ABT group, $p = 0.16$). Thus, one would need to prescribe ABT for 91 patients to prevent 1 readmission for febrile UTI as a result of catheter removal.

Of the 41 patients displaying symptoms of UTI after catheter removal, 40 had a positive urine culture before beginning treatment for their UTI. The remaining patient with UTI had been empirically treated for his UTI at another institution, where his urine culture (negative) was obtained after antibiotic treatment began. Of the 40 patients with positive cultures, 19 patients were reported with positive cultures and treated in other institutions. In 21 patients the complete information about

Table 1. Clinical characteristics, perioperative data and complications within 30 days of surgery

		Antibiotic prophylaxis at time of catheter removal	
		no (n = 452)	yes (n = 261)
Clinical characteristics	Age, years	60 (55, 64)	60 (55, 65)
	BMI, kg/m^2	27 (25, 30)	28 (26, 31)
	Prostate volume, g	32 (25, 47)	30 (24, 44)
	Diabetes	27 (6%)	22 (8%)
	Hypertension	188 (42%)	102 (39%)
	Coronary artery disease	50 (11%)	24 (9%)
	ASA (n = 595) ≤2	315 (87%)	206 (88%)
	>2	46 (13%)	28 (12%)
Perioperative data	Operative time, min	210 (180, 240)	270 (240, 320)
	Estimated blood loss, ml	250 (200, 400)	250 (200, 300)
	Transfused	25 (5.5%)	9 (3.4%)
	Length of stay (days) / range	2 (1, 2) / 1, 22	2 (2, 2) / 1, 14
	Emergency room visit	72 (16%)	34 (13%)
	Readmission	35 (7.7%)	19 (7.3%)
Mortality		0	1 (0.4%)
Morbidity	All complications	186 (41%)	101 (39%)
Procedure-specific complications	Anastomotic leak	25 (5.5%)	23 (8.8%)
	Symptomatic lymphocele	31 (6.9%)	7 (2.7%)
	Lymphorrhea	16 (3.5%)	17 (6.5%)
	Pelvic abscess	4 (0.9%)	2 (0.8%)
	UTI (whether or not considered related to catheter removal)	42 (9.3%)	11 (4.2%)
	Wound infection	22 (4.9%)	7 (2.7%)
	Urinary retention	10 (2.2%)	8 (3.1%)
	Ileus	9 (2.0%)	3 (1.1%)
	Deep vein thrombosis or pulmonary embolism	9 (2.0%)	7 (2.7%)
	Obturator palsy	7 (1.5%)	5 (1.9%)
	Ureteral injury	1 (0.2%)	0
Complications by grade	Grade I	91 (20%)	52 (20%)
	Grade II	34 (8%)	16 (6%)
	Grade III	61 (13%)	32 (12%)
	Grade IV	0	0
	Grade V	0	1 (0.4%)

Data are given as median (interquartile range) or frequency (percentage).

pathogens was available (table 3). *Escherichia coli* was the most common pathogen (n = 11), and 3 patients had mixed infection. Three of the 21 patients (2 in ABT group, 1 in no-ABT group) had pathogens resistant to quinolones.

Clinical characteristics hypothesized to affect UTI (age, BMI, ASA score, prostate volume, and operative time) are listed in table 4 for the 452 patients not receiving prophylaxis. None of these clinical characteristics were significantly associated with having a UTI. For verification, we repeated these analyses in the subset of 261 patients given prophylaxis and found no significant associations with UTI (all $p > 0.4$, data not shown).

Discussion

Antibiotic prophylaxis consists of a brief course of antibiotics administered before or at the start of a diagnostic or therapeutic intervention, used to minimize the infec-

Table 2. Symptoms which prompted UTI investigation in the 41 patients with catheter removal-related UTI

Symptoms	Antibiotic prophylaxis at time of catheter removal		
	no	yes	total
LUTS compatible with UTI	19	7	26
Fever	11	0	11
Hematuria	1	0	1
Other[a]	2	1	3
Total	33	8	41

[a] Abdominal pain, epididymitis, diarrhea.

Table 3. Urinary cultures in the 41 patients with catheter removal-related UTI

Urinary cultures	Antibiotic prophylaxis at time of catheter removal	
	no	yes
E. coli	8[a]	2
Enterococcus sp.	2	1
Klebsiella	2	0
Pseudomonas	2	0
Enterobacter cloacae	1	0
E. coli + *Enterococcus* sp.	0	1[b]
Enterococcus sp. + *Staphylococcus aureus*	0	1[b]
Enterococcus sp. + *Klebsiella oxytoca*	1	0
Positive[c]	16	3
Negative[d]	1	0
Total	33	8

[a] One case was resistant to quinolones.
[b] Resistant to quinolones.
[c] The cases were reported as positive culture but no further information was given.
[d] The patient was empirically treated for UTI at an outside hospital, where urinary culture was obtained after initiation of antibiotic treatment.

tious complications resulting from such interventions. Although it is common practice to administer antibiotic prophylaxis for many urologic procedures, there is still little evidence for its use in most of these procedures [6].

LRP is classified as a clean-contaminated surgery [12]. In the guidelines authorized by the Centers for Disease Control and Prevention, a clean-contaminated wound (class II) is defined as 'an operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination'. While is it widely accepted that systemic perioperative antibiotics reduce the risk of surgical site infections and UTI, there is scant evidence supporting the use of antibiotics in LRP patients to prevent catheter-related UTI or catheter removal-related UTI. The Best Practice Policy panel of AUA recommends a course of intravenous cephalosporins lasting <24 h in clean-contaminated urological operations involving the opening of the urinary tract. The panel also advocates 24 h of oral antibiotics (fluoroquinolones or TMP-SMX) at the time of removing an external urinary catheter if the patient has infection-related risk factors. Alternatively, a full course of culture-directed antimicrobial can be administered for documented bacteriuria, or treatment can be omitted if urine culture shows no growth [13].

These recommendations are based on two randomized controlled trials involving 146 patients after transurethral surgery. In these studies, patients receiving cefotaxime (single dose in one study, 3-day course in the other) at the time of catheter removal had significantly reduced the postoperative complication rate and length of hospital stay compared to a control group not receiving antimicrobials at catheter removal [2, 3]. However, there are no specific recommendations concerning prophylaxis in LRP. The AUA guidelines suggest that urinary tract surgery should be considered a risk factor for bacteremia in the presence of bacteriuria, and therefore AP for catheter removal may be warranted [13].

In the present non-randomized retrospective study, the use of ABT significantly reduced the incidence of symptomatic UTI following catheter removal, from 7.3 to 3.1%. The severity of UTI symptoms was also less intense in the ABT group, with all patients presenting with LUTS alone and none with fever. In the group without ABT, fever was the main symptom for 33% (11/33) of men developing UTI. And although readmission for febrile UTI was rare, it was observed only in the patients who did not receive ABT (n = 5, 0.7% overall).

Assuming the effectiveness of perioperative prophylaxis in reducing postoperative infections and given that the prostate has been removed, most cases of postoperative bacteriuria and UTI could well be catheter-related. Given the retrospective nature of this study, we were unable to determine the incidence of asymptomatic bacteriuria, as only patients who had UTI symptoms were investigated. However, we know from the publications on short-term catheterization that the rate of bacteriuria is 5–10% for each day the catheter is in place [4]. Among

Table 4. Univariate logistic regression analysis to evaluate the association of patient clinical characteristics with catheter removal-related UTI in the 452 patients without antibiotic prophylaxis

Predictor	No UTI (n = 419)	UTI (n = 33)	Odds ratio	95% CI	p value
Age, years	60 (55, 64)	58 (56, 63)	1.00	0.95, 1.05	0.9
BMI, kg/m^2 (n = 389)	27 (25, 30)	27 (26, 30)	1.01	0.93, 1.09	0.9
ASA (n = 361)					
≤2	293 (88%)	22 (81%)	ref.	ref.	
>2	41 (12%)	5 (19%)	1.62	0.58, 4.52	0.4
Operative time	210 (180, 240)	210 (180, 225)	0.94[a]	0.86, 1.03	0.16
Prostate volume, g (n = 409)	32 (25, 47)	30 (24, 42)	0.98	0.96, 1.01	0.17

[a] Odds ratio per 10-min increase in operative time.
Descriptive data are given as median (interquartile range) or frequency (percentage).

patients with UTI, the median time to catheter removal was 7 days, which equates to a rate of bacteriuria of at least 35% at the time of catheter removal. The best strategy to manage catheter-acquired bacteriuria after LRP has not been investigated, but studies in the non-urologic setting have shown benefits for antibiotic treatment once bacteriuria has been identified. In a randomized controlled trial comparing oral antimicrobials with no treatment for asymptomatic bacteriuria following short-term catheter use in women, bacteriuria resolved in 81% of patients treated with antimicrobials. By contrast, bacteriuria resolved in only 36% of untreated patients, and another 17% of untreated patients went on to develop UTI symptoms [14]. In a double-blind, placebo-controlled trial of prophylactic ciprofloxacin in surgical patients with postoperative bladder drainage scheduled for 3–14 days, 75% of the placebo group were bacteriuric at catheter removal compared with 16% of ciprofloxacin-treated patients. Also, 20% of placebo-treated patients had symptomatic UTI, including 3 with septicemia, compared with 5% of the ciprofloxacin group [15].

When deciding if administration of ABT is appropriate, it is important to consider the number needed to treat to prevent an infection and the risk and costs of adverse effects. Fluoroquinolones are generally efficacious in the urinary tract, have a long half-life, and are rarely associated with allergic reactions [16, 17]. Fluoroquinolones are also generally well tolerated: the most common adverse reactions involve the gastrointestinal tract, with 3–17% of patients reporting mostly mild nausea, vomiting, and/or abdominal discomfort. Central nervous system side effects, predominantly mild headache and dizziness, have been seen in 0.9–11% of patients. Hypotension, tachycardia, crystalluria, thrombocytopenia, leukopenia, anemia, and Achilles tendon rupture have occurred quite rarely [18]. Regarding the cost benefit of prophylaxis, it is estimated that each episode of symptomatic UTI will incur additional costs of USD 676, and catheter-related bacteremia is likely to cost at least USD 2,836 [19]. Our analysis showed that we need to administer fluoroquinolone prophylaxis to 24 LRP patients to prevent 1 UTI after catheter removal, and to 91 patients to prevent 1 hospital readmission for febrile UTI. Our retrospective analysis revealed no major side effects from the prophylaxis given, and considering the high cost of re-hospitalization and the potential risk of sepsis, we feel that it is reasonable to treat this number of patients with antibiotics.

Another concern is the development of antibiotic-resistant strains of bacteria. On a large scale, there is a clear correlation between the increase of antibiotic-resistant bacteria and the rise of antibiotic use in clinical practice [20]. In this study, we were not able to assess the impact of prophylaxis use on the development of resistant strains, since post-prophylaxis fluoroquinolone sensitivity was determined for only 21 patients (approximately half of the patients with symptomatic UTI), and there were no pre-prophylaxis cultures. In a pilot randomized controlled trial of 48 non-urologic patients which compared 2-day ciprofloxacin prophylaxis vs. placebo at the time of catheter removal, UTI rates were not significantly different: 16% in the ciprofloxacin group vs. 13% in the placebo group. The pathogens were resistant to ciprofloxacin in 88% of UTI cases [9]. In contrast, however, several studies in a number of urologic settings have confirmed the effectiveness of oral fluoroquinolone prophylaxis, making this the first-choice recommendation for endoscopic pro-

cedures from the panel of AUA [13]. In our study, only 14% (3/21) of patients with symptomatic UTI and sensitivity culture had ciprofloxacin-resistant pathogens. We feel this is acceptable and does not preclude fluoroquinolones being used as a prophylactic agent.

The limitations of the present study include its retrospective and non-randomized methodology, the lack of systematic urine cultures, the fact that side effects of ABT were not recorded in all patients, and the unmeasured confounding potential relating to the surgeon, since one surgeon routinely prescribed ABT whereas the other surgeon did not. Another possible confounding factor is the time to catheter removal, as patients who received ABT tended to have longer time to catheter removal than patients in the no-ABT group; this was based on the preference of the surgeon. It is possible that early removal of the catheter is associated with infection, but we were unable to control for this due to the high correlation between receiving ABT and increased time to catheter removal. Despite these limitations, the results of our study suggest that after LRP, the use of ABT at the time of catheter removal reduces the risk of postoperative UTI. These results warrant the development of future randomized placebo-controlled studies with rigorous sensitivity testing, to more exactly determine the benefit of prophylactic antibiotics at catheter removal for this population.

Conclusions

In this non-randomized retrospective study, the use of ABT at the time of catheter removal reduced the risk of postoperative UTI after LRP. One would need to prescribe AP to 24 patients to prevent 1 case of UTI.

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