



Fig. 3. Metal stenting of ampullary cancer

After biliary sphincterotomy, the length of each stricture was determined and the origin of the cystic duct insertion was noted in patients who had a gallbladder. The stent delivery system was advanced proximal to the stricture over a guide wire, where the stent was partially deployed and positioned within the stricture. When anatomically feasible stents were deployed so as to avoid occlusion of the cystic duct insertion, particularly in patients with a gallbladder.

#### Results and Discussion

Complications of endoscopic papillectomy occurred in 7 cases and were as follows: bleeding — 4, acute mild pancreatitis — 2, perforation — 1. Epinephrine spray and argon-plasma coagu-

lation was used to attain hemostasis in 2 patients, hemoclip placement — in 1 case and angiographic management was necessary in 1 patient. All cases of pancreatitis were treated conservatively. In 1 case of perforation surgery was performed. During follow-up (mean 30 months) 12 of 21 patients (49%) had no recurrence, 5 had recurrent adenoma (mean time interval to recurrence 27 months), two — died of unrelated illnesses and 2 are awaiting follow-up. All residual tumors were eradicated by repeated endoscopic procedures.

#### Conclusions

(1) Endoscopic therapy appears to be a reasonable alternative to surgery for management of benign papillary tumors. (2) Papillary adenoma after endoscopic resection recurs in about a third of cases. (3) Recurrences are usually small and benign, and can be successfully treated endoscopically. (4) Further studies with long-term follow up are needed to determine the ultimate outcome of endoscopic treatment in patients with papillary neoplasms. (5) Metal biliary stenting is effective procedure in the treatment of unresectable cases.

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## ANTIBIOTIC PROPHYLAXIS ON THE TIME OF CATHETER REMOVAL FOLLOWING LAPAROSCOPIC RADICAL PROSTATECTOMY

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**Objective.** To assess the interaction between antibiotic prophylaxis and bacteriuria, leukocyturia after catheter removal following laparoscopic radical prostatectomy (LRP).

**Patients and methods.** A prospective randomized study enrolled 180 patients undergoing LRP, who were randomized either for receiving 7 days of prophylactic antibiotics starting at urinary catheter removal, or not. A urine specimen was collected for urinalysis on removal of the catheter, 1, 4 and



8 weeks after operation. Another urine specimen was collected for urine culture on removal of the catheter and 4 weeks later. The groups were compared for the bacteriuria, leukocyturia occurring within 8 weeks after catheter removal.

**Results.** Antibiotic prophylaxis was given to 80 of 145 LRP patients (55.17%), while the remaining 65 patients did not receive antibiotic prophylaxis. The total incidence of bacteriuria after catheter removal following LRP was 20% (29/145), which was showed no significant differences between the two groups (with or without prophylaxis, 16/80, 13/65,  $P>0.05$ ). However, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between 2 groups ( $P=0.025$ ). Moreover, postoperative change in urine leukocyte counts were not significantly different between the 2 groups ( $P>0.05$ ).

**Conclusion.** Bacteriuria and leukocyturia should be safely managed with culture-specific antibiotic prophylaxis and careful monitoring after catheter removal following LRP. There is no detectable significant benefit in using antibiotic prophylaxis to reduce the urine leukocyte counts after LRP.

**Key words:** prostate cancer, radical prostatectomy, bacteriuria, leukocyturia.

## Introduction

After laparoscopic radical prostatectomy (LRP), short-term catheterization is usually used to ensure that the bladder remains empty during a period of vesicourethral anastomotic healing. Bacteriuria is one of the most common complication after LRP, and the reported rate of bacteriuria increases about 5–10% for each day [1]. Antibiotic prophylaxis is widely accepted during the perioperative period. However, the benefit of antibiotic prophylaxis during removal of the catheter is controversial [2; 3]. In addition, urine culture results are not usually available before 24 hours after collection, most of physicians are often prescribe the empiric antibiotics as a result of urinalysis (urinary leukocyte counts) for the patient [4]. Herein, the present study was undertaken to assess the interaction between antibiotic prophylaxis and bacteriuria (symptomatic or asymptomatic), and leukocyturia occurring within 8 weeks immediately after catheter removal in patients undergoing LRP.

## Patients and Methods

Consecutive men who underwent LRP at our institution from January 2010 to December 2011 by a single surgeon (Xin Gao) were enrolled in this study. The study was approved by the Institutional Ethical Committee and all patients provided written informed consent before entry to the study. The perioperative management of both groups was similar. Intravenous ciprofloxacin (0.5 g) was administered half an

hour before surgery plus 3-day doses postoperatively as surgical prophylaxis. The vesicourethral anastomosis was performed using a 3-0 Vicryl suture in a continuous or intermittent manner at the discretion of the surgeon [5]. The drains and indwelling urinary catheters were removed before discharge. Patients who presented with clinical urinary tract infection (UTI) before catheter removal, required additional transurethral manipulations (urethrotomy, dilatation of the urethra), or received prolonged antibiotics ( $>7$  days) for other complications were excluded. Based on whether to receive antibiotics at the time of urinary catheter removal, the patients divided into 2 groups. Antibiotic prophylaxis group routinely prescribed a 7-day oral course of antibiotics (ciprofloxacin, 500 mg, once daily) starting the day at catheter removal. Patients allergic to ciprofloxacin were given (Cefaclor, 375 mg, twice daily). Patients in the other group did not receive any antibiotics at this time.

Demographic and clinical data, including age, history disease, prostate-specific antigen (PSA), Prostate volume, Neoadjuvant androgen ablation therapy, operative time, estimated blood loss, transfusion, duration of catheter, final Gleason score and complications were recorded prospectively. Two urine specimens of each patient, one for urinalysis (urinary leukocyte counts) was collected immediately after catheter removal, 1, 4 and 8 weeks after catheter removal, and one for urine culture

immediately after catheter removal and 4 weeks after catheter removal. In our institution, all urine samples were collected in a sterile device that reduces the manipulation of the sample to a minimum. Patients with at least  $10^5$  cfu/ml in any of these 2 postoperative urine cultures were considered to have present bacteriuria. Leukocyturia was defined as 18.0 leukocytes/ul according to the result of urinalysis (Sysmex UF-1000i). At follow-up period, all patients were seen by a study-blind specialist in urology to assess subjective symptoms after catheter removal.

Data were presented as median (interquartile) for continuous variables and as frequencies (percentage) for categorical variables. Statistical analysis was performed using the t-test,  $\chi^2$  test or Fisher's exact test. Postoperative changes in the urine leukocyte counts between the 2 groups were compared by two-factor repeated measure ANOVA. All analysis was done using SPSS 15.0 software (SPSS, Chicago, Illinois, USA) and  $P$  values of less than 0.05 was considered statistical significance.

## Result

Between January 2010 and December 2011, a total of 177 patients were randomized (T1c-T3b). 32 patients were excluded receiving prolonged antibiotic therapy for clinical UTI before catheter removal (11), chest infection (5), remote infection (4), surgical site infection (3), intraoperative rectal injury (2), and for not completing the follow-up required for this study (7). Statisti-



Table 1

**Clinical Characteristics, Perioperative Data and Complications within 1 Year of Surgery**

Indices	Antibiotic prophylaxis at catheter removal		P
	No (n=65)	Yes (n=80)	
Clinical characteristics			
Age, years	70 (57, 77)	67 (55, 74)	0.932
Hypertension	20 (30.7%)	29 (36.3%)	0.488
Diabetes	15 (23.1%)	23 (28.8%)	0.440
Previous TURP	6 (9.2%)	5 (6.3%)	0.542
Serum PSA, ng/ml	17.6 (6.7, 34.6)	23.4 (2.3, 40.8)	0.092
Prostate volume, ml	39.7 (22.7, 89.6)	35.3 (21.9, 108.6)	0.239
Neoadjuvant androgen-ablation therapy	7 (10.8%)	9 (11.3%)	0.927
Perioperative data			
Operative time, min	172 (121, 308)	165 (115, 350)	0.047
Estimated blood loss	132 (65, 450)	116 (50, 389)	0.052
Transfusion	3 (4.6%)	2 (2.5)	0.657
Catheter duration, days	9 (7, 21)	8 (7, 14)	0.058
Final Gleason score > 7	44 (67.7%)	51 (63.7%)	0.619
Postoperative complications			
Urinary retention	1 (1.5%)	0	—
Incontinence	2 (3.1%)	3 (3.8%)	1.000
Anastomotic stricture	2 (3.1%)	1 (1.3%)	0.578

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

Table 2

**Summary of Bacterial Isolates and Species Resistant to Ciprofloxacin from Two Groups Patients within 4 Weeks after Catheter Removal Following LRP**

Species	No. of cultures (Species resistant to ciprofloxacin)	
	No-antibiotic group (n=65)	Antibiotic group (n=80)
Escherichia coli	6 (1)	5 (4 <sup>a</sup> )
Pseudomonas aeruginosa	4	3 (3 <sup>b</sup> )
Klebsiella pneumoniae	1 (1)	4 (2 <sup>c</sup> )
Staphylococcus epidermidis	1 (1)	2 (1)
Coagulase Negative Staphylococcus	1	0
Enterobacter cloacae	0	1 (1)
Enterococcus faecalis	0	1
Total	13 (3)	16 (11)

Note. a — two cases with fever when urine culture was obtained; b/c — one case with dysuria when urine culture was obtained.

cal analysis was therefore based on 145 patients. Demographic and clinical characteristics showed no significant difference between the patients remaining in both groups except the operative time ( $P=0.047$ , Table 1). The urinary catheters were left in the place for  $11 \pm 3.5$  days in the prophylaxis group and for  $(10.0 \pm 2.7)$  days in the group without prophylaxis ( $P=0.069$ ). Perioperative prophylaxis was given in all patients for a median duration of 3 days.

Among 145 patients analyzed, antibiotic prophylaxis was given to 80 patients (55.17%), 76 patients received ciprofloxacin, and 4 patients received Cefaclor for known or suspected allergy to the former.

Among 145 patients, 29 (20%) developed a postoperative bacteriuria in the both groups (Table 2). In the prophylaxis group, these cases of postoperative bacteriuria were discovered on removal of the catheter (7), 4 weeks after catheter withdrawal (9). The pathogens in 11 patients were resistant to ciprofloxacin. In the non-therapy group, 9 patients had bacteriuria on removal of the catheter, 4 patients 4 weeks after catheter removal. 10 patients in non-antibiotic group were sensitive to ciprofloxacin. There was no significant difference in the bacteriuria rate (symptomatic or asymptomatic) on the time of catheter removal and 4 weeks later between the antibiotic prophylaxis and non-antibiotic group ( $P=0.330$ ,  $0.385$  respectively). However, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between 2 groups ( $P=0.025$ ). Lower urinary tract symptoms (LUTS) such as frequency, urgency and burning sensation were not significant difference between the 2 groups ( $P=0.134$ ). In antibiotic group, 3 patients with fever starting at the 2, 3, 5 days after urinary catheter removal respectively, and fever was observed in 2 patients in no-antibiotic group

only (fever  $< 38^\circ\text{C}$ ). These fever suspicious for UTI continued antibiotic therapy in antibiotic group and all decreased gradually thereafter. No serious infectious sequelae occurred up to 4 weeks after LRP. No adverse or aller-

gies events from receiving the antibiotic prophylaxis were noted.

In total, 145 urine samples were collected immediately prior to catheter removal. Of 1160 urine specimens, the mean con-



**Postoperative Change in Urine Leukocyte Counts and Urine Culture Results between the 2 Groups within 8 Weeks after Catheter Removal**

Time point after catheter removal	Antibiotic prophylaxis at catheter removal		P
	No (n=65)	Yes (n=80)	
Urine leukocyte counts	—	—	Group=0.097; time=0.042; Group*time= 0.106@
At catheter removal	444.81±97.06	436.82±106.53	0.932*
1st week	243.32±89.46	215.68±57.42	0.488*
4th week	170.67±63.89	142.70±52.78	0.440*
8th week	25.17±16.87	27.16±35.65	0.542*
Urine culture results			
At catheter removal	9 (13.8%)	7 (8.8%)	0.330#
8th week	4 (6.2%)	9 (11.3%)	0.385#
Resistant to quinolones	3 (23.1%)	11 (68.8%)	0.025#

Note. @ — Two-factor repeated measure ANOVA. Factor 'group' consists of antibiotic and non- antibiotic groups, while factor 'time' consists of at catheter removal, 1 week, 4 week, and 8 week for urinalysis (urine leukocyte counts) and at catheter removal, 1 week for Urine culture results. 'Group × time' indicates interaction; \* — t-test; # —  $\chi^2$  test or Fisher's exact test.

centration of leukocyte counts were highest on the time of catheter removal and decreased gradually thereafter (with vs without antibiotics: (436.82±106.5) vs (444.81±97.06) leukocytes/ul). In addition, postoperative change in urine leukocyte counts were not significantly different between the 2 groups within 8 weeks after catheter removal ( $P>0.05$ , Table 3). ANOVA for repeated measures be used to perform the data analysis. The results showed that the interaction between antibiotic therapy and time effects was not significant ( $P=0.106$ ), the main effect of the treatment was not significant ( $P=0.097$ ), while the time effect was significant ( $P=0.042$ , Table 3).

## Discussion

We know from the publications that the incidence of bacteriuria is 5–10% for each day the catheter is in the place [1]. Among the patients with LRP in our institute, the median time to catheter removal was 8 days, which equates to a rate of bacteriuria of at least 40% on the time of catheter removal. There are two critical times for the development of infectious complications following prostatic surgery: the perioperative period and the time of catheter removal [3; 6]. The AUA guidelines recommend that 24 h of oral antibiotics (fluoroquinolones or TMP-SMX) on the time of urinary catheter removal if the patient has infection-related risk factors, and urinary tract surgery should be considered a risk factor for bacteremia [7]. However, there are few specific recommendations and studies concerning antibiotic prophylaxis at the time of catheter removal following LRP.

Several studies try to deciding if administration of antibiotic prophylaxis at catheter removal following radical prostatectomy is appropriate. In prospectively collected data, retrospective analysis study of prophylactic ciprofloxacin in LRP patients af-

ter catheter removal, urinary tract infection (UTI) was observed less frequently among patients receiving antibiotic therapy (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. They suggested that it is reasonable to treat LRP patients with antibiotics after catheter removal [8]. Jessica A and colleagues [9] prospectively examined urine culture results collected from 334 RP patients who received prophylactic antibiotics 1 day before, the day of, and for 5 days after catheter removal. They found out that 25% (83/334) had positive culture results, of which 7% were resistant to ciprofloxacin. They also suggested a high frequency of bacteriuria but low risk of clinical infectious complications using extended fluoroquinolone

prophylaxis at catheter removal after RP.

However, in the present randomized prospective study, there was no significant difference in the bacteriuria rate at the time and 8 weeks later after catheter removal between the antibiotic prophylaxis and non-antibiotic groups ( $P=0.330$ , 0.385 respectively). By contrast, antibiotic resistance occurred most frequently in the antibiotic prophylaxis group and was significant difference between the two groups ( $P=0.025$ ). Fever is infrequently encountered after catheter removal following LRP, its treatment is usually up to the physician's discretion. Based on our experience, we suggest that fever greater than 38.5°C might be a reasonable criteria for administration of antibiotics. In case of the necessity of antibiotic therapy, repeat urine cultures for bacterial species and antimicrobial susceptibilities might seem rational. As we suppose, another concerning, that identified bacteriuria resulting in a peri-anastomotic inflammatory



response leads to anastomosis fibrosis, ischaemia and scarring, which may contribute to anastomotic stricture and would seem to favor antibiotic administration. Due to the growing number of resistant strains of bacteria, we feel that it is more reasonable to treat the patient with culture-specific antibiotic prophylaxis and careful monitoring [10; 11].

The presence of bacteriuria is relatively common of patients after LRP [8; 9]. As yet, however, few investigations have been done the change of urine leukocyte counts after LRP. In several studies of leukocyturia after transurethral resection of the prostate (TURP), a high concentration of leukocytes in urine samples were present on removal of the catheter and 1 week after operation, but at 4 weeks postoperatively, the mean leukocyte counts in urine had become less than before. They presumed that the leukocyturia was probably associated with exudation of inflammatory cells of the surgical wounds, but leukocyturia cannot reflect the possibility of postoperative bacteriuria [12; 13]. As urinalysis is one of the most common diagnostic screening tests in clinical practice, and urine culture results are available not before 24 h after collection, an antibacterial drug is usually empirically prescribed after urinalysis but before the urine culture results are known [4]. In present study, urine leukocyte counts were highest on the time of catheter removal and decreased gradually thereafter. Postoperative changes in the urine leukocyte counts between the two groups by two-factor repeated measure ANOVA show that the time effect was significant, but not the effect of antibacterial drugs.

Several limitations of our study warrant mention. First of all, our study population was relatively small. Additionally, in our institution, a seven day treatment with orally taken quinolones is the first-line treatment,

and the length of antibacterial administration is arbitrary. Another possible confounding factor is the time to catheter removal, our populations tended to have longer time to catheter removal than patients in western country studies [14]. It is possible that early removal of the catheter is reduce the risk of bacterial ascension. Finally, we did not treat our control group patient with placebo, as the results of urinalysis and urinary culture are unlikely to be affected by blinding the patients.

### Conclusion

Notwithstanding the limitations, our results suggest that the risk of bacteriuria and leukocyturia after catheter removal following LRP is real, which should be safely managed with culture-specific antibiotic prophylaxis and careful monitoring. There is no detectable significant benefit in using antibiotic prophylaxis to reduce the urine leukocyte counts after LRP.

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