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Research Article

Hospitalization Due to Febrile Urinary Tract Infection After Prostate Biopsy: A Comparative Analysis of 1805 Cases

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Abstract

Purpose: Patients with a history of urinary tract infection, antibiotic use, hospital admission, bacteriuria, diabetes mellitus, or other comorbidities may be at increased risk of infectious complications (10). Oral or intravenous antibiotics are essential before TR-PB. Cephalosporines could be a good alternative to fluoroquinolones for TR-PB prophylaxis. This study aims to show the cause of hospitalization due to febrile urinary tract infection after TR-PB.

Methods: We performed a total of 1805 prostate biopsies in the above-mentioned period. Two groups of patients were formed based on their infection status. Group 1, 1748 patients had no infectious complications after TR-PB. Group 2, 57 patients had infections related to the prostate biopsy procedure. The primary endpoint was the development of infection-related complications, including microbiologically confirmed urinary tract infection (UTI) and/or bacteremia. Secondary outcomes assessed included bacteriuria, bacteremia, hospitalizations related to infection.

Results: There were significant differences between the two arms in terms of Charlson comorbidity indexes, core number, diabetes mellitus, hypertension, IPSS, history of urinary tract infection, prior biopsy history ($p < 0.05$). Multivariate Cox regression analysis revealed that diabetes mellitus (HR 2.567, 95% CI 1.367-4.821, $p < 0.003$), hypertension (HR 3.842, 95% CI 2.176-6.782, $p < 0.001$), history of urinary tract infection (HR 3.526, 95% CI 1.459-8.518, $p < 0.005$) and core number (HR 1.278, 95% CI 1.095-1.491, $p < 0.002$) were independent predictors of infection after prostate biopsy.

Conclusion: Hypertension, diabetes mellitus, history of urinary tract infection and core number are independent risk factors for infection after TR-PB.

Keywords: Prostate Biopsy; Diabetes Mellitus; Urinary Tract Infection; Cephalosporin

Introduction

Prostate biopsy may be necessary when a digital rectal examination reveals an abnormal prostate, the blood test for prostate-specific antigen (PSA) is elevated, or imaging studies show changes in the prostate gland. A transrectal or transperineal approach is typically used to perform this procedure. Transrectal prostate biopsies (TR-PB) have been associated with a higher rate of infectious complications [1]. Antibiotic prophylaxis reduces infection following TR-PB [2], but despite this preventive measure, 3–10% of patients still develop an infectious complication [3-5].

Bacteriuria, UTIs, bacteremia, and sepsis are potential infectious complications that can occur following TR-PB [6]. Hospitalization is necessary in 1-3% of cases, and the sepsis occurrence rate is 0.8%, with a reported incidence of 5-7% [7,8]. On the other hand, antibiotics should be used with caution due to the increasing risk of antibiotic resistance [9].

Patients with a history of urinary tract infection, antibiotic use, hospital admission, bacteriuria, diabetes mellitus, or other comorbidities may be at increased risk of infectious complications [10]. Oral or intravenous antibiotics are essential before TR-PB. Cephalosporines could be a good alternative to fluoroquinolones for TR-PB prophylaxis. Cephalosporines has activity against many fluoroquinolone-resistant strains of Escherichia coli and is relatively inexpensive with a good safety profile. This study aims to show the cause of hospitalization due to febrile urinary tract infection after TR-PB.

Materials and Methods

This is a retrospective study performed between January 2015 and December 2022. The present study protocol was reviewed and approved by the Institutional Review Board of XXXX University (approval number: 2025/28-01) and it was conducted in accordance with the principles of the Declaration of Helsinki. Complications were analyzed in a cohort of men who underwent transrectal prostate biopsies for suspected prostate cancer. Routinely, urine culture was not performed. Our protocol for perioperative antibiotic prophylactic included cephalosporin. If the patient had a positive urine culture history, we used antibiotics according to the urine culture antibiogram. We performed a total of 1805 prostate biopsies in the above-mentioned period. The procedure involved 10-12 transrectal core biopsies. Local anesthesia was applied using 2% lidocaine gel. An 18-gauge, single-use disposable biopsy needle was used for the procedure. The patient data set comprised a range of variables, including demographics, comorbidities, urinary tract infections history, prostate biopsy history, antibiotics history, serum Prostate-Specific Antigen (PSA) and Prostate Imaging-Reporting and Data System (PI-RADS) score. Following the finalization of biopsy pathologies, histopathology results, complications of transrectal biopsy, treatment management after transrectal biopsy complications, antibiotics administered for prostatitis, microbiological details of urine culture and blood culture were recorded. Also, International Prostate Symptom Score (IPSS) evaluated before biopsy procedure. Two groups of patients were formed based on their infection status.

Group 1, 1748 patients had no infectious complications after TR-PB. Group 2, 57 patients had infections related to the prostate biopsy procedure. All patients received information about potential complications before the biopsy procedure and were advised to contact the doctor responsible if there are any complications. The primary endpoint was the development of infection-related complications, including microbiologically confirmed urinary tract infection (UTI) and/or bacteremia. UTI was diagnosed when bacteria were detected in the urine and antibiotics were subsequently administered to treat the specific bacteria identified in the urine culture. Secondary outcomes assessed included bacteriuria, bacteremia, hospitalizations related to infection, emergency department visits due to infection, the emergence of new resistant organisms, and the influence of comorbidities on infections. All outcomes were assessed within a 30-day period following the procedure.

Data analysis was conducted with SPSS software, version 22 (IBM Corp, Armonk, NY). Numerical data were summarized using the median and quartiles, while categorical data were summarized using frequencies and percentages (n%). To compare categorical data, the chi-square test was utilized. For comparing numerical data between two groups, the Mann-Whitney U test was applied. Hazard ratios (HR) and 95% confidence interval (CI) were determined, and $p < 0.05$ was considered significant.

Results

Of the patients evaluated, 1805 met the inclusion criteria, with 1748 assigned to group 1 and 57 to group 2. 1769 (98%) patients received cephalosporins prophylaxis (Table 1). Patients in group 1 had a mean age of 64.8 years, while those in group 2 had a mean age of 64.1 years. The mean body mass index was 26.9 in group 1 and 27.2 in group 2. Median serum PSA levels were 7.6 ng/mL in group 1 and 7.5 ng/mL in group 2. Finally, median prostate volumes were 50 cc in group 1 and 51 cc in group 2. No significant differences were observed between the two groups regarding age, BMI, IPSS, antibiotics history, mpMRI, PI-RADS Score, prostate volume, and core biopsy volume. However, there were significant differences between the two arms in terms of Charlson comorbidity indexes, core number, diabetes mellitus, hypertension, IPSS, history of urinary tract infection, prior biopsy history, biopsy histopathology ($p < 0.05$) (Table 2).

Antibiotics class	n (1805)	%
Cephalosporin	1769	98
Trimethoprim-sulfamethoxazole	10	0.56
Carbapenem	10	0.56
Quinolone	8	0.44
Other	8	0.44

Table 1: Prophylactic antibiotics classification used in pre-biopsy.

	Prostatitis patients (No) (n = 1748)	Prostatitis patients (Yes) (n = 57)	p-value
Age (years), mean+SD	64.8 ± 7.9	64.1 ± 8.5	0.516[T]
Charlson Comorbidity Index, mean+SD	2.6 ± 1.1	3.4 ± 1.6	0.001[T]
International Prostate Symptom Score, mean+SD	19.2 ± 7.1	21.7 ± 7.2	0.010[T]
Core number, mean+SD	11.03 ± 1.87	11.8 ± 2.16	0.002[T]
Malignant core number, mean+SD	4.83 ± 3.2	4.78 ± 3.4	0.942[T]
Body Mass Index, median (min-max)	26.9(19-37)	27.2(20.2-38.8)	0.336[M]
PSA (ng/mL), median (min-max)	7.6 (0.2-1000)	7.5(1-1000)	0.709[M]
Prostate volume, median (min-max)	50(9-250)	51(8-213)	0.209[M]
PSA-density, median (min-max)	0.15(0.01-50)	0.12(0.04-12.9)	0.186[M]
Core volume(mL), median (min-max)	135(22-715)	153(56-595)	0.216[M]
Diabetes mellitus, n (%)	166(9.5)	17(29.8)	0.001[c]
Hypertension, n (%)	407(21.4)	32(56.1)	0.001[c]
Prior biopsy history, n (%)	236(13.5)	16(28.1)	0.002[c]
History of urinary tract infection, n (%)	65(3.7)	7(12.3)	0.001[c]
Antibiotics history, n (%)	301(17.2)	13(22.8)	0.273[c]
Alpha-blocker history, n (%)	766(43.8)	35(61.4)	0.009[c]
Multiparametric Prostate MRI, n (%)	880(50.3)	35(61.4)	0.100[c]
PI-RADS Score, n (%) 1 2 3 4 5	 34(3.9) 79(9) 317(36) 317(36) 133(15.1)	 0 2(5.7) 14(40) 15(42.9) 4(11.4)	0.619[c]
Complications, n (%) Hematuria Fever >38 oC Urinary retention Anal bleeding	 14(0.8) 6(0.3) 7(0.4) 6(0.3)	 2(3.5) 47(82.5) 6(10.5) 1(1.8)	0.012[c]

Post-Biopsy sepsis, n (%)	0	5(8.8)	0.001[c]
Need for Intensive Care Unit, n (%)	0	4(7)	0.001[c]
Urine culture, n (%) Positive Negative		 15(26.3) 42(73.7)	
Microbiological Details of Urine Culture, n (%) *Escherichia coli* *Klebsiella. p* *Pseudomonas. A* Other		 32(56.1) 4(7) 1(1.8) 5(8.8)	
Blood culture, n (%) Positive Negative		 42(73.7) 15(26.3)	
Microbiological Details of Blood Culture, n (%) *Escherichia coli* *Klebsiella. p* *Pseudomonas. A* Other (Specify ....)		 9(15.8) 1(1.8) 1(1.8) 4(7.0)	
Drug-susceptibility of bacteria isolated from urine culture, n (%) Sensitive Resistant		 34(59.6) 23(40.4)	
Drug-susceptibility of bacteria isolated from blood culture, n (%) Sensitive Resistant		 41(71.9) 16(28.1)	
Blood culture, n (%) No Yes	 1653(94.6) 95(5.4)	 54(94.7) 3(5.3)	0.955[c]
Pathology of biopsy, n (%) BPH Prostate cancer Chronic prostatitis Granulomatous Prostatitis Other	 884(50.6) 763(43.6) 66(3.8) 1(0.1) 34(1.9)	 23(40.4) 22(38.6) 9(15.8) 0 3(5.3)	0.001[c]
Malignancy of biopsy rate, n (%) No Yes	 982(56.2) 766(43.8)	 34(59.6) 23(40.4)	0.603[c]
Biopsy ISUP Grade, n (%) 1 2 3 4 5	 223(29.1) 185(24.2) 93(12.1) 132(17.2) 133(17.4)	 5(21.7) 6(26.1) 0 5(21.7) 7(30.4)	0.226[c]

RRP ISUP Grade, n (%)			0.552[c]
1	47(18.1)	3(37.5)	
2	85(32.8)	3(37.5)	
3	55(21.2)	1(12.5)	
4	37(14.3)	0	
5	35(13.5)	1(12.5)	

Table 2: Baseline characteristics of patients.

Abbreviations: PSA; Prostate specific antigen, BPH; Benign prostatic hyperplasia, RRP; Radical retropubic prostatectomy.

C: Chi-square analysis; T: Student's T-test; M: Mann-Whitney U Test.

Of the 42 prostatitis patients who underwent urine culture had growth; 32 (76.1%) of the growing microorganisms were Escherichia coli. The distribution of microorganisms is given in Table 3.

Microorganisms	n = 42	%
Escherichia coli	32	76.19
Klebsiella pneumoniae	4	9.52
Pseudomonas aeruginosa	1	2.38
Others	5	11.91

Table 3: The distribution of microorganisms' prostatitis patient's urine culture.

Univariate analysis identified Charlson comorbidity index, diabetes mellitus, core number, cardiovascular disease, hypertension, prior biopsy history, and history of urinary tract infection as significant risk factors for infection after prostate biopsy.

Multivariate Cox regression analysis revealed that diabetes mellitus (HR 2.567, 95% CI 1.367-4.821, $p < 0.003$), hypertension (HR 3.842, 95% CI 2.176-6.782, $p < 0.001$), history of urinary tract infection (HR 3.526, 95% CI 1.459-8.518, $p < 0.005$) and core number (HR 1.278, 95% CI 1.095-1.491, $p < 0.002$) were independent predictors of infection after prostate biopsy, as shown in Table 4.

Variable	Univariate model		Multivariate model	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Ageing	0,989 (0.956-1.023)	0.516		
Body Mass Index	1.062 (0.948-1.189)	0.298		
Charlson Comorbidity Index	1.544 (1.295-1.841)	0.001		
Diabetes mellitus	4.050 (2.246-7.303)	0.001	2.567 (1.367-4.821)	0.003
Cardiovascular disease	3.599 (1.977-6.550)	0.001		
Hypertension	4.217 (2.471-7.200)	0.001	3.842 (2.176-6.782)	0.001
Prior biopsy history	2.500 (1.381-4.528)	0.002		
History of urinary tract infection	3.625 (1.582-8.304)	0.002	3.526 (1.459-8.518)	0.005
Antibiotics History	1.420 (0.756-2.670)	0.276		
Alpha-blocker History	2.040 (1.187-3.505)	0.010		
PSA (ng/mL)	1.001 (0.999-1.003)	0.226		
Prostate volume	1.005 (0.998-1.013)	0.171		
PSA Density	1.026 (0.958-1.098)	0.476		
Multiparametric Prostate MRI	1.569 (0.913-2.697)	0.103		
PI-RADS score	1.119 (0.785-1.595)	0.534		
Core number	1.270 (1.091-1.479)	0.002	1.278 (1.095-1.491)	0.002
Core volume	1.004 (1.001-1.008)	0.017		

Table 4: Univariate and Multivariate logistic regression analysis of risk factors for infection after prostate biopsy.

Discussion

TR-PB is the current method of choice for histopathological diagnosis of prostate cancer [11]. Disadvantage of TR-PB is the high post-biopsy infection rate, which was 3.1% in our cohort and is comparable to the available literature. A concerning finding in some studies is a post-procedural infection rate as high as 7% [12].

The number of cores taken in prostate biopsy is also a controversial issue as a risk factor. Naughton., *et al*. found no significant difference between six and twelve fragments in prostate biopsies about morbidities [13]. Raaijmakers., *et al*. additional sample biopsy did not produce any increase in morbidity [14].

In this present study, we found that patients who had prior biopsy before undergoing TR-PB had a greater risk of infection after TR-PB. In addition, Simsir., *et al*. [15] found that an increased number of biopsy cores and a history of previous biopsies were associated with an increased risk of infectious complications following TR-PB. A higher number of samples was associated with an increased risk of infectious complications. A possible explanation for the increased risk of urinary tract infections with a higher number of samples is that each sampling procedure potentially introduced contamination from the rectal ampulla into the prostate.

Diabetes mellitus is a recognized risk factor for developing infectious complications. The presence of diabetes mellitus can create conditions that promote the proliferation of Escherichia coli. It may also cause hypoxia and fibrosis in diabetic prostate tissue, which may increase the chance of infection after TR-PB [16,17]. According to our multivariate logistic regression analysis, patients with a history of diabetes had a significantly higher risk of developing post-biopsy infections.

Comorbidity assessment is important because patients with more comorbidities, decreased overall physical function and impaired immunological function are at increased risk of developing infection after biopsy [18]. In our study, a higher CCI score was significantly associated with an increased risk of infection after TR-PB.

Choi., *et al*. reported an increase in quinolone resistance in recent years [19]. Also, Steensels., *et al*. also showed that quinolone-resistant infections are increasing after TR-PB. Quinolones have been reported to be the most used prophylactic antibiotic before TR-PB [20]. Because of the high prevalence of quinolone resistance in our country, for prophylaxis, cephalosporins group antibiotics (%98) were used instead of quinolone. A history of urinary tract infections may have contributed to the development of a post-biopsy infection. This could be due to the presence of asymptomatic bacteriuria or residual bacteria within the prostate gland. These factors may have increased the patient's susceptibility to a clinical infection following the prostate biopsy procedure. The results of our study, which revealed an elevated risk of post-biopsy infection associated with any antibiotic treatment for UTIs, agree with the findings of a previous research study [21].

This study had several limitations. Two limitations of this study include its retrospective design and the use of data from a single center. Furthermore, the study did not assess the impact of blood glucose control or the specific diabetes treatments received by patients. A large, prospective study is needed to confirm these results.

Conclusions

In conclusion, cephalosporin group antibiotics were used due to the antibiotic resistance epidemiology of our region. There are many risk factors for hospitalization after TR-PB. Our data show that hypertension, diabetes mellitus, history of urinary tract infection and core number are independent risk factors for infection after TR-PB.

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