



Research Article

Is antibiotic prophylaxis still mandatory for transperineal prostate biopsy? Results of a comparative study



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ABSTRACT

Introduction and objectives: This study aimed to assess the incidence of urinary tract infections (UTIs) after transperineal prostate biopsy (TP-PB) comparing patients who underwent antibiotic prophylaxis (AP) with patients who had no prophylaxis.

Materials and methods: This prospective, double-center trial was conducted between August and December 2020. Patient candidates to PB were included with 1:1 allocation to case (Group A-no AP) and control group (Group B-standard AP). All TP-PBs were performed in an outpatient setting under local anesthesia. Data collected 2 weeks after the procedure included incidence of UTIs or bacteriuria, evaluated with a urine culture (UC), main symptoms, and complications related to TP-PBs.

Results: A total of 200 patients were included (100 patients in each group). The mean age was 66.2 ± 7.7 in Group A and 67.4 ± 8 years in Group B ($P = 0.134$). Mean prostate volume was 65.5 ± 26.7 vs. 51 ± 24.6 cc ($P < 0.001$), number of biopsy cores was 17.8 ± 2.4 vs. 14.9 ± 0.8 ($P < 0.001$), and PSA value was 15.9 ± 28.1 vs. 13.3 ± 22.3 ng/ml ($P = 0.017$). Overall PCa detection rate was 55% vs. 59% ($P = 0.567$). Postoperative UTI occurred in one patient in Group A vs. zero in Group B. Asymptomatic bacteriuria was present in 3 vs. 5 patients ($P = 0.470$) and was not treated with antibiotics. Postoperative hematuria was observed in 13 patients vs. 29 ($P < 0.05$), and acute urinary retention was observed in one patient in each group.

Conclusions: The incidence of bacteriuria and UTIs in TP-PBs is not related to AP. Therefore, AP could be discontinued in TP-PB candidates without the risk of increasing UTI-related complications.

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1. Introduction

Prostate biopsy (PB) is the reference exam for Prostate Cancer (PCa) diagnosis and is one of the most common procedures performed in Urology departments. The traditional PB technique is the transrectal (TR) method guided by transrectal ultrasound (TRUS).¹ Despite the rapidity of this procedure and its feasibility in an outpatient setting, many recent pieces of evidence associate TR-PB with increasing rates of infective complications, and up to 5% of

patients undergoing TR-PB need hospitalization due to sepsis.^{2,3} Linder et al documented in a prospective randomized trial 44% incidence of bacteriuria and 16% of bacteremia after TR biopsy in men with preoperative negative urine culture.⁴

A recent systematic review by Loeb S et al.⁵ outlined a recent rise in the incidence of infective complications after TR-PB; data from the Global Prevalence Study of Infections in Urology reported an incidence of febrile urinary tract infection (UTI) of 3.5%, with 3.1% requiring hospitalization after PB.⁶ Recent attention was given after the report of a case of death after TR-PB in a 68-year-old Norwegian man that led to the subsequent local adoption of the TP approach, as the TR one was related to an overall hospitalization rate of 10% for UTIs within the first 60 days after biopsy.⁷

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Moreover, the indiscriminate adoption of empirical fluoroquinolones and combination regimen as standard prophylaxis has led to an increase of antibiotic resistance, therefore worsening the incidence of post-PB UTI.^{8,9} For that reason, different antibiotic schemes are applied in Urologic departments without a specific standardization. As PB is a commonly performed procedure, a high overall volume of antibiotic therapy is delivered to this population.

In alternative to TR, growing evidence supports the routine use of transperineal (TP) prostate biopsy.¹⁰

Despite an apparent longer time of procedure and a steep learning curve for the operator, the TP technique offers several advantages in terms of sampling quality, mostly for the anterior zone of the prostate, and reduces the risk of UTI avoiding passing the needle through the rectal wall.¹¹

The 2021 EAU Guidelines on Urological Infections advise performing a prophylactic antibiotic therapy before prostate biopsy without making a clear division between the TR and the TP technique. However, it is evidenced that the relative risk of UTI is more common in the TR methods, where an additional rectal preparation with povidone-iodine is recommended in association with antibiotic prophylaxis (AP).^{12,13}

Several randomized studies demonstrated a significant incidence of UTI in patients undergoing TR PB without AP (from 5 to 26% of the study population).^{14,15} However, there are only a few data on the incidence of post-PB UTI in patients undergoing TP PB without antibiotics prophylaxis, and no randomized or comparative trials have been reported.

This study aimed to compare the infection rate after TP biopsy in a series of men with or without AP.

2. Material and methods

2.1. Study design

This was a prospective, comparative double-center study carried out between August and December 2020. We enrolled all consecutive patients with clinical indication to prostate biopsy (rising PSA, suspicious MRI finding, or positive digital rectal examination) to select a population of 200 subjects with 1:1 allocation to case and control group. The statistical power of the sample size was considered as 100 for each arm. TP-PB was performed in two urological departments of two Tertiary Hospitals with the same setting, except for the AP, which was administered only in one center. The AP scheme was based on the latest European Association of Urologist (EAU) guidelines 9 and consisted of oral cephalosporin, cefixime 400 mg once a day, for 3 days starting 24 hours before the procedure.

Clinical data were recorded in our database, and all patients underwent a urine culture before the biopsy and 14 days after the procedure. Three weeks after the procedure, all the patients were evaluated in our outpatient clinic to control complications and biopsy-related symptoms, such as UTI (painful micturition, bladder, suprapubic, or renal pain, cloudy and foul-smelling urine), gross hematuria, urethrorrhagia, hematospermia, urinary retention. The study was approved by the local ethical committee all patients signed informed consent, and (Protocol BIO_IVU Version 1.0 – registry number 18582).

2.2. Exclusion criteria

Patients with a clinical history of recurrent UTI or with documented UTI; patients with cardiac mechanical valvular prostheses or with a previous history of endocarditis; patients who did not sign the informed consent.

2.3. Biopsy technique

All TP-PB were performed in an outpatient setting; patients were placed in dorsal lithotomy position with gynecological heel stirrups. All procedures were performed under local anesthesia (Lidocaine hydrochloride 7.5% 10 mL plus Ropivacaine 0.75% 10 mL) administered in the ventral prostatic apical region after disinfection of perineal skin with 10% povidone-iodine solution. In some cases (i.e., anxious or hyperalgesia patients; planned saturation biopsy), intravenous sedation with Midazolam 2 mg was performed. Patients were instructed to have an enema the day before the procedure and have a light breakfast with clear liquids (tea or water) at least two hours before the biopsy.

The procedures were performed by experienced urologists in TP-PB: GMP in the center without AP, and NT or AT in the center with standard AP. TP-PBs were performed by a single-access free-hand ultrasound-guided PB according to Martorana et al.¹⁶ using the BK Pro Focus ultrasound scanner with a 4–12 MHz biplanar rectal probe. A biopsy needle (disposable Bard Monopty 18G × 20 cm) was inserted through a single hole in the midline of the perineum, 1.5 cm from the anus. The number of cores was variable according to the indication (first biopsy; MRI cognitive fusion biopsy; saturation biopsy) and prostate volume.

2.4. Statistical analysis

Statistical analysis was performed with IBM-SPSS v.17 for Windows (IBM Corp, Armonk, NY, USA). Student *t* test and the Mann–Whitney *U* test were performed to compare continuous parametric and nonparametric variables, as appropriate. Continuous variables were reported as mean ± SD. All values in the text are expressed as mean ± SD. Statistically significant results were $P \leq 0.001$. Spearman correlations were used to test for the strength of linear association between variables along with the Wilcoxon and Mann–Whitney.

Power calculation was done, and we estimated that with 100 participants for each arm, the study would have 80% or greater power to detect a mean difference between the group of patients who underwent AP and the group of men without AP, assuming a standard deviation of 2 and a two-sided type I error rate of 0.05.

3. Results

Main patients' preoperative characteristics are presented in Table 1. The only significantly different baseline domains were mean prostate volume (65.5 ± 26.7 mL in Group A vs. 51 ± 24.6 in Group B, $P < 0.001$) and the number of biopsy cores (17.8 ± 2.4 in Group A vs. 14.9 ± 0.8 in Group B, $P < 0.001$), while also mean PSA and positive DRE findings were different among the two Groups. The prostate cancer detection rate was similar (55 vs. 59 cases, $P = 0.569$). Table 2 reports the histologic findings among the two Groups. Only one patient reported a post-PB UTI in Group A, presented with fever and dysuria six hours after the procedure and managed in the outpatient department with oral antibiotics and anti-inflammatory drugs, promptly recovered after five days. The urine culture showed *Escherichia Coli* infection. No similar cases were reported in Group B. The 14-days urine culture reported three cases of asymptomatic bacteriuria in Group A and five cases in Group B ($P = 0.470$). Asymptomatic bacteriuria was not treated with antibiotics. One patient in Group A–no AP developed a febrile urinary tract infection by *E. coli* that was resistant to fluoroquinolones. In patients with asymptomatic bacteriuria, polymicrobial contamination was present in two patients and *E. coli* with no antibiotic resistance in one. In the group Group B–standard AP, five patients developed asymptomatic bacteriuria with the

Table 1
Baseline patients' characteristics

	Group A (n = 100)	Group B (n = 100)	P
Mean age (years)	66.2 ± 7.7	67.4 ± 8	0.134
Anticoagulant or antiplatelet therapy	12	14	0.674
Previous history of urinary tract infection	0	3	–
Diabetes mellitus	14	13	0.836
Positive DRE	31	48	0.013
Mean PSA (ng/mL)	15.9 ± 28.1	13.3 ± 22.3	0.017
Mean prostate volume (mL)	65.5 ± 26.7	51 ± 24.6	<0.001
Mean MRI PIRADS score	3.9 ± 0.9	n.a.	–
Mean biopsy cores (n)	17.8 ± 2.4	14.9 ± 0.8	<0.001

PSA, prostate-specific antigen; DRE, digital rectal examination; MRI, magnetic resonance imaging; PIRADS, prostate imaging reporting and data system.

Table 2
Prostate biopsy histologic findings

	Group A (n = 100)	Group B (n = 100)
Negative (BPH, normal prostate cells)	45	41
ASAP	3	2
GS 6 (3 + 3)	24	11
GS 7 (3 + 4)	15	16
GS 7 (4 + 3)	6	18
GS 8 (4 + 4)	6	3
GS 9 (4 + 5)	1	5
GS 9 (5 + 4)	0	2
GS 10 (5 + 5)	0	1
STUMP	0	1

GS, Gleason score; ASAP, atypical small acinar proliferation; STUMP, stromal tumors of uncertain malignant potential.

following pathogens: *Klebsiella oxytoca* multidrug-resistant in one and *E. coli* resistant to fluoroquinolones in three patients, and polymicrobial contamination was present in one patient. No significant different rate in the other post-PB-reported complications was found between the two groups (Table 3).

4. Discussion

Antibiotic resistance is one of the greatest concerns for the modern healthcare system, both from a clinical and economic point of view.¹⁷ It is estimated to be attributable to at least 300 million excess deaths in the next 35 years.¹⁸ PB is a commonly performed procedure, as it is the mandatory diagnostic exam for the detection of prostate cancer, with around one million PB performed yearly in the United States. A national US study¹⁹ showed a high rate of 30-day hospitalization after PB of 6.9%, significantly higher than the control population, mostly related to UTI. A large case series of TR-PB patients by Zaytoun et al.²⁰ showed that more than half of cases of febrile UTI or septicemia were caused by fluoroquinolone-

Table 3
Complications after TP-PB

	Group A (n = 100)	Group B (n = 100)	P
Clinical UTI	1	0	1
Asymptomatic bacteriuria	3	5	0.470
Gross hematuria	3	5	0.470
Urethrorrhagia	2	1	0.560
Acute urinary retention	3	1	0.312
Hemospermia	12	15	0.534

UTI, urinary tract infection.

resistant pathogens. Therefore, a rising interest is now given to the TP approach.

In the existent literature, few studies investigated the incidence of UTI after TP-PB. One of the main advantages of TP-PB is that the needle passes through the skin, which can easily be prepared in a cleaned fashion, and not through the rectal wall. Therefore, it can be postulated that the standard AP for TR-PB is probably excessive for the TP-PB procedure.

All the available literature found a reduced incidence of UTI with the TP route. Gunzel et al.²¹ recently reported an important series of 766 TP-PBs performed under local anesthesia without any AP. Four patients (0.6%) developed a post-biopsy infection, and one experienced urosepsis. Those results are similar to other TP-PB series in which antibiotics were systematically administered; therefore, the authors concluded that the procedure could be considered safe also without AP.

A review article from a multicentric worldwide urologists' group²² underlines the clear advantages of TP-PB over the TR ones in the prevention of UTI-related events, advocating a "TR-exit" by the end of 2022. The principal advantages over the TRs are reported as reduced bacterial contamination with the consequent reduction in UTIs and better access for the sampling of the anterior zone. Moreover, a recent paper by Marengo Jimenez et al.²³ reported a significantly lower rebiopsy rate after TP-PB compared to TR ones.

The prospective study by Pepdjonovic et al.²⁴ included 577 TP-PB patients that underwent biopsy with a single dose of endovenous cephazolin. The authors did not report any hospital readmission for infective complications, concluding that even single-dose AP was effective for UTI prevention. Different from our study, the procedure was performed under general anesthesia, and they performed a template-guided biopsy, therefore resulting in multiple perineal skin punctures.

Another recent retrospective single-center study²⁵ described a wide series of 2192 TP-PB patients performed in a decade. The authors analyzed the overall incidence of complications, focusing on documented UTI, defined as one of the following events during the 3 weeks after PB: fever ($\geq 38.3^\circ\text{C}$) and/or active urinary tract symptoms such as urgency, frequency, and dysuria with pyuria and/or leukocytosis. The authors found an incidence of infectious complications of 1.87% (41/2192). The multivariate logistic regression analysis of risk factors for UTI showed a positive correlation for patients with diabetes ($P = 0.021$) and history of urinary retention ($P = 0.013$). Even if those findings are relevant, patients were not investigated with urine culture, and the study lacks a control group.

Other recent retrospective TP-PB series documented the feasibility of TP-PB without AP. Sigle A et al.²⁶ documented only two cases of febrile UTI over a 184 patients' population (1.08%); Szabo RJ²⁷ reported a similar series of 242 TP-PBs in which 212 (88%) did not receive any prophylaxis. The Author documented no cases of sepsis and only one case of perineal abscess (0.4% of total).

Castellani D et al.²⁸ presented a Systematic Review and Meta-Analysis of comparative studies in which TP-PB was performed with or without antibiotics, reporting a similar pooled rate of UTI after TP-PB, estimated to 0.11% in the AP group and 0.31% in the group without AP (RR: 2.09, 95% CI: 0.54–8.10, $P = 0.29$).

All the existing data reported on TP-PB performed without AP are in line with our findings. Indeed, our data supported that performing TP-PB without any AP was safe. Our research, for the first time, has provided data on this topic through a comparative study, and this has been its strength and originality. Patient outcomes were not significantly different for UTI-related complications and symptoms, regardless of the use of AP. Therefore, we documented that the influence of AP in the prevention of UTI and related complications was not relevant. Positive urine culture samples after TP-PB were comparable between the two study groups, with

irrelevant numbers of bacteriuria that was also found in the control group. Thus, asymptomatic bacteriuria seems not to be related to the administration of standard AP. This was a comparative study and not a randomized trial; this is the main limitation of our research. However, our data represent a further step after the initial results on this item from noncomparative and nonrandomized studies. Our data open the door to the changing of an established “paradigm” in terms of PB AP. Moreover, this can be another strong point in favor of the adoption of the TP approach rather than the TR one. Indeed, avoiding AP is only safe and feasible by performing TP-PB. Increased use of TP-PB without AP, instead of the TR-PB which requires it, would have a major impact on reducing the worldwide annual administration of antibiotics. Indeed, the worldwide number of prostate biopsies per year is enormous and, consequently, the related use of antibiotics for prophylaxis.

5. Conclusions

This was the first comparative study that evaluated the TP-PB in two groups of patients with the same setting, except for the administration of AP. We demonstrated that TP-PB without AP was safe. AP did not have a relevant impact on postprocedure UTI and related complications. Wider use of TP-PB without AP would critically reduce the unnecessary administration of antibiotics worldwide.

Conflicts of interest

All Authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Key of definitions for abbreviations

AP	Antibiotic prophylaxis
PB	Prostate biopsy
PCa	Prostate cancer
PSA	Prostate-specific antigen
TP	Trans-perineal
TR	Trans-rectal
UTI	Urinary-tract infections

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