

Comparison of Bacteriuria, Hematuria, and Pain Complications after Transrectal and Transperineal Prostate Biopsy in Patients with Suspected Prostate Cancer

Kurnia Penta Seputra¹, Harry Achsan Chaerul¹, Besut Daryanto^{1*}, Dewi Santosaningsih², Khairul Asri Mohd Ghani³

¹Department of Urology, Faculty of Medicine Universitas Brawijaya, Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia, 65112

²Department of Clinical Microbiology, Faculty of Medicine Universitas Brawijaya, Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia, 65112

³Department of Urology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia, 43400

*Corresponding Author

Besut Daryanto

Department of Urology, Faculty of Medicine Universitas Brawijaya, Dr. Saiful Anwar General Hospital, Malang, Indonesia, 65112

Email: urobes.fk@ub.ac.id

Introduction. Prostate cancer is the most common cancer in men with the second-highest mortality rate in the United States. In Indonesia, 1,102 patients with an average age of 67.18 years have been diagnosed with prostate cancer in the last 8 years. The primary diagnostic approach for prostate cancer involves two biopsy methods: transrectal prostate biopsy (TRPB) and transperineal prostate biopsy (TPPB). This study aims to evaluate the complications of bacteriuria, hematuria, and pain levels after the procedures between TRPB and TPPB.

Methods. This study is an analytical observational study with a cohort design. The sample consists of 34 patients suspected of prostate cancer, undergoing prostate biopsy with a 1:1 technique comparison between TPPB (17) and TRPB (17). Data were analyzed using SPSS software version 28.

Result. The Friedman test and paired T-test results show a significant difference in urine culture and urinalysis before and after transrectal biopsy, but no significant difference in pain assessment. For transperineal biopsy, a significant difference was only found in pain assessment before and after the biopsy. The Mann-Whitney test results show a significant difference in the incidence of bacteriuria and hematuria, with TPPB showing lower rates and higher VAS in the TPPB group.

Conclusion. TPPB tends to be better at avoiding the risk of bleeding and infection complications, while TRPB is better at avoiding pain. Therefore, TPPB is more beneficial for patients.

Keywords: bacteriuria, hematuria, pain, prostate biopsy

Introduction

Prostate cancer is the most common cancer in men and ranks as the second-highest cause of death in the United States. In Indonesia, the number of prostate cancer patients in three central education hospitals in Jakarta, Surabaya, and Bandung, over the last 8 years are 1,102 patients with an average age of 67.18 years [1].

There are two principles in approaching the diagnosis of prostate cancer, namely transrectal prostate biopsy (TRPB) and transperineal prostate biopsy (TPPB) [2]. Transrectal prostate biopsy has become the most commonly used technique because it saves time with relatively few invasive side effects, and it is performed as a standard procedure in many countries. On the other hand, the TPPB approach requires a longer procedure time as it is traditionally done under general anesthesia or total anesthesia. Although generally considered a

safe and well-tolerated procedure, post-biopsy complications are reported to occur in 50% of cases, including pain, hematuria, hematospermia, urinary retention, and infection [3].

Until now, the superiority of one method over another remains debated. Potential drawbacks of the TRPB approach include an increased risk of urinary tract infections (UTIs) and fever after the procedure. On the other hand, transperineal prostate biopsy (TPPB) was associated with an increased rate of post-procedure urinary retention [4]. In Indonesia, a study was conducted in 2019 comparing TRPB and TPPB in terms of examination duration, pain perception, and complications. The results of the study indicated that hematuria and rectal bleeding were more prevalent in TRPB compared to TPPB [5]. However, there is still no study comparing urinary tract infection complications after TRPB and TPPB procedures in Indonesia. Based on these

considerations, this research aims to evaluate bacteriuria complications, hematuria assessed through urine culture, and post-procedure pain in patients suspected of prostate cancer who underwent biopsy via both transrectal and transperineal approaches.

Materials and Methods

The research design employs an analytical observational design with a cohort approach. The study took place at Dr. Saiful Anwar Malang General Hospital from May 2023 to October 2023 with a suspected diagnosis of prostate cancer patients who are planned to undergo transperineal (TPPB) and transrectal (TRPB) biopsy procedures. Inclusion criteria include (a) Patients diagnosed with suspected prostate cancer receiving treatment in the outpatient or inpatient Urology Department at Dr. Saiful Anwar General Hospital Malang during the study period and planned for biopsy; (b) Patients with normal vital signs before the biopsy procedure; (c) Patient with or without previous urinary tract infection who received antibiotic therapy for 7 days before urine culture specimen collection; (d) Patients willing to participate in the study and sign the informed consent after receiving an explanation.

Each patient will undergo urine culture examination to identify bacteriuria, urinalysis to identify hematuria and bacteriuria, and VAS score to identify the pain scale before undergoing TPPB and TRPB procedures. After that, one day after the procedure, another VAS score examination will be conducted, and seven days after the procedure, urinalysis and urine culture examinations will be performed again. In this study, a comparative analysis will be conducted on bacteriuria, hematuria, and pain scale based on the visual analogue scale (VAS) before and after underwent prostate biopsy through transrectal (TRPB) and transperineal (TPPB) approaches.

Result

Study Characteristics

In this study, there were a total of 34 patients who met the criteria with a 1:1 ratio, consisting of 17 cases of patients who underwent transrectal biopsy and 17 cases of patients who underwent transperineal biopsy.

The group of subjects undergoing transperineal biopsy (TPPB) has an average age of 65 years,

while transrectal biopsy (TRPB) has an average age of 66 years. Regarding complaints before the procedure, the majority of subjects experienced only urinary retention, totaling 18 subjects (52.9%). This was followed by subjects experiencing only Lower Urinary Tract Symptoms (LUTS) with 12 subjects (35.3%), and subjects experiencing both urinary retention and LUTS with 2 subjects (5.8%) (Table 1).

Table 1. Subject characteristics

Characteristic	Mean ± SD or Sum (Percentage)
Age (n=34)	
TPPB	65 ±4.1 years old
TRPB	66 ± 10.7 years old
Pre-procedure complaints (n=34)	
Urine retention	18 (52.9%)
LUTS	12 (35.3%)
Both	2 (5.8%)
Others	1 (2.9%)
No Data	1 (2.9%)

Urinalysis examination seven days after the transperineal in Table 2 showed that all urine samples indicate sterile urine in the group of patients who underwent transperineal biopsy. Meanwhile, in the group of patients underwent transrectal biopsy, urine culture examination seven days after the transrectal biopsy revealed that 7 subjects (41.2%) had bacteriuria, including *Escherichia coli* (7 patients, 100%), *Enterobacter cloacae* (1 patient, 14.3%), and *Pseudomonas aeruginosa* (1 patient, 14.3%).

Table 2. Proportion of bacteriuria post TRPB and TPPB procedure among subjects

Procedure	Bacteriuria (%)	Total	Proportion
TPPB	0 (0.00)	17	0.000
TRPB	7 (41.18)	17	0.412

Urinalysis examination seven days after the transperineal in Table 3 showed non-hematuria results in the group of patients who underwent transperineal biopsy. Meanwhile, in transrectal biopsy, 6 subjects (35.3%) had hematuria.

Table 3. Proportion of haematuria post TRPB and TPPB procedure among subjects

Procedure	Haematuria (%)	Total	Proportion
TPPB	0 (0.00)	17	0.000
TRPB	6 (35.3)	17	0.353

In the group of patients underwent transperineal biopsy, the Visual Analogue Score (VAS) values were distributed in the range of VAS 1 to 2, while in the group of patients underwent transrectal biopsy, the VAS values for patients were in the range of VAS 1 to 3. One day after the procedure, the VAS values increased in the transperineal biopsy group, while VAS values decreased in the other group.

Post TPPB Analysis

Table 4 demonstrated that among the 17 patients who underwent transperineal biopsy, there was a significant difference in the VAS score (p-value=0.001) but not in the incidence of hematuria (p-value=1.000) or bacteriuria (p-value=1.000).

Table 4. Characteristics of pain among subjects

Characteristic	Pre-procedure	Post-procedure
TPPB	range: 1-2	range: 1-5
VAS 1	8 (47.0%)	1 (5.88%)
VAS 2	9 (52.9%)	6 (35.3%)
VAS 3	0 (0%)	0 (0%)
VAS 4	0 (0%)	4 (23.6%)
VAS 5	0 (0%)	5 (29.4%)
TRPB	range: 1-3	range: 1-2
VAS 1	5 (29.4%)	11 (64.7%)
VAS 2	10 (58.8%)	6 (35.3%)
VAS 3	1 (5.9%)	0 (0%)

Post TRPB Analysis

The incidence of bacteriuria varied significantly amongst the 17 individuals who had transrectal biopsies (p-value=0.008). Furthermore, of the seven patients with bacteriuria, three also had fever, while the other four showed no symptoms. Additionally, there was a significant difference in the incidence of hematuria (p-value=0.014), although there was no significant difference in the VAS score before and after the biopsy process (p-value=0.072) (Table 5).

Table 5. Comparisons of bacteriuria, haematuria, and pain before and after TPPB procedure

Complication	Pre-Procedure	Post-Procedure	p-value
Bacteriuria	0 (0%)	0 (0%)	1.000*
Haematuria	0 (0%)	0 (0%)	1.000*
Pain (VAS Score)	1.59	3.24	0.001*

*Friedman, significant <0.05

**Paired T-Test, significant <0.05

Analysis of Differences in Post Procedure Complications Between TPPB and TRPB

Table 6 presents that there was a significant difference between two groups in the comparison of bacteriuria incidence, hematuria incidence, and VAS score (p-value=0.003, p-value=0.007, p-value=0.001).

Table 6. Comparisons of bacteriuria, haematuria, and pain before and after TRPB procedure

Complication	Pre-Procedure	Post-Procedure	P value
Bacteriuria	0 (0%)	7 (41.18%)	0.008*
Haematuria	0 (0%)	6 (35.30%)	0.014*
Pain (VAS Score)	1.71	1.24	0.072**

*Friedman, significant <0.05

**Paired T-Test, significant <0.05

Discussion

This study shows a difference in age between the two groups of subjects and depicts that age plays a significant role in the risk of prostate cancer [6]. Prostate cancer is very rare in men under the age of 40, and the incidence of prostate cancer dramatically increases after the age of 55. This finding is also observed in the global scale of prostate cancer rates, both in less developed and developed countries [7].

In this study, the majority of subjects experienced urinary retention as their main complaint, followed by lower urinary tract symptoms (LUTS), and 2 patients who experienced both urinary retention and LUTS. In a cohort study of 68 patients underwent transperineal procedures and 66 patients underwent transrectal procedures in 2017, significant LUTS symptoms were also found in the sample characteristics (p-value <0.05) [8].

This can occur because the growth of prostate cancer cells can block the urethra or compress the bladder, hindering the flow of urine from the bladder out of the body. Additionally, structural changes caused by prostate cancer can damage the structure of the urethra and bladder, making it less elastic or narrower. This can obstruct the flow of urine [9].

Surgical therapy becomes necessary when medical therapy does not yield satisfactory results. All urology experts are aware that older men experiencing acute urinary retention and subsequently underwent Transurethral Resection of the Prostate (TURP) can sometimes be diagnosed with prostate cancer based on the pathology of the removed prostate. The exact frequency of cancer varies from one study to another but typically ranges between 5-10%.

LUTS can result from pressure on the bladder, where the growth of prostate cancer can cause an increase in bladder pressure. This can lead to the bladder contracting more frequently and more forcefully, resulting in LUTS symptoms such as frequent urination and urgency (a strong urge to urinate). Additionally, prostate cancer often causes partial narrowing or obstruction of the urethra as the enlarged prostate gland compresses the urethra. This can disrupt urine flow and lead to symptoms such as weak urine stream, difficulty initiating urination, or a feeling of incomplete bladder emptying [2].

Analysis After TPPB Procedure

The results of this study show an incidence rate of bacteriuria in patients underwent TPPB of 0% (n=0/17). These results also indicate no significant difference between pre- and post-TPPB procedure. Bacteriuria was assessed from urine culture results on the 7th day after the TPPB procedure. This finding aligns with other studies that demonstrate no incidence of post-TPPB bacteriuria in 114 patients [10]. A similar scenario was found in another comparative study of 200 patients who underwent TPPB, where only 8 out of those 200 were proven to have bacteremia after TPPB [11]. Theoretically, TPPB has an advantage in preventing cross-contamination caused by bacteria in the rectal mucosa, as the TPPB procedure involves the needle penetrating the previously disinfected skin [12].

In this study, it was found that out of 17 patients who underwent TPPB, none experienced hematuria post the TPPB procedure. Due to this, the difference between pre- and post-procedure is not significant. The results of this study align with another conducted by Bass et al [13], where out of

131 patients underwent TPPB, none reported hematuria complaints. However, some other studies reported incidents of post-procedure hematuria. Jones et al. found an incidence of patients with hematuria requiring irrigation to be 1% (n=4/402) (14). Another study reported a hematuria incidence of 5.3% (n=7/130) post TPPB [12]. On the other hand, a study conducted on patients taking anticoagulant and antiplatelet drugs experienced hematuria incidences of 76.5% and 47.5%, respectively [10].

Hematuria occurring after prostate biopsy is caused by the mechanical trauma from the use of biopsy needles inserted into the prostate gland and surrounding tissues [15]. In theory, TRPB has a higher risk of bleeding compared to TPPB because the rectum has many blood vessels. This bleeding can be avoided by performing TPPB [5].

Patients undergoing TPPB in this study reported a pain level with an average VAS of 3 from the score 1-5. The pain level was assessed one day after the TPPB procedure. Several other studies also show similar results regarding the pain levels perceived by patients after the procedure. A study conducted by Huang et al [12], showed VAS 3 from the score 2-4, assessed immediately after the procedure. In another study by Marra et al [16], the researchers found that the VAS reported by patients reached the number 5 from the score 3-6. This is suspected because the researchers used a multiple puncture technique, causing the pain scale to increase. The use of a biopsy gun in the TPPB procedure to penetrate the sensitive skin of the perineum and the neurovascular bundle surrounding the prostatic capsule causes intense and often unbearable pain. General or spinal anesthesia may be required when this procedure is performed without adequate pain control and sedation [12]. Low pain scores can be achieved using coaxial needles to avoid sampling from multiple points. Several studies have also demonstrated that the use of coaxial needles results in milder pain and shorter procedure times [17].

Analysis after TRPB Procedure

This study found that 7 out of 17 patients underwent transrectal biopsy significantly experienced bacteriuria, with an incidence of 41.1%. Additionally, 3 patients reported fever, and 1 person had a urinary tract infection. Urine culture results on the 7th day also showed significant bacterial growth, with *Escherichia coli* (n=7), *Pseudomonas aeruginosa* (n=1), and *Enterobacter cloacae* (n=1) found in the seven patients with bacteriuria. Some previous studies have shown high

rates of bacteriuria after TRPB procedures. A quite significant difference was found in a comparative study between urine cultures of patients who underwent TRPB and a control group, with percentages of 5.4% and 0.9%, respectively. This study also found that 8.8% of bacterial urine cultures in patients had resistance to Fluoroquinolone. An epidemiological study conducted by Bennett et al [19] stated that the prevalence of asymptomatic bacteriuria after TRPB in Asia was 7.3%. Another systematic review also found a bacteriuria incidence rate of 18% in patients given single-dose prophylactic antibiotics [20].

TRPB carries a high risk of complications, such as bacteriuria, because the biopsy needle used in TRPB contacts the rectal mucosa. The rectum itself is rich in vascularity, so TRPB can introduce pathogenic microbes from feces into the bloodstream easily through the puncture wounds in the rectal wall formed during the procedure [5]. This high infection rate is suspected due to the increasing prevalence of antibiotic-resistant bacteria, such as Enterobacteria resistant to Fluoroquinolones, Carbapenems, and multiple drugs, including *Escherichia coli* and *Bacteroides* [21]. *Escherichia coli* is a major cause of urinary tract infections, as evidenced in this study where all samples contained *E. coli* (100%). This is because *E. coli* bacteria have many virulence factors contributing to their ability to cause disease. The most common surface virulence factor is fimbriae, such as type 1 fimbriae and P fimbriae. The presence of these fimbriae helps in adhesion to the host cell surface (uroepithelium), tissue invasion (most crucial in the pathogenesis of Uropathogenic *Escherichia coli* (UPEC) causing urinary tract infections), biofilm formation, and induction of cytokines [22-24].

The incidence of post-TRPB procedure hematuria was 35.3% (6 of 17 patients). This result showed a significant increase compared to the pre-procedure condition. However, this finding is lower than in previous studies, where in a cohort study with a large number of patients underwent TRPB procedures, the incidence of hematuria was reported to be up to 65.8% within 35 days, but only 6.2% found it bothersome [15]. Another study by Huang et al [12] found a hematuria incidence rate of 13.8% seven days after the procedure. In a prospective cohort study, the estimated incidence of hematuria was 20% after 14 days post-biopsy [25].

According to Loeb et al [26], hematuria is a common complication following TRPB procedures, with the incidence percentage ranging between 10-84%, depending on the definition of hematuria,

duration, and data collection methods. Moreover, higher figures are observed in studies applying doctor-patient interview methods compared to retrospective questionnaire approaches. The influence of the number of biopsies on the incidence of hematuria is still debated, as one study indicates that the number of core biopsies does not significantly affect the incidence of hematuria, while other research reports an increase in hematuria rates in line with the addition of core biopsy numbers [15, 27-28].

The average VAS reported by patients in this study was 1. Pain intensity was also assessed one day after the procedure. This result is lower than in previous studies, where VAS in TRPB patients was around 3. The difference lies in the duration of VAS data collection in that study, which was immediately after the procedure [12]. Similar results were found in another study comparing patients willing and unwilling to undergo TRPB, reporting VAS of 3 and 5, respectively, one month after the procedure [29]. On the other hand, a study by Sivaraman et al [17], showed similar results, with a VAS of 1 from the scale of 0-6.

Pain involves various factors. In the context of prostate biopsy, pain can be influenced by various aspects, such as individual characteristics and the type of anesthesia used. Additionally, to minimize unnecessary treatment and side effects in prostate cancer treatment, active surveillance often requires periodic prostate biopsies. Lack of compliance with scheduled biopsies has also been shown to be a factor that can cause pain [29]. During the biopsy process, pain can occur at several stages, such as when inserting the probe, performing periprostatic infiltration, and taking biopsy samples, and this pain can last for several hours afterward [26]. Some previously reported predictors of pain include anorectal compliance, younger age, prostate volume, number of biopsy cores, and lateral decubitus position, which may affect blood flow in the prostate. Anxiety is also an important factor to consider, especially in younger patients [15].

Post-analysis of Complication Differences after TPPB and TRPB Procedures

The most significant difference in complications after TPPB and TRPB lies in the incidence of post-procedural bacteriuria, with incidences of 0% and 41.1%, respectively. Urine culture results from 7 patients who underwent TRPB also showed the growth of *E. coli* bacteria, while in TPPB, all samples remained sterile. Patients undergoing TRPB also reported additional

complaints related to bacteriuria, such as fever and urinary tract infections (UTI), which were not observed in patients underwent TPPB. All patients received management according to their symptoms.

As discussed earlier, TRPB poses a higher risk of causing bacteriuria and other infections because, in the process of TRPB, the biopsy needle initially contacts the rectal mucosa. The rectal wall is rich in blood vessels, facilitating the entry of bacteria into the bloodstream [5]. This can be prevented by performing biopsies using the transperineal technique because, in TPPB, the skin can be disinfected beforehand, minimizing the infection rate [12].

Furthermore, the difference in the incidence of bacteriuria between TPPB and TRPB may be influenced by the choice of prophylactic antibiotics in the two different groups. In TPPB, all patients were given prophylactic Gentamicin 160 mg, while many patients undergoing TRPB were given Ciprofloxacin prophylaxis 1000 mg. Both groups were not given any additional antibiotics. A study found that *E. coli* is more resistant to Ciprofloxacin than Gentamicin [30]. Moreover, the administration of a single antibiotic may have a higher risk of infection compared to the administration of combination antibiotics [31]. On the other hand, the prevalence of drug-resistant bacteria is higher in developing countries, making prophylactic antibiotic administration less effective in patients undergoing TRPB [14].

Another complication that showed a significant difference is hematuria, with results of 35.3% and 0% in the TRPB and TPPB groups, respectively. These results indicate a lower incidence compared to a study by Halfian et al [5], where the incidence of hematuria in TRPB patients was 30% (n=3/10), while in the TPPB group, it was 20% (n=2/10). Similar results were also found in a cohort study from 2021 to 2022, where patients underwent TRPB had a much higher incidence of hematuria compared to TPPB, with 66.8% (n=13/283) and 48.8% (n=340/513), respectively [32].

In general, bleeding and hematuria can resolve on their own without treatment, but in patients taking blood thinners, complaints can be more severe [10]. A study conducted in 2012 found a weak but significant influence of Aspirin on the risk of post-biopsy hematuria. However, the results for Warfarin did not have an independent effect on hematuria [29]. On the other hand, a study on the effects of anticoagulants and antiplatelets in patients undergoing TPPB found no significant difference between the two groups in the incidence of hematuria [10]. Unfortunately, in this study, data

on the use of blood thinners were not collected from the patients.

Another significant difference in complications is the pain scale perceived by patients, where those undergoing TPPB reported higher VAS values (3; 1-5), while those undergoing TRPB experienced almost no pain complaints. This study's results align with one systematic review, where TPPB patients reported more post-procedural pain complaints [9]. However, these findings differ from a study by Halfian et al [5], where researchers found no significant difference between the two methods. Pain during the biopsy procedure originates from two sources: when the TRPB probe is inserted into the rectum, innervated by pudendal nerve branches below the linea dentate inferior rectal, and during multiple needle punctures into the prostatic capsule, innervated by autonomic branches of the neurovascular bundle (NVB) between the posterolateral part of the prostate and the rectum [5]. The perineum is theoretically a sensitive area, and the neurovascular bundle surrounding the prostatic capsule can cause intense pain when penetrated by the biopsy needle. General anesthesia or spinal anesthesia may be required when performing this procedure without proper pain control and sedation [12]. The choice of anesthesia technique also influences the postoperative pain scale. Local anesthesia procedures involving pudendal nerve blocks show lower postoperative pain effects. On the other hand, prostate biopsy procedures using general anesthesia rarely involve pudendal nerve blocks [33]. This may impact the postoperative pain results in this study, where TPPB patients underwent general anesthesia while TRPB procedures only used local anesthesia.

In general, TPPB can be chosen to avoid patients from the risk of bleeding and infection complications, while TRPB spares patients from experiencing pain (10).

A key limitation of this study lies in the presumed sterility of the urine in patients who underwent a 7 days course of prophylactic antibiotics prior to culture collection. Relying on empiric prophylaxis without establishing a baseline negative culture post-treatment introduces significant clinical risk, particularly in patients with an active UTI. In such cases, persistent bacterial colonization or antimicrobial resistance may compromise efficacy. Consequently, performing a biopsy without definitive microbiological confirmation of sterility increases the risk of severe post procedural infectious complications.

Conclusion

From the study results, it can be concluded that TRPB and TPPB have different side effects. Thus, TPPB is more beneficial for the patients. Recommendations for future research include considering the use of a larger sample, controlling for other variables that have the potential to influence the variable being tested, and understanding the long-term impact of the variables under investigation. It is suggested to continue monitoring participants for a longer period to gain deeper insights into the relationship between research variables and observed outcomes.

Conflict of Interest

The authors define no conflict of interest.

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