COMPLICATION AND SAFETY OF TRANSPERINEAL PROSTATE BIOPSY USING NOVEL AFFORDABLE VY PROBE (TPPB-VY) IN CLINICAL PRACTICE : A PILOT STUDY

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ABSTRACT

Objective: *This study was aimed to know the complication and safety of TPPB-VY in clinical practice.* ***Material & Methods****: TPPB were performed in 34 patients between January 2019 and Juni 2021. Ethical approval of this study was sought from the hospital authorities (IRB number: LB.02.01/X.6.5/ 55/2020). Patients underwent systematic 10-12 core TPPB depend on the prostate volume with intravenous light sedation. The patient was included to the study if PSA ≥ 4 ng/ml and/or Digital Rectal Examination (DRE) results suggestive of prostate cancer. Procedures were performed without any antibiotic prophylaxis or an enema before the procedure and post procedure the patients just get an oral fluoroquinolones and low potent analgetics (if needed). The complication include pain level post procedure (using VAS), perineal hematoma, fever and retention post biopsy were recorded.* ***Results:*** *In all, 34 patients were included in the study. The result showed that perineal pain perceived by patients post procedure were 76.47% (26 out of 34 patients) but the VAS score just mild around 0-2. There were 23.53% (8 out of 34 patients) hematuria, 5.88% (2 out of 34 patients) acute urinary retention and 2.9 % (1 out of 34 patients) perineal hematoma. No fever or clinical infection was observed and 82.35% (28 out of 34 patients) patients presented with minor complications (ClavienDindo I). Only one of the patients were hospitalized due to the post-biopsy complication that need intervention.* ***Conclusion:*** *This is the first study TPPB using Novel Affordable VY probe. The results show clinically insignificant complication without infection. TPPB using Novel Affordable VY probe is feasible and safe.*

Keywords: *TPPB-VY, prostate cancer, VY probe, complications, safety.*

ABSTRAK

Tujuan: *Penelitian ini bertujuan untuk mengetahui komplikasi dan keamanan TPPB-VY dalam praktek klinis.* ***Bahan & Cara:*** *TPPB dilakukan pada 34 pasien antara Januari 2019 dan Juni 2021. Persetujuan etik penelitian ini diminta dari otoritas rumah sakit (nomor IRB: LB.02.01/X.6.5/55/2020). Pasien menjalani TPPB 10-12 inti sistematis tergantung pada volume prostat dengan sedasi ringan intravena. Pasien dimasukkan ke penelitian jika hasil PSA ≥ 4 ng/ml dan/atau Digital Rectal Examination (DRE) menunjukkan kanker prostat. Prosedur dilakukan tanpa profilaksis antibiotik atau enema sebelum prosedur dan pasca prosedur pasien hanya mendapatkan fluoroquinolones oral dan analgetik potensi rendah (jika diperlukan). Komplikasi meliputi tingkat nyeri pasca prosedur (menggunakan VAS), hematoma perineum, demam dan retensi pasca biopsi dicatat.* ***Hasil:*** *Secara keseluruhan, 34 pasien dilibatkan dalam penelitian ini. Hasil penelitian menunjukkan bahwa nyeri perineum yang dirasakan oleh pasien pasca prosedur adalah 76.47% (26 dari 34 pasien) tetapi skor VAS hanya ringan sekitar 0-2. Terdapat 23.53% (8 dari 34 pasien) hematuria, 5.88% (2 dari 34 pasien) retensi urin akut dan 2.9% (1 dari 34 pasien) hematoma perineum. Tidak ada demam atau infeksi klinis yang diamati dan 82.35% (28 dari 34 pasien) pasien mengalami komplikasi ringan (ClavienDindo I). Hanya satu pasien yang dirawat di rumah sakit karena komplikasi pasca-biopsi yang memerlukan intervensi.* ***Simpulan:*** *Ini adalah studi pertama TPPB menggunakan probe Novel Affordable VY. Hasilnya menunjukkan komplikasi yang tidak signifikan secara klinis tanpa infeksi. TPPB menggunakan probe Novel Affordable VY layak dan aman.*

Kata kunci: *TPPB-VY, kanker prostat, pemeriksaan VY, komplikasi, keamanan.*

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INTRODUCTION

Prostate cancer is one of the most common cancers in men. In the United States, prostate cancer is ranked as the third leading cause of cancer death. In 1990, an estimated 160.000 men were diagnosed with prostate cancer. One of the main problems that may be found in prostate cancer patients is the

invisible course of the disease, in which only about 30-40% of patients presented with a tumor that was still located in the prostate while the rest presented with a more advanced stage.[1-2]

TransRectal Prostate Biopsy (TRPB) is the standard examination in diagnosing prostate cancer. However, this procedure carries a high risk of complications, with approximately 50% of patients receiving biopsy using this method experienced complaints of hematuria, rectal bleeding, and acute urinary retention after the procedure. Other serious complications, such as anemia and fainting, may be present, although were rarely found. This procedure also carried a risk of sepsis, which was believed to be caused by direct inoculation of bacteria from the rectal mucosa by the biopsy needle into the prostate, blood vessels, or urinary tract.[3]

Another diagnostic method of biopsy approach should be considered because of the high risk of complications using TRPB.[3] Approximately one million prostate biopsies are performed annually in the United States. The incidence of clinical infection post-TRPB was also increased, possibly due to quinolone antibiotic resistance.[4]

In order to reduce the rates of complications in patients undergoing prostate biopsy, an alternative biopsy approach should be considered. A TPPB has been proposed as an alternative to TRPB. Research by Xiang et al. found that the TPPB reduced the rate of complications that occurred after biopsy (such as fever and rectal bleeding) compared to TRPB with approximately the same level of accuracy.[5] Despite the safety and low morbidity of such procedure, possible complications should be promptly assessed.[6]

OBJECTIVE

This study aimed to discover the complications and safety of novel affordable VY probe in clinical practice. To the authors' knowledge, this is the first study of a TPPB using Novel Affordable VY probe.[7]

MATERIAL & METHODS

This study was an observational, analytic, retrospective research investigating the complications and safety of the TPPB procedure. Data of patients who underwent TPPB in Hasan Sadikin Academic Medical Center between January 2019 and June 2021 were collected from the urology unit's database and medical records. Patients with PSA level ≥ 4 ng/ml and/or DRE results suggestive of prostate cancer who underwent TPPB with a minimum of 7 days follow-up period were included in the study. Patients with incomplete or grossly inadequate data were excluded from the study.

Patients underwent systematic (12 core), or combined (targeted + systematic) TPPB. Procedures were performed without any antibiotic prophylaxis or an enema before the procedure. After the procedures, patients were only given oral fluoroquinolones and low potent analgesics. Histopathology result was used to confirm the diagnosis of prostate cancer in this study. Patient demographics, estimated prostate volume, PSA level, and complications of this procedure such as perineal pain (measured with visual analogue scale (VAS) score), hematuria, fever, perineal hematoma, and urinary retention post biopsy were collected.

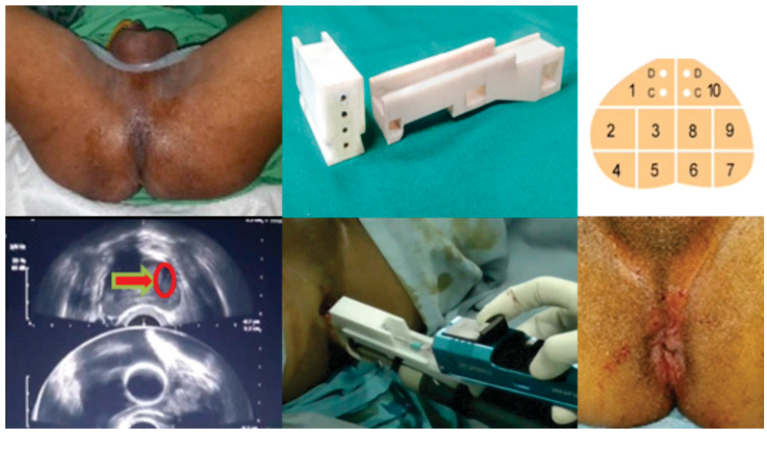

Figure 1. TPPB using Novel Affordable VY Probe. A) Patient position for biopsies. B) VY probe. C) Mapping Prostate Biopsy. D,E) Hypoechoic lesion on left anterior prostate. F) Post TPPB biopsy without perineal hematoma.

RESULTS

There were 34 patients receiving TPPB in Hasan Sadikin Academic Medical Center between January 2019 and June 2021. All patients met the inclusion criteria and none were excluded from the study. Characteristics of study subjects are presented in Table 1.

The mean age of the study population was 65.32 ± 8.5 years (range 49-85). Among a total of 34 study subjects, 26 (76.47%) had TRUS-visible lesions, while the remaining 8 had no lesion (23.53%). The mean age, prostate volume, PSA level, and operation time of patients in the group with TRUS-visible lesion and without TRUS-visible lesion group are reported in Table 1. Differences in age and prostate volume were not significant between both groups ($p>0.05$, analyzed with independent t-test and Mann Whitney, respectively), thus both groups were comparable in terms of patient age and prostate volume.

The mean serum PSA level in the group with lesion (149.67 ± 327 ng/mL), albeit higher, was also not statistically significant compared to the without lesion group (23.17 ± 20.56 ng/mL) (analyzed with Mann Whitney test, $p =0.255$). The difference in duration of operation number of biopsy cores between both groups were not statistically significant (analyzed with independent t-test, $p=0.22$ and chi-square test, $p=0.20$, respectively). As many as 8 patients (23.53%) received only systematic biopsy, 0 patient received only targeted biopsy, while the remaining 26 patients (76.47%) received a combination of systematic and targeted biopsy. A statistically significant difference between proportion of biopsy method was found, with lesions found in 26 patients (76.47%) using combination of systematic and targeted biopsy, while no lesions was found in patients using targeted method or systematic method only (Fisher exact test, $p<0.001$). Of the 34 men who underwent TPPB, 12 (35.29%) were diagnosed with prostate cancer.

The severity of prostate biopsy complications was assessed using the Clavien–Dindo classification (Table 2), which consisted of 5 different grades.

Table 2. Complication classified according to modified Clavien-Dindo classification.

Grade	Complication
1	Perineal pain Hematuria Urinary retention Perineal hematoma Urinary tract infection
2	Intraoperative hemorrhage Urinary tract infection with signs of bacteremia
3	Complications requiring surgical, endoscopic or radiological intervention
4	Life threatening complications (including CNS complications)
5	Death

In this study, a total of 28 study subjects (82.35 %) presented with minor complications (ClavienDindo I). Documentation of complications, presented in Table 2, showed that perineal pain post procedure was perceived by 76 % of patients (26 out of 34 patients). However, the range of VAS score

Table 1. Characteristics of study subjects.

Characteristics	Hypoechoic Lesion	No lesion
Patients (n (%))	26 (76.47)	8 (23.53)
Mean age (y)	67.08 ± 7.531	59.63 ± 9.471
Mean prostate volume (mL)	55.19 ± 31.45	76.16 ± 59.4
Mean PSA (ng/mL)	756.29 ± 1878.33	32.33 ± 26.93
Mean procedure time (minutes)	28.35 ± 10.7	24.63 ± 4.96
Number of biopsy cores		
10-core, n(%)	8 (66.67)	4 (33.33)
12-core, n(%)	7 (70)	3 (30)
Biopsy method		
Targeted biopsy only (n(%))	0 (0)	0 (0)
Systematic biopsy only (n(%))	0 (0)	8 (100)
Combined (targeted+systematic biopsy) (n(%)	26 (100)	0 (0)

Table 3. Complication of TPPB-VY.

Complication	TRUS-visible lesion n (%)	Without TRUS-visible lesion n (%)	Total n (%)
Perineal Pain	19 of 26 (73.08%)	7 of 26 (26.92%)	26 of 34 (76.47%)
Hematuria	5 of 8 (62.5%)	3 of 8 (37.5%)	8 of 34 (23.53%)
Urinary Retention	1 of 2 (50%)	1 of 2 (50%)	2 of 34 (5.88%)
Urethral Bleeding	0 (0%)	0 (0%)	0 (0%)
Urinary Tract Infections	0 (0%)	0 (0%)	0 (0%)
Perineal Hematoma	1 of 1 (100%)	0 (0%)	1 of 34 (2.94%)

obtained from those who reported pain was 0 to 2, indicating that only mild pain was perceived. As much as 23.53% of patients (8 out of 34 patients) experienced hematuria, 5.88% (2 out of 34 patients) suffered from acute urinary retention and only 2.9 % (1 out of 34 patients) suffered perineal hematoma. Data analysis using chi-square test showed that complication rates in both groups (with lesion and without lesion) were not significantly different ($p>0.05$). Other complications such as fever or clinical infection, urinary tract infection, urethral bleeding and rectal bleeding were not found. None of the patients were hospitalized due to post-biopsy complications.

DISCUSSION

The incidence of prostate cancer is increasing in Indonesia, although still lower than in Western and other Asian countries.Age was considered a major risk factor of prostate cancer, with the median age being 72 years. In the UK 36% of cases are diagnosed in men aged 75 years and only 1% are diagnosed in under 50 years. It was reported that in some Asian countries (Japan, Hong Kong, and South Korea) an increase of incidence rates was more pronounced after 60 years of age.[1-2] This value was not much different from the mean age of our study population, which was found to be 65.32 ± 8.5 years (range 49-85).

Diagnosis of prostate cancer is based on a digital rectal examination and a core needle biopsy. Prostate biopsy specimens are taken from the apex, middle and base in male patients who have abnormal DRE results or elevated serum PSA, or both. In this study, detection rate of prostate cancer using TPPB was found to be 35.29% (12 of 34 patients), this value was not much different from another study conducted in China which reported a detection rate of 31.4%. Other previous studies conducted in 2003, 2005, and 2007 reported that prostate cancer detection rate by TPPB were 38%, 41.3%, and 30.2%, respectively.

The conventional method of a systematic prostate biopsy is performed using transrectal ultrasound to obtain 10 to 12 tissue samples in a grid-like pattern. Many studies from Western countries have reviewed improvements in the detection rate by extended TPPB. Emiliozzi et al reported an increasing detection rate with higher core numbers, particularly in patients with a PSA of 4-10 ng/ml (30% in 6-core TPPB vs. 49% in 12-core TPPB). Pepe et al confirmed these data by comparing 12 versus 18 cores, with detection rates reaching 35% and 51%, respectively. These findings were also supported by a study conducted in Indonesia which reported that prostate cancer detection rate was significantly higher in patients receiving 10-core biopsy compared to those receiving 6-core biopsy (31.6% vs. 22.4%, $p < 0.001$).[8-12] In this study, we used 12-core TPPB. The detection rate of prostate cancer was lower in the 12-core group compared to the 10-core group (29.41% vs. 35.29%). However, this difference was not statistically significant (chi-square test, $p=0.665$), we believe this finding may be due to small sample size.

The mean serum PSA level in the prostate cancer group (531.41 ± 1068.53 ng/mL) was significantly higher compared to the non-prostate cancer group. This is in accordance with previous study in Indonesia which documented an increased rate of prostate cancer in higher PSA levels.[7]

A statistically significant difference of lesion detection proportion in biopsy method was found in this study (Fisher exact test, $p<0.001$). This is in accordance with general consensus which had been reached from previous studies, that the combination of targeted and systematic biopsy provided the most detailed detection evaluation.[13]

A literature review conducted by Galfano et al concluded that minor complications are more frequently found in TPPB, although reports of these complications were scarce because they rarely need treatments. Our study found that a total of 28 patients (82.35%) presented with minor complications (ClavienDindo I). Perineal pain post procedure was

found in 26 out of 34 patients (72.7%). This value was higher than a report from previous studies which documented mild perineal pain in only 31% and 38.1% of patients. Further studies should be conducted in order to find out the cause of difference in these findings, it may be caused either by our limited sample size, differences in methods of data collection, or the types of of anesthesia given to the patients. The range of VAS score obtained from those who reported pain was 0 to 2, indicating that only mild pain was perceived, which was in agreement with previous study.[8-12]

As much as 23.53% of patients (8 out of 34 patients) experienced hematuria and only 5.88% (2 out of 34 patients) suffered from acute urinary retention. This was in accordance with other studies which reported that self-limiting hematuria occured in percentages ranging from 8.6% to 52% while rates of acute urinary retention ranged from 0-7 to 2%. The same studies reported a percentage of only 1-6% for perineal hematoma, which was not found in our study.

Fever or clinical infections were not found in this study, although no prophylactic antibiotics or enema was administered pre procedure. This finding was supported by previous studies which documented that the rates of fever post procedure were low, ranging from 0-5 to 2%. The explanation for this was that the TPPB is considered a sterile procedure, because the biopsy needle does not pass through the rectum. For this reason, antibiotic prophylaxis should be recommended only for patients with a high risk of infection, such as diabetic or immunosuppressed patients, those with a poor general health status, cardiac prostheses, or cardiac valve pathologies, and those with an indwelling catheter or high postvoiding residual. In these patients, fluoroquinolones are indicated as first-choice antimicrobials. A study conducted in Japan also noted that a preparation enema may be pointless in TPPB because the needle is not contaminated by fecal material.[8-12]

Other possible complications of TPPB, such as hemospermia, and rectal bleeding were not discovered in our study. This was in contrast with finding from a previous study which documented an incidence of hemospermia in 79% of its study subjects, further evaluations should be done in order to investigate what causing this distinctive finding.

Data analysis using chi-square test showed that complication rates in both groups of our study (with lesion and without lesion on TRUS) were not significantly different ($p>0.05$), which meant presence of lesion found on TRUS was not associated with the incidence of biopsy complications. Based on our findings of complication rates, this preliminary study demonstrated clinical feasibility and safety of TPPB.

CONCLUSION

This is the first study of a transperineal ultrasound guided biopsy using Novel Affordable VY probe. The results of this study showed that the procedure had clinically insignificant complications and no infection was found. Thus, the use of Novel Affordable VY probe can be considered as feasible and safe.

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