

Patient experience after transperineal template prostate biopsy compared to prior transrectal ultrasound guided prostate biopsy

[Author's unedited version]

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Introduction Transperineal template prostate biopsy (TTPB) is reported to have higher cancer detection and lower complication rate compared to transrectal ultrasound guided prostate biopsy (TRUSPB).

However there is no report of the same patient's experience with both types of biopsy.

Aim: To compare the patient reported experience in the same cohort of patients who underwent both TRUSPB and TTPB, using validated questionnaires.

Material and methods We retrospectively utilised the Patient Reported Outcome Methods (PROM) tool validated for TRUSPB and the international index of erectile function (IIEF-5) questionnaire to collect longitudinal data at follow-up in same cohort of patients who underwent both TTPB and TRUSPB between January 2015 and February 2016.

Results Out of 44 TTPB performed during the period, 35 patients had undergone both TRUSPB and TTPB. Patient reported pain post biopsy was significantly higher with TRUSPB (86% vs. 61%; $p = 0.01$). Post- biopsy urinary retention rates were significantly higher in the TTPB group (16.7% vs. 5.7%; $p = 0.05$, t test). Furthermore incidence of patient reported sexual dysfunction rates based on the IIEF-5 was significantly higher in the TTPB group ($p = 0.001$, t test).

Conclusions Although overall TTPB was better tolerated in this cohort of patients with lower risk of health care contact, patients reported higher incidence of urinary retention and sexual dysfunction after TTPB compared to TRUSPB. Thus patients should be adequately informed about potential risks with each biopsy as they may have significant impact on quality of life.

INTRODUCTION

Prostate biopsy has evolved considerably since its inception. TransRectal UltraSound guided prostate biopsy (TRUSPB) was first described by K.K. Hodge in 1989 [1]. The 12-core TRUSPB is a simple office based procedure and is currently used as a routine diagnostic procedure for prostate cancer. However, poor sensitivity with false negative rates of up to 23%, a high complication rate along with increasing antibiotic resistance have led to a renewed interest in Transperineal Template Prostate Biopsy (TTPB) which was previously only an underused alternative to TRUSPB [2]. TTPB has the advantage of improved sampling of anterior and apical regions of the prostate, decreased risk of underestimation of disease volume and grade and negligible rates of post-biopsy sepsis which is highly relevant in the

era of emerging antimicrobial resistance [3]. It is also a useful alternative in patients with rectal conditions requiring previous radiotherapy or surgery. The disadvantages of TTPB include the need for general anaesthetic, longer time, training, specific equipment which is not widely available and cost of all of the above [4]. The increasing utilisation of Magnetic Resonance Imaging (MRI) in prostate cancer has led to multi-parametric MRI-guided biopsies that have led to improvement in cancer detection, more accurate Gleason grading and a reduction in the potential number of cores, thus reducing complication rates. Additionally, MRI-TRUS fusion biopsies would improve detection of significant prostate cancer via both TP and Transrectal routes [5].

Literature comparing the complication rates between the standard TRUSPB and TTPB shows a similar side-effect profile and tolerability after both procedures, with the exception of sepsis which is higher with TRUSPB as per reports [6, 7]. A validated patient reported outcome questionnaire for assessing patient reported outcomes after prostate biopsy was first presented in the ProBE- Prostate Biopsy Effects study – a prospective cohort study embedded in the Prostate Testing for Cancer and Treatment (ProtecT) study [8]. An adapted version of this questionnaire has since been utilised in a multi-center study of 389 men undergoing TTPB and the results were then compared with previously reported TRUSPB outcomes from the ProBE study [9]. Even though similar questionnaires were used the patient cohorts were different. There is no report of the same patient's experience with both types of biopsy. The aim of this study was to compare the patient reported experience in the same cohort of patient after TRUSPB and TTPB using validated questionnaires.

MATERIAL AND METHODS

A standardised questionnaire-based cohort study on retrospectively collected data was performed in a single center in Ireland. An adapted version of the previously validated ProBE questionnaire and International Index of Erectile Function 5 (IIEF-5) (shortened) questionnaire were utilised. Ethics approval was obtained from the local hospital group ethics committee.

Over a 9-month period from 15th May 2015 to 15th February 2016, 44 patients underwent TTPB and 35 of 44 underwent both TRUSPB and TTPB. The patients were contacted by telephone and asked to fill both questionnaires based on their experience with the two different types of prostate biopsy. The principle investigator who was independent of the operating team contacted all patients and filled out the questionnaires via telephone to minimise bias. Patients who could not be contacted were excluded from the study. Four urologists performed the TRUSPB and two of those performed the TTPB.

Biopsy procedure

TTPB was performed as a day case procedure under general anaesthetic (GA) in the lithotomy position with antibiotic prophylaxis (ciprofloxacin 750 mg PO 12 hours before and gentamicin 240 mg IV stat pre-procedure). A biplanar TRUS probe mounted on a stabilizer and stepper with a brachytherapy template grid was utilised. After calculating the prostatic volume, an 18-gauge biopsy needle is directed through the template grid to obtain biopsies under direct ultrasound guidance. Mean of 20 cores are taken from each of the anterior, mid and posterior prostate sectors targeting the peripheral zone. Additional targeted cores [2, 3] from cancer-suspicious MRI visible lesions are taken. The multi-parametric MRI studies were reported by two consultant uro-radiologists in accordance with the European Society of Uro-Radiology standards. The MRI is used cognitively with some cases utilizing the MRI-ultrasound fusion software (BiopSee™, Darmstadt, Germany). Patients were discharged on the same day after voiding with appropriate post-biopsy instructions.

TRUS biopsies were performed under local anesthetic (LA) using a standard ultrasound and biopsy probe with prophylactic antimicrobial cover (Ciprofloxacin 750 mg P.O morning and evening of biopsy and Gentamicin 240 mg IV at the time of biopsy), 12 core biopsies were taken – 6 from each side.

Anesthetic choice and effect on questionnaire

Since TTPB was performed under GA and TRUSPB was performed under LA, in order to avoid bias the patients were asked of their experience after discharge. It was clarified that the questionnaire was not trying to assess patient experience during the procedure or immediately after it.

Symptoms

Likert scale grading was used to describe the severity of symptoms such as haematuria, haematochezia, heamospermia, fever, shivers and pain self-reported as absent or present and then graded from 'none', 'mild', 'moderate' to 'severe'. The IIEF-5 questionnaire was completed at baseline and post procedure. Attitude to re-biopsy

This was described as "would you have a preference for one of these procedures based on your experience after the biopsy?" This was modified from the original ProBE questionnaire.

Utilisation of healthcare resources

This was described as contact with general practitioner (GP) or readmission and requirement of analgesia, antibiotics or catheterisation post procedure.

Outcome measures

Our primary outcome measures were post-procedure pain, infection, hospital readmission, voiding dysfunction, urinary retention, sexual dysfunction, bleeding, attitude to re-biopsy and healthcare resource utilization post biopsy. The secondary outcome measure was the cancer detection rate for TTPB in our institution.

Statistical analysis

Data obtained from case report forms were transferred to a computer spreadsheet. Entries were then checked for any errors. All data were tested where appropriate for normality. P values less than 0.05 were considered statistically significant. SPSS (Version 21.0. Armonk, NY, USA) and excel were utilised for statistical analysis. The statistical significance was calculated by using the Student's t test and chi-square test where appropriate.

RESULTS

A total of 44 male patients underwent TP biopsy in our center over the 9-month period. The median age of the cohort was 61 years (48 to 73 years).

Thirty-five out of the 44 (79.5%) patients had undergone a previous TRUS biopsy and were included in the study.

The median follow-up period post TTPB at the point of data collection was 40 weeks (8 to 48 weeks).

Symptoms and severity

Patient reported pain post biopsy was significantly higher after TRUSPB compared to TTPB (30/35 vs. 22/35; 86% vs. 61%; $p = 0.01$). Post-biopsy urinary retention rates were significantly higher after TTPB compared to TRUSPB (16.7% vs. 5.7%; $p = 0.05$, t test). The other patient reported symptoms did not differ significantly between the two biopsies. Table 1 outlines patient symptoms post-TTPB and TRUSPB.

Sexual function

There was a significant difference in patient reported rates of sexual dysfunction based on the IIEF questionnaire between the two biopsies ($p = 0.001$, t test), with the incidence being higher after TTPB group (Table 2). Of the four patients reporting erectile dysfunction (ED) after TTPB; 2 were recovering (3 months from biopsy, negative biopsy and Gleason 3+3), 1 underwent prostatectomy (Gleason score 4+3) and 1 had to undergo treatment for ED (biopsy 11 months ago, caverject injections; Gleason 3+3). The median age of this cohort was 63 years (59–73 years).

Contact with healthcare

The incidence of general practitioner contact was 12% higher after TRUSPB ($n = 7$) as compared to TTPB ($n = 3$) ($p = 0.001$, chi square test). The incidence of hospital admission post biopsy was also significantly higher (7%, $p = 0.02$) after TRUSPB ($n = 4$) as compared to TTPB ($n = 2$).

Attitude to re-biopsy

A total of ten patients (10/35) said they would not mind undergoing either of the procedures again whereas 15/36 (42%) patients would prefer TTPB if given a choice while 11/36 (31%) would rather undergo TRUSPB. The difference in the attitude to re-biopsy was not significant statistically ($p = 0.32$, chisquare test).

TP biopsy outcome

The median PSA of patients who underwent TTPB was 8.35 (0.8 to 29). The indications for TTPB in patients who had a previous TRUSPB included negative biopsy, positive MRI, TRUS sepsis and ASAP. A mean of 20 cores were taken during the TTPB (11-28). Four MRI-fusion TTPB were performed. The overall cancer detection rate was 66% with 58.6% representing non-significant cancers (Gleason score ≤ 6) versus 41.3% with significant cancers (Gleason score ≥ 7).

DISCUSSION

This is the first study comparing patient reported experience with TRUSPB and TTPB in the same cohort of patients using a validated questionnaire. The patient cohort undergoing the TTPB provided a historical comparative group. This was to reduce bias with self-reported symptoms after biopsy as different patient cohorts are likely to have different perceptions in pain thresholds, different thresholds to contact healthcare and different personal experiences at different hospitals.

The response rate of the study was 79.5% with a median time at follow-up of 40 weeks post TTPB. Rosario et al. 8 reported a 89% response rate at 35 days post biopsy and Wadhwa et al. 9 reported 51.6% response at baseline and follow-up. Overall attitude to re-biopsy did not differ significantly between TRUSPB a, though there was an 11% higher rate of patients

who preferred TTPB to TRUSPB. This was reflected in the previous two studies where ProBE questionnaire was utilised, the attitude to re-biopsy was less negative in TTPB study as compared to the TRUSPB cohort (12% in TTPB versus 20% in TRUSPB).

Wadhwa et al. [9] reasoned that a later point of data collection from the biopsy could potentially contribute to less favourable attitude towards TRUSPB in the PROBE study as could the fact that most patients undergoing a TTPB had a prostate biopsy before and hence were better prepared for the same. This study involved much longer time intervals from biopsy to data collection compared to the two prior studies; hence the effect of time should be minimal.

The explanation for the above attitude could lie in the overall outcomes reported by patients post TTPB. There was a statistically significant higher incidence of healthcare contact (both hospital admission and GP input) after TRUSPB, the indications being moderate to severe pain, haematuria and infective symptoms. The indications for admission post TTPB included urinary retention, haematuria and pain. In the study by Wadhwa et al 5.5% patients required contact with healthcare for urinary retention post TTPB compared to 8.3% in our study. Rosario et al reported a 10.4% rate of GP consultation and 1.3% incidence of hospital admission post TRUSPB for infective symptoms, haematuria, haematospermia and haematochezia; this was lower than our reported rates of 20% requiring GP contact and 11% patients requiring hospital admission post-TRUSPB. However the trend of higher incidence of GP consultation and hospital admission after TRUSPB compared to TTPB remains universal. Randomised controlled trials comparing the two types of biopsies have reported higher rate of major complications like sepsis and rectal bleeding with TRUSPB [11]. A recent meta-analysis comparing the two types of biopsies has shown comparable complications with the two techniques [12].

Pain after discharge was significantly higher after TRUSPB than TTPB while urinary retention was significantly more common after TTPB. When performed under LA, authors report a higher incidence of pain during and after TTPB compared to TRUSPB [11, 12]. This study was focused on pain after the procedure and did not look at pain during the procedure due to the difference in anesthetic technique. The other self-reported outcomes on the questionnaire were not statistically different after the two biopsies in this cohort. Higher rates of haematospermia were reported after TTPB but only 1 out of 8 patients described this as a moderate problem. Though the higher rate of haematospermia post TTPB is previously described, patients tend to describe haematospermia as a major/moderate symptom more frequently (26.6% and 17%) in contrast to our findings [8, 9, 10]. This could be due to increased awareness/expectation of this as a routine side-effect in our cohort.

Another significant difference in the patient experience with both biopsies is the reduction in erectile function after TTPB compared to no reports of erectile dysfunction post TRUSPB. Wadhwa et al also reported this in their study. This erectile dysfunction post TP biopsy is described as temporary and reverses within 3–6 months [10]. One of our patients did not experience a reversal of his ED post TP biopsy and is currently on treatment, this patient did not have any issues with erectile function before the biopsy.

The limitations of this study include the longer interval between both biopsies and data collection and variation in point of data collection post biopsy, which would raise a potential recall bias. However, all the patients were unequivocal about their experience and said they clearly recall of the biopsy and events post procedure which is reflected on almost similar reports as previous studies. This study was only able to evaluate pain after the biopsy at discharge, not during the biopsy due to difference in the type of anaesthesia used for both biopsy techniques. The investigator ensured patients did not rate pain during the procedure while answering the questionnaire. This method of data collection also provided a long- term follow-up post biopsy allowing for development and/or resolution of certain symptoms, which would not be available in previous studies with shorter follow up. This study was unique in the way that the use of same cohort of patients potentially eliminates confounders like baseline patient differences and effect of time on data collection.

CONCLUSIONS

This was a first of its kind study comparing the same patient experience after two different types of prostate biopsies, in an attempt to reduce certain reporting biases on prostate biopsy tolerability among patients.

Although overall TTPB was better tolerated after discharge in this cohort of patients with lower risk of health care contact, patients reported higher incidence of urinary retention and sexual dysfunction after TTPB compared to TRUSPB. Thus, patients should be adequately informed about potential risks with each biopsy as they may have significant impact on quality of life, in order to better equip these patients for complications after biopsies.

Conflicts of interest

The authors declare no conflicts of interest.

Table 1. Patient self-reported symptoms after TP and TRUS biopsy

	TP Biopsy (n = 35)		Previous TRUS biopsy (n = 35)		Difference
	Overall	Moderate/Severe	Overall	Moderate/Severe	
Pain	22 (61%)	3 (8.3%)	30 (86%)	9 (26%)	P=0.01
Haematuria	23 (66%)	3 (8.3%)	22 (63%)	5 (14.2%)	P=0.39
Haematochezia	1 (2.7%)	0	2 (5.7%)	1 (2.8%)	P=0.34
Haematospermia	8 (22%)	1 (2.7%)	6 (17.2%)	1 (2.8%)	P=0.25
Incontinence	1 (2.7%)	1 (2.7%)	0	0	P=0.09
Retention	6 (16.6%)	3 (8.3%)	2 (5.7%)	1 (2.8%)	P=0.05
Fever +/- shivers	4(11%)	4 (11%)	6 (17%)	6 (17%)	P=0.20
GP review required	3 (8.3%)		7 (20%)		P= 0.001
Admission required	2 (5.5%)		4 (11%)		P=0.002

Table 2. Erectile dysfunction based on IIEF-5 score

TP biopsy			TRUS biopsy			P value, ttest
PRE mean (sd)	POST	P value, t test	PRE	POST	P value, ttest	
21.2 (3.3)	19.3 (5.9)	0.02	21.2 (3.3)	21 (3.7)	0.32	0.04

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