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ORIGINAL ARTICLE

Factors influencing urinary retention after transperineal template biopsy of the prostate: outcomes from a regional cancer centre

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Abstract

Introduction Multi-parametric MRI (MP-MRI) prior to prostate biopsy is the investigation of choice for an elevated age-related PSA and abnormal digital rectal examination. MP-MRI in combination with transperineal template mapping biopsy has facilitated the development of the concept of targeted biopsies, either cognitively or with software fusion. Urinary retention is a recognised complication of transperineal prostate biopsy, with reported incidence being 1.6–11.4%. We present patient and procedure-related factors, which influence occurrence of urinary retention after transperineal template biopsy.

Patients and methods Retrospective data collection of 243 consecutive cases of transperineal template biopsies performed at a single institution were recorded and analysed. Biopsies were taken using a standard 5-mm template in 4–6 sectors, depending on the prostate volume.

Results 31/243 (12.8%) patients developed urinary retention, defined as patient discomfort and inability to micturate and bladder scan of ≥ 600 ml. Patients in the retention group were significantly older (mean 68.7 vs. 65.8 years, $P = 0.034$). Prostate volume was significantly greater in comparison with the non-retention group (mean 75.4 vs. 57.2 cc, $P = 0.0016$). The number of biopsies taken was positively correlated with urinary retention (median 35 vs. 32 biopsies, $P = 0.045$), and this was independent of prostate size ($R^2 = 0.2$). Presenting PSA, pre-operative flow and histopathological outcome were independent of urinary retention.

Conclusions Factors resulting in an increased risk of urinary retention are advancing age (> 68.7 years); a larger prostate volume (> 75 cc); greater number of biopsies (> 35); greater severity of lower urinary tract symptoms prior to biopsy and diabetes. Targeted biopsies alone, instead of a full template, may avoid urinary retention in the high-risk groups identified.

Keywords Transperineal template biopsy · Prostate biopsy · Prostate cancer · Urinary retention

Introduction

There has been a paradigm shift in the traditional workup of suspected prostate cancer, from a raised age-related prostate-specific antigen (PSA) leading to transrectal ultrasound-guided (TRUS) biopsy in all patients, to the incorporation of multi-parametric MRI (MP-MRI) into the diagnostic workup. The former currently remains the standard pathway as outlined by the National Institute for Health and Clinical Excellence (NICE) guidelines, but more recent research has questioned the validity of this pathway [1, 2].

PSA as a diagnostic marker in isolation is unreliable, with a normal PSA of < 4 ng/ml potentially masking prostate cancer in up to 15% of patients [3]. TRUS biopsy of the prostate is associated with side effects including sepsis and urinary retention; furthermore, it is also reported to under-stage clinically significant cancers [2, 4]. Infection and sepsis risk after transperineal template biopsy is consistently reported as being less than in standard TRUS biopsy [5].

The new paradigm considers MP-MRI as the first-line investigation for an elevated age-related PSA and a suspicion of prostate cancer, along with abnormal findings on digital rectal examination. There is good correlation between use of MP-MRI in the diagnosis of prostate cancer, with meta-analyses reporting a specificity of 0.88 and sensitivity of 0.74 [6]. Recent publication of the PROMIS trial indicates that MP-MRI can be a useful triage for patients with a raised PSA and suspected prostate cancer, with up to 27% of

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patients with clinically insignificant prostate cancer potentially being able to avoid unnecessary primary biopsy [2]. PROMIS has shown that sensitivity of MP-MRI is superior to TRUS biopsy (93 vs. 48%); therefore, if MP-MRI can highlight a focal lesion, a targeted biopsy can aid diagnosis. The 2010 NICE guidance reports that correct cancer detection is achieved in 38–76% of patients undergoing prostate biopsy via the transperineal route [7].

MP-MRI taken in combination with transperineal template mapping biopsy has facilitated the development of targeted biopsy of the prostate, either cognitively or more recently, with MRI–ultrasound fusion software. However, MRI is not a suitable imaging modality for all patients, particularly those with permanent pacemakers, some types of arthroplasty, or other conditions which preclude a patient from MRI scanning.

This transperineal route for prostate biopsy was initially derived from the procedure used to implant brachytherapy seeds and requires a stepper device and template grid [8]. As with TRUS biopsy, urinary retention is a recognised potential complication, requiring catheterisation and a further hospital episode [4, 7, 9]. Studies referenced by NICE report incidence of urinary retention as ranging from 1.6 to 11.4% [7, 9].

We present patient- and procedure-related factors, which influence occurrence of urinary retention after transperineal template biopsy.

Patients and methods

284 consecutive patients underwent transperineal template biopsies of the prostate at a single regional cancer centre from January to December 2015. 41 patients were excluded due to incomplete data, resulting in 243 cases available for retrospective data collection and full analysis.

Patients were consented and prescribed a phosphate enema on arrival. The transperineal template biopsy procedure was performed under gentamycin and co-amoxiclav cover, with the patient in an extended lithotomy position. A 14 Ch Foley catheter was inserted at the beginning of the procedure to enable aerated gel to be introduced per urethra. Biopsies were taken in a standard systematic fashion with 5-mm template mapping biopsies taken in 4–6 sectors, depending on the prostate volume. Some patients underwent additional biopsies of a target lesion by cognitive fusion, as identified on MRI. The urinary catheter was routinely removed at the end of procedure.

Systematic extraction of data parameters was performed to include: patient demographics, comorbidities, previous prostate disease, presenting PSA, prostate volume, number of biopsy cores taken, severity of LUTS (lower urinary tract symptoms) or International Prostate Symptom Score (IPSS), pre-operative flow (Q_{max}) and post-void residual volume (PVR), use of pre- and post-procedural alpha-blocker (400 µg Tamsulosin), histological and oncological outcomes.

The primary outcome measure was occurrence of post-procedural urinary retention. This was defined as the requirement for insertion of a urethral catheter, due to inability to pass urine, patient discomfort and/or a PVR of ≥ 600 ml after a period of observation. Descriptive statistics and *t* tests were used to analyse and present the data, with a significant difference being taken as $P = 0.05$.

Results

Six patients did not undergo pre-procedural MP-MRI imaging. These patients were unable to have an MRI due to claustrophobia, presence of a non-MRI-safe pacemaker, metalwork, or other patient factors rendering them unsuitable to undergo this imaging modality.

Overall incidence of urinary retention in our cohort was 31/243 (12.8%). Results are summarised in Fig. 1. In all patients who developed urinary retention, this occurred < 24 h after the procedure. Patients were catheterised and attended a trial without catheter (TWOC) clinic appointment 1 week later. Of the 31 patients, voiding function returned

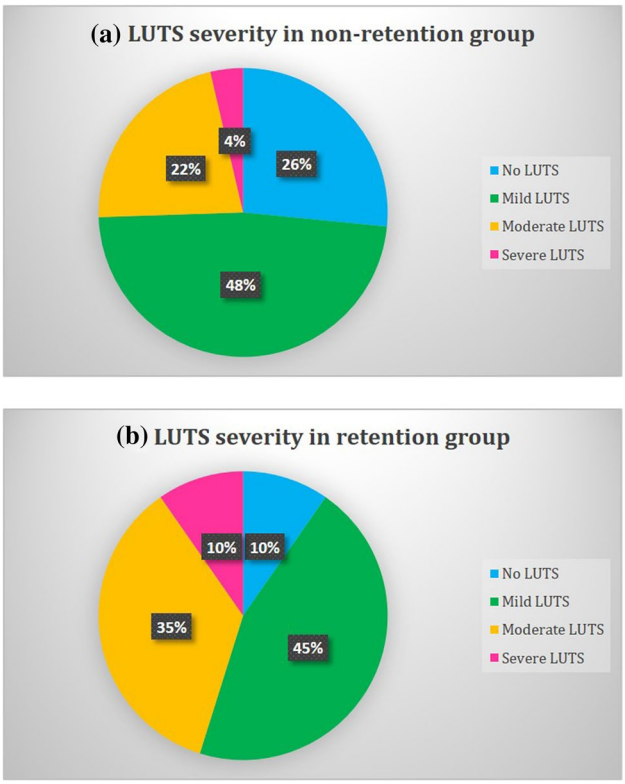

Fig. 1 Pre-existing severity of LUTS in **a** non-retention group, vs. **b** retention group

following TWOC in 28 patients (90.3%). Two patients were taught clean intermittent self-catheterisation due to inadequate voiding and a large PVR volume, and one patient managed to void after a second TWOC attempt.

Patient age was associated with urinary retention, with patients in the retention group being significantly older (mean 68.7 vs. 65.8 years, $P=0.034$) (Table 1). Similarly, prostate volume was significantly greater in comparison with the non-retention group (mean 75.4 vs. 57.2 cc, $P=0.0016$). The number of biopsies taken was positively correlated with development of urinary retention (median 35 vs. 32 biopsies, $P=0.045$), and unrelated to prostate size ($R^2=0.2$).

Presenting PSA, pre-operative flow rate (Q_{max}) and histopathological outcome were independent of urinary retention. Although not reaching statistical significance, a greater pre-operative post-void residual volume was associated with occurrence of urinary retention (mean 192 vs. 104 ml, $P=0.056$).

98% (238/243) patients were given a single prophylactic dose tamsulosin (400 µg) on the day of procedure, with the aim of preventing urinary retention. 56/243 (23%) patients were already taking regular tamsulosin. All patients in the retention group had received tamsulosin on the day of procedure and a significantly greater proportion of urinary retention patients (41.9%, 13/31) were already taking tamsulosin regularly, in comparison with 20.4% (43/212) in the non-retention group ($P=0.008$). This corresponds with the greater severity of LUTS in the retention group compared with the non-retention group. Post-operatively, patients who were not initially taking tamsulosin were given a post-operative course of 5–7 days.

A number of common co-morbidities were also analysed, these included cardiovascular disease, hypertension, diabetes, hypercholesterolaemia (Table 2). Of these, diabetes was the only factor to be significantly associated with a greater risk of urinary retention, 16.1% of patients who developed retention were diabetic (5/31), compared with 5.2% (11/212) in the non-retention group ($P=0.02$). There were no readmissions for sepsis in this entire cohort.

Pre-operative LUTS influences the occurrence of urinary retention. In the retention group, a total of 45% (14/31) of patients had moderate or severe LUTS, whereas in the

Table 1 Factors influencing urinary retention

	All patients $n=243$	Retention 31/243 (12.8%)	Non-retention 212/243 (87.2%)	Difference P
Age (years)				0.034
Mean	66.2	68.7	65.8	
Range	41–80	56–79	41–80	
Presenting PSA (ng/ml)				0.224
Mean	8.34	9.71	8.16	
Range	0.3–41.0	1.1–24.8	0.3–41.0	
Prostate volume (cc)				0.0016
Mean	59.6	75.4	57.2	
Range	15–250	20–189	15–250	
Number of biopsies				0.045
Median	33	35	32	
Range	10–54	23–52	10–54	
Pre-op flow rate, Q_{max} (ml/s)				0.552
Mean	15.9	14.2	16.0	
Pre-op post-void residual (ml)				0.056
Mean	111	192	104	
Tamsulosin on the day of procedure	238/243 (97.9%)	31/31 (100%)	207/212 (97.6%)	0.390

Table 2 Associated comorbidities and influence on urinary retention

Number of patients	All patients $n=243$	Retention 31/243 (12.8%)	Non-retention 212/243 (87.2%)	Difference P
Hypertension	79 (32.5%)	14 (45.2%)	65 (30.1%)	0.11
Diabetes	16 (6.6%)	5 (16.1%)	11 (5.2%)	0.02
Cardiovascular disease	13 (5.4%)	1 (3.2%)	12 (5.7%)	0.58
Hypercholesterolaemia	26 (10.7%)	3 (9.7%)	23 (10.8%)	0.84

non-retention group this was only 26% (49/192, $P=0.024$) (Fig. 1). Similarly, 26% (51/192) patients in the non-retention group had no pre-existing LUTS, whereas this was only 10% (3/31) for those who subsequently developed retention ($P=0.041$).

When considering the entire cohort, the overall cancer detection rate was 59.3% (144/243). Cancer detection in patients who subsequently developed urinary retention was 48.4% (15/31), and greater in the non-retention group, 60.8% (129/212), but not reaching statistical significance ($P=0.19$).

Discussion

These data precede the publication of the PROMIS trial, therefore, it was initially premature to suggest that the standard of care has changed so rapidly that MRI- or US-fusion-targeted transperineal biopsies have become a standard practice. However, these findings provide the necessary data that can be applied in these cases to progress to targeted biopsies alone in future. With the PROMIS trial results, recommendations regarding the role of MP-MRI in the diagnosis of prostate cancer are likely to change, both in the UK and Europe [2]. It is likely that targeted biopsy will become the diagnostic procedure of choice, following MP-MRI in the detection of prostate cancer. There are data from TRUS biopsy outcomes to suggest this, but not proven for the transperineal route yet. This becomes more relevant as there has been a recent increase in biopsy via the transperineal route. The MRI scan will, not only facilitate a mechanism for geographical localisation of the lesion, but also enable a full template mapping biopsy to be performed, if necessary. In the event of multi-focal disease, the latter will ensure that all potential foci of significant prostate cancer have been biopsied.

The transperineal route can be recommended due to the lower rates of sepsis and access to the anterior gland, which is more challenging via the TRUS route [10]. A study by Pepe et al. reiterates that cognitively targeted transperineal biopsies are far superior at diagnosing clinically significant prostate cancers in the anterior zone when compared to transrectal TRUS cognitive fusion methods [11]. Cognitive fusion was used in this series; software fusion can also be utilized particularly if targeted biopsies without the full template are considered. However, fusion software is currently costly and not yet widely accessible. In this series all biopsies were performed under general or regional anaesthesia; more recently, targeted transperineal biopsies under local anaesthetic have become feasible [12].

Incidence of urinary retention in our cohort was 12.8%. NICE guidance for transperineal template biopsy of the prostate quotes the incidence of urinary retention as 1.6–11.4% [7, 13]. A large single-centre study of 3000 patients by Pepe et al. reported a low mean incidence of urinary retention of 6.7% across varying numbers of biopsies [14]. Whereas, Merrick et al. reported incidence of 39.4%; therefore, our rates, though slightly higher than NICE reporting, are comparable with other groups [15]. The onset of urinary retention post-procedure in these studies was within 48 h [16].

A systematic review by Loeb et al. reported a 1.7% incidence of urinary retention in patients undergoing TRUS biopsy [4]. However, the standard protocol for TRUS biopsy only involves 12 cores, rather than transperineal, where usually at least 24 cores are taken. Reducing the number of biopsies taken may reduce the incidence of urinary retention; furthermore, a shorter operating time may be afforded if targeted biopsies are taken rather than a full template. This is, however, dependent on the operator's cognitive targeting and being able to identify the corresponding anatomical lesion as guided by MP-MRI reporting.

Several studies report a positive correlation between a greater number of needle biopsies and frequency of urinary retention, though not statistically significant in some studies [13, 14, 16, 17]. In the current series, taking 35 or more biopsies was associated with occurrence of urinary retention. Prostate volume varies greatly, and in our cohort, a larger prostate size > 75 cc was found to be associated with urinary retention. This is comparable to the 68 cc reported by Willis et al. [17]. As clinically expected, patients with a larger prostate would have greater potential to develop urinary retention, due to the reactive oedema and obstructive effects following multiple needle punctures.

Other indicators which may predispose patients to urinary retention relating to prostate volume include ratio of transition zone volume to total prostate volume and a higher IPSS, thus LUTS severity [4]. In our series, LUTS severity was a significant predisposing factor to development of urinary retention; therefore, this could be a pre-operative risk factor that should be considered when counselling patients about the risks. A greater pre-operative PVR was associated with the occurrence of urinary retention, though not fully reaching 95% significance.

As template biopsy becomes more frequently performed and in preference to TRUS biopsies, it is important to assess the complications and subsequent impact on patients. Awareness of these clinically significant risk factors relating to urinary retention as a post-operative complication is useful in counselling and consenting patients prior to template biopsy. The role of prophylactic tamsulosin (400 µg) has been evaluated; however, some patients who attend for template biopsy are already taking long-term alpha-blockers (23% in our series) [8]. Tamsulosin is given to some patients before template biopsy is performed (single dose on the morning of procedure) and continued for 5–7 days; or in some cases for 28 days post-procedure. This practice

appears to be operator dependent, with no established protocol. Published literature reports a similar varying practice ranging from a 10-day course of tamsulosin (400 µg) starting 2 or 3 days pre-operatively, to a 2-week course of 800 µg tamsulosin starting 2 days pre-procedure [15, 18, 19]. The current evidence for the use of tamsulosin to prevent urinary retention post-transperineal template biopsy of the prostate is unclear and formal guidelines relating to indications and recommendations for its pre-procedural use are lacking.

Diabetes and older age have also been linked with post-procedure acute urinary retention, which is also described in our population [4]. The increased risk of urinary retention may be associated with neuropathic autonomic dysfunction, as a recognised complication of diabetes. In our series, pre-operative urinary flow rate, presenting PSA and histological outcome were not found to be significantly related to incidence of post-operative urinary retention.

Limitations of this study could be in the diagnosis of urinary retention, as accurate monitoring and timing of onset of urinary retention relied on some subjectivity. Urinary retention was defined as a bladder scan of ≥ 600 ml post-void residual, patient discomfort and/or the inability to void. Acute painful retention is easily diagnosed, but a PVR > 600 ml may also be considered as chronic retention. The diagnosis of the latter can thus be subjective and it is conceivable that some of these patients may have voided after a longer period of observation. This may explain why the incidence of post-operative urinary retention in this cohort was slightly higher than other studies.

Conclusions

In this study, several factors were investigated for their role in the development of post-operative urinary retention. The risk factors resulting in a significantly increased risk of urinary retention are advancing age (> 68.7 years), a larger prostate volume (> 75 cc), a greater number of biopsies (> 35), a greater severity of LUTS prior to biopsy and pre-existing diabetes. Rates of urinary retention may have been greater without pre-procedural tamsulosin; however, a conclusion cannot be reached regarding its isolated efficacy without intentional randomisation.

A greater number of biopsies are significantly correlated with incidence of post-procedural urinary retention; this suggests that targeted biopsies alone may avoid this complication in the high-risk groups identified. This would be dependent on reliable MRI target reporting, followed by favouring either cognitive targeted, or MRI–ultrasound software fusion biopsies. The advantages of the transperineal route are well-documented and this should be the preferred method over TRUS in future.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

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