

Sepsis rates after template prostate biopsy with single-dose prophylactic antibiotic

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Citation: Rafiq M, Gabriel M, Reddy U, Rochester M, Farag F. Sepsis rates after template prostate biopsy with single-dose prophylactic antibiotic. Cent European J Urol. 2022; 75: 205-208.

Article history

Submitted: Sept. 19, 2021

Accepted: April 1, 2022

Published online: April 23, 2022

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Introduction Urosepsis is a significant risk associated with prostate biopsy. Resistance of microorganisms to antibiotics is a challenging issue for clinicians in everyday practice. In the current study, we investigated the rates of sepsis and hospital admissions following transperineal (TP) prostate biopsies using a single dose of gentamicin.

Material and methods Data for consecutive patients who underwent TP prostate biopsies (March 2019–March 2020) were included. Patients received a single-dose of prophylactic gentamicin 120 mg IV and had skin preparation with antiseptic povidone-iodine or chlorhexidine solution prior to the procedure. Patient's electronic records were reviewed for rates of sepsis and readmission to hospital within 7 days following TP prostate biopsy.

Results A total of 365 consecutive patients were included in the study. After exclusion of non-eligible patients, 280 patients were included in final analysis. The median age was 67 years (32–83), the median prostate-specific antigen (PSA) level was 8.5 ng/ml (0.2–58), and the median prostate size was 44 cc (10–188). Approximately 58% of patients had one or more comorbidities in the form of diabetes mellitus (DM), hypertension, asthma, chronic kidney disease, or ischemic heart disease. Adenocarcinoma was found in 71.7% of patients. None of the 280 patients developed sepsis. Urinary tract infection (UTI) occurred in 2.8% of patients with E.coli, none of them required hospital readmission.

Conclusions Our single centre experience showed a 0% sepsis rate after TP prostate biopsy with single prophylactic dose of gentamicin. Future randomized controlled trials (RCTs) should explore the possibility of performing these procedures without antibiotic prophylaxis in order to reduce the unnecessary use of antibiotics.

Key Words: transperineal prostate biopsy <> urinary tract infections <> sepsis

INTRODUCTION

Cancer of the prostate gland is the most common form of malignancy in men with a worldwide lifetime incidence of up to 4% [1]. Prostate biopsy, either transrectal or transperineal (TP), is the current standard diagnostic tool to establish a diagnosis of prostate carcinoma. It is an invasive procedure and can be associated with a number of complications such as haematuria, haemospermia, urinary

tract infections (UTIs), prostatitis, urinary retention and epididymo-orchitis [2].

Transrectal ultrasound guided prostatic biopsy procedures have been associated with significant rates of UTIs (up to 6%) and sepsis (up to 1%) [3]. Therefore, in the current practice, this approach requires either povidone-iodine rectal preparation or antibiotic prophylaxis [4].

Worldwide urological practice is undergoing a significant change from the traditional transrectal

ultrasound guided prostatic biopsy for the diagnosis of prostatic cancer to TP prostatic biopsy approach [5] due to its superior efficacy in finding anterior prostatic cancer with significantly less sepsis and UTIs [6, 7].

The European Association of Urology (EAU) guidelines made great efforts to recommend a standardised protocol for antibiotic prophylaxis for TP prostate biopsy procedures.

In the current study, we investigated the rates of sepsis and hospital admissions following TP prostate biopsies under cover of a single dose of prophylactic gentamicin 120 mg IV.

MATERIAL AND METHODS

Data for patients who underwent TP prostate biopsies to investigate elevated serum prostate-specific antigen (PSA) at Norfolk and Norwich University Hospital between March 2019 and March 2020 were considered eligible for inclusion in the study. Patients with positive midstream urine sample for infection within 4 weeks prior to biopsy date, long-term urethral catheters, uncontrolled diabetes mellitus and those on immunosuppressives and chemotherapies were excluded from the study.

All patients had a mid-urethral stream (MSU) sample checked to rule out UTI prior to procedure, and another MSU sample within 4 weeks after biopsy date as per local trust protocol. All procedures were performed under general anaesthesia as a day case by more than one surgeon in a standard extended dorsal lithotomy position, using biplanar transrectal ultrasound (TRUS) probe mounted on a stabiliser and stepper with a template grid. Prior to the procedure, all patients received a single dose of prophylactic gentamicin 120 mg slow IV 30 min prior to the procedure regardless of the patient's creatinine clearance and had skin preparation with antiseptic povidone-iodine or chlorhexidine solution. Patients' electronic records were reviewed for demographics, comorbidities, blood levels of PSA, multiparametric magnetic resonance imaging (mpMRI) of the prostate results, histopathological outcomes, rates of sepsis and UTIs, and readmission to hospital within 7 days following TP prostate biopsy date.

RESULTS

Data for 365 consecutive patients who underwent TP prostate biopsies between March 2019 and March 2020 were included in the study. After exclusion of non-eligible patients, data of 280 patients were included in the final analysis. Table 1 shows the baseline demographics and histopathological out-

comes of the patients included in final data analysis. The median age was 67 years (range 32–83), the median blood level of PSA was 8.5 ng/ml (range 0.2–58), and the median prostate size was 44 cc (range 10–188). Comorbidities included diabetes mellitus (DM), hypertension, asthma, chronic kidney disease, and ischemic heart disease, with approximately 19% of patients showing multiple comorbidities. Further histopathological examination of the obtained biopsies confirmed the presence of prostatic adenocarcinoma in 71.7% of patients. None of the 280 patients developed sepsis with no recorded admission to the hospital due to sepsis. Eight out of 280 patients (2.8%) developed UTI with *E. coli* growth in urine culture and sensitivity, their median age was 72 years (range 58–74), and median prostatic volume of 40 cc (range 20–62), three patients had a single comorbidity of cerebrovascular accident, ischemic heart disease, and hypertension. Three patients had prostate adenocarcinoma on further histopathological examination. None of these eight patients required hospital readmission and all of them were treated as outpatients with oral ciprofloxacin.

DISCUSSION

Resistance of microorganisms, especially to fluoroquinolones, is a challenging issue for clinicians in everyday practice [8, 9] and since March 2019 it has become discouraged by the European Commission due to serious side effects with alternatives suggested including cephalexin and aminoglycosides [4]. Therefore, it is worth investigating alternatives to fluoroquinolones either using different antibiotics or only skin preparation with antiseptics or both when applying the TP route in obtaining prostatic biopsies.

In a recent systematic review published in 2020 with a meta-analysis of data pooled from 59 randomized controlled trials (RCTs) including 14,153 patients, rates or infections were significantly higher in procedures done without antibiotic prophylaxis compared to those covered with antibiotics (RR 0.56, 95% CI = 0.40–0.77). The authors reported inferior outcomes when a shorter course of prophylactic antibiotics was used in comparison to longer term courses up to 7 days (RR = 1.89, 95% CI = 1.37–2.61). They recommended fosfomycin as an alternative to fluoroquinolones to use as prophylaxis at time of prostate biopsy in countries where fluoroquinolones are discouraged [10].

On the other hand, another systematic review published in 2021 with a meta-analysis of data retrieved from 90 RCTs including 16,941 patients has shown that rectal preparation with povidone-

Table 1. Baseline demographics and histopathological outcomes of patients included in final analysis

Number		
Age in years [median (range)]	67 (32–83)	
Comorbidities %	58%	
Blood level of PSA (ng/ml)	8.5 (0.2–58)	
Prostate volume (CC)	44 (10–188)	
mpMRI (PIRADS N/%) Total number = 221 patients	PIRADS I	18 (8.1%)
	PIRADS II	44 (19.9%)
	PIRADS III	35 (15.8%)
	PIRADS IV	75 (34%)
	PIRADS V	49 (22.2%)
No cancer 28%		
Adenocarcinoma diagnosis 72%	Gleason Score 6	10%
	Gleason Score 7	50%
	Gleason Score 8	5%
	Gleason Score 9	5%
	Gleason Score 10	2%
Post-op UTI N (%)	8 (2.8%)	
Post-op sepsis %	0%	
Post-op AUR	1 (0.4%)	
Vasovagal episode	1 (0.4%)	

N – number of patients; PSA – prostate-specific antigen; AUR – acute urinary retention; mpMRI – multiparametric magnetic resonance imaging; UTI – urinary tract infections; PIRADS – Prostate Imaging Reporting and Data System

iodine can reduce not only the risk of infections following the prostate biopsy procedures (RR = 0.50, 95% CI = 0.38–0.65) but also the need for hospital admission (RR = 0.38, 95% CI = 0.21–0.69). The authors clearly demonstrated that the TP approach was associated with significantly lower infections compared to the transrectal approach (RR = 0.55, 95% CI = 0.33–0.92) [6].

In the current study, none of our patients developed sepsis following TP biopsy procedures, while 1.7% of patients in our series developed UTIs. None of our patients required hospital admission due to sepsis and/or UTI which is in keeping with the worldwide figures of almost zero percent hospital admission following TP biopsies [2]. However, sepsis due to the TP approach has been recorded in some series although this happened very occasionally. In the series of Baba et al. [11] of 485 patients who received a single dose of cefazolin together with skin preparation using benzalkonium chloride, the authors reported an infection rate up to 0.8% including one case of epididymitis and 3 cases of prostatitis, one of them developed septic shock. In a series of 409 patients, Symons et al. [12] used a combination of gentamicin 240 mg IV preoperatively and a three day course of norfloxacin 400 mg twice daily prior to TP biopsies. The authors reported one case of sepsis secondary to *E.coli* infection following the procedure and

UTIs with pyrexia in 13 patients (3.2%). Pepdjonovic et al. [13] reported occurrence of acute clinical prostatitis in one patient out of 577 patients who underwent TP prostate biopsies under cover of single IV dose of cefazolin and no hospital admission was required in their series. On the other hand, Vyas et al. [14] carried out TP biopsies in 634 patients under cover of single IV dose of amikacin 500 mg followed by ciprofloxacin 500 mg twice daily for three days. The authors reported no cases of sepsis and only one case of epididymo-orchitis. The Japanese Research Group of Urinary Tract Infection in a multicentre study investigated the role of a number of antibiotics as prophylactic in prostate biopsies across 46 centres in Japan [15]. Levofloxacin was the most commonly used drug in their study. The authors reported only 0.57% rate of genitourinary infection in TP approach compared to 0.83% rate in transrectal approach, but this was not a statistically significant difference. The TP approach was associated with significantly lower rates of febrile infections compared to transrectal approach (0.16% vs 0.71%, $p = 0.04$). In contrary to our series, patients with potential risks to develop infections following the procedure were included in the final analysis, and the authors found that the incidence of post-TP biopsies infections in their series was associated with some risk factors including indwelling catheters, use of immunosuppressives and steroids. Our study showed 2.8% rate of UTI following TP biopsies, this is significantly higher than Setia et al. [16], who in 2021 reported UTI events in only 0.44% of patients who underwent TP biopsies without antibiotics and no UTI in the group of patients who underwent the procedure utilizing prophylactic antibiotics. It could be argued that the prophylactic dose of gentamicin utilized in our study is suboptimal and doesn't take into account the variations between patients in terms of creatinine clearance and body weight, however, Setia et al. reported no UTIs even after omission of antibiotic prophylaxis in their study making the rule of antibiotics in TP procedures questionable. A systematic review published in 2022 [17] on 2368 patients who underwent TP biopsies using antibiotic prophylaxis versus 1294 patients who underwent TP biopsies without antibiotics, reported pooled rates of post-procedure sepsis of 0.13% in the antibiotics group vs 0.09% in the no-antibiotics group (RR 1.09, 95% CI: 0.21–5.61, $p = 0.92$). The pooled rates of post-procedure fever were 0.69% in the antibiotics group vs 0.47% in the no antibiotics group, (RR 1.02, 95% CI 0.02–44.5, $p = 0.9$). The genitourinary infections rates were 0.11% in the antibiotics group vs. 0.31% in the no-antibiotics group

(RR 2.09, 95% CI 0.54–8.10, $p = 0.29$). The pooled rates of post-procedure readmission for infections were 0.13% in the antibiotics group vs 0.23% in the no-antibiotics group (RR: 1.29, 95% CI: 0.31–5.29, $p = 0.73$) and no death events were reported in relation to these admissions.

To date, no good quality RCT has been carried out to investigate the real role of antibiotics and/or skin preparations in prophylaxis against genitourinary infections and sepsis, and in view of the increasing rates and severity of the emerging resistance of microorganisms to the currently available antibiotics, the need for such a study is highly needed.

Our study has some limitations, most importantly the lack of a control group, however, one of the purposes of carrying out this study was to highlight the need for large well designed prospective randomised controlled

studies to address the real difference in sepsis/UTIs outcomes between TP biopsies using prophylactic antibiotics and those without prophylactic antibiotics.

CONCLUSIONS

Our single centre experience showed a 0% sepsis rate after transperineal prostate biopsy with single prophylactic dose of gentamicin. Future randomised controlled trials should explore the possibility of carrying out these procedures without antibiotic prophylaxis with the aim to reduce the unnecessary use of antibiotics and development of multi-resistant microorganisms to broad spectrum antibiotics.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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