Infection complications after transrectal ultrasound-guided prostate biopsy: A radiology department's experience and strategy for improvement

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Abstract

Introduction: Transrectal ultrasound (TRUS)-guided prostate biopsy is a common procedure performed to diagnose prostate cancer. The risk of infection complications is well-described in the literature, and strategies to avoid such complications continue to evolve over time. We performed a retrospective review of our infection complications and propose a strategy for improvement.

Methods: We reviewed clinical outcomes from patients undergoing TRUS-guided prostate biopsy at our institution from November 2018 to November 2020. We reported the antimicrobial prophylaxis received, whether the biopsy was systematic or targeted, and we examined the rate of clinically significant infection complications and hospitalization.

Results: Among 312 men who underwent TRUS-guided prostate biopsy during the study period, seven (2.2%) had an infection. Four patient groups with distinct antimicrobial regimen were identified; the largest of these patient groups received a three-day course of cefixime and a single dose of fosfomycin (59%). The proportion of patients with infection complications across these groups did not demonstrate a statistically significant difference (p=0.803). There was no significant difference in proportion of infection between systematic and targeted biopsy groups (3.0% vs. 0%, p=0.204). The proportion of patients hospitalized was 1.3%, with a mean length of stay of four days.

Conclusions: We report a rate of clinically significant infection following TRUS-guided prostate biopsy of 2.2%. Due to our referral pathway, we have an inconsistent approach to antimicrobial prophylaxis, although there was no statistically significant difference in infection rate between the groups. We propose a standardized approach that may lead to improved patient outcomes.

Introduction

Prostate cancer remains a leading cause of illness in men, with a one in eight estimated lifetime risk of developing the disease.[1] Despite previous concerns about overdiagnosis and overtreatment, prostate cancer remains the most common cancer and the third leading cause of male death from cancer in Canada.[2]

Prostate biopsy is the gold standard test for diagnosing prostate cancer.[3] The most commonly used biopsy technique remains transrectal ultrasound-guided (TRUS-guided) biopsy.[4] The more recent advent of the transperineal approach has shown reduced infection complications, although there is increased procedure time, cost, and required expertise, with no significant change in cancer detection rate.[5] The standard TRUS-guided biopsy approach involves a 12-core systematic biopsy, which is often the first-line diagnostic test.

TRUS-guided prostate biopsy is generally well-tolerated, with a low risk of major complications. There are two broad categories of postprocedural complication: bleeding and infection. The most frequent complication is bleeding,[6] which may manifest as hematochezia, hematuria, or hematospermia.

Infection complications after TRUS-guided biopsy have been widely reported and vary from asymptomatic bacteriuria (44%)[7] to post-procedural fever (4.2%) and hospitalization (0.8%).[8] Infection complications remain the single most modifiable complication of TRUS-guided biopsy and, for this reason, it was the primary focus of our study. Studies showed that risk factors, such as diabetes and a history of urinary retention, increase the risk of infection.[9] Antimicrobial prophylaxis significantly reduces bacteriuria, bacteremia, fever, and hospitalization due to infection,[10] and although this is the standard of care, a general trend of an increase in infection complications over time has been observed.[11,12] Ciprofloxacin resistance was shown to contribute to increasing infection complications in one study,[13] and more recently, the American Urological Association (AUA) guidelines 2020 have updated their recommendation for TRUS-guided biopsy

(class III/contaminated procedure) antimicrobial prophylaxis from first-line fluoroquinolone (ciprofloxacin/levofloxacin) to cephalosporin (first- generation ± aminoglycoside or third-generation monotherapy), with choice based on local antimicrobial resistance patterns.[14]

The purpose of our retrospective study was to review our experience and compare our practices to the ever-evolving best practice. We propose an improvement strategy for our service that could be applied to other similar centers where radiologists perform TRUS-guided biopsies for multiple referrers.

Methods

Study design and population

A retrospective chart review was conducted on patients who underwent TRUS-guided prostate biopsy at our institution from November 2018 to November 2020. Only patients who were referred from external institutions, for whom followup was not readily available, were excluded from the study.

Data collection and analysis

Patient characteristics were collected, including age, date of procedure, preprocedural antibiotic prophylaxis regimen, and type of biopsy (systematic vs. targeted). In addition, medical comorbidities were recorded for patients who were found to have had an infection complication. The study's primary outcome was the rate of clinically significant infection following TRUS-guided biopsy, which was defined as symptomatic infection requiring medical attention and/or a therapeutic course of antibiotics from the time of biopsy to clinical followup. Secondary outcomes included the incidence of hospitalization and the length of hospital stay to treat infection complications and whether the cultured organism was resistant to the prophylactic antibiotic agent used. Data was collected from the electronic patient record and medical notes from the followup urology clinic visit.

All statistical analyses were performed with SPSS version 22 (IBM Corp, Armonk, NY, U.S.). Data was presented as mean with range or mean ± standard deviation for continuous variables and as percentage for categorical variables. In univariable analysis, variables were compared between groups using the independent t-test for continuous variables. The Chi-squared test or Fisher exact test was performed for categorical variables. Statistical significance was defined as $p<0.05$.

Biopsy preparation, technique, and antibiotic prophylaxis

In our practice, fellowship-trained abdominal radiologists performed TRUS-guided prostate biopsy for patients referred by a urologist. Procedures were most commonly performed in the outpatient clinic.

The week before the scheduled biopsy, patients were instructed to stop taking antiplatelet agents (acetylsalicylic acid and clopidogrel). Warfarin and direct oral anticoagulants (DOACs) were held for 48–72 hours in line with clinical guidelines.[15] All patients were administered oral antibiotic therapy for a duration of three days, on the day before, the day of, and the day after the procedure, with some groups receiving an additional single dose of fosfomycin on the day of the procedure. At our institution, antimicrobial prescribing practices vary depending on the referring physician. Patients received one of the following four oral antibiotic prophylaxis regimens: ciprofloxacin 500 mg twice a day; ciprofloxacin 500 mg twice a day and one dose of fosfomycin 3 g; cefixime 400 mg daily; cefixime 400 mg daily and one dose of fosfomycin 3 g. In addition, our patients were prescribed a phosphate enema to be taken the night before the procedure unless they have advanced chronic kidney disease, in which case a tap water enema was used. Patients were advised to fast except for clear fluids from midnight the night before the procedure.

We performed our TRUS-guided prostate biopsies by positioning patients in the left lateral decubitus position and inserting the ultrasound probe transrectally. Periprostatic local anesthesia was administered using a 22-gauge spinal needle placed through the biopsy guide channel under ultrasound guidance into the area where the prostatic innervation enters the gland. This was identified by angling the probe laterally until the notch between prostate and seminal vesicle was visualized. The needle was placed into this space and 5 cc of lidocaine 2% was injected on each side. Successful placement was confirmed by observing the injectate cause separation of the seminal vesicles and prostate from the rectal wall.

If the biopsy was targeted, usually 2–4 cores per lesion of interest were taken using cognitive fusion technique following review of prior magnetic resonance imaging (MRI). If the biopsy was systematic (non-targeted), we took 12 cores in total, consisting of a single core from each zone as follows: medial and lateral peripheral zone at the apex, base, and mid-gland bilaterally. All samples were collected in individual labeled sample containers.

When all samples were collected, the ultrasound probe was removed and the patient proceeded to sit in the waiting area with advice to empty their bladder before leaving the department to exclude acute urinary retention.

All patients were followed up by the referring urologist within two weeks of the procedure. The followup is used to discuss results and further management and record any periprocedural complications, including symptoms of infection or requirement for a treatment course of antibiotics.

The institutional research ethics board reviewed and approved the study and informed consent was waived.

Results

A total of 312 men underwent TRUS-guided prostate biopsy at our institution over the study period. The mean age was 66.56 years (range 39–90). The majority were older than 65 years of age (61.2%).

Among 312 patients, seven (2.2%) patients had an infection. Infection rates across the four antibiotic groups did not demonstrate a statistically significant difference (p=0.803). The proportion of patients with an infection who underwent systematic biopsy was 2.9% (7/238) as compared to 0% (0/74) in those who underwent targeted biopsy (p=0.204); the difference was not statistically significant.

Demographics of patients who experienced an infection complication, medical comorbidities, and the manifestation and outcome of the infection are outlined (Table 1). The proportion of patients hospitalized was 1.3% (4/312) and mean length of stay (LOS) was four days (range 3–5). Four of the seven patients had a positive urine culture. The organisms cultured were *Escherichia coli* (*E. coli*) in three cases and *Pseudomonas aeruginosa* in one. In the remaining three cases, no organism was isolated on culture despite compelling evidence of urinary tract infection, including fever and elevated white cell count with no alternative source of infection identified. The antimicrobial resistance of the cultured organisms included two cases of extended-spectrum beta-lactamase (ESBL) and one case resistant to ciprofloxacin.

The majority (59%) of patients received a three-day course of cefixime and a single dose of fosfomycin as their antibiotic prophylaxis regimen (Table 2).

Of the seven infection complications, two were inpatients at the time of biopsy. One patient presented in urinary retention secondary to a large prostate mass and another had completed treatment for urosepsis and found to have a markedly elevated prostate-specific antigen (PSA) and sclerotic bone lesions on imaging. Of our entire patient cohort, 92.4% were biopsied as elective outpatients.

Discussion

In this retrospective study, our findings demonstrated a proportion of clinically significant infection following TRUS biopsy of 2.2% and a proportion of hospitalization of 1.3% with no admissions to the intensive care unit.

Due to our patient referral pathway, we reported four distinct empiric antimicrobial prophylaxis regimens, and although there was no statistically significant difference in infection rates between the groups, our study was not powered enough to examine this outcome and the absence of a difference is likely related to the sample size and small event rate. The retrospective nature of our study leads to information bias since the study operations, data collected, data entry, and data quality assurance could not be preplanned. We commit to further analysis of our performance on a prospective basis.

Our study identified areas where we may improve our performance while modernizing our practice to reflect the latest guidelines and highest level of evidence. Rectal swab culture screening before biopsy to tailor antibiotics has been suggested as a potential solution to antimicrobial resistance. Post-biopsy infection rates were significantly higher in groups given empiric prophylaxis (4.6%) vs. targeted antibiotics (0.72%) in a systematic review of nine cohort studies by Cussans et al.[16] Although this cautious approach may seem unwieldy, it has been shown to be cost-effective in some patient populations.[17] Taylor et al evaluated targeted antimicrobial prophylaxis based on rectal swab results vs. standard empirical prophylaxis and found that 38 men would have to undergo rectal swab before TRUS-guided biopsy to prevent one infection complication and the calculated cost of targeted vs. empirical prophylaxis in 100 men undergoing TRUS-guided biopsy was $1346 vs. $5598.[18]

Duration of prophylactic antimicrobial therapy has varied over time and between various institutions from single-dose to up to three days.[10] The most recent European Association

Table 1. Characteristics of patients with infection complications

Case	Age	Comorbidities	Patient status	Length of stay post-biopsy (days)	Complications	Urine culture	Biopsy result
1	72	Bladder cancer, hypothyroidism, nephrolithiasis	Outpatient	3	Urosepsis	Negative	Adenocarcinoma Gleason 6 (3+3)
2	89	Type II diabetes, hypertension, nephrolithiasis, urinary retention	Inpatient	4	Urinary tract infection	*E. Coli* (ESBL)	Adenocarcinoma Gleason 9 (4+5)
3	68	Hypertension, dyslipidemia	Inpatient	4	Urosepsis	*E. Coli* (ESBL)	Negative
4	59	COPD, dyslipidemia, tuberculosis	Outpatient	3	Urosepsis	*E. Coli*	Negative
5	79	None	Outpatient	0	Prostatitis	Negative	Adenocarcinoma Gleason 6 (3+3)
6	65	None	Outpatient	0	Urinary tract infection	Negative	Adenocarcinoma Gleason 6 (3+3)
7	77	hypertension	Outpatient	0	Urinary tract infection	Pseudomonas	Negative

COPD: chronic obstructive pulmonary disease; ESBL: extended spectrum beta-lactamase.

Table 2. Proportion of post-biopsy infection stratified by antibiotic prophylaxis regimen

Antibiotic prophylaxis regimen	Infection complication
Ciprofloxacin (n=38)	1 (2.6%)
Cefixime/fosfomycin (n=184)	5 (2.7%)
Ciprofloxacin/fosfomycin (n=11)	0
Cefixime (n=79)	1 (1.3%)

of Urology (EAU) 2021 and AUA 2020 guidelines suggested a single-dose regimen for low- risk patients undergoing TRUS-guided biopsy.[14,19]

Evidence supporting the protective effect of pre-biopsy bowel preparation varies based on the agent used for rectal cleansing.[20] Studies evaluating the use of sodium phosphate or saline enemas found no protective effect against post-TRUS-guided biopsy infections;[21,22] however, studies evaluating the effect of povidone-iodine rectal cleansing strongly supported its use in reducing infection complications.[23,24] In a recent systematic review and meta-analysis of nonantibiotic strategies for the prevention of infection complications following prostate biopsy, consisting of 90 randomized controlled trials, Pradere et al found rectal preparation with povidone-iodine reduced infection complications and hospitalization.[25] A meta-analysis of nine studies including 1936 patients showed 61 infections among 930 men in the povidone-iodine group and 131 among 1006 in the control group (relative risk 0.50, 95% confidence interval 0.38–0.65). The same study found transperineal biopsy significantly reduces infection complications compared to TRUS-guided biopsy. The authors recommended transperineal approach or TRUS-guided biopsy with povidone-iodine rectal preparation to minimize infection complications.[25] Both findings are also reflected in the most recent EAU guidelines 2021 (level 1a evidence) with the recommendation to perform prostate biopsy using the transperineal approach due to lower risk of infection complications.[19] There remain many factors preventing widespread use of transperineal approach, including cost, procedure duration, available expertise, and anesthetic support.

Incorporating some of these practices and refining our evidence-based approach may lead to a further improvement in our burden of infection complications. A standard approach to antimicrobial prophylaxis and rationalizing our use of enemas may result in more efficient use of resources and enhance our patient experience.

Upon review of the best available evidence, we propose a single antimicrobial regimen that incorporates our current practice and best available evidence from AUA and EAU guidelines.[14,19] Our proposed new, simplified regimen will consist of a single 400 mg dose of cefixime (third-generation cephalosporin) on the morning of the procedure for low-risk patients with an option to extend to three days for high-risk patients (diabetes or history of urinary retention). Although we recognize the merit in rectal swabbing for targeted antimicrobial prophylaxis, particularly in high-risk patients, our infection rate and local antimicrobial resistance patterns do not currently justify this additional measure.

We currently require our patients to use a phosphate enema the night before the biopsy; this is often not performed properly and can cause patient discomfort/distress. There is insufficient evidence for this practice, and we will no longer advocate for its use. We believe that there is sufficient evidence to recommend the use of a povidone-iodine enema, which can be easily administered as a suppository as an additional measure to mitigate risk of infection.

In our current practice, procedures have been postponed and rescheduled when patients have not taken their antibiotic or phosphate enema the previous day. This new, simplified regime should reduce postponements, with resultant improved departmental efficiency.

Finally, we recognize there could be a role for careful patient selection and timing of TRUS-guided biopsy. Our preference is to perform biopsies electively as an outpatient rather than as an inpatient when patients may be recovering from an acute illness. We believe that the standardization of our practice will make future audit and research more accurate and significant while enhancing our already high performance in infection complication mitigation. This strategy may easily be considered and adopted by other services providing TRUS-guided prostate biopsy.

Conclusions

We currently have a low number of infection complications; however, our antimicrobial prescribing practice is inconsistent and deviates from current best practice. We have identified a simplified regimen that can be adopted by other radiologist-led services to improve workflow and patient experience without compromising patient safety. We plan to prospectively examine future outcomes and monitor our infection complication rate following initiation of our standardized approach to maintain quality assurance in our practice.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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