The Impact of Repeat Biopsies on Infectious Complications in Men with Prostate Cancer on Active Surveillance

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Abbreviations and Acronyms

AS = active surveillance

ESBL = extended spectrum beta-lactamase

FQ = fluoroquinolone

PSA = prostate specific antigen

TRUS = transrectal ultrasound

UTI = urinary tract infection

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Purpose: Prostate biopsy related infectious complications are associated with significant morbidity. The risk of infectious complications in patients with prostate cancer on active surveillance remains under studied.

Materials and Methods: A total of 591 consecutive men who underwent prostate biopsy were prospectively enrolled in a study evaluating prostate biopsy related complications between January 2011 and January 2012. Of these men 403 were previously diagnosed with prostate cancer and were included in this study. They underwent a 14-core transrectal ultrasound guided prostate biopsy as part of an active surveillance regimen. A nurse contacted all men within 14 days of biopsy, and information was collected on potential complications, antibiotics received and bacterial culture results.

Results: Fourteen patients (3.5%) had infectious complications including 13 requiring hospitalization. Five patients had positive urine cultures, and fluoroquinolone resistant isolates were identified in 4 patients, including 2 with extended spectrum beta-lactamase producing isolates. We evaluated the impact of risk factors including diabetes, benign prostatic hyperplasia and antibiotic regimen. However, only the number of previous prostate biopsies was significantly associated with an increased risk of infectious complications ($p = 0.041$). For every previous biopsy the odds of an infection increased 1.3 times (OR 1.33, 95% CI 1.01–1.74).

Conclusions: In men with prostate cancer on active surveillance the number of previous prostate biopsies is associated with a significant risk of infectious complications and every previous biopsy increases the risk of infectious complication. Fluoroquinolone resistant and extended spectrum beta-lactamase producing isolates represent the most commonly identified organisms. Men with prostate cancer on active surveillance should be informed of the risks associated with serial repeat prostate biopsies.

Key Words: prostatic neoplasms, biopsy, infection, sepsis, treatment outcome

In 2012 an estimated 241,740 men were diagnosed with prostate cancer.[1] Prostate needle biopsy with TRUS guidance is the standard technique to obtain a histological diagnosis of prostate cancer and some men endure multiple negative prostate needle biopsy results before diagnosis.[2]

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Similarly, many men diagnosed with low risk prostate cancer managed with AS will endure several years of serial TRUS biopsies. AS has emerged as the preferred management strategy for men with low risk prostate cancer and the National Comprehensive Cancer Network guidelines recommend annual prostate biopsy.[3,4] Approximately 1 million prostate needle biopsies are performed annually in the United States and the numbers will increase as more men are enrolled in AS.[5] The impact of increasing the frequency of prostate needle biopsies on the risk of infection related complications in patients on AS is under studied.

Several observational studies have reported that significant morbidity is associated with initial prostate needle biopsy. In a study using administrative data of elderly men enrolled in Medicare, the rates of 30-day hospitalization after initial prostate biopsy were 2.65-fold higher than among randomly selected control subjects.[5] In that same study the authors demonstrated that the risk for 30-day hospitalization after initial prostate needle biopsy because of infection had increased between 1991 and 2007. An analysis of patients enrolled in the European Organization for Research and Treatment of Cancer prostate cancer screening clinical trial revealed a high proportion of urine cultures with trimethoprim sulfa resistant isolates after prostate needle biopsy.[6] These observations suggest an increasing incidence of antimicrobial resistance contributing to infectious complications after prostate needle biopsy.

Despite accumulating evidence demonstrating an increase in infectious complications after prostate needle biopsy, the impact of repeat prostate needle biopsies in a population of men undergoing AS for low risk prostate cancer is unknown. We conducted a prospective observational study during 1 year at a single institution to determine the incidence and characteristics of infectious complications after prostate needle biopsy in men diagnosed with prostate cancer on AS.

MATERIALS AND METHODS

Patient Cohort

Men who underwent at least 1 prostate biopsy at Memorial Sloan-Kettering Cancer Center between January 2011 and January 2012 and were diagnosed with prostate cancer on biopsy were eligible for inclusion in this study (403). Each man underwent only 1 biopsy during this period, and data were collected prospectively from the most recent biopsy and used for analysis.

Prostate Biopsy Technique and Prophylactic Antibiotic Use

The standard technique for prostate needle biopsy at our institution involved TRUS guidance using an 18 gauge needle, and obtaining 14 cores from the apical, mid and base regions as well as the transitional zone of the prostate. Individual physicians determined the antibiotics used for prophylaxis before prostate needle biopsy. Most physicians at our institution prescribed an oral FQ antibiotic beginning the evening before the biopsy and continued for 24 hours after the procedure.

Assessment of End Point

Our primary outcome of interest was infection within 14 days after biopsy, which we defined as hospitalization for infection, positive blood or urine culture, or fever greater than 100.3F. This was assessed by telephone call by our nursing staff to the patient within 14 days. In addition, nursing staff contacted doctors or outside hospitals to collect information on antibiotic use, urine and blood culture results as well as symptoms of infection at presentation, and recorded these data in a prospective database.

Followup Schedule

For patients enrolled on AS the standard followup regimen includes routine serum PSA measurement and digital rectal examination every 6 months, and repeat TRUS guided prostate needle biopsy as often as annually or once every 3 years based on disease characteristics.

Statistical Methods

We evaluated the impact of the number of prior biopsies on the risk of post-biopsy infectious complications. The null hypothesis tested was that the number of prior biopsies is not associated with an increased risk of infectious complications. In addition, we sought to identify if the previous class of prophylactic antibiotics, diagnosis of diabetes and increasing age are associated with the risk of infectious complications after prostate biopsy. We used univariate logistic regression to test for these associations. Due to a limited number of events, we were unable to use multivariate models in this analysis. All analyses were conducted using Stata® 12.0.

RESULTS

Of the 403 men in this study more than half (55%) had undergone only 1 previous prostate biopsy. Only 40 (10%) of 403 patients had undergone 4 or more previous biopsies (table 1). FQ antibiotics were given to 92% of patients before undergoing the on-study biopsy. Intramuscular gentamicin was administered to 114 (28%) patients.

There were 14 patients (3.4%, 95% CI 1.7–5.3) who had an infection after prostate biopsy, of whom 5 had positive urinary cultures and 9 had negative urinary cultures. Among the patients with growth on urine culture 4 were found to have ciprofloxacin resistant Escherichia coli including 2 with an ESBL producing isolate. One patient had aminoglycoside resistant Enterococcus.

The number of previous biopsies was significantly associated with an increased risk of post-biopsy infection. On average, the odds of infection increased