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BRIEF REPORT

Infection-Related Hospital Admissions After Prostate Biopsy in United States Men

Richard Evans,[1] Aram Loeb,[2] Keith S. Kaye,[3,4] Michael L. Cher,[2,5] and Emily T. Martin[1]

[1]Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor; [2]Department of Urology and [3]Division of Infectious Diseases, Wayne State University School of Medicine, Karmanos Cancer Institute and Detroit MedicalCenter, Michigan; [4]Department of Internal Medicine, University of Michigan Medical School, Ann Arbor; [5]Department of Pathology, Wayne State University School of Medicine, Karmanos Cancer Institute and Detroit Medical Center, Michigan

Antibiotic prophylaxis during prostate biopsy is widespread; however, rates of postbiopsy infections have been rising. In an analysis of insurance claims data for 515 045 prostate biopsies, 1.55% were hospitalized with infectious complications, with a mean total payment $14 498.96. Infection was the second most common reason for 30-day hospital readmission.

Keywords. antibiotic prophylaxis; biopsy; MarketScan; postoperative complications; prostate.

The incidence of infectious complications after prostate biopsy has been rising over the past 2 decades [1, 2] with estimates of this increase ranging from 100% (2003–2011) [1] to 300% (1996–2005) [2]. These infectious complications—comprised mainly of bacteriuria, bacteremia, urinary tract infection, prostatitis, epididymoorchitis, and sepsis—have surpassed all other major complications associated with the procedure [3]. In recent years, as infectious complications related to biopsy procedures has been rising, so has the prevalence of fluoroquinolone-resistant *Escherichia coli* [4–6].

The American Urological Association (AUA) recommends the use of fluoroquinolone antibiotics as prophylaxis for prostate biopsy procedures [7]. Thus, common antibiotic prophylactic strategies for prostate biopsy may be insufficient to prevent procedure-associated complications, particularly given the rise of fluoroquinolone-resistant (FQR) Gram-negative pathogens. Screening men for colonization with FQR organisms before initiation of prophylactic antibiotics has been proposed as a strategy to reduce the incidence of postbiopsy infection [8]. The development and implementation of such screening programs are resource intensive and require an understanding of the overall risk of postbiopsy complications and costs.

In this study, the objective was to (1) generate national-level, all-cause, and infection-related readmission rates and costs after prostate biopsy in the United States as well as (2) describe current use of antibiotic prophylaxis and treatment, by conducting an analysis of prostate biopsies captured over 8 years in a national insurance claims database.

METHODS

Database

We used inpatient and outpatient data from the Truven Health Analytics MarketScan Commercial Claims and Encounters (CCAE) and Medicare Supplemental and Coordination of Benefits (MDCR) databases to perform a retrospective cohort study for years 2005–2012. The MarketScan database is a national collection of pharmaceutical claims from both employer-sponsored and individual health plans encompassing over 40 million people each year. The inpatient data contain professional and facility encounters and all services associated with an inpatient visit, whereas the outpatient data contain encounters to physician offices, hospital, or other outpatient facilities and emergency rooms. The number of health plans and enrollees included in CCAE and MDCR varies by year.

Data Collection

Men ≥40 years of age with a Current Procedural Terminology-4 (CPT-4) code indicating prostate biopsy (55700) were identified from outpatient services and inpatient admissions tables for years 2005–2012, and inpatient admission data were queried for a period of 30-days after prostate biopsy. All patients included in the follow-up analysis were required to be continuously enrolled in at least 1 insurance plan for at least 30-days postbiopsy for inclusion. Patients hospitalized for infectious complications were identified by querying *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes indicating infection; these included but were not limited to sepsis, prostatitis, cellulitis, and abscess (Supplementary Table 1). Antibiotic data were gathered using the MarketScan-supplied outpatient pharmaceutical claims containing outpatient prescription drug claims from mail-order programs or retail pharmacies. Prescribed prophylactic antibiotics were defined as antibiotic doses given from 2 days prior through 2 days after biopsy.

Incidence and Cost Estimation

The denominator used in incidence rate estimation was derived from male-only Medicare beneficiaries enrolled from 2005 to

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Correspondence: E. T. Martin, MPH, PhD, Associate Professor, University of Michigan School of Public Health, Department of Epidemiology, 1415 Washington Heights, Ann Arbor, MI 48109-2029 (etmartin@umich.edu).

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Table 1. Population Counts and Trends for (n = 515045) Prostate Biopsies Registered in the MarketScan Database From 2005–2012 and Their Subsequent Hospitalization Within 30 Days of Prostate Biopsy

	Eligible Biopsies		Biopsies Hospitalized Within 30 Days		Infectious Complications Within 30 Days	
Year	Number	Percent of Total per Year	Number	Rate of Hospitalization per 10000 Biopsies	Number	Rate of Complication per 10000 Biopsies
2005	45437	5.4	1438	316	559	123
2006	46129	5.3	1422	308	648	140
2007	47942	7.8	904	188	472	98
2008	62934	5.3	1985	315	1090	173
2009	62095	5.3	1958	315	1120	180
2010	66081	5.2	2018	305	1255	189
2011	80470	5.5	2485	308	1580	196
2012	103957	7.4	3767	362	1260	121

2012. Mean cost of hospital stay for admittance was calculated using the total gross payments to all providers who submitted claims for covered services rendered during an admission including total gross payments to the hospital.

Statistical Analyses

All proportions and rates were calculated with SAS software 9.4 (SAS Institute, Cary, NC). Chi-square tests of independence were used to estimate *P* values comparing each prophylactic antibiotic by hospitalization status.

RESULTS

We identified 515045 prostate biopsies performed from the MarketScan database from years 2005 to 2012. The median age at the time of biopsy was 62 with a range of 59 (40–95). Of the 515045 prostate biopsies identified in MarketScan, 15977 were followed by an admission to the hospital as an inpatient within 30 days of the initial procedure, for a 30-day hospitalization rate of 3.1%. When only 1 biopsy per patient is considered, this represents 13205 individual patients admitted soon after biopsy (2.9%). The median length of stay during hospitalization was 3 days (interquartile range = 2), and the mean total payment for the duration of the hospitalization was $15238.71 (standard deviation [SD] = $23148). A total of 7984 (50%) individuals hospitalized within 30-days after biopsy were hospitalized for management of an infection. The mean cost of hospitalization for this subgroup was $14498.96 United States Dollars (USD) (SD = $26975). Septic conditions represented 67.4% of all infectious complications (n = 5385) (Supplementary Table 3). Less than 1% (n = 45) of those hospitalized after prostate biopsy died during hospitalization, and 71% (n = 32) of those who died had an infection documented during their hospitalization.

Over the 8-year time period, infectious postbiopsy complications cost 115 million USD, for an average of 14 million USD per year. When extrapolated out to the entire male Medicare population, we thus estimate the total US cost of infection-related postbiopsy complications to be $5 billion, or 623 million annually.

Prophylactic antibiotic data were available for 16.4% (n = 84242) of all prostate biopsies identified in MarketScan (Supplementary Table 4). Fluoroquinolone antibiotics ciprofloxacin and levofloxacin were the most commonly prescribed prophylactic antibiotics, representing 49.4% (n = 46190) and 28.5% (n = 26684) of all biopsies, respectively. For the 15977 biopsies with subsequent 30-day hospitalization, 3203 (20%) had antibiotic data available. Of these, fluoroquinolones ciprofloxacin and levofloxacin were also the most commonly administered prophylactic antibiotics for this subset of patients (34.4% [n = 1370] and 20.5% [n = 814], respectively).

DISCUSSION

In a national sample of men undergoing prostate biopsies from January 2005 to December 2012, 3.1% were hospitalized within 30 days. Of these, 50% (1.55% of the total) were admitted for management of infection. Cost for inpatient admissions due to these infectious complications averaged 14500 USD.

Previous reports regarding complications after prostate biopsies have focused on infections with FQR *E coli* and extended spectrum β-lactamase-producing pathogens [6, 8]. However, the AUA-recommended fluoroquinolone antibiotics, ciprofloxacin and levofloxacin, were administered to 70% of all biopsy patients as prophylaxis for the prevention of infection after prostate biopsy, yet infection remains the most common reason for 30-day hospital readmission in this study. This was true even in those who received recommended prophylactic therapy. This indicates that many of these complications could be due to the emergence of multidrug-resistant pathogens, as has been noted in smaller prospective studies.

Rectal swab culture screening before biopsy to tailor antibiotics has been proposed as a potential solution to this growing resistance problem: in a systematic review of 9 cohort studies by Cussans et al [9], postbiopsy infection rates were found to be significantly higher in groups given empirical prophylaxis (4.6%) compared with groups receiving targeted antibiotics (0.72%). A decision-analysis to weigh the cost of rectal culture-guided prophylaxis against the cost from empirical prophylaxis was carried out by Li et al [10] in 2015. Their analysis found rectal culture-guided prophylaxis reduced total costs—per men undergoing prostate biopsy—by 40% and a 90%

reduction in overall infection rate. One cohort study by Taylor et al [11] among US men showed even higher cost-savings per postbiopsy infections averted by prior rectal-culture screening (USD 4499) as of 2012.

Important distinctions may be made for those who received multiple versus singular biopsies in regards to FQR colonization and post-transrectal ultrasound-guided prostate biopsy complications. In our study population, there were 46 611 patients with at least 2 biopsies between 2005 and 2012, and, of those hospitalized with an infectious complication, 1903 had at least 2 biopsies. Having multiple prostate biopsies was found to be a significant risk factor for incurring an infection after routine prostate biopsy, and the odds of a serious infection that resulted in hospitalization after routine prostate biopsy increased by a factor of 1.3 if the patient has had a biopsy in the past (odds ratio = 1.33; 95% Wald confidence interval, 1.21–1.46). These results may have potential clinical implications because repeat prostate biopsies are not commonly reported as risk factors for postbiopsy complications.

Our study has several limitations that must be acknowledged. First, the nature of claims-based data prevents us from identifying other contributing factors to hospitalization that may not be apparent from the administrative data. It is further possible that the 5836 biopsies admitted for "diseases and disorders of the male reproductive system" could have an underlying infectious etiology, thus leading to an underestimate of the proportion of readmissions attributable to infection. Second, we are unable to ascertain fluoroquinolone resistance in the organisms isolated from hospitalized biopsies, and thus important information regarding rates of fluoroquinolone resistance during the study period are not estimable. However, an increasing trend in *E coli* fluoroquinolone resistance of 10% from 2005 to 2012 has been documented [12], adding considerable weight to the argument of FQR organisms being implicated in the infectious complications identified here. Despite these limitations, the use of a large national database for this analysis has made data readily available in a large sample across multiple states and across many years, allowing us to establish a national-level estimate of the burden of postbiopsy prostate infection complications with different patterns of clinical care.

CONCLUSIONS

Despite widespread use of fluoroquinolone antibiotic prophylaxis for prevention of infection after prostate biopsy, infection was the most common reason for 30-day hospital readmission. This may be due, at least in part, to the emergence of multidrug-resistant pathogens. These avoidable admissions provide significant financial strain to the healthcare system, resulting in an average cost of 14 500 USD per infection or 14 million annually. Continued efforts are needed to optimize prophylaxis strategies, and best practice guidelines are needed to prevent complications and reduce patient cost and hospital utilization.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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