Hospital-specific antibiograms and antibiotic prophylaxis for prostate biopsies: a reexamination of AUA recommendations

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Introduction: *To assess whether standard American Urological Association (AUA) and other recommendations for prostate biopsy prophylaxis provide sufficient coverage of common urinary organisms responsible for post biopsy infections by comparing local antibiograms in Philadelphia-area hospitals.*

Materials and methods: *De-identified culture results derived from antibiograms were collected from six academic and community hospitals in the Philadelphia region. Analysis specifically focused on four major bacterial causes of urinary tract infection following prostate biopsy (Escherichia coli (E. coli), Klebsiella pneumoniae, Proteus mirabilis and Enterococcus faecalis) along with commonly recommended antibiotics including fluoroquinolones (FQ's), trimethoprim/sulfamethoxazole, ceftriaxone, and gentamicin.*

Results: *Bacterial sensitivities to each antibiotic across institutions showed variation in E.coli sensitivities to FQs ($p < 0.001$), trimethoprim/sulfamethoxazole ($p < 0.001$), ceftriaxone ($p < 0.001$) and gentamicin ($p < 0.001$). Klebsiella pneumoniae and Proteus mirabilis exhibited similar variations. Sensitivity comparisons for Enterococcus faecalis was unable to be performed due to absent or incomplete data across institutions.*

Conclusion: *Institutional antibiograms vary within our regional hospitals. Standardized recommendations for commonly used antibiotic prophylaxis such as fluoroquinolones may be inadequate for peri-procedural prostate biopsy prophylaxis based on local resistance patterns. Valuable information about the potential effectiveness of antibiotic prophylaxis for prostate biopsies can be found in local institutional antibiograms, and should be consulted when considering antibiotic prophylaxis for prostate biopsy procedures.*

Key Words: antibiogram, prostate biopsy prophylaxis, prostate infection, AUA guidelines, bacterial sensitivity, bacterial resistance

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Introduction

Prostate biopsy is the only method for detecting localized prostate cancer with over 1 million biopsies estimated to be performed annually in the United States.[1] Despite the frequent use of fluoroquinolone (FQ) antibiotic prophylaxis directed against the most common strains of bacteria that cause post procedure infections, the rate

of infectious complications encountered from transrectal ultrasound-guided prostate biopsy is estimated at 1%-6%.[1-3] A single dose of oral FQ or first, second or third-generation cephalosporins in accordance with American Urological Association (AUA) recommendations are recommended as drugs of choice for the prevention of post-biopsy infection.[4-6] Studies have demonstrated the efficacy of prophylactic antibiotics prior to prostate biopsy in reducing rates of bacteriuria, bacteremia, fever, UTI and hospitalization compared to non-treated controls.[7]

In recent years, however, the rate of post-biopsy infections have increased, in part due to a high prevalence of FQ-resistant E. Coli, the most common pathogen found in post-biopsy infections.[8-10] The Food and Drug Administration has since decreed that quinolone antibiotics should only be used in patients who have "no alternative".[11] This information led the Canadian Urological Association (CUA) to recommend providers consult local hospital antibiograms to inform providers on their choice of antibiotic prophylaxis, rather than risk suboptimal antibiotic coverage in the ever-changing landscape of antibiotic resistance with specific antibiotic of choice type of recommendations.[7] Hospital antibiograms represent a periodic summary of antimicrobial susceptibilities of bacterial isolates evaluated in the hospital's clinical microbiology lab.[12] This data is often used to assess local susceptibility rates, to aid in selecting empiric antibiotic therapy, and to monitor resistance patterns over time in an institution. A 2017 literature review by Liss et al encompassing 346 articles concluded that post-biopsy infection risk assessment including consultation of local antibiograms should be recommended.[13] In spite of these broad discussions of antibiograms and antibiotic resistance, to date, no study has specifically evaluated this data in determining antibiotic use in the setting of prostate biopsy prophylaxis recommendations.

TABLE 1. **Antibiogram data from six hospitals in the greater Philadelphia area. Three common bacterial causes of post-prostate biopsy infection were compared for sensitivities to four common antibiotics used to treat post biopsy infection. Bacterial sensitivities are shown here ranked in descending order (left to right) according to percentage of bacteria exhibiting sensitivity to the antibiotics.**

Bacterial Strain	Institution	Highest sensitivity (%)		2nd (%)		3rd (%)		4th (%)
Escherichia coli	A	CTX (91.0)	>	GM (88.9)	>	TMP/SMX (70.0)	>*	FQ (68.8)
	B	CTX (93.0)	>	GM (91.0)	>	FQ (80.0)	>	TMP/SMX (75.9)
	C	GM (88.9)	=	CTX (86.9)	>	FQ (68.0)	>*	TMP/SMX (68.0)
	D	CTX (96.0)	>	GM (92.9)	>	FQ (77.9)	>	TMP/SMX (73.0)
	E	CTX (89.0)	=	GM (87.9)	>	FQ (69.2)	>*	TMP/SMX (69.2)
	F	CTX (97.7)	=	GM (94.9)	>	FQ (79.9)	>*	TMP/SMX (76.9)
Klebsiella pneumoniae	A	GM (92.0)	>	CTX (80.9)	=	FQ (77.9)	>*	TMP/SMX (75.9)
	B	GM (94.9)	=	FQ (93.9)	=	CTX (92.9)	>	TMP/SMX (83.9)
	C	GM (94.7)	>	FQ (86.1)	=	CTX (83.9)	>*	TMP/SMX (82.1)
	D	GM (98.9)	=	CTX (96.2)	=	FQ (90.7)	>*	TMP/SMX (90.0)
	E	GM (93.0)	>	FQ (89.9)	=	CTX (88.0)	>*	TMP/SMX (87.0)
	F	GM (100.0)	=	CTX (96.5)	=	FQ (95.6)	>*	TMP/SMX (89.4)
Proteus mirabilis	A	CTX (95.9)	>	GM (91.0)	>	TMP/SMX (83.0)	>	FQ (70.8)
	B	CTX (96.0)	=	GM (93.8)	=	FQ (90.0)	>	TMP/SMX (86.9)
	C	CTX (90.6)	=	GM (87.8)	=	TMP/SMX (81.2)	>	FQ (74.0)
	D	CTX (98.7)	>	GM (91.7)	>	TMP/SMX (82.3)	>*	FQ (72.8)
	E	GM (90.1)	>	TMP/SMX (78.1)	=	CTX (76.8)	>	FQ (67.8)
	F	CTX (100.0)	=	GM (94.6)	=	TMP/SMX (89.2)	>*	FQ (85.1)

Institutions: [A]: Thomas Jefferson University Hospital; [B]: Hospital of the University of Pennsylvania; [C]: Temple University Hospital; [D]: Einstein Healthcare; [E]: Cooper University; [F]: Crozer-Chester Medical Center
Antibiotics: [CTX]: ceftriaxone; [GM]: gentamicin; [FQ]: fluoroquinolone; [TMP/SMX]: trimethoprim sulfamethoxazole
[>]: sensitivity to antibiotic (left) is significantly greater than sensitivity to antibiotic (right)
[=]: sensitivity to antibiotic (left) is non-significantly greater than sensitivity to antibiotic (right)
[*]: sensitivity to antibiotic (left) is non-significantly greater than sensitivity to antibiotic (right); however, sensitivity to antibiotic (right) is significantly lower than antibiotic with highest sensitivity (far left)

We analyzed antibiogram data from six hospitals servicing the Philadelphia metropolitan area and compared resistance patterns of the most common pathogens encountered in reported transrectal prostate biopsy infections to antibiotics routinely recommended for prostate biopsy prophylaxis. The goal was to provide information on how standard recommendations for transrectal biopsy antibiotic prophylaxis would compare to resistance patterns across several hospitals.

Materials and methods

Six academic and community healthcare centers servicing the greater Philadelphia-Delaware Valley area (Thomas Jefferson University, University of Pennsylvania, Temple University, Einstein Healthcare, Cooper University Hospital and Crozer-Chester Medical Center) were included in the study. A representative from each of the six institutions was responsible for procuring and providing the institution's most current antibiogram data.

De-identified bacterial culture results derived from the available antibiograms were collected from each institution. The four most common uropathogens were compared across institutions for sensitivities to the commonly recommended antibiotics for prophylaxis in prostate biopsies (FQ, trimethoprim/sulfamethoxazole, gentamicin, and ceftriaxone). The data analysis focused on the following bacterial strains: E.coli, Klebsiella pneumoniae, and Proteus mirabilis, as these represent the most common infectious bacterial agents associated with prostate biopsy.[14]

For five institutions, raw data, including number of cultures studied for each bacterium was available. One institution provided percentage of bacterial sensitivities without number of total cases.

Pearson Chi-square test was used to compare sensitivities to determine if significant variation was present across institutions. Analysis was performed for each of the four bacteria's sensitivities to each of the four antibiotics, for a total of 16 separate analyses.

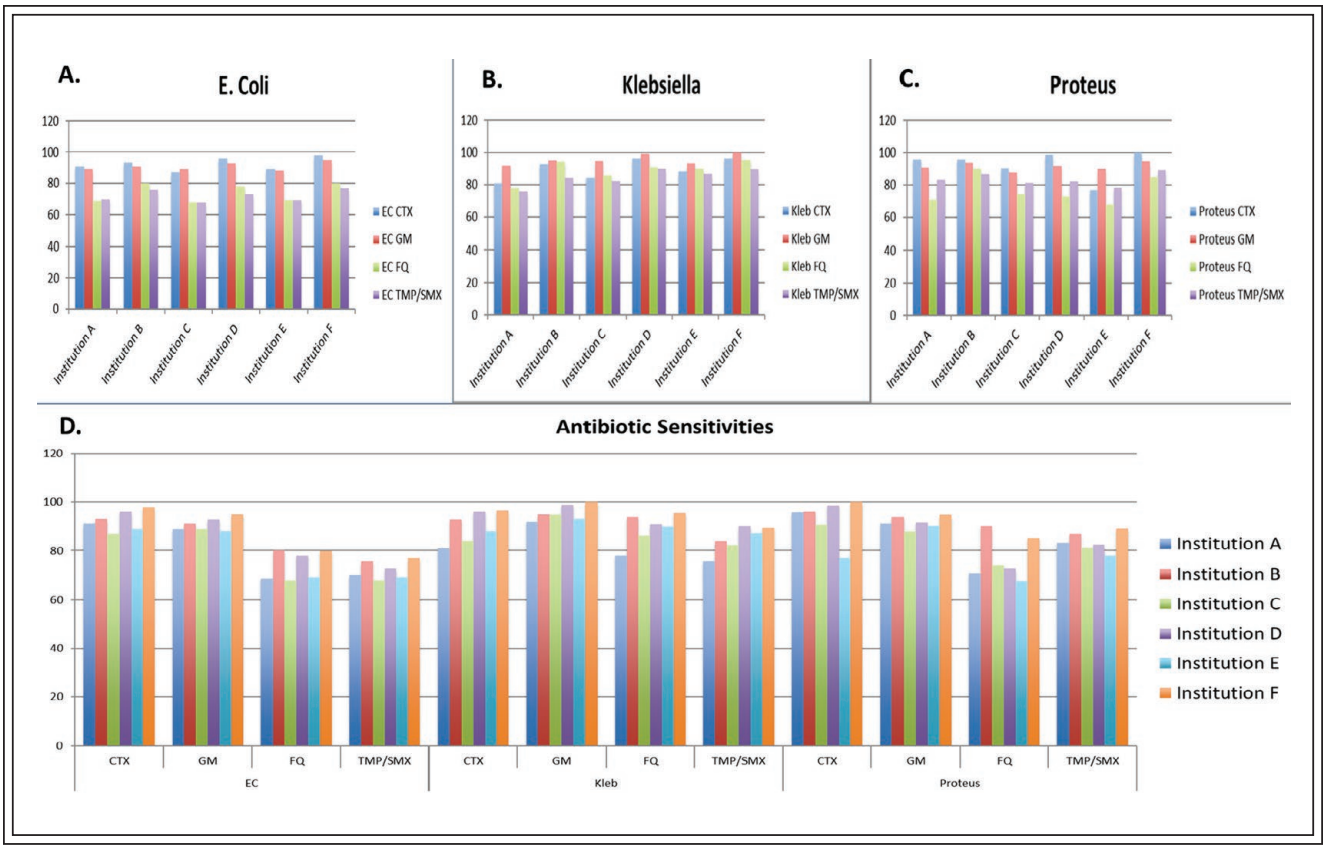

Figure 1. Antibiogram data from six hospitals in the greater Philadelphia area. Sub-figures A, B, and C presents individual hospital percent sensitivities in the x-axis to antibiotics of isolates per institution by bacterium. Sub-Figure C displays combined individual hospital percent sensitivities in the x-axis to antibiotics of isolates per institution by bacterium and antibiotic.

Results

Results are presented in Table 1 and Figure 1. Out of 16,503 total bacterial cultures with sensitivity, 10,974 were E. Coli, 3,750 were Klebsiella and 1,779 were Proteus. E. coli had the greatest average sensitivity to ceftriaxone (92.3%) of the antibiotics studied across all institutions. Gentamicin sensitivity was next highest (90.8%) and FQ sensitivity was third (74.3%). Statistically significant variation in E. coli sensitivity to FQ ($p < 0.001$), trimethoprim/sulfamethoxazole ($p < 0.001$), ceftriaxone ($p < 0.001$) and gentamicin ($p < 0.001$) was observed between all institutions. Enterococcus faecalis sensitivity to > 1 antibiotic was unavailable at all six institutions.

Of the four antibiotics studied, bacteria had the highest sensitivity to current AUA recommended antibiotics (ceftriaxone, FQ) in just 55.6% of bacterial isolates across all institutions. Bacterial cultures demonstrated the least sensitivity to FQs in 33.3% of cases, and was ranked either 3rd or 4th in terms of sensitivity in 83% of cases.

Discussion

Our findings suggest that routine prophylaxis for prostate biopsies using AUA recommended FQs might not be the best choice for the top three pathogenic organisms in all of the local antibiograms in the Philadelphia area hospitals studied. Additionally, cephalosporins, the alternative AUA-recommended top choice, represented by ceftriaxone in our study, was the sole best option in only 50% of antibiograms for the most common organism (E. Coli) in this series. However, the additional AUA recommendation of culture-directed antibiotic prophylaxis are supported as the antibiograms more clearly inform antibiotic choice. Using the pre biopsy culture results many allow urologists to decrease the chance of encountering bacterial resistance than by using algorithmic decision-making alone.

With over a million prostate biopsies estimated to be performed annually in the United States, the significant rise in antibiotic-resistant bacteria has become a major concern. This increasing resistance is even noted with our antibiotics of last resort such as carbapenem-resistant Enterobacteriaceae (including E. coli and Klebsiella species).[1] One of the reasons cited for this rise in resistances is suspected overuse of antibiotics in humans and in the livestock industries. The World Health Organization has shown detectable levels of antibiotics in municipal water supplies, and with this exposure to the public, the process of bacteria becoming resistant is compounded by factors such as over-prescribing of antibiotics.[1,15] Not surprisingly, a Canadian study of 75,000 patients who underwent prostate biopsy found a 400% increase in hospitalizations for infection from 1996 to 2005.[16] With the significant rise in resistance and concurrent rise in infectious complications after prostate biopsy, increased attention should be given to recommendations that guide our selection of prophylactic antibiotics.

In response to the increasing infection rates, recent studies have focused on novel ways to tailor and perhaps steward antibiotic use with pre procedure urine cultures or rectal culture swabs. Using data from the Michigan Urological Surgery Improvement Collaborative (MUSIC) registry in Michigan, they noted that many of the hospital related infections with prostate biopsy could be avoided by implementing new protocols (e.g. culture specific or augmented antibiotic prophylaxis).[17] A study by Duplessis et al, analyzed 235 rectal swabs from patients before prostate biopsy to check for FQ resistance. Of those evaluated, 32 (14%) had FQ resistant isolates.[18] Similar results were observed in a study by Cohen et al, which reported on the rectal swabs of 637 men and observed that 23.4% of patients harbored strains of FQ resistant E. coli.[19] In this study the authors also concluded that number of prior biopsies is not significantly associated with bacterial resistance. These studies finding high resistance in rectal flora, the cause of most post prostate biopsy infections. This is consistent with the our local antibiogram resistance patterns and supports our findings of common resistance to the specific AUA recommended antibiotic prostate biopsy prophylaxis options. Using these recommended agents, nearly a quarter of patients treated with FQs might be at risk for infection due to bacterial resistance.

Recognizing the need for guidance on urology-specific antimicrobial prophylaxis, the AUA formed a Committee lead By Dr. Stuart Wolf that created the AUA's 2008 "Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis",[18] wherein the AUA developed nationwide recommendations for urologic procedures including prostate biopsy prophylaxis. These recommendations for broad gram-negative coverage in the form of FQ administered prior to biopsy, with these recommendations were expanded to include cephalosporins for increased coverage.[12] By 2013, in the face of worsening bacterial resistance to FQs, the European Urological Association (EAU) officially acknowledged that in regard to prostate biopsy prophylaxis the "choice of regimens remains

debatable".[20] However, our study of Philadelphia area institutions found significant variations in antibiotic sensitivity for each of the most common pathogens limiting applicability of using a standardized regimen. Importantly, in none of our local antibiograms analyzed were FQs the most effective prophylactic choice.

Our study has a number of limitations. Antibiograms' tracking of resistance trends has some limitations as they snapshot bacterial culture sensitivity profiles, and cannot account for rapidly developing changes in sensitivities and resistances. Our study is limited in that not all of the institutional antibiograms are updated annually leading to potential confounding from different years being analyzed. Furthermore, differing antibiotic use and stewardship patterns may cause differing bacterial sensitivities and this may explain the antibiogram differences both between institutions. Another potential limitation is that the local antibiograms used in this study do not provide information on patient age or other factors that may play a role on the incidence of antibiotic resistance. Further, our data is representative of the Philadelphia area and may not be generalizable to the rest of the United States. Lastly, no data was available on specific clinical outcomes related to trans-rectal prostate biopsy infection rates. Despite these limitations, it is possible to draw valuable conclusions from the sensitivity information present between hospitals and between antibiotics. Although our data questions the use of standardized antibiotic regimen, with stewardship in the use of antibiotics increasingly similar sensitivities may be seen in the future.

The differences we observed within the antibiogram profiles indicate that recommendations for standardized antibiotic prophylaxis may not be optimum even within a relatively small geographic area such as ours. Within our own region, there were high resistance levels to AUA recommended antibiotics of choice, but also variations between institutional antibiograms. Validation of our observations and nation-wide research is needed to evaluate if similar findings exist in other regions. In theory using local institutional antibiograms, providers can prescribe antibiotic regimens that may provide better antimicrobial coverage and improved efficacy than following AUA guidelines that may be based on older and nation-wide average sensitivity data.

This approach potentially carries several advantages. Infections associated with prostate biopsy can lead to urosepsis in rare cases, and thus any precaution to avoid potentially fatal downstream effects from infection should be pursued. Further, tailoring antibiotics with bacterial sensitivities would help combat the growing problem of increased bacterial resistances, which threatens many specialties and procedures, and would help to reduce the development of multidrug-resistant organisms. The variation in sensitivity observed across our institutions reinforces the concept of consulting hospital-specific antibiograms over broad regional or national recommended regimens. The AUA white paper includes consideration of culture-directed antibiotics and express concern with considering antibiograms as representative of outpatient flora. However, the counter argument, that those floras that are found in culture results are more likely to represent the pathogenic strains is equally valid.

Conclusions

Hospital-specific antibiograms provide valuable information about bacterial sensitivities that may inform the use of prophylactic antibiotics for ultrasound directed prostate biopsies. There are increasing concerns for using FQs, the most commonly recommended antibiotic for prostate biopsy prophylaxis. Further investigations should examine infection rates from biopsy specific urine and rectal cultures, and the broader public health cost impact in tailoring antibiotic choice to local antibiogram sensitivities. □

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