Studies split on pre-prostate TRUS biopsy screening

Anne Ford

October 2016—Take a bar graph, any bar graph, and compare it to the natural landscape of the United States. If most of it resembles the Great Plains but the right-hand side starts looking more like Rocky Mountain territory . . . well, something interesting is going on.

Dr. Zembower

That's the case with a graph recently put together by Teresa R. Zembower, MD, MPH, associate professor of medicine in the infectious diseases division at Northwestern University Feinberg School of Medicine and an infectious disease specialist, Northwestern Medicine, Chicago. The graph depicts the incidence, by year, of all the PubMed articles between 1975 and 2015 that contain the words "infection" and "prostate biopsy."

"You can see that sometime around 2010, that's when people started noticing there was something different [going on]," Dr. Zembower said in "Pre-prostate Biopsy Screening for Quinolone-resistant Gram-Negative Rods: Worthwhile or Wasteful?" a talk at the ASM Microbe meeting in June. "People said, 'Uh-oh. Something is wrong. We're seeing infections like we've never seen before.'"

Urinary tract infection, prostatitis, prostate abscess, epididymitis, bacteremia, and sepsis. Suddenly, even with ciprofloxacin prophylaxis, these and other complications of prostate biopsy are becoming much more common. "Since 2010, the incidence is up to seven percent in some institutions," Dr. Zembower reported, citing studies published in the *Journal of Urology, European Urology,* and other publications. "Hospitalizations are up to four percent, largely due to cipro-resistant bacteria." Hospitalizations within 30 days due to infection rose between 1991 and 2007, she says. "And 30-day UTIs or bacteremia incidence increased from 0.71 per 100 biopsies to 2.15 per 100 biopsies between 2002 and 2011. It's quinolone-resistant Gram-negatives that are causing this, mostly *E. coli.*"

As this upward trend in infectious complications of prostate biopsy continues, institutions find themselves under increasing pressure to develop effective methods of fighting it. In her presentation, Dr. Zembower outlined the pros and cons of one such method—pre-biopsy screening for quinolone-resistant Gram-negative rods.

But first, where is all this *E. coli* coming from? "We note that roughly 20 percent of men who are undergoing prostate biopsy are actually colonized in their rectums with cipro-resistant *E. coli*," Dr. Zembower said. "That's scary enough, but these cipro-resistant *E. coli* also tend to be multidrug resistant—resistant to ampicillin, ampicillin sulbactam, trimethoprim sulfa, aminoglycosides—and some of them are ESBLs [extended-spectrum beta-lactamase-producing organisms]."

Many of the risk factors for infection are not easily modifiable—an immunocompromised or an uncircumcised state, diabetes, indwelling catheter, exposure to antibiotics within six months, larger prostate, health care workers and their families, and colonization with fluoroquinolone-resistant *E. coli*. Some things can be done in an attempt to prevent infection, however, such as disinfecting the biopsy needle between cores, treating the asymptomatic bacteriuria before biopsy, minimizing bleeding, and using a transperineal approach in high-risk patients, which

some institutions are doing, she says, but which has a higher risk of procedure-related complications.

But the main form of useful prophylaxis is antimicrobial. It's just not clear what kind is best. As Dr. Zembower put it, "Although everybody agrees you should give something, people disagree about what you should give. The American Urological Association and CMS do have guidelines on what's appropriate prophylaxis for prostate biopsy. Quinolones are first-line. Cephalosporins are also agents of choice. And then the alternatives are more for the people who can't take those choices, so aztreonam plus/minus clindamycin, and then the AUA says that the prophylaxis duration should be 24 hours or less."

Two main prophylaxis strategies have emerged, Dr. Zembower said—a targeted approach and an augmented approach. The targeted approach involves taking a pre-biopsy rectal swab culture and plating the results. "Usually it's done on a selective media that's enhanced with cipro, but there's no standard way to do this," she said. "We use a MacConkey plate with one microgram per mL of cipro. We get that commercially. Some people use 10 micrograms per mL of cipro. Some people have used broth enhancement techniques. So it's not standardized. But you use the culture, whatever your lab uses, and you direct your prophylaxis to that. So since the plate has cipro in it, if nothing grows, you give cipro. That's what we do. And if something grows, you target your prophylaxis to the antimicrobial susceptibility profile."

Why opt for this strategy? "It allows you to give a narrower spectrum," she said. "It may be adaptable to different practice settings. I think it's durable. I think that's the big advantage, that as antibiotic resistance changes, you'll be able to detect it." On the downside, it's a cumbersome approach that does require at least one extra patient visit and has no standardized procedure.

In contrast, the augmented approach entails adding something to ciprofloxacin or using a non-quinolone regimen. While easier and faster, this strategy has its downside as well, of course. "The cons are the theoretical selection of resistance and probably multidrug resistance," Dr. Zembower said. "And also remember, a lot of these patients who have cipro-resistant organisms have multidrug-resistant organisms, so you may miss the organism as well if you're just adding empirically. And then there is obviously, anytime you're adding something, the potential for adverse drug reactions."

She pointed to a recent systematic review that looked at nine cohort studies on the role of targeted prophylactic antimicrobial therapy before transrectal ultrasound-guided prostate biopsy in reducing infection rates (Cussans A, et al. *BJU Int.* 2016;117[5]:725–731). The review, which looked at empiric ciprofloxacin versus targeted prophylaxis, found that post-biopsy infection and sepsis rates were significantly higher in the empiric group than in the targeted group, and that 27 men would need to receive targeted prophylaxis for one infective complication to be prevented. The authors concluded that targeted prophylactic therapy before TRUSP is associated with lower sepsis rates, and they recommend changing current pathways to adopt this approach.

"I don't think this is a surprise," Dr. Zembower said. "We know cipro as a one-size-fits-all for everybody undergoing prostate biopsy is probably pretty dangerous these days, especially if you have a pretty high-risk patient population."

She highlighted another recent study, "Comparative Effectiveness of Single versus Combination Antibiotic Prophylaxis for Infections after Transrectal Prostate Biopsy," which considered augmented versus single prophylaxis, mostly with cipro (Marino K, et al. *Antimicrob Agents Chemother.* 2015;59[12]:7273–7275). It was a single center retrospective cohort of 455 men who received various prophylaxis regimens—monotherapy versus combination therapy.

"Cipro alone—again, no surprise—underperformed," with a 7.5 percent infection rate, said Dr. Zembower. "But intramuscular gentamicin, which a lot of urology offices use, really underperformed, with a 17.2 percent infection rate." Compare that with cipro plus cefpodoxime, which had an infection rate of just 1.1 percent, or cipro plus anything else, which came in at 2.3 percent. The study's conclusion: Institutions with high antibiotic prophylaxis failure rates should consider combination regimens derived from their local antimicrobial susceptibility data.

“Again, not a surprise. If you add something to cipro because cipro is underperforming everywhere, you’re probably going to get better results,” she said.

A third study she reviewed came from a statewide intervention in Michigan to reduce hospitalizations after prostate biopsy (Womble PR, et al. *J Urol.* 2015;194[2]:403–409). “They looked at retrospective data collection using conventional prophylaxis, and then they did their quality intervention and looked at prospective data using either an augmented or targeted approach,” Dr. Zembower said. “They found that there was a significant difference in the augmented and targeted approach. They both worked better than the traditional approach, but they were equally efficacious.” The statewide intervention reduced post-biopsy infection-related hospitalizations by 53 percent.

A similar study out of 13 Kaiser Permanente urology clinics considered retrospective data collection using empirical prophylaxis, either monotherapy or augmented therapy versus targeted therapy, and looked at sepsis within 30 days (Liss MA, et al. *J Urol.* 2015;194[2]:397–402). “They saw no statistical difference in infection rates in the targeted versus empiric groups,” Dr. Zembower said. “But they’re a fan of the targeted approach, and they have been from the beginning. They think the targeted approach allows physicians to limit the use of multiple antimicrobial agents, and that’s its advantage.”

“Our results,” the authors wrote, “suggest that rectal cultures allow correct antibiotic recommendations in almost all cases.”

Of the several studies published on this topic in 2015, Dr. Zembower said, about half point to the targeted or augmented approach being superior to empiric therapy, and the other half say they’re no better. “So it’s still an unknown question.”

This much is known, she said: About 20 percent of men undergoing TRUSP are enterically colonized at the start with quinolone-resistant Gram negatives, primarily *E. coli,* and these *E. coli* are often multidrug resistant. An increased incidence and severity of post-TRUSP infections are associated with monotherapy with quinolones and with some other drugs as pre-procedure prophylaxis. Studies suggest that the targeted and augmented approaches are comparable in terms of infection outcomes, and additional studies are needed not only to compare the strategies but also to monitor for further emergence of drug resistance. No study has done the latter.

“I worry about, first, driving resistance,” Dr. Zembower said, “and, second, having another 2010 where we missed drug resistance and then we’re back to saying, ‘Okay, now what are they colonized with?’”
[hr]

Anne Ford is a writer in Evanston, Ill.