Fluoroquinolone-Resistant Intestinal Organisms and Infections After Prostate Biopsy: Shifting Sands of the Prevention Narrative

Deepak Batura
Department of Urology, London North West Healthcare NHS Trust, United Kingdom

(See the Major Article by Liss et al on pages 979–87.)

Keywords. prostate biopsy; complications; healthcare-associated infections; fluoroquinolone resistance; prevention.

Transrectal ultrasound-guided prostate biopsies continue to be the gold-standard procedure for the diagnosis of prostate cancer. Prostate biopsies are being performed in growing numbers. This is due to rising longevity, an increase in screening programs, and larger numbers of men in active surveillance protocols and men requiring rebiopsy. An increasing incidence of severe infective illness after transrectal prostate biopsies in this decade has led to a rising tide of interest in infections after biopsies. Although overall morbidity has remained mostly contained, the management of these infections imposes a considerable financial and resource burden on healthcare systems [1].

There has been an increasing awareness that the rate of ciprofloxacin-resistant infections after biopsy correlates with the carriage of fluoroquinolone-resistant bacteria in the intestinal microbiota of men undergoing biopsy. This knowledge has been based on the observed similarity between bacteria present in the intestinal flora and those cultured from clinical isolates of men who go on to develop infections. This single-center observational study by Liss et al [2], published in this issue of Clinical Infectious Diseases, has built on what has hitherto been assumed, and has demonstrated that there were no differences between pulsed-field gel electrophoresis (PFGE) patterns or antimicrobial susceptibility profiles in Escherichia coli infection isolates and E. coli rectal isolates in 9 men with paired isolates, strongly suggesting that rectal E. coli is the source of infections. Interestingly, the authors have also noted that non–sequence type (ST) 131 clones were as likely to cause infection as ST131 clones, implying that the underlying virulence of ST131 may be exaggerated in the context of infections after prostate biopsy. In their patients, the increased proclivity for fluoroquinolone-resistant bacteria to cause infections could not be explained by any differences in detection of the ST131 clone, which is purportedly more virulent, or by virulence characteristics between the infecting and colonizing strains. Therefore, it is conceivable that direct inoculation of the bacteria into the prostate lessens the need for special virulence characteristics to initiate infection.

The study was a retrospective review of data on 1638 biopsies. However, due to the inherent weaknesses of retrospective studies, incomplete data capture, and nonavailability of rectal cultures done beforehand, the cohort was whittled down to less than half that number (764 patients). Furthermore, selecting only 78 patients for PFGE analysis led to a similarity analysis being conducted in only 9 men, and thus the finding of similar E. coli PFGE profiles between clinical isolates and rectal isolates lacks the statistical robustness that one would have liked to see. Thus, a larger study exploring this similarity would be a welcome addition to literature on the topic.

Liss et al also found that hospital admissions in the preceding year were predictive of infections, but there is currently no mechanism to explain this observation. Equally intriguing has been the observation that 65 men who had rectal cultures 1–2 weeks before biopsy had a significantly lower prevalence of resistant E. coli colonization than men who had a culture done on the day of biopsy. In the absence of any intervention during the interval...
between rectal swabbing and biopsy, this observation in 8.5% of evaluable subjects is probably due to chance but could represent another area for further study.

The authors have also shown that supplemented antimicrobial prophylaxis was used in 20.9% of their patients, with ampicillin being most commonly used (94%). This is despite ampicillin co-resistance being present in 99% of men who received enhanced prophylaxis. It is therefore unsurprising that infection rates did not differ between the patients who received supplemental antibiotics and those who did not. The choice of supplemental antibiotic raises questions given this level of resistance; more so when their patients’ rectal and clinical isolates showed negligible resistance to carbapenems (0%-1%), β-lactamase inhibitors (1%), and amikacin (0%). It would not be inappropriate to speculate that outcomes could have changed with a different choice of antimicrobial for enhanced prophylaxis [3, 4].

The study by Liss et al has once again reiterated the clinical significance of fluoroquinolone resistance as a risk factor for postbiopsy infections. In areas with very high rates of fluoroquinolone resistance, such as Southeast Asia and Africa, rates of infective complications are likely to be larger [5]. As these geographic areas are resource limited in healthcare provision, the morbidity of these infections is likely to be correspondingly more severe. It is in this context that a search for alternate strategies to reduce biopsy-related infections assumes an even larger role.

Effective antibiotic stewardship and decreasing the use of fluoroquinolones in poultry and livestock would be effective public health interventions to decrease the reservoir of fluoroquinolone-resistant E. coli. However, given the slow implementation of these measures and increasing international travel helping to spread these bacteria, we are a long way from effective public health control. Until these long-term measures gain traction, the Hippocratic principle of nonmaleficence, or primum non nocere, demands that the prevention narrative should include other measures.

It is not unusual for urologists to give a 2- to 4-week course of ciprofloxacin for clinical prostateitis or to try and decrease prostate-specific antigen (PSA) levels and thus eliminate false-positive PSA results and unnecessary biopsy [6]. This practice has no valid justification but continues to be used by many. This could contribute to fluoroquinolone resistance in these men by the time they have a biopsy.

The authors propose adding supplemental antibiotics on a tailored basis, guided by prebiopsy rectal swabs. This is, in essence, targeted prophylaxis, which has been useful in reducing postbiopsy infections [7]. Other measures include prophylaxis based on local antibiotic-resistant patterns through antibiograms. Approaches such as the use of povidone-iodine rectal washouts or using chlorhexidine-coated biopsy needles have also been proposed.

In an attempt to improve diagnostic yield, the number of cores of tissue sampled has increased from the traditional 6 to 12, with many more cores being taken in “saturation” biopsies. Increasing the number of cores increases the risk of infection. With increasing validation of multiparametric magnetic resonance imaging (MRI) and fusion biopsy techniques making accurate tissue sampling possible, it is hoped that the number of cores can be kept down. MRI and fusion techniques could also help in reducing the high rate of repeat biopsies, which can occur in up to 20% of men.

A more limited use of PSA screening as proposed in the American Urological Association guidelines of 2013, assisted by risk nomograms, could help reduce the number of biopsies being performed. The use of biomarkers such as PCA3 and use of gene tests to determine cancer predisposition might further help reduce biopsy rates. Transperineal biopsies are more complex to perform than transrectal biopsies and usually require a general anesthetic. Despite this, the transperineal route, with its lower rate of infective complications, should certainly be included in the biopsy construct.

Note

Potential conflict of interest. Author certifies no potential conflicts of interest.

The authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References