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ORIGINAL ARTICLE

Prevention and management of infection associated with transrectal ultrasound guided prostate biopsy in Ireland

Clíodhna Frances Ní Bhuachalla, Eileen Nolan, David Galvin, Claire M Buckley, Fidelma Fitzpatrick
National Cancer Control Programme (NCCP) National Prostate Biopsy Infection Project Board, NCCP, Dublin, Ireland

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Abstract

The incidence of transrectal ultrasound (TRUS)–guided prostate biopsy associated infection is reportedly increasing, particularly antimicrobial resistant (AMR) infections. To inform development of an inaugural national policy on prevention and management of infection post TRUS biopsy, we conducted a national survey of ten prostate cancer centres that perform approximately 90% of public prostate biopsies in Ireland. An on-line questionnaire regarding prostate biopsy pathways, pre-biopsy AMR risk assessment and antimicrobial prophylaxis regimens, and post-biopsy infection surveillance and management was circulated to all centres. AMR organisms considered included *Enterobacteriaceae* (with particular reference to *Escherichia coli*) with fluoroquinolone and/or aminoglycoside resistance, extended spectrum beta-lactamase (ESBL) or carbapenamase production. Data from 1st January 2011 to 30th June 2013 were collected retrospectively from July to September 2013. Data were analysed using Microsoft Excel® software. The results of this survey demonstrated marked variation of practices nationally. Three centres reported risk assessing for AMR colonisation pre-biopsy. AMR screening was not conducted routinely in any centre. Antimicrobial prophylaxis regimens, surveillance programmes and empiric therapy guidelines for sepsis also varied between centres. A range of infectious complications were reported, both bloodstream infection (BSI) and non-BSI, however, due to use of non-standardised case definitions, national infection rates could not be generated. At the time of the survey, there were no Irish guidelines and centres followed American and/or European

Corresponding Author
Dr C.F. Ni Bhuachalla
NCCP, King's Inns House, 200 Parnell Street, Dublin1, Ireland.
Email: c_ni_bhuachalla@hotmail.com

guidelines. Following our survey the National Cancer Control Programme published a "National Policy on the Prevention and Management of Infection post Transrectal Ultrasound-guided Prostate Biopsy" in June 2014 to assist in standardising practice and reducing risk of infectious complications.

Key words: Transrectal ultrasound-guided (TRUS) prostate biopsy; Prostate; Infections; Drug resistance, microbial, Antibiotic prophylaxis; Epidemiological surveillance; disease management

Introduction

Transrectal ultrasound (TRUS)-guided prostate biopsy is a standard diagnostic tool for prostate cancer.[1] Public Rapid Access Prostate Clinics (RAPC), established by the Irish National Cancer Control Program (NCCP) in 2009, facilitate same day management of suspected prostate cancer and target men with indications for prostate biopsy.[2] This one-stop diagnostic model facilitates rapid assessment and diagnosis, reducing patient anxiety and streamlining prostate cancer diagnosis and management.

Infectious complications following TRUS biopsy are increasing, specifically antimicrobial resistant (AMR) infections, and include urinary tract infection (UTI), prostatitis, bloodstream infection (BSI), and severe sepsis.[3] *Escherichia coli* causes approximately 75%–90% of infections with increasing reports of fluoroquinolone resistance and/or production of an extended spectrum ß-lactamase (ESBL).[3] AMR infection risk factors include recent fluoroquinolones, AMR colonisation or infection and recent international travel.[1,3-5] Recent Irish AMR data demonstrated approximately 26.2% of invasive *E. coli* isolates tested were resistant to ciprofloxacin, approximately 10.1% of invasive *E. coli* isolates tested were found to be ESBL-producing and the first carbapenamase-producing *E. coli* from an invasive infection was confirmed.[6]

In light of reported increased incidence of infectious complications, and absence of Irish TRUS biopsy data, we conducted a national survey of public prostate cancer centres. The aim of this survey was to ascertain national practices to inform development of a national policy on prevention and management of infection post-TRUS biopsy.

Methods

An on-line questionnaire regarding prostate biopsy pathways, pre-biopsy AMR risk assessment and antimicrobial prophylaxis, and post-biopsy infection surveillance and management was circulated to ten public prostate cancer centres (all 8 NCCP centres and the 2 largest centres of 15 other public hospitals performing TRUS biopsies). These ten centres perform approximately 90% of public prostate biopsies nationally. Data from 1st January 2011 to 30th June 2013 were collected retrospectively from July to September 2013 using SurveyMonkey®. Data were analysed using Microsoft Excel® software.

Gathering and analysing national cancer data is consistent with the standard works and terms of reference of the NCCP thus institutional review board approval was deemed not to be required.

Results

All ten centres responded. All centres performed TRUS biopsies on-site, four also performed transperineal prostate biopsies. Biopsies were performed in interventional radiology (n=5), RAPC facilities (n=3) or urology outpatients (n=2). All centres used oral fluoroquinolone antimicrobial prophylaxis; ciprofloxacin (n=8), ofloxacin (n=2). Five centres used a second agent; intravenous (IV) gentamicin, IV amikacin or oral metronidazole. Antimicrobial prophylaxis dosing schedules varied; single dose (n=2), 24 hours (n=4), 48 hours (n=1), 72 hours (n=2), 5 days (n=1). Dosing of ciprofloxacin varied with either 500mg (n=4) or 750mg (n=4) prescribed.

No centre routinely performed pre-procedure AMR screening though one was conducting a pilot study on ESBL *Enterobacteriaceae* rectal screening. Three centres reported using a formal risk assessment tool to assess for AMR colonisation pre-biopsy. Risk factors assessed are described in Table I. No formal risk assessment tools or written protocols were returned.

Seven centres reported having a post-biopsy infection surveillance programme in place, although none

Table I. Risk assessment for AMR colonisation pre-biopsy

Number of centres	Risk factor assessed
n=3	• Previous AMR colonisation • Immunocompromise
n=2	• Recent fluoroquinolone use • Previous antimicrobials • Previous urological procedure
n=1	• Previous post-biopsy sepsis • Presence of indwelling material • Renal tract abnormality • Recent hospitalisation • Diabetes mellitus • Age

used standardised internationally comparable case definitions for infection categorisation. Methodology for infection follow-up varied and included telephone follow-up (n=3), clinic review (n=5) or a combination of methods (n=2). Table II summarises infectious complications reported.

Seven centres had a protocol for infection management post-TRUS biopsy. Empiric antimicrobial prescribing guidelines varied; meropenem (n=3), meropenem with gentamicin (n=1), co-amoxiclav with gentamicin (n=1) or piperacillin/tazobactam (n=1). Empiric use of ciprofloxacin or amikacin was not reported. Four centres recommended prior discussion of empiric antimicrobial therapy with a clinical microbiologist or infectious diseases physician.

Discussion

This national survey revealed marked variation in practices in Irish centres performing TRUS biopsies. While all centres used fluoroquinolone prophylaxis in line with international guidelines[4,5] there was no standardisation in relation to pre-biopsy AMR assessment and prophylaxis regimens, and post-biopsy surveillance and infection management.

Table II. Number of prostate biopsies performed and post-biopsy infectious complications reported in ten Irish prostate cancer centres from 1st January 2011- 30th June 2013

Year	2011	2012	2013*
Number of prostate biopsies performed	3,466 (n=8)	3,771 (n=9)	2,338 (n=7)
Number of post-biopsy BSI[1]			
0-5 BSI	3 centres	3 centres	5 centres
6-10 BSI	1 centre	3 centres	0
>10 BSI	1 centre	1 centre	1 centre
Number of post-biopsy non BSI[2]			
0-5 non BSI	2 centres	1 centre	4 centres
6-10 non BSI	1 centre	3 centres	0
>10 non BSI	0	2 centres	0

[1] BSI: bloodstream infection

[2] Non BSI: urinary tract infection (n=5), prostatitis (n=2), orchitis (n=1) epididymitis (n=1), spinal abscess (n=1)

* Reported figures up until 30th June 2013.

TRUS biopsy is a widely performed, generally safe elective procedure but can be associated with infectious complications. Post-TRUS biopsy UTI rates of 2–6% are reported, with 30–50% of those patients developing BSI. A quarter of patients hospitalised with post-TRUS biopsy *E. coli* BSI had severe sepsis requiring intensive care unit admission.[3] True incidence of infection may be underestimated, as reports usually concentrate on hospitalised patients rather than primary care patients (e.g., while 4.2% of patients had a fever in the two weeks post-procedure, only 0.8% were hospitalised).[3]

Irish prostate centres reported a small but significant number of post-TRUS biopsy infections. As standardised case definitions for infection surveillance were not employed, we could not produce Irish infection rates for benchmarking with other countries. However, national AMR surveillance data indicates that AMR *Enterobacteriaceae* spp. BSI is increasing.[6] Standardising national surveillance methodology permits meaningful comparison of infection rates and analysis of outcomes. We recommend that Irish centres systematically capture UTI and BSI post-TRUS biopsy, using standardised European case definitions from 'Hospitals in Europe Link for Infection Control Surveillance (HELICS)' standards to enable comparison with other European centres,[7] and conduct systems analysis of all BSI. The NCCP national policy outlines a national surveillance framework.[8]

Irish centres did not routinely screen patients for AMR and three centres (30%) risk assessed patients. While individual studies indicate the usefulness of pre-biopsy rectal AMR screening to guide targeted antimicrobial prophylaxis,[9] currently this approach is not recommended in international guidelines.[4] Others recommend that urologists consider AMR screening after risk assessment.[5] Pre-biopsy AMR screening to direct antimicrobial prophylaxis could certainly be justified in light of increasing reports of post-prostate biopsy AMR infections.[1,3] In order to evaluate the cost effectiveness of a national prostate biopsy AMR screening programme in Ireland, we would require standardised surveillance on the burden of infection and reconfiguration of existing care pathways of RAPCs to enable prior AMR screening. The optimal specimen type and laboratory protocol for screening has yet to be defined.[3]

Study results demonstrated varied prophylaxis regimens. There are no definitive data to support the use of three day over 1 day dosing regimens, or multiple over single dose schedules.[10] Prophylaxis should commence within 60 minutes of the biopsy and be discontinued within 24 hours.[4] For patients without risk factors for AMR *Enterobacteriaceae* we recommend single dose 750mg oral ciprofloxacin,[4,5] and a 2 drug regimen if AMR risk factors present.[8] Transperineal prostate biopsy is less frequently associated with infection,[3] and may be the preferred approach where risk of sepsis is high.

Limitations of this study are inclusion of public data only and that national infection rates could not be generated from the survey data.

Although international guidelines recommend a standardised approach to TRUS biopsy we found considerable practice variation in Ireland. At the time of the survey, there were no Irish guidelines and centres followed American,[4] and/or European guidelines.[5] Following our survey the NCCP published a national policy on the prevention and management of infection post-TRUS biopsy in June 2014[8] with several infection-related key performance indicators for quarterly national monitoring. Effective implementation of this policy requires clear communication between all stakeholders and should assist in reducing infectious complications by standardising practice.

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