NPCA
National Prostate Cancer Audit

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Prostate Biopsy Short Report

NPCA: Short Report

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About HQIP, the National Clinical Audit and Patient Outcomes Programme and how it is funded:

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RCS
The British Association of Urological Surgeons
BUG
HQIP Healthcare Quality Improvement Partnership

Executive Summary

The majority of prostate biopsies are taken through the transrectal (TR) route with sepsis remaining the most serious and well recognised complication of this procedure. Taking prostate biopsies through the transperineal (TP) approach has been developed in recent years as it is better at sampling the anterior tissue of the prostate gland, which is generally neglected by the transrectal approach. This short report aims to evaluate the current national practice in the use of TP biopsies and how the risk of complications is affected by the biopsy approach.

73,630 men diagnosed with prostate cancer in the English National Health Service between 1st April 2014 and 31st March 2017 were identified using cancer registry data. Welsh data was not used as we did not have access to appropriate outpatient data. Administrative hospital data were used to identify biopsy route, overnight hospital stay immediately after biopsy, 30-day hospital admissions because of sepsis, urinary retention or haematuria and 30-day mortality. Multivariable generalised linear regression models were performed to calculate adjusted risk differences in these outcomes between TR and TP biopsies.

In summary, the proportion of men undergoing a TP biopsy has nearly doubled within 3 years (14% to 25%), indicating a shift towards the use of this approach in certain hospitals. For every 1000 biopsies performed, 3.6 *fewer* men would be readmitted due to sepsis, and 10.6 *more* men would be readmitted due to urinary retention, if all biopsies were performed via the TP route. There was no difference in hospital readmissions due to haematuria or in 30-day mortality risk.

Although the TP approach reduced the risk of infection, the higher risk of urinary retention following a TP biopsy has often been overlooked by clinicians when considering TR and TP approaches. However, it is important to highlight that changes in contemporary practice are moving towards some hospitals taking TP biopsies under local anaesthetic, utilising image mapping technology in order to take fewer, but more targeted biopsies. Future observations from the National Prostate Cancer Audit will be able to see if the risk of retention reduces as more hospitals adopt these techniques.

Introduction

Over 40,000 men are diagnosed with prostate cancer in England each year and the majority of these men will have undergone a prostate biopsy for diagnosis (1). The transrectal (TR) route is currently the most common technique in most countries but a newer technique using the transperineal (TP) route has been developed. This approach is better able to sample the whole prostate and proponents of this technique report perceived lower risk of post-biopsy sepsis (2).

Some UK hospital providers have now implemented a TP approach as their primary route for prostate cancer diagnosis (3, 4), but the majority of biopsies nationally are still undertaken using the TR route (5). There is currently limited high level evidence for the universal adoption of this methodology, a fact reflected in the current National Institute for Health and Care Excellence (NICE) guidelines. NICE only make reference to the use of TR biopsies but do not currently recommend its use universally (1, 6). In a similar vein, the European Association of Urology (EAU) and the American Urology Association (AUA) guidelines both quote the results of a recent meta-analysis indicating lower rates of sepsis following TP biopsies, compared to TR biopsies, but they do not advise that the TP route

should be used preferentially (7, 8). The AUA guidelines state that it remains unclear whether the risk of overall complications is significantly different when comparing TP to TR biopsies (9, 10).

According to two meta-analyses comparing complication rates of TR and TP biopsies, differing rates of complications were observed (7, 11). In this short report we assess how prostate biopsies are performed across England and we compare the risk of complications between TR and TP biopsies using nationwide data from the National Prostate Cancer Audit (NPCA) and Hospital Episode Statistics (HES) (1).

Methods

Data Sources and Patient Population

All patients newly diagnosed with prostate cancer between 1st April 2014 and 31st March 2017 were identified from the English cancer registry using the ICD-10 diagnosis code C61 and the corresponding date of diagnosis. The NPCA only collects data on men who have a diagnosis of prostate cancer and so men who may have undergone a TP or TR biopsy but did not receive a prostate cancer diagnosis were not included in this analysis. The data set was linked at patient-level to HES and death records from the Office for National Statistics (ONS). HES is an administrative routine database of all hospital outpatient appointments and inpatient admissions in England, and the ONS maintains the official register of all deaths in England.

OPCS-4 procedure codes were used to identify men undergoing a TR (M70.3) and/or a TP biopsy (M70.2). To account for the time interval between patient biopsy and the date of diagnosis, the start date of the HES database was extended by 3 months (January 1st 2014). This ensured that biopsy data was available for all patients who had received a prostate cancer diagnosis since NPCA data collection began (1st April 2014). For each patient, the biopsy date closest to the date of diagnosis was taken as the incident biopsy ensuring that a single biopsy per patient was included. 73,630 men were identified after the exclusion of men whose hospital location was missing (n=8), men who underwent biopsies in private hospitals (n=1008) and men for whom the biopsy method was unknown (n=815).

Outcome variables and coding framework

The 30-day risks of readmission due to sepsis, urinary retention or haematuria, and the 30-day mortality risk were calculated. The complications which occurred within the initial admission when the biopsy took place were also included. Sepsis, urinary retention and haematuria were identified using the ICD-10 and OPCS-4 codes displayed in **Table 1** (12). This method ensured that only complications severe enough to require a hospital admission were included which aligns with the Clavien-Dindo classification of a severe surgical complication (grade 3) (13). Previous studies have also used these outcomes to measure the most common complications following a prostate biopsy (7, 11, 12, 14). To distinguish between a true readmission and an inpatient stay after prostate biopsy, a complication code must occur in a different hospital episode to that of the prostate biopsy code.

Control Variables

HES was used to identify patient age, ethnicity, co-morbidities and socioeconomic deprivation status. The cancer registry was used to identify patient ethnicity in instances where HES records were incomplete.

Men were categorised into four ethnic groups (White, Asian, Black and Other). The Royal College of Surgeons (RCS) Charlson score was used to identify any co-morbid conditions captured in the HES record within one year prior to each patient's prostate biopsy (15). This score has been validated previously using HES in patients undergoing surgery (16). Socioeconomic deprivation status was determined for patients from the English 2012 Index of Multiple Deprivation (IMD) based on their area of residence and divided according to quintiles of the national distribution (17).

Statistical analysis

Four generalised linear models were used to estimate the adjusted risk differences in 30-day readmissions due to sepsis, urinary retention, haematuria, and 30-day mortality between TR and TP cohorts. These models assumed a binomial distribution for the outcomes and used an identity link function. Analyses were adjusted for the year of biopsy, patient age, RCS Charlson score, socioeconomic deprivation status and ethnicity given they may affect the likelihood of developing complications. All models also took account of clustering within hospitals (18). Missing values for ethnicity (n=4987, 6.7%) were imputed using multiple imputation by chained equations. 20 data sets were created and Rubin's rules used to combine estimates. Wald tests were used to calculate *P* values with significance set at $P<0.05$.

Results

73,630 men were included in the study, of whom 59,907 underwent a TR biopsy (81%) and 13,723 underwent a TP biopsy (19%). Approximately 86% were aged 60 or above, 23% had at least one recorded co-morbidity and 87% of men had a white ethnicity (**Table 2**). 133 English NHS Trusts were identified in the HES database as performing prostate biopsies. **Figure 1** indicates the proportion of men undergoing a TP biopsy according to each of the English NHS Trusts identified. Only five Trusts performed more than 90% of their prostate biopsies via the TP route, with most Trusts performing the majority of their biopsies via the traditional TR route (88%). The proportion of men undergoing a TP biopsy has nearly doubled within 3 years (14% to 25%), indicating a shift towards the use of this approach in certain hospitals.

Figure 2 shows the 30-day risk of each type of complication (sepsis, retention, haematuria) according to the route of biopsy (TP versus TR). The overall 30-day risk of a complication following a TP biopsy was 3.0%, compared to 2.5% following a TR biopsy. Men were less likely to be readmitted due to sepsis if they had a TP instead of a TR biopsy: 806 men (1.35%) were readmitted due to sepsis after TR, compared to 142 men (1.03%) after TP biopsy (adjusted risk difference -0.36%; 95% CI -0.56 to -0.15; $P=0.001$) (**Table 3**). The adjusted risk difference of sepsis did not vary with biopsy year. Factored for 1000 biopsies, 3.6 fewer men would be readmitted due to sepsis if all biopsies were performed via the TP route.

Men were more likely to be readmitted with urinary retention if they had a TP rather than a TR biopsy: 571 men (0.95%) were readmitted after TR biopsy, compared to 265 men (1.93%) after TP biopsy (adjusted risk difference 1.06%, 95% CI 0.71 to 1.41; $P<0.001$) (**Table 3**). The adjusted risk difference of retention did not vary with biopsy year. Factored for 1000 biopsies, 11 more men would be readmitted due to urinary retention if all biopsies were performed via the TP route.

There was no significant difference between TR and TP cohorts for readmissions due to haematuria within 30 days (0.66% vs 0.71%, $P=0.546$) or for 30-day patient mortality (0.10% vs 0.07%, $P=0.197$).

Summary and conclusions

This is the largest population-based study to compare complications following TR and TP prostate biopsies, but also highlights the large variation across the country in terms of biopsy method used. The results show that in statistical terms patients are more likely to be readmitted to hospital due to sepsis if they have a TR biopsy rather than a TP biopsy. However, the risk reduction achieved via the TP route was not as marked as what has been previously reported (19). Sepsis remains a serious and well recognised complication related to a prostate biopsy and every effort should be made to reduce this. However, whilst the TP route reduces the risk of sepsis, that reduction was modest, did not vary across the three years of the study and the reduction occurred from a very low base risk for both biopsy methods (TP: 1.03 versus TR: 1.35%).

By contrast, the risk of being readmitted with urinary retention is greater following a TP biopsy, compared to a TR biopsy, however results from the two meta-analyses making this comparison showed no significant difference (7, 11). The higher risk of developing retention is potentially associated with the use of a general anaesthetic and the larger number of cores taken with TP template biopsies (factors we were unable to account for) (20). However, changes in contemporary practice are moving towards hospitals being able to utilise image mapping technology in order to take fewer, but more targeted, biopsies, as well as under local anaesthetic (4, 17). Future research is needed to see whether these newer approaches will reduce the risk of developing post-biopsy urinary retention following TP, as well as TR, biopsies. At present information about the use of image mapping, and whether local anaesthetic was used, is not collected in the Audit but new COSD (Cancer Outcomes and Services Dataset) data items will be available from 2020. It is also important to stress that decision making about biopsy route is not only based on the risk of complications but must also balance the potential differences in cancer diagnosis and the higher burden of TP biopsies on the use of resources.

In summary, current practice indicates that for every readmission due to sepsis prevented by performing a TP biopsy, there will be a further three readmissions due to urinary retention (risk difference of retention vs sepsis: 1.06 / 0.36), but both techniques are equivalent in terms of readmissions due to haematuria and in 30-day mortality risk. More TP biopsies are expected to be carried out in order to reduce a perceived higher risk of post-biopsy sepsis following TR sampling. It will therefore be important to monitor this trend and to report further on whether the risk of post-biopsy urinary retention is reduced with this approach, especially with the increasing use of local anaesthetic and/or targeted biopsies. Although the majority of complications following a prostate biopsy will have become apparent within 30 days, an assessment of longer term or recurring complications is also needed for a complete comparison of both biopsy methods. This will be performed in a subsequent short report when additional information about biopsy technique is available.

Table 1. Coding framework

Codes:	Description of code
Sepsis	
ICD-10 codes within the first 7 diagnostic fields	
N30.0	Acute cystitis
N39.0	Urinary tract infection, site not specified
N41.0	Acute prostatitis
N41.2	Abscess of prostate
N41.3	Prostatocystitis
N41.9	Inflammatory disease of the prostate, unspecified
N45.0	Orchitis, epididymitis and epididymo-orchitis with abscess
N45.9	Orchitis, epididymitis and epididymo-orchitis without abscess
N49	Inflammatory disorder male genital organs
R36	Urethral discharge
B96.1	Klebsiella pneumoniae as the cause of diseases classified to other chapters
B96.2	Escherichia coli as the cause of diseases classified to other chapters
B96.4	Proteus as the cause of diseases classified to other chapters
B96.5	Pseudomonas as the cause of diseases classified to other chapters
B96.8	Other specified bacterial agents as the cause of diseases
A41.8	Other specified sepsis
A41.9	Sepsis, unspecified
A49.9	Bacterial infection, unspecified
ICD-10 codes within the first diagnostic field and as part of an emergency admission	
I48	Atrial fibrillation and flutter
N17.9	Acute renal failure, unspecified
Haematuria	
ICD-10 codes within the first 7 diagnostic fields	
R31	Unspecified haematuria
N42.1	Congestion and haemorrhage of prostate
OPCS-4 codes within the first 3 procedure fields and as part of an emergency admission	
M45.9	Unspecified diagnostic endoscopic examination of bladder
M45.8	Other specified diagnostic endoscopic examination of bladder
X33.9	Unspecified other blood transfusion
Urinary retention	
ICD-10 codes within the first seven diagnostic fields	
R33	Retention of urine
ICD-10 codes within the first 2 diagnostic fields and as part of an emergency admission	
Z46.6	Fitting and adjustment of urinary device

Table 2. Patient characteristics and biopsy type for men diagnosed with prostate cancer between 1st April 2014 and 31st March 2017

	Transrectal biopsy		Transperineal biopsy		Total	
	No.	%	No.	%	No.	%
Total	59,907	81.4	13,723	18.6	73,630	100
Biopsy year						
2014	14,744	24.6	2,340	17.1	17,084	23.2
2015	19,750	33.0	4,334	31.6	24,084	32.7
2016	19,875	33.2	5,162	37.6	25,037	34.0
2017	5,538	9.2	1,887	13.8	7,425	10.1
Age group (years)						
< 60	7,941	13.3	2,534	18.5	10,475	14.2
60-69	22,898	38.2	6,090	44.4	28,988	39.4
70-79	24,113	40.3	4,676	34.1	28,789	39.1
≥ 80	4,955	8.3	423	3.1	5,378	7.3
RCS Charlson comorbidity score						
0	46,744	78.0	9,841	71.7	56,585	76.9
1	9,152	15.3	2,952	21.5	12,104	16.4
≥2	4,011	6.7	930	6.8	4,941	6.7
Socioeconomic deprivation status						
1 (least deprived)	14,169	22.7	4319	25.6	18,488	23.3
2	14,593	23.4	3874	23.0	18,467	23.3
3	13,453	21.5	3544	21.0	16,997	21.4
4	10,976	17.6	2883	17.1	13,859	17.5
5 (most deprived)	9286	14.9	2230	13.2	11,516	14.5
Ethnicity						
White	52,599	87.8	11,752	85.6	64,351	87.4
Asian	959	1.6	274	2.0	1,233	1.7
Black	1,896	3.2	708	5.2	2,604	3.5
Other	765	1.3	292	2.1	1,057	1.4
Missing	3,688	6.2	697	5.1	4,385	6.0
Abbreviations: RCS = Royal College of Surgeons						

Table 3. Regression analyses comparing transrectal (TR) and transperineal (TP) biopsy for sepsis, urinary retention, haematuria and mortality.

	TR n (%)	**TP n (%)**	**Unadjusted Risk difference (%)**	**95% CI (%)**	***P***	**Adjusted risk difference (%)**	**95% CI (%)**	***P***
Total	59,907	13,723						
Sepsis	806 (1.35)	142 (1.03)	-0.31	-0.51 to -0.01	**0.003**	-0.36	-0.56 to -0.15	**0.001**
Urinary retention	571 (0.95)	265 (1.93)	0.98	0.62 to 1.34	**<0.001**	1.06	0.71 to 1.41	**<0.001**
Haematuria	396 (0.66)	97 (0.71)	0.05	-0.17 to 0.26	0.671	0.07	-0.15 to 0.28	0.546
Mortality*	59 (0.10)	9 (0.07)	-0.03	-0.08 to 0.02	0.196	-0.03	-0.07 to 0.01	0.197
Adjustments made for biopsy year, age, ethnicity, RCS Charlson score and socioeconomic deprivation status * Adjusted for age								

Figure 1. Proportion of prostate biopsies performed via the transperineal route for men diagnosed with prostate cancer between 1st April 2014 and 31st March 2017.

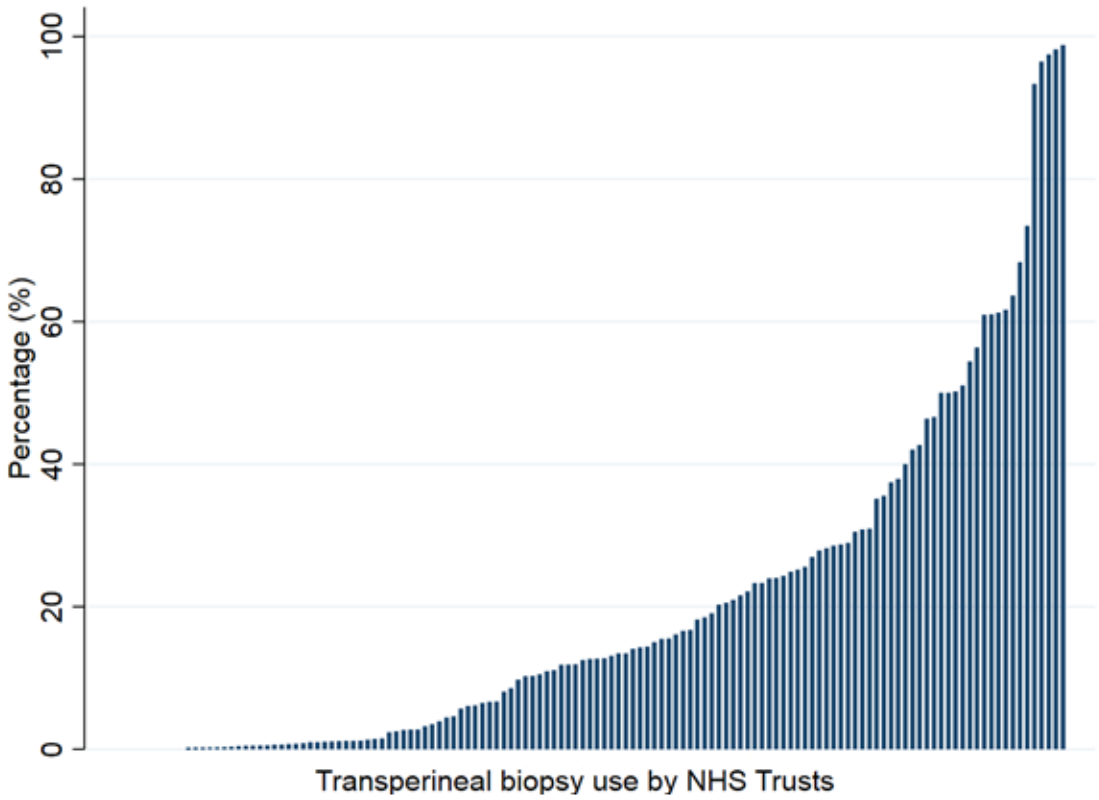
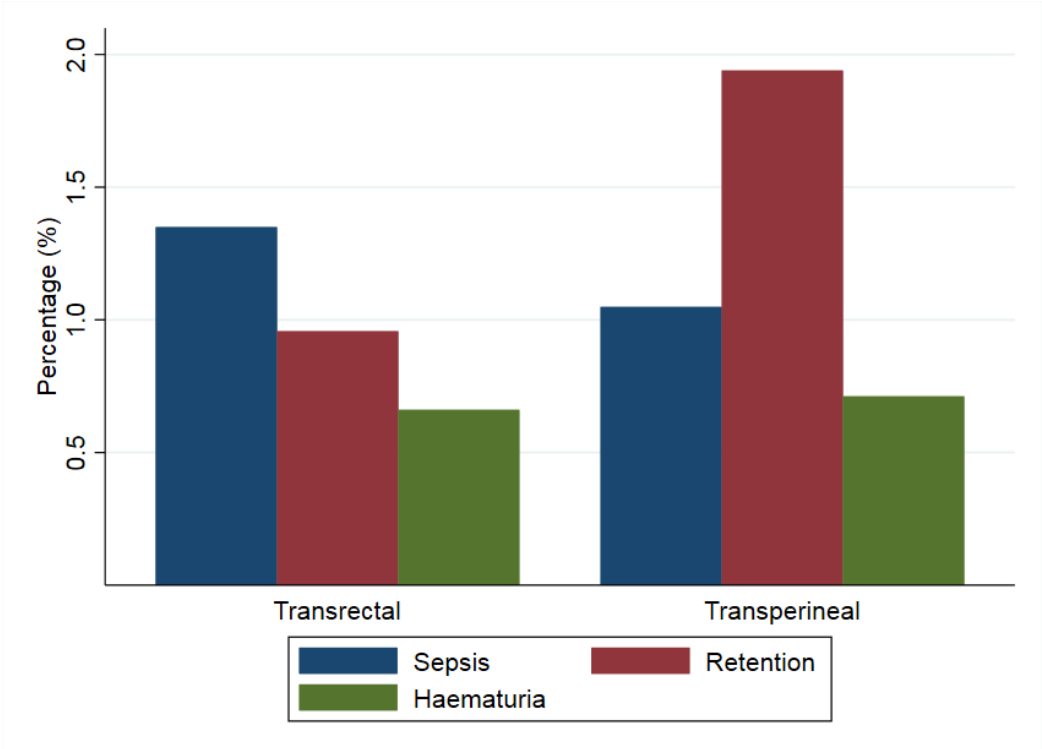


Figure 2. 30-day complications following prostate biopsy stratified by biopsy route (transrectal versus transperineal) for men diagnosed with prostate cancer between 1st April 2014 and 31st March 2017.



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Glossary

Co-morbidity
Medical condition(s) or disease process(es) that are additional to the disease under investigation (in this case, prostate cancer).

Cancer Outcomes and Services Dataset (COSD)
The national standard for reporting on cancer in the NHS in England. Trusts submit a data file to the National Cancer Registration and Analysis Service (NCRAS) every month.

Charlson Co-morbidity Score
A commonly used scoring system for medical co-morbidities. The score is calculated based on the absence and presence of specific medical problems in the Hospital Episode Statistics (HES) database.

Healthcare Quality Improvement Partnership (HQIP)
It aims to promote quality improvement in healthcare and increase the impact of clinical audit on the services provided by the NHS and independent healthcare organisations.

Hospital Episode Statistics (HES)
A database that contains data on all inpatients treated within NHS trusts in England. This includes details of admissions, diagnoses and treatments.

International Classification of Diseases, Tenth Revision (ICD-10)
This is the World Health Organisation international standard diagnostic classification, and is used to code diagnoses and complications within the Hospital Episode Statistics database of the English NHS.

NHS Trust
An NHS organisation that provides acute care services in England. A trust can include one or more hospitals.

Office for National Statistics (ONS)
Government department responsible for collecting and publishing official statistics about the UK's society and economy. This includes cancer registration data.

Royal College of Surgeons of England (RCS)
An independent professional body committed to enabling surgeons to achieve and maintain the highest standards of surgical practice and patient care. As part of this it supports audit and the evaluation of clinical effectiveness of surgery.

Targeted Biopsy
This is a type of transrectal or transperineal biopsy which uses information from an MRI scan to take biopsies from abnormal areas of the prostate. This involves taking fewer sample than a template biopsy.

Template Biopsy
This is a type of transperineal biopsy where the doctor uses a template (or grid) with lots of holes over the perineum. An ultrasound probe guides the biopsy needle through the template and into the prostate. This allows biopsies to be taken from all parts of the prostate.

Transrectal Biopsy
This involves using thin needles to takes tissue samples from the prostate after numbing the area with local anaesthetic. The biopsy is done through the rectum (back passage).

Transperineal Biopsy
Taking biopsies of the prostate through the perineum. This is performed under general anaesthetic and needle placement can be more precise than transrectal ultrasound biopsies.