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ORIGINAL ARTICLE

Prophylactic Antibiotics and Hospitalisations following Transrectal Prostate Biopsy:

a local retrospective cohort study

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Background

Prostate biopsy is an important tool in prostate cancer diagnosis. However, transrectal prostate biopsy is associated with a number of complications, including infectious complications. This local cohort study aims to assess the incidence of such complications and 30-day readmission rates, and any predisposing factors for said complications including patient co-morbidities, type of prophylactic antibiotics used and biopsy approach.

Methods

A retrospective review was carried out for men over 18 years of age who underwent transrectal prostate biopsy from January 2021 to December 2021.

Results

A total of 373 patients were included. 184 (49.4%) underwent systematic biopsy, 115 (30.8%) underwent combined and 59 (15.8%) underwent targeted biopsy. The commonest antibiotic prophylaxis regime is ciprofloxacin, metronidazole and gentamicin. 30-day readmission count was 19 (5.1%). The commonest complication requiring readmission was lower UTI (n=14 (73%)), 70% of these has Escherichia coli cultured in the urine.

Conclusion

This study replicated the findings that infectious complications are the most common cause of readmission after transrectal biopsy and that E.coli is the most common causative organism for infectious complications post biopsy. This study does not replicate the findings from similar studies which showed that the number of cores yielded correlates with the risk of infection post biopsy, nor does it confirm that increased age, DM or a high BMI increases the risk of developing post biopsy infection.

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The gold standard of prostate cancer detection is a transrectal ultrasound (TRUS) guided biopsy. Transrectal biopsies of the prostate are easily done as a day case setting without the need for general anaesthesia. Patients undergoing transrectal biopsy of the prostate are given antibiotic prophylaxis due to the risk of infectious complications.[1] MRI guided transrectal prostate biopsies have become more frequent due to the ability to target areas of suspicion which results in improved detection of prostate cancer. In addition, by reducing the amount of cores retrieved complication rates are reduced without the need to compromise prostate cancer diagnosis.[2]

Bleeding is the most common complication.[3] A variety of factors have been documented which affect the frequency of bleeding post prostate biopsy. The use of anticoagulation medication and the number of cores retrieved during the procedure increase the incidence of bleeding.[4]

Antimicrobial prophylaxis significantly reduces post operative infectious complications and in turn the need for hospitalisation.[5] The most common antibiotics prescribed are fluoroquinolones for a variable duration, but studies have shown that antibiotic prophylaxis for more than 24 hours provides no significant benefit.[6,7] Infectious complications such as UTI, epididymitis and sepsis still arise despite patients' compliance to antimicrobials and the use of techniques to reduce such risk.[4]

The risk of urinary retention post TRUS prostate biopsy is low and is not correlated to the number of cores taken during the procedure.[8] This is usually short lasting and rarely requires any form of intervention.[9]

The purpose of this study is to assess whether co-morbidities, the type of prophylactic antibiotics used and the approach for prostate biopsy sampling influence post operative complications while also looking at the complication rate and what complications arose within a 30-day time period. This will help to better guide antibiotic prescribing to improve the outcome of transrectal ultrasound guided prostate biopsies.

METHODS

A retrospective review was carried out for men over 18 years of age who underwent transrectal prostate biopsy from January 2021 to December 2021 (12 months). These dates where selected to allow the opportunity to gather information on the different prophylactic antibiotics used. Data was collected from a Mater Dei Hospital (MDH) database. All the prostate biopsies were performed under the supervision of five consultant urologists and one consultant radiologist.

Data was collected over a period of 3 months from 16th February 2022 until 20th May 2022. Using the local healthcare software system (iSOFT and patient dashboard), discharge summaries and inpatient/ outpatient records in MDH and Gozo General Hospital (GGH).

Preoperative variables for patients who underwent transrectal prostate biopsy included patient demographics, type of biopsy, number of cores taken, comorbidities including diabetes and immunosuppression, on anticoagulation or antiplatelets, catheterised 24 hours prior to the biopsy, previous antibiotic use within 30 days before biopsy, prophylactic antibiotics used and the duration of antibiotics. Post operative 30-day readmission was documented, length of stay, reason for readmission, Clavien-Dindo severity and antibiotic treatment given and duration.

Statistical analysis was performed using Fisher's exact test for categorical variables. Independent sample t-test and one-way ANOVA analysis was used for continuous variables. Results were considered significant if $p < 0.05$. IBM SPSS Statistics (Version 26) was used for data analysis. Approval for this study was obtained from the University of Malta Research Ethics Committee FREC number- UREC-DP2112004MED.

RESULTS

A total of 373 patients were included in this retrospective review. Mean age was 70.03 years. The commonest biopsy type was TRUS systematic (n=184(49.3%)) followed by TRUS combined (n=115(30.8%) and TRUS targeted (n=59(15.8%)). Out of 373 patients, 66 patients (17.7%) suffered from diabetes mellitus, 10 (2.7%) were immunocompromised 7 (1.9%) of which were on immunomodulators. 4 (1.0%) patients had previous antibiotic use within 30 days before the prostate biopsy. This could be due to patients who would have been given antibiotics in the community and therefore not picked up in the study. None of the patients had an indwelling catheter. 103 (27.6%) patients were on antiplatelets or anticoagulation.

The minimum number of cores taken was 3 with a maximum of 28. The least number of cores was taken

in TRUS targeted while the maximum in TRUS systematic. The average number of cores in TRUS targeted was the least amounting to 6.46 cores, TRUS combined had an average of 10.63 cores while TRUS systematic had an average of 14.62 cores. Studies show that more cores increase the risk of sepsis but this was not represented in our study cohort. Age (p=0.990), BMI (p=0.31) and Diabetes Mellitus (p=0.25) were not statistically significant in patients who were readmitted with prostate biopsy complications. Table 1 summarises the numerical findings including the p values for correlation with admission rates.

There was no statistical significance between the antibiotics used and the readmission rate. This can be attributed to the fact that the main concern is the transrectal route and that we need to move towards the transperineal approach for prostate biopsy sampling. The commonest antibiotic prophylaxis regime is ciprofloxacin, metronidazole and gentamicin with gentamicin being given as a stat dose at the induction of prostate biopsy.

Table 1 *Summary of Results showing the p values for Correlation with admission rates where applicable (Pearson – Chi Square for categorical variables, Pearson correlation for continuous variables)*

Demographics	**Range**	**Mean**	***p*-value**
Age	47.09 - 88.06	70.03	0.99
BMI	19-40	28.96	0.31
Potential Risk Factor for Post Biopsy Complication	**(n=)**	**%**	**p-value**
Diabetes Mellitus	66	17.69	0.25
Immunosuppressed	10	2.68	0.54
On Immunomodulators	7	1.87	
Indwelling Catheter	0	0.00	
On Antiplatelets or Anticoagulants	103	27.61	
Had previous Antibiotics within <30days	4	1.07	0.64
Type of Biopsy	**(n=)**	**%**	**p-value**
TRUS systematic	184	49.3	
TRUS combined	115	30.8	
TRUS targeted	59	15.8	
Overall	373	100	0.125
No of Cores per Biopsy Type	**Range**	**Average**	**p-value**
TRUS systematic	4-28	14.62	
TRUS combined	5-20	10.63	
TRUS targeted	3-14	6.46	
Overall	3-28	11.99	0.49
No of Prophylactic Antibiotics	**Range**	**Average**	**p-value**
Number of Antibiotics	0-4	1.95	0.844

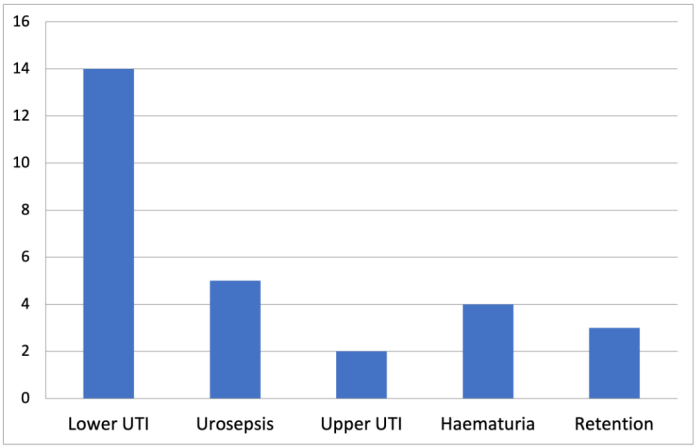

Figure 1 *Number of patients requiring hospitalisation after developing a complication post transrectal prostate biopsy*

From 373 patients the 30-day readmission count was 19 (5.1%). The commonest complication requiring readmission was lower UTI (n=14 (73%)). The other 27% included upper UTI, retention, haematuria and urosepsis (**Figure 1**). The average interval from prostate biopsy to readmission was 6 days with an average length of stay of 7.5 days. All readmissions were treated with intravenous antibiotics (**Figure 2**). From 19 readmissions 7 had positive urine cultures on readmission, 70% of these has Escherichia coli cultured in the urine.

DISCUSSION

Prostate cancer is a worldwide major health concern. It is the second most common cancer diagnosis in men with approximately 1.4 million diagnoses globally in 2020.[9] Diagnosis of prostate cancer is dependent on clinical history, digital rectal examination, prostate specific antigen (PSA) measurement, as well as imaging techniques and prostate biopsy.

The European Association of Urology (EAU) Prostate Cancer guidelines[10] recommend the use of Magnetic Resonance Imaging (MRI) prior to biopsy in both biopsy-naive and in those with prior negative biopsy in the detection of Prostate Cancer base on the MRI-FIRST study.[11] These guidelines go on to recommend a combined targeted and systematic approach when MRI is positive in biopsy-naïve men, whilst targeted biopsy alone is indicated in men with previous negative biopsy but a positive MRI, and systemic biopsy alone is only indicated in those with a prior negative biopsy with a negative MRI but a high clinical suspicion of Prostate cancer.[10] In this study the vast majority (49.3%) of the 373 patients underwent a systemic biopsy alone. Although the study did not stratify patients into biopsy-naïve and prior negative biopsy, or into MRI positive or negative, this finding indicates a lack of adherence to EAU recommendations. This is important when bearing in mind that systematic biopsy alone had an average 14.6 core yield, as oppose to 6.46 in the targeted group of this study. Although this study did not conclude that an increased number of cores is associated with increased risk of sepsis, this has been shown in other studies.[2] This study also reports no association with Diabetes Mellitus (p=0.25) in terms of readmissions with prostate biopsy complications. However, this is likely to be due to the small number of Diabetes Mellitus sufferers (p=66) included in the study resulting in a statistical analysis which is far from powered.

The 30-day readmission rate in this study was of 5.1%, with 3.75% of patients being readmitted in view of a lower UTI. In a retrospective observational study performed in Ängelholm and Helsingborg, Scania, Sweden, the authors found an overall infection rate of 5.4% post biopsy with 3.9% of the patients

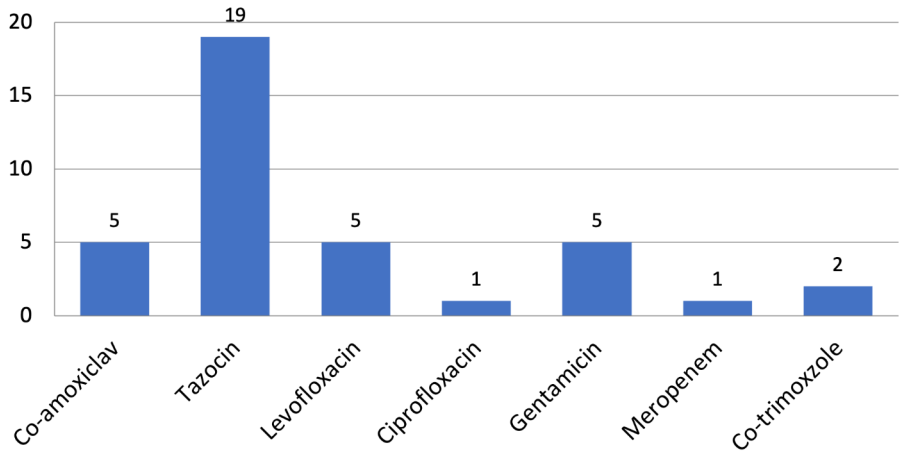

Figure 2 *Intravenous Antibiotics used to treat infectious complications in patients requiring hospitalization following transrectal prostate biopsy*

requiring hospitalisation for intravenous antibiotics[12], the latter percentage is very similar to that reported here. No attempt was made in our study to detect the number of patients who contracted an infection and were treated in primary care, and therefore an overall infection rate cannot be reported.

Infectious complications are significantly higher following transrectal biopsy when compared to transperineal biopsy[13], and hence the EAU guidelines now strongly suggest performing prostate biopsy using the transperineal approach.[10] However, in cases were a transrectal approach is used several steps may be taken to reduce the risk of infectious complications including the use of povidone-iodine for rectal cleansing, and the use of prophylactic antibiotics.[10] This study showed that a combination of ciprofloxacin, metronidazole and gentamicin was the most prescribed prophylactic regime locally. Whilst augmented prophylaxis (with the use of two or more antibiotic classes) is suggested by the EAU[11], the prophylactic, empirical use of fluroquinolones (like ciprofloxacin) is now strongly discouraged by the European Medicine Agency (EMA) due to the severe and potentially irreversible adverse reactions which may affect several organ systems.[14] Alternative prophylactic antibiotics have also been suggested, including fosfomycin trometamol.[10] In a metanalysis which included 59 randomized controlled trials, Pilatz et alshowed that antibiotic prophylaxis reduces infectious complications from transrectal biopsy, and that fosfomycin trometamol was an alternative to fluoroquinolone with reduced rates of infectious complications.[15] In the local cohort included in this study fosfomycin trometamol was used alone or as part of an augmented prophylaxis protocol in 126 patients (33.8%), of which 5 (3.9%) required readmission.

This study showed that E. coli was the most common organism cultured in the urine and blood in patients with post prostate biopsy infection. This is in keeping with the results from a study performed in Canada by Lange et al in which E. coli was the cause of urosepsis after transrectal biopsy in 67% of the patients with positive cultures.[16]

CONCLUSION

This study replicated the findings that infectious complications are the most common cause of readmission after transrectal biopsy, and that the rate of readmission due to infectious complications is in the region of 3.9%. Moreover, it replicated the finding that E.coli is the most common causative organism for infectious complications post biopsy. The study highlights the urgent requirement for local antibiotic prophylactic guidelines for transrectal prostate biopsy. The infection rate also emphasises the EAU recommendation in favour of transperineal biopsy, and hence implies a need for local expertise in this technique. This study does not replicate the findings from similar studies which showed that the number of cores yielded correlates with the risk of infection post biopsy, nor does it confirm that increased age, DM or a high BMI increases the risk of developing post biopsy infection.

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