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ORIGINAL ARTICLE

Retrospective Review of the Diagnostic Pathway of Suspected Prostate Cancer in Mater Dei Hospital

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Background

A well-established prostate cancer diagnostic pathway is used in Europe[1] to increase early diagnosis of clinically significant prostate cancers. This retrospective review was aimed to assess the efficiency and accuracy of this pathway within the department of urology at Mater Dei Hospital.

Method

Data collected included demographic data, digital rectal examination (DRE) findings prior to magnetic resonance imaging (MRI) and prostate specific antigen (PSA) values preceding MRI. PSA doubling time and PSA velocity were calculated. The cohort was divided into three groups according to the MRI result - negative, positive or equivocal for prostate cancer. Prostate gland volume, Prostate Imaging-Reporting and Data System (PI-RADS) score, TNM stage and histology results were documented and compared.

Results

41% of the cohort had a DRE suggestive of cancer. The cohort had a mean PSA value of 4.912 ng/ml, mean PSA density of 0.152 ng/ml, mean PSA velocity of 0.306 ng/ml/year and mean PSA doubling time of 64 months. The mode PIRADS count was 2. Most cancers were staged at T3a . The mean prostate size was 61.46 cubic centi-metres. 93.4% of patients with an MRI of the prostate suggestive of cancer had a prostate biopsy. 79.5% provided samples suggestive of cancer. The most common grade of cancer was Gleason 7 disease.

Conclusion

Allowing for limitations of a retrospective review and a small cohort, this study has shown that using the European pathway for diagnosis of prostate cancer increases diagnosis of significant prostate cancer.

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INTRODUCTION

A well-established prostate cancer diagnostic pathway is used in Europe[1] to increase early diagnosis of clinically significant prostate cancers. This retrospective review was aimed to assess the efficiency and accuracy of this pathway within the department of urology at Mater Dei Hospital.

MATERIALS AND METHODS

A cohort of patients was selected for a retrospective review of the diagnostic pathway for prostate cancer. All individuals who underwent a multi-parameteric magnetic resonance imaging (MRI) of the prostate in 2019 were included. Patients who were on active surveillance or were previously assessed for prostate cancer were excluded. MRIs performed for reasons other than prostate cancer diagnosis were also excluded.

Demographic data pertaining to date of birth and age was collected from digital records. Clinical findings acquired from a digital rectal examination prior to MRI were noted. Prostate Specific Antigen (PSA) values preceding the MRI were collected and used to calculate PSA Doubling Time and PSA velocity.

Every MRI was interpreted by a single experienced urology radiologist. The cohort was divided into three groups according to the MRI results - negative, positive or equivocal for prostate cancer. The prostate gland volume, the Prostate Imaging-Reporting and Data System (PI-RADS) score and the TNM stage were collected.

The definitive diagnosis is based on histopathological assessment of tissue samples obtained using traditional trans-rectal systematic ultrasound guided prostate biopsy or MRI trans-rectal ultrasound guided fusion prostate biopsy.[1]A significant prostate cancer was defined as a cancer with a minimum Gleason score of six and a tumour volume of at least 0.5 cubic centi-metres.[4]

Electronic case summaries of patients who required a prostate biopsy were analysed and any biopsy related complications were noted. The complications were graded according to the Clavien-Dindo Classification system (Clavien et al, 2009).

Statistical analysis was performed using Chi-squared test for categorical variables. Independent sample t-test and one-way ANOVA analysis for continuous variables. Results were considered significant if $p < 0.05$. IBM SPSS Statistics (Version 26) was used for data analysis. Clearance was obtained from the data protection office.

Table 1 *Reasons for Exclusion*

Reason for Exclusion	Total
On active surveillance	38
Previously investigated	352
MRI for non-cancer disease	63
Others	8

RESULTS

The cohort was made up of 1180 patients. 720 patients were included. 460 patients were excluded. The most common reason for exclusion was previous investigation for prostate cancer (Table 1). The mean age of the cohort was 68 years old.

PSA values at referral ranged from 0.47 ng/ml to 19.54 ng/ml with a mean of 4.912 ng/ml. Figure 1 illustrates the most common PSA values. 41% of the cohort had a digital rectal examination suggestive of cancer, 34% of the cohort had no documented digital rectal exam and the rest had a normal digital rectal examination.

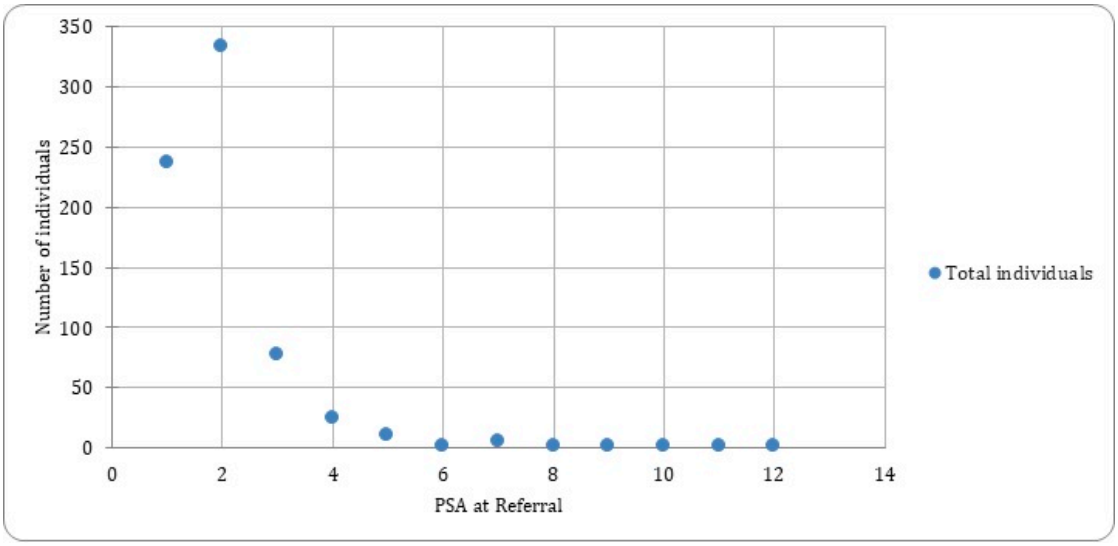

Figure 1 *PSA value at referral*

The mean PSA density for the whole cohort was 0.152 ng/ml, mean PSA velocity was of 0.306 ng/ml/year with a mean PSA doubling time of 64 months. In the prostate cancer group PSA density was 0.23ng/ml and a mean PSA velocity of 1.91 ng/ml/year. In the non-prostate cancer group the mean PSA density is 0.11ng/ml and a mean PSA velocity of 0.36 ng/ml/year.

From the 720 MRI prostate reviewed, 261 suggested prostate cancer, 336 were not suggestive of prostate cancer and 126 were equivocal. The mode PIRADS count was 2. Most cancers were staged as T3a according to the TNM staging system.[1] The mean prostate size was calculated to be 61.46 cubic centi-metres, ranging from 13 to 369 cubic centi-metres.

From the cohort selected 244 individuals (33.8%) were further investigated using a prostate biopsy. This means 93.4% of patients with a MR of the prostate suggestive of cancer. Most common biopsy performed was targeted trans-rectal ultrasound guided systematic biopsy. Prostate cancer was diagnosed in 194 out 244 men undergoing prostate biopsy (79.5%). The most common grade of cancer was Gleason 7 disease (Figure 2).

Eleven patients out of 244 men suffered a complication related to their biopsy, post biopsy sepsis in 10 patients and haematuria in one patient. According to the Clavien-Dindo classification, 7 out of 11 patients were noted to have a grade 2 complication whilst the rest were not documented.

A statistically significant correlation was made between increasing age and the incidence of significant prostate cancer ($p<0.001$). Similarly, patients with a higher PSA value at referral were more likely to have a significant cancer ($p<0.001$. MRI derived PIRADS score was also correlated to histological results, with a higher PIRADS score represented a higher risk for a significant cancer ($p<0.001$).

DISCUSSION

Prostate cancer is the second most common cancer in males.[9] An accurate universal diagnostic pathway is essential to reduce the morbidity and mortality related to prostate cancer. Screening has been a crucial tool in the latter for most cancers but screening for prostate cancer is a controversial topic. Studies have shown that screening increases diagnosis of less advanced disease but does not increase the overall prostate cancer specific survival benefit.[8]

This retrospective study included individuals who were referred urgently for investigation of an elevated prostate specific antigen result. The cohort was investigated according to guidelines published by the European Association of Urology.[1] The aim was to diagnose significant prostatic cancer[4] and eliminate insignificant prostate cancer according to Epstein's criteria. This is essential to prevent over treatment.

In this study, it was noted that higher PSA velocity and PSA doubling time values were associated with significant prostate cancer. However, these values do have a prognostic value[10-11] following treatment of prostate cancer. As serum PSA is influenced by many factors, there is no universal value that is diagnostic of prostate cancer. Nonetheless, the higher the value, the greater the likelihood of prostate cancer.[1] The latter consolidates the importance of monitoring the PSA velocity and PSA doubling time of patients.

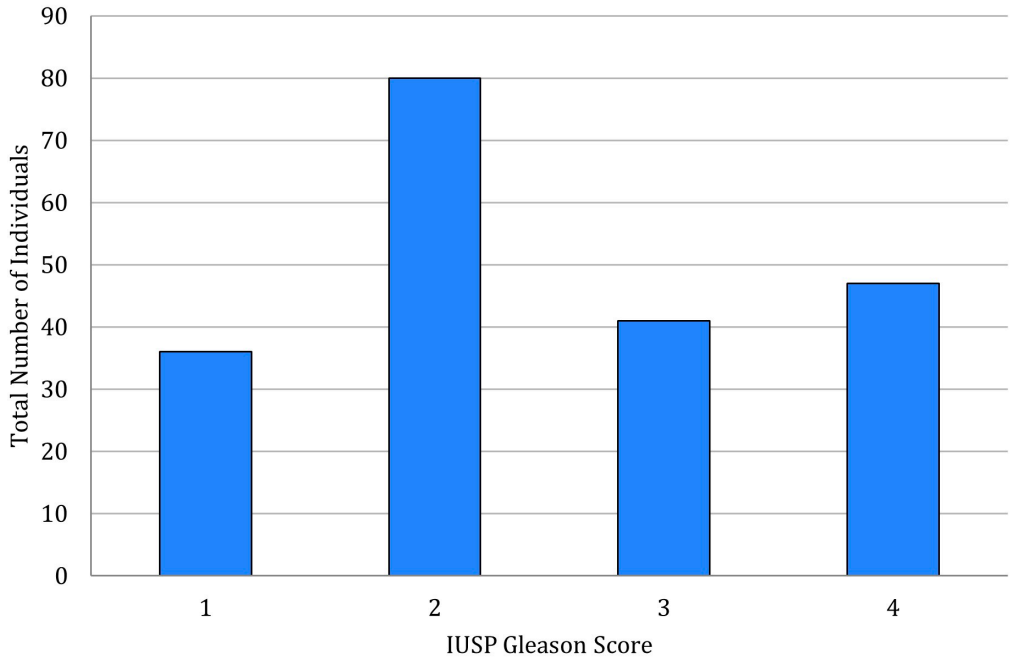

Figure 2 *IUSP Gleason score on first biopsy*

Multiparametric MRI is central to the diagnosis of prostatic cancer with a sensitivity and specificity of 95% according to a Cochrane meta-analysis.[11] This imaging modality has increased the amount of significant prostate cancers diagnosed. In this cohort, most patients were found to be in stage T3a according to the TNM staging system on MRI. The locally advanced stage may reflect delays in referral and investigation of suspected prostate cancer in the local scenario. Despite the great benefit of using MRI, it is inaccessible to patients with MRI incompatible devices. Also, MRI is relatively contra-indicated in patients who are claustrophobic, have a high body mass index or suffer from kidney disease if Gadolinium contrast is required.[12]

Most patients in the cohort who were referred for biopsy underwent a targeted prostate biopsy. The local urology department has strived to shift towards this sampling method as it has been shown to be more accurate and less invasive compared to other methods.[7]

CONCLUSION

Allowing for limitations of a retrospective review and a small cohort, this study has shown that using the European pathway for diagnosis of prostate cancer increases diagnosis of significant prostate cancer.

REFERENCES

1. EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2021V4.pdf, n.d.
2. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up- Annals of Oncology [WWWDocument],n.d.URL https://www.annalsofoncology.org/article/S0923-7534(20)39898-7/fulltext
3. Overview | Prostate cancer: diagnosis and management | Guidance | NICE [WWW Document], n.d. URL https://www.nice.org.uk/guidance/ng131 (accessed 1.14.22).
4. Defining clinically significant prostate cancer on the basis of pathological findings - PubMed [WWW Document], n.d. URL https://pubmed.ncbi.nlm.nih.gov/30565298/ (accessed 1.14.22).
5. Diagnostic Pathway with Multiparametric Magnetic Resonance Imaging Versus Standard Pathway: Results from a Randomized Prospective Study in Biopsy-naïve Patients with Suspected Prostate Cancer - PubMed [WWW Document], n.d. URL https://pubmed.ncbi.nlm.nih.gov/27574821/ (accessed 1.14.22).
6. Prostate cancer diagnostic pathway: Is a one-stop cognitive MRI targeted biopsy service a realistic goal in everyday practice? A pilot cohort in a tertiary referral centre in the UK | BMJ Open [WWW Document], n.d. URL https://bmjopen.bmj.com/content/8/10/e024941 (accessed 1.14.22).
7. Hayes, J.H., Barry, M.J., 2014. Screening for prostate cancer with the prostate-specific antigen test: a review of current evidence. JAMA 311, 1143–1149. https://doi.org/10.1001/jama.2014.2085
8. Siegel, R.L., Miller, K.D., Fuchs, H.E., Jemal, A., 2021. Cancer Statistics, 2021. CA Cancer J Clin 71, 7–33. https://doi.org/10.3322/caac.21654
9. Identification of high-risk prostate cancer: role of prostate-specific antigen, PSA doubling time, and PSA velocity - PubMed [WWW Document], n.d. URL https://pubmed.ncbi.nlm.nih.gov/18640768/ (accessed 1.14.22).
10. Systematic review of pretreatment prostate-specific antigen velocity and doubling time as predictors for prostate cancer - PubMed [WWW Document], n.d. URL https://pubmed.ncbi.nlm.nih.gov/19064972/ (accessed 1.14.22).
11. Consensus criteria for the use of magnetic resonance imaging in the diagnosis and staging of prostate cancer: not ready for routine use - PubMed [WWW Document], n.d. URL https://pubmed.ncbi.nlm.nih.gov/21256671/ (accessed 1.14.22).
12. Ghadimi M, Sapra A. Magnetic Resonance Imaging Contraindications. [Updated 2021 May 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551669/