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A review of prostate cancer prevalence among patients referred to Rapid Access Prostate Clinics with abnormal digital rectal examination in the community

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Abstract

Aims

Prostate cancer (PCa) is a leading cause of male cancer death. Digital rectal examination (DRE) is part of PCa assessment. National Cancer Control Programme (NCCP) created Rapid Access Prostate Cancer Clinic (RAPC) referral proforma for General Practitioners. We aim to investigate differences in PCa detection rates between patients with abnormal community DRE only, versus patients with abnormal DRE in RAPC and community.

Methods

Retrospective review of NCCP referrals with abnormal DRE findings to Galway University Hospital RAPC from 1/1/2018-1/10/2021. Data collected included DRE findings, age and Prostate Specific Antigen levels, and performed investigations. Patients were divided into 2 groups; 1. Abnormal DRE in community only and 2. Abnormal DRE in community and RAPC. Statistical analysis with Two-sample proportion testing.

Results

Total of 2,312 NCCP referrals, 545 (23.6%) reported abnormal DRE. 339 patients had suspicious community DRE only, 88 subsequently diagnosed with PCa. 166 patients had suspicious DRE in RAPC, 108 subsequently diagnosed with PCa. Statistically significant difference in proportions of PCa between groups (95% CI 0.305-0.477).

Conclusion

Abnormal DRE in RAPC setting is more likely to result in detection of prostate cancer than abnormal community DRE. Appropriateness of DRE testing for PCa in primary care settings must be questioned.

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Introduction

Prostate cancer (PCa) accounts for 9.7% of all male cancers[1]. In Ireland, PCa remains a prominent health challenge, with cases increasing annually by 3.7%. Nonetheless, outcomes for PCa patients are positive, with a 10 year survival rate of 89%[2].

Assessment of PCa features a combination of PSA testing, digital rectal examination (DRE), imaging, and biopsy procedures. DRE is a well-established examination in the assessment of many pathologies, including PCa[3]. However, due to its intrusive nature men can be reluctant to assent to DRE testing[4]. Negative patient perceptions about DREs could mean that clinicians too may be reluctant to undertake testing. Furthermore, there appears to be a paucity of effective education on DREs at undergraduate level, leading to lack of confidence among students and practitioners, as well as inadequate performance and interpretation of findings[5].

The National Cancer Control Programme (NCCP) was created in 2007 with the aim of reducing cancer incidence and cancer-related mortality, while improving quality of life for cancer patients[6]. NCCP established Rapid Access Prostate Clinics (RAPCs) in 2009, and subsequently developed national referral guidelines to streamline the RAPC referral process for General Practitioners (GPs). These guidelines stipulate criteria for RAPC referral, including abnormal DRE findings and PSA levels above age-reference range[7]. Galway University Hospital is the specialist centre for PCa in the Saolta Network, providing PCa care for a population of approximately 1 million patients[8].

GPs rely on clinical DRE findings and PSA levels to determine appropriateness for RAPC referral. Rates of inter-examiner agreement between doctors regarding DRE findings has been disputed. Smith and Catalona (1995) assessed inter-examiner agreement rates among consultant and trainee urologists, finding only a “fair” level of inter-observer agreement existed. Walsh et al (2014), reported a concordance rate of 76% between primary care and RAPC DRE findings, with 39% of patients referred from primary care with abnormal DRE diagnosed with PCa. Philip et al (2005) found DRE had a positive predictive value of 47% in PCa detection in patients with PSA levels between 2.5–10 ng/mL. Naji et al. (2018) found that DREs performed by GPs have poor pooled sensitivity (0.51) and poor pooled specificity (0.59) for PCa detection. In contrast, Borden Jr et al. (2007) found that individuals with an abnormal prostate on DRE had a two-fold greater risk of being diagnosed with PCa than those without. Jones et al. (2018), in systematic review, found that the pooled sensitivity for DRE in PCa detection was only 28.6%, and pooled negative predictive value was 84.2%.

The appropriate approach to PCa assessment, at least in the primary care setting, remains unestablished. Therefore we must question whether it is of any real benefit to include this as a

parameter for RAPC referral. The aim of this study is to evaluate the outcomes of patients referred to the RAPC in Galway University Hospital with abnormal community DRE findings. In particular, we will focus on PCa detection rate in those patients who had abnormal DRE with GP testing only versus those patients who had abnormal DRE in both the primary care and RAPC setting.

Methods

A retrospective review of all referrals to the RAPC service of Galway University Hospital between 1/1/2018-1/10/2021 was performed. Referrals sent on NCCP forms on which DRE findings were documented as "suspicious" or "malignant" were selected for the study. Referrals not submitted on NCCP proforma, and referrals with DRE findings documented as "normal" or "benign" were excluded. Non-NCCP referrals were excluded as DRE findings are a mandatory component of NCCP forms only, and NCCP forms are the recommended method for RAPC referral.

Data collected for each patient included age, DRE findings and grade of examining doctor at first RAPC review, and PSA level. Information on modality and outcome of performed investigations was obtained. Referral letters were extracted from triage folders located on secure hospital computers. Imaging was obtained from hospital radiology systems, biopsy results obtained from hospital laboratory systems, and clinic correspondence extracted from electronic patient records. DRE findings on RAPC review described as "firm", "soft" or "benign" were considered non-suspicious for malignancy, and DRE findings described as "extremely firm", "hard", "malignant" or "nodular" were considered suspicious for malignancy. Median values and ranges were calculated for ages and PSA results. The non-attendance (DNA) rate was calculated. Patients who DNAd and those without documented RAPC DRE were excluded from further analysis.

Data on performed investigations was collected, including whether patients proceeded to upfront biopsy or RAPC review first. While those patients who proceeded directly to TRUS did not have a formal RAPC review prior to their biopsy per se, all biopsies are performed by RAPC doctors and each patient has a documented DRE at time of biopsy, therefore these cases were included. A database of included patients was created, which was then divided into subgroups based on performance of biopsy and results, whether initial PSA was within NCCP age reference rage, and whether DRE findings on RAPC review were consistent with GP findings (i.e. prostate felt suspicious at RAPC review). Statistical analysis was performed using Jamovi (version 2.2.5) software.

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Results

Total of 2,896 referrals to the RAPC service of Galway University Hospital during the study period, of which 2,312 (79.8%) were referred via the NCCP proforma. Two-hundred and ninety-one (12.6%) of these NCCP referrals did not have DRE findings recorded, despite the use of the proforma.

Five-hundred and forty-five (23.6%) of all NCCP referrals had a documented abnormal DRE. RAPC attendance rates among NCCP-referred patients with abnormal DREs were extremely high, with only 20 patients (3.7%) failing to attend clinic. Of these, 2 patients did not attend because they sought treatment privately. Surprisingly, in 20 (3.7%) of patients referred via NCCP pathway with abnormal prostate examination, DRE findings were not documented in outpatient correspondence.

Median age for all years was 62 (range 33-76), and median PSA for all years was 5.16 (range 0.14-830). One-hundred and thirty-eight (25.3%) referrals had PSA within NCCP-stipulated age reference range.

Of the 20 patients referred with abnormal DRE who did not have a documented prostate examination in the RAPC, 7 (35%) were examined by a consultant, 11 (55%) by a registrar, and 2 (10%) by Senior House Officer (SHO).

For the purposes of further data interpretation and analysis, patients who did not attend the RAPC (20) or who did not have a documented DRE on RAPC review (20) were excluded, leaving 505 as the new total number of patients for analysis.

The majority of prostate examinations on RAPC review were performed by registrars (n=351; 69.5%). Eighty-two (16.2%) of DREs were performed by consultants, and 72 (14.3%) were performed by SHOs.

Two-hundred and fifty-four (50.3%) patients were referred directly for a TRUS-guided prostate biopsy. By comparison, two-hundred and fifty-one (49.7%) patients proceeded to RAPC review first. A total of 351 patients went on to have a biopsy. Of those biopsied, 196 were found to have PCa, representing a positivity rate of 55.8% among patients who were biopsied. Multiparametric MRI (mpMRI) scans were performed in a total of 337 patients (66.8%), with 89 (26.4%) of these patients receiving an mpMRI scan prior to biopsy.

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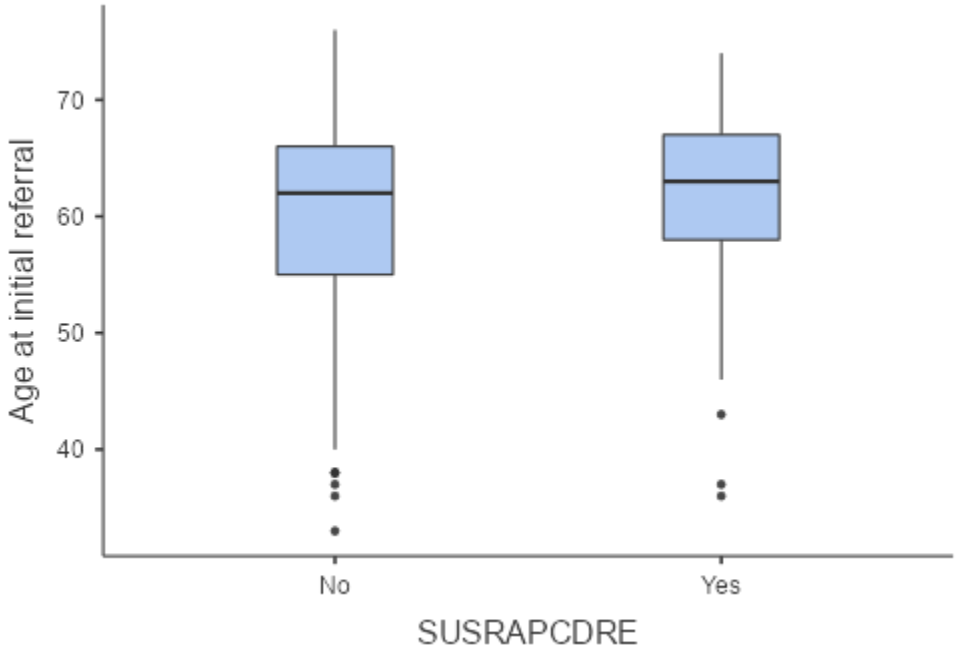
A total of 378 (74.8%) of patients from across all 4 years had a raised PSA in conjunction with abnormal community DRE. With regards to patients who had a PSA outside their age range, 182 (48.1%) went on to have a histological diagnosis of prostate cancer. Regarding the 127 patients who had a PSA within their age range, 14 (2.7% of study cohort) had a subsequent diagnosis of prostate cancer. Gleason 6 prostate cancer (7/14) was the most common histological diagnosis in this group, while 2 had non-PSA secreting tumours (small cell and sarcoma). There were 3 cases of Gleason 4+3, 1 case of Gleason 3+4, and 1 case of Gleason 5+4 tumours. Overall the proportion of clinically significant tumours (≥ Gleason 7) diagnosed in those patients with a normal PSA was 3.9%.

The 505 patients included for analysis were then subdivided into 2 cohorts; 1: Patients who had abnormal DRE on community testing but not in the RAPC, and 2: Patients who had abnormal DRE both in the community and RAPC. Statistical analysis was performed using Jamovi (version 2.2.5) software. There were no significant differences between the 2 groups in terms of baseline characteristics of age and PSA value at time of referral, but both groups have a considerable number of outliers in terms of PSA values (Figures 1 and 2).



SUSRAPC DRE = Suspicious DRE on RAPC review

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Figure 1. Age at time of referral for both groups: Abnormal DRE in community vs abnormal DRE in RAPC

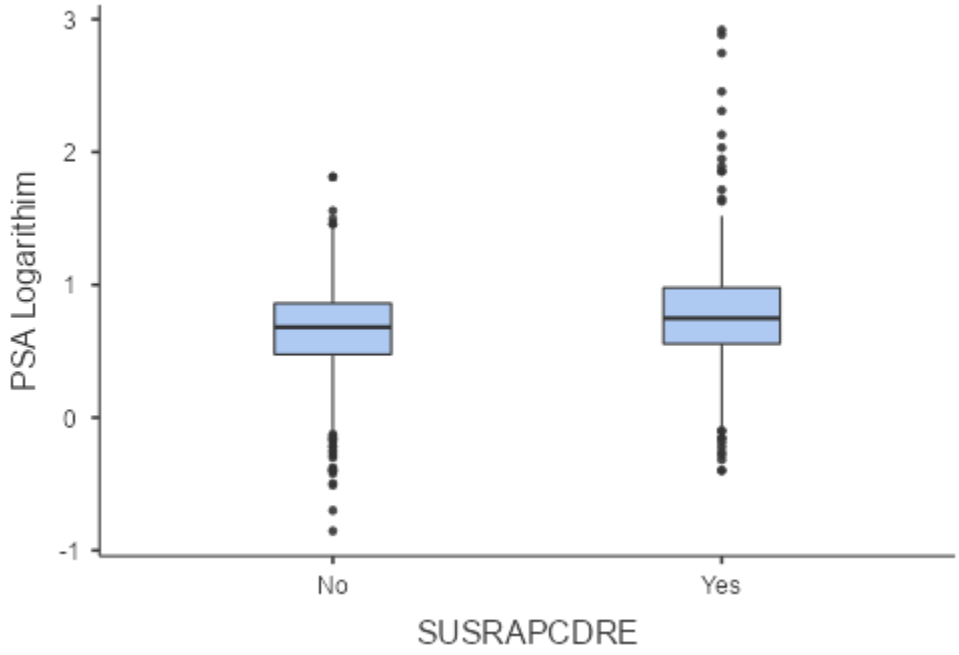

Figure 2. PSA (logarithmic scale) at time of referral for both groups: Abnormal DRE in community vs abnormal DRE in RAPC

Three-hundred and thirty-nine (67.1% of total) patients had a suspicious DRE in the community only, and of these, 88 (26% of subgroup) were diagnosed with PCa. One-hundred and sixty-six patients (32.9% of total) had a suspicious DRE in community and RAPC settings, and of these 108 (65.1% of subgroup) were subsequently diagnosed with a prostate cancer (Figure 3, Table 1). Two-sample proportion (Binomial) testing was performed to elicit the difference in proportion of prostate cancers detected between groups. There was a statistically significant difference in proportion of 39.1% between the 2 groups (95% Confidence Interval 0.305-0.477), in favour of those patients who had a suspicious DRE on RAPC review. This demonstrates that an abnormal DRE in the RAPC setting is more likely to result in detection of prostate cancer than an abnormal community DRE.

RAPC DRE findings	Number of patients in subgroup	Number of biopsies performed	Number of prostate	Subgroup percentage of	Total

			cancers detected	cancer detected	
Suspicious	166	150	108	65.1%	
Non suspicious	339	201	88	26.0%	
					505

Table 1. Frequency table of PCa incidence based on DRE findings

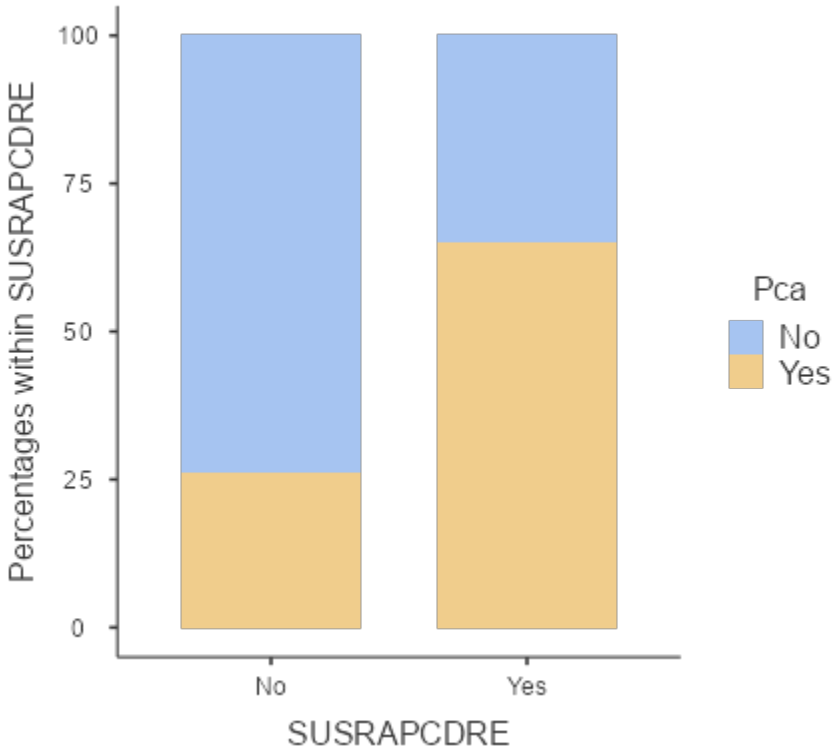

Figure 3. Stacked bar chart of Prostate cancer frequency between DRE groups

Discussion

The creation of RAPC services and proformas is important in streamlining PCa assessment in Irish healthcare[2]. However, despite this, 20% of patients were referred via alternative pathways. Despite being a referral criterion in NCCP proformas, 12.6% of NCCP referrals did not record DRE findings. Melia et al. (2008) found that the introduction of guidelines had no impact on GP

referral patterns. Further education on appropriate use of proformas may be required to ensure they are utilized properly.

Most referred patients underwent investigation, with 352 (69.5%) of patients proceeding to prostate biopsy, and 337 (66.7%) patients undergoing mpMRI. PCa was detected in 196 (38.8%) of the 505 included patients, with higher rates of PCa detected among patients with abnormal DREs in the RAPC setting specifically (108/166 patients, 65.1%). The overall PCa prevalence among patients with abnormal DRE findings in the primary care setting only was 26% (88 of 339 patients), despite representing a much larger cohort. The difference in PCa rates between the 2 cohorts was statistically significant (95% Confidence Interval 0.305-0.477), suggesting that an abnormal DRE in the RAPC setting is more likely to result in PCa diagnosis. The lower yield of community DRE testing with regards to prostate cancer detection could be as a consequence of inadequate education or supervision of skill acquisition at the undergraduate and junior doctor level, which has been discussed in the literature [15]. It is worth noting that 14 patients with normal PSA but abnormal community prostate exam went on to have a diagnosis of prostate cancer. While half of these patients had low risk prostate cancer on biopsy findings, abnormal community DRE was the trigger for RAPC review and subsequent prostate cancer diagnosis for the remaining half.

A potential limitation of this study is with regards to how patients were selected to proceed to prostate biopsy. Two-hundred and one patients (59.2% of cohort) who had abnormal DRE solely on GP testing proceeded to prostate biopsy. Conversely, 150 (90.3% of cohort) patients who had abnormal DRE on RAPC review had a biopsy. There could be an element of selection bias here in that the higher proportion of PCa found in the cohort of patients who had abnormal DRE on RAPC examination is due to higher biopsy rates. It is worth considering, however, that 50.3% of patients referred with abnormal community DRE only were referred directly for a TRUS biopsy, where they would have been examined by a RAPC doctor. As a further consideration, 351 (69.5%) patients proceeded to biopsy. Therefore data for the remaining 30.5% of patients who were not biopsied is incomplete.

The range of terminology used to describe DRE results poses a challenge to interpreting whether findings are malignant or benign [16]. In this study, terms used to categorise DRE findings as suspicious or non-suspicious were outlined above. It is possible that in ascribing the outcomes of “benign” or “suspicious” to the above terms that we could have misinterpreted the examiner’s findings.

This study demonstrates that abnormal DRE findings in the community are of limited value in the detection of prostate cancer. By contrast, abnormal DRE findings in RAPC clinics are far more

likely to result in a prostate cancer diagnosis. Higher detection rates in RAPC clinics could be due to greater clinician experience and education. Given the relatively poor inter-observer agreement for DRE examinations, their invasive nature, as well as their low sensitivity for PCa detection, we need to re-evaluate whether this is an appropriate community test for PCa assessment.

Declaration of Conflicts of Interest:

None declared.

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