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Original Article

Evaluation of the changing landscape of prostate cancer diagnosis and management from 2005 to 2016

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ABSTRACT

Background: Approaches to prostate cancer (PCa) diagnosis and treatment have evolved significantly over past decades. There has been an increasing focus on minimizing overdiagnosis and overtreatment of clinically insignificant PCa. The objective of this study was to evaluate the changes in the diagnostic approach and initial treatment strategy that has evolved over time in an Australian urological private practice.

Materials and methods: Men with newly diagnosed PCa were identified from the private practice electronic and paper medical records from 2005 to 2016 and data was consolidated into six groups of 2-year intervals. Diagnostic strategy was analyzed with particular reference to the use of multiparametric magnetic resonance imaging (mpMRI) scan and ^{68}Ga-prostate specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) scans. National Comprehensive Cancer Network risk group stratification was correlated with initial treatment strategy and compared over time.

Results: Chart review identified 839 men who had a mean age of 65.8 years. In 2011–2012, prebiopsy mpMRI scan was introduced. Its uptake correlated with a decrease in numbers of men diagnosed with low risk cancer ($r = -0.80$, $P = 0.04$) and an increase in numbers of men diagnosed with high-risk cancer ($r = 0.90$, $P = 0.01$). The use of ^{68}Ga-PSMA PET/CT was associated with decreasing use of CT and bone scans performed. Open radical prostatectomy had a declining trend particularly when robotic surgery (robotic assisted radical prostatectomy (RARP)) was introduced. Pelvic lymph node dissections performed progressively decreased. An increased use of luteinizing hormone receptor hormone (LHRH) antagonists was seen in favor of LHRH agonists. Whilst use of high dose rate brachytherapy declined, there was an increased use of low dose rate brachytherapy.

Conclusion: Prebiopsy mpMRI has been associated with an increased proportion of newly diagnosed men having clinically significant PCa. Over time, ^{68}Ga-PSMA PET/CT scans, robotic assisted radical prostatectomy (RARP) and LHRH antagonists have increased in use, whilst CT and bone scans, and pelvic lymph node dissections have decreased.

1. Introduction

Prostate cancer (PCa) has been the second commonest cause of Australian male cancer related mortality from 2013 to 2016.[1] In light of this worrying statistic, there has been significant beneficial progress in the approaches to diagnosis and treatment of PCa, particularly over the past decade.[2–4]

Prostate specific antigen (PSA) testing has been associated with increased early detection of PCa, but any decline in PCa-related mortality has been modest.[5] However, PSA testing has been associated with the overdiagnosis of many indolent tumors followed by subsequent overtreatment.[6] Transrectal ultrasound-guided biopsies have been the mainstay of PCa diagnosis. The introduction of the prebiopsy multiparametric magnetic resonance imaging (mpMRI) scan can potentially minimize the diagnosis of clinically insignificant disease and improve the detection of clinically relevant disease.[7]

The introduction of ^{68}Ga-prostate specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) scans has significantly increased the detection accuracy of metastatic disease compared to the standard imaging protocols of radionuclide bone scans and abdominopelvic CT scans.[8]

The approach to initial treatment of early stage PCa has changed significantly over recent years. Increasingly, low-risk cancer is

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being managed conservatively, which has reduced overtreatment of low risk disease. However, an Australian study based in Victoria found that a majority of patients have undergone initial treatment with aggressive interventions such as androgen deprivation therapy (ADT), radical prostatectomy (RP), and radiotherapy, regardless of their risk category of PCa.[9]

Little data is available that describes the uptake of new technology into urological practice and how it has impacted the management of newly diagnosed PCa patients. The objective of this study is to report on changes in the approach to the diagnosis, investigation, and initial treatment of PCa in an Australian academic specialist prostate private practice over a 12-year period.

2. Materials and methods

We retrospectively reviewed medical records from patients with newly diagnosed PCa from the years 2005 to 2016 inclusive. Their records were identified using a combination of key word searching in the private practice software program and a provided list of men who had biopsy proven PCa from the pathology laboratory utilized by this practice. Men previously diagnosed with PCa and referred for second opinion or continued management were excluded from this study.

The practice introduced a paperless system on September 14, 2011 whereby from this date onwards, patients with newly diagnosed PCa would have their files kept exclusively as electronic records in the practice database. For patients who were diagnosed prior to this date, electronic medical records were used if the patient's paper files had been uploaded into the database. If the complete patient medical record had not been scanned into the database, paper records would be sourced and reviewed. Institutional ethics committee approval was obtained (HREC Project ID: 2017-001).

Data collected prior to prostate biopsy included age, International Prostate Symptom Score (IPSS), digital rectal examination findings, PSA, and mpMRI scans were recorded. The risk categorization for PCa was deduced from the PSA level, local clinical stage, and Gleason score according to current National Comprehensive Cancer Network guidelines. Furthermore, the use and results of extent of disease imaging were recorded.

The patient's initial treatment strategy was classified as active surveillance, watchful waiting, or intervention. Intervention was defined as including ADT, RP, and radiotherapy.

RP was reported as either the open RP (ORP) or RARP, with or without pelvic lymph node dissections (PLND).

Patients who underwent ADT were distinguished as either being treated with luteinizing hormone receptor hormone (LHRH) agonists or LHRH antagonists. There was no inclusion of bilateral orchiectomy as this was never undertaken in this practice.

Prostate radiotherapy included external beam radiation therapy (EBRT) and low dose rate (LDR) brachytherapy or high dose rate (HDR) brachytherapy. It was also reported if the insertion of SpaceOar polyethylene glycol spacing prosthesis and/or fiducial seeds was a component of the treatment.

Data was consolidated into six groups of 2-year time periods. Age and IPSS were presented as means and standard deviations. Due to small numbers of substantial outlier PSA levels for some of the time frames examined, the median PSA and corresponding interquartile ranges were reported. Data in the other categories was counted and summated. Percentages were ascertained for each field of summary data in Tables 1 and 2, relative to the number of patients from the specific year group. For the initial treatment approaches in Table 3, the proportion of the subtype of each therapy was relative to the total number of the certain treatment, for instance the proportions of LHRH agonists and antagonists were relative to the total ADT therapy. The percentage for total treatment strategy was calculated relative to the total number of patients from the particular 2-year interval.

To investigate trends and make comparisons between datasets, the Pearson's correlation coefficient (r value) and P value were determined. Statistical significance for any correlation was defined as $P < 0.05$.

All analyses were executed using Microsoft Excel (Mac 2011 Version 14.6.9, Microsoft Corporation, Redmond, WA, USA) statistical analysis functions.

3. Results

A total of 839 patient records were retrospectively analyzed from 2005 to 2016 inclusive. Baseline data is summarized in Table 1. Over the 12 years, the overall mean age was 65.8 years and mean IPSS was 8 with no apparent change in the variables over the years. In the years 2007 and 2016, two men did not have their local clinical stages determined because they did not undergo a digital rectal examination. One patient did not have a rectum as a result of previous abdominoperineal excision of the rectum. The other man was unable to have the examination performed due to an anal stricture. There was no correlation between the number of biopsies taken and whether transperineal biopsy was performed (r = -0.06, $P = 0.90$).

In 2011–2012, the prebiopsy mpMRI was first introduced in the private practice and rapidly increased by 85.6% in use in patient care from 2011 to 2016, as shown in Table 1. This appeared to be associated with a decreasing percentage of men diagnosed with low-risk PCa (r = -0.80, $P = 0.04$) and an increasing percentage of men diagnosed with high-risk PCa (r = 0.90, $P = 0.01$) as shown in Fig. 1.

Both CT and bone scans were steadily increasing in use (r = 0.93, $P = 0.02$) from 2005 to 2012, as per Table 2. However, with the

Table 1
Summary data presenting the investigations for diagnosis of prostate cancer (PCa) for 2005–2016.

Yr	2005–2006	2007–2008	2009–2010	2011–2012	2013–2014	2015–2016
No. patients	71	160	164	159	143	142
Age (± SD)	67.8 (8.8)	66.8 (9.4)	64.6 (9.3)	63.7 (8.6)	65.4 (8.3)	67.9 (8.2)
PSA (IQR)	8.40 (8.90)	7.12 (6.68)	6.58 (4.84)	6.20 (3.75)	6.40 (5.23)	6.50 (4.46)
IPSS (± SD)	7 (6)	10 (8)	9 (7)	8 (7)	7 (6)	8 (7)
T1c (%)	40 (56.3)	87 (54.4)	103 (62.8)	115 (72.3)	88 (62.0)	78 (55.3)
≥ T2 (%)	31 (43.7)	72 (45.0)	61 (37.2)	44 (27.7)	54 (38.0)	63 (44.7)
Transperineal biopsy	1 (1.4)	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.4)	3 (2.1)
Prebiopsy mpMRI (%)	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.8)	87 (60.8)	127 (89.4)
Low risk (%)	26 (36.6)	37 (23.1)	41 (25.0)	39 (24.5)	19 (13.3)	20 (14.1)
Intermediate risk (%)	29 (40.8)	86 (53.8)	87 (53.0)	74 (46.5)	79 (55.2)	72 (50.7)
High risk (%)	16 (22.5)	36 (22.5)	36 (22.0)	46 (28.9)	45 (31.5)	49 (34.5)

IPSS, international prostate symptom score; IQR, interquartile range; mpMRI, multiparametric magnetic resonance imaging; PSA, prostate specific antigen; SD, standard deviation.

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