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Title:
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Date:
2018-03-01

Citation:
Sathianathen, N. J., Lamb, A. D., Lawrentschuk, N. L., Goad, J. R., Peters, J., Costello, A. J., Murphy, D. G. & Moon, D. A. (2018). Changing face of robot-assisted radical prostatectomy in Melbourne over 12 years. ANZ Journal of Surgery, 88 (3), pp.E200-E203. https://doi.org/10.1111/ans.14169.

Persistent Link:
https://hdl.handle.net/11343/293464

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The changing face of robot-assisted radical prostatectomy in Melbourne over 12 years

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Running Header: Australian RARP trends

Word Count:

- Abstract: 233
- Main text: 1,516

Figures included: 4

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ans.14169

Abstract

Introduction

This study aims to characterise the trends in disease presentation for RARP over a twelve-year period in Melbourne, Australia.

Methods

All patients undergoing a RARP between 2004 and October 2016 while under the care of six high-volume surgeons were included in the study. Data was collected prospectively regarding patient demographics and clinical details of their cancer.

Results

Over the 12-year timespan of the study, 3,075 men underwent a RARP with a median age of 63.01 years.

Temporal analysis demonstrated that the median age of patients undergoing prostatectomy advanced with time with the median age in 2016 being 65.51 years compared to 61.0 years in 2004 ($p<0.001$). There was also a significant trend to increased D'Amico risk groups over time with the percentage procedures for high-risk patients increasing from 12.6% to 28.10% from 2004 to 2016 ($p<0.001$).

Upgrade rates between biopsy and pathological Gleason grade scoring significantly trended down over the period of the study ($p<0.001$). There was also a shift to increased pathological stage over the 12 years with 22.1% of men having T3 disease in 2004 compared to 49.8% in 2016.

Conclusion

Our analysis demonstrates increasing treatment of older men with higher risk tumours, consistent with international trends. While this largely reflects a shift in case selection, further work is needed to assess whether the stage shift may relate partially to a decline in screening and increased presentation of higher risk disease

Keywords: prostatectomy, prostate cancer, robotic surgical procedures, laparoscopic surgery

Introduction

The prostate cancer (CaP) landscape has undergone substantial transformation over the last decade. Despite CaP continuing to be the most common solid organ malignancy amongst males in this period, we have witnessed an increased uptake of active surveillance, a shift in screening and biopsy guidelines, and the advent of new technologies, which have all influenced the characteristics of CaP as we know it today.

The incidence of prostate cancer rose sharply with the introduction of PSA (prostate specific antigen) testing in 1988(1). Then in 2002 a second spike was observed when some clinicians lowered the PSA threshold for further investigation from the norm at that time of 4.0 ng/mL after more than a fifth of men were demonstrated to have clinically significant disease with a PSA below the aforementioned threshold(2). As expected, this resulted in the number of prostate biopsies in a single Australian state increased by 59% between 2000 and 2004(3).

More recently, we have seen a reversal of these trends following the grade D recommendation from the United States Preventive Services Task Force (USPSTF) whom concluded that the harms of PSA screening outweighed its benefits. The downstream impact of these recommendations in the local setting have included a

decrease in PSA testing, prostate biopsy and radical prostatectomy since 2012(4). The decrease in radical prostatectomy rates are also partly explained by the increased use of active surveillance for low risk cancers(5).

Furthermore, technological developments in the field over the last decade have been colossal. Traditional open radical prostatectomy has largely been surpassed robot-assisted radical prostatectomy (RARP) both here in Australia and overseas where the technology is accessible(6). Similarly, use of the transperineal technique and pre-biopsy MRI have enhanced biopsy practices(7, 8).

Thus given these immense changes in the PCa setting, our study aims to characterise the demographic and disease trends of men undergoing RARP over the last decade in Australia.

Methods

A database with all men undergoing a RARP between January 2004 and October 2016 whilst under the care of six, high-volume, consultant surgeons (DGM, DAM, NLL, AJC, JG and JP) were included.

Available patient demographic and oncological data was collected. Oncological data included PSA at diagnosis, clinical stage, mode of diagnostic biopsy, biopsy pathology, final specimen pathology, pathological stage and the presence of a positive surgical margin. Patients were classified into groups based on the date of their RARP procedure and these groups were then compared to define trends.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics (Statistical Package for the Social Science, version 22.0, SPSS Inc., Chicago, Illinois, USA). One-way ANOVA, Kruskal-Wallis and Chi-square tests were used for univariate analysis. P values were all two-sided and were considered to be statistically significant if less than 0.05.

Results

Over the 12-year timespan of the study, 3,075 consecutive men met the inclusion criteria with a median age of 63.01 years (Appendix 1). The median PSA at the time of diagnosis was 6.35 ng/mL, 57.7% of the cohort was diagnosed with D'Amico intermediate disease and nearly two-thirds (62.1%) had T2 disease on their whole-mount specimen (Figure 1).

Temporal analysis demonstrated that the median age of patients undergoing RARP advanced with time with the median age in 2016 being 65.51 years compared to 61.0 years in 2004 ($p<0.001$; Figure 2). There was no significant change in PSA values over time ($p=0.489$).

There was also a significant trend to increased D'Amico risk groups over time (Figure 1) with the percentage procedures for high-risk patients increasing from 12.6% to 28.10% from 2004 to 2016 ($P<0.001$). Conversely, a lower proportion of men undergoing RP were D'Amico low risk with this group accounting for 40.9% of procedures in 2004 but only 6.2% in 2016.

Information regarding the mode of biopsy was available for 489 patients starting in 2010. All biopsies were performed transrectally in 2010 and 2011. From 2011 there is increase in the proportion of biopsies performed using the transperineal technique from 2.1% in 2012 to 49.2% in 2016 ($p<0.001$). Upgrade rates between biopsy and pathological Gleason grade scoring significantly trended down over the period of the study with 44.1% in 2004, 31.6% in 2010 and 24.5% in 2016 ($p<0.001$; Figure 3). On secondary analysis, men who were upgraded from their biopsied pathology scores were 2.27 times more likely [OR 95% CI 1.38 to 3.45] to have undergone TRUS biopsy than TP ($p=0.001$).

There was also a shift to increased pathological stage over the 12 years with 22.1% of men having T3 disease in 2004 compared to 49.8% in 2016 (Figure 4). However, positive surgical margin (PSM) status was available for 1,141 patients in our study from 2008 onwards and these rates decreased from 27.3% in 2008 to 12.1% in 2016 (p=0.0419).

Discussion

Amongst men undergoing RARP in Melbourne over the last twelve years, our study demonstrated a transition in patient demographics towards older individuals (Figure 2). Interestingly, this is a reversal of the trends previously seen when the median age of patients undergoing RP declined over the final decade of the 1990s(9). The increased utilisation of PSA screening and subsequent early detection of disease during the time period studied by Moul et al was likely the driving factor behind the decreasing median age. Furthermore, the number of radical prostatectomies also increased considerably since the introduction of PSA testing which began to trigger concerns regarding over-treatment of prostate cancer when taking into account the indolent nature of low-risk disease. This subsequently resulted in the USPSTF issuing a grade D recommendation regarding PSA testing, which has considerably impacted the prostate cancer landscape both in Australia and internationally. Zargar and colleagues reported that, since the release of the USPSTF findings, the number of

PSA tests, prostate biopsies and radical prostatectomies have all decreased in the state of Victoria(4). It is possible that these changes have led to delayed diagnosis and subsequently treatment. It should be noted that case selection is also an important factor contributing to the observed trends but its effect is not easily measureable.

The aforementioned changes in screening guidelines, which occurred during the timespan of our study, may also have played a role in the change in stage that was observed. The introduction of PSA testing in the late 1980s resulted in an surge of patients being diagnosed with non-palpable disease(10), however enthusiasm surrounding PSA screening has waned over time and may have influenced the stage migration. Furthermore, radical surgery alone was historically not an acceptable treatment option for locally advanced CaP, however, contemporary evidence has suggested otherwise and subsequently, surgeons have been more willing to operate on this subgroup(11). Additionally, the uptake of active surveillance for low-risk cancers has been widespread amongst urologists. Canadian data demonstrated an increased use of active surveillance from 2002 to 2010(12). Similarly, amongst all men diagnosed with prostate cancer in a single Australian state between 2008 and 2012, just under a quarter of the cohort received no treatment with curative intent at 12 months follow-up(5). This included over a third of men with low-risk disease who were placed on active surveillance. This resulting decrease in the numbers of

men with D'Amico low risk cancer undergoing treatment with curative intent was also seen in our cohort and will have contributed to the trend in stage seen in men undergoing RARP.

Consistent with the aforementioned observations, there was increase in the proportion of men with pathological stage T3 disease, consistent with other international series (13). Despite operating on higher risk patients, positive surgical margin rates decreased with time (27.3% to 12.1% p=0.0419). Lightfoot and colleagues also demonstrated a similar trend in their large study of patients with T3 disease undergoing RARP where the PSM rate decreased 70.6% to 32.3% over a six-year period(14). This appropriately reflects increasing surgical experience even when performing complex cases (15). It should be further noted that positive surgical margin status data was only available for approximately one-third of the total cohort (n=1,141) and no data prior to 2008.

There was an observed down trend in biopsy upgrade rates, which is thought to be associated with the increased use of transperineal biopsy (TPB) in our cohort (Figure 3). Compared to transrectal biopsies, the transperineal technique has been reported to improve the detection of clinically significant cancer(16). Furthermore, there have been noticeable benefits in the sampling of the anterior prostate, which is notoriously poorly sampled by transrectal biopsy. In a group of men who either had

a new diagnosis of cancer or upgrading of their disease using TPB and a previous negative TRUS, 79% had involvement of their anterior and/or transition zones(17). Although no patient in our study underwent a fusion biopsy given current practice of cognitive targeting in Melbourne(16), we expect that upgrade rates will further decline in the future with improving detection and sampling ability.

Our study demonstrates a substantial change in the characteristics of men undergoing RARP in Melbourne over the last decade. Since 2004, there have been significant trends to operating on older patients and those with higher-risk disease. These changes have primarily been driven by the alteration in PSA screening guidelines and uptake of active surveillance for low risk disease, and by recognition that good outcomes can be achieved in higher risk patients.

Niranjan Sathianathen certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None

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Figure 1: D’Amico risk groups over the timeframe of the study (p<0.001)

Figure 2: Age trend during period of study, p<0.001

Figure 3: Mode of biopsy and upgrade rates between bioptic and pathological Gleason score*

Figure 4: Pathological stage and positive surgical margin rate (data not available prior to 2008)

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Appendix 1 Patient Characteristics

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	P value
n	127	167	154	211	234	253	233	287	312	257	302	293	245	
Median Age	61.00	60.97	61.75	60.85	61.90	62.70	62.40	63.30	63.78	63.22	63.51	65.00	65.51	<0.001
Median PSA	7.50	6.30	6.35	6.00	6.45	6.25	6.10	5.73	6.00	6.30	6.70	6.80	6.60	0.489
D'Amico														<0.001
Low (%)	52 (41)	52 (31)	32 (21)	47 (22)	56 (24)	67 (26)	52 (22)	73 (25)	75 (24)	37 (15)	25 (8)	31 (11)	15 (6)	
Med (%)	59 (47)	91 (54)	86 (56)	119 (56)	123 (53)	136 (54)	130 (56)	159 (55)	174 (56)	149 (59)	206 (69)	176 (60)	159 (66)	
High (%)	16 (13)	24 (14)	36 (23)	45 (21)	52 (23)	50 (20)	51 (22)	55 (19)	63 (20)	66 (26)	69 (23)	85 (29)	68 (28)	
Biopsy*														<0.001
TRUS (%)	-	-	-	-	-	-	19 (100)	65 (100)	92 (98)	70 (91)	58 (63)	48 (58)	30 (51)	
TP (%)	-	-	-	-	-	-	0 (0)	0 (0)	2 (2)	7 (9)	34 (37)	35 (42)	29 (49)	
Stage														<0.001
T2 (%)	99 (78)	138 (83)	91 (59)	156 (74)	177 (76)	172 (68)	149 (64)	194 (68)	188 (60)	135 (53)	144 (48)	135 (47)	116 (50)	
T3 (%)	28 (22)	28 (17)	63 (41)	55 (26)	57 (24)	81 (32)	84 (36)	93 (32)	123 (40)	121 (47)	156 (52)	153 (53)	115 (50)	

***Data on mode of biopsy not available prior to 2010**

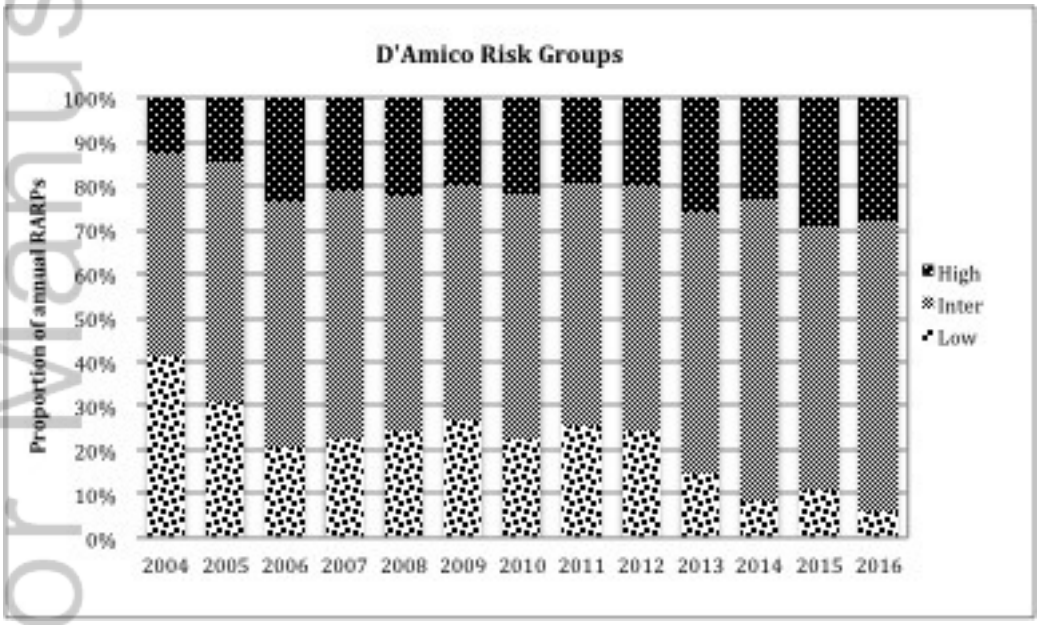
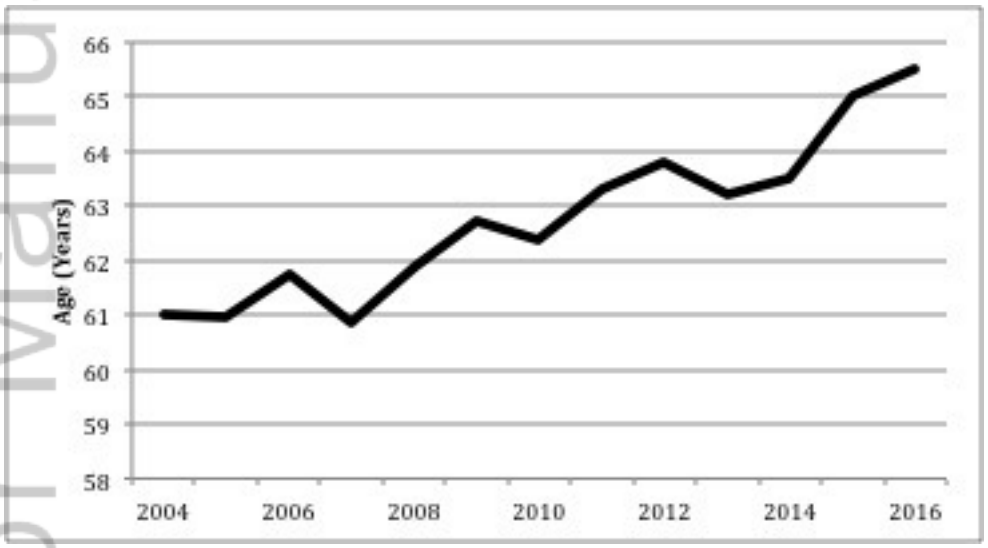


Figure 1.jpg



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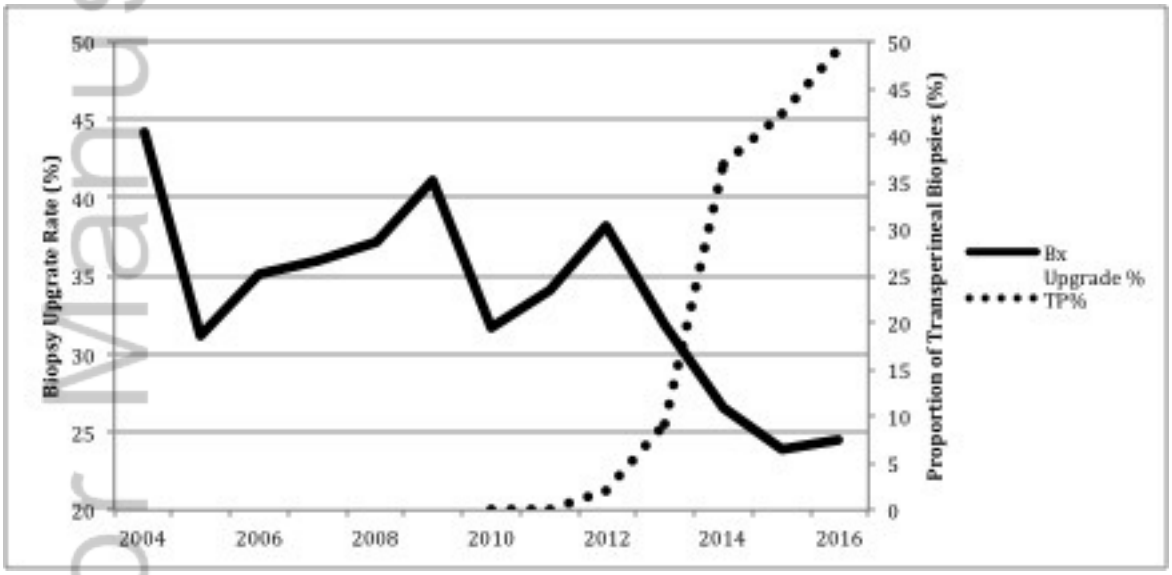

Figure 3.jpg

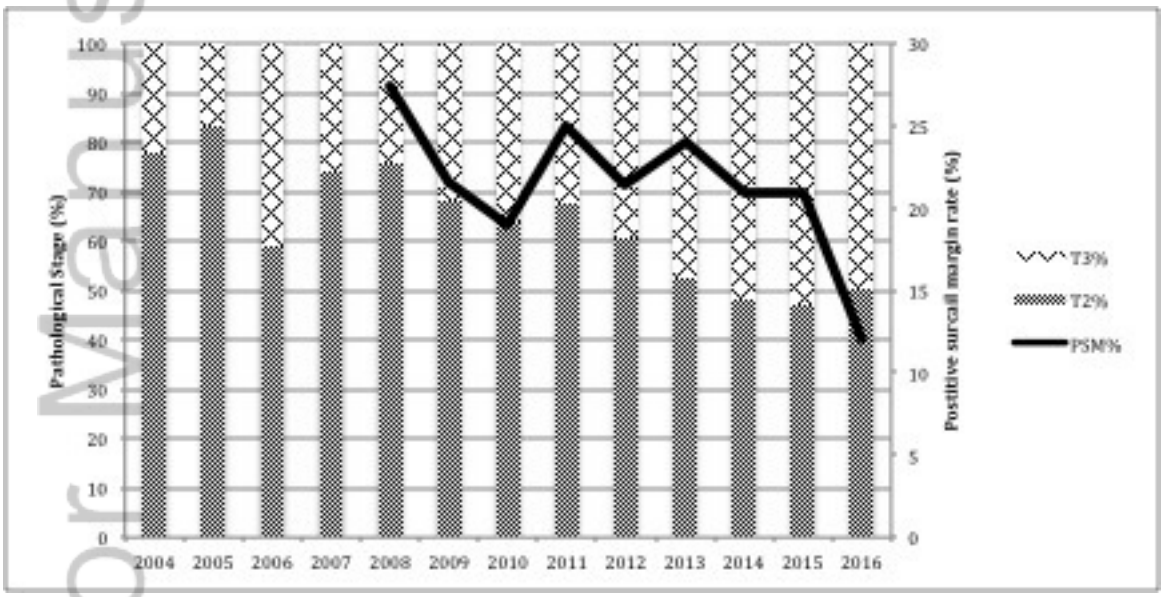

Figure 4.jpg