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Original Article
Clinical Investigation

South African single surgeon experience: Comparison of oncological outcomes, robot-assisted radical prostatectomy versus open perineal radical prostatectomy

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Abbreviations & Acronyms
BCR = biochemical recurrence
EAU = European Association
ORP = open radical prostatectomy
Post-t = postoperative pathological T stage
Pre-t = preoperative T stage
PSA = prostate specific antigen
PSM = positive surgical margin
RARP = robot-assisted radical prostatectomy

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Background: Studies comparing oncological outcomes between robot-assisted radical prostatectomy (RARP) and open radical prostatectomy (ORP) are often limited by bias because of their multi-institutional and multiple surgeon design. Studies from a single institution and single surgeon are uncommon.
Objective: To compare oncological outcomes between RARP and ORP at a single institution by a single surgeon.
Design, setting and participants: A retrospective cohort study of 2376 men with localized prostate cancer who underwent either RARP or ORP, from 1995 to 2020 at single institution, by one surgeon was done. The first 100 cases were discounted in both cohorts to account for the learning curve.
Measurements: Positive surgical margin (PSM) and biochemical recurrence (BCR) rates were measured for each cohort.
Results: A total of 1566 men underwent ORP and 810 underwent RARP. BCR rates of 29.2% were found in the ORP group versus 19.5% in the RARP group ($p < 0.001$). PSM rates of 15.4% were found in the ORP group versus 9.0% in the RARP group ($p < 0.001$). A multivariate analysis of preoperative prostate specific antigen (PSA) and tumor stage (T) shows no statistically significant association with recurrence when controlled for surgical technique.
Conclusions: RARP produces better oncological outcomes when compared to ORP when performed by one experienced surgeon at a single institution.
Patient summary: In this large study of men with prostate cancer still localized to the prostate. We found that better cancer removal and chances of cancer recurrence are reduced by a robot-assisted prostate removal technique, compared to the traditional open technique.

Key words: oncological outcomes, perineal radical prostatectomy, positive surgical margins, prostate cancer, radical prostatectomy, robot-assisted radical prostatectomy.

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INTRODUCTION

The landscape of surgical management of localized prostate cancer has changed dramatically in the last 20 years. There has been a rapid shift from the standard open radical prostatectomy (ORP), either retropubic or perineal approach, to laparoscopic radical prostatectomy and in the last 15 years robot-assisted radical prostatectomy (RARP) has become the preferred approach globally.[1] This migration in technique has led to a tome of research comparing post-operative complications, functional and oncological outcomes. The validity of the conclusions from these studies remains limited because of multiple factors, including utilization of multiple surgeons, different institutions and selection biases.[2–4] This study aimed to control for these confounders by comparing the results of a single surgeon's experience performing consecutive perineal radical prostatectomy and RARP in one institution, in order to evaluate the impact of surgical technique on oncologic outcomes.

DESIGN, SETTING AND PARTICIPANTS

In this retrospective cohort study, the oncological outcomes of men with localized prostate cancer who opted for surgical management were analyzed. These men were all treated at the Pretoria Urology Hospital in South Africa, with either an ORP or RARP. All the procedures were performed by one surgeon between the year 1995 and 2020. The ORP group were all performed via the transperineal approach. The RARP procedure was performed using the standard transperitoneal approach with the Da Vinci Si model. There were no significant changes to surgical technique and approach in the period of this investigation.

The prostatectomy specimens were reviewed for the presence of positive surgical margins (PSM) in each cohort. All the patients were followed up for a minimum of 24 months and evaluated for biochemical recurrence (BCR) with prostate specific antigen (PSA) serum measurements. BCR was defined as a PSA more than 0.2 ng/mL during follow up.

The rates of PSM and BCR were compared between men who underwent ORP versus RARP. A multivariate analysis was performed to determine whether other factors such as preoperative PSA, tumor stage, Gleason score and surgical technique were independent predictors of oncologic outcomes.

Ethics approval was obtained from the University of Pretoria's Faculty of Health Sciences Research Ethics Committee. All patients provided written informed consent before the undertaking of each procedure.

TABLE 1 Primary outcomes between open radical prostatectomy (ORP) and robot-assisted radical prostatectomy (RARP).

Variable	Description	ORP	RARP	*p*-Value
		N = 1566	*N* = 810	
Age (years)	Less than 50	94 (6.0%)	25 (3.1%)	<0.001
	50 to 59	468 (30.1%)	203 (25.3%)	
	60 to 69	746 (48.0%)	365 (45.6%)	
	70 and above	247 (15.9%)	208 (26.0%)	
Pre-prostate specific antigen	10 or less	1140 (74.0%)	590 (73.8%)	0.260
	Between 10 and 20	331 (21.5%)	161 (20.2%)	
	Above 20	70 (4.5%)	48 (6.0%)	
Recurrence	Yes	458 (29.2%)	158 (19.5%)	<0.001
	No	1108 (70.8%)	652 (80.5%)	
Positive surgical margin	Yes	241 (15.4%)	73 (9.0%)	<0.001
	No	1325 (84.6%)	737 (91.0%)	
Preoperative T stage	T1	1071 (69.7%)	54 (7.1%)	<0.001
	T2a	97 (6.3%)	75 (9.8%)	
	T2b	128 (8.3%)	39 (5.1%)	
	T2c	237 (15.4%)	531 (69.3%)	
	T3	4 (0.3%)	67 (8.7%)	
Postoperative pathological T stage	T2a	125 (8.2%)	58 (7.5%)	<0.001
	T2b	98 (6.4%)	38 (4.8%)	
	T2c	1072 (70.0%)	615 (78.7%)	
	≥T3	241 (15.4%)	73 (9.0%)	

RESULTS

Between 1995 and 2013, there were 1566 men who underwent ORP, and between 2013 and 2020, there were 810 men who underwent RARP. This number was reached after discounting the initial 100 cases in each cohort to account for learning curve. There was no statistically significant difference in the basic demographics of age and race. There was also no statistically significant difference in European Association (EAU) Risk Stratification between the two groups. There was a statistically significant difference between the two groups with regards to preoperative T stage (Pre-t) and postoperative pathological T stage (Post-t). There were more high stage tumors in the RARP group Pre-t T2c (69.3%) and T3 (8.7%), compared to the ORP group Pre-t T2c (15.4%) and T3 (0.3%). This is in contrast with the tumors upstaged to ≥T3 in the pathological postoperative T stage, 9.0% versus 15.4% in the RARP and ORP groups, respectively.

The RARP group had a statistically significant lower rate of PSM compared to ORP; 9.0 versus 15.4% ($p < 0.001$), see Table 1. The rate of BCR was also significantly better in the RARP group compared to ORP after a minimum follow up of 24 months; 19.5 versus 29.2% ($p < 0.001$), see Table 1.

A multivariate analysis was also done to determine whether preoperative PSA, Tumor stage and surgical technique independently associated with BCR. Preoperative tumor stage was not associated with BCR; odds ratio 0.53 (015–1.95), ($p = 0.34$). There was a statistically significant association between preoperative PSA and rate of BCR; PSA between 10 and 20 ng/mL had an odds ratio of 2.58 (2.07–3.23), ($p < 0.001$), and PSA more than 20 ng/mL; odds ratio 3.94 (2.63–5.9), ($p < 0.001$). Surgical technique also had a statistically significant association with BCR; odds ratio 0.42 (0.32–0.55), ($p < 0.001$), See Tables 2 and 3.

DISCUSSION

The uptake of RARP as the technique of choice for the surgical management of localized prostate cancer has grown substantially over the past two decades, overtaking traditional open techniques and classical laparoscopy.[5,6] This has not been without controversy; with many claiming the uptake was due to effective marketing as opposed to sound evidence based medicine, and some even going as far as to say it was a solution to a non-problem.[6] These concerns have since been laid to rest as far as perioperative and functional outcomes are concerned, most notably by the LAPPRO Trial and other randomized studies.[2,7–9] The glaring gap, however, still remains when the question of oncological control is asked. The evidence has been equivocal at best and conflicting at worst.[10]

With regards to PSM, early reports on the oncological outcomes of laparoscopy and RARP, emphasized serious concern over the apparent high PSM rates, compared to traditional techniques. These findings, however, were heavily influenced by surgeon experience, learning curve and institutional experience.[11,12] Further investigations showed

TABLE 2 Influence of preoperative prostate specific antigen (PSA) in each group.

Factor	Level	No recurrence	Recurrence	*p*-Value
Overall		*N* = 1761	*N* = 616	
Pre-PSA	10 or less	1378 (79.7%)	352 (57.7%)	<0.001
	Between 10 and 20	295 (17.1%)	197 (32.3%)	
	Above 20	57 (3.3%)	61 (10.0%)	
Open radical prostatectomy		*N* = 1108	*N* = 458	
Pre-PSA	10 or less	877 (80.7%)	263 (57.9%)	<0.001
	Between 10 and 20	183 (16.8%)	148 (32.6%)	
	Above 20	27 (2.5%)	43 (9.5%)	
Robot-assisted radical prostatectomy		*N* = 652	*N* = 158	
Pre-PSA	10 or less	501 (77.9%)	89 (57.1%)	<0.001
	Between 10 and 20	112 (17.4%)	49 (31.4%)	
	Above 20	30 (4.7%)	18 (11.5%)	

TABLE 3 Multivariable logistic regression for factors associated with recurrence.

Factor	Odds ratio 95% confidence interval	*p*-Value
Group		
Open radical prostatectomy	Reference	
Robot-assisted radical prostatectomy	0.42 (0.32; 0.55)	<0.001
pre_t		
pre_t1	Reference	
pre_t2a	0.51 (0.18; 1.42)	0.196
pre_t2b	0.57 (0.2; 1.58)	0.277
pre_t2c	0.42 (0.16; 1.13)	0.085
pre_t3a	0.5 (0.16; 1.56)	0.231
Pre-prostate specific antigen		
10 or less	Reference	
Between 10 and 20	2.58 (2.07; 3.23)	<0.001
Above 20	3.94 (2.63; 5.9)	<0.001

equivocal outcomes, with no difference between RARP and ORP, whilst later studies showed improved PSM rates in favor of RARP.[5,13–16] This conflict can be best explained by the inconsistent control for independent factors influencing PSM, such as, preoperative PSA, clinical tumor stage and surgeon experience.[5,13–16] Our study population in the two groups had no statistical difference with regards to preoperative PSA and demographic factors. There was, however, statistically significant difference between the two groups with regards to preoperative and postoperative/pathological tumor stage. Interestingly this difference showed that higher stage tumors (T2c and above) were treated in the RARP group compared to ORP, with better PSM and BCR outcomes in the RARP. This trend has been noted in other series[13–16] and perhaps underlines the increased confidence that the surgeon has to treat higher stage tumors because of the increased visibility and precision of the RARP technique. More importantly; with one experienced surgeon from a single institution performing all procedures, the question of surgeon experience is dealt with effectively. This underlies the validity of our finding, that, PSM rates are significantly improved by RARP. Like other investigators who demonstrated improved PSM with RARP, we suspect improved magnification and 3D visualization of the prostatic anatomy, especially at the apex may explain these findings.[15,17,18]

The BCR is another important metric for oncological control in prostate cancer treatment. Much like PSM, previous literature comprising of randomized control trials and their systematic reviews and meta-analyses showed no difference in BCR rates between RARP and ORP.[2,19] The weakness of these investigations is that the majority of them are either multi-institutional or multi-surgeon operated, or both. This undermines the validity of their findings because of the variation in surgeon experience and postoperative oncological treatment of the patients was left to physician discretion, and this too was variable. Our study controlled for these variations in its design and therefore supports the validity of the finding of reduced BCR rates in the RARP group. One might argue that it follows, that if PSM rates are reduced, then BCR rates will be reduced, and therefore, our findings are moot in this regard. Unfortunately, this has not been borne out in the literature, with many investigations disputing that PSM is an independent predictor of BCR.[4,14,15,19] It is therefore a reassuring finding from our study that operative technique is a significant predictor of BCR along with the previously described preoperative metrics. The strength of our findings is further supported by the demographic and preoperative similarities between the two groups. Although PSA was found to be a statistically significant predictor of BCR, the number of patients with PSA between 10 and 20, and above 20 was not different between the two study populations.

Single surgeon series from other countries and institutions have only hinted at the superiority of RARP over ORP with regards to oncological control, only concluding that it is non-inferior to ORP, lacking statistical grounds to show superiority.[1,4,7,20,21] Our study is novel in its assertion that in the hands of an experienced surgeon, RARP shows improved oncological control.

The main limitations of our study were its retrospective nature and the use of a historical control, the authors acknowledge the advancements in diagnostic and staging modalities for prostate cancer in this time period and concede this might have had a limited impact on the poorer oncological outcomes the ORP cohort who operated much earlier. Future research with prospective cohorts and randomized control trials with single surgeons over a long term period are still required to further corroborate these findings. A further limitation is the omission of the analysis of nerve sparing technique as an independent predictor of oncological control, it is the authors' view that this is a question deserving of its

own investigation and therefore outside the scope of this paper. Lastly, the authors also intend to investigate separately the functional outcomes, namely; potency, continence and complication rate (console time and estimated blood loss) to complete the pentafecta.

In the hands of an experienced surgeon, RARP shows statistically superior oncological control when compared to ORP. This is a helpful finding when counseling patients who opt for surgical management of localized prostate cancer.

AUTHOR CONTRIBUTIONS

Khayalethu C. S. Dlamini: Conceptualization; investigation; methodology; validation; writing – review and editing; formal analysis; project administration; writing – original draft; visualization. **Lance J. Coetzee:** Conceptualization; investigation; methodology; supervision; resources; writing – review and editing; validation. **Kgomotso Mathabe:** Supervision; funding acquisition.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

University of Pretoria Health Science Research Ethics Committee (Ethics No 745/2020).

INFORMED CONSENT

Not applicable.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL

Not applicable.

ANIMAL STUDIES

Not applicable.

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