Superior Quality of Life and Improved Surgical Margins Are Achievable with Robotic Radical Prostatectomy After a Long Learning Curve: A Prospective Single-surgeon Study of 1552 Consecutive Cases

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Abstract

Background: Comparative studies suggest functional and perioperative superiority of robot-assisted radical prostatectomy (RARP) over open radical prostatectomy (ORP).

Objective: To determine whether high-volume experienced open surgeons can improve their functional and oncologic outcomes with RARP and, if so, how many cases are required to surpass ORP outcomes and reach the learning curve plateau.

Design, setting, and participants: A prospective observational study compared two surgical techniques: 1552 consecutive men underwent RARP (866) or ORP (686) at a single Australian hospital from 2006 to 2012, by one surgeon with 3000 prior ORPs.

Outcome measurements and statistical analysis: Demographic and clinicopathologic data were collected prospectively. The Expanded Prostate Cancer Index Composite quality of life (QoL) questionnaire was administered at baseline, 1.5, 3, 6, 12, and 24 mo. Multivariate linear and logistic regression modelled the difference in QoL domains and positive surgical margin (PSM) odds ratio (OR), respectively, against case number.

Results and limitations: A total of 1511 men were included in the PSM and 609 in the QoL analysis. RARP sexual function scores surpassed ORP scores after 99 RARPs and increased to a mean difference at 861st case of 11.0 points (95% confidence interval [CI], 5.9–16.1), plateauing around 600–700 RARPs. Early urinary incontinence scores for RARP surpassed ORP after 182 RARPs and increased to a mean difference of 8.4 points (95% CI, 2.1–14.7), plateauing around 700–800 RARPs. The odds of a pT2 PSM were initially higher for RARP but became lower after 108 RARPs and were 55% lower (OR: 0.45; 95% CI, 0.22–0.92) by the 866th RARP. The odds of a pT3/4 PSM were initially higher for RARP but decreased, plateauing around 200–300 RARPs with an OR of 1.15 (0.68–1.95) at the 866th RARP.

Limitations include single-surgeon data and residual confounding.

Conclusions: RARP had a long learning curve with inferior outcomes initially, and then showed progressively superior sexual, early urinary, and pT2 PSM outcomes and similar pT3 PSM and late urinary outcomes. Learning RARP was worthwhile for this high-volume surgeon, but the learning curve may not be justifiable for late-career/low-volume surgeons; further studies are needed.
1. Introduction

Radical prostatectomy is a treatment option for localised prostate cancer in men with a life expectancy exceeding 10–15 yr [1]. Open radical prostatectomy (ORP) is the gold standard technique; however, robot-assisted radical prostatectomy (RARP) is gaining popularity. Recent studies report superior quality of life (QoL) and equivalent positive surgical margin (PSM) outcomes with RARP compared with ORP [2–5], but there remains a paucity of high-quality evidence. Randomised trials are underway [6–8]. However, according to trial protocols, participating surgeons perform ORP or RARP but not both. Hence the skill and experience of individual surgeons may confound results.

Men undergoing RARP during a surgeon’s learning curve may be subject to treatment selection bias, with selection potentially based on factors such as current QoL, age, disease characteristics, desire for nerve sparing, and prior hormonal therapy. Despite this, many of these potential confounders were not adjusted for in previous studies, thereby producing results vulnerable to confounding from treatment selection bias. No studies have attempted in-depth modelling of the learning curve effect on functional and oncologic outcomes across >800 cases, adjusting comprehensively for confounders. Describing the learning curve up to 850 cases for one highly experienced high-volume open surgeon may guide open surgeons who are considering learning RARP.

The objectives of this study were to determine if an experienced surgeon could improve QoL and PSM outcomes by learning RARP, and if so, to determine how many RARPs were required to achieve superiority and to reach the learning curve plateau for each outcome.

2. Patients and methods

2.1. Patients and study design

Between March 2006 and September 2012, a single surgeon (PS), who had performed >3000 prior ORPs, performed his first 866 RARPs independently (following supervised training by an expert surgeon) (Fig. 1) at St. Vincent’s private hospital in Sydney, Australia. PS’s initial robotic training consisted of limited experience in laparoscopic surgery, an accredited intensive robotic training workshop, and an animal

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**Fig. 1 – Flow diagram showing patient participation.**

ADT = androgen-deprivation therapy; EPIC = Expanded Prostate Cancer Index Composite; HRQoL = health-related quality of life; ORP = open radical prostatectomy; RARP = robot-assisted radical prostatectomy.
laboratory training course. He received initial mentoring and proctoring by an experienced surgeon for 20 cases until deemed competent and further proctoring by a leading expert to approximately case number 50 to further refine his technique. He also obtained observerships with three leading robotic surgeons prior to and during the first year of robotics.

PS also performed 686 ORPs during the period of the study. All 1552 men in consultation with a multidisciplinary team chose their preferred surgical method and consented to be enrolled in a prospective research database. Overall, 1511 patients with complete data were included in the PSA analysis. All were invited to participate in the prospective Expanded Prostate Cancer Index Composite (EPIC) QoL study of which 837 agreed; 609 had sufficient data for inclusion in this QoL analysis. The hospital’s ethics committee approved the study.

2.2. Outcome measures

2.2.1. Quality-of-life outcome measures

Participants in the EPIC QoL study received a self-administered questionnaire at baseline and at 1.5, 3, 6, 12, and 24 mo following treatment. The questionnaire included questions from EPIC [9], developed from the UCLA Prostate Cancer Index [10], to assess health-related quality of life (HRQoL) in men with prostate cancer. The EPIC questions measure QoL scores for Urinary, Bowel, Sexual, and Hormonal summary domains, and each Domain Summary Score is composed of Function and Bother subscales. In addition, the Urinary Domain summary score includes distinct Incontinence and Irritation/Obstruction subscales. All scores (and also differences in mean scores) are determined on 100-point scales, where lower scores indicate poorer QoL.

2.2.2. Positive surgical margin outcome measures

All prostatectomy specimens were processed according to International Society of Urological Pathology/American Joint Committee on Cancer guidelines with whole-mount step sectioning at 3-mm intervals. A PSM was defined as tumour involving the inked margin of the cut surface.

2.3. Surgical technique

The ORP technique was performed as described by Walsh [11]. Retrograde nerve sparing was performed selectively based on preoperative risk stratification (using the Partin nomogram) [12] and adjusted according to operative findings. Extent of nerve sparing was defined as 0 (no neurovascular nerve bundle [NVB] preservation), 0.5 (partial NVB preservation), or 1 (complete NVB preservation) for each side; a total score of 0–2 was recorded postoperatively. Bladder neck reconstruction, eversion, and six-suture urethrovesical anastomosis were performed.

The transperitoneal RARP technique used was previously described by Rocco and colleagues [13], using the da Vinci Si robotic system (Intuitive Surgical, Sunnyvale, CA, USA). Prior suture ligation of the dorsal venous complex (except where there was a significant aberrant pudendal artery) followed by division, selective bladder neck preservation, and combined antegrade/retrograde nerve sparing were performed, adjusted according to visual feedback in selected high-risk cases. A Rocco posterior stitch, suspension stitch, and continuous anastomosis were performed.

2.4. Statistical analyses

Multivariate linear regression analyses with generalized estimating equation adjustment to account for repeated outcome observations on the same individual were used to estimate adjusted mean differences in QoL scores between treatments according to surgeon experience [14]. Separate regression models were fitted for each HRQoL domain subscale, with each model sharing a common formulation. Subscale-specific scores were defined as the dependent variable in each model with the corresponding baseline score as a continuous independent variable.

Categorical covariates included time since surgery (1.5, 3, 6, 12, 24 mo), age (38–54, 55–59, 60–64, 65–77 yr), year of surgery (2006–2007, 2008–2009, 2010–2012), socioeconomic status of residence area (divided into quintiles using the Socio-Economic Indexes for Areas) [15], remoteness of residence (major city, inner regional, outer regional, remote/very remote based on Accessibility/Remoteness Index of Australia) [16], baseline prostate-specific antigen (PSA) (<4, 4–10, >10 ng/ml), pathologic stage (pT1c–pT2c, pT3A–pT4), biopsy Gleason score (<7, 7, >7), hormonal preoperative therapy (no, yes), adjuvant therapy (no, yes), and operation type (ORP vs RARP). Models were not adjusted for NVB preservation because this variable potentially is situated on causal pathways between surgery type and QoL outcomes (and additional adjustment for NVB did not materially change any estimates anyway). QoL scores were found not to be associated with the surgeon’s ORP case number (presumably the surgeon had plateaued in his ORP learning curve; Table 1). Consequently, mean ORP QoL scores were modelled in the regression equations as constant.

The RARP learning curve relationship between mean QoL score and RARP case number was found to be most suitably modelled in the regression equations by natural log functions. To assess whether the learning curve was significantly modified by time after surgery, terms for interaction between learning curves and a dichotomous variable (1.5–6 and 12–24 mo after surgery) were added to the regression models.

The relationship between PSM risk and surgeon’s experience was modelled using logistic regression. Independent variables included those in the linear regression models except for baseline QoL score, time since surgery, and adjuvant therapy. The surgeon’s learning curves for ORP and RARP were again modelled as constant and natural log functions, respectively. Modification of the learning curve by pathologic stage (pT2 vs pT3–4) was modelled using interaction terms. In the absence of published studies defining a “plateau point” in the learning curve, an increase of 1 point in QoL score or 10% decrease in the PSM odds ratio (OR) per 150 additional cases was proposed.

Table 1 – Slope coefficients for the associations between quality of life/positive surgical margin outcomes and surgeon’s open radical prostatectomy (ORP) case number during the study period for ORP patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Slope coefficient</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual function</td>
<td>-0.004</td>
<td>0.833</td>
</tr>
<tr>
<td>Sexual bother†</td>
<td>0.011</td>
<td>0.739</td>
</tr>
<tr>
<td>Urinary function</td>
<td>0.014</td>
<td>0.338</td>
</tr>
<tr>
<td>Urinary bother†</td>
<td>0.017</td>
<td>0.253</td>
</tr>
<tr>
<td>Urinary irritative obstruction*</td>
<td>0.008</td>
<td>0.728</td>
</tr>
<tr>
<td>Urinary incontinence*</td>
<td>0.015</td>
<td>0.226</td>
</tr>
<tr>
<td>Positive surgical margin †</td>
<td>-0.002</td>
<td>0.169</td>
</tr>
</tbody>
</table>

| Data are for ORP patients only.          |
| Slope coefficient obtained from linear regression of quality of life (QoL) outcome on surgeon’s ORP case number during the study period. General estimating equations were used to account for the repeated QoL measurements on the same individuals at different time intervals. |
| Slope coefficient obtained from logistic regression of positive surgical margin outcome on surgeon’s ORP case number during the study period. Note: Linear and logistic regression models were adjusted for age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, and hormonal preoperation therapy. Linear (QoL) regression models were additionally adjusted for baseline QoL score, time after surgery, and adjuvant therapy. |
3. Results

Table 2 summarises the baseline demographics and clinical characteristics. They were similar between the 1511 men in the PSM analysis and the subset included in the QoL analysis (see supplemental data, Supplemental Table 1, comparing baseline characteristics of the QoL and PSM analysis groups). There were differences between the RARP and ORP groups at baseline as demonstrated in Table 2: a larger proportion of ORP patients had their operation in 2006–2007 than RARP patients (53% vs 8%); the ORP group had a higher median PSA (6.8 vs 5.8 ng/ml) and higher proportions with PSA >10 (25% vs 12%), Gleason score >7 (18% vs 11%), pathologic stage >T2 (42% vs 38%), and neoadjuvant therapy (11% vs 4%). Patients in the ORP group were less likely to undergo complete NVB preservation.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HRQoL analyses' (n = 609)</th>
<th>Surgical margin analyses' (n = 1511)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ORP (n = 230)</td>
<td>RARP (n = 379)</td>
</tr>
<tr>
<td></td>
<td>Median Age at surgery, yr</td>
<td>60.9 62.2</td>
</tr>
<tr>
<td></td>
<td>Quartiles</td>
<td>56–65 57–66</td>
</tr>
<tr>
<td></td>
<td>Age group (%)</td>
<td>38–54 48 (21) 53 (14) 0.165</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55–59 49 (21) 87 (23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60–64 62 (27) 117 (31)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65–77 71 (31) 122 (32)</td>
</tr>
<tr>
<td></td>
<td>Calendar year of surgery (%)</td>
<td>2006–2007 74 (32) 37 (10) &lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2008–2009 119 (52) 162 (43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2010–2012 37 (16) 180 (47)</td>
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<tr>
<td></td>
<td>SES of residence area (%)</td>
<td>1 (highest SES) 109 (47) 220 (58) 0.112</td>
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<tr>
<td></td>
<td></td>
<td>2 47 (20) 65 (17)</td>
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<tr>
<td></td>
<td></td>
<td>3 38 (17) 42 (11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 25 (11) 35 (9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 (lowest SES) 11 (5) 17 (4)</td>
</tr>
<tr>
<td></td>
<td>Place of residence (%)</td>
<td>Remote/Very remote 3 (1) 5 (1) 0.143</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outer regional 41 (18) 46 (12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inner regional 49 (21) 70 (18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Major city 137 (60) 258 (68)</td>
</tr>
<tr>
<td></td>
<td>PSA at baseline Median, ng/ml</td>
<td>6.7 5.9</td>
</tr>
<tr>
<td></td>
<td>Quartiles</td>
<td>4.8–10.4 4.2–7.8</td>
</tr>
<tr>
<td></td>
<td>PSA group (%) &lt;4 ng/ml</td>
<td>28 (12) 82 (22) &lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4–10 ng/ml 144 (63) 258 (68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;10 ng/ml 58 (25) 39 (10)</td>
</tr>
<tr>
<td></td>
<td>Pathologic stage (%) pT2 129 (56) 250 (66) 0.015</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>pT3–pT4 101 (44) 129 (34)</td>
</tr>
<tr>
<td></td>
<td>Gleason score on biopsy (%) &lt;7 16 (7) 55 (15) 0.007</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 176 (77) 281 (74) 478 (71)</td>
</tr>
<tr>
<td></td>
<td>Hormonal preoperative therapy (%)</td>
<td>No 206 (90) 369 (97) &lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes 24 (10) 10 (3) 72 (11)</td>
</tr>
<tr>
<td></td>
<td>Adjuvant therapy (%) No 219 (95) 373 (98) 0.020</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes 11 (5) 6 (2) n/a</td>
</tr>
<tr>
<td></td>
<td>NVB score (%) 0, 0.5 16 (7) 15 (4) &lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1, 1.5 69 (30) 57 (15) 186 (28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 145 (63) 307 (81) 466 (66)</td>
</tr>
</tbody>
</table>

HRQoL = health-related quality of life; ORP = open radical prostatectomy; NVB = neurovascular nerve bundle; PSA = prostate-specific antigen; RARP = robot-assisted radical prostatectomy; SES = socioeconomic status.

* All patients included in the HRQoL analyses are also included in the surgical margin analyses.

* Adjuvant therapy data are not shown for the surgical margin cohort because adjuvant therapy occurs postsurgery and thus cannot causally affect the surgical margin.
(66% vs 79%). Both groups in the QoL cohort had similarly high follow-up rates (86–99% for ORP and 88–98% for RARP; Table 3). Unadjusted (crude) QoL and PSM results are summarised in Table 4.

3.1. Quality-of-life results

3.1.1. Sexual domains
No significant interaction between follow-up period and the RARP learning curves for sexual function and sexual bother were found \( (p = 0.1 \) and \( p = 0.3 \), respectively). Hence a single learning curve was modelled for each outcome (Figs. 2 and 3). Mean (expected) scores were lower for RARP compared with ORP at the first RARP, at \( −23.5 \) (95% CI, −36.8 to −10.2) and \( −13.5 \) points lower (−36.3 to 9.4) for sexual function and bother, respectively. Scores improved and became higher than ORP scores after 99 and 123 RARPs, respectively. At the final surgery (861st RARP in the QoL cohort), sexual function and sexual bother scores were 11.0 (95% CI, 5.9–16.1) and 5.4 (2.7 to 13.5) points better, respectively, for RARP compared with ORP. Improvements plateaued around 600–700 and 300–400 RARPs, respectively.

3.1.2. Urinary quality-of-life domains
Significant interactions were found between follow-up period and the learning curves for all four urinary domain subscales (\( p < 0.001 \) for each). Hence results are presented for two time periods.

### 3.1.2.1. Early postoperative period (1.5–6 mo)
Mean scores for the first RARP were \( −28.3 \) (95% CI, −46.5 to −10.0), \( −14.5 \) (−26.6 to −2.4), \( −11.4 \) (−21.9 to −0.9), and \( −3.9 \) (−11.4 to 3.6) points lower than ORP scores for incontinence, function, bother, and irritation-obstruction, respectively (Fig. 4a, 5a, 6a, 7a). Scores for RARP rapidly improved, becoming higher than ORP scores after 182, 144, 58, and 18 operations, respectively. By the final RARP case (\( n = 861 \) in the QoL cohort, mean RARP scores were 8.4 (95% CI, 2.1–14.7), 5.2 (1.1–9.3), 7.5 (3.9–11.2), and 5.1 (2.5–7.7) points higher, respectively. Differences between scores plateaued around 700–800, 300–400, 300–400, and 100–200 RARPs, respectively.

### 3.1.2.2. Late postoperative period (12–24 mo)
Mean scores for the first RARP were \( −15.0 \) (95% CI, −31.5 to 1.5), \( −6.8 \) (−17.2 to 3.5), −12.1 (−22.3 to −1.9), and −6.6 (−13.8 to 0.5)

### Table 3 – Quality-of-life interview completion rates by treatment group

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Questionnaire return status</th>
<th>Months since surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Due for return</td>
<td>Returned</td>
</tr>
<tr>
<td>ORP, ( n(%) )</td>
<td></td>
<td>230 (100)</td>
</tr>
<tr>
<td>RARP, ( n(%) )</td>
<td></td>
<td>379 (100)</td>
</tr>
</tbody>
</table>

ORP = open radical prostatectomy; RARP = robot-assisted radical prostatectomy.

### Table 4 – Means/proportions and standard deviations for outcome measurements by treatment and follow-up time

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Baseline</th>
<th>6-mo follow-up</th>
<th>24-mo follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ORP</td>
<td>RARP</td>
<td>ORP</td>
</tr>
<tr>
<td>Sexual function; mean (SD)</td>
<td>59.8 (25.5)</td>
<td>61.0 (24.5)</td>
<td>25.8 (21.6)</td>
</tr>
<tr>
<td>Sexual bother; mean (SD)</td>
<td>76.6 (28.6)</td>
<td>76.9 (28.2)</td>
<td>47.6 (30.6)</td>
</tr>
<tr>
<td>Sexually potent, % (SD %)</td>
<td>56.6 (49.7)</td>
<td>63.1 (48.3)</td>
<td>8.8 (28.4)</td>
</tr>
<tr>
<td>Urinary function; mean (SD)</td>
<td>95.6 (8.2)</td>
<td>95.7 (10.4)</td>
<td>88.0 (12.7)</td>
</tr>
<tr>
<td>Urinary bother, mean (SD)</td>
<td>86.8 (14.2)</td>
<td>87.9 (14.2)</td>
<td>86.6 (13.3)</td>
</tr>
<tr>
<td>Urinary irritative obstruction, mean (SD)</td>
<td>88.9 (12.4)</td>
<td>90.2 (11.1)</td>
<td>91.2 (9.6)</td>
</tr>
<tr>
<td>Urinary incontinence, mean (SD)</td>
<td>94.8 (10.6)</td>
<td>94.2 (14.2)</td>
<td>81.9 (19.7)</td>
</tr>
<tr>
<td>Continent, % (SD %)</td>
<td>84.1 (36.6)</td>
<td>85 (35.8)</td>
<td>49.1 (50.1)</td>
</tr>
<tr>
<td>Positive surgical margin, % (SD %)</td>
<td>9 (28.6)</td>
<td>6.7 (25.1)</td>
<td>32.5 (46.9)</td>
</tr>
</tbody>
</table>

ORP = open radical prostatectomy; RARP = robot-assisted radical prostatectomy; SD = standard deviation.

Baseline measurements represent measurements taken shortly before surgery, except for surgical margins that represent measurements from tissue taken during the operation.

Sexual potency was defined as sexual function score >60.

1. Continent was defined as Expanded Prostate Cancer Index Composite questionnaire responses to Q12 = 0 and Q8 = 5 (no pads required and rarely or never leak urine).
Fig. 2 – Adjusted differences in mean sexual function scores (robot-assisted radical prostatectomy [RARP] minus open radical prostatectomy [ORP]) by surgeon RARP experience (number of prior RARPs) for measurements taken between 1.5 and 24 mo after surgery.

* Adjusted for time after surgery, baseline sexual function score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.

\* Difference in means (95% confidence interval) at first RARP.
\** Difference in means at last RARP (n = 861).
\^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.

\# Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.
CI = confidence interval.

Fig. 3 – Adjusted differences in mean sexual bother scores (robot-assisted radical prostatectomy [RARP] minus open radical prostatectomy [ORP]) by surgeon RARP experience (number of prior RARPs) for measurements taken between 1.5 and 24 mo after surgery.

* Adjusted for time after surgery, baseline sexual bother score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.

\* Difference in means (95% confidence interval) at first RARP.
\** Difference in means at last RARP (n = 861).
\^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.

\# Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.
CI = confidence interval.

Fig. 4 – Adjusted differences in mean urinary function scores (robot-assisted radical prostatectomy [RARP] minus open radical prostatectomy [ORP]) by surgeon RARP experience (number of prior RARPs) for measurements taken between (a) 1.5–6 mo after surgery and (b) 12–24 mo after surgery.

* Adjusted for time after surgery, baseline sexual bother score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.

\* Difference in means (95% confidence interval) at first RARP.
\** Difference in means at last RARP (n = 861).
\^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.

\# Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.
CI = confidence interval.
points lower than ORP scores for incontinence, function, bother, and irritation-obstruction, respectively (Fig. 4b, 5b, 6b, 7b). RARP scores improved rapidly early in the learning curve but plateaued sooner than RARP scores for 1–6 mo. RARP scores became higher than ORP scores after 579, 284, and 222 RARPs for incontinence, bother, and irritation-obstruction, respectively, and they never became higher for function. Differences between scores plateaued around 200–300, 50–100, 200–300, and 200–300 RARPs for incontinence, function, bother, and irritation-obstruction, respectively (Figs. 4–7).

3.2. Oncologic results: positive surgical margins

Because there was a significant interaction between the PSM risk learning curve and pathologic stage ($p = 0.036$), PSM learning curves are reported by pathologic stage (Fig. 8). In pT2 disease, the odds of a PSM were 6.19 times higher (95% CI, 1.20–31.80) for RARP than ORP at first RARP but became lower after 108 RARPs and plateaued around 400–500 RARPs. At the final RARP ($n = 866$) in the study, the odds of a PSM were 55% lower for RARP compared with ORP (OR: 0.45 [95% CI, 0.22–0.92]). In pT3–4 disease, the odds of a PSM were initially 4.71 times higher (95% CI, 0.90–24.60) for RARP and plateaued around 200–300 cases. The odds of a PSM remained 17% higher with RARP at the final RARP; however, the confidence limits were wide (OR: 1.17 [95% CI, 0.70–1.97]).

4. Discussion

In this study, an experienced high-volume open surgeon improved his surgical margins and a number of his QoL outcomes by learning RARP. This study adds to the evidence base because it uses a validated QoL tool (EPIC), adjusts for more confounders than previous studies, extends the learning curve analysis to approximately 850 cases, and demonstrates a benefit for highly experienced open surgeons.

Unadjusted potency and continence rates (Table 4) may appear lower than some series; this is due to the strict definitions of continence and potency imposed by the EPIC QoL tool, the inclusion of all men with baseline erectile dysfunction and impotence, and the absence of adjustment for other confounders in these raw figures.

The improved potency outcomes with RARP in this study are consistent with a recent meta-analysis of six comparative studies that reported erectile dysfunction in 47.4% of men 12 mo following ORP, compared with 24.2% following RARP (OR: 2.84; $p = 0.002$) [3]. Degree of nerve sparing was not adjusted for in our study because RARP may improve
Fig. 6 – Adjusted differences in mean urinary incontinence scores (robot-assisted radical prostatectomy [RARP] minus open radical prostatectomy [ORP]) by surgeon RARP experience (number of prior RARPs) for measurements taken between (a) 1.5–6 mo after surgery and (b) 12–24 mo after surgery.

\( \text{Adjusted for time after surgery, baseline sexual bother score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.} \)

\* Difference in means (95% confidence interval) at first RARP.

\** Difference in means at last RARP (n = 861).

\^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.

\# Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.

CI = confidence interval.

Fig. 7 – Adjusted differences in mean urinary irritative obstruction scores (robot-assisted radical prostatectomy [RARP] minus open radical prostatectomy [ORP]) by surgeon RARP experience (number of prior RARPs) for measurements taken between (a) 1.5–6 mo after surgery and (b) 12–24 mo after surgery.

\( \text{Adjusted for time after surgery, baseline sexual bother score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.} \)

\* Difference in means (95% confidence interval) at first RARP.

\** Difference in means at last RARP (n = 861).

\^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.

\# Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.

CI = confidence interval.
precision in intrafascial nerve sparing through enhanced magnification, greater degrees of freedom, downscaled movements, controlled gentle retraction, antegrade approach, and reducing venous bleeding. Intrafascial nerve sparing may damage fewer cavernous nerve fibres and reduce traction neurapraxia, improving potency outcomes [17,18].

The improved early urinary outcomes seen with RARP are consistent with previous studies by our group [19] and others [20]. In a 2012 meta-analysis of 51 studies, incontinence at 12 mo was 11.3% after ORP and 7.5% after RARP (OR for incontinence: 1.53; p = 0.03) [21]. Improved early continence may be due to the improved distribution of tension, reduced anastomotic leaks, and reduced suture knot fibrosis with a continuous 12-suture anastomosis. Robotics may facilitate apical preservation of the pubourethral ligaments, fascia, and delicate neurovascular supply to the external sphincter.

The finding of lower pT2 PSM risk with RARP after approximately 100 cases suggests that RARP may be oncologically superior after a modest learning curve for organ-confined (pT2) disease, even for an experienced open surgeon. A previous smaller study demonstrated the same finding [22]. Two meta-analyses [2,5] and a literature review [4] showed equivalent pT2 PSM rates, but they did not model PSM risk across the learning curve. One published study reported higher pT2 PSM rates for RARP, but results were confounded by comparing the ORP series of one surgeon with the RARP series of another [23].

For extraprostatic (pT3) disease in this study, RARP achieved a similar PSM risk to ORP late in the learning curve. A recent meta-analysis reported lower PSM rates for ORP than RARP in pT3 disease, but adjustment for confounders was limited and the learning curve was not analysed [2]. One recent study showed equivalent PSM outcomes for RARP and ORP in higher risk disease for experienced robotic surgeons [24]. A multi-institutional review of 3794 patients showed a learning curve of >1000 cases before the pT3 PSM rate plateaued [25]. Therefore, RARP for high-risk disease should be avoided early in the learning curve but appears equivalent in experienced robotic surgeons.

Surgeon experience across a learning curve of >1000 cases and heterogeneity (due to unmeasured surgeon factors) were previously shown to be significant predictors of biochemical recurrence after ORP [26,27]. Experienced open surgeons therefore argue that individual surgeon skill and experience are more important predictors of outcomes than operative approach, and that their excellent ORP results are due to having reached a plateau in the learning curve [28,29], beyond which they are unlikely to improve further by learning RARP. Our PSM results suggest that although RARP exhibited a similarly long learning curve to that shown in ORP studies, the assumption that ORP outcomes cannot be improved upon by RARP for an experienced surgeon may be inaccurate. RARP involves a long learning curve, and patients early in the learning curve may experience worse QoL and PSM outcomes than if they

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**Fig. 8 – Adjusted robot-assisted radical prostatectomy (RARP) versus open radical prostatectomy (ORP) [reference group] odds ratios for positive surgical margin by surgeon RARP experience (number of prior RARPs) stratified by pathologic stage.**

- Adjusted for time after surgery, baseline sexual bother score, age at surgery, calendar year of surgery, socioeconomic status of residence, place of residence, baseline prostate-specific antigen, pathologic stage, Gleason score on biopsy, hormonal preoperation therapy, and adjuvant therapy.
- * Difference in means (95% confidence interval) at first RARP.
- ** Difference in means at last RARP (n = 861).
- ^ Number of prior RARPs required for RARP mean score to exceed ORP mean score.
- # Number of prior RARPs where an additional 150 operations will result in a one-unit increase in the mean difference.
- CI = confidence interval.
had undergone ORP by the same surgeon [19,25]. A trifecta of superior early continence, sexual function, and pT2 PSM risk required >300 cases in our study, as did achieving similar late continence and pT3 PSM risk outcomes.

If our results are validated in future studies, it would suggest that learning RARP may be worthwhile for young or high-volume surgeons but may not be for late-career (<10 yr of practise remaining) or midcareer low-volume (<25 cases per year) surgeons because it may take a low-volume surgeon 5 yr to achieve equivalent outcomes and 15 yr to achieve superior outcomes. Fellowship training likely shortens the learning curve [30–32], but undertaking a 12-mo robotic fellowship is impractical for established surgeons. For these surgeons, a combination of intensive workshops, advanced simulator dry labs, live animal/cadaveric wet labs, and observerships and closely supervised preceptorships may shorten the learning curve.

The most important limitation of this study is that it is a single-surgeon study. The learning curve may vary widely between surgeons, just as an individual surgeon is an independent predictor of outcomes even for highly experienced surgeons [27]. This limits the generalizability of the study to surgeons with different levels of training, experience, caseload, and case complexity. External factors may contribute to the learning curve too, such as the level of training and experience with robotic surgery of the surgical assistant, operating room nurses, anaesthetists, and technical staff.

Our study is subject to other limitations. First, a major limitation is that PSM is a weak surrogate for subsequent oncologic outcomes; biochemical recurrence, cancer progression, and survival end points are preferable but require longer follow-up. Second, although statistical adjustments can compensate for the nonrandomised nature of observational studies, some residual confounding is likely to remain due mostly to unidentified confounding factors. Thus some unidentified confounder may be the causal factor explaining the differences in outcomes rather than the RARP technique itself. This major limitation of an observational study such as ours may alter (to an unknown extent) our results and therefore precludes us from drawing definitive conclusions. Randomised trials are underway and may provide more definitive conclusions; however, published protocols suggest individual surgeon factors may confound results because participating surgeons will perform only ORP or RARP rather than both techniques. Finally, only 609 men had sufficient QoL data for analysis because some men met exclusion criteria, declined participation, or dropped out. Despite this, there were no baseline differences between the QoL and overall cohorts to suggest a selection bias, and the retention rate was high (Table 2).

5. Conclusions

In this single-surgeon analysis, RARP had a long learning curve with inferior outcomes initially but then progressively superior sexual, early urinary, and pT2 PSM outcomes, and equivalent pT3 PSM and late urinary outcomes. Although our study suggests that switching to RARP could be worthwhile for some high-volume surgeons, high-quality studies are needed that analyse the learning curves of surgeons with varying case volumes, experience, laparoscopic training, and robotic fellowship training.

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Study concept and design: Stricker, Thompson, Rasiah.

Acquisition of data: Böhm, Haynes, Thompson, Matthews.

Analysis and interpretation of data: Thompson, Egger, Stricker.

Drafting of the manuscript: Thompson, Egger.

Critical revision of the manuscript for important intellectual content: Böhm, Haynes, Rasiah, Stricker.

Statistical analysis: Thompson, Egger.

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Supervision: Stricker, Rasiah.

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Appendix A. Supplementary data

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References


