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Superior Biochemical Recurrence and Long-term Quality-of-life Outcomes Are Achievable with Robotic Radical Prostatectomy After a Long Learning Curve—Updated Analysis of a Prospective Single-surgeon Cohort of 2206 Consecutive Cases

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Abstract

Background: Our earlier analysis suggested that robot-assisted radical prostatectomy (RARP) achieved superiority over open radical prostatectomy (ORP) in terms of positive surgical margin (PSM) rates and functional outcomes.
Objective: With larger sample size and longer follow-up, the objective of this study update is to assess whether our previous findings are upheld and whether the improved PSM rates for RARP after an initial learning curve compared with ORP—as observed in our earlier analysis—ultimately resulted in improved biochemical control.
Design, setting, and participants: Prospective observational study comparing two surgical techniques; 2271 consecutive men underwent RARP (1520) or ORP (751) at a single centre from 2006 to 2016.
Outcome measurements and statistical analysis: Demographic and clinicopathological data were prospectively collected. The EPIC-QOL questionnaire was administered at baseline and 1.5, 3, 6, 12, and 24 mo. Multivariate linear regression modelled the difference in quality of life (QOL) domains against case number; logistic and Cox regression modelled the differences in PSM and biochemical recurrence (BCR) hazard ratios (HR), respectively.
Results and limitations: A total of 2206 men were included in BCR/PSM analysis and 1045 consented for QOL analysis. Superior pT2 surgical margins, early and late sexual outcomes, and early urinary outcomes were upheld and became more robust (narrowing of 95% confidence intervals [CIs]). The risk of BCR was initially higher for RARP, improved after 191 RARPs, and was 35% lower (hazard ratio [HR] 0.65, 95% CI 0.47–0.90) at final RARP, plateauing after 226 RARPs. Improved late (12–24 mo) urinary bother scores (adjusted mean difference [AMD] = 4.7, 95% CI 1.3–8.0) and irritative–obstructive scores (AMD = 3.8, 95% CI 0.9–5.6) at final RARP were demonstrated. Limitations include observational single surgeon data, possible residual confounding, and short follow-up.
Conclusions: The results from this updated analysis demonstrate that RARP can be beneficial for patients of high-volume surgeons, although more randomised studies and studies with survival outcomes are needed.
Patient summary: Robot-assisted radical prostatectomy was able to improve functional and oncological outcomes in this single surgeon's learning curve.

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1. Introduction

Radical prostatectomy (RP) is one treatment option for men with localised prostate cancer (PCa) and life expectancy exceeding 10–15 yr [1]. Open retropubic radical prostatectomy (ORP) is the traditional gold standard; however, robot-assisted radical prostatectomy (RARP) is increasingly performed in the USA, Europe, and Australia. The widespread uptake of RARP was initially justified by studies reporting reduced length of stay, a modest decrease in blood loss, superior quality of life (QOL), and equivalent positive surgical margin (PSM) outcomes with RARP compared with ORP; however, these conclusions were based on level 3 evidence from nonrandomised, retrospective studies [2–5].

Three randomised trials are underway [6–8], including the early reported outcomes by Yaxley et al [6], showing no difference between RARP and ORP in terms of complications, PSM, and early urinary and sexual function outcomes. Their results suggest that RARP increased costs with minimal benefit to patients. Public and private funding bodies typically require a cost, QOL, or oncological benefit to be demonstrated to justify the funding of robotic surgery procedures. In the UK, for example, the National Health Service (NHS) is currently considering withdrawing funding for robotic cystectomy based on the lack of benefit in recent randomised trials [9,10].

However, in the aforementioned trial by Yaxley et al [6] all ORPs were performed by a highly experienced, high-volume open surgeon, while all RARPs were performed by another surgeon earlier in his career. As a consequence, each surgeon's unique skills may have confounded the study outcomes. Other limitations include the short follow-up and small sample size. We previously [11] attempted to address these limitations by comparing ORP and RARP outcomes for a single surgeon (to eliminate individual surgeon skill as a confounder) across the RARP learning curve (to account for the effect of the learning curve) using data from a prospective cohort study. Our study demonstrated the important effect of the learning curve on superior sexual, early urinary, and pT2 PSM outcomes for RARP after a long learning period. However, we were unable to demonstrate superior late urinary outcomes or assess biochemical recurrence (BCR) outcomes due to follow-up limitations. With more patients and longer follow-up now being available, the objective of this study update was to determine if our findings were upheld and to assess whether the lower rates of PSM for RARP after an initial learning curve compared with ORP, as observed in our previous analysis, ultimately resulted in lower rates of BCR.

2. Patients and methods

2.1. Patients and study design

This was a prospective, nonrandomised, observational study comparing ORP and RARP. Patient data were included in the analyses of QOL and/or oncological outcomes if the patient consented to participate and had undergone prostatectomy for PCa from the study surgeon (P.S.) between 3 March 2006 and 26 February 2016 (the latter date being the cut-off for these analyses). Patients with incomplete or insufficient data were excluded from the relevant analyses (Supplementary Fig. 1). Between 2006 and 2016, P.S. (who performed ~3000 prior ORPs) performed his first 1520 RARPs and an additional 751 ORPs. The ORP and RARP surgical techniques used were described previously [11]. Of 2271 eligible men, 2206 (97%) with complete data were included in the PSM and BCR analyses (Supplementary Fig. 1). All were invited to participate in a prospective QOL cohort study: 1090 men were enrolled and 1045 had sufficient data for analysis (baseline plus ≥ postoperative questionnaire completed). The institutional ethics committee approved the study (HREC approval SVH 13/018 & SVH 12/231).

2.2. Outcome measures

2.2.1. QOL, BCR, and PSM outcome measures

A full description of the QOL and PSM outcome measures used has been published previously [11]. Participants received a self-administered EPIC-QOL [12] questionnaire at baseline and then at 1.5, 3, 6, 12, and 24 mo following treatment. To avoid the potential influence that medical staff or the use of interviewers might have on QOL measurements, QOL outcomes were patient reported with questionnaires administered by mail, by clinical data managers who have no role in patient care and minimal personal contact with patients. PSM was defined as a tumour extending the inked margin of the cut surface. BCR was defined as postoperative prostate-specific antigen (PSA) ≥0.1 ng/l on follow-up (at least 4 wk after surgery).

2.3. Statistical analyses

A full description of the statistical methods used has been published previously [11]. Multivariate linear regression analyses with generalised estimating equations were used to estimate adjusted mean differences in QOL scores between RARP and ORP (y-axis) and plotted according to surgeon experience (ie, number of previous cases performed, x-axis), for each health-related quality of life domain [13]. The relationship between PSM risk or BCR risk and surgeon's experience was modelled using logistic and Cox regression, respectively.

RARP learning curves were modelled as natural log functions. ORP learning curves were modelled as constant because outcomes were found not to be associated with the surgeon's ORP case number (Supplementary Table 1). We adjusted effect estimates for a number of established, measurable confounders (Figs. 1 and 2, and Supplementary Fig. 2–9). Potential confounders included in the QOL models were also included in the PSM/BCR models, with the exception of time since surgery and adjuvant therapy. Modifications of the learning curves by pathological stage (pT2 vs pT3/pT4) and time after surgery (1.5–6 and 12–24 mo after surgery) were assessed and modelled using interaction terms. In keeping with our previous analysis, an increase of 1 point in QOL score or 10% decrease in the PSM odds ratio (OR) or BCR hazard ratio (HR) per 150 additional cases defined the plateau in the learning curve.

In sensitivity analyses, data were reanalysed after excluding patients who received preoperative hormonal treatment (all outcomes) and those who received adjuvant therapy (for QOL and BCR outcomes, since PSMs cannot be causally affected by adjuvant therapy).

3. Results

Baseline demographics and clinical characteristics were similar between the 2206 men in the PSM/BCR analysis and the subset of 1045 men included in the QOL analysis (Table 1). There were significant differences between the RARP and ORP groups (ORP patients had higher proportions

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