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Platinum Priority – Prostate Cancer

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Biochemical Recurrence After Robot-assisted Radical Prostatectomy in a European Single-centre Cohort with a Minimum Follow-up Time of 5 Years

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Abstract

Background: Robot-assisted radical prostatectomy (RARP) is an increasingly commonly used surgical treatment option for prostate cancer (PCa); however, its longer-term oncologic results remain uncertain.
Objective: To report biochemical recurrence–free survival (BRFS) outcomes for men who underwent RARP ≥5 yr ago at a single European centre.
Design, setting, and participants: A total of 944 patients underwent RARP as monotherapy for PCa from January 2002 to December 2006 at Karolinska University Hospital, Stockholm, Sweden. Standard clinicopathologic variables were recorded and entered into a secure, ethics-approved database made up of those men with registered domiciles in Stockholm. The median follow-up time was 6.3 yr (interquartile range: 5.6–7.2).
Outcome measurements and statistical analysis: The outcome of this study was biochemical recurrence (BCR), defined as a confirmed prostate-specific antigen (PSA) of ≥0.2 ng/ml. Kaplan-Meier survival plots with log-rank tests, as well as Cox univariable and multivariable regression analyses, were used to determine BRFS estimates and determine predictors of PSA relapse, respectively.
Results and limitations: The BRFS for the entire cohort at median follow-up was 84.8% (95% confidence interval [CI], 82.2–87.1); estimates at 5, 7, and 9 yr were 87.1% (95% CI, 84.8–89.2), 84.5% (95% CI, 81.8–86.8), and 82.6% (95% CI, 79.0–85.6), respectively. Nine and 19 patients died of PCa and other causes, respectively, giving end–of–follow-up Kaplan-Meier survival estimates of 98.0% (95% CI, 95.5–99.1) and 94.1% (95% CI, 90.4–96.4), respectively. Preoperative PSA >10, postoperative Gleason sum ≥4 + 3, pathologic T3 disease, positive surgical margin status, and lower surgeon volume were associated with increased risk of BCR on multivariable analysis. This study is limited by a lack of nodal status and tumour volume, which may have confounded our findings.
Conclusions: This case series from a single, high-volume, European centre demonstrates that RARP has satisfactory medium-term BRFS. Further follow-up is necessary to determine how this finding will translate into cancer-specific and overall survival outcomes.

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1. Introduction

Prostate cancer (PCa) is the most common nondermatologic cancer in Western men [1]. More than 90% of cases are organ-confined at diagnosis and are thus amenable to treatment by radical prostatectomy (RP), which has been shown to be superior to watchful waiting at 15-yr follow-up [2]. With the introduction of the robotic platform, the new millennium has seen an exponential rise in robot-assisted RP (RARP), which now accounts for many RPs done in developed countries [3]. However, there remains a lack of long-term oncologic data regarding this procedure, with one small RARP series of 184 patients that reports on biochemical recurrence (BCR) outcomes with a minimum follow-up of 5 yr [4]. The largest series in the literature reports prostate-specific antigen (PSA) relapse outcomes for 1384 patients with a median follow-up of 5.2 yr; it is from an American centre [5]. In this paper, we report BCR data on 904 patients treated at a single European centre who underwent RARP monotherapy from 2002 to 2006 and had a median follow-up of 6.3 yr.

2. Patients and methods

A total of 944 men with clinically localised or locally advanced (cT1–cT3) PCa underwent RARP by nine surgeons at Karolinska University Hospital, Stockholm, Sweden, from January 2002 to December 2006. Postoperative PSAs were taken at 6 wk, 6 mo, 12 mo, 18 mo, and 24 mo, and annually thereafter. The date of last follow-up updating for all patients was December 31, 2011. Forty of 944 of the men (4.2%) received adjuvant therapy (radiotherapy and/or hormones) and fulfilled the sole exclusion criterion; no patient received neoadjuvant therapy. Standard preoperative and postoperative clinicopathologic data on all subjects were prospectively entered into a secure, ethics-approved database. Information regarding pelvic lymphadenectomy was not available, as it was not routinely recorded when this study started in 2002, and thus we cannot be certain that our current indications for performing lymphadenectomy in intermediate- and high-risk disease were adhered to in all cases included in this study. RP specimens were subjected to whole-mount processing, sectioned according to the Stanford procedure, and evaluated by seven uropathologists. Postoperative PSA data for patients not presenting to our clinic but rather to other physicians' clinics were obtained from the records of laboratories in Stockholm, ensuring virtually complete data collection. BCR was defined as a confirmed PSA $\geq$0.2 ng/ml.

Clinicopathologic characteristics of a continuous nature were tested for normality using the Shapiro-Wilks test, and characteristics not normally distributed were reported as median and interquartile range (IQR). The study outcome was BCR, defined as a confirmed PSA $\geq$0.2 ng/ml. Kaplan-Meier survival analysis was used to visualise BCR-free survival (BRFS) outcomes, which were stratified by preoperative PSA, clinical risk group (low risk: preoperative PSA $\leq$10 and preoperative Gleason sum $\leq$6; intermediate risk: preoperative PSA 10–19.9 or preoperative Gleason sum 7; high risk: preoperative PSA $\geq$20 or preoperative Gleason sum $\geq$8 or cT3), postoperative Gleason sum, pathologic stage, surgical margin status, surgical margin status by pathologic stage, and surgeon volume (defined as the total number of RARP cases performed by an individual surgeon). Event-time distributions for the time to failure were compared using log-rank tests. Univariable and backward elimination (inclusion criterion: $p < 0.05$) multivariable Cox proportional hazard regression models incorporating age, prostate volume, surgeon volume, clinical stage, preoperative PSA, preoperative Gleason sum, pathologic stage, postoperative Gleason sum, and surgical margin status were used to determine variables predictive of BCR, and hazard ratios (HRs) were computed for these risk factors. Patients with non-PCa deaths prior to BCR were censored at the time of death. All analyses were performed using SAS v.9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

Demographic and clinicopathologic summary statistics for the study cohort are reported in Table 1 and 2. The median age was 62.2 yr (IQR: 58.2–65.8), and the median preoperative PSA was 6.4 ng/ml (IQR: 4.8–9.0). The median prostate volume was 38.0 ml (IQR: 30.0–49.0), and the median surgeon volume was 131.8 (IQR: 51.3–245.5). A total of 60.2% of the study cohort was deemed low risk, 33.4% were intermediate risk, and 6.4% were high risk. The positive surgical margin rate was 21.6%; the overall BRFS was 84.8% (95% confidence interval [CI], 82.1–87.1) at a median follow-up time of 6.3 yr (IQR: 5.6–7.2) (Fig. 1A). The BRFS for all patients at 5, 7, and 9 yr was 87.1% (95% CI, 84.8–89.2), 84.5% (95% CI, 81.8–86.8), and 82.6% (95% CI, 79.0–85.6), respectively. The median time to BCR was 2.3 yr (IQR: 1.0–3.7). Nine and 19 patients died of PCa and other causes, respectively, with 16 of 19

Table 1 – Clinical characteristics

Clinical characteristics	Median	IQR
Patient age, yr	62.2	58.2–65.8
BMI, kg/m^2	25.6	24.0–27.3
Preoperative PSA, ng/ml	6.4	4.8–9.0
Prostate volume, ml	38.0	30.0–49.0
Surgeon volume	131.8	51.3–245.5
	n	%
Clinical T stage (missing *n* = 7)		
cT1	551	61.4
cT2	318	35.5
cT3	28	3.1
Preoperative PSA (missing *n* = 1)		
$\leq$10	736	81.5
>10	167	18.5
Clinical risk category (missing *n* = 3)		
Low	542	60.2
Intermediate	301	33.4
High	58	6.4
Surgeon volume (missing *n* = 2)		
1–50	222	24.6
51–100	142	15.7
101–150	132	14.6
>150	406	45.0
Surgeries, no.		
2002	20	2.2
2003	70	7.7
2004	184	20.4
2005	266	29.4
2006	364	40.3
Nerve-sparing status (missing *n* = 16)		
Bilateral	340	38.3
Unilateral	310	34.9
None	238	26.8

IQR = interquartile range; BMI = body mass index; PSA = prostate-specific antigen.