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Salvage Versus Primary Robot-assisted Radical Prostatectomy: A Propensity-matched Comparative Effectiveness Study from a High-volume Tertiary Centre

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Article info

Abstract

Background: Salvage robot-assisted radical prostatectomy (sRARP) is a potential treatment option for locally recurrent prostate cancer (PCa) after nonsurgical primary treatment. There are minimal data comparing outcomes between propensity-matched sRARP and primary robot-assisted radical prostatectomy (RARP).

Objective: The primary objective is to compare perioperative, oncological, and functional outcomes of sRARP with primary RARP, and the secondary is to compare outcomes between sRARP after whole and focal gland therapy.

Design, setting, and participants: A 1:1 propensity-matched comparison was carried out of 135 sRARP cases with primary RARP cases from a cohort of 3852 consecutive patients from a high-volume tertiary centre.

Outcome measurements and statistical analysis: Perioperative, oncological, and functional outcomes including complication rates, positive surgical margins, biochemical recurrence (BCR), continence, and erectile dysfunction (ED) were retrospectively collected.

Results and limitations: There were no significant differences in patient characteristics between sRARP and primary RARP groups. In the salvage and primary groups, median (interquartile range) follow-up periods were 521 (304–951) and 638 (394–951) d, grade III–V Clavien-Dindo complication rates were 1.5% and 0% (p = 0.310), BCR rates were 31.9% and 14.1% ($p < 0.001$) at the last follow-up, pad-free continence rates were 78.8% and 84.3% at 2 yr ($p = 0.337$), and ED rates were 94.8% and 76.3% ($p < 0.001$), respectively. Comparing the whole and focal gland groups, BCR rates

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were 36.7% and 29.1% ($p = 0.687$) at follow-up, pad-free continence rates were 53.1% and 89.3% at 2 yr ($p < 0.001$), and ED rates were 98% and 93% ($p = 0.214$), respectively.

Conclusions: Salvage RARP has similar perioperative outcomes to primary RARP with inferior potency rates. Post–focal therapy sRARP has similar recurrence and continence rates to primary RARP. Post–whole gland therapy, complication, and recurrence rates are higher, and there is a higher risk of urinary incontinence.

Patient summary: We report the largest propensity-matched comparison of salvage robot-assisted radical prostatectomy (RARP) after focal and whole gland therapy. Salvage RARP is a feasible procedure for the treatment of locally recurrent prostate cancer in high-volume centres; however, patients should be counselled appropriately as to the different outcomes.

1. Introduction

Nonsurgical primary treatment for prostate cancer (PCa) includes whole gland therapy such as radiotherapy or brachytherapy, and focal gland therapy such as high-intensity focused ultrasound (HIFU), cryotherapy, or electroporation. Biochemical recurrence (BCR) and clinical recurrence rates for nonsurgical primary therapy can range from 20% to 70%, and represent a significant risk of metastatic progression and cancer-specific mortality [1,2]. Salvage radical prostatectomy (sRP) is a potential treatment option for patients who have locally recurrent PCa.

Historically, sRP has shown inferior oncological and functional outcomes to primary radical prostatectomy with higher postoperative complication rates. The poor outcomes associated with sRP may be due to the technical hazards of surgery such as adhesions, fibrosis, poor tissue quality, and distortion of surgical planes that result from the primary treatment modality [3].

Outcomes for sRP have improved with the use of minimally invasive robot-assisted techniques. Salvage robot-assisted radical prostatectomy (sRARP) techniques have been developed to make the procedure more feasible with improved outcomes. Robotic procedures have the benefit of better vision and dexterity [4].

There is limited literature on sRARP as it is an uncommon and technically challenging procedure. Most studies are descriptive and therefore unable to assess whether outcomes of sRARP are comparable with those of RARP when adjusted for covariates such as age, body mass index (BMI), comorbidities, preoperative prostate-specific antigen (PSA), Gleason score, and clinical T stage. Despite a lack of level 1 evidence and the American and European urology associations describing focal therapy as experimental or investigational, the use of focal therapy for the treatment of local PCa is growing in popularity due to its perceived favourable side-effect profile compared with RARP [5–7]. However, the outcomes of salvage surgery after focal therapy have not been well compared with primary RARP. Clearly, it is not possible to randomise between primary RARP and sRARP, as these are different disease states, and therefore, the next best level of evidence can be obtained

only by comparing risk-matched cohorts of sRARP with those of primary RARP.

Herein, we compared the perioperative, oncological, and functional outcomes of patients undergoing sRARP with those of propensity-matched patients undergoing primary RARP. Furthermore, we compared sRARP outcomes in patients who had previous primary whole gland therapy with those of patients having focal gland therapy.

2. Patients and methods

2.1. Study population

A total of 3852 consecutive patients underwent primary RARP or sRARP in a single, high-volume tertiary centre between January 2012 and March 2020, and had a minimum follow-up of 6 mo. Of these patients, 135 underwent sRARP after whole gland therapies such as radiotherapy, brachytherapy, and whole gland HIFU, and focal gland therapies such as focal HIFU, cryotherapy, and electroporation.

Primary treatment failure was defined as nadir plus 2 ng/ml following radiotherapy and three serial rises in PSA following minimally invasive treatments [6]. All patients had biopsy-proven local disease as well as staging investigations including multiparametric magnetic resonance imaging, bone scan, computed tomography, and prostate-specific membrane antigen positron emission tomography scans. Patients who had primary radiotherapy routinely received pelvic lymph node radiation, and therefore no pelvic lymph node dissection (PLND) was undertaken in this cohort in an attempt to prevent vascular and lymphatic complications [8]. In all other patients, PLND was decided based on the Briganti nomogram and European Association of Urology (EAU) guidelines, and in conjunction with informed patient choice [6].

2.2. Data collection

Data were collected retrospectively using local cancer registry databases, electronic medical records, general practitioner records, and patient questionnaires. Preoperative data including age, BMI, American Society of Anaesthesiologists (ASA) score, non–age-adjusted Charlson comorbidity index (CCI), PSA, T stage, Gleason score, EAU risk classification, and primary therapy were collected [9]. PSA, T stage, and Gleason score were collected after the primary treatment and before the surgical intervention. Perioperative data including operative time, estimated blood loss (EBL), blood transfusion, nerve sparing, PLND, length of stay (LOS), and 30-d Clavien-Dindo complications were also collected, as were postoperative oncological data including positive surgical margins

(PSMs), T stage, Gleason score, BCR, clinical recurrence, and the use of further androgen deprivation therapy (ADT), radiotherapy, and chemotherapy. PSMs <3 or >3 mm were reported as negative and positive [10]. BCR was defined as PSA >0.2 ng/ml [6]. Functional data including full continence, defined as zero pads per day, and social continence, defined as one pad per day, were collected at 3-, 6-, 12-, and 24-mo intervals. Data on ED, defined as inability to have sexual function on at least 50% of attempts without the use of invasive aids, and survival at the last follow-up were also collected.

2.3. Statistical analysis

Data analysis was performed in IBM SPSS Statistics Data Editor version 23 (IBM Corporation, Armonk, NY, USA). To control for potential confounders, propensity scoring was used to achieve 135 1:1 matched samples from 135 sRARP cases [11]. Cases were matched by estimated propensity score to their nearest neighbour within a caliper distance of 0.02. Propensity scores were calculated using a logistic regression model considering the following baseline covariables known to influence outcomes: age, BMI, CCI, PSA, and T stage. Gleason score was avoided due to the unreliability in the tissue after prior treatment. All significance tests performed were two tailed. The independent t test, Mann-Whitney U test, and chi square test were used to evaluate differences between the primary and salvage groups. Kaplan-Meier survival analysis and log-rank tests were used to determine time to recurrence.

3. Results

3.1. Primary versus salvage

3.1.1. Characteristics
Full clinical and pathological characteristics are shown in Table 1. There were no statistical differences between age, BMI, ASA score, CCI, preoperative PSA, T stage, and Gleason score between the primary and salvage groups. Of the patients, 0%, 24.4%, 75.6% in the salvage group and 0%, 19.3%, and 80.7% in the primary group were classified as having low, intermediate, and high risk, respectively, according to EAU risk stratification ($p = 0.307$; Table 1). Two patients received whole gland radiotherapy followed by focal gland HIFU prior to sRARP. Eight patients had two focal treatments before undergoing sRARP: four had two HIFU treatments, two had HIFU followed by cryotherapy, and two had electroporation followed by HIFU.

3.1.2. Perioperative
The median operation time was 165 min in the salvage group and 140 min in the primary group ($p = 0.004$). Unilateral and bilateral nerve sparing were feasible, respectively, in 23% and 3.7% in the salvage group compared with 28.1% and 20.7% in the primary group ($p < 0.001$) due to technical feasibility and tumour location. There were fewer PLND procedures in the salvage group as zero patients undergoing primary radiotherapy received PLND due to safety concerns. There were no statistical differences in EBL, blood transfusion, or LOS between the primary and salvage groups. There was no statistically significant difference in the 30-d Clavien-Dindo III–V complication rates between salvage (1.5%) and primary (0%) surgery. Two patients in the salvage group suffered from grade ≥III Clavien-Dindo complications requiring surgical intervention (Table 2).

One patient suffered from rectal injury with intraoperative primary repair following whole gland radiotherapy, and one patient suffered from a haematoma requiring reoperation and washout after HIFU therapy.

3.1.3. Oncological
The median follow-up in the salvage group was 521 d compared with 638 d in the primary group ($p = 0.245$). PSMs <3 and >3 mm were 22.2% and 15.6%, respectively, in the salvage group compared with 14.8% and 8.9%, respectively, in the primary group ($p = 0.022$). Overall recurrence rates were 31.9% (biochemical 22.2%, lesion 9.6%) in the salvage group and 14.1% (biochemical 9.6%, lesion 4.4%) in the primary group ($p < 0.001$) at median follow-up. Recurrence-free survival rates are shown in Figure 1, with worse rates for the salvage cohort ($p < 0.01$). All patients with BCR or lesion recurrence had further ADT; 9.6% of the salvage patients who recurred had further salvage radiotherapy and 1.5% had chemotherapy (Table 3). PLND was undertaken in 18.5% of the patients in the salvage group and 43% in the primary group ($p < 0.001$). Overall survival was 95.6% in the salvage group compared with 99.3% in the primary group ($p = 0.125$).

3.1.4. Functional
Full continence was achieved at 3, 6, 12, and 24 mo, respectively, in 25.9%, 53.3%, 67.2%, and 78.8% in the salvage group, compared with 25.9%, 43.7%, 71.6%, and 84.3% in the primary group. There were no statistically significant differences between the groups. ED at the last follow-up was 94.8% in the salvage group compared with 76.3% in the primary group ($p < 0.001$; Table 4).

3.2. Whole versus focal gland

3.2.1. Characteristics
There were no statistically significant differences in age, BMI, ASA score, or CCI between the whole and focal gland salvage groups. There were more high-risk patients in the whole gland salvage group (83.7%) than in the focal gland salvage group (70.9%, $p = 0.099$; Table 1). Full data comparing whole and focal gland treatment subtypes are available in the Supplementary Tables 1 and 2.

3.2.2. Perioperative
Between whole and focal gland therapy, there were no statistically significant differences in operative time EBL, transfusion, or length of stay. Unilateral and bilateral nerve sparing were feasible, respectively, in 8.2% and 2% of the whole gland group compared with 31.4% and 4.7% of the focal group due to technical feasibility and tumour location ($p = 0.001$). Complication rates were significantly greater in the whole gland group (22%) than in the focal group (8%, $p = 0.025$; Table 2).

3.2.3. Oncological
The median follow-up time in the whole gland group was 490 d compared with 542 d in the focal group ($p = 0.669$). PSMs <3 and >3 mm were, respectively, 16.3% and 18.4% in

Table 1 – Patient characteristics

	Salvage subtypes						Salvage total	Primary total	p value
	Whole gland	Matched primary	p value	Focal gland	Matched primary	p value	Whole/focal p value			
Patients, n	49	49	–	86	86	–	–	135	135	–
Age (yr), median (IQR)	70 (63, 73)	68 (65, 74)	0.765	70 (64, 72)	69.5 (67, 73)	0.118	0.509	70 (64, 73)	69 (66, 73)	0.158
BMI, median (IQR)	27.7 (26, 30)	28 (27, 30)	0.285	27.8 (26, 30)	28 (26, 29)	0.751	0.798	27.7 (25.9, 30.6)	28 (26, 29)	0.736
ASA, n (%)										
1	1 (2.0)	0	0.257	3 (3.5)	4 (4.7)	0.134	0.568	4 (3.0)	4 (3.0)	0.061
2	43 (87.8)	48 (98.0)		76 (88.4)	80 (93.0)			119 (88.1)	128 (94.8)	
3	5 (10.2)	1 (2.0)		7 (8.1)	2 (2.3)			12 (8.9)	3 (2.2)	
CCI ≥1, n (%)	8 (16.3)	10 (20.4)	0.804	17 (19.8)	17 (19.8)	>0.999	>0.999	25 (18.5)	27 (20.0)	>0.999
PSA preop, median (IQR)	5.50 (3.65, 11.00)	6.00 (4.40, 7.85)	0.754	5.90 (3.58, 10.35)	6.00 (5.00, 8.38)	0.636	0.742	5.8 (3.6, 10.7)	6 (4.9, 8.1)	0.813
T stage preop, n (%)										
T1	1 (2.0)	3 (6.1)	0.746	2 (2.3)	2 (2.3)	0.346	0.089	3 (2.2)	5 (3.7)	0.614
T2	21 (42.9)	19 (38.8)		50 (58.1)	43 (50.0)			71 (52.6)	62 (45.9)	
T3	27 (55.1)	27 (55.1)		34 (39.5)	41 (47.7)			61 (45.2)	68 (50.4)	
Gleason preop, n (%)										
3 + 3	2 (4.1)	0	0.083	4 (4.7)	0	0.063	0.002	6 (4.4)	0 (0)	0.613
3 + 4	12 (24.5)	20 (40.8)		42 (48.8)	37 (43.0)			54 (40.0)	57 (42.2)	
3 + 5	0	1 (2.0)		1 (1.2)	0			1 (0.7)	1 (0.7)	
4 + 3	16 (32.7)	18 (36.7)		23 (26.7)	24 (27.9)			39 (28.9)	42 (31.1)	
4 + 4	8 (16.3)	4 (8.2)		8 (9.3)	15 (17.4)			16 (11.9)	19 (14.1)	
4 + 5	9 (18.4)	5 (10.2)		8 (9.3)	8 (9.3)			17 (12.6)	13 (9.6)	
5 + 4	2 (4.1)	1 (2.0)		0	2 (2.3)			2 (1.5)	3 (2.2)	
EAU risk, n (%)									)	
Low	0	0	>0.999	0	0	0.223	0.099	0	0	0.307
Intermediate	8 (16.3)	8 (16.3)		25 (29.1)	18 (20.9)			33 (24.4)	26 (19.3)	
High	41 (83.7)	41 (83.7)		61 (70.9)	68 (79.1)			102 (75.6)	109 (80.7)	

ASA = American Society of Anaesthesiologists score; BMI = body mass index; CCI = Charlson comorbidity index (non–age adjusted); EAU = European Association of Urology; IQR = interquartile range; n = numbers; PSA = prostate-specific antigen.

Table 2 – Perioperative outcomes

				Salvage subtypes						
	Whole gland	Matched primary	p value	Focal gland	Matched primary	p value	Whole/focal p value	Salvage total	Primary total	p value
Op time (min), median (IQR)	160 (125, 180)	130 (120, 180)	0.075	165 (135, 180)	150.5 (120, 180)	0.026	0.715	165 (135, 180)	140 (120, 180)	0.004
Nerve sparing, n (%)										
No	44 (89.8)	30 (61.2)	0.003	55 (64.0)	39 (45.3)	<0.001	0.001	99 (73.3)	69 (51.1)	<0.001
Unilateral	4 (8.2)	14 (28.6)		27 (31.4)	24 (27.9)			31 (23.0)	38 (28.1)	
Bilateral	1 (2.0)	5 (10.2)		4 (4.7)	23 (26.7)			5 (3.7)	28 (20.7)	
Pelvic lymph node dissection, n (%)										
No	43 (87.8)	25 (51.0)	<0.001	67 (77.9)	52 (60.5)	0.002	0.153	110 (81.5)	77 (57.0)	<0.001
Extended	6 (12.2)	20 (40.8)		18 (20.9)	22 (25.6)			24 (17.8)	42 (31.1)	
Obturator fossa	0	4 (8.2)		1 (1.2)	12 (14.0)			1 (0.7)	16 (11.9)	
EBL (ml), median (IQR)	150 (100, 200)	150 (65, 300)	0.634	200 (100, 300)	150 (100, 300)	0.334	0.080	200 (100, 300)	150 (98, 300)	0.505
Transfusion, n (%)	0	0	–	0	0	–	–	0	0	–
LOS, median (IQR)	1 (1, 2)	1 (1, 2)	0.074	1 (1, 2)	1 (1, 2)	0.171	0.462	1 (1, 2)	1 (1, 2)	0.100
Clavien-Dindo complication, n (%)										
Grade 0	38 (77.6)	47 (95.9)	0.006	79 (91.9)	82 (95.3)	0.146	0.025	117 (86.7)	129 (95.6)	0.006
Grade 1	7 (14.3)	1 (2.0)		2 (2.3)	3 (3.5)			9 (6.7)	4 (3.0)	
Grade 2	3 (6.1)	1 (2.0)		4 (4.7)	1 (1.2)			7 (5.2)	2 (1.5)	
Grade 3–5	1 (2.0)	0		1 (1.2)	0			2 (1.5)	0	0.310

EBL = estimated blood loss; IQR = interquartile range; LOS = length of stay.

the whole group, compared with 25.6% and 14% in the focal group ($p = 0.787$). Recurrence occurred in 36.7% (biochemical 22.4% and lesion 14.3%) of whole gland cases and 29.1% (biochemical 22.1% and lesion 7%) of focal cases ($p = 0.687$) at median follow-up. Recurrence-free survival rates for whole and focal gland therapy are shown in Figure 2. Overall survival was 89.8% in the whole gland group compared with 98.8% in the focal group at the last follow-up ($p = 0.014$; Table 3).

3.2.4. Functional

In the whole gland group, full continence was achieved at 3, 6, 12, and 24 mo in 14.3%, 32.7%, 48.9%, and 53.1%, respectively, compared with 32.6%, 65.1%, 77.8%, and 89.3% in the focal group. Full continence rates were statistically significantly greater in the focal group than in the whole gland group ($p = 0.02, 0.001, 0.001,$ and 0.001, respectively) at 3, 6, 12, and 24 mo. ED at the last follow-up was 98% in the whole gland group compared with 93.0% in the focal gland group ($p = 0.214$; Table 4).

4. Discussion

To our knowledge, this is the largest study globally comparing propensity-matched cohorts of sRARP with those of primary RARP. We discuss our findings in comparison with the findings of other descriptive studies and previous small-scale matched studies. We have further evaluated the outcomes of salvage surgery following primary whole gland treatments compared with focal treatments.

4.1. Feasibility

Our grade III–V Clavien-Dindo complication rate of 1.5% in the sRARP cohort is lower than that reported in previous literature (6–33%) [12]. Our complication rates were statistically greater after whole gland therapy (22%) than after focal therapy (8%, $p = 0.025$). Furthermore, when comparing salvage surgery after whole gland therapy with the matched primary cohort, the complication rate was significantly higher (22% vs 4%, $p = 0.006$); however, this was not the case for salvage surgery after focal gland therapy (8% vs 5%, $p = 0.146$). Previous literature has shown that the complication rates can be up to 33% after whole gland and 9% after focal therapy [13,14]. Complication rates after sRARP are not statistically greater than primary RARP; however, they are clinically relevant. The retrospective nature of data collection may underestimate the complication rate in both groups. Our superior perioperative outcomes in comparison with literature may be due to the use of robot-assisted surgery and our experienced surgeons operating in a high-volume centre.

4.2. Oncological outcomes

PSM rates in the salvage group were significantly higher than those in the primary group. However, there was no difference between the whole and focal gland groups. Our
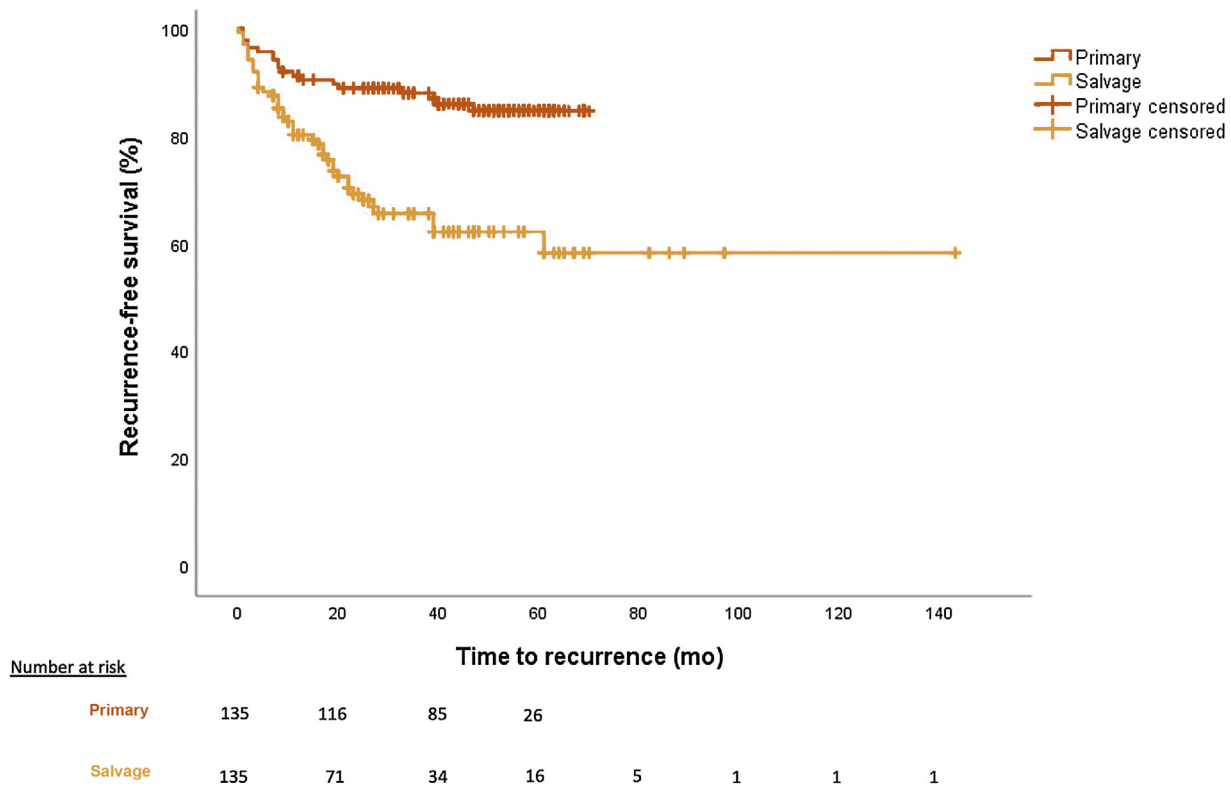
Fig. 1 – Recurrence-free survival for primary RARP versus sRARP ($p < 0.001$).
RARP = robot-assisted radical prostatectomy; sRARP = salvage RARP.

recurrence rates were significantly greater in the salvage group (31.9%) than in the primary group (14.1%) at 22 mo of follow-up ($p < 0.001$). Furthermore, recurrence-free surviv- al was inferior in the salvage group than in the primary group ($p < 0.001$). Furthermore, when comparing salvage surgery after whole gland therapy with the matched primary cohort, the recurrence rate was significantly higher (36.7% vs 12.2%, $p = 0.004$); however, this was not the case for salvage surgery after focal gland therapy (29.1% vs 15.1%, $p = 0.059$). All patients who suffered from recurrence had further ADT, and 9.6% had further radiotherapy. Bates et al [15] propensity matched 53 sRARP patients to primary RARP and found a BCR rate of 33% in the salvage group compared with 15% in the primary group at 26 mo ($p = 0.029$). However, our sRARP cohort included 77% EAU high-risk and 23% intermediate-risk patients, compared with 26% high-risk and 28% intermediate-risk patients in Bates et al's [15] study. Our recurrence rates are similar to those in other studies with medium-term follow-up. Kaffenberger et al [16] report 18% BCR at 16 mo and Nunes-Silva et al [14] report 46% at 24 mo. In the largest systematic review of sRP, Chade et al [12] reported 5- and 10-yr BCR-free survival of 47–82% and 28–53%, respectively.

On comparison of patients who had recurrence with recurrence-free patients, we found preoperative PSA (7.2 vs 5.5 ng/ml) and T stage (T2 29%, T3 71% vs T2 47%, T3 53%) to be higher. EAU guidelines suggest that referral for salvage therapy should be made when the PSA value is below 10 [6]. We would recommend that patients be referred for

salvage treatment at an earlier stage immediately following biochemical failure. Further studies are required to identify the ideal PSA and T-stage threshold to deliver better sRARP oncological outcomes.

4.3.   Functional outcomes

Owing to tumour location, loss of tissue planes, tissue adherence, as well as pre-existing ED, nerve sparing was feasible only in 27% of the salvage cohort compared with 49% in the primary cohort ($p < 0.001$). We found that continence improves with time in the salvage cohort, and patients should be counselled carefully about this. At 3, 6, 12, and 24 mo, full continence was achieved in 26%, 53%, 67%, and 79%, respectively. Continence rates are also superior for salvage surgery after focal therapy to those for salvage surgery after whole gland therapy. With better surgical reconstruction techniques and Retzius-sparing technique, continence rates have improved over time for RARP [17–19]. In 2004, Stephenson et al [20] reported a 5-yr sRARP continence rate of 39% after radiotherapy. However, more recent work in 2010 showed continence rates of 71% for sRARP [21].

Salvage RARP after focal therapy had better continence outcomes than whole gland therapy with medium-term continence rates varying from 73% to 91% [14,22]. In our study, full continence rates were greater at all time intervals after focal therapy than after whole gland therapy. At 24 mo, full continence was 89% after focal

Table 3 – Oncological outcomes

	Salvage subtypes							Salvage total	Primary total	p value
	Whole gland	Matched primary	p value	Focal gland	Matched primary	p value	Whole/focal p value			
Follow-up (d0, median (IQR)	490 (261, 1053)	530 (328, 841)	0.702	541.5 (312, 890)	649 (401, 1109)	0.096	0.669	521 (304, 951)	638 (394, 951)	0.245
Surgical margins, n (%)										
Negative	32 (65.3)	39 (79.6)	0.087	52 (60.5)	64 (74.4)	0.117	0.787	84 (62.2)	103 (76.3)	0.022
Positive <3 mm	8 (16.3)	7 (14.3)		22 (25.6)	13 (15.1)			30 (22.2)	20 (14.8)	
Positive >3 mm	9 (18.4)	3 (6.1)		12 (14.0)	9 (10.5)			21 (15.6)	12 (8.9)	
T stage postop, n (%)										
T1	0	0	0.317	0	0	0.467	0.069	0	0	0.339
T2	16 (32.7)	21 (42.9)		42 (48.8)	45 (52.3)			58 (43.0)	66 (48.9)	
T3	33 (67.3)	28 (57.1)		44 (51.2)	41 (47.7)			77 (57.0)	69 (51.1)	
Upstaging, n (%)	20 (40.8)	17 (34.7)	0.678	40 (46.5)	31 (36.0)	0.253	0.522	60 (44.4)	48 (35.6)	0.195
Gleason postop, n (%)										
3 + 3	0	1 (2.0)	0.467	1 (1.2)	3 (3.5)	0.427	0.016	1 (0.7)	4 (3.0)	0.288
3 + 4	17 (34.7)	17 (34.7)		46 (53.5)	44 (51.2)			63 (46.7)	61 (45.2)	
3 + 5	0	0		0	0			0	0	
4 + 3	19 (38.8)	14 (28.6)		26 (30.2)	18 (20.9)			45 (33.3)	32 (23.7)	
4 + 4	3 (6.1)	1 (2.0)		5 (5.8)	7 (8.1)			8 (5.9)	8 (5.9)	
4 + 5	10 (20.4)	13 (26.5)		8 (9.3)	12 (14.0)			18 (13.3)	25 (18.5)	
5 + 4	0	3 (6.1)		0	2 (2.3)			0	5 (3.7)	
Upgrading, n (%)	15 (30.6)	13 (26.5)	0.839	14 (16.3)	13 (15.1)	>0.999	0.051	29 (21.5)	26 (19.3)	0.779
Total recurrence, n (%)	18 (36.7)	6 (12.2)	0.004	25 (29.1)	13 (15.1)	0.059	0.687	43 (31.9)	19 (14.1)	0.001
Biochemical only	11 (22.4)	4 (8.2)		19 (22.1)	9 (10.5)			30 (22.2)	13 (9.6)	
Lesion	7 (14.3)	2 (4.1)		6 (7.0)	4 (4.7)			13 (9.6)	6 (4.4)	
Further ADT, n (%)	18 (36.7)	7 (14.3)	0.013	26 (30.2)	14 (16.3)	0.059	0.438	44 (32.6)	21 (15.6)	0.002
Further radiotherapy, n (%)	2 (4.1)	0	0.500	11 (12.8)	0	0.001	0.099	13 (9.6)	0	<0.001
Further chemotherapy, n (%)	1 (1.7)	0	>0.999	1 (1.2)	0	>0.999	0.685	2 (1.5)	0	0.500
Overall survival, n (%)	44 (89.8)	49 (100)	0.063	85 (98.8)	85 (98.8)	>0.999	0.014	129 (95.6)	134 (99.3)	0.125

ADT = androgen deprivation therapy; IQR = interquartile range.

Table 4 – Functional outcomes

	Salvage subtypes						Salvage total	Primary total	p value
	Whole gland	Matched primary	p value	Focal gland	Matched primary	p value	Whole/focal p value			
Full continence, n (%)										
3 mo	7 (14.3)	10 (20.4)	0.607	28 (32.6)	25 (29.1)	0.742	0.020	35 (25.9)	35 (25.9)	>0.999
6 mo	16 (32.7)	21 (42.9)	0.424	56 (65.1)	38 (44.2)	0.007	<0.001	72 (53.3)	59 (43.7)	0.137
12 mo	23 (48.9)	35 (72.9)	0.043	63 (77.8)	61 (70.9)	0.345	0.001	86 (67.2)	96 (71.6)	0.583
24 mo	26 (53.1)	41 (85.4)	0.027	67 (89.3)	72 (83.7)	0.481	<0.001	93 (78.8)	113 (84.3)	0.337
Social continence, n (%)										
3 mo	10 (20.4)	30 (61.2)	<0.001	46 (53.5)	49 (57.0)	0.749	<0.001	56 (41.5)	79 (58.5)	0.007
6 mo	27 (55.1)	37 (75.5)	0.078	71 (82.6)	62 (72.1)	0.164	0.001	98 (71.0)	99 (73.3)	>0.999
12 mo	30 (61.2)	43 (87.8)	0.011	79 (91.9)	74 (86.0)	0.332	<0.001	109 (80.7)	117 (86.7)	0.268
24 mo	39 (79.6)	45 (91.8)	0.180	81 (94.2)	83 (96.5)	0.687	0.010	120 (88.9)	128 (94.8)	0.115
Erectile dysfunction, n (%)	48 (98.0)	36 (73.5)	0.002	80 (93.0)	67 (77.9)	0.015	0.214	128 (94.8)	103 (76.3)	<0.001

Full continence = zero pads per day; social continence = one pad per day.
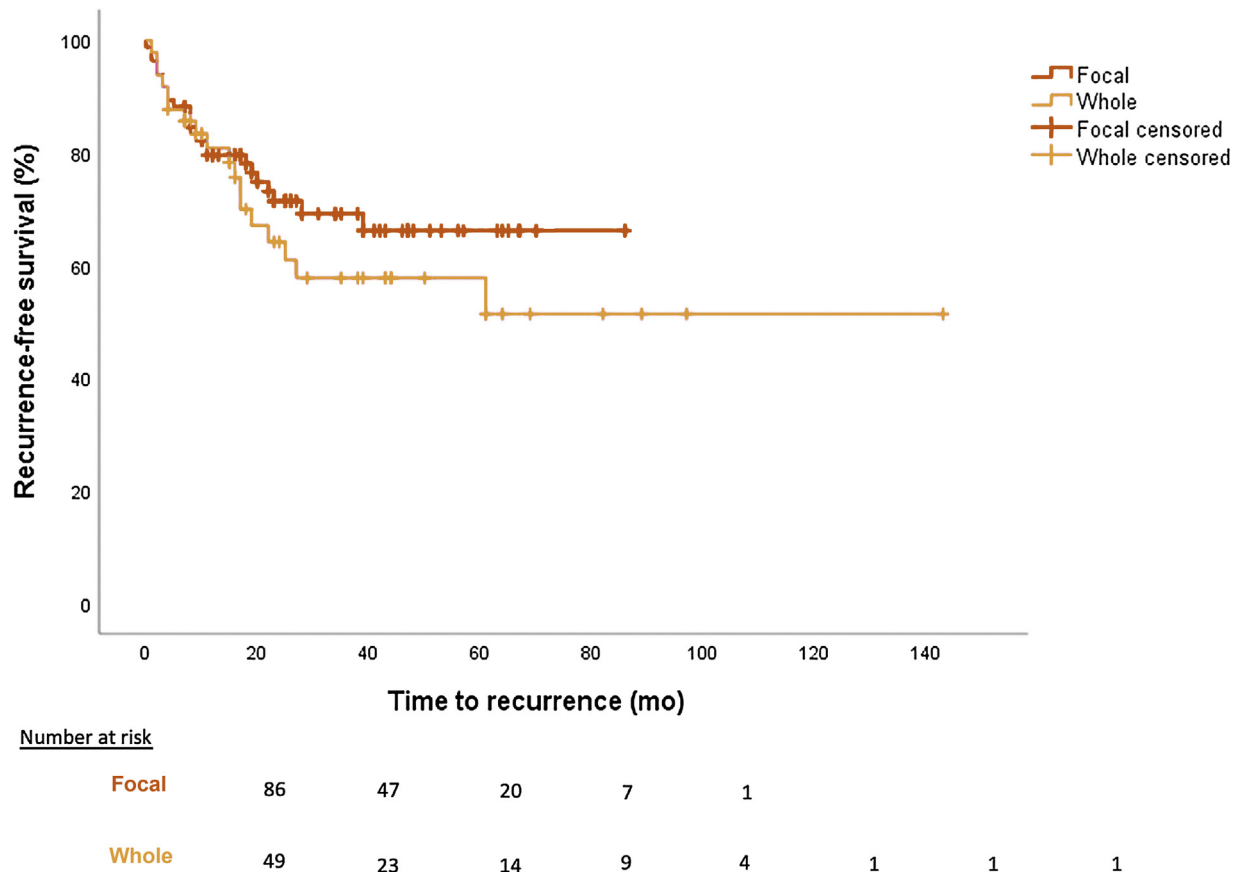

Fig. 2 – Recurrence-free survival of sRARP whole gland versus focal gland treatment ($p = 0.375$).
sRARP = salvage robot-assisted radical prostatectomy.

gland therapy and 53% after whole gland therapy ($p < 0.001$). Onol et al [23] found poor ED rates similar to those of our study, but improved continence outcomes after focal therapy compared with those after whole gland therapy. Our data show a significantly greater rate of ED of 95% in the salvage group compared with 77% in the primary group ($p < 0.001$). ED rates up to 100% are widely

reported after sRARP due to the resection of the neurovascular architecture [12,15,16].

4.4.   Limitations

Our study is the largest propensity-matched comparison of sRARP; however, this is a retrospective, single-centre study

with medium-term follow-up. Patients who had previous primary treatment and then RARP will have different preoperative pathology from patients who receive primary RARP; however propensity score matching has been attempted to control these variations. Further, all surgeries were undertaken in a high-volume centre by experienced surgeons. Larger, multicentre prospective studies with longer-term follow-up are needed to better appreciate the outcomes of sRARP.

5.   Conclusions

Salvage RARP is a feasible operation with perioperative outcomes comparable with those of primary RARP in similar propensity-matched cohorts. Recurrence rates are higher with sRARP, and this may be due to the high-risk, aggressive characteristics of our sRARP cohort. Continence rates are comparable between the primary and salvage cohorts, although ED rates are inferior in the salvage group. Salvage RARP after whole gland therapy shows inferior continence rates to focal therapy and a matched primary RARP cohort. Perioperative outcomes are acceptable; however, complication rates are higher after whole gland therapy. In high-volume centres, sRARP is a safe and feasible treatment for locally recurrent PCa, but patients should be counselled about poorer outcomes compared with primary RARP, especially with regard to erectile function and particularly in those who received primary whole gland therapy.

CRediT authorship contribution statement

Arjun Nathan: Conceptualization, Methodology, Investigation, Data curation, Writing - original draft. **Monty Fricker:** Formal analysis. **Ruben De Groote:** Conceptualization, Methodology, Writing - review & editing. **Amandeep Arora:** Investigation. **Yuzhi Phuah:** Investigation. **Kiran Flora:** Investigation. **Sonam Patel:** Investigation. **Veeru Kasivisvanathan:** Writing - review & editing. **Ashwin Sridhar:** Supervision, Writing - review & editing. **Greg Shaw:** Supervision, Writing - review & editing. **John Kelly:** Supervision, Writing - review & editing. **Tim Briggs:** Supervision, Writing - review & editing. **Prabhakar Rajan:** Supervision, Writing - review & editing. **Prasanna Sooriakumaran:** Supervision, Writing - review & editing. **Senthil Nathan:** Supervision, Writing - review & editing.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euros.2021.03.003.

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