ORIGINAL ARTICLE



Oncologic outcomes of patients with incidental prostate cancer who underwent RARC: a comparison between nerve sparing and non-nerve sparing approach

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Abstract

Background Incidental Prostate cancer (iPCa) is a relatively common finding during histopathological evaluation of radical cystectomy (RC) specimens. To reduce the high impact of RC on erectile function, several sexual-preserving techniques have been proposed. The aim of this study was to evaluate and compare the oncologic outcomes of patients with iPCa who underwent nerve spring and no-nerve sparing robot-assisted radical cystectomy (RARC).

Methods The clinicopathologic data of male patients who underwent RARC at our institution between 2006 and 2016 were retrospectively analysed. Patients with iPCa at definitive pathological examinations were stratified in two groups, according to the preservation of the neurovascular bundles (nerve sparing vs no nerve sparing). Significant PCa was defined as any Gleason score $\geq 3 + 4$. Biochemical recurrence (BR) was defined as a sustained PSA level > 0.2 ng/mL on two or more consecutive appraisals. BR rate was assessed only in patients with incidental prostate cancer and at least 2 years of follow-up. Differences in categorical and continuous variables were analysed using the chi-squared test and the Mann–Withney *U* test, respectively. Biochemical recurrence curves were generated using the Kaplan–Meier method and compared with the Log-rank test.

Results Overall, 343 male patients underwent RARC for bladder cancer within the study period. Nerve-sparing surgery was performed in 143 patients (41%), of these 110 had at least 2 years of follow up after surgery. Patients who underwent nerve-sparing surgery were significantly younger (p < 0.001). Clinically significant PCa was found in 24% of patients. No significant differences regarding preoperative PSA value (p=0.3), PCa pathological stage (p=0.5), Gleason score (p=0.3) and positive surgical margin rates (p=0.3) were found between the two groups. After a median follow-up of 51 months only one patient, in the no-nerve-sparing group had developed a biochemical recurrence (p=0.4).

Conclusions In our series most of the iPca detected in RC specimens can be considered as insignificant with a low rate of BR (0.9%). Nerve-sparing RARC is a safe procedure which did not affect oncological outcomes of patients with iPCa.

Keywords Bladder cancer · Robotic surgery · Prostate cancer

Abbreviations

PCa	Prostate cancer
iPCa	Incidental prostate cancer
BCa	Bladder cancer
RARC	Robot-assisted radical cystectomy
RC	Radical cystectomy
NS	Nerve sparing
BR	Biochemical recurrence

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Background

Radical cystectomy (RC) represents the standard treatment in non-metastatic muscle-invasive bladder cancer (MIBC) and high-risk, recurrent non-invasive disease, according to the European Association of Urology guidelines [1]. Due to the high prevalence of postoperative erectile disfunction linked with RC, several sex-sparing approaches have been proposed in selected patients. These techniques range from cystectomy with a complete/partial prostate preservation to a nerve-sparing cystectomy, reporting satisfactory functional outcomes [2, 3]. However, these procedures, especially those in which a partial prostatectomy is performed, have raised some concerns because of the risk of local invasion of the prostate by the bladder cancer and for the risk of concomitant Prostate Cancer [4].

Incidental Prostate cancer (iPCa) is a relatively common finding during histopthological workup of RC specimens, with a reported rate of prevalence ranging from 4 to 60% [5]. This substantial disparity can be affected by several parameters such as epidemiological and racial differences and to the thoroughness of the pathological work-up [4]. Furthermore, recent systematic review and meta-analysis, have shown that most of the iPCa detected can be considered as insignificant, showing a very low rate of biochemical recurrence (BR) [6, 7].

In the last two decades, the introduction of robotic surgery has evolved the approach to the surgical management of urologic cancers. The application of robotics was initially driven by robot-assisted radical prostatectomy (RARP), and increasingly the widespread adoption of robot-assisted radical cystectomy (RARC) is evident [8]. During RARP, robotic surgery enables an easier identification of nerve sparing (NS) planes compared with the open or laparoscopic approach, allowing surgeons to modify the degree of NS depending on PCa risk group.[9].

To date, there has been no publication reporting on the oncological outcomes of patients with iPCa who underwent RARC and the potential clinical implication of a NS procedure. The aim of our study was to assess the role of NS on oncological outcomes of patients with iPCa who underwent RARC.

Patients and methods

Patients selection and data collection

After institutional review board approval, a retrospective analysis of our database was carried out. We identified male patients who underwent RARC for non-metastatic Bladder Cancer (cTa-cT4N0M0), between March 2006 and December 2016, at our institution. The database was frozen in February 2018. Surgical technique was performed as previously reported in detail [10].

Patients

The following demographic and clinicopathologic variables were reviewed: Age, Body mass index (BMI), American Society of Anaesthesiologist (ASA) score, neoadjuvant chemotherapy, clinical and pathological stage, urinary diversion type. Patients with incidental prostate cancer at definitive pathological examinations and patients with the previous diagnosis of prostate cancer were stratified according to the preservation of the neurovascular bundles (NS vs non NS).

Pathologic evaluation

All the surgical specimens were extensively processed to determine the presence of both bladder and prostate cancer. The prostate gland was processed with a complete sampling with 3 mm slices, the apex of the prostate and the bladder neck were also separately analysed.

Urothelial bladder cancer and prostate cancer were staged according to the American Joint Committee on Cancer Union Internationale Contre le Cancer TNM classification, 7th edition.[11]. Gleason Grade was assigned according to the 2005 ISUP Consensus Conference on Gleason Grading of Prostatic Carcinoma [12]. Clinically significant PCa was defined as any Gleason score $\geq 3+4$ [13]. Positive soft tissue surgical margin was defined as the presence of tumour at inked areas of soft tissue on the specimen.

Follow-up regimen

Postoperatively, patients were seen at least every 6 months in the first 2 years. Patients with incidental prostate cancer or with the revious diagnosis of prostate cancer were scheduled for serum PSA evaluation at every 6 months for the first year and annually thereafter. Postoperative PSA data for patients not presented to our clinic but rather to other physicians' clinics were obtained from the electronic patient records linked to the patient's personnel number from laboratories throughout Stockholm, ensuring virtually complete data collection. Biochemical recurrence was defined as a sustained PSA level > 0.2 ng/mL on two or more consecutive appraisals. Follow-up data included data of adjuvant treatment and survival status. Biochemical recurrence rate was assessed in all patients with incidental prostate cancer and at least 2 years of follow-up.

Statistical analysis

Differences in categorical and continuous variables were analysed using the chi-squared test and the Mann–Whitney U test, respectively. The biochemical recurrence curves were generated using the Kaplan–Meier method and compared with the Log-rank test. All *p*-values were two-sided and statistical significance was defined as a p < 0.05.

Statistical analysis was performed using SPSS Statistics 20 (IBM Corp, Armonk, NY, USA).

 Table 1
 Patient's characteristics

Results

Overall, 343 male patients underwent RARC for BCa, at our institutions, within the study period. Table 1 shows clinicopathologic features of the 343 patients stratified according to the preservation of the neurovascular bundles. iPCa was found in 140 patients (40.8%). NS RARC was performed in 143 patients (41%).

Patients who underwent NS surgery were significantly younger (p < 0.001), had lower ASA score (p < 0.001) and lower rate of clinical MIBC (p = 0.01). No differences regarding preoperative PSA value and prostatic positive surgical margin rate were found between the two groups (p=0.6).

Table 2 summarizes clinicopathologic characteristics of 110 patients with iPCa and with a follow up longer than 2 years, stratified according to the preservation of the neurovascular bundles. In this cohort, 44 (40%) patients underwent NS surgery. Patients receiving NS surgery were younger (p < 0.001) and had lower clinical BCa stage (p < 0.001). No significant differences regarding preoperative PSA value (p = 0.3), PCa pathological stage (p = 0.5) and Gleason score (p = 0.3) were detected between two groups. Overall, clinically significant PCa was found in 33

	Overeall $(n = 110)$	Nerve sparing $(n=45)$	Non nerve sparing $(n=65)$	P value
Age				< 0.001
Mean \pm SD	68.6±3.9	63.2 ± 8.8	72.4 ± 6.2	
Median (IQR)	70 (64–75)	64 (57–70)	72 (69–76)	
ASA score, n (%)				< 0.001
1	39 (11.4)	26 (18.2)	13 (6.5)	
2	152 (44.3)	73 (51)	79 (39.5)	
3	141 (41.1)	43 (30.1)	98 (49.0)	
4	11 (3.2)	1 (0.7)	10 (5)	
BMI				0.571
Mean \pm SD	26.6 ± 3.9	26.2 ± 3.2	26.2 ± 4.4	
Median (IQR)	26 (24–28)	26 (24–28)	26.0 (23-29)	
Preoperative PSA				0.6
Mean \pm SD	3.0 ± 5.0	2.5 ± 29	3.3 ± 6.1	
Median (IQR)	1.6 (0.8–3.4)	1.5 (0.8–3.0)	1.6 (0.8–3.8)	
Clinical bladder stage, n (%)				0.011
<ct2< td=""><td>97 (28.3)</td><td>54 (37.5)</td><td>43 (21.5)</td><td></td></ct2<>	97 (28.3)	54 (37.5)	43 (21.5)	
cT2a-b	183 (53.4)	68 (47.5)	115 (57.5)	
cT3	42 (12.2)	14 (10)	28 (14)	
cT4	21 (6.1)	7 (5)	14 (7)	
Neoadjuvant chemotherapy, n (%)	122 (35.6)	60 (42)	62 (31)	0.03
Urinary diversion, n (%)				< 0.001
Ileal conuit	217 (63.3)	34 (23.8)	183 (91.5)	
Neobladder	126 (36.7)	109 (76.2)	17 (8.5)	
Follow up (months)				0.08
$Mean \pm SD$	42 ± 25	45.6 ± 26.1	40 ± 24	
Median (IQR)	38 (24–56)	39 (26-60)	36 (23–53)	
Death for bladder cancer (%)	61 (17.8)	18 (12.5)	43 (21.5)	0.08
Prostate cancer, n (%)				< 0.001
No	170 (49.6)	84 (58.7)	86 (43)	
Previous diagnosis	33 (9.6)	4 (2.8)	29 (14.5)	
Incidental	140 (40.8)	55 (38.5)	85 (42.5)	
Prostate surgical margins, n (%)				0.6
Positive	7 (2)	4 (3)	3 (1.5)	

All *p*-values were two-sided and statistical significance was defined as a p < 0.05

Table 2Clinical andpathological characteristics ofpatients with incidental Prostatecancer who underwent RARC,and follow-up longer than24 months

	Overall	Nerve sparing	No nerve sparing	
	(n = 110)	(<i>n</i> =44)	(<i>n</i> =66)	
Age				< 0.001
Mean \pm SD	69.0 ± 8.0	64 ± 8.1	72.4 ± 6.0	
Median (IQR)	70 (64–75)	64 (59–71)	72.5 (69–76)	
ASA score, n (%)				0.180
1	13 (11.8)	7 (15.6)	6 (9.1)	
2	45 (41)	21 (46.7)	24 (36.9)	
3	48 (43.6)	17 (37.8)	31 (47.7)	
4	4 (3.6)	_	4 (6.2)	
BMI	((11))		. (0.2)	0.32
Mean \pm SD	26.2 ± 3.8	26.5 ± 3.1	25.9 ± 4.4	
Median (IQR)	26 (24–28)	27 (25–28)	26 (23–28)	
Preoperative PSA value	20 (2 · 20)	27 (20 20)	20 (20 20)	0.34
Mean ± SD	3.3 ± 3.8	2.75 ± 2.8	3.7 ± 4.4	
Median (IQR)	2.1 (1.2–3.9)	1.8 (1.1–3–1)	2.4 (1.2–4.1)	
Clinical bladder stage, n (%)	211 (112 015)	110 (111 0 1)	2 (1.2)	0.07
<ct2< td=""><td>35 (31.8)</td><td>20 (44.4)</td><td>15 (23.1)</td><td>0.07</td></ct2<>	35 (31.8)	20 (44.4)	15 (23.1)	0.07
cT2a-b	57 (51.8)	21 (46.7)	36 (55.4)	
cT3	10 (9.1)	2 (4.4)	8 (12.3)	
cT4	8 (7.3)	2 (4.4)	6 (9.2)	
Urinary diversion, n (%)	0 (1.5)	2 (4.4)	0 (9.2)	< 0.001
Ileal conduit	73 (66.4)	15 (33.3)	58 (89.2)	0.001
Orthotopic neobladder	37 (33.6)	30 (66.7)	7 (10.8)	
Neoadjuvant chemotherapy, n (%)	40 (36.4)	18 (40)	22 (33.8)	0.5
Pathologic bladder cancer stage, n (%)	10 (30.1)	10 (10)	22 (33.6)	0.04
pT0	36 (32.7)	15 (33.3)	21 (32.3)	0.01
pTis	7 (6.4)	2 (4.4)	5 (7.7)	
pTa-pT1	12 (10.9)	10 (21.2)	2 (3.3)	
pT2	22 (20)	10 (21.2)	12 (18.4)	
pT3	24 (21.8)	7 (15.6)	17 (25.1)	
pT4	9 (8.2)	1 (2.2)	8 (12.3)	
Bladder surgical margins, n (%)	> (0.2)	1 (2:2)	0 (12.5)	0.14
Positive	3 (2.7)	_	3 (4.5)	0.11
Pathologic prostate cancer stage, n (%)	0 (217)		5 (110)	0.5
pT2	94 (84.5)	41 (90.1)	53 (80.3)	0.5
pT3a	14 (12.7)	4 (8.9)	11 (16.7)	
pT3b	2 (1.8)	-	2 (3)	
Pathologic gleason Score, n (%)	2 (1.0)		2(3)	0.3
$\leq 3+3$	77 (70)	33 (73)	44 (68)	0.5
3+4	21 (19)	6 (13.3)	15 (23)	
4+3	9 (8)	5 (11)	4 (6)	
4+5 3+5	9 (8) 1 (0.9)	- (11)	4 (0) 1 (1.5)	
4+4	1 (0.9)	- 1 (2)	- (1.3)	
++++ >4+4	1 (0.9)	1 (2)	- 1 (1.5)	
		-		0.3
Clinically significant Prostate cancer, n (%) Prostate surgical margins, n (%)	33 (30%)	12 (26)	21 (32)	0.3
Prostate surgical margins, <i>n</i> (%) Positive	3 (2.7)	2 (4.4)	1 (1 5)	0.5
	5 (2.7)	2 (7.4)	1 (1.5)	

All *p*-values were two-sided and statistical significance was defined as a p < 0.05

patients (30%), of these 12 (26%) and 21 (32%) were in the NS and in the non-NS group, respectively (P=0.3).

Table 3 shows postoperative outcomes of patients with incidental prostate cancer and follow up longer than 24 months. Within a mean follow up of 51 months, biochemical recurrence was found in only one patient (0.9%) in the "non-NS" group (p = 0.41). None of the 110 patients died for prostate cancer. However, 20 patients (18%) died for BCa: 6 in the NS and 14 in the non-NS group, respectively (p = 0.46).

Table 4 shows the clinicopathologic features and the postoperative outcomes of 33 patients with the previous diagnosis of PCa at time of RARC, stratified by the NS technique. In this cohort, the PSA follow-up was measured starting from the date of diagnosis of PCa. Overall, 23 patients (70%) were treated for PCa before RARC. Within a mean followup of 182 months, 2 (6%) patients experienced biochemical recurrence after cystectomy, one per group (p = 0.09).

The figures depict the biochemical recurrence rate in our cohort, according to the preservation of the neurovascular bundles and the date of diagnosis of PCa.

Figure 1 shows the overall Biochemical recurrence rate. Figure 2 shows the biochemical recurrence rate in patients with iPCa and in those with the previous diagnosis of PCa (p = 0.02). Figure 3 shows the biochemical recurrence rate in patients with incidental PCa, stratified by the preservation of the neurovascular bundles (p = 0.3).

Discussion

The frequency of incidentally discovered PCa, during histopathological RC workup, is variable and the clinical implication of this finding is still unclear. The reported incidence of iPCa varied considerably among the previous series, ranging from 4 to 60% of all RC cases [14]. This wide variation depends upon ethnicity and age of the patients studied, differences in histopathologic sampling like slice size, and factors related to the rate of PCa-screening in different societies [14]. In the present study, the rate of iPCa was 41%, which is consistent with those reported in other Western countries series with a 3 mm

slice thickness sampling [7]. Unfortunately, to date, preoperative risk factors such as age, PSA value and digital rectal examination (DRE) seems not reliable enough to accurately predict the risk of a concomitant PCa, thus no exact consensus exists regarding which patients are suitable for a planned nerve-sparing RC. Newer technologies such as prostate magnetic resonance imaging and the prostate cancer antigen 3 test may better help identify higher-risk patients with clinically significant PCa in the future [15]. Overall, in the present study, the median PSA value of patients with iPCa was 2.1 ng/mL (1.2-3.9) and no statistically significant differences were found, concerning PSA value between patients who underwent NS and non-NS RARC. These findings are in line with those described by Bruins et al. who reported, in a series of 1476 patients, a median PSA value of 1.66 ng/mL (0.1-80) [6]. Similarly, Ward et al. analysing a cohort of patients who underwent RC, with normal DRE and PSA below 2.0 ng/ mL and found a 23% rate of iPCa [16].

Analysing the pathology stage of tumors, we found that most of the iPCa (84.5%) was organ confined (\leq pT2); 70% had Gleason score \leq 6, that is considered as a non-clinicallysignificant disease [13] and only 2 (1.8%) patients had Gleason Score \geq 8. These findings are in line with those reported by Pettus et al. [17] and Pignot et al. [18] who found that 29% and 25% of iPCa was clinically significant, respectively.

A limited number of studies have reported oncological outcomes of iPCa in RC specimens, most of them have a short follow-up, and no consensus about the impact on survival has been reached. Large-multi-institutional series have reported that about 3% of patients who underwent RC, developed a BR and rarely PCa was the cause of death in these patients [6, 14]. These findings are consistent with those reported by Tanaka et al. [19], Pan et al. [20], Gakis et al. [21] and Winkler et al. [22] who analyzed the mortality rates in patients undergoing RC, and identified no single PCa-related cause of death. In contrast with these results, Heidegger et al., reported a BR rate of 28% and identified 6 patients (11%) that died from PCa [23]. A recent metaanalysis showed that 1.9% of patients developed a BR, indicating that most of the incidentally discovered PCa were non-clinically significant [7].

Table 3Postoperative outcomesof patients with incidentalprostate cancer who underwentRARC, and follow-up longerthan 24 months

	Overall	Nerve sparing	No nerve sparing	р
	(<i>n</i> =110)	(<i>n</i> =44)	(n = 66)	
Biochemical relapse, n (%)	1 (0.9)	_	1 (1.5)	0.4
Adjuvant Hormonal treatment, n (%)	1 (0.9)	-	1 (1.5)	0.4
Death for Bladder cancer (%)	20 (18%)	6 (13.3)	14 (21.5)	0.46
Follow up (months)				0.65
Mean ± SD	51.2 ± 22.5	52 ± 22	50.7 ± 23	
Median (IQR)	47 (32–64)	50 (33-65)	47 (32–61)	

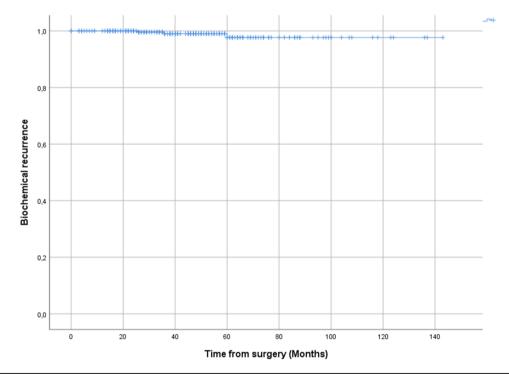
Table 4Clinicopathologiccharacteristics and postoperativeoutcomes of patients underwentRARC for urothelial carcinomaof the bladder and previousdiagnosis of Prostate Cancer

	Overall $(n=33)$	Nerve sparing $(n=4)$	No nerve sparing $(n=29)$	р
Age				0.06
Mean \pm SD	72.8 ± 5.4	68.5 ± 2.8	73.4 ± 5.4	
Median (IQR)	73.1 (70–77)	68.5 (66–71)	73 (70–77)	
ASA Score, n (%)	× ,			0.8
2	15 (44.5)	2 (50)	13 (44.8)	
3	18 (55.5)	2 (50)	16 (55.2)	
BMI	× ,	~ /		0.27
Mean \pm SD	26.3 ± 3.9	24.2 ± 2.2	26.6 ± 4	
Median (IQR)	25.5 (23–28)	24 (22–26)	26 (23–30)	
Preoperative PSA value	~ /		× ,	0.37
Mean ± SD	3.6 ± 7	4.3 ± 3.9	3.5 ± 7.3	
Median (IQR)	0.2 (0.1–5.9)	4 (0.6–8.3)	0.1 (0.1–4.5)	
Clinical bladder stage, n (%)	0.2 (0.2 200)	(010 010)		0.1
<ct2< td=""><td>16 (48.5)</td><td>4 (100)</td><td>12 (42)</td><td></td></ct2<>	16 (48.5)	4 (100)	12 (42)	
cT2a-b	13 (39.4)	</td <td>13 (45)</td> <td></td>	13 (45)	
cT3	1 (3)		1 (3)	
cT4	9 (9.1)		3 (10)	
Clinical PCa stage, n (%)	2 (212)		- ()	0.2
T1c	15 (45.5)	4 (100)	11 (38)	0.2
T2	15 (45.5)	-	15 (52)	
T3	3 (9)	_	3 (10)	
Clinical Gleason score, n (%)	5 ())		5 (10)	0.057
$\leq 3+3$	18 (54.6)	3 (75)	15 (52)	0.007
3+4	7 (21.2)	-	7 (24)	
4+3	4 (12.1)	_	4 (14)	
3+5	1 (3)	_	1 (3)	
4+4	1 (3)	1 (25)	-	
>4+4	2 (6.1)	-	2 (7)	
Preoperative treatment for PCa, n (%)	2 (0.1)		2(1)	0.03
Clinical observation	10 (30.3)	3 (75)	7 (24)	0.05
External Beam Radiotherapy	9 (27.3)	5 (15)	9 (31)	
Brachytherapy	3 (9.1)	_	3 (10.2)	
Radical prostatectomy	7 (21.2)	_	7 (24)	
Hormonal treatment	4 (12.1)	1 (25)	3 (10.2)	
Pathological bladder cancer stage, n (%)	4 (12.1)	1 (23)	5 (10.2)	0.9
pT0	13 (39.5)	_	13 (45)	0.9
pT0 pT1	4 (12)	2 (50)	2 (7)	
pT2	1 (3)	1 (25)	2 (1) -	
pT2 pT3	10 (30.3)	1 (25)	9 (31)	
pT4	5 (15.2)	1 (23)	5 (17)	
Pathologic Prostate cancer stage, n (%)	5 (15.2)	-	5(17)	0.019
pT0	16 (48.5)	_	16 (55.7)	0.019
pT2	6 (18.2)	_	6 (20.6)	
	0 (18.2) 7 (21.2)	- 2 (50)		
pT3a pT3b	4 (12.1)	2 (50) 2 (50)	5 (17) 2 (7)	
Pathologic Gleason Score, <i>n</i> (%)	4 (12.1)	2 (30)	2(7)	0.049
	16 (19 5)		16 (55 7)	0.045
Non-reported	16 (48.5) 5 (15.2)	_	16 (55.7)	
$\leq 3+3$	5 (15.2) 2 (0,1)	-	5 (17) 2 (7)	
3+4	3 (9.1)	1 (25)	2 (7)	
4+3	4 (6)	2 (50)	2 (7)	

Table 4 (continued)

	Overall $(n=33)$	Nerve sparing $(n=4)$	No nerve sparing $(n=29)$	р
3+5	2 (6)	_	2 (7)	
4+4	2 (6)	1 (25)	1 (10.3)	
>4+4	1 (3)	_	1 (3)	
Positive Surgical margins, n (%)				
Bladder cancer	5 (15)	1 (25)	4 (13.8)	0.55
Prostate cancer	2 (6)	1 (25)	1 (3)	0.09
Biochemical relapse, n (%)	2 (6)	1 (25)	1 (3.4)	0.09
Adjuvant Hormonal treatment, n (%)	2 (6)	1 (25)	1 (3.4)	0.09
Death for Bladder cancer (%)	6 (18.2)	-	6 (20.3)	0.3
Time from PCa diagnosis to RARC (months)				0.09
Mean±SD	152 ± 325	35 ± 30.9	168±344	
Median (IQR)	63 (30–113)	29.5 (9-67)	64 (42–138)	
Follow up (months from PCa diagnosis)				0.07
Mean±SD	182 ± 323	63 ± 28.6	199±341	
Median (IQR)	103 (54–156)	62 (36–91)	109 (59–168)	

All *p*-values were two-sided and statistical significance was defined as a p < 0.05



Biochemical recurrence					
24 months 60 months 96 months 140 months					
Number at risk (%)	258	72	15	1	

Fig. 1 Biochemical recurrence rate of 343 patients who underwent RARC

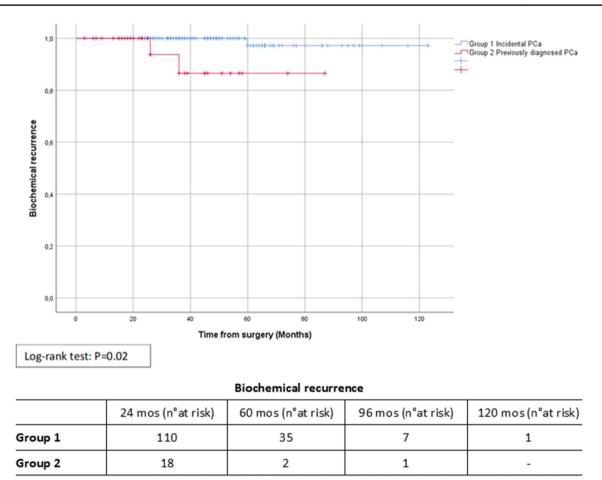


Fig. 2 Biochemical recurrence rate in 143 patients with prostate cancer, stratified by incidental PCa or previously diagnosed PCa

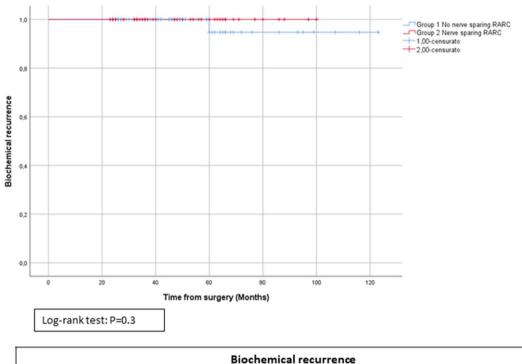
Several results of our study are noteworthy. First, to our knowledge this is the first series that reports the oncological outcomes of patients with iPCa who have undergone RARC, comparing the BR rate according to the preservation of the neurovascular bundles. Our results are consistent with previous studies, showing that most of the iPCa diagnosed at time of RC are clinically insignificant and doesn't affect the oncological outcomes of patients. The two groups were similar regarding the preoperative PSA value, the ASA score, the pathological Gleason Score, the pathological PCa stage, the surgical margins rate and the mortality rates from bladder cancer. In our series, only one patient in the non-NS group developed a BR and received hormonal treatment. The vast majority were not clinically impacted by their iPCa, while 18% of patients died for Bladder cancer. These findings indicate that the oncological outcomes of patients with iPCa at RC is mainly driven by the prognosis of the bladder cancer. Analyzing 33 patients with the previous diagnosis of PCa, at the time of RARC, only 4 had undergone NS procedures. In these subgroups, two patients developed BR, one per group (p=0.09). With the limitation of the exiguous sample in analysis, these findings indicate that selective NS RARC provides satisfactory oncological outcomes even in patients with the previous diagnosis of PCa at the time of RARC.

Our study has several limitations: first and foremost, its retrospective design. Furthermore, patients who underwent NS-RARC were younger, had a lower rate of muscleinvasive bladder cancer and were more likely to receive an orthotopic urinary diversion. All these findings may lead to relevant biases, which cannot be excluded.

From the clinical point of view, the importance of this study is to highlight that NS RARC can be offered to patients with organ-confined bladder cancer without worsening the life expectancy of the patients.

Conclusions

Concomitant PCa occurs in more than 40% of all RC specimens and the majority have characteristics of non-clinically significant disease. The oncological prognosis of patients who undergo RC are primarily driven by the bladder cancer stage. Nerve-sparing RARC is a safe procedure that ensures a low rate of BR without affecting the oncological outcomes



Biochemical recurrence							
	24 mos (n°at risk) 60 mos (n°at risk) 96 mos (n°at risk) 115 mos (n°at risk)						
Group 1	66	18	4	1			
Group 2	44	16	3	-			

Fig. 3 Biochemical recurrence rate in 110 patients with incidental PCa at time of RARC, stratified by nerve-sparing surgery

of patients and may be routinely offered to patients with organ-confined bladder cancer disease.

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Compliance with ethical standards

Conflict of interest Francesco Chessa, Axel Moller, Justin Collins, Oscar Laurin, Markus Aly, Riccardo Schiavina, Cristofer Adding, Concetta Distefano, Alessandro Bertaccini, Olof Akre, Abolfazl Hosseini, Eugenio Brunocilla and Peter Wiklund declare that they have no conflict of interest.

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