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ORIGINAL ARTICLE

The impact of previous prostate surgery on the outcomes of laparoscopic radical prostatectomy

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ABSTRACT

BACKGROUND: The aim of this study was to evaluate the outcomes in laparoscopic radical prostatectomy (LRP) in patients who had undergone prior prostate surgery (PPS).

METHODS: In this study 946 consecutive LRP patients were included and a retrospective comparison between those patients who had received PPS (group A) and those who had not received PPS (group B) was carried out. The preoperative, intraoperative and postoperative data was collected in a prospectively-maintained database. All complications occurring ≤30 days after surgery were recorded and defined according to the Dindo-modification of the Clavien system.

RESULTS: Longer operative time, greater blood loss, longer catheterization time, higher incidence of lymphocele, rectal injury and anastomotic stricture were found to be more frequent in group A. No statistically significant difference was noted between the two groups in terms of positive surgical margin rate and Biochemical recurrence free survival (BCRFS). Complete urinary continence rate resulted significantly higher in group B patients at both 1-year and 2-year follow-up. Potency rate resulted better in group B patients even if a statistically significant difference for both unilateral and bilateral nerve sparing techniques was not reached.

CONCLUSIONS: LRP procedure can be safely performed on patients who have previously undergone PPS without compromising oncologic safety whereas a negative impact on functional outcome in terms of achieving a complete urinary continence rate and sexual potency should be expected.

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Key words: Prostatic neoplasms - Laparoscopy -Prostatectomy – Complications.

Currently, radical prostatectomy (RP) is the only surgical treatment for localized prostate cancer (PCa) that has shown a cancer-specific survival benefit when compared with conservative management.[1]

The rate of incidental PCa detection revealed by transurethral resection of the prostate (TURP) or open prostatectomy (OP) in patients with both negative PSA plasma levels and negative digital rectal examination is about 6%.[2]

A history of having undergone a TURP has been reported as a risk factor for the onset of anastomotic stricture, erectile dysfunction (ED) and urinary incontinence (UI) as consequences of open RP,[3-5] while no detrimental ef-

fect on oncological safety has been reported.[6, 7]

In the last decade, laparoscopic radical prostatectomy (LRP) has been increasingly performed for the surgical treatment of PCa and LRP is now considered a well-established alternative to open surgery.[8] Furthermore, it has been demonstrated that LRP can reduce the surgical trauma for the patient when compared to open surgery.[9] Nevertheless, few studies have assessed the effects of PPS on LRP outcomes.[10-15] One of the most recent and comprehensive reports on this patient category concludes that LRP after TURP can be performed within the confines of good oncological safety; however inferior intraoperative and postoperative outcomes and compromised postoperative sexual recovery have been reported.[10, 14]

The objective of this study is to assess the effects of PPS, including TURP, OP and laser treatments, on the oncologic and functional outcomes of a large series of LRP.

Materials and methods

Study design and population

The retrospective, single-surgeon study included 946 consecutive LRPs for localized PCa, performed between February 2010 and February 2015. Ninety-eight patients (10.4%) presented with a history of PPS for benign prostate enlargement (BPE) treatment. All patients were informed about other possible therapies for incidental PCA (active surveillance, brachytherapy, High-intensity focused ultrasound [HIFU] and external beam radiation) and the choice to perform LRP was based on a joint decision arrived at by the patients and physicians.

Preoperative, intraoperative and postoperative data was collected in a prospectively-maintained database, while a retrospective comparison between patients who had undergone PPS (group A) and those who had not (group B), was made for the purpose of this study.

In group A the diagnosis of PCa was either incidental, based on pathological specimens retrieved during prostatic surgery, or performed by prostate biopsy during routine follow-up. The study was approved by the committee on research ethics at the institution in which the research was conducted and any informed consent from human subjects was obtained as required.

Surgical technique

LRP was performed in all patients by a single surgeon (SS) with the extraperitoneal approach, in accordance with our previously described technique.[16] The only differing approach adopted in this specific subset of patients was a wider opening of the bladder wall of 1-2 cm proximally to the vesico-prostatic junction in order to maintain better visualization of the bladder neck and ureteral ostium, especially during posterior dissection. In cases of patients presenting a Gleason score of >6 and/or PSA level >10 ng/mL, a lymphadenectomy at the level of the obturator fossa and external iliac vessels was performed. Ureteral stents had never been preoperatively placed in the PPS (group A) patients.

Each prostatectomy specimen was examined by two uro-pathologists at our institution. Uro-pathologists have a wide experience in the field and all specimens were reviewed by both of them independently.

Tumor staging was assigned according to the 2002 American Joint Committee on Cancer TNM staging system,[17] and the differentiation was assigned according to the Gleason scheme. Positive surgical margin (PSM) was defined as the tumor extending to the inked surface of specimen, and in areas without a definite identifiable capsule, the definition previously described by Rosen *et al*. was followed.[18, 19]

No single patient had undergone LRP within the first 4 months after TURP in order to diminish the periprostatic inflammation due to the first intervention.

Each patient underwent a cystography on the 7th postoperative day to evaluate the urethral anastomosis for leakage.

Of the PPS patients, the nerve-sparing technique (NSS) was performed in 39 patients (40%) (unilateral NSS, 13 patients [33%] and bilateral NSS, 3 patients 7%]), whereas out of the non-PPS patients, the NSS had been used in 390 patients (46%) (unilateral NSS, 305 pa-

tients [36%] and the bilateral NSS in 85 patients [10%]).

Bilateral NSS was performed in pre-operatively potent patients with a PSA<10, Gleason≤7 and only two positive biopsy cores out of at least 12, while Unilateral NSS was performed in cases of Gleason-score 4+3 or with more than two positive cores out of at least 12 biopsy after frozen section.

Patient follow-up

All patients were scheduled for follow-up visits at our institution at 1, 3, 6 mo and subsequent 6-mo intervals. A minimum 2-year follow-up was available for all 946 patients while a 5-year follow-up was available in 589 cases. Erectile function was assessed by using the International Index of Erectile Function (IIEF-5) and Erection Hardness Score (EHS) while urinary continence was assessed by using the International Consultation on Incontinence Modular Questionnaire (ICIQ)-UI Short Form.[21] Patients were considered sexually potent if an IIEF-5 score≥21 and EHS≥3 were both achieved, independent of the use of oral agents.[22] All questionnaires were self-administered to patients. All complications occurring ≤30 days after surgery were recorded and defined according to the Dindo-modification of the Clavien system.[20]

Outcome analysis

A retrospective cross-sectional evaluation of surgical, oncologic and functional results was carried out to compare groups 1 and 2. Student's *t*-test was used for normally distributed variables and χ^2 for comparing two proportions. For all statistical basis of comparison, significance was considered as $P<0.05$. Biochemical recurrence-free survival (BCRFS) was compared between groups based on the Kaplan–Meier method using SPSS 17.0 (SPSS Inc, Chicago, IL, USA). The sample size was based on the differences in postoperative oncologic and functional (urinary continence and potency) outcomes using an effect size of 1.0, an alpha level of 0.05, and a power of 0.80. The determination of the sample size and effect size was appropriate for the number of treatment groups in this type of research and was consistent with previous published guidelines.[23]

Results

Baseline characteristics

Patients' demographics, pre-operative tumor and surgical characteristics are summarized in Table I.

TABLE I.—*Patients' demographics, pre-operative tumor and surgical characteristics.*

	Group A	Group B	P value
Patients, N.	98	848	
Age, years, mean±SD	67.2±3.5	65.1±3.5	0.38
Total PSA, ng/dL, mean±SD	7.1±2.1	9.8±2.8	<0.001
Pre-operative IIEF-EF mean±SD	22.7±2.4	21.9±2.6	0.15
Pre-operative IPSS mean±SD	10.3±4.1	11.6±5.5	0.12
Clinical stage, N. (%)			
T1a-T1b	26 (27)	38 (4.5)	
T1c	51 (52)	491 (58)	
T2a	11 (11)	182 (21.5)	
T2b	7 (7)	72 (8.5)	
T3a	1 (1)	38 (4.5)	
T3b	2 (2)	27 (3)	
Prostate Weight, g, mean±SD	31.0±9.2	53.0±11.9	<0.001
Previous prostatic surgical intervention, N. (%)			
Monopolar TURP	81 (82.6)	0	
Holmium Laser TURP (HOLEP)	11 (11.2)	0	
Open prostatectomy	6 (6.1)	0	

SD: Standard Deviation

In Group A, diagnosis of PCa was made incidentally in 27% of the cases and by performing a prostate biopsy in 52% of the cases. Both PPS and non-PPS groups presented similar data for age (group A: 67.2±3.5 years; group B: 65.1±3.5), and tumor characteristics (clinical stage and Gleason Score), whereas a significantly higher preoperative PSA level (group A: 7.1±2.1; group B 9.8±2.8; P<0.001) and mean prostate weight (group A: 31.0±9.2; group B 53.0±11.9; P<0.001) were detected in group B patients. Monopolar TURP was the most frequently performed prostatic surgery before LRP in 81(82.6%) cases, followed by laser TURP (HoLEP) in 11 (11.2%) cases and OP in 6 (6.1%) cases.

Preoperatively, the mean IIEF-5 was 22.7±2.4 and 21.9±2.6 in group A and group B, respectively (P=0.15) and the mean preoperative IPSS was 10.3±4.1 and 11.6±5.5 in both groups, respectively (P=0.12).

Intra, postoperative and oncologic outcomes

Table II details the intraoperative, postoperative data and complications. Mean operative time resulted significantly longer in group A patients (group A: 208 minutes *vs.* group B 193 minutes; P<0.001). Similarly, mean blood loss was higher in group A patients (group A: 606 mL *vs.* group B: 624 mL; P<0.05). Length of hospital stay was similar between groups, while a significantly longer catheterization time was observed in group A (group A: 9.6 days *vs.* group B: 7,7 days; P<0.001). Overall surgical complication rate was found to be significantly higher in group A than in group B (16% *vs.* 3.3%, respectively; P>0.001), with a

TABLE II.—*Intraoperative, postoperative data and complications and oncologic outcomes.*

	Group A	Group B	P value
Patients, N.	98	848	
Intra- and postoperative data			
Overall operative time, min, mean	208	193	<0.001
Blood loss, mL, mean	606	624	<0.05
Hospital stay, days, mean	6.6	6.5	0.58
Catheterization time, days, mean	9.6	7.7	<0.001
Nerve sparing surgery (NSS), N. (%)	16 (16)	390 (46)	
Unilateral NSS, N. (%)	13 (13)	305 (36)	
Bilateral NSS, N. (%)	3 (3)	85 (10)	
Surgical complications overall (Clavien classification), N. (%)	16 (16)	28 (3.3)	<0.001
Conversion to open surgery	0 (0)	0 (0)	1.0
Wound infections or hematoma	2 (2)	6 (0.7)	0.17
Lymphocele	2 (2)	11 (1.3)	0.75
Rectal injury	2 (2)	1 (0.1)	<0.01
Anastomotic stricture	9 (9.2)	10 (1.2)	<0.001
Oncologic outcomes			
Gleason score after LRP			
Gleason 6	3 (3)	42 (5)	
Gleason 3+4	17 (17)	71 (8)	
Gleason 4+3	52 (53)	398 (47)	
Gleason 8-10	26 (27)	337 (40)	
pTNM Stage, N. (%)			
pT2a	17 (18)	152 (18)	
pT2b	36 (37)	322 (38)	
pT2c	30 (31)	118 (14)	
pT3a	11 (10)	161 (19)	
pT3b	4 (4)	93 (11)	
Positive surgical margins (PSM), N. (%)			
Overall	20 (20)	136 (16)	0.28
pT2	11/83 (13)	106/592 (18)	
pT3a	7/11 (43)	51/161 (31.5)	
pT3b	2/4 (51)	38/93 (40.5)	

statistically significant difference for the incidence of rectal injury (CLAVIEN III B) (group A: 2% *vs.* group B: 0.1%; P<0.01) and anastomotic stricture (CLAVIEN III B) (group A: 9.2 *vs.* group B: 1.2; P<0.001).

Table II also describes oncologic outcomes. No patient showed absence of prostate cancer at definitive pathologic examination (pT0). Positive surgical margin rate was increased, though not in a statistically significant way, in group A patients with pT3a and pT3b stages. As shown in Figure 1, no statistically significant difference was noted between the two groups in terms of BCRFS.

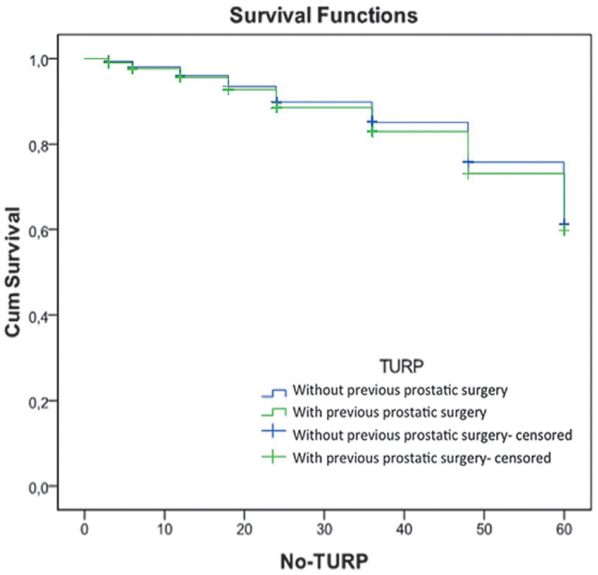

Figure 1.—Biochemical recurrence free survival according to presence/absence of previous prostatic surgery.

Functional results: urinary continence and sexual potency

Functional results in terms of urinary continence and erectile function are reported in Table III. Complete urinary continence rate resulted significantly higher in group B patients at both 1-year (group A: 84.7% *vs.* group B: 91.7%; P<0.05) and 2-year follow-ups (group A 90.8% *vs.* group B 98.1%; P<0.001). Similarly, potency rate resulted higher in group B patients even though statistically significant differences for both unilateral and bilateral NSS at 1 and 2 year follow-ups were not reached. Table IV summarizes functional results in terms of urinary continence and erectile function based upon the different type of prostatic surgery performed before LRP.

A trifecta outcome was achieved at 24 months by 7% of Group A patients *vs.* 19.9% of Group B patients (P<0.05). In patients who underwent monolateral NS procedure trifecta was reached at 24 months by 40% and 41.6% in group A and group B respectively (P>0,05), while in bilateral NS at 24 months trifecta was achieved by 66.6% and 81.1% of patients in group A and group B respectively (P>0.05) (Table V).

TABLE III.—*Functional outcomes: urinary continence rates and potency rates according to type of nerve-sparing surgery.*

		Continence rate		
		Group A N. (%)	Group B N. (%)	P value
12 months		83 (84.7)	777 (91.7)	<0.05
24 months		89 (90.8)	831 (98.1)	<0.001
Potency Rates According To Type of Nerve-Sparing Surgery				
	Type of nerve-sparing surgery	Potency rate*		
		Group A N. (%)	Group B N. (%)	P value
12 months	Unilateral	4 (30.7)	99 (32.5)	0.382
	Bilateral	1 (33.3)	39 (45.7)	0.243
24 months	Unilateral	5 (40.4)	132 (43.3)	0.667
	Bilateral	2 (66.6)	73 (85.7)	0.219

*Patients were considered sexually potent if an IIEF-5 score≥21 and EHS≥3 were achieved, independent of the use of oral agents.

TABLE IV.—*Functional outcomes: urinary continence rates and potency rates according to type of prostatic surgery before LRP.*

		Continence rate				
		Group A Overall N. (%)	Group A Monopolar TURP N. (%)	Group A Laser (HoLEP) N. (%)	Group A Simple prostatectomy N. (%)	P value
12 months		83 (84.7)	70 (84.5)	9 (84.1)	4 (82.3)	0.517
24 months		89 (90.8)	74 (90.9)	10 (90.5)	5 (90.4)	0.495
		Potency rates * according to type of nerve-sparing surgery				
	Type of nerve-sparing surgery	Group A overall N. (%)	Group A Monopolar TURP N. (%)	Group A Laser (HoLEP) N. (%)	Group A Simple prostatectomy N. (%)	P value
12 months	Unilateral	4 (30.7)	3 (29.4)	1 (29.2)	0 (0)	0.674
	Biateral	1 (33.3)	1 (33.3)	0 (0)	0 (0)	1
24 months	Unilateral	6 (40.4)	4 (40.4)	2 (40.9)	0 (0)	0.867
	Bilateral	2 (75.0)	2 (75.0)	0 (0)	0 (0)	1

*Patients were considered sexually potent if an IIEF-5 score≥21 and EHS≥3 were achieved, independent of the use of oral agents.

TABLE V.—*Trifecta outcome at 12 and 24 months.*

Trifecta			
	Group A N. (%)	Group B N. (%)	P value
12 months			
Total	5 (5)	129 (15.2)	<0.05
Monolateral NS	4 (30.7)	94 (30.8)	NS
Bilateral NS	1 (33.3)	35 (41.1)	NS
24 months			
Total	7 (7)	169 (19.9)	<0.05
Monolateral NS	5 (40.4)	127 (41.6)	NS
Bilateral NS	2 (66.6)	69 (81.2)	NS

Discussion

In recent years, LRP has been established as a safe and effective treatment for PCa in specialized centers.[8, 24-30]

Performed by any of the surgical approaches, previous TURP may impose difficulties for the surgical team during RP due to infections of the prostate and seminal vesicles and perforation of the prostate's capsule during TURP, with extravasation of irrigation fluid, which could result in periprostatic fibrosis and distortion of the surgical planes, making the dissection difficult.[31-33]

To date, the largest study evaluating the surgical and functional outcome of LRP following TURP was published by Menard *et al.* in 2008 [10] which concluded that no negative impact on oncologic outcome and urinary continence was found while worsened intra-operative and postoperative outcomes and more difficult preservation of sexual potency were observed at the time.

Compared to previously published articles that considered exclusively TURP operations,[7-12] our study also includes other procedures like Holmium laser enucleation (HoLEP) and OP. Based upon our experience, PPS did not have any impact on LRP, with the exception of making it more difficult to access the Retzius space in the group A patients who had undergone OP, due to the adhesions induced by sutures of bladder and abdominal walls, although this cannot be supported by any data due to the extremely limited number of cases. However, such a condition can lead to prolonged duration of the access phase to the Retzius space and trocar placement, so in very

difficult cases the trocars were placed under endoscopic visualization.

As expected, lower preoperative PSA levels and mean prostate weight were found in the PPS patients when compared to the non-PPS patients.

Regarding intraoperative data, worse results were observed in the patients who had undergone PPS with a statistically significant difference in terms of operative time and mean blood loss.

A significantly longer catheterization time in the group A was observed in the postoperative data, while no difference between the two groups for mean hospital stay was found. The longer catheterization time in the PPS patients can be explained by the difficulty in performing a bladder-neck sparing technique.

A statistically significant higher overall complication rate was observed in patients who had previously undergone PPS with a higher incidence of rectal injury and anastomotic stricture. The 16% figure that appears quite high is heavily affected by the 9.2% of anastomotic strictures. The significantly higher rate of anastomotic strictures in these same patients could be explained by the impaired healing process at the level of the anastomosis due to scarring and fibrosis of the previously resected bladder neck.

Similarly, Jaffe *et al*, in their retrospective study analyzing surgical outcomes for men undergoing LRP after TURP concluded that PPS patients have worse surgical and postoperative outcomes with respect to operative time, length of stay and overall complication rate.[32]

As recounted by Menard *et al*. [10], operative difficulties were mainly encountered while performing resection of the posterior plane of the prostate and during dissection of the apex and identification of the urethral stump, particularly following recent TURP.

Similarly, although a minimum 4 month interval was imposed following PPS prior to performing LRP in order to reduce the negative effect of the periprostatic fibrosis induced by previous prostatic operation, we frequently found the surgical steps approaching the posterior prostatic plane and the apex more complex. This could perhaps explained by the significantly longer operative time and more frequent incidence of rectal injuries. Both of the two cases of rectal injury were intraoperatively detected and repaired by a 2-layer running suture of the rectal hole and its effectiveness was checked by injecting saline solution throughout a rectal catheter). In the postoperative setting, patients had received a prolonged parenteral nutrition.)

Notwithstanding the technical difficulties encountered during surgery of the PPS patients, no impact on the oncologic outcome after LRP was observed as indicated in the 5-year actuarial progression free-survival rate which was found to be similar in both groups. However, our data on positive surgical margins shows a higher percentage in T3a and T3b patients, even if not statistically significant. This data is in contrast with the results reported by Jaffe *et al.* who found a statistically significant higher positive margin rate in patients with a history of TURP undergoing LRP.[32]

Better functional results were found in the patients without PPS with the exception of the sexual potency rate however no difference on functional outcome was detected in terms of impact of the different type of PPS performed before LRP. The lack of a statistically significant difference related to sexual recovery between groups could be explained by the small number of patients in group A, who had received a NSS in group A. This affects also the trifecta outcome and could explain the relatively low rate of trifecta achievement in our series.

In our experience the urinary continence rate was impaired at both the 1-year and 2-year follow-up in the patients whose had undergone PPS Two possible explanations can be taken into consideration to support this finding: 1) the more complex surgical approach to the prostatic apex and urethral stump which could have led to the impairment of the urinary sphincter; 2) the presence of 9.2% of group A patients who, due to necessary treatment for the stricture of the vesico-urethral anastomosis, were not able to fully follow and complete their rehabilitation process.

Our findings confirm that sexual recovery

strictly relied on the type of NSS utilized and highlight the fact that performing a NSS in patients who have undergone PPS is undoubtedly more challenging.

In our opinion the greater, though not significant, difference between groups over time is related to the fact that a true preservation of the neurovascular bundle (NVB) was technically feasible in a limited number of PPS patients so that their response rate to oral agents remained lower than that observed in non-PPS patients.

Limitations of the study

Several limitations to the present study must be acknowledged however. Firstly, as this was a retrospective study, imparting an inherent selection bias could be overcome. A second main limitation includes the wide difference between the cohorts of patients that can affect the reliability of statistical comparison. Moreover, the scarce number of specific subgroups limits the statistical significance of the inter-group comparison. In addition, continence was not assessed using pad but only by self-administered questionnaire and we do not perform an earlier evaluation of continence at 3 and 6 months. Overall follow-up was relatively short.

Conclusions

The findings of our study confirm that LRP following PPS can be performed without compromising oncologic safety. However, operating on post-PPS patients is technically more demanding as supported by our study's intra- and postoperative results and overall complication rate and requires surgeons with advanced laparoscopic expertise. Adequate preoperative counseling is also recommended.

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