

Real Life Comparative Analysis of Robotic Assisted versus Laparoscopic Radical Prostatectomy in a Single Centre and Single Surgeon Experience

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Article

Real Life Comparative Analysis of Robotic Assisted versus Laparoscopic Radical Prostatectomy in a Single Centre and Single Surgeon Experience

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Simple Summary: In the comparison between RARP and LRP approach, a clear advantage of the robotic approach is a significant reduction in operating times, days of hospitalization and postoperative catheterization compared to laparoscopic surgery. It is not possible to describe any certain oncological advantage both in terms of surgical margins and pathological lymph nodes removed. In RARP cases a reduction to the limit of significance is described in terms of biochemical recurrence. RARP produces a more rapid recovery of urinary continence at 3 months postoperatively without significant advantages in terms of erectile potency recovery.

Abstract: Background: The advantage of a robotic assisted (RARP) over a laparoscopic (LRP) approach in radical prostatectomy (RP) remains to be demonstrated. **Aim** of the study is to use a homogeneous population in real life and single surgeon surgery, to analyze the oncological and functional results based on the type of the surgical approach. **Methods:** This is a prospective trial on non-metastatic prostate cancers (PC) patients considered after multidisciplinary decision to RP, using RARP or LRP. A real-life setting was analyzed at our Urological Departments, using homogeneous criteria for the management of PC cases and a one surgeon experience on 444 cases (284 LRP and 160 RARP). **Results:** Mean operative time was significantly lower in RARP (173.33±44.3 min) than in LRP (153.21±25.1 min) ($p<0.001$). In cases submitted to an extended lymph node dissection (eLND), the mean number of lymph nodes removed was 15.16±7.83 and 19.83±4.78 respectively in LRP and RARP procedures ($p<0.001$), but positive lymph nodes (pN1) were similarly found in 15.8% of LRP patients and 13.6% of RARP patients ($p=0.430$). Surgical margins (SM) positivity was not significantly higher in RARP group (20.0%) when compared to LRP group (15.9%) ($p=0.145$). During the postoperative follow-up, a biochemical recurrence (BCR) was detected in 14.4% and 7.5% of cases in the LRP and RARP group respectively ($p=0.014$). Better results of PAD test at 3-month interval using RARP approach (mean pad weight 75.57±122 grams and 14±42 grams respectively in LRP and RARP ($p<0.01$)) were described. **Conclusions:** In the comparison between RARP and LRP approach, a clear advantage of the robotic approach is a significant reduction in operating times, days of hospitalization and postoperative catheterization compared to laparoscopic surgery. It is not possible to describe any certain oncological advantage both in terms of surgical margins and pathological lymph nodes removed. In RARP cases a reduction to the limit of significance is described in terms of biochemical recurrence. RARP produces a more rapid recovery of urinary continence at 3 months postoperatively without significant advantages in terms of erectile potency recovery.

Keywords: keyword 1: prostatic neoplasm; 2: radical prostatectomy; 3: robotic surgery; 4: laparoscopic surgery

1. Introduction

Robotic-assisted radical prostatectomy (RARP) has become the most widely used robotic intervention and the most frequently performed technique for the treatment of non-metastatic prostate cancer [1-6].

However, its advantage over the laparoscopic (LRP) approach remains to be demonstrated but the greater simplicity of execution and the shorter learning curve make it favored [1-4]. The European Urological Association (EAU) recommends informing patients' candidates for prostatectomy that no surgical approach (laparoscopic versus robotic) has clearly demonstrated superiority in terms of both oncological and functional results [7]. However, several clinical trials have shown an advantage of RARP over LRP in terms of recovery of sexual potency and surgical margins (SM) status in organ-confined PC [1-6;8-16]. The presence of SM+ represents the most immediate indication of failure for RP to achieve patient cure. However, more and more frequently its treatment is not immediate and is replaced by vigilant monitoring, delaying treatment in case of early biochemical recurrence [8-16].

Even in this setting, a randomized study can allow us to compare two homogeneous populations to verify significant differences between the different approaches. However, the limit of the randomized study is the distance that can be produced from a real-life situation as well as the difficulty of execution. Moreover, a study that reaches a significant number of RP sample through the coexistence of different surgeons with different approaches and experiences, introduces a relevant factor of variability that can reduce the validity of the results [1-6;17-25].

In the present study we report the long-term case history of a population of patients with non-metastatic PC considered suitable, according to EAU guidelines and after multidisciplinary discussion, for radical prostatectomy, performed by a single surgeon with experience of over 10 years. This population represents a homogeneously treated sample in a perfect real-life situation at a high-volume institution for the treatment of PC and with a multidisciplinary (MDT) group regulating decisions relating to the management of each individual patient.

Aim of the study is to use this homogeneous population in real life to analyze the oncological and functional results based on the type of surgical approach but also based on the clinical and pathological characteristics of the neoplasms.

2. Materials and Methods

This is a prospective trial on non-metastatic PC patients considered after MDT decision to RP, using RARP or LRP. A real-life setting was analyzed at our Urological Departments, using homogeneous criteria for the management of PC cases and a one surgeon experience is reported.

2.1. Population

Patients with a histological diagnosis of non-metastatic PC considered for RP as primary therapeutic option and submitted to surgery by a single surgeon (AS), were consecutively enclosed in the analysis. The analysis was approved by our internal ethical committee and all patients gave their informed consensus for each procedure. All diagnostic and therapeutic procedures reflected our routine clinical practice in a department at high-volume for the management of PC disease. All diagnostic and therapeutic decisions for the management of patients and selection for surgery were discussed in a MDT group. In particular for low-risk PC patients, possible options between active surveillance, surgery and radiotherapy were offered and presented with the possible advantages, limitations and side effects. In patients at intermediate or high risk, the two options surgery and radiotherapy were equally presented to the patient. Inclusion criteria were histological diagnosis of adenocarcinoma, no distant metastases at clinical staging, RP as chosen primary treatment option, estimated life-expectancy of ≥ 10 years. Exclusion criteria were androgen deprivation therapies,

chemotherapies, pelvic radiation therapies or treatments with other agents that could influence prostate tumor growth. From January 2013 to December 2023, 444 consecutive patients with PC submitted to RP in our Department of Urology by a single surgeon (AS), corresponding to defined inclusion and exclusion criteria were included in our analysis (Table1).

Table 1. Characteristics of the whole population included in the study. Mean \pm SD, median, (range).
Number of cases (%).

Number cases	444
Age (years)	67.49 \pm 6.53; 68: (47-73)
BMI	26.05 \pm 3.55; 26.0: (18.0- 39.40)
Charlson Index	3.86 \pm 1.06; 4: (0-7)
Familiarity	
Yes	35 (7.9%)
no	409(92.1%)
Digital Rectal Examination	
Normal	376 (84.7%)
Suspicious	68 (15.3%)
Preoperative total PSA (ng/ml)	8.61 \pm 5.74; 7.30: (3.0-64.0)
PSAD	0.22 \pm 0.186; 0.17: (0.1-0.59)
Prostate volume (cc)	48.17 \pm 14.79; 45.0: (20.0-120.0)
mMR PIRADS score	(data available in 208 cases)
PIRADS 2	6 (2.9%)
PIRADS 3	44 (21.1%)
PIRADS 4	111 (53.4%)
PIRADS 5	47 (22.6%)
Prostate Tumor size (mm) at mMR	12.8 \pm 6.53; 11.0: (4.0-39.0)
Preoperative CT and bone scan	
No	374 (84.3%)
yes	70 (15.7%)
Preoperative PET CT scan	
no	434 (97.7%)
choline	6 (1.3%)
PSMA	4 (1.0%)
Clinical T staging	
T1	12 (2.7%)
T2a	30 (6.7%)
T2b	192 (43.2%)
T2c	173 (39.0%)
T3a	30 (6.8%)
T3b	7 (1.6%)
T4	0
Clinical N staging	
N0	440 (99.1%)
N1	4 (0.9%)
Number of suspected lymph node at imaging	3.0 \pm 1.4; 3: (2-4)
Prostate biopsy type	
Random	163(36.7%)
Target	17 (3.8%)
Target + random	264 (59.5%)

Prostate biopsy number of cores	12.61±3.65;12 (4-27)
Biopsy outcomes	
% positive samples PC	41.31±26.13; 34: (2-100)
% positive clinical significant PC	53.47±28.5; 50.0: (8.0-100.0)
Max% PC tissue per core	58.35±24.7; 50.0: (6.0-100.0)
Prostate biopsy laterality +	
Monolateral	203 (45.7%)
bilateral	241 (54.3%)
ISUP grading at biopsy	
1	149 (33.6%)
2	135 (30.4%)
3	86 (19.4%)
4	57 (12.8%)
5	17 (3.8%)
Risk Class (D'Amico)	
Low risk	142 (32.0%)
Intermediate risk	200 (45.0%)
High risk	102 (23.0%)
Nomograms results (% estimated risk for N+) in intermediate and high risk cases	
Briganti 2012	23.40±19.11; 17.5: (2-85)
Briganti 2019	17.58±31.4; 12.85: (2-95)
Surgical technique at radical prostatectomy	
Laparoscopic	284 (64%)
Robotic assisted	160 (36%)
Operative time (minutes)	160.05±33.73; 160: (90-300)
Nerve sparing technique at surgery	
No	317 (71.4%)
Yes	127 (28.6%)
Monolateral	52 (40.9%)
Bilateral	75 (59.1%)
Extended lymph node dissection	
no	309 (69.6%)
yes	135 (30.4%)
Pathological stage (T)	
pT2	246 (55.4%)
pT3a	150 (33.8%)
pT3b	48 (10.8%)
pT4	0
Pathological stage (N)	
N0	115 (85.2%)
N+	20 (14.8%)
Number Lymph nodes removed at surgery	
Total cases	17.22±6.81; 18: (4-47)
N+ cases	17.95±9.38; 19: (6-47)
N0 cases	17.07±6.24; 18: (4-35)
Percentage positive lymph nodes in pN+ cases	14.80 ±11.60; 10.4: (4.0-26.6)

Site of positive lymphnodes (number of cases)	
Obturator right	10 (50.0%)
Obturator left	13 (65.0%)
External iliac right	4 (20.0%)
External iliac left	6 (30.0%)
Internal iliac right	7 (35.0%)
Internal iliac left	9 (45.0%)
ISUP grading at surgery	
1	92 (20.7%)
2	183 (41.2%)
3	89 (20.1%)
4	48 (10.8%)
5	32 (7.2%)
Surgical margin at surgery (R)	
Negative	367 (82.7%)
positive	77 (17.3%)
Positive surgical margin site	
apex	31 (40.2%)
lateral	23 (29.9%)
basal	6 (7.8%)
posterior	12 (15.6%)
multiple	5 (6.5%)
Positive surgical margin grading	
3	55 (71.4%)
4	21 (27.3%)
5	1 (1.3%)
Positive surgical margin radial distance (mm)	2.97±1.1; 3 (1-7)
Positive surgical margin	
Single	72 (93.5%)
multiple	5 (6.5%)
PNI at surgery	
positive	269 (60.5%)
negative	175 (39.5%)
Cribriiform/IDC at surgery	
positive	20 (4.5%)
negative	424 (95.5%)
Postoperative hospitalization (days)	3.41±0.56;3 (3-7)
Catheterization time (days)	10.27±2.0; 10: (6-16)
Postoperative anastomotic leakage	
no	441 (99.3%)
yes	3 (0.7%)
Postoperative blood transfusion	
no	442 (99.5%)
yes	2 (0.5%)
Postoperative lymphocele	
no	436 (98.2%)
yes	8 (1.8%)
Postoperative anastomotic stricture	
no	432 (97.3%)
yes	12 (2.7%)
Postoperative rectal injury	

no	444 (100%)
yes	0 (0%)
Postoperative total PSA (ng/ml)(at 1 month)	0.09±0.17; 0.02: (0.01-2.0)
Postoperative follow-up (months)	56.4±37.8; 48 (12-120)
Biochemical progression	
No	391 (88.1%)
Yes	53 (11.9%)
Time to biochemical progression (months)	18.67±24.57;12 (1-48)
Adjuvant therapy	
no	391 (88.1%)
RT	37 (8.3%)
RT+ADT	16 (3.6%)
IIEF-5 preoperative (patients submitted to nerve sparing)	20.75±5.83; 23: (12-25)
Postoperative use of tadalafil	
No	317 (71.4%)
yes	127 (28.6%)
IIEF-5 postoperative (6 months) (patients submitted to nerve sparing)	9.68±3.74; 9: (6-19)
IIEF-5 postoperative (12 months) (patients submitted to nerve sparing)	10.41±24.10; 8: (5-21)
Penile prosthesis	
no	420 (94.6%)
yes	24 (5.4%)
Postoperative Pelvic floor rehabilitation	
no	355 (79.9%)
yes	89 (20.1%)
Postoperative PAD test	
1 months (grams)	99.37±33.0; 20.0: (0-404)
3 months (grams)	45.14±95.9; 4.0 (0-480)
6 months (grams)	34.86±70.5; 2.0 (0-420)
12 months (grams)	14.82±28.7; 0: (0-100)
No PADS postoperative status	407 (91.6%)
Artificial Sphincter	
no	432 (97.3%)
yes	12 (2.7%)

2.2. Clinical Parameters

The whole population of 444 cases is described in Table 1. Patients, after prostatic specific antigen (PSA) increase, were submitted to multiparametric magnetic resonance imaging of the prostate (mMRI) with PI-RADS score determination. Targeted samples on sites indicated by mMRI were associated to random samples in each prostate lobe. Before surgery, clinical staging and risk category (D'Amico and EAU classification) assessment was homogeneously performed, using PSA determination and imaging (mMRI, CT and bone scan, PET-CT scan). Validated predictive nomograms in terms of risk for positive lymph node involvement were used [13,17]. In cases with familiarity and high risk PC, a genetic evaluation for pathogenic variants (PV) of Damage DNA Repair (DDR) genes was performed on surgical samples as part of a prospective trial.

2.3. Pathologic Evaluation

All histological specimens from prostatic biopsy and RP were analyzed by our uro-pathologist with a long experience in PC field. Gleason score and grade groups according to the World Health organization (WHO)/ISUP 2014 guidelines at biopsy and at surgery, pathologic staging using TNM classification, SM status were routinely defined in all cases. In particular, SM were considered positive when carcinoma was transected by an inked SM; this could be in a setting of organ-confined or extracapsular disease.

2.4. Surgical Procedure

Surgical technique was not assigned randomly, and no specific selection was performed regarding the two approaches. As routine clinical practice in our department, each procedure (RARP and LRP) was discussed with the patient and performed by the same single surgeon (AS) who had a high expertise (> 10 years for LRP and > 5 years for RARP) in each approach, consistent with best practice. All surgical procedures (LRP and RARP) were performed using the same intraperitoneal standard technique for RP, starting from the bladder neck and proceeding to the prostate apex. A nerve-sparing (NS) (intrafascial, monolateral or bilateral) procedure was performed based on mMRI results, risk classes, the risk of extracapsular disease and after discussion with the patient on the probability to maintain potency balanced with possible harm. In particular, for either RARP or LRP: - intrafascial NS was performed in cases with low or intermediate risk classes PC, low risk of ipsilateral extracapsular PC extension, good preoperative sexual potency - patients with clinical high-risk of ipsilateral extracapsular disease were excluded from a NS surgery; - extended lymph node dissection (eLND) was performed in all high-risk cases and in the intermediate-risk class in cases with $\geq 5\%$ probability for positive nodes based on predictive nomograms; intra-operative evaluation of SM was not performed; - surgical intraperitoneal technique was equal using RARP or LRP. Intra and perioperative complications were reported, in particular anastomotic leakage, lymphocele, rectal injury, such as operative time, blood transfusion, catheterization time and postoperative hospitalization.

2.5. Functional Analysis

Post-operative functional complications, such as urethral stricture, urinary incontinence (UI) and erectile dysfunction (ED) were analyzed during a follow-up of 12 months. A UI was defined as a persistent urinary leakage ≥ 5 g at a 24-hour pad test. The use of a postoperative pelvic floor rehabilitation and pad test modifications during treatment was described such as the need for an artificial sphincter procedure. A significant ED was defined as an International Index of Erectile Function-5 (IIEF-5) score between 1-10. Postoperative tadalafil rehabilitation was performed in all cases submitted to NS procedure.

2.6. Oncological Outcomes

All patients were followed at regular intervals (each 3 months for the first two years and then every 6 months) to determine time to biochemical (confirmed total PSA progression ≥ 0.2 ng/ml), radiological (radiologically confirmed at PET CT scan and/or mpMRI), local or distant recurrence, as recommended by the EAU guidelines. The decision for adjuvant therapy to surgery or early biochemical progression was taken homogeneously in all cases after discussion in the MDT and based on the EAU guidelines.

2.7. Statistical Analysis

For statistical evaluation SPSS Statistics program was used. Descriptive statistical methods, such as number of cases, mean \pm SD, median and range were used. For the comparison of quantitative data and pairwise intergroup comparisons of variables a Mann Whitney test or ANOVA one-way test were performed. For comparison of qualitative data Fisher's Exact test and chi-square test were used. Univariate and multivariate Cox proportional analysis considering clinical and pathological parameters were used. Statistical significance was evaluated at $p < 0.05$. Kaplan Maier analysis to

define the cumulative rate of risk for biochemical progression was performed in the population stratified on the basis of different variables.

3. Results

Baseline characteristics of the whole population of 444 cases considered for RP are described in Table 1. 284 patients (64.0%) were submitted to a laparoscopic approach (LRP) whereas 160 patients (36.0%) to a robotic assisted surgery (RARP). Mean age of the population was 67.49±6.53 with a range of 47-73 years and mean preoperative total PSA was 8.61±5.74, ranged between 3.0-64.0ng/ml.

An intermediate- and high-risk PC was present in 45.0% and 23.0% of cases, respectively. An eLND was performed in 135 (30.4%) cases (mean number of removed lymph nodes: 17.22±6.81), whereas a NS technique in 127 (28.6%) cases. At the final pathologic evaluation an extracapsular disease (pT3) was found in 44.6% of cases (pT3a 33.8% and pT3b 10.8%). SM+ were found in 77 (17.3%) cases and positive lymph nodes (pN1) in 20 cases (14.8%). Mean surgical operative time was 160.05min (range 90-300), mean time for hospitalization was 3.41±0.56 days (range 3-7 days) and mean time of catheterization was 10.27 days (range 6-16 days). During the first post-operative 12-month follow-up, rates of urethral stricture, blood transfusion and lymphocele were 2.7%, 0.5% and 1.8%, respectively. Mean IIEF-5 changed from a preoperative 20.75±5.83 to a postoperative 10.41±24.10. A no PADS status was obtained in 91.6% of cases after surgery.

Mean postoperative follow-up was 56.4 ±37.8 months (range 12-120) with a 11.9% rate of biochemical recurrence (BCR) at a mean time of 18.67±24.57 months. Adjuvant therapies were prescribed in 11.9 % of cases, radiotherapy (RT) in 8.3% and RT + androgen deprivation therapy (ADT) in 3.6%.

3.1. Differences in Pathological, Oncological and Functional Outcomes according to Surgical Approach

Clinical parameters such as preoperative PSA, prostate tumor size and ISUP grading were not significantly (p>0.50) different between cases submitted to RARP and LRP. A higher percentage (13.8%) of cases submitted to RARP were clinically staged T3 when compared to cases submitted to LRP (5.3%) (p<0.001). Patients undergoing RARP were significantly younger (median 66vs69 years; p<0.001) and had a slightly but significantly higher Charlson Comorbidity Index (CCI) when compared to LRP patients (Table 2).

Table 2. Distribution of preoperative and postoperative parameters on the basis of the surgical approach. Mean±SD, median, (range). Number of cases (%). (LRP= laparoscopic; RARP= robotic assisted).

	LRP	RARP	P value
Number cases	284	160	
Age (years)	68.65±6.582; 69: (48-73)	66.35±5.973; 66 (47-68)	<0.001
BMI	26.17±11.16; 25.6:(17-39.4)	25.127±4.317; 25.0 (17-34)	0.124
Charlson Index	3.34±1.42; 4 (2-7)	4.10±0.722; 4 (0-7)	<0.001
Familiarity			0.217
Yes	25 (8.8%)	10 (6.2%)	
no	259 (91.2%)	150 (93.8%)	
Digital Rectal Examination			0.327
Normal	245 (86.3%)	131 (81.9%)	
Suspicious	39 (13.7%)	29 (18.1%)	
Preoperative total PSA (ng/ml)	8.79±6.175; 7.5: (3.0-64.0)	8.23±4.89; 6.9 (3.0-30.0)	0.328
PSAD	0.16±0.10; 0.14: (0.04-0.59)	0.22±0.18; 0.17 (0.07-0.59)	0.546

Prostate volume (cc)	49.67±16.07; 49.5: (22-120)	47.56±14.39; 45 (20-120)	0.409
mMR PIRADS score (data available in 208 cases)			0.042
PIRADS 2	3 (4.3%)	3 (2.2%)	
PIRADS 3	21 (30.0%)	23 (16.7%)	
PIRADS 4	33 (47.1%)	78 (56.5%)	
PIRADS 5	13 (18.6%)	34 (24.6%)	
Prostate Tumor size (mm) at mMR	10.76±5.11; 10.0: (6-39)	13.59±6.94;12.0 (4-38)	0.10
Preoperative CT and bone scan			0.251
No	245 (86.3%)	129(80.6%)	
yes	39 (13.7%)	31 (19.4%)	
Preoperative PET CT scan			0.117
no	283 (99.6%)	151 (94.3%)	
choline	1 (0.4%)	5 (3.2%)	
PSMA	0	4 (2.5%)	
Clinical T staging			<0.001
T1	9 (3.2)	3 (1.9%)	
T2a	19 (6.7%)	11 (6.9%)	
T2b	110 (38.7%)	82 (51.2%)	
T2c	131 (46.1%)	42 (26.2%)	
T3a	12 (4.2%)	18 (11.3%)	
T3b	3 (1.1%)	4 (2.5%)	
Clinical N staging			0.545
N0	282 (99.3%)	158 (98.7%)	
N1	2 (0.7%)	2 (1.3%)	
Number of suspected lymph node at imaging	4±1.4; 4: (3-4)	2±1.35; 2 (1-3)	0.64
Biopsy outcomes			
% positive samples PC	40.6±26.26; 29: (8-100)	41.60±26.09;35 (4-57)	0.772
Prostate biopsy laterality +			<0.001
Monolateral	102 (35.9%)	101 (63.1%)	
bilateral	182 (64.1%)	59 (36.9%)	
ISUP grading at biopsy			0.610
1	98 (34.5%)	51 (31.9%)	
2	74 (26.1%)	61 (38.1%)	
3	58 (20.4%)	28 (17.5%)	
4	42 (14.8%)	15 (9.4%)	
5	12 (4.2%)	5 (3.1%)	
Risk Class (D'Amico)			0.849
Low risk	92 (32.4%)	50 (31.3%)	
Intermediate risk	126 (44.3%)	74 (46.2%)	
High risk	66 (23.3%)	36 (22.5%)	
Operative time (minutes)	173.33±44.34; 160 (90-300)	153.21±25.11; 142.5 (90-300)	<0.001
Nerve sparing technique at surgery			<0.001

No	223 (78.5%)	94 (58.7%)	0.187
Yes	61 (21.5%)	66 (41.3%)	
Monolateral	27 (43.3%)	25 (31.7%)	
Bilateral	34 (56.7%)	41 (68.3%)	
Extended lymph node dissection			0.160
no	146 (73.2%)	74 (63.1%)	
yes	76 (26.8%)	59 (36.9%)	
Pathological stage (T)			0.910
pT2	157 (55.3%)	89 (55.6%)	
pT3a	91 (32.0%)	59 (36.9%)	
pT3b	36 (12.7%)	12 (7.5%)	
pT4	0	0	
Pathological stage (N)			0.430
N0	64(84.2%)	51 (86.4%)	
N+	12(15.8%)	8 (13.6%)	
Number Lymph nodes removed at surgery			<0.001
Total cases	15.16±7.83; 15: (4-47)	19.83±4.78; 20 (6-34)	
N+ cases	17.45±11.8; 15 (6-47)	19.6±7.1; 20 (6-34)	
N0 cases	14.7±6.8; 14 (4-35)	19.8±4.1; 20 (11-31)	
ISUP grading at surgery			<0.001
1	73 (25.7%)	19 (11.9%)	
2	98 (34.5%)	85 (53.1%)	
3	54 (19.0%)	35 (21.9%)	
4	37 (13.0%)	11 (6.9%)	
5	22 (7.8%)	10 (6.2%)	
Surgical margin at surgery (R)			0.145
Negative	239 (84.1%)	128 (80.0%)	0.037
positive	45 (15.9%)	32 (20.0%)	
Positive surgical margin site			
apex	22 (48.9%)	9 (28.1%)	
lateral	11 (24.4%)	12 (37.5%)	
basal	2 (4.4%)	4 (12.5%)	
posterior	7 (15.6%)	5 (15.6%)	0.225
multiple	3 (6.7%)	2 (6.3%)	
Positive surgical margin grading			0.008
3	34 (75.6%)	21 (65.6%)	
4	11 (24.4%)	10 (31.3%)	
5	0 (0%)	1 (3.1%)	
Positive surgical margin radial distance (mm)	3.45±0.84; 3 (2-6)	2.63±1.14; 2.5 (1-7)	0.762
Positive surgical margin			0.10
Single	42 (93.3%)	30 (93.7%)	
multiple	3 (6.7%)	2 (6.3%)	
PNI at surgery			

positive	179 (62.6%)	90 (56.2%)	
negative	105 (37.4%)	70 (43.8%)	
Cribriiform/IDC at surgery			0.01
positive	7 (2.5%)	13 (8.1%)	
negative	277 (97.5%)	147 (91.9%)	
Postoperative hospitalization (days)	3.75±0.74;3 (3-7)	3.11±0.36;3 (3-5)	0.057
Catheterization time (days)	11.53±1.45; 12 (8-14)	9.60±2.06; 10 (6-16)	<0.001
Postoperative anastomotic leakage			0.245
no	284 (100%)	157 (98.1%)	
yes	0 (0%)	3 (1.9%)	
Postoperative blood transfusion			0.294
no	284 (100%)	158 (98.7%)	
yes	0(0%)	2 (1.3%)	
Postoperative lymphocele			0.16
no	278 (97.9%)	158 (98.7%)	
yes	6 (2.1%)	2 (1.3%)	
Postoperative anastomotic stricture			0.51
no	272 (95.8%)	160 (100%)	
yes	12 (4.2%)	0 (0%)	
Postoperative rectal injury			--
no	284 (100%)	160 (100%)	
yes	0	0	
Postoperative total PSA (ng/ml)(at 1 month)	0.06±0.2; 0.02: (0.01-2.0)	0.04±0.92; 0.02 (0.01-1.0)	0.047
Postoperative follow-up (years)	64.4±28.8; 62 (24-120)	49.2±36.0; 48 (12-120)	0.385
Biochemical progression			0.014
No	243 (85.6%)	148 (92.5%)	
Yes	41 (14.4%)	12 (7.5%)	
Time to biochemical progression (months)	21.77±26.49; 12 (1-120)	18.58±13.2; 13 (1-36)	0.105
Adjuvant therapy			0.55
no	247 (87.0%)	143 (90.0%)	
yes	37 (13.0%)	16 (10.0%)	
Adjuvant therapy type			0.358
-RT	27 (73.0%)	10 (62.5%)	
-RT + ADT	10 (27.0%)	6 (37.5%)	
IIEF-5 postoperative (6 months) (patients submitted to nerve sparing)	9.60±3.78; 9 (6-19)	10.25±3.94; 9.5 (7-15)	0.750
IIEF-5 postoperative (12 months) (patients submitted to nerve sparing)	10.14±4.77; 10 (5-21)	18.0±3.75; 18 (8-18)	0.117
Postoperative Pelvic floor rehabilitation			0.106
no	230 (81.0%)	125 (78.2%)	

yes	54 (19.0%)	35 (21.8%)	
Postoperative PAD test			
1 months (grams)	163.84±222.0; 50 (0-400)	68.17± 374.17; 11 (0-404)	0.680
3 months (grams)	75.57±122.20; 20 (0-480)	14.02±42.09; 0 (0-250)	<0.001
6 months (grams)	39.47±76.08; 5 (0-420)	13.62±28.60; 0 (0-80)	0.023
12 months (grams)	14.76±29.41; 0 (0-100)	15.33±23.2; 1 (0-50)	0.964

The distribution of PC risk classes did not significantly ($p=0.849$) differ between the two groups. In cases submitted to mMR, PIRADS 4 and 5 lesions were more frequent in the RARP group than in the LRP group (56.5% and 24.6% vs 47.1% and 18.6%, respectively; $p=0.042$) (Table 2). At biopsy, the percentage of positive cores did not significantly differ between the two groups ($p=0.772$). The percentage of bilateral positive biopsies was higher in the LRP group ($p<0.01$) (Table 2).

The percentage of cases submitted to a NS procedure was 21.5% and 41.3% respectively ($p<0.01$), whereas the percentage of cases submitted to eLND was 26.8% and 36.9% respectively in the LRP and RARP group ($p=0.56$). In cases submitted to eLND, the mean number of lymph nodes removed was 15.16 ± 7.83 and 19.83 ± 4.78 respectively in LRP and RARP procedures ($p<0.001$). Mean operative time was 173.33 ± 44.3 min and 153.21 ± 25.1 min respectively in LRP and RARP ($p<0.001$) (Table 2).

3.1.1. Pathological Outcomes

The distribution of pathological T stage was not significantly different ($p=0.910$) in the two groups. When an eLND was performed, positive lymph nodes (pN1) were found in 15.8% of LRP patients and 13.6% of RARP patients ($p=0.430$). Pathological ISUP 2 and 3 were more frequent in the RARP group, while the LRP group had a higher percentage of ISUP 1, 4 and 5 cases ($p<0.001$), (Table 2). SM positivity was not significantly higher in RARP group (20.0%) when compared to LRP group (15.9%) ($p=0.145$). In cases submitted to LRP, the highest rate of SM+ was at the apex (48.9%) followed by the lateral site (24.4%), whereas in cases submitted to RARP was at the lateral site (37.5%) followed by the apex (28.1%) ($p=0.037$). Extra-prostatic extension of positive SM was 3.45 ± 0.84 and 2.63 ± 1.14 in the LRP and RARP group respectively ($p=0.008$). SM+ grading was 4 in 24.4% and 31.3% of cases respectively in LRP and RARP procedures ($p=0.225$) (Table 2). During the postoperative follow-up, a BCR was detected in 14.4% and 7.5% of cases in the LRP and RARP group respectively ($p=0.014$) with a similar mean time to progression (21.77 ± 26 months and 18.58 ± 13 months respectively in LRP and RARP) ($p=0.1059$). Kaplan Maier curve describing cumulative biochemical recurrence (BCR) free survival rates according to the surgical approach are showed in Figure 1.

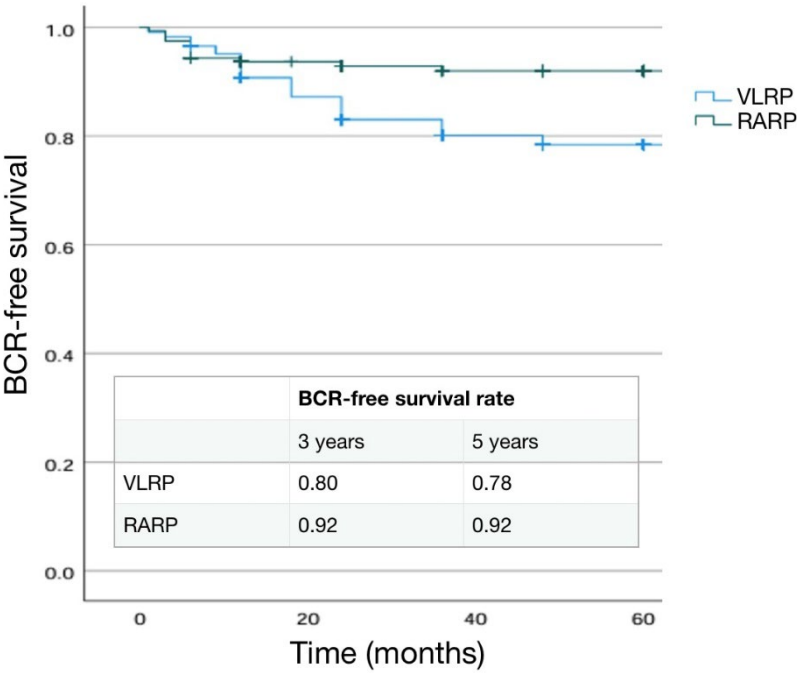


Figure 1. Kaplan Maeier analysis. Estimated rates of Biochemical free-survival (BFS) according to the surgical approach. LRP(Laparoscopic) versus Robotic assisted (RARP).

Adjuvant therapies were prescribed in 13.0% (73.0% RT and 27.0% RT + ADT) and 10.0% (62.5% RT and 37.5%RT+ADT) in LRP and RARP cases respectively (p=0.358) (Table 2).

3.1.2. Functional Outcomes

Postoperative catheterization time was shorter in RARP cases (mean 9.60±2.0) than in LRP cases (mean 11.53±1.45)(p<0.001) (Table 2). The percentage of postoperative side effects after surgery was similar between the two approaches and it is described in Table 2 and 3.

Table 3. a. Postoperative side effects according to the surgical approach (LRP= Laparoscopic versus RARP= Robotic assisted). Number of cases and % of cases. Mean±SD, median, (range).

Parameter	LRP	RARP	P value
Postoperative anastomotic leakage			0.245
No	284(100%)	157 (98.1%)	
yes	0	3 (1.9%)	
Postoperative blood transfusion			0.294
no	284 (100%)	158 (98.7%)	
yes	0	2 (1.3%)	
Postoperative lymphocele			0.16
no	278 (97.9%)	158 (98.7%)	
yes	6 (2.1%)	2 (1.3%)	
Postoperative anastomotic stricture			0.51
no	272 (95.8%)	160 (100%)	
yes	12 (4.2%)	0	
Postoperative rectal injury			x

no	824 (100%)	160 (100%)	
yes	0	0	
Postoperative hospitalization (days)	3.75±0.74; 3 (3-7)	3.11±0.36; 3 (3-5)	0.037
Catheterization time (days)	11.53±1.45; 12 (8-14)	9.60±2.06; 10 (6-16)	<0.001

Table 3. b. Postoperative urinary continence results according to the surgical approach (LRP= Laparoscopic versus RARP= Robotic assisted). Number of cases and % of cases and mean +/- SD, median and range.

Parameter	LRP	RARP	P value
Postoperative Pelvic floor rehabilitation			0.106
no	230 (81.0%)	125 (78.2%)	
yes	54 (19.0%)	33 (21.8%)	
Postoperative PAD test (1 month) (grams)	163.84±222.0; 50 (0-400)	68.17± 374.17; 11 (0-404)	0.68
Postoperative PAD test (3 months) (grams)	75.57±122.20; 20 (0-480)	14.02±42.09; 0 (0-250)	<0.001
Postoperative PAD test (6 months) (grams)	39.47±76.08; 5 (0-420)	13.62±28.60; 0 (0-80)	0.023
Postoperative PAD test (12 months) (grams)	14.76±29.41; 0 (0-100)	15.33±23.2; 1 (0-50)	0.964

Table 3. c. Postoperative Sexual recovery results according to the surgical approach (LRP=Laparoscopic versus RARP=Robotic assisted). Number of cases and % of cases and mean +/- SD, median and range.

Parameter	LRP	RARP	P value
Nerve sparing technique at surgery			<0.001
No	223 (78.5%)	94 (58%)	
Yes	61 (21.5%)	66 (42%)	
Monolateral	27 (43.3%)	25 (31.7%)	0.187
Bilateral	34 (56.7%)	41 (68.3%)	
IIEF-5 postoperative (6 months)	9.60±3.78; 9 (6-19)	10.25±3.94; 9.5 (7-15)	0.750
IIEF-5 postoperative (12 months)	10.14±4.77; 10 (5-21)	18.0±3.75; 18 (18-18)	0.117

Postoperative pelvic floor rehabilitation was used in 19.0% and 21.8% of cases respectively in LRP and RARP groups (p=0.106) (Table 2 and 3). Postoperative PAD test was similar at 1- and 12-month intervals (p>0.05) between LRP and RARP procedures, whereas better results at 3-month interval using RARP approach (mean pad weight 75.57±122 grams and 14±42 grams respectively in LRP and RARP (p<0.01)) were described (Table 3). In cases submitted to NS procedures, IIEF5 mean score was 9.60±3.78 at 6-month and 10.14±4.77 at 12-month interval for LRP group and 10.25±3.94 and 18.0±3.75 for RARP group (p>0.05) (Table 2,3).

3.1.3. Main Significant Differences in Results

In the RARP group: - higher percentage of NS procedure; - higher mean number of lymph nodes removed; - lower mean operative time; - higher (but not statistically significant) rate of SM+; lower

rate of BCR; lower catheterization time; lower mean pad weight at 3- and 6-month interval; higher (but not statistically significant) IIEF-5 score at 12-month.

3.2. Differences in Pathological, Oncological and Functional Outcomes according to Risk Classes

The distribution of the population according to the risk classes showed 142 cases (32.0%) in the low, 200 cases (45.0%) in the intermediate and 102 cases (23.0%) in the high risk class. Clinical parameters such as age, BMI and Charlson Index were not significantly ($p>0.50$) different between the 3 classes (Table 4).

Table 4. Distribution of preoperative and postoperative parameters on the basis of risk classes.
Mean \pm SD, median, (range). Number of cases (%).

	Low risk	Intermediate Risk	High risk	P value
Number cases	142	200	102	
Age (years)	67.73 \pm 6.60; 67: (50-73)	67.42 \pm 6.61; 68 (49-22)	67.46 \pm 6.12; 69 (47-71)	0.906
BMI	25.73 \pm 3.70; 25.3 (18-37)	25.84 \pm 3.35; 25.4 (18.5- 37)	26.81 \pm 3.63; 26 (21-39.4)	0.121
Charlson Index	3.82 \pm 1.02; 4 (2-7)	3.89 \pm 1.08; 4 (0-7)	3.88 \pm 1.06; 4 (1-6)	0.903
Familiarity				0.138
Yes	0	19 (9.5%)	17 (16.7%)	
no	142 (100%)	181 (90.5%)	85 (83.3%)	
Digital Rectal Examination				<0.001
Normal	134 (94.4%)	176 (88.0%)	66 (64.7%)	
Suspicious	8 (5.6%)	24 (12.0%)	36 (35.3%)	
Preoperative total PSA (ng/ml)	6.73 \pm 3.12;6.4 (3.0-19.0)	8.41 \pm 3.91;7.5 (3.0-23.0)	11.74 \pm 9.3;9.3 (3.0-64.0)	<0.001
PSAD	0.14 \pm 0.49;0.13 (0.08-0.26)	0.23 \pm 0.17;0.19 (0.06-0.54)	0.3 \pm 0.3;0.24 (0.11-0.59)	0.048
Prostate volume (cc)	47.78 \pm 15.48;45 (25-120)	47.4 \pm 13.72;45 (20-87)	51.53 \pm 16.77; 52.5 (25-90)	0.403
mMR PIRADS score (data available on 208 cases)				<0.001
PIRADS 2	6 (10.7%)	0 (0%)	0 (0%)	
PIRADS 3	14 (25.0%)	26 (26.2%)	4 (7.7%)	
PIRADS 4	32 (57.1%)	58 (58.6%)	20 (38.5%)	
PIRADS 5	4 (7.2%)	15 (15.2%)	28 (53.8%)	
Prostate Tumor size (mm) at mMR	10.15 \pm 4.78; 9.5 (4.0-30.0)	11.83 \pm 4.66; 10 (5.0-27.0)	18.25 \pm 8.72; 16 (7.0-39.0)	<0.001
Preoperative CT and bone scan				<0.001
No	133 (93.7%)	88 (87.5%)	66 (64.8%)	
yes	9 (6.3%)	25 (12.5)	36 (35.2%)	
Preoperative PET CT scan				0.027
no	142 (100%)	195 (97.5%)	97 (95.1%)	
choline	0	4 (2.0%)	2 (2.0%)	
PSMA	0	1 (0.5%)	3 (2.9%)	

Surgical technique at radical prostatectomy				0.850
Laparoscopic	92 (64.8%)	126 (63.0%)	66 (64.7%)	
Robotic assisted	50 (35.2%)	74 (37.0%)	36 (35.3%)	
Operative time (minutes)	150.50±27.35;140 (120-300)	155.0±20.06;157.5 (90-210)	183.51±50.711; 175 (90-300)	<0.001
Nerve sparing technique at surgery				<0.001
No	73 (51.4%)	145 (72.5%)	99 (97.0%)	
Yes	69 (48.6%)	55 (27.5%)	3 (3.0%)	
Monolateral	19 (27.5%)	31 (56.4%)	2 (66.7%)	<0.001
Bilateral	50 (72.5%)	24 (43.6%)	1 (33.3%)	
Extended lymph node dissection				<0.001
no	142 (100%)	167 (83.5%)	0 (0%)	
yes	0 (0%)	33(16.5%)	102(100%)	
Pathological stage (T)				<0.001
pT2	110 (77.5%)	108 (53.0%)	28 (27.4%)	
pT3a	28 (19.7%)	80 (39.9%)	42 (41.2%)	
pT3b	4 (2.8%)	12 (7.1%)	32 (31.4%)	
Pathological stage (N)				<0.001
N0	--	26 (73.1%)	89 (87.2%)	
N+		7 (26.9%)	13 (12.8%)	
ISUP grading at surgery				<0.001
1	75 (52.8%)	14 (7.0%)	3 (2.9%)	
2	57 (40.2%)	109 (54.5%)	17 (16.7%)	
3	9 (6.3%)	58 (29.0%)	22 (21.6%)	
4	1 (0.7%)	12 (6.0%)	35 (34.5%)	
5	0 (0%)	7 (3.5%)	25 (24.5%)	
Surgical margin at surgery (R)				0.003
Negative	129 (90.8%)	162(80.8%)	76 (74.5%)	
positive	13 (9.2%)	38 (19.2%)	26 (25.5%)	
Positive surgical margin grading				<0.001
3	13 (100%)	33 (86.8%)	9 (34.6%)	
4	0 (0%)	5 (13.2%)	16 (61.5%)	
5	0 (0%)	0 (0%)	1 (3.9%)	
Positive surgical margin radial distance (mm)	2.86±0.945; 3 (2-4)	2.65±0.89; 2.5 (2-6)	3.34±1.25; 3 (1-7)	0.104
Postoperative total PSA (ng/ml)(at 1 month)	0.03±0.08; 0.02 (0.01-1.0)	0.04±0.093; 0.02 (0.01-1.0)	0.12±0.3; 0.03 (0.01-2.0)	<0.001
Biochemical progression				<0.001
-No	136 (95.8%)	183 (91.5%)	72 (70.6%)	
-Yes	6 (4.2%)	17 (8.5%)	30 (29.4%)	
Time to biochemical progression (months)	19.0±15.83; 15 (6-48)	23.88±28.22; 18 (1-120)	15.72±24.12; 6 (1-4120)	0.576

Adjuvant therapy no	139 (97.9%)	186 (93.0%)	66 (64.7%)	<0.001
yes	3 (2.1%)	14 (7.0%)	36 (35.3%)	
Adjuvant therapy type				0.290
-RT	3 (100%)	13 (92.9%)	21 (58.3%)	
-RT + ADT	0	1 (7.1%)	15 (41.7%)	

Mean preoperative PSA significantly increased with increasing risk classes ($p<0.001$). In cases submitted to mMR, the highest percentages of PIRADS 4 and 5 lesions were found respectively in the intermediate and high risk groups ($p<0.01$) (Table 4).

A similar proportion of cases was submitted to LRP versus RARP in the three classes ($p=0.850$). The percentage of cases submitted to a NS procedure was 48.6%, 27.5% and 3.0% respectively in the low, intermediate and high risk class, whereas the percentage of cases submitted to eLND in the intermediate class (based on a risk $> 5\%$ at predictive nomogram) was 16.5% and 100% in the high risk class; ($p<0.001$). Operative time was shorter in low risk cases (mean 150.50 ± 27.35 min) when compared to intermediate (mean 155.0 ± 20.06 min) and high risk cases (mean 183.51 ± 50.71 min) ($p<0.001$). (Table 4).

3.2.1. Pathological Outcomes

The distribution of pathological ISUP varied greatly between the three groups, with only one patient in the low risk class with a pathological ISUP of 4-5 and only 3 patients in the high risk group with a pathological ISUP of 1 ($p<0.01$). When an eLND was performed, positive lymph nodes (pN1) were found in a higher percentage of cases in the intermediate risk group when compared with the high risk class (26.9%vs12.8%; $p<0.01$) (Table 4). SM positivity was higher in the high risk group (25.5%) when compared to the intermediate (19.2%) and low risk (9.2%) ($p=0.003$). SM+ grading was 4 in 0%, 13.2% and 61.5% of cases respectively in low, intermediate and high risk cases ($p<0.00$)(Table 4).

A BCR was detected in 4.2%, 8.5% and 29.4% of cases in the low, intermediate and high risk group respectively with a similar mean time to progression (19.0 ± 15.83 months, 23.88 ± 28.22 months and 15.72 ± 24.12 months respectively).Adjuvant therapies were prescribed in 2.1% (100% RT), 7.0% (92.9% RT and 7.1% RT + ADT) and 35.3% (58.3% RT and 41.7%RT+ADT) in low, intermediate and high risk cases respectively ($p<0.001$) (Table 4).

3.2.2. Main Significant Differences in Results

Increasing risk class: -increase in operative time; - increase in SM+ rate, SM+ grading; -increase in BRC rate, use of adjuvant therapies.

3.3. Differences in Pathological, Oncological and Functional Outcomes according to pT Stage

A pathologic extraprostatic tumor was found in 198 cases (44.9%) with pT3a in 34.0% and pT3b in 10.8% of cases. Preoperative PSA significantly ($p<0.001$) increased from pT2 to pT3b cases (Table 5).

Table 5. Distribution of preoperative and postoperative parameters on the basis of pT. Mean \pm SD, median, (range). Number of cases (%).

	pT2	pT3a	pT3b	P value
Number cases	246	150	48	
Age (years)	66.76 \pm 6.45; 67 (48-71)	68.25 \pm 6.587; 68 (47-72)	68.79 \pm 6.75; 68 (54-73)	0.032
BMI	25.71 \pm 3.56; 25.3 7-37.2)	26.25 \pm 3.41; 25.7 (19-39.4)	27.21 \pm 3.8; 26.1 (19-37)	0.077
Charlson Index	3.77 \pm 1.08; 4 (0-7)	4.05 \pm 1.01; 4 (0-7)	3.8 \pm 1.05; 4 (1-6)	0.179

Familiarity				0.211
Yes	14 (5.7%)	15 (10%)	6 (12.5%)	
no	232 (94.3%)	135 (90%)	42 (87.5%)	
Digital Rectal Examination				<0.001
Normal	226 (91.9%)	118 (78.7%)	52 (66.7%)	
Suspicious	20 (8.1%)	32 (21.3%)	16 (33.3%)	
Preoperative total PSA (ng/ml)	7.64±4.52;6.85 (3.0-48.0)	8.59±4.77;7.5 (3.0-33.0)	13.55±10.14; 11.2 (4.0-64.0)	<0.001
PSAD	0.19±0.15;0.15 (0.1-0.50)	0.22±0.15;0.18 (0.1-0.59)	0.35±0.36; 0.23 (0.1-0.50)	0.112
Prostate volume (cc)	48.0±4.53; 45 (20-120)	49.08±14.4;47 (24-90)	43.91±15.87;40 (25-75)	0.56
mMR PIRADS score				0.01
PIRADS 2	6 (5.2%)			
PIRADS 3	31 (26.9%)	11 (15.1%)	2 (10.0%)	
PIRADS 4	61 (53.1%)	41 (56.2%)	9 (45.0%)	
PIRADS 5	17 (14.8%)	21 (28.7%)	9 (45.0%)	
Prostate Tumor size (mm) at mMR	10.9±4.78; 10 (4-30)	14.10±5.98; 12 (5-35)	20.53±11.33; 18 (8-39)	<0.001
Clinical T staging				<0.001
T1	8 (3.2%)	4 (2.7%)	0	
T2a	29 (11.8%)	1 (0.6%)	0	
T2b	106 (43.1%)	76 (50.7%)	10 (20.8%)	
T2c	96 (39.0%)	51 (34.0%)	26 (54.2%)	
T3a	7 (2.9%)	18 (12.0%)	5 (10.4%)	
T3b	0	0	7 (14.6%)	
Biopsy outcomes				<0.01
% positive samples PC	33.15±21.7.25 (5-100)	48.11±26.58; 44 (2-100)	59.66±29.42; 52.5 (10-100)	
ISUP grading at biopsy				<0.001
1	113 (45.9%)	31 (20.7%)	5 (10.4%)	
2	77 (31.4%)	50 (33.3%)	8 (16.7%)	
3	34 (13.8%)	37 (24.7%)	15 (31.3%)	
4	20 (8.1%)	24 (16%)	13 (27.0%)	
5	2 (0.8%)	8 (5.3%)	7 (14.6%)	
Surgical technique at radical prostatectomy				0.193
Laparoscopic	157 (63.8%)	91 (60.7%)	36 (75.0%)	
Robotic assisted	89 (36.2%)	59 (39.3%)	12 (25.0%)	
Operative time (minutes)	159.02±35.57;160 (90-300)	160.42±33.21; 160 (90-300)	165.28±26.53; 177.5 (100-200)	0.764
Pathological stage (N)				<0.01
N0	11 (100%)	68 (88.9%)	36 (75.0%)	
N+	0 (0%)	8 (11.1%)	12 (25.0%)	
ISUP grading at surgery				<0.001
1	85 (34.6%)	7 (4.7%)	0	
2	114 (46.3%)	65 (43.3%)	4 (8.3%)	
3	32 (13.0%)	39 (26.0%)	18 (37.5%)	

4	13 (5.3%)	27 (18.0%)	8 (16.7%)	
5	2 (0.8%)	12 (8.0%)	18 (37.5%)	
Surgical margin at surgery (R)				<0.001
Negative	218 (88.6%)	119 (79.2%)	30 (62.5%)	
positive	28 (11.4%)	31 (20.8%)	18 (37.5%)	
Positive surgical margin grading				0.001
3	24 (85.7%)	25 (80.6%)	6 (33.3%)	
4	4 (14.3%)	5 (16.2%)	12 (66.7%)	
5	0 (0%)	1 (3.2%)	0 (0%)	
Positive surgical margin radial distance (mm)	2.72±0.966; 3 (1-4)	2.67±0.84; 3 (2-5)	3.71±1.28; 3.5 (2-7)	0.01
PNI at surgery				<0.001
positive	103 (41.9%)	123 (82.0%)	43 (89.6%)	
negative	143 (58.1%)	27 (18.0%)	5 (10.4%)	
Cribriform/IDC at surgery				0.001
positive	2 (0.8%)	10 (6.7%)	8 (16.7%)	
negative	244 (99.2%)	140 (93.3%)	40 (83.3%)	
Postoperative total PSA (ng/ml)(at 1 month)	0.03±0.31;0.02 (0.01-0.1)	0.05±0.143; 0.02 (0.01-1.0)	0.21±0.419; 0.04 (0.01-2.0)	<0.001
Biochemical progression (number of cases and %)				<0.001
-No	234 (95.1%)	127 (84.7%)	30 (62.5%)	
-Yes	12 (4.9%)	23 (13.3%)	18 (37.5%)	
Time to biochemical progression (months)	34.25±42.26; 15 (3-120)	16.1±11.38; 12 (1-36)	11.28±15.18; 2 (1-48)	0.032
Adjuvant therapy				<0.001
no	242(98.4%)	133 (88.7%)	16 (33.3%)	
yes	4 (1.6%)	17 (11.3%)	32 (62.7%)	
Adjuvant therapy type				0.033
-RT	4 (100%)	14 (82.4%)	19 (59.5%)	
-RT + ADT	0	3 (17.6%)	13 (40.6%)	

In cases submitted to mMR, the percentage of PIRADS 5 lesion significantly increased with increasing pT stage ($p=0.01$) (Table 5). At biopsy, the percentage of positive cores, bilateral incidence, and ISUP 4-5 were significantly higher ($p<0.001$) in the pT3 groups (Table 5). A similar proportion of cases was submitted to LRP or RARP approach with similar mean operative times in pT2 and pT3 cases ($p>0.05$) (Table 5).

3.3.1. Pathological Outcomes

The percentage of ISUP 4-5 PC at surgery increased with pathological stage ($p<0.001$), as the percentage of positive lymph node (pN1) (0% in pT2, 11.1% in pT3a and 25.0% in pT3b; $p<0.01$) (Table 5). SM positivity was higher in the pT3b (37.5%) than in pT3a (20.8%) and pT2 (11.4%) cases ($p<0.001$). pT3b patients demonstrated a significantly longer mean extra-prostatic extension of SM+ (3.71±1.28) than the other groups ($p=0.01$), and SM+ grading was 4 in 14.3%, 16.2% and 66.7% of cases respectively in pT2, pT3a and pT3b cases ($p=0.001$) (Table 5). A BCR was detected in 4.9%, 13.3% and 37.5% of cases in the pT2, pT3a and pT3b group respectively with a shorter mean time to progression in the pT3b group (34.25±42.2, 16.1±11.3 and 11.28±15.1 in the pT2, pT3a and pT3b groups, respectively; $p=0.032$). Adjuvant therapies were prescribed in 1.6% (100% RT), 11.3% (82.4% RT and 17.6% RT+ADT) and 62.7% (59.5% RT and 40.6%RT+ADT) in pT2, pT3a and pT3b cases respectively

($p < 0.001$) (Table 5). Kaplan Maier curve describing cumulative biochemical recurrence (BCR) free survival rates according to pT stage are showed in Figure 2

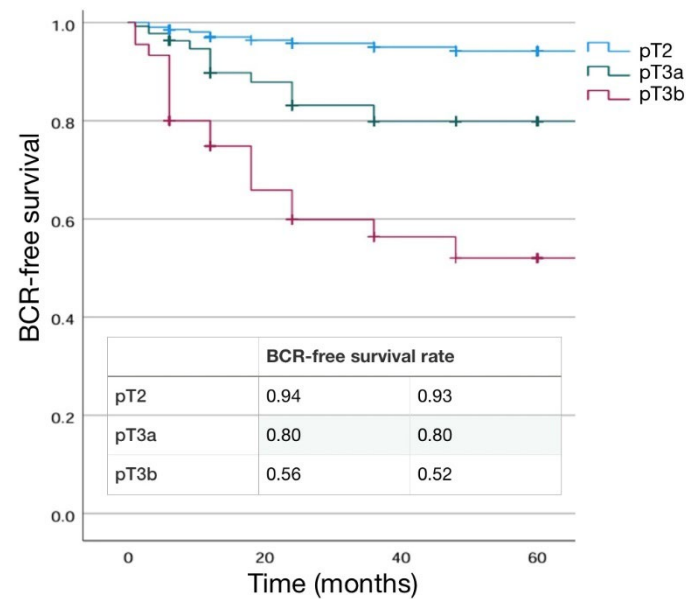


Figure 2. Kaplan Maeier analysis. Estimated rates of Biochemical free-survival (BFS) according to the pT stage.

3.3.2. Main Significant Differences in Results

Increasing pT stage: - increase in preoperative PSA; - increase in PIRADS 5 lesions and percentage of positive biopsy cores; - increased rate of positive lymph nodes (pN+), SM+; increase in SM+ grading, BCR rate, use of adjuvant therapies.

3.4. Differences in Pathological, Oncological and Functional Outcomes according to pN Stage

A low percentage (14.8%) of cases submitted to eLND showed pathological lymph node involvement, with a similar distribution between LRP (15.8%) and RARP (13.6%) approach. Clinical parameters such as age, BMI and Charlson index were not significantly ($p > 0.50$) different between pN0 and pN1 cases (Table 6).

Table 6. Distribution of preoperative and postoperative parameters on the basis of pN status. Mean \pm SD, median, (range). Number of cases (%).

	pN0	pN1	P value
Number cases	115	20	
Age (years)	66.16 \pm 6; 67 (47-72)	67.37 \pm 6.66; 68 (56-71)	0.40
BMI	26.1 \pm 3.3; 25.1 (19-39.4)	27.01 \pm 3.86; 26.65 (19.32-8)	0.41
Charlson Index	3.75 \pm 1.14; 4 (0-7)	4 \pm 0.6; 4 (3-5)	0.454
Familiarity			0.145
Yes	3 (1.5%)	10 (50.0%)	
no	201 (98.5%)	10 (50.0%)	
Digital Rectal Examination			<0.001
Normal	156 (76.5%)	9 (45.0%)	
Suspicious	48 (23.5%)	11 (55.0%)	
Preoperative total PSA (ng/ml)	8.72 \pm 5.29; 7.5 (3.0-48.0)	16.54 \pm 8.83; 16 (5.0-30.0)	<0.001

PSAD	0.22±0.175; 16 (0.1-0.6)	0.51±0.441;0.33 (0.1-0.7)	0.012
Prostate volume (cc)	48.38±15.21; 47 (20-120)	53.11±21.86;50 (25-90)	0.386
Prostate Tumor size (mm) at mMR	11.94±4.77; 10 (5-28)	27.7±10.47;30 (11-39)	<0.001
Clinical T staging			<0.001
T1	4 (3.5%)	0	
T2a	12 (10.4%)	0	
T2b	45 (39.1%)	3 (15.0%)	
T2c	29 (25.2%)	8 (40.0%)	
T3a	21 (18.3%)	6 (30.0%)	
T3b	4 (3.5%)	3 (15.0%)	
Clinical N staging			<0.001
N0	114 (99.1%)	17 (85.0%)	
N1	1 (0.9%)	3 (15.5%)	
Number of suspected lymph node at imaging	2±1; 2 (1-3)	4±1; 4 (3-4)	0.21
Nomograms results (% risk for N+)			
Briganti 2012	24.5±17.12; 17: (2-82)	26.4±15.46; 20: (7-85)	0.175
Briganti 2019	23.4±16.45; 16: (2-82)	26.9±21.36; 21: (4-78)	0.143
Biopsy outcomes			0.001
% positive samples PC	38.78±24.76; 30 (2-100)	72.54±24.7;75 (35-100)	
ISUP grading at biopsy			0.304
1	7 (6.1%)	1 (5.0%)	
2	10 (8.7%)	5 (25.0%)	
3	42 (36.5%)	6 (30.0%)	
4	43 (37.4%)	6 (30.0%)	
5	13 (11.3%)	2 (10.0%)	
Surgical technique at radical prostatectomy			0.62
Laparoscopic	64 (55.6%)	12 (60.0%)	
Robotic assisted	51 (44.4%)	8 (40.0%)	
Operative time (minutes)	166.01±34.74; 160 (90-300)	170±26.06;175 (135-220)	0.68
Pathological stage (T)			<0.001
pT2	11 (9.6%)	0	
pT3a	68 (59.1%)	8 (40.0%)	
pT3b	36 (31.3%)	12 (60.0%)	
Number Lymph nodes removed at surgery			0.60
Total cases	17.07±6.24; 18 (2-35)	17.95±9.38; 18.5 (6-47)	
Site of positive lymphnodes			--
Obturator	---	20 (100%)	

External iliac		8 (40.0%)	
Internal iliac		9 (45.0%)	
ISUP grading at surgery			0.001
1	1 (0.9%)	0	
2	14 (12.2%)	2 (10.0%)	
3	44 (38.2%)	8 (40.0%)	
4	36 (38.3%)	2 (10.0%)	
5	20 (17.4%)	8 (40.0%)	
Surgical margin at surgery (R)			0.001
Negative	83 (72.1%)	11 (55.0%)	
positive	32 (27.9%)	9 (45.0%)	
Positive surgical margin grading			0.384
3	19 (59.4%)	4 (44.4%)	
4	12 (37.5%)	5 (55.6%)	
5	1 (3.1%)	0 (0%)	
Positive surgical margin radial distance (mm)	3.03±1; 3 (1-7)	3.79±1.72; 3 (1-7)	0.136
PNI at surgery			0.02
positive	70 (60.9%)	4 (15.8%)	
negative	45 (39.1%)	16 (84.2%)	
Cribriform			<0.001
negative	105 (91.3%)	14 (73.7%)	
positive	10 (8.7%)	6 (26.3%)	
Postoperative total PSA (ng/ml)(at 1 month)	0.05±0.19; 0.02 (0.01-2.0)	0.28±0.376;0.09 (0.01-1.0)	<0.001
Biochemical progression			<0.001
-No	94 (81.7%)	9 (45.0%)	
-Yes	21 (18.3%)	11 (55.0%)	
Time to biochemical progression (months)	28.3±34.6; 12 (1-120)	4.18±7.37; 3 (1-24)	0.030
Adjuvant therapy			<0.001
no	85 (73.9%)	6 (30.0%)	
yes	30 (26.1%)	14 (70.0%)	
Adjuvant therapy type			<0.001
-RT	24 (80.0%)	4 (28.6%)	
-RT + ADT	6 (20.0%)	10 (71.4%)	

Mean total PSA was significantly higher in pN1 patients (16.54±8.83 vs 8.72±5.29 in the pN1 and pN0 groups, respectively; $p<0.001$) (Table 6). A clinical suspicious for lymph node involvement at preoperative imaging was found in 0.9% of cases in pN0 and 15.5% of cases in pN1 cases ($p<0.001$). At biopsy, the percentage of positive cores and bilateral incidence were significantly higher ($p=0.001$) in the pN1 group. The distribution of ISUP grading ($p=0.304$) and mean and median nomograms results were similar between pN0 and pN1 groups ($p>0.05$) (Table 6).

3.4.1. Pathological Outcomes

The mean number of lymph nodes removed was similar in the two groups ($p=0.60$). In pN1 cases the site of positive lymph nodes (pN+) was obturator (100%), internal iliac (45.0%) and external iliac (40.0%). (Table 6). The percentage of pathological ISUP 5, pT3b stage and PNI were significantly higher in pN1 patients ($p=0.001$, 0.001 and 0.02 respectively) (Table 6). Also SM positivity was higher in the pN1group (45.0%) than in pN0 (27.9%) cases ($p=0.001$) and SM+ grading was 4 in 37.5% and

55.6% of cases respectively in pN0 and pN1 cases (p=0.384)(Table 6). A BCR was detected in 18.3% and 55.0% of cases in the pN0 and pN1 group respectively (p<0.001) with a shorter mean time to progression in the pN1 group (4.18±7.37 months and 28.3±34.6 months respectively in pN1 and pN0). Adjuvant therapies were prescribed in 26.1% (80% RT and 20% RT + ADT) and 70.0% (28.6% RT and 71.4%RT+ADT) in pN0 and pN1 cases respectively (p<0.001) (Table 6). Kaplan Maier curve describing cumulative biochemical recurrence (BCR) free survival rates according to the pN stage are showed in Figure 3

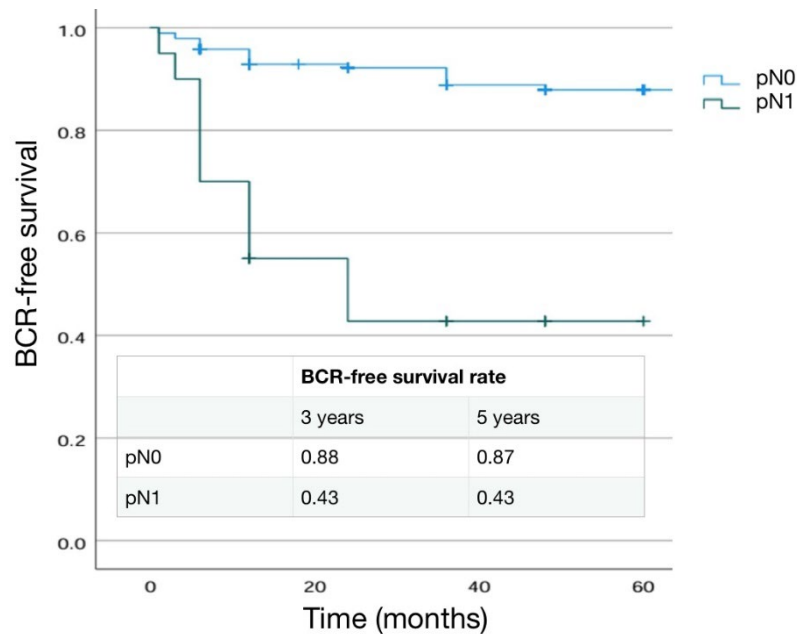


Figure 3. Kaplan Maeier analysis. Estimated rate of Biochemical free-survival (BFS) according to the pN stage.

3.4.2. Main Significant Differences in Results

In pN1 cases: - higher clinical suspicious cN1; higher preoperative PSA and percentage of positive core at biopsy; - higher pT3b rate, ISUP 5 rate, SM+ rate and SM+ grading; - higher BCR rate and use of adjuvant therapies.

3.5. Differences in Pathological, Oncological and Functional Outcomes according to Surgical Margins

Positive surgical margins were found in 17.3% of cases with a no significant difference between the LRP (15.9%) and the RARP (20.0%) group (p=0.145). Clinical parameters such as age, Charlson Index and BMI were not significantly (p>0.50) different between SM- and SM+ cases (Table 7).

Table 7. Distribution of preoperative and postoperative parameters on the basis of Surgical margins (SM). Mean±SD, median, (range). Number of cases (%).

	Negative SM	Positive SM	P value
Number cases	367	77	
Age (years)	67.44±6.62; 68 (47-73)	67.78±6.14; 69 (52-72)	0.68
BMI	25.88±3.44; 25,4 (18.0-39.4)	26.89±4.04; 26.2 (19-37)	0.83
Charlson Index	3.81±1; 4 (0-7)	4.14±0.93; 4 (1-6)	0.7
Familiarity			0.96
Yes	23 (6.3%)	12 (15.6%)	
no	344 (93.7%)	65 (84.4%)	
Digital Rectal Examination			0.01

Normal	315 (85.8%)	61 (79.2%)	
Suspicious	52 (14.2%)	16 (20.8%)	
Preoperative total PSA (ng/ml)	8.0±1.07; 4 (3.0-7.0)	11.54±8.8;9.6 (3.0-64.0)	<0.001
PSAD	0.21±0.14; 0.17 (0.1-0.50)	0.28±0.318;0.18 (0.2-0.59)	0.253
Prostate volume (cc)	47.78±14.65; 445 (20-120)	49.97±15.77;46.5 (25-90)	0.452
Prostate Tumor size (mm) at mMR	11.98±5.66; 10 (4-39)	16.52±8.67; 14 (5-38)	<0.001
Clinical T staging			<0.001
T1	12 (3.2%)	0	
T2a	30 (8.2%)	0	
T2b	160 (43.6%)	32 (42.1%)	
T2c	142 (38.7%)	31 (39.5%)	
T3a	22 (6.0%)	8 (10.5%)	
T3b	1 (0.3%)	6 (7.9%)	
Clinical N staging			0.002
N0	366 (99.7%)	74 (96.1%)	
N1	1 (0.3%)	3 (3.9%)	
Biopsy outcomes			
% positive samples PC	38.31±25.167; 30 (5-100)	54.664±26.78;50 (2-100)	<0.001
ISUP grading at biopsy			0.14
1	131 (35.7%)	18 (23.4%)	
2	107 (29.1%)	28 (36.4%)	
3	69 (18.7%)	17 (22.0%)	
4	50 (13.6%)	7 (9.1%)	
5	10 (2.7%)	7 (9.1%)	
Surgical technique at radical prostatectomy			0.345
Laparoscopic	239 (65.1%)	45 (59.2%)	
Robotic assisted	128 (34.9%)	32 (40.8%)	
Operative time (minutes)	160.03±36.02; 160 (90-300)	160.63±22.39;160 (120-220)	0.92
Nerve sparing technique at surgery			0.450
No	259 (70.4%)	5	
Yes	108 (29.6%)	8 (74.7%)	
Monolateral	42 (38.9%)	19 (25.3%)	
Bilateral	66 (61.1%)	10 (52.6%)	0.230
		9 (47.4%)	
Pathological stage (T)			<0.001
pT2	218 (59.4%)	28 (36.4%)	
pT3a	119 (32.4%)	31 (40.2%)	
pT3b	30 (8.2%)	18 (23.4%)	
ISUP grading at surgery			0.006
1	84 (23%)	8 (10.4%)	
2	152 (41.3%)	31 (40.3%)	

3	70 (18.9%)	19 (24.7%)	
4	41 (11.2%)	7 (9.1%)	
5	20 (5.7%)	12 (15.6%)	
Positive surgical margin site apex lateral basal posterior multiple		31(40.2%) 23 (29.9%) 6 (7.8%) 12 (15.6%) 5 (6.5%)	--
Positive surgical margin grading 3 4 5		55 (71.4%) 21 (27.3%) 1 (1.3%)	--
Positive surgical margin radial distance (mm)	x	2.97±1.1; 3 (1-7)	--
PNI at surgery positive negative	215 (58.5%) 152 (41.5%)	54 (70.1%) 23 (29.9%)	0.05
Cribriiform/IDC at surgery positive negative	12 (3.3%) 355 (96.7%)	8 (10.4%) 69 (89.6%)	0.20
Postoperative total PSA (ng/ml)(at 1 month)	0.04±0.97; 0.02 (0.01-1.0)	0.13±3.4;0.03 (0.01-2.0)	<0.001
Biochemical progression -No -Yes	338 (92.1%) 29 (7.9%)	53 (68.8%) 24 (31.2%)	<0.001
Time to biochemical progression (months)	25.45±29.4; 18 (1-120)	9.73±11.57; 4.5 (1-48)	0.022
Adjuvant therapy no yes	359 (91.6%) 10 (8.4%)	34 (44.1%) 43 (55.9%)	<0.001
Adjuvant therapy type -RT -RT + ADT	4 (40.0%) 6 (60.0%)	33 (76.7%) 10 (23.3%)	0.037

The SM+ group had a significantly higher mean preoperative PSA (11.54±8.8 vs 8±1.07; $p<0.001$). A higher percentage of clinical stage cT1, cT2a and cT2b in the SM- group and a higher percentage of cT2c, cT3a and cT3b cases in the SM+ group was present ($p<0.001$) (Table 7). At biopsy the percentage of positive cores was significantly higher ($p<0.001$) in the SM+ group. The distribution of ISUP grading was similar between SM- and SM+ groups ($p=0.14$) (Table 7).

The percentage of cases submitted to a NS procedure was 29.6% and 25.3% respectively ($p=0.450$) and mean operative time was 160.03±36.02 min and 160.63±22.39 min respectively in SM- and SM+ ($p=0.92$) (Table 7).

3.5.1. Pathological Outcomes

The distribution of pathological ISUP grading and T stage were significantly different ($p=0.006$ and <0.001 respectively) in the two groups. In particular, pT3 cases were more frequent in SM+ patients than in SM- patients (63.6% and 40.6%) (Table 7). The site for positive SM was posterior-lateral in 45.5% of cases, basal in 7.8% and apex in 40.2% of cases. Median extra-prostatic radial extension of positive SM was 3mm (range 1-7) and SM+ grading was 4 in 27.3% and 3 in 71.4% of

cases (Table 7). A BCR was detected in 7.9 % and 31.2% of SM- and SM+ cases respectively with a shorter mean time to progression in SM+ cases (25.45 ± 29.4 months and 9.73 ± 11.57 months respectively in SM- and SM+). Adjuvant therapies were prescribed in 8.4% (40% RT and 60% RT + ADT) and 55.9% (76.7% RT and 23.3%RT+ADT) in SM- and SM+ cases respectively ($p<0.001$)(Table 7). Kaplan Maier curve describing cumulative biochemical recurrence (BCR) free survival rates according to the SM status are showed in Figure 4

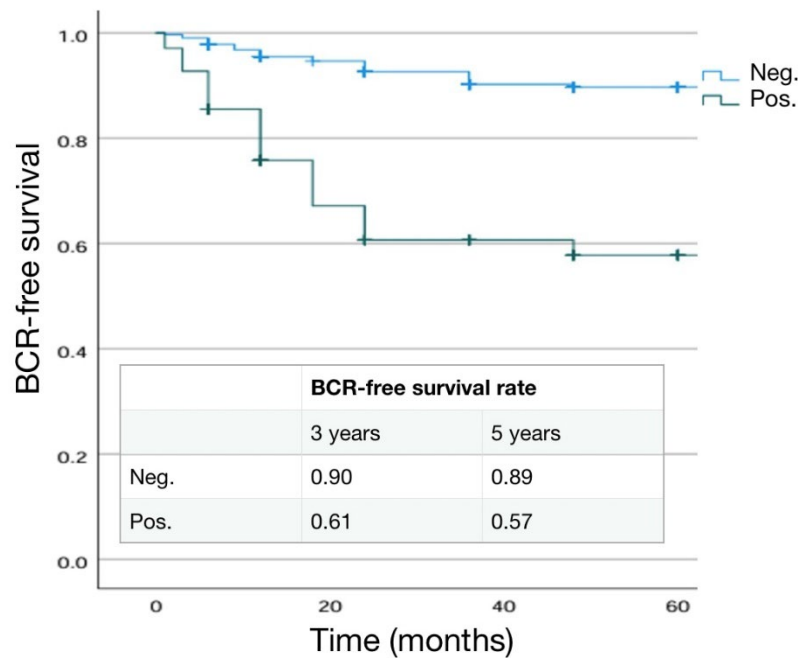


Figure 4. Kaplan Maeier analysis. Estimated rates of Biochemical free-survival (BFS) according to surgical margin (SM) status.

3.5.2. Main Significant Differences in Results

In SM+: - higher preoperative PSA; - higher percentage of positive core at biopsy; increase in BCR rate; increase in adjuvant therapy use

3.6. Differences in Pathological, Oncological and Functional Outcomes according to Biochemical Recurrence

Biochemical recurrence (BCR) was evaluated at a mean postoperative follow up of 56.4 ± 37.8 years. A BCR was detected in 11.9% of cases with a mean time of 18.67 ± 24.57 months, with a lower percentage in cases submitted to RARP (7.5%) than in cases submitted to LRP (14.4%) ($p=0.014$).

Clinical parameters such as age and Charson Index were not significantly ($p>0.50$) different between BCR- and BCR+ cases (Table 8).

Table 8. Distribution of preoperative and postoperative parameters on the basis of Biochemical recurrence (BCR). Mean±SD, median, (range). Number of cases (%).

	No BCR	Yes BCR	P value
Number cases	391	53	
Age (years)	67.13±6.588; 68 (47-72)	68.62±6.7; 70 (49-73)	0.131
BMI	25.74±3.43; 25 (18-37)	27.21±3.61;26.7 (21.4-39.4)	0.017
Charlson Index	3.85±1.02; 4 (0-7)	3.86±1.39; 4 (0-7)	0,96
Familiarity			0.12
Yes	28 (7.2%)	7 (13.2%)	
no	363 (92.8%)	46 (86.8%)	

Digital Rectal Examination			
Normal	340 (86.9%)	36 (67.9%)	<0.001
Suspicious	51 (13.1%)	17 (32.1%)	
Preoperative total PSA (ng/ml)	8.14±5.04; 7.1 (3.0-64.0)	11.37±7.03; 9.65 (4.0-30.0)	<0.001
PSAD	0.2±0.145; 0.17 (0.1-0.59)	0.26±0.48; 0.28 (0.1-0.47)	0.007
Prostate volume (cc)	48.15±14.6; 45 (20-120)	48.55±18.37; 50 (25-90)	0.933
Prostate Tumor size (mm) at mMR	11.95±5.14; 10 (4-30)	23.21±11.18; 20 (10-39)	<0.001
Clinical T staging			<0.001
T1	12 (3.1%)	0	
T2a	30 (7.7%)	0	
T2b	173 (44.2%)	19 (35.8%)	
T2c	148 (37.8%)	25 (47.2%)	
T3a	26 (6.7%)	4 (7.5%)	
T3b	2 (0.5%)	5 (9.4%)	
Clinical N staging			<0.001
N0	390 (99.7%)	50 (94.3%)	
N1	1 (0.3%)	3 (5.7%)	
Biopsy outcomes			<0.001
% positive samples PC	38.68±25.2; 30 (2-100)	59.21±27.57; 50 (14-100)	
ISUP grading at biopsy			<0.001
1	143 (36.6%)	6 (11.3%)	
2	123 (31.4%)	12 (22.6%)	
3	70 (17.9%)	16 (30.2%)	
4	46 (11.8%)	11 (20.8%)	
5	9 (2.3%)	8 (15.1%)	
Surgical technique at radical prostatectomy			0.034
Laparoscopic	243 (62.1%)	41 (77.4%)	
Robotic assisted	148 (37.9%)	12 (22.6%)	
Nerve sparing technique at surgery			0.002
No	270 (69.1%)	47 (88.7%)	
Yes	121 (30.9%)	6 (11.3%)	
Monolateral	48 (28.9%)	4 (80.0%)	
Bilateral	73 (71.1%)	2 (20.0%)	0.016
Pathological stage (T)			<0.001
pT2	234 (59.8%)	12 (22.6%)	
pT3a	127 (32.5%)	23 (43.4%)	
pT3b	30 (7.7%)	18 (34.0%)	
pT4	0	0	
Pathological stage (N)			0.014
N0	94 (91.3%)	21 (65.6%)	
N+	9 (8.7%)	11 (34.4%)	

ISUP grading at surgery			P<0.001
1	88 (22.5%)	4 (7.5%)	
2	172 (43.0%)	11 (20.8%)	
3	75 (19.0%)	14 (24.4%)	
4	40(11.4%)	8 (15.1%)	
5	16 (4.1%)	16 (20.2%)	
Surgical margin at surgery (R)			<0.001
Negative	338 (86.4%)	29 (54.7%)	
positive	53 (13.6%)	24 (45.3%)	
Positive surgical margin grading			<0.001
3	45 (84.9%)	10 (41.7%)	
4	7 (13.2%)	14 (58.3%)	
5	1 (1.9%)	0	
Positive surgical margin radial distance (mm)	2.67±0.82; 3 (1-4)	3.75±1.35; 3.5 (2-7)	0.001
PNI at surgery			<0.001
positive	225 (57.5%)	44 (83.0%)	
negative	166 (42.5%)	9 (17.0%)	
Cribriiform/IDC at surgery			0.217
positive	15 (3.8%)	5 (9.4%)	
negative	376 (91.2%)	48 (90.6%)	
Postoperative total PSA (ng/ml)(at 1 month)	0.03±0.03; 0.02 (0.01-0.1)	0.24±0.433;0.07 (0.01-2.0)	<0.001
Time to biochemical progression (months)		18.67±24.57;12 (1-120)	--
Adjuvant therapy			<0.001
no	359 (91.8%)	32 (60.4%)	
yes	32 (8.2%)	21 (39.6%)	
Adjuvant therapy type			0.042
-RT	26 (81.2%)	11 (55.0%)	
-RT + ADT	6 (18.8%)	10 (45.0%)	

On the contrary, BCR+ patients had a significantly higher preoperative mean BMI (27.21±3.61 vs 25.74±3.43; p=0.017) (Table 8). At biopsy the percentage of positive cores and bilateral incidence were significantly higher (p<0.001) in the BCR+ group. The distribution of ISUP grading also varied significantly between the two groups. In fact, only 2% of patients that did not develop a BCR were found to have an ISUP of 5 at biopsy, while 15.1% of those who experienced a BCR had an ISUP grade of 5 at diagnostic biopsy (p<0.001) (Table 8).

The percentage of cases submitted to a NS procedure was 30.9% and 11.3% respectively, in the BCR- and BCR+ group (p=0.02) (Table 8).

3.6.1. Pathological Outcomes

As expected, BCR+ patients were more likely to have a higher pathological stage and ISUP grading at final pathology (p<0.001). Similarly, positive lymph nodes (pN1) in the case of an eLND were found in a higher percentage of cases in the BCR+ group (8.7% in BCR- and 34.4% in BCR+; p=0.014) (Table 8). SM positivity was higher in the BCR+ (45.3%) than in BCR- (13.6%) cases (p<0.001). Mean extra-prostatic extension of positive SM was higher in BCR+ patients (3.75±1.35 vs 2.67±0.8; p=0.001) and SM+ grading was 4 in 13.2% and 58.3% of cases respectively in BCR- and BCR+ cases (p<0.001)(Table 8). Kaplan Maier curve describing cumulative biochemical recurrence free survival rates according to the different variables are showed in Figure 1-5.

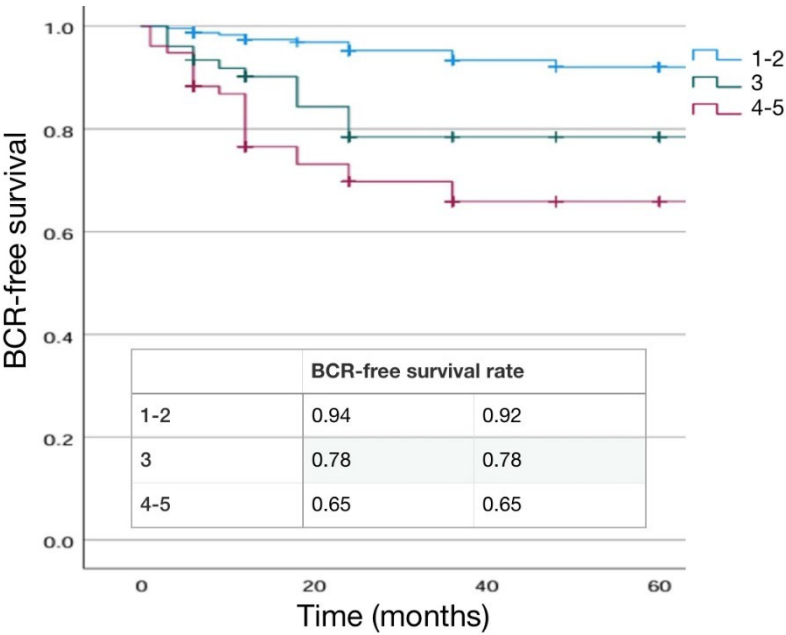


Figure 5. Kaplan Maeier analysis. Estimated rates of Biochemical free-survival (BFS) according to the ISUP grading at surgery.

3.6.2. Main Significant Differences in Results

In BCR+: - higher preoperative PSA; - higher percentage of positive prostatic core at biopsy; - higher pT stage and ISUP grading; - higher percentage of SM+ and SM+ grading.

3.7. Logistic Regression Analysis

Table 9 shows a logistic regression analysis assessed to identify variables able to condition adverse pathological, oncological and functional conditions in our population of non-metastatic PC submitted to surgery.

Table 9. a Risk for **extracapsular extention** (pT3a and pT3b) at surgery on the basis of different preoperative parameters at univariate and multivariate analysis.

	Univariate			Multivariate		
Parameter	OR	95%CI	P value	OR	95%CI	P value
Preoperative PSA						
<10 ng/ml	1.0			1.0		
≥ 10 ng/ml	3.46	2.19-5.44	<0.001	1.79	0.78-4.0	0.16
PIRADS score						
3	1.0			1.0		
4	1.98	0.92-4.37	0.079	1.30	0.53-3.15	0.50
5	4.84	1.97-11.93	<0.001	1.70	0.55-5.16	0.30
Prostate biopsy +						
monolateral	1.0			1.0		
bilateral	1.40	0.95-2.07	0.087	2.0	1.48-6.22	0.064
Max percentage PC tissue per core				Not included		
< 25%	1.0					
25-50%	1.33	0.76-2.35	0.285			
51-75%	1.33	0.76-2.35	0.285			

>75%	2.0	0.75-5.33	0.102			
ISUP grading						
1 e 2	1.0			1.0		
3	5.41	3.23-0.97	<0.001	2.10	0.95-5.02	0.06
4-5	10.63	5.79-19.52	<0.001	6.40	1.72-24.44	0.006
Risk Classes						
Low	1.0					
Intermediate	1.20	0.87-2.45	0.276	1.0		
High	2.90	1.74-4.89	<0.001	2.80	1.1-6.2	0.04

Table 9. b Risk for **upgrading** (ISUP 1-2 in ISUP 3-5) at surgery on the basis of different preoperative parameters at univariate and multivariate analysis.

	Univariate			Multivariate		
Parameter	OR	95%CI	P value	OR	95%CI	P value
Preoperative PSA						
<10 ng/ml	1.0			1.0		
≥ 10 ng/ml	3.42	1.65-7.10	<0.001	2.20	0.7-8.69	0.15
PIRADS score				Not included		
3	1.0					
4	1.57	0.4-6.09	0.51			
5	0.58	0.56-5.96	0.64			
Prostate biopsy +						
monolateral	1.0			1.0		
bilateral	2.06	1.01-4.18	0.042	1.71	0.8-3.54	0.1
Max percentage PC tissue per core				Not included		
< 25%	1.0					
25-50%	1.0					
51-75%	1.20	0.66-2.15	0.385			
>75%	1.33	0.75-2.53	0.102			
Risk Classes						
Low	1.0					
Intermediate	1.0			1.0		
High	2.90	1.74-4.89	<0.001	3.28	1.45-7.4	0.04

Table 9. c Risk for **lymph node involvement** (pN1) at surgery on the basis of different preoperative parameters at univariate and multivariate analysis.

	Univariate			Multivariate		
Parameter	OR	95%CI	P value	OR	95%CI	P value
Preoperative PSA						
<10 ng/ml	1.0			1.0		
≥ 10 ng/ml	4.27	1.65-11.02	0.001	1.31	0.63-2.71	0.47
PIRADS score						
3	1.0			1.0		
4	1.07	1-1.15	0.10	2.55	1.08-6	0.03

5	1.28	1.08-1.53	0.003	3.97	1.36-11.54	0.01
Prostate biopsy +						
monolateral	1.0			1.0		
bilateral	5.20	1.48-18.36	0.005	1.35	0.96-1.89	0.78
Max percentage PC tissue per core				Not included		
< 25%	1.0					
25-50%	1.0					
51-75%	1.0					
>75%	1.50	0.67-3.39	0.27			
Risk classes						
Low	1.0					
Intermediate	1.0			1.0		
High	7.32	2.06-25.94	<0,001	4.50	1.7.11.9	0.002
Number of lymph nodes removed at surgery						
<10	1.0			1.0		
10-15	3.36	0.7-12	0.10	1.70	0.62-11	0.5
>15	5.69	1.78-18.17	0.001	4.10	1.009-26.5	0.049
Nomogram risk						
≤7%	1.0			1.0		
>7%	1.30	1.07-1.49	0.10	1.61	0.17-15.1	0.60
Surgical technique						
Laparoscopy	1.0			1.0		
Robotic assisted	1.20	0.5-3.15	0.60	2.0	0.34-12.66	0.60
ISUP grading						
1 e 2	1.0			1.0		
3	9.45	1.93-46.32	0.003	2.21	3.0-11.52	0.005
4-5	9.28	1.96-43.86	<0.001	5.89	3.0-11.52	<0.003
pTstage						
pT2	1.0			1.0		
pT3a	1.08	1.01-1.15	0.012	1.20	0.76-1.96	0.40
pT3b	1.70	1.28-2.25	<0.001	3.34	1.5-7.4	0.003

Table 9. d Risk for **positive surgical margin** at surgery on the basis of different preoperative parameters at univariate and multivariate analysis.

	Univariate			Multivariate		
Parameter	OR	95%CI	P value	OR	95%CI	P value
Preoperative PSA						
<10 ng/ml	1.0			1.0		
≥ 10 ng/ml	3.57	2-5.63	<0.001	2.98	1-8.8	0.04

Prostate volume				Not included		
<50 cc	1.0					
≥ 50 cc	1.04	0.47-2.33	0.90			
PIRADS score						
3	1.0			1.0		
4	1.57	0.54-4.54	0.40	0.89	0.2-3.2	0.80
5	3.32	1.08-10.23	0.03	1.90	0.7-9.5	0.20
Prostate biopsy +				Not included		
monolateral	1.0					
bilateral	1.14	0.68-1.09	0.60			
Risk classes						
Low	1.0					
Intermediate	1.0			1.0		
High	1.44	0.81-2.54	0.20	4.98	1.0-22.8	0.40
Surgical technique						
Laparoscopic	1.0			1.0		
Robotic assisted	1.27	0.7-2.1	0.35	1.20	0.5-1.8	0.40
Nerve sparing technique at surgery						
no	1.0			1.0		
yes	0.80	0.46-1.44	0.48	2.10	0.5-7.9	0.30
Operative time				Not included		
≤ 120 min	1.0					
>120 min	1.57	0.34-7.27	0.56			
pTstage						
pT2	1.0			1.0		
pT3a	2.0	1.15-3.52	0.01	2.0	1.1-3.65	0.20
pT3b	4.60	2.27-9.32	<0.001	4.60	2-10.67	<0.001
ISUP grading at surgery						
1-2	1.0			1.0		
3	1.65	0.90-3.0	0.10	1.37	0.73-2.66	0.30
4-5	1.84	1.0-3.41	0.05	1.40	0.74-2.70	0.30

Table 9. e Risk for **biochemical progression** after surgery on the basis of different preoperative parameters at univariate and multivariate analysis.

	Univariate			Multivariate		
Parameter	OR	95%CI	P value	OR	95%CI	P value
Preoperative PSA						
<10 ng/ml	1.0			1.0		
≥ 10 ng/ml	3.0	1.68-5.57	<0.001	4.12	1.2-19.21	0.007
PIRADS score						
3	1.0			1.0		
4	1.05	1-1.09	0.06	1.02	0.9-1.20	0.90

5	1.42	1.17-1.71	<0.001	1.90	0.7-9.50	0.20
Prostate biopsy +						
monolateral	1.0			1.0		
bilateral	2.64	1.37-5.10	0.003	4.52	0.81-25.10	0.08
Risk classes						
Low	1.0					
Intermediate	1.0			1.0		
High	4.35	2.47-8.44	<0.001	9.66	1.85-50.32	0.007
Surgical technique						
Laparoscopic	1.0			1.0		
Robotic assisted	0.38	0.19-0.75	0.007	0.66	0.17-2.55	0.66
Nerve sparing technique at surgery						
no	1.0			1.0		
yes	0.24	0.09-0.62	0.002	0.30	0.10-2.20	0.30
Operative time						
≤ 120 min	1.0			1.0		
>120 min	1.10	0.99-1.14	0.23	0.98	0.65-1.62	0.90
pTstage						
pT2	1.0			1.0		
pT3a	3.42	1.64-7.14	<0.001	1.20	0.70-3.0	0.40
pT3b	11.10	4.80-25.75	<0.001	2.82	0.99-8.21	0.06
ISUP grading at surgery						
1-2	1.0			1.0		
3	3.21	1.47-7.0	0.005	1.87	0.83-5.72	0.190
4-5	6.76	3.32-13.70	<0.001	3.73	1.50-9.50	0.006
Lymphnode involvement						
pN0	1.0			1.0		
pN1	2.46	1.82-5.13	0.010	8.32	1.53-45.0	0.014
Number of Lymph nodes removed						
<10	1.0			1.0		
10-15	3.18	0.99-10.21	0.60	1.7	0.40-3.20	0.40
>15	2.86	1.24-6.60	0.010	2.2	0.80-4.50	0.20
Surgical margins						
Negative	1.0			1.0		
positive	4.97	2.39-10.34	<0.001	7.20	1.80-28.30	0.004
Surgical margins grade						
3	1.0			1.0		
4	5.0	5.57-45.0	<0.001	4.96	2.37-10.37	<0.001
PNI at surgery						

negative	1.0			1.0		
positive	4.50	1.92-10.55	<0.001	1.50	0.63-4.50	0.32

3.7.1. Predictors for the Risk of Extracapsular Extension

On univariate analysis, the risk of extracapsular extension at pathological staging after surgery did not significantly vary according to percentage of positive tissue per core at biopsy and biopsy laterality whereas it significantly increased according to preoperative PSA (OR= 3.46; 95% CI= 2.19-5.44; $p<0.002$), PIRADS score (highest OR=4.84; 95% CI=1.97-11.93; $p<0.001$), ISUP grading (highest OR=10.63; 95% CI 5.79-19.52; $p<0.001$) and risk class (high risk: OR=2.9; 95% CI=1.74-4.89; $p<0.001$). On multivariate analysis, ISUP grading 4-5 and high risk class were the only variables able to independently and significantly influence the risk for extracapsular extension ($p=0.006$ and $p=0.04$ respectively) (Table 9a).

3.7.2. Predictors for the Risk of Upgrading at Surgery

On univariate analysis, the risk of upgrading after surgery (ISUP 1-2 in ISUP 3-5) did not significantly vary according to PIRADS score at mMR and percentage of positive tissue per core. Considering the intermediate risk class as standard reference, the risk of upgrading significantly increased 2.9 times (95%CI 1.74-4.89; $p<0.001$) in cases with a high risk tumor. On multivariate analysis, only high risk class remains a variable able to independently and significantly influence the risk for upgrading ($p=0.04$) (Table 9b).

3.7.3. Predictors for the Risk of Lymph Node Involvement

On univariate analysis, the risk of lymph node involvement at pathological evaluation (pN1) did not significantly vary according to the percentage of positive tissue per core biopsy, Briganti 2019 nomogram risk using a 7% cut-off (OR=1.3; 95% CI=1.07-1.49, $p=1.61$) and surgical approach (OR=1.2; 95%CI= 0.5-3.12; $p=0.60$). On univariate analysis, variables able to significantly increase the risk of lymph node involvement were preoperative PSA with a $> 15\text{ng/ml}$ value (OR=5.69; 95%CI 1.78-18.17; $p=0.001$), high risk class (OR 7.32; 95%CI 2.06-25.94, $p<0.001$), number of lymph nodes removed at surgery >15 vs <10 (OR 5.69; 95%CI=1.78-18.17; $p=0.001$), ISUP grading 3 vs 1-2 and 4-5 vs 1-2 (OR=9.45; 95%CI=1.93-46.32; $p=0.003$ and OR=9.28; 95%CI=1.96-43.86; $p<0.001$ respectively) and pT stage, pT3a vs pT2 and pT3b vs pT2 (OR= 1.08; 95%CI=1.01-1.15; $p=0.012$ and OR=1.7; 95%CI=1.28-2.25; $p<0.001$).

On multivariate analysis, PIRADS score 4 vs 3 and 5 vs 3 ($p=0.01$ and $p=0.03$), high risk class (0.002), ISUP grading 3 vs 1-2 and 4-5 vs 1-2 ($p=0.005$ and $p<0.003$), pT3b vs pT2 ($p=0.003$) and number of removed lymph node >15 versus <10 ($p=0.049$) were the variables able to independently and significantly influence the risk for lymph node involvement (Table 9c).

3.7.4. Predictors for the Risk of Positive Surgical Margins

On univariate analysis, the risk of positive surgical margins at pathological evaluation did not significantly vary according to prostate volume, positive biopsy laterality, risk class, NS technique (OR=0.8; 95%CI=0.46-1.44; $p=0.48$), surgical approach (OR=1.27; 95%CI=0.7-2.1; $p=0.35$), operative time $>120\text{min}$ vs $<120\text{min}$ (OR= 1.57; 95%CI 0.34-7.27; $p=0.56$). On the contrary, the risk of SM+ increased with preoperative PSA $>10\text{ng/dl}$ vs $<10\text{ng/dl}$ (OR=3.57; 95%CI=1-5.63; $p<0.001$), PIRADS score 5 vs 3 (OR3.32; 95%CI 1.08-10.23; $p=0.003$), pT3a vs pT2 and pT3b vs pT2 (OR=2; 95%CI 1.15-3.52; $p=0.01$ and OR=4.6; 95%CI 2.27-9.32; $p<0.001$) and ISUP grading 4-5 vs 1-2 (OR=1.84; 95%CI 1-3.41; $p=0.05$).

On multivariate analysis, only preoperative PSA and pT3b vs pT2 remained variables able to independently and significantly influence the risk for SM+ ($p=0.04$ and $p<0.001$, respectively) (Table 9d).

3.7.5. Predictors for the Risk of Biochemical Recurrence

On univariate analysis, the risk of biochemical recurrence (BCR) during the postoperative follow-up was significantly related to several variables. In particular, the risk for BCR increased with preoperative PSA >10ng/ml vs <10ng/ml (OR=3; 95%CI 1.68-5.57; $p<0.001$), PIRADS score 5 vs 3 (OR=1.42; 95%CI 1.17-1.71; $p<0.001$), positive biopsy laterality (OR= 2.64; 95%CI= 1.37-5.1; $p=0.003$), risk class (OR=4.35; 95%CI 2.47-8.44; $p<0.001$), pT3a vs pT2 and pT3b vs pT2 (OR=3.42; 95%CI 1.64-7.14; $p<0.001$ and OR=11.1; 95%CI 4.8-25.75; $p<0.001$ respectively), ISUP grading 3 vs 1-2 and 4-5 vs 1-2 (OR=3.21; 95%CI 1.47-7; $p=0.005$ and OR=6.76; 95%CI 3.32-13.7; $p<0.001$), lymph nodes removed >15 vs <10 (OR=2.86; 95%CI 1.24-6.6; $p=0.01$), SM positivity (OR=4.97; 95%CI 2.39-10.34; $p<0.001$), grading at SM+ 4 vs 3 (OR=50; 95%CI 5.57-451; $p<0.001$) and PNI positivity at final pathology (OR 4.5; 95%CI 1.92-10.55; $p<0.001$). Finally, the risk for BCR was lower in patients who underwent a RARP when compared to a LRP and in those submitted to a NS technique (OR=0.38; 95%CI=0.19-0.75; $p=0.007$ and OR=0.24; 95%CI 0.09-0.62; $p=0.002$).

On multivariate analysis, PSA>10 ng/ml ($p=0.007$), high risk class ($p=0.007$), ISUP 4-5 ($p=0.006$), lymph node involvement ($p=0.014$), SM positivity ($p=0.004$) and SM+ grading 4 ($p<0.001$) remained significant and independent predictors for the development of a BCR. (Table 9e)

4. Discussion

Radical prostatectomy remains a primary treatment for non-metastatic prostate cancer, with minimally invasive techniques like laparoscopic radical prostatectomy and robotic-assisted radical prostatectomy being widely adopted. As these techniques continue to evolve, updated evidence is critical for understanding their comparative effectiveness, safety, and patient outcomes [26-30].

LRP, although effective, requires significant technical expertise. Surgeons must develop advanced laparoscopic skills, particularly in high-volume centers, to achieve outcomes that match those of RARP [31-36]. A study by Bhayani and Pavlovich [1] reaffirms the steep learning curve associated with LRP, emphasizing the need for extensive training and experience to achieve optimal patient outcomes. Stolzenburg JU [2] reported that while LRP remains effective in experienced hands, the advantages of RARP in preserving functional outcomes, particularly continence, are becoming more pronounced with robotic technology.

RARP, in some experiences, has been associated with lower positive surgical margin rates, particularly in high-risk prostate cancer cases, and better preservation of urinary continence and sexual function due to enhanced nerve-sparing capabilities [12,14-16,20-22]. A recent systematic review by Ma J et al [3] highlighted the technological superiority of RARP in terms of precision and ergonomics, contributing to better surgical outcomes and shorter learning curves for surgeons compared to LRP. A meta-analysis by Huang X et al [4] found that RARP had significantly better functional outcomes than LRP, especially in terms of early continence recovery and sexual function preservation, making it the preferred choice in several centers. A multi-institutional study by Dell'Oglio et al [5] confirmed that RARP continues to demonstrate superior functional outcomes compared to LRP, with lower rates of postoperative complications.

The latest guidelines of the European Association of Urology reflect the growing preference for RARP in centers where it is available, citing its advantages in functional outcomes. However, LRP remains a recommended alternative and the EAU Guidelines on Prostate Cancer (2024) emphasize that both LRP and RARP are viable options, with the choice depending on the availability of technology and surgeon expertise [7]. RARP may be favored for its superior functional outcomes, particularly in terms of continence and potency preservation [12,14-16,20-22]. The decision between these techniques should be individualized based on patient characteristics, surgeon experience, and available resources, in line with the latest European guidelines [7].

In the present study we report the long-term case history of a population of patients with non-metastatic PC considered suitable, according to EAU guidelines and after multidisciplinary discussion, for radical prostatectomy, performed by a single surgeon with experience of over 10 years with LRP and over 5 years with RARP. This population represents a homogeneously treated sample in a perfect real-life situation at a high-volume institution for the treatment of PC and with a multidisciplinary (MDT) group regulating decisions relating to the management of each individual

patient. *Limitations and strengts:* Strengths of the study are the analysis of a real-world situation in a high-volume center and with an MDT group that determines homogeneous evaluation and treatment criteria. Furthermore, as a university training center, all LRP and RARP procedures were performed by a single surgeon with an operating team of urology residents. The limitations are mainly the lack of randomization in the selection of patients for the two procedures (LRP versus RARP). No selection parameters were considered to determine the surgical procedure; however, the non-randomization produced some differences between the population undergoing LRP and that undergoing RARP. In particular, age was significantly higher in the LRP group, whereas the percentage of PIRADS 4-5 at mMR and the percentage of clinical locally advanced stage (cT3) was significantly higher in the RARP group. Except for these parameters, the two populations are sufficiently homogeneous at baseline.

In the comparison between the robotic and laparoscopic approach, a first advantage of the robotic approach is a significant reduction in operating times, days of hospitalization and postoperative catheterization compared to laparoscopic surgery (despite the greater experience of the operator > 10 years in LRP compared to robotics > 5 years). Perioperative and postoperative complications such as anastomotic leakage, need of blood transfusion, urethral stricture have practically disappeared with both approaches. Both approaches have similarly resulted in a drastic reduction in postoperative complications in clinical practice; the greater simplicity of the robotic approach produces an advantage also in terms of operating, catheterization and hospitalization times.

With a homogeneous indication for extended lymph node dissection (all high risk cases and >5% risk at Briganti nomogram in intermediate risk), a similar percentage of cases was submitted to eLND using RARP or LRP. RARP was able to remove a significantly higher number of lymph nodes, however the percentage of pN1 was similar and limited in both approaches (LRP 15.8%, RARP 13.6%). The role of extended lymphadenectomy in RP remains debated due to the low percentages of pN1 reported in most experiences, regardless of the number of lymph nodes removed at surgery and despite indications obtained by nomograms []. In our experience, at multivariate analysis, together with PIRADS score, high risk class, ISUP grading and pT stage, also the number of removed lymph node >15 versus < 10 was a variable able to independently and significantly influence the risk for pathologic lymph node involvement (OR 4.10; 95%CI 1.0-26.5; p=0.049), whereas surgical approach was not a significant variable.

Our experience did not confirm significant differences in terms of risk for SM+ related to the surgical approach although the percentage was slightly higher after RARP. A higher but not statistically significant percentage of positive surgical margins was found after RARP when compared to LRP, but with lower extraprostatic radial distance in RARP group. At the multivariate analysis only a pathologic involvement of seminal vesicles (pT3b stage) was able to significantly and independently increase the risk of SM+.

The only parameter significantly influenced by the surgical approach in our population was biochemical recurrence at postoperative follow-up. The RARP approach was associated with a significantly lower percentage of BCR (7.5%) when compared to LRP (14.4%) (p=0.014). Time to biochemical progression was similar between LRP and RARP cases but in the RARP group the risk for BCR was significantly reduced at univariate analysis. However, at multivariate analysis the surgical approach did not remain a significant and independent variable able to influence BCR rates, as opposed to surgical margins positivity and grade, lymph node involvement and ISUP grading.

The second crucial point in the comparative analysis between RARP and LRP, is the possibility for a functional long-term advantage []. In our experience, the percentage of nerve sparing techniques was double in the RARP group when compared to the LRP. Robotic vision probably determines greater safety in performing a nerve sparing approach, leading to an extension of the indications in clinical practice. In our clinical practice we extensively use pelvic floor rehabilitation with electrostimulation and biofeedback starting 30 days after removal of the catheter, homogeneously in RARP (21.8%) and LRP (19.0%) cases []. RARP was capable of speeding up the reduction of postoperative urinary losses with a significantly lower PAD weight at 3 and 6 months postoperatively compared to LR (mean pad weight 75.57±122grams and 14±42 grams respectively in LRP and RARP (p<0.01)) while at 12 months the recovery of continence was high in both approaches (no PADS in 91.6% of cases). In cases submitted

to a nerve sparing procedure, the two approaches produced no statistically significant differences in terms of IIEF-5 score reduction at 6 and 12 months postoperatively ($p>0.05$). However, the 12-month IIEF-5 mean and median score showed better results using RARP (18.0 ± 3.75 ; 18) than LRP (10.14 ± 4.77 ; 8). Considering ED as postoperative International Index of Erectile Function-5 (IIEF-5) score between 1-10, the 12-month percentage of ED was 57.3% in LRP and 45.4% in RARP.

5. Conclusions

In the comparison between the robotic and laparoscopic approach, a clear advantage of the robotic approach is a significant reduction in operating times, days of hospitalization and postoperative catheterization compared to laparoscopic surgery. Perioperative and postoperative complications such as anastomotic leakage, need of blood transfusion, urethral stricture have practically disappeared with both approaches. It is not possible to describe any certain oncological advantage both in terms of surgical margins and pathological lymph nodes removed. A reduction to the limit of significance is described in terms of biochemical recurrence to the advantage of the robotic approach. RARP produces a more rapid recovery of urinary continence at 3 months postoperatively without significant advantages in terms of erectile potency recovery.

6. Patents

The choice of a robotic assisted approach for radical prostatectomy procedure can provide a clear advantage in terms of reduction of operating time, days of hospitalization and catheterization compared to the laparoscopic surgery. Perioperative complications such as anastomotic leakage, need of transfusion, urethral stricture have practically disappeared with both approaches. It is not possible to report any certain oncological advantages of one technique on the other. Robotic approach produces a more rapid recovery of urinary continence at 3 months postoperatively without significant advantages in terms of erectile potency recovery.

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