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ORIGINAL ARTICLE

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Ten-year functional and oncological outcomes of a prospective randomized controlled trial comparing laparoscopic versus robot-assisted radical prostatectomy

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Abstract

Background: Among prostate cancer (PCa) treatment options, mini-invasive surgical approaches have gained a wide diffusion in the last decades. The aim of this study was to present oncological, functional, and quality of life data after 10 years of follow-up of a prospective randomized controlled trial (RCT) (ISRCTN11552140) comparing robot-assisted radical prostatectomy (RARP) versus laparoscopic radical prostatectomy (LRP) for the treatment of PCa.

Methods: Patients with localized PCa were randomized to undergo LRP or RARP between January 2010 and January 2011. Functional (continence and potency) and oncological (prostate-specific antigen, biochemical recurrence [BCR] and BCR-free survival [BCRFS]) variables were evaluated. BCRFS curves were estimated by the Kaplan–Meier method and compared using the log-rank test. Machine learning partial least square-discriminant analysis (PLS-DA) was used to identify the variables characterizing more the patients who underwent RARP or LRP.

Results: Seventy-five of the originally enrolled 120 patients remained on follow-up for 10 years; 40 (53%) underwent RARP and 35 (47%) LRP. Continence and potency recovery rates did not show significant differences ($p = 0.068$ and $p = 0.56$, respectively), despite a Δ12% for continence and Δ8% for potency in favor of the robotic approach. However, the quality of continence (in terms of International Consultation on Incontinence Questionnaire-Short Form [ICIQ-SF] score) and erection (in terms of International Index of Erectile Function-5 [IIEF-5] score) was significantly better after 10 years in the robotic group ($p = 0.02$ and $p < 0.001$).

Francesco Porpiglia and Cristian Fiori contributed equally to the senior authorship.

PLS-DA revealed that LRP was characterized by the worst functional-related outcomes analyzing the entire follow-up period. Four (10%) and six (17%) patients experienced BCR in RARP and LRP groups, respectively ($p = 0.36$), with an overall 10-year BCR-free survival of 88% and 78% ($p = 0.16$).

Conclusions: Comparable continence and potency rates were observed between RARP and LRP after a 10-year follow-up. However, the RARP group exhibited superior totally dry rate and erection quality. No difference in terms of oncological outcomes was found.

KEYWORDS

erectile dysfunction, incontinence, LRP, prostate cancer, RARP

1 | INTRODUCTION

In case of localized prostate cancer (PCa), radical prostatectomy should be proposed as one of the treatment options.[1] Even if for decades standard retropubic approach has represented the reference standard, under the pressure of ever more minimally invasive surgery (MIS),[2] laparoscopic radical prostatectomy (LRP) at first, and then robot-assisted radical prostatectomy (RARP) was introduced as alternatives.

Notwithstanding the already demonstrated advantages of MIS in perioperative outcomes, such as estimated blood loss (EBL), transfusions, length of hospital stay, and complications,[3] the main issue is still represented by the real benefit in terms of oncological and functional outcomes.

Discordant findings were reported,[3] even if both RARP[4,5] and LRP[6] revealed to be oncologically safe.

Only few studies directly compared LRP and RARP[7–9] with a well-established a priori prospective randomized protocol; however, long-term follow-up data are lacking.

We previously reported short- (1 year)[9] and mid-term (5 years)[10] results from a prospective single-center, single-surgeon randomized study comparing LRP and RARP.

We now present oncological, functional, and quality-of-life data after 10 years of follow-up.

2 | MATERIALS AND METHODS

The following section has been reported in accordance with CONSORT statement to trial of nonpharmacologic treatment[11] (File S1).

2.1 | Trial design

This is a single-center prospective parallel two arms randomized control trial (1:1 for two groups) for patients with localized PCa, who underwent to LRP or RARP. The trial was registered on International Standard Randomized Controlled Trial Number (ISRCTN) registry (registry number ISRCTN11552140).

2.2 | Participants

Eligible participants were all adults aged 50–75 years old, affected by localized or locally advanced PCa (clinical stage T1–T2 or T3, N0, M0), with biopsy Gleason score (GS) 2–10 and prostate-specific antigen (PSA) < 20 ng/mL. All patient candidates for surgery were consecutively included in the study, except for patients who do not provide informed consent to participate in the study.

2.3 | Study setting

The study took place at San Luigi Gonzaga University Hospital, Orbassano (Turin, Italy) January 2010 to January 2011. This study was approved by our local ethical committee (protocol N. 136/2009) (File S2: Protocol).

2.4 | Intervention

All surgical procedures were carried out by an experienced surgeon (F. P.). Before the start of our study, the surgeon executed >600 LRP (starting in 2000) and 100 RARP (starting in 2008). Both RARP and LRP were performed according to our previously described transperitoneal anterograde approach.[12,13] When clinically and oncologically indicated, unilateral or bilateral neurovascular bundle preservation (nerve-sparing [NS] procedure) and extended pelvic lymph node dissection (LND) according to Briganti nomogram were performed.[9]

2.5 | Outcomes

- The primary objective of the study was to compare the functional outcomes after the intervention (in terms of continence and potency recovery) during the follow-up.
  - Continence definition: patients were defined "continent" in case of use of only one safety pad per day or if they did not use any pad at all (see Section 2.8.1).

- Potency definition: In subjects who were submitted to NS surgery, potency was defined as the ability to obtain an erection sufficient for sexual intercourse, with or without the aid of a phosphodiesterase type 5 inhibitor (see Section 2.8.1).
- The secondary endpoints were (i) the evaluation of oncological, in terms of BCR and (ii) perioperative outcomes.

2.6 | Sample size

Originally, the sample size was calculated to record significant differences (a level <0.05) of around 25% (according to our previously published experience[9]) between the incidence proportions of evaluated outcome (continence at Month 3 after surgery, see Section 2.5, "Outcomes") with an adequate power ($1-\beta$ = 80%). To fulfill these conditions a total of 52 + 52 = 104 patients is needed. Taking into consideration a dropout or lost-to-follow-up rate of 15%, eight extra patients were enrolled for each group (60 patients in each arm).

At last, we enrolled 120 males with histologically confirmed prostate cancer (T1–2N0M0) clinically staged according to TNM 2009.[14]

2.7 | Randomization (sequence generation)

We used a computerized 1-to-1 simple randomization list (www.randomization.com) to randomize patients to either RARP or LRP groups.

2.8 | Data collection

2.8.1 | Functional outcomes and complication measurements

Continence, preoperatively and postoperatively, was defined extracting a single question from the Expanded Prostate Cancer Index Composite (EPIC) questionnaire[15]: How many pads or adult diapers per day do you usually use to control leakage?

Continence was assessed at 1, 3, 6, and 12 months, and then every 6 months until 10 years after the procedure. At 10 years, the International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) was also administered. Potency was assessed at 1, 3, 6, and 12 months, and then every 6 months until 10 years after surgery. Late complications during the follow-up period and any other procedure performed after surgery were recorded. Patients who were submitted to a surgical procedure for incontinence were considered as incontinent at the functional analysis.

The outcomes of surgeries were reported separately.

2.8.2 | Oncological outcomes measurements

Serum PSA levels were assessed at 1, 3, 6, and 12 months, and then every 6 months. Patients who underwent adjuvant treatments during follow-up, such as radiotherapy (RT) and hormonal treatment (HT), were recorded.

BCR was defined as (1) any postoperative cancer therapy, such as RT, HT, or chemotherapy; or (2) PSA > 0.2 ng/mL with a single confirmation repeated measurement.[16]

All mortality events occurring from the date of surgery to the date of the last follow-up were used.

2.8.3 | Quality of life outcomes measurements

To evaluate patient satisfaction after surgery and general health status as subjective perception, Questions 46 ("Overall, how satisfied are you with the treatment you received for your prostate disease intervention?" 1 = *extremely dissatisfied* to 5 = *extremely satisfied*] and 1 ("In general, would you say your health is 1 = *excellent* to 5 = *poor*]) of the EPIC questionnaire were answered during the last follow-up visit.[15]

2.9 | Statistical analysis

Means and standard deviations were used to describe continuous variables, median and interquartile ranges for the discrete ones. Categorical variables were summarized by frequency tables.

Mann–Whitney and Fisher's exact tests were used to compare continuous and categorical variables between RARP and LRP groups. Continence and erectile function recovery rates were reported at every year of follow-up after RP and compared by χ^2 test. Cumulative hazard function (HF) of time to continence and potency was used; furthermore, binomial logistic regression was performed to identify patients' surgical predictors for continence and potency. For survival analyses, BCRFS curves were estimated by the Kaplan–Meier method and compared using the log-rank test.

A sparse version partial least square-discriminant analysis (PLS-DA) was tested as supervised multivariate data analysis to identify the variables that characterize more the patients who underwent RARP or LRP.[17,18] Briefly, PLS-DA is a supervised/classification model where the a priori classification of each of the objects under exam is known. It aims to calculate specific boundaries in the multidimensional space that allow to separate the different individuals (i.e., scores) within their corresponding classes (in this case, RARP vs. LRP). In particular, discrimination models always provide an outcome regarding the classification of the patients and, in parallel, provide loading values (i.e., loadings) showing the contributions of the different variables to the categories and the individuals under investigation. For further details on this specific machine-learning method see File S3.

Data processing was carried out using R software (version 4.0.2) and R Studio (version 1.3.959).

3 | RESULTS

3.1 | Participants flow and losses or exclusion

Of the 120 patients enrolled in the study, 45 (37.5%) were lost during the 10-year follow-up ended in January 2021 (Table S1). Among them, nine died (20% out of 45): only one patient died of PCa (11% out of nine). Among the 75 patients who completed the 10-year follow-up, 40 (53%) underwent RARP and 35 (47%) underwent LRP (Figure 1).

3.2 | Baseline data

As shown in Table S1, the preoperative baseline characteristics of the 75 analyzed patients remained comparable, as well as the clinical stage. NS rate and number of LND were similar between the two groups. Furthermore, no differences were found in terms of postoperative pathological findings (International Society of Urological Pathology, pathological stage), no patient was pN1; PSMs rate was 27.5% versus 25.7% ($p = 0.86$).

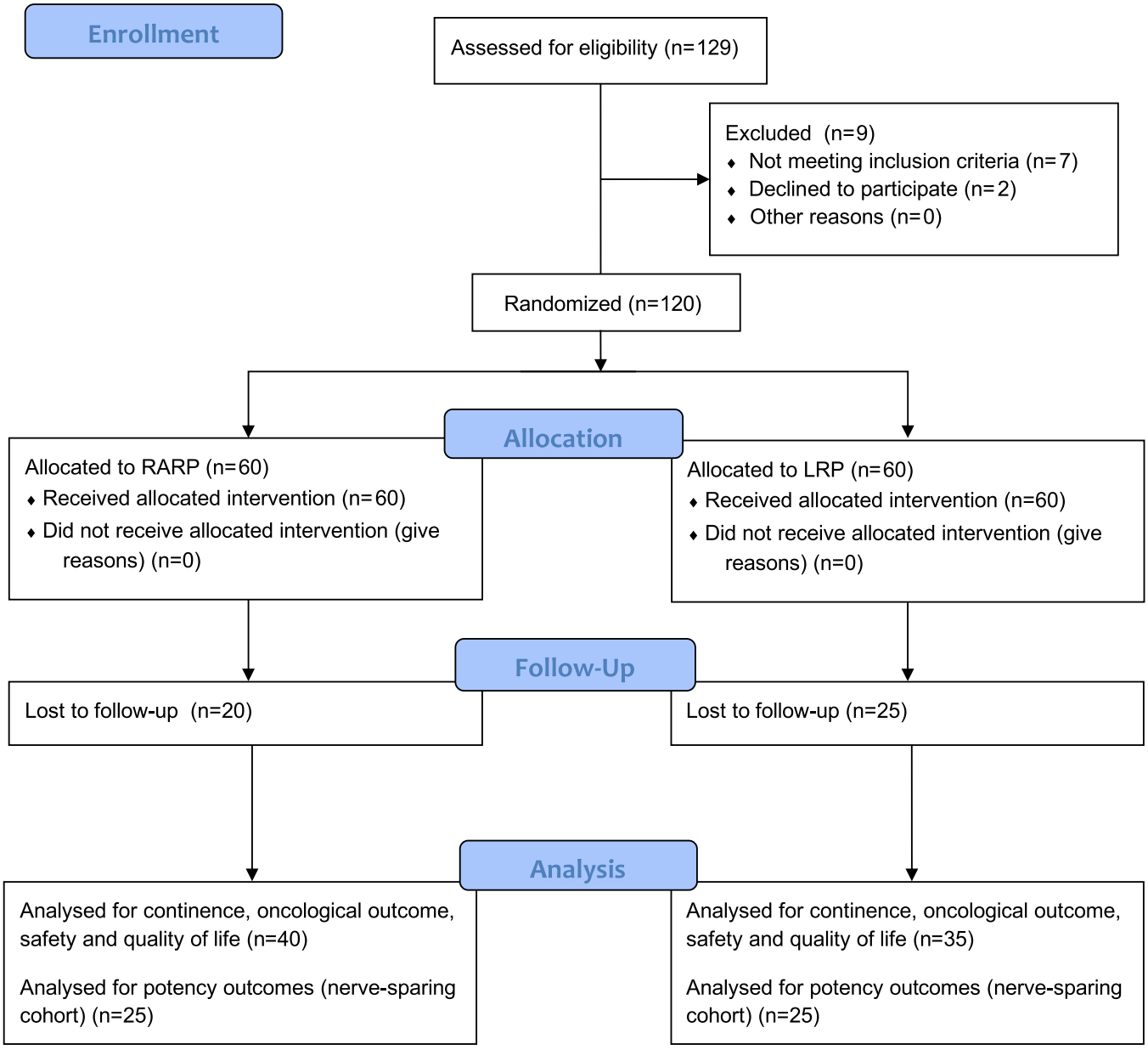

FIGURE 1 Study flow CONSORT diagram. LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Continence and potency outcomes.

	Overall cohort					Study cohort				
	All patients	RARP	LRP	*p* Value (c^2 test)	OR (95% CI)	All patients	RARP	LRP	*p* Value (c^2 test)	OR (95% CI)
Continence, *n* (%)										
1 year	107/120 (89.2%)	57/60 (95.0%)	50/60 (83.3%)	<0.001	2.029 (0.807–5.103)	68/75 (90.6%)	40/40 (100.0%)	28/35 (80.0%)	0.003	20.675 (1.048–408.068)
2 years	109/120 (90.8%)	58/60 (96.7%)	51/60 (85.0%)	<0.001	1.433 (0.575–3.567)	68/75 (90.6%)	39/40 (97.5%)	29/35 (82.8%)	0.029	4.571 (0.473–44.17)
3 years	108/118 (90.8%)	57/59 (96.6%)	51/59 (86.4%)	<0.001	1.312 (0.529–3.259)	68/75 (90.6%)	39/40 (97.5%)	29/35 (82.8%)	0.029	3.272 (0.317–33.83)
4 years	106/116 (91.4%)	56/58 (96.6%)	50/58 (86.2%)	<0.001	1.333 (0.535–3.32)	69/75 (92.0%)	39/40 (97.5%)	30/35 (85.7%)	0.060	2.087 (0.177–24.615)
5 years	104/115 (90.4%)	55/57 (96.5%)	49/58 (84.5%)	<0.001	1.206 (0.484–3.005)	68/75 (90.6%)	39/40 (97.5%)	29/35 (82.8%)	0.029	2.087 (0.177–24.615)
6 years	73/81 (90.1%)	39/42 (92.9%)	31/39 (79.4%)	0.07	1.091 (0.437–2.722)	69/75 (92.0%)	39/40 (97.5%)	30/35 (85.7%)	0.060	1 (0.059–16.928)
7 years	72/80 (90%)	39/41 (95.1%)	31/39 (79.4%)	0.03	1.109 (0.441–2.788)	69/75 (92.0%)	39/40 (97.5%)	30/35 (85.7%)	0.060	2.087 (0.177–24.615)
8 years	70/78 (89.7%)	38/41 (92.7%)	30/37 (81.1%)	0.125	1 (0.396–2.524)	67/75 (89.3%)	38/40 (95.0%)	29/35 (82.8%)	0.089	3.272 (0.317–33.83)
9 years	69/76 (90.8%)	37/40 (92.5%)	29/36 (80.5%)	0.124	1 (0.396–2.524)	66/75 (88.0%)	37/40 (92.5%)	29/35 (82.8%)	0.199	1.568 (0.239–10.298)
10 years	65/75 (86.6%)	37/40 (92.5%)	28/35 (80.0%)	0.068	1.5 (0.599–3.754)	65/75 (86.6%)	37/40 (92.5%)	28/35 (80.0%)	0.068	1.568 (0.239–10.298)
Potency, *n* (%)										
1 year	47/70 (67.1%)	28/35 (80.0%)	19/35 (54.3%)	0.001	21.317 (1.128–402.835)	33/50 (66.0%)	20/25 (80.0%)	13/25 (52.0%)	0.036	3.692 (1.052–12.957)
2 years	50/70 (71.4%)	29/35 (82.9%)	21/35 (60.0%)	<0.001	6.5 (0.721–58.613)	37/50 (74.0%)	21/25 (84.0%)	15/25 (60.0%)	0.049	3.5 (0.921–13.306)
3 years	46/70 (65.7%)	27/35 (77.1%)	19/35 (54.3%)	<0.001	3.655 (0.363–36.854)	33/50 (66.0%)	19/25 (76.0%)	14/25 (56.0%)	0.135	2.488 (0.741–8.35)
4 years	46/70 (65.7%)	27/35 (77.1%)	19/35 (54.3%)	<0.001	2.364 (0.205–27.248)	33/50 (66.0%)	19/25 (76.0%)	14/25 (56.0%)	0.135	2.488 (0.741–8.35)
5 years	44/70 (62.9%)	26/35 (74.3%)	18/35 (51.4%)	<0.001	2.364 (0.205–27.248)	31/50 (62.0%)	18/25 (72.0%)	13/25 (52.0%)	0.145	2.373 (0.734–7.675)
6 years	33/52 (63.4%)	18/26 (69.2%)	15/26 (57.7%)	0.387	1.147 (0.069–19.047)	31/50 (62.0%)	18/25 (72.0%)	13/25 (52.0%)	0.145	2.373 (0.734–7.675)
7 years	31/51 (60.7%)	17/25 (68%)	14/26 (53.8%)	0.301	2.364 (0.205–27.248)	30/50 (60.0%)	17/25 (68.0%)	13/25 (52.0%)	0.248	1.961 (0.621–6.193)
8 years	30/50 (60%)	16/25 (64%)	14/25 (56%)	0.563	1.781 (0.28–11.328)	30/50 (60.0%)	16/25 (64.0%)	14/25 (56.0%)	0.563	1.397 (0.449–4.35)
9 years	30/50 (60%)	16/25 (64%)	14/25 (56%)	0.563	1.156 (0.218–6.135)	30/50 (60.0%)	16/25 (64.0%)	14/25 (56.0%)	0.563	1.397 (0.449–4.35)
10 years	30/50 (60%)	16/25 (64%)	14/25 (56%)	0.563	2.056 (0.454–9.307)	30/50 (60.0%)	16/25 (64.0%)	14/25 (56.0%)	0.563	1.397 (0.449–4.35)

Note: *p* values' column refers to the comparison between percentages, while OR is significant if the associated 95% CI does not contain 1.

Abbreviations: CI, confidence interval; LRP, laparoscopic radical prostatectomy; OR, odds ratio; RARP, robot-assisted radical prostatectomy.

3.3 | Functional outcomes

Concerning the continence outcomes, in our study cohort, after achieving the peak of 97.5% and 82.8% in RARP and LRP groups, respectively ($p < 0.029$), at the fifth year postintervention, the continence rate slightly decreased for both approaches reaching the 92.5% for robotics and 80% for laparoscopy. A significant statistical advantage was not reached, due to the low sample size of patients who completed the follow-up (Table 1 and Table S2), notwithstanding the Δ of 12% for continence recovery between the two groups.

However, at 10 years, the ICIQ-SF showed a significantly higher rate of completely dry patients in the robotic group (10/40 vs. 1/35) with higher amount of urine loss in the laparoscopic group: 10% of RARP patients and 17% of LRP patients reported a moderate to large amount of urine loss ($p = 0.02$) (Tables S3 and S4).

Cumulative HF for time to continence showed a hazard ratio (HR) of 2.18 ($p < 0.001$; 95% confidence interval [CI]: 1.52–3.11) in favor of robotic approach (Figure 2A).

At binomial logistic regression analysis for continence recovery, no significant predictors were identified (Table S5).

A trend similar to continence was observed also for potency recovery in patients who benefitted from an NS procedure. After 10 years of follow-up, 64% and 56% of this cohort were potent in RARP and LRP Group ($p = 0.56$), respectively (Table 1).

A benefit of the robotic approach in erectile function recovery was documented by the outcomes of the International Index of Erectile Function (IIEF) questionnaire (Table S4). As demonstrated by the IIEF sum scores, a Δ of 3.1 points was observed between the two groups at the end of the follow-up ($p = <0.001$). Furthermore, compared to the preoperative values, a decrease of −15.3% and −25.9% was observed in RARP and LRP groups, respectively.

Cumulative HF for time to potency did not show difference ($p = 0.29$) (Figure 2B). At binomial logistic regression analysis the younger age (odds ratio [OR]: 0.84, 95% CI: 0.73–0.96; $p = 0.014$) and a bilateral NS procedure (OR: 13.7, 95% CI: 3.5–53.4; $p < 0.001$) were found to be significant predictors for potency recovery (Table S6).

3.4 | Oncological outcomes

Among the 75 patients that completed the follow-up, four (10%) and six (17.1%) patients experienced BCR in RARP and LRP groups, respectively ($p = 0.36$), with an overall 10 years BCR-free survival of 87.7% and 78.0% ($p = 0.16$) (Figure 2C).

Among the 75 patients analyzed, eight in the RARP group and three in the LRP group underwent RT during the first 5 years of follow-up (three and one as adjuvant RT; while five and two as salvage RT, respectively); no patients received RT between five and 10 years of follow-up. Concerning androgen deprivation therapy, four and three patients have begun HT during the 10 years of follow-up; among them only two (5%) and three (8.5%) during the second 5 years. Comparable overall mortality was recorded (10.0% vs. 14.2%; $p = 0.56$), as well as cancer-specific mortality ($p = 0.15$) (Table S1). Furthermore, no differences were found between the two groups in terms of oncologic results after stratification by D'Amico risk group (Table S7).

3.5 | Late complications, quality of life, and satisfaction evaluation

After the first 5 years of follow-up (3/40; Clavien-Dindo Grade III), 7.5% and (0/35) 0% of surgery-related complications occurred in RARP and LRP groups, respectively ($p = 0.09$). In addition, six (15.0%) and seven (20.3%) patients underwent further surgical treatment for urological pathologies during the follow-up ($p = 0.56$) (Table S8); and in all the cases after the first 5 years. At 10 years of follow-up, 38/40 patients (95%) and 31/35 (88.5%) were completely satisfied or satisfied with the surgical procedure for prostate cancer ($p = 0.30$) in RARP and LRP groups, respectively. At follow-up conclusion, 35/40 (87.5%) and 29/35 (82.8%) patients defined their health status as excellent, very good, or good ($p = 0.57$) in RARP and LRP groups, respectively.

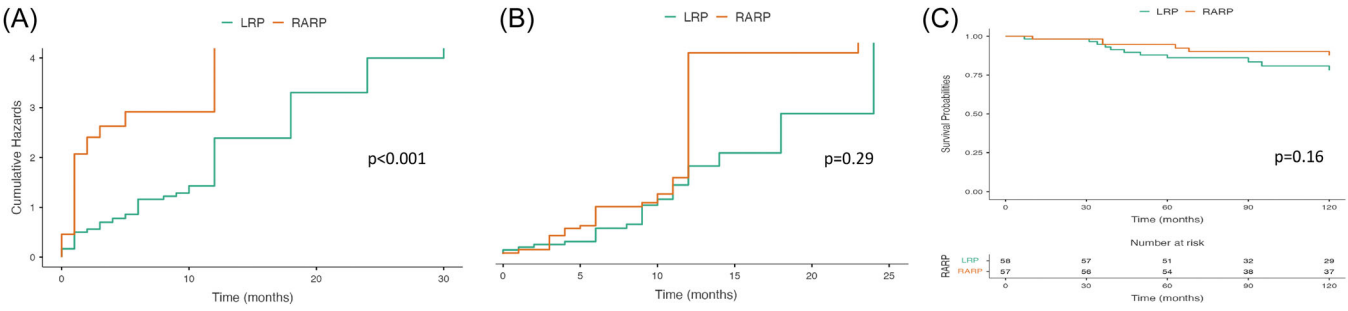

FIGURE 2 Cumulative hazard function (HF) of time to continence (A) and potency (B). Kaplan–Meier curve representation of biochemical recurrence-free survival (C). LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy. [Color figure can be viewed at wileyonlinelibrary.com]

3.6 | Machine learning data analysis

Analyzing the entire data set, the PLS-DA showed that RARP and LRP individuals are separated along the abscissa axis of the scores plot (Figure 3A), showing good overall discrimination. In particular, the variables in the left quadrants of the loading plot (Figure 3B) are more characteristic for the LRP group. As shown in the graph these variables are related with worst functional outcomes (e.g., higher rate of therapy for incontinence, longer continence time restore, and higher number of pads/die). On the other hand, the variables in the right quadrants are more consistent for the RARP group (e.g., higher rate of continence at first, second, and third years and higher scores, that means best, at EPIC_Q46 at fifth year).

Furthermore, specifically for our primary endpoint, we have set a second model including only the variables that potentially have an impact on postoperative functional outcomes. Again, RARP and LRP patients are separated along the abscissa axis of the scores plot (Figure 3C). The variables in the left quadrants of the loading plot (Figure 3D) are more correlated to the LRP group suggesting worst performances in terms of continence outcomes during the entire 10 years of follow-up.

4 | DISCUSSION

Herein, we present, for the first time, the long-term outcomes of a prospective randomized controlled trial (RCT) comparing LRP and RARP. We found significant advantages for RARP in terms of continence and potency recovery in the first 5 years of follow-up; while, in the second half, despite a Δ12% for continence and Δ8% for potency in favor of robotic approach the statistical significance was

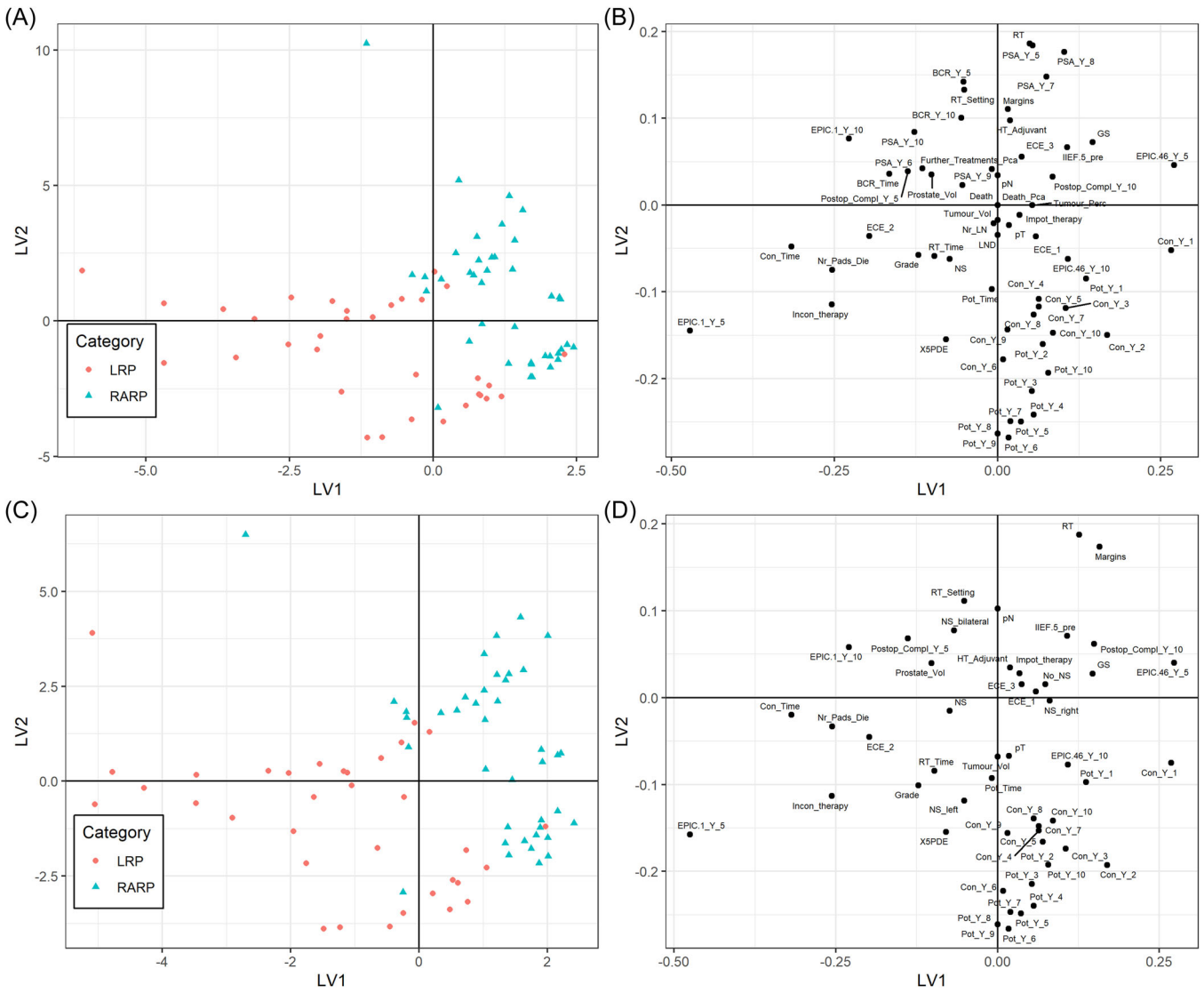

FIGURE 3 Sparse partial least square-discriminant analysis scores (A) and (C) and loadings (B) and (D) plots evaluating all the entire data set (A) and (B) of our collected variables or only the variable related with functional outcomes (C) and (D). In (A) and (C), individuals who underwent the RARP technique are marked with blue triangles, whereas individuals who underwent the LRP technique are marked with red circles. In (B) and (D), each dot represents a parameter that was monitored during the 10-year follow-up period. LRP, laparoscopic radical prostatectomy; RARP, robot-assisted radical prostatectomy. [Color figure can be viewed at wileyonlinelibrary.com]

not reached ($p = 0.068$ and $p = 0.56$, respectively). In fact, no differences were found between the surgical approaches at the logistic regression analysis.

This is probably linked to the occurrence of different confounding factors during this long follow-up, such as the need for postoperative RT or HT, further surgical interventions, and aging.

Therefore, in our multivariable analysis, no variables resulted to be significant for continence recovery while only age and bilateral NS procedure for potency. Moreover, one should note that this study was powered to detect difference in continence at 3 months and so it was not planned to give findings at 10 years anyway; furthermore, the number of patients considered was reduced compared to the original population (−37.5%), and this aspect might have played a role in the calculation of statistical difference between the groups.

Focusing on continence, even if age is a well-known risk factor for postoperative incontinence with an estimated rise of 6% every year,[19] the aging of the patients during the long follow-up period with the concomitant increase of incontinence rate, does not influence the quality of life as reported with EPIC and ICQUI-SF questionnaire.

In the last years, continence mechanisms were deeply explored[20] and, with robotics, different surgical techniques were proposed aimed to maximize postoperative continence recovery.[21–23]

The impact of the surgical technique is mostly reflected in the first years after the intervention, as recently demonstrated in an evidence-based analysis published by Carbonara et al. (OR: 0.38; 95% CI: 0.18–0.8; $p = 0.01$).[24] Furthermore, the benefit of the robotic approach was revealed to be significant also after 2 years of follow-up.[25] On the other hand, the long-term data are controversial: if a large Dutch retrospective series including 1370 patients with a median follow-up time of 7.08 years, proved the advantages of RARP versus LRP for continence recovery ($p = 0.002$)[26]; on the contrary, Lantz et al. did not find advantages for robotics compared to open prostatectomy in their 8 years follow-up study.[4]

Similar trends were reported in our series for potency recovery in the nerve-sparing cohort. We can speculate that the robotic approach, with its enhanced visualization and mobility, allows to perform a more accurate nerve-sparing, reducing the stress and damage on the neurovascular bundles' fibers, resulting in a faster and higher rate of erection, according to Literature for the early potency (12 months) recovery.[24] However, despite the Δ8% in favor of robotics in our NS series, a significant benefit was not reached, in accordance with the experience of Lindenberg and colleagues,[26] even if the better IIEF-5 at the end of the follow-up was recorded ($p < 0.001$).

Briefly, summarizing our findings on functional outcomes, we can affirm that

- No statistical differences in terms of continence and potency recovery rate after 10 years of follow-up were reported
- However, we found a Δ12% for continence and Δ8% for potency in favor of the robotic approach at the end of the follow-up.
- The statistical inconsistency was caused by the loss of 45 (37.5%) patients and subsequent insufficient power of the study together with the occurrence of confounding factors such as adjuvant/salvage RT.
- Analyzing the quality of continence (amount of urine loss, and percentage of completely dry patients) with the ICIQ-SF questionnaire and the quality of erections with IIEF-5 questionnaire, we found that in the robotic group, the patients reached better outcomes ($p = 0.02$ and $p < 0.001$).
- In fact, the two study cohorts differ in terms of functional performances at PLS-DA analysis.

Concerning oncological outcomes, in this RCT we found similar rates of PSMs both in our overall cohort of 120 patients ($p = 0.38$)[9] and in the specific cohort of 75 patients that have achieved the 10th year of follow-up ($p = 0.86$). This data is reflected by the BCR rate that resulted to be similar between the two groups at the end of the follow-up ($p = 0.36$). Furthermore, BCRFS was in line with our previously published experience at 5 years postintervention (81.6% for RARP and LRP groups),[10] showing a rate of 87.7% and 78% for RARP and LRP group, respectively ($p = 0.167$). Similarly, Menon et al. reported BCRFS rates of 95.1%, 86.6%, and 81.0% after 1, 5, and 7 years, respectively, after RARP.[23] This optimal cancer control obtained with robotic approach is not surprising, in fact in a recently published paper by Bravi et al., as opposed to open and laparoscopic radical prostatectomy, surgeons performing RARP achieve adequate cancer control at the beginning of their learning curve.[27] In our series, oncological outcomes were comparable between the two cohorts also in high-risk group patients (Table S3), even if the surgeon had different learning curve with the two surgical approaches at the time of surgery.[9]

Focusing on safety results and late complications both approaches resulted to have a low rate of surgery-related adverse events (Table S4) and need of further surgical interventions to solve these issues (Tables S4 and S5). In fact, only 3/40 (7.5%) and 6/35 (17.15%) patients needed further surgical treatments related to their previous prostate cancer surgery. In a population-based analysis, Wu et al.[28] found that RARP was associated with fewer acute and chronic postoperative complications than open or laparoscopic prostatectomy. In fact, at 3 years, the odds of chronic surgical complications, apart from BPH symptoms and urethral strictures, were lower in patients who received RARP.

All the above-mentioned factors (both functional and oncological) translate into excellent long-term satisfaction outcomes with both techniques as revealed by the EPIC questionnaire, with roughly 90% of the patients that were satisfied and 85% that defined their health status at least good (see Section 3.5). However, the faster recovery of continence and potency with RARP resulted in a higher satisfaction in the robotic cohort at 1 and 5 years of follow-up.[9,10]

After all these considerations we can introduce the concept of pentafecta,[29] showing that 22/40 (55%) patients in the RARP group and 18/35 (51.4%) in the LRP achieved this goal ($p = 0.88$). Among the 35 patients who did not reach this objective, 22 (62.8%) failed just one parameter which, in most cases, was erectile dysfunction.

Finally, our study does not evaluate the difference in terms of costs between RARP and LRP. Even if RARP is associated with higher median direct costs, medical costs, and total hospital charges, its costs dropped once the peak of the learning curve was reached, achieving better functional and oncological outcomes in comparison with LRP.[24] Furthermore, the advent of open market, with the introduction of new robotic platforms[30] will determine a further decrease in the costs of robotics, increasing the accessibility of this technology. With a last technical consideration, we would like to emphasize that current refinements of RARP (such as retzius-sparing and single site extravesical approaches)[21,31,32] may simply not be feasible to the same high standard without articulated instrumentation, three-dimensional vision, camera deflection, or the relative speed advantage of robotics, and it furtherly corroborate the benefits of robotic surgery.

This study is not devoid of limitations: firstly, the low sample size can affect the results, even if the number of enrolled patients was statistically validated. It should be stressed that the power of the study was calculated based on approximately 25% between the incidence proportions of tested outcome (continence at Month 3 after the intervention)[9]; therefore, despite the comparable pre-operative baseline data of this cohort of 75 patients, our findings can be affected by the missing of the data of patients lost at follow-up. Furthermore, this is a single surgeon, single-center series and therefore this data may not be generalizable for all practitioners.

5 | CONCLUSIONS

At 10 years of follow-up, comparable rates of continence and potency were observed between RARP and LRP. Nevertheless, the RARP cohort demonstrated higher percentage of patients achieving total dryness and experiencing valid erections as indicated by higher IIEF-5 scores.

Furthermore, both RARP and LRP resulted to be oncologically safe even after a long-term follow-up.

The loss of 37.5% of the patients during the follow-up period can partially affect these findings.

AUTHOR CONTRIBUTIONS

Francesco Porpiglia and Cristian Fiori: Conceptualization. **Sabrina De Cillis, Federico Piramide, Gabriele Volpi, Stefano Granato, Davide Zamengo, Alberto Piana, and Gabriele Bignante**: Data curation. **Eugenio Alladio, Federico Piramide, Edoardo Vallariello, and Ilaria Stura**: Formal analysis. **Enrico Checcucci, Daniele Amparore, Matteo Manfredi, Michele Di Dio, Riccardo Autorino, Francesco Porpiglia, and Cristian Fiori**: Supervision. **Enrico Checcucci and Sabrina De Cillis**: writing—original draft. **Gabriele Volpi and Daniele Amparore**: writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data presented in this study are available on request from the corresponding author.

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SUPPORTING INFORMATION

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