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Retrograde Release of the Neurovascular Bundle with Preservation of Dorsal Venous Complex During Robot-assisted Radical Prostatectomy: Optimizing Functional Outcomes

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Abstract

Background: Robot-assisted laparoscopic radical prostatectomy (RARP) presents consistent oncological outcomes for prostate cancer; yet continence and potency results are not uniform. We present a technical modification for RARP which preserves the nerves and vascular structures anterior to the prostate aiming to optimize functional outcomes.
Objective: To present oncological and functional results of a modified technique for RARP.
Design, setting, and participants: Prospective, noncontrolled case series including 128 consecutive patients undergoing RARP performed by a single surgeon (R.F.C).
Surgical procedure: RARP with retrograde release of the neurovascular bundle and preservation of dorsal venous complex.
Measurements: Potency was defined as a Sexual Health Inventory for Men score of ≥17; continence was defined as use of no pads. Oncological results analyzed were positive surgical margins (PSM) rates and biochemical recurrence (BCR)-free survival. BCR was defined as prostate-specific antigen >0.2 ng/ml. Complications were graded according to the Clavien-Dindo classification.
Results and limitations: Median patient age was 63.5 yr. Median skin-to-skin time was 78 min. Median length of hospital stay was 1 d, with seven patients (5.5%) hospitalized for more than 24 h. Median intraoperative bleeding was 200 ml and two patients required postoperative blood transfusion (1.6%). Four patients (3.1%) had grade ≥3 complications. Biochemical recurrence (BCR) occurred in nine of 128 patients (7%) and median time to BCR was 6 mo. Overall PSM rate was 13.3% (17 of 128 patients). PSM rate was 9% among patients with pT2 disease (8/89) and 27% in patients with pT3 (9/38). Continence was reached immediately in 85.9% of the patients and 98.4% were continent at1 yr. At 1 mo postoperatively, 60 patients were potent (53%), while 98 patients among 113 (86%) were potent 1 yr after surgery. A limitation of this study is that it was a noncomparative study.
Conclusions: Retrograde release of the neurovascular bundle with preservation of dorsal venous complex during RARP is safe and associated with excellent oncological and functional outcomes. Future comparative studies are needed.
Patient summary: Robot-assisted radical prostatectomy (RARP) presents consistent oncological outcomes for prostate cancer; yet continence and potency results are not uniform. We present a technical modification for RARP aiming to preserve the nerves and vascular structures anterior to the prostate. We evaluated 128 consecutive patients with clinically localized or locally advanced prostate cancer undergoing RARP with our modified technique of retrograde release of the neurovascular bundles with dorsal vein sparing. We have shown that this technique is safe, effective and associated with early recovery of continence and sexual function after surgery.

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1. Introduction

Robot-assisted radical prostatectomy (RARP) presents consistent oncological outcomes with low complication rates [1]. The magnification and bloodless operative field of RARP allow for accurate dissection of the periprostatic fascias enhancing preservation of the neurovascular bundles (NVBs). Yet, functional results following RARP (erectile function and continence) are not consistent in multiple series using standard NVB preservation techniques. Although functional results of RARP appear to be superior to laparoscopic surgery [2] and, in some series, to open surgery [3], rates of return of potency in the robotic approach have ranged from 62% to 80% [2,4]. Despite the fact that tumor staging and patient characteristics (age, preoperative erectile function) play major roles in predicting postoperative potency, improvements in surgical technique could lead to more refined preservation of the NVBs enhancing functional recovery [5,6].

Recently, the anatomical basis of the neuronal architecture described by Walsh [7] was reviewed. Microanatomical studies have demonstrated a complex neural organization with distribution around the prostate, including the anterior surface of the prostate [8,9]. Electrophysiological investigation confirmed the functional ability of these nerve fibers to promote erection [10]. These findings may indicate that the nerve-sparing (NS) surgery including these anterior fibers can optimize the functional results of RARP.

The aim of this study is to illustrate a technical modification of RARP allowing the preservation of nervous and vascular structures anterior to the prostate and report our 1-yr outcomes with this modified technique.

2. Patients and methods

2.1. Study design and patient selection

We evaluated 128 consecutive patients with clinically localized or locally advanced prostate cancer (clinical stage T1, T2, or T3—TNM) undergoing RARP with modified retrograde release NVBs with dorsal vein and endopelvic fascia sparing from October 2015 to January 2016. All patients underwent preoperative bone scans and magnetic resonance imaging (MRI) to confirm local staging and surgical planning. All procedures were performed by a single surgeon (R.F.C.) with experience of over 1000 cases of RARP prior to the beginning of this series. Data were prospectively collected and retrospectively analyzed after Institutional Review Board approval of the study.

2.2. Preoperative parameters evaluated

For each patient, we collected the following clinical and pathological information: age, body mass index (BMI), Charlson comorbidity index, total prostate-specific antigen (PSA) level, prostate volume in ultrasound-guided transrectal prostate biopsy, D'Amico risk classification, biopsy Gleason score, and clinical cancer stage (cTNM).

Baseline urinary and sexual functions were assessed before RARP with the self-administered validated questionnaires Expanded Prostate Cancer Index Composite (EPIC) and Sexual Health Inventory for Men (SHIM), respectively [11,12]. In preoperative evaluation, 15 individuals were considered impotent (SHIM <17) and therefore were excluded from the postoperative potency analysis. Continence was defined as the use of no pads; all patients were continent prior to surgery.

2.3. Surgical technique

All cases were performed using a six-port transperitoneal technical modification of RARP [13], and port placement was the same as previously described [14]. We used the Da Vinci surgical system Si (Intuitive Surgical, Sunnyvale, CA, USA) throughout the cases.

The innovation of this technique is to perform the early retrograde release of the NVBs without opening the endopelvic fascia and without ligating the dorsal venous complex (DVC).

Retrograde neurovascular dissection was performed bilaterally in all cases. Partial NS was performed using anatomical landmarks as described by Patel et al [15]. The decision to perform partial NS was taken based on MRI findings and using our previously published nomogram [16]. A modified periurethral suspension stitch and posterior reconstruction of the rhabdosphincter were performed in all procedures [17].

Pelvic lymph node dissection (PLND) was performed in all cases. Extended PLND, which comprises the removal of tissue along the external iliac vein, from the obturator fossa, internal iliac vessels, and common iliac artery until the ureter, was performed in patients with a risk of lymph node involvement of $>5\%$ in the Briganti nomogram [18]; a limited PLND (removed tissue along the external iliac vein and from the obturator fossa) was performed in patients with an estimated risk of $<5\%$.

In sequence, the key steps of surgical technique are as follows:

1. The patient is placed in the Trendelenburg position at a 30° angle. Pneumoperitoneum is induced with a Veress needle and the trocars are inserted.
2. Using a 0° lens, an incision of the anterior peritoneum to access the Retzius space is performed; the overlying fatty tissue adjacent to the prostate is dissected.
3. Using a 30° lens turned downward, the anterior bladder neck is incised without opening the endopelvic fascia or ligating the DVC (Fig. 1A).
4. After suspending the Foley catheter, the posterior bladder neck is incised so as to obtain vas deferens and seminal vesicle exposition; the lateral bladder attachments are not ligated in order to preserve the anterolateral neurovascular structures.
5. Athermal dissection of the vas deferens and seminal vesicles is performed. Afterward, the Denonvilliers fascia is incised and the posterior plane of dissection is developed according the planned NS strategy; to allow for more lateral dissection of this plane, we flip the camera to 30° up. In patients in whom full NS was planned, the incision was performed in the interfascial plane bilaterally; when incremental NS was performed, the posterior plane was developed underneath the Denonvilliers fascia.
6. Our technical modification is the release of the NVB starting at the level of the bladder neck, developing an avascular plane underneath the DVC (Fig. 1B). This dissection continues laterally respecting the anatomical landmarks of the NVB described by Patel et al [15] (Fig. 1C); full NS is performed when NVB dissection occurs medially to the prostatic artery, communicating this plane with the posterior plane previously developed; if a partial NS is desired, we dissect it laterally to the prostatic artery. The NVB dissection is performed bilaterally.
7. The prostatic apex is dissected maximizing preservation of the urethral stump; this dissection is carried out underneath the DVC using blunt and sharp dissection, avoiding injury to the anterior vascular structures. Posteriorly, the urethra is incised and the prostate is removed.

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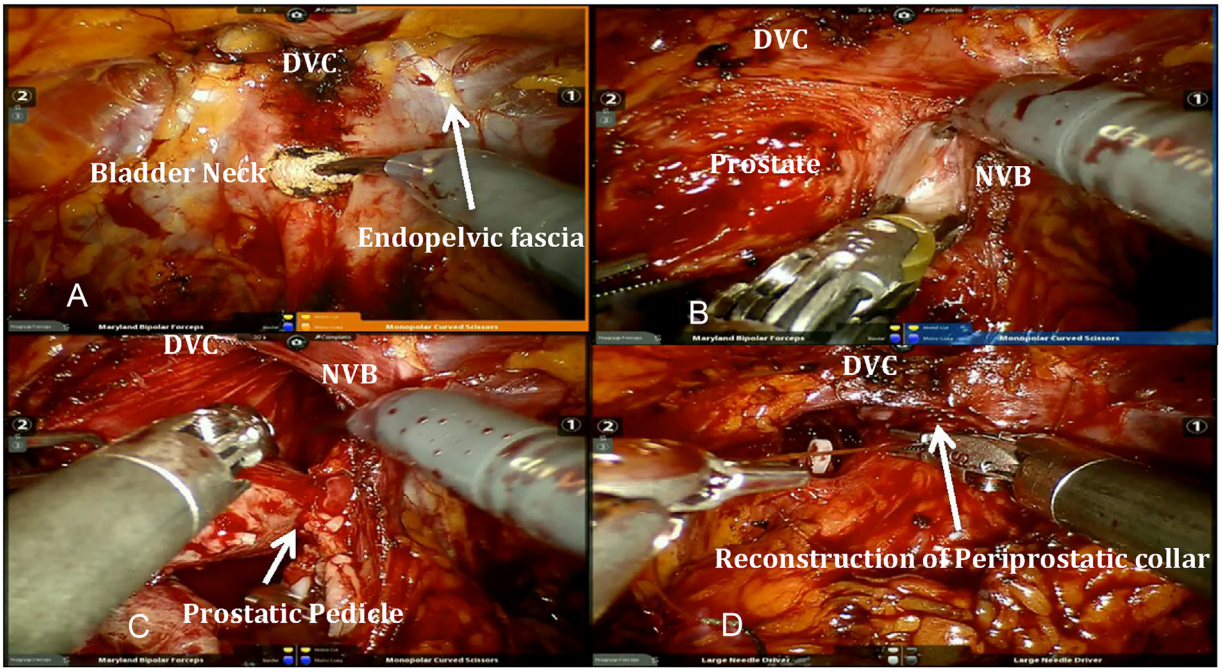

Fig. 1 – Surgical steps. (A) The anterior bladder neck being incised with the endopelvic fascia and the dorsal venous complex preserved. (B) Retrograde release of the right neurovascular bundles. (C) Dissection of the right neurovascular bundles before ligation of the prostatic pedicle. (D) The endopelvic fascia and periprostatic collar are reconstructed with a continuous suture.

8. In sequence, modified posterior reconstruction of the rhabdosphincter is carried out and vesicourethral anastomosis is performed using a modified van Velthoven continuous suture (3.0 Polydioxanone Suture—double armed—16 cm × 16 cm).
9. Finally, the endopelvic fascia and periprostatic collar are reconstructed with a continuous suture (Fig. 1D). A modified anterior suspension stitch is performed (3.0 Polydioxanone Suture—double armed—16 cm × 16 cm).

2.4. Intraoperative data collection and perioperative care

The data collected intraoperatively included operative time, estimated blood loss (blood aspirated from the surgical field), blood transfusion, NVB preservation (partial or complete), PLND, and complications. Perioperative care is detailed in the Supplementary material.

2.5. Histopathological evaluation and postoperative definition of positive surgical margins

RARP specimens were processed according to the recommendations of the American Society of Clinical Pathologists [19]. Clinical staging was done according to the TNM system. Positive surgical margins (PSMs) were defined as the presence of tumor tissue on the inked surface of the specimen.

2.6. Postoperative evaluation, penile rehabilitation, and surgical complications

The urinary catheter was removed 7 d after surgery routinely.

The length of the hospital stay was calculated by subtracting the date of admission from the date of discharge. Rehospitalizations within 28 d after the surgery were considered "readmissions".

Postoperative follow-up comprised clinical examination, PSA level, continence evaluation with a self-administrated questionnaire (EPIC), and potency evaluation using a self-administered questionnaire (SHIM) at 1, 3, 6, and 12 mo after surgery.

Early penile rehabilitation was recommended for all patients, with regular use of phosphodiesterase type 5 (PDE5) inhibitors starting 7 d after surgery, until recovery of sexual function.

Complications occurring during surgery or within 90 d after surgery were classified according to the Clavien-Dindo classification.

2.7. Postoperative definition of biochemical recurrence, continence, potency, and trifecta and pentafecta rates

Biochemical recurrence (BCR) was defined as two consecutive values of PSA >0.2 ng/ml after RARP [20].

The definition of continence was based on the answer to the EPIC questionnaire item regarding the range of incontinence severity: "How many pads or adult diapers per day did you usually use to control leakage during the past 4 wk?" Continence was defined as the use of "no pads" (score 0). The rate of continence recovery was defined considering only continent patients prior to RARP. Immediate continence was defined as continence immediately after the removal of the bladder catheter at 7 d postoperatively.

Patients were considered potent after surgery if the recovered SHIM score was ≥17. Time to recovery of erectile function was considered the date of the first sexual intercourse after surgery. Patients taking PDE5 inhibitors to achieve intercourse were considered potent. Patients for whom intercourse depended on a vacuum erection device, penile injection, transurethral alprostadil, or a penile prosthesis were not considered potent. The rate of erectile function recovery was defined considering only patients who were potent prior to RARP.

Trifecta rate is the likelihood of achieving urinary continence, potency, and cancer control concurrently following surgery. Pentafecta rate is the likelihood of achieving trifecta plus absence of complication and absence of PSMs concurrently following surgery [21].

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2.8. Statistical analysis and data report

Collected data were summarized with means and standard deviation for normally distributed continuous variables. Discrete variables were reported with median and interquartile ranges. Potency and continence were reported with a Kaplan-Meier estimate and log rank test for comparisons.

Statistical analysis was performed using SPSS version 20.0 (IBM, USA).

3. Results

3.1. Clinical, demographic, and pathological characteristics

Demographic and preoperative characteristics of 128 patients are summarized in Table 1.

Overall median age was 63.5 yr (interquartile range [IQR]: 57.25–68). Median preoperative PSA was 5.25 (IQR: 4.1–7.2). The most common Gleason score in biopsies was 7 (62.5%)—50% pattern 3 + 4 and 50% pattern 4 + 3. The majority of patients had clinically localized disease and were detected by elevated PSA (T1c = 32%); 49.2% of the patients had palpable disease at rectal examination (T2) and 18.8% had signs of extracapsular extension in the preoperative clinical evaluation (DRE and MRI).

Table 1 – Demographic and preoperative features

Variable	
Age (yr), mean ± SD	62.6 ± 0.707
BMI, mean ± SD	27.93 ± 2.984
Charlson comorbidity index, median (IQR)	2 (1–3)
PSA median (IQR)	5.25 (4.1–7.2)
	N (%)
Clinical stage	
T1c	41 (32)
cT2	63 (49.2)
cT3	24 (18.8)
Biopsy Gleason score	
6	29 (22.7)
7	80 (62.5)
≥8	19 (14.8)
D'Amico risk classification	
Low risk	26 (20.3)
Intermediate risk	70 (54.7)
High risk	32 (25)
Pathological stage	
≤pT2	90 (70.3)
≥pT3, pT4	38 (29.7)
Specimen Gleason score	
≤6	19 (14.8)
7	83 (64.8)
≥8	26 (20.4)
Prostate weight range (g)	
20–40	90 (70.3)
41–60	23 (18.0)
>60	15 (11.7)
SHIM score, median (IQR)	21.5 (23–20)
<17	15 (11.7)
≥17 and ≤21	49 (38.3)
>21	64 (50)

BMI = body mass index; IQR = interquartile range; PSA = prostate-specific antigen; SD = standard deviation; SHIM = Sexual Health Inventory for Men.

3.2. Perioperative outcomes and complications

Median skin-to-skin time was 78 min (IQR: 70–85). Median length of hospital stay was 1 d (IQR: 1–1); only seven patients (5.5%) were hospitalized for more than 24 h. Median intraoperative bleeding was 200 ml (IQR: 170–230); only two patients received blood transfusion perioperatively, both with a relevant history of coronary artery disease and presenting with postoperative hypotension with a drop in hemoglobin level.

In this series, 41 patients (32%) underwent extended lymphadenectomy and 87 (68%) underwent limited lymphadenectomy.

Readmission was necessary in two (1.6%) patients. The reasons were pulmonary thromboembolism (0.8%) treated with intravenous heparin and strangulated hernia (0.8%) treated with enterectomy plus hernia repair; both presented uneventful recovery after treatment.

Overall, we identified 14 postoperative surgical complications of any grade in 14 patients (10.9%). No intraoperative complications were recognized. Complications are available in Table 2.

3.3. Histopathological findings

Table 3 summarizes the histopathological findings from patients undergoing RARP.

Median prostate weight was 43 g (IQR: 24–44.75). The majority of patients (70.3%) presented organ-confined disease; seminal vesicle invasion (pT3b) was identified in 10 of the patients (7.8%) and extraprostatic extension (pT3a) was found in 28 cases (21.9%). There was no case of pT4 in histopathological findings.

The most common Gleason score in the surgical specimen was 7, which corresponded to 64.8% of the patients (33 Gleason 3 + 4, 39.8%; 50 Gleason 4 + 3, 60.2%). One case presented pT0 (0.8%), even after the review of biopsy and surgical specimen.

Overall PSM rate was 13.3% (17/128). Stratified by pathological stage, PSM rate was 9% among patients with pT2 and 23.7% among patients with pT3. Most of the PSMs (nine cases; 52.9%) were circumferential, followed by six cases in the prostate apex (35.3%) and two in the bladder neck (11.8%).

All patients underwent lymphadenectomy. The median number of resected lymph nodes was 20 (IQR: 13.5–26.5), and six patients (4.7%) presented positive nodes: four (9.76%) in extended lymphadenectomy and two (2.3%) in limited lymphadenectomy.

Table 2 – Complications according to Clavien-Dindo classification

Complications	Occurrences (%)	Clavien grade
Lymphocele	7 (5.4)	I
Blood transfusion	2 (1.6)	II
Pulmonary thromboembolism	1 (0.8)	II
Infected lymphocele	1 (0.8)	IIIa
Bladder clots	1 (0.8)	IIIb
Strangulated hernia	1 (0.8)	IIIb
Strictures of fossa navicularis	1 (0.8)	IIIb

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Table 3 – Pathological features

Variable	*N* (%)
Pathological stage	
pT2	89 (69.5)
pT3a	28 (21.9)
pT3b	10 (7.8)
Specimen Gleason score	
6	18 (14.0)
7	83 (64.8)
≥8	26 (20.4)
Positive surgical margins	
Overall, *N* (%)	17 (13.3)
In pT2 cancers, *n*/*N* (%)	8/89 (9)
In pT3 cancers, *n*/*N* (%)	9/38 (23.7)
pT3a, *n*/*N* (%)	8/28 (28.6)
pT3b, *n*/*N* (%)	1/10 (10)

Note that with respect to pathological stage and Gleason, the sum of percentages does not result in 100% because the pathological stage of one patient was pT0.

3.4. *Oncological results*

Median follow-up period was 19 mo (IQR: 17–22); minimum follow-up was 13 mo.

BCR occurred in 7% of cases (9/128), and median time to BCR was 6 mo after surgery (IQR: 6–12; Supplementary Fig. 1). Median PSA at the time of BCR was 0.3 (IQR: 0.2–0.825).

Patients with BCR were reassessed with pelvic MRI, bone scintigraphy, or positron emission tomography with prostate-specific membrane antigen (PSMA). In two cases, bone metastases were detected and the treatment option was luteinizing hormone-releasing hormone therapy. The other five cases, in which no metastasis was observed, treatment was conducted with salvage pelvic radiotherapy ± androgen deprivation therapy.

3.5. *Continence outcomes*

At 1 yr postoperatively, continence rate was 98.4% (126/128). Only two patients (1.6%) remained incontinent at the end of follow-up, and are being treated with pelvic floor physiotherapy and anticholinergics, both using only one pad. The immediate continence rate was 85.9%. Figures 2A and 2B show continence rates over time and continence recovery Kaplan-Meier curve, respectively. Median time to recovery of continence was 7 days (IQR: 7–7). To date, no patient presented with an anastomotic stricture.

3.6. *Erectile function outcomes*

At 1 mo postoperatively, 60 patients were potent (SHIM ≥17) (53.1%), while 98 patients among 113 (86.7%) were potent 1 yr after surgery. Figure 3A shows the potency rate over time, and Figure 3B shows a Kaplan-Meier curve of erectile dysfunction recovery. Median time to recovery of potency was 30 days (IQR: 30–120). In our series, based on the grade of the NVB preservation on each side of the prostate, we have the following data: 67 patients underwent full bilateral NS (59.3%), 40 underwent partial + full NS (35.4%), and six underwent less than partial + full NS (5.3%). We stratified the median time to erectile dysfunction recovery by full bilateral NS versus full + partial NS (Supplementary Fig. 2). There was no statistically significant difference between the two groups (p = 0.345).

3.7. *Trifecta and pentafecta rates*

The overall trifecta rates were 51.2%, 69%, 81.4%, and 83.2% at 1, 3, 6, and 12 mo after RARP, respectively. The overall pentafecta rates were 41.6%, 57.6%, 64.6%, and 69% at 1, 3, 6, and 12 mo after RARP, respectively.

4. Discussion

In this prospective series, we reported the 1-yr results of a modified technique for RARP in which the endopelvic fascia and the DVC are preserved. Our results show surgical safety, low rate of complications and excellent oncological and functional outcomes. The rate of potency and continence seem to outperform the results of standard techniques reported in the literature.

Studies have demonstrated a complex neural organization of the NVBs, with a distribution around the prostate

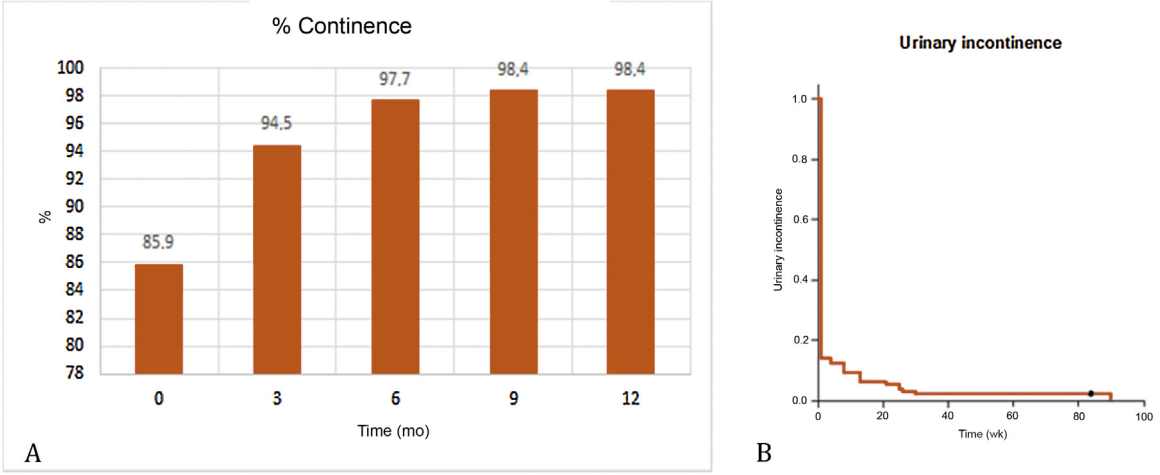

Fig. 2 – (A) Percentage of continent patients by time (in months). (B) Kaplan-Meier curve of incontinence (in weeks).

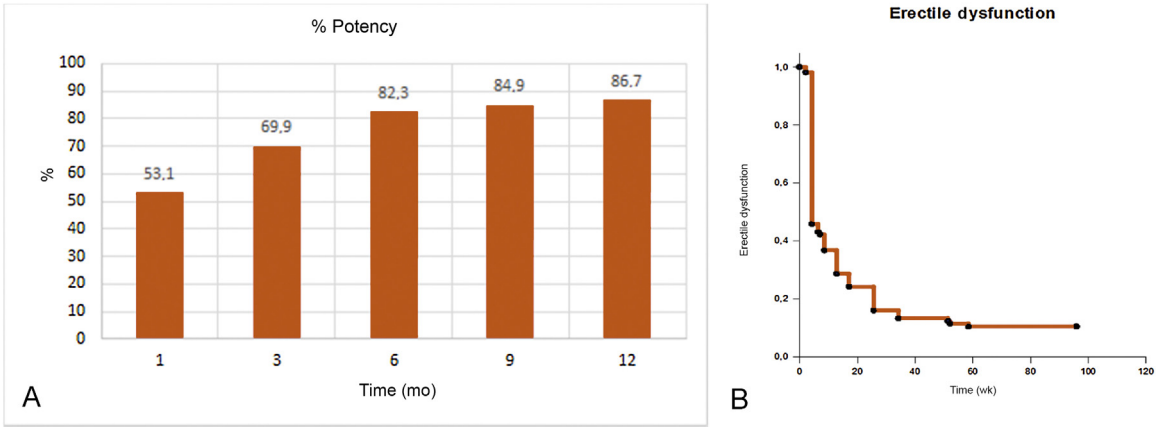

Fig. 3 – (A) Percentage of sexually potent patients by time. (B) Kaplan-Meier curve showing erectile dysfunction by time.

and seminal vesicles [8] and a hammock-like arrangement in a trizonal distribution [22]. Authors described the presence of autonomic ganglion cells in the pelvic plexus around the bladder and the prostate [23,24]. Savera et al [25] identified erectile nerves in the "veil of Aphrodite" along the anterolateral aspect of the prostate. NVBs were found to be occupying a potential avascular triangular space bounded by the anterior layer of the Denonvilliers fascia posteriorly, prostatic fascia medially, and lateral pelvic fascia laterally [24].

From this knowledge, we have developed technical modifications in RARP that preserves the nerves and vessels on the anterior surface of the prostate without opening the veil of Aphrodite and the endopelvic fascia. This allows, from the anatomical point of view, the achievement of an excellent NS surgery.

In addition, this technique avoids the section of the puboprostatic ligaments, which, together with the endopelvic fascia, stabilizes the external urinary sphincter. It also maintains the integrity of the DVC and the small arteries running through the Santorini plexus. Although the latter do not have a well-defined role, they have been suggested to have an accessorial function in blood supply of the striated sphincter [26]. Importantly, such modifications did not result in significant increases to the risk of bleeding or complications. Of note, our complication rate was 10.9%, as compared with 9% in a comprehensive review of the literature [27]. Similarly, our mean bleeding value was 200 ml, which is comparable with the 166 ml found in the same meta-analysis [27]. The transfusion rate of 1.5% is compatible with a 2% rate reported in the literature, ranging from 0.5% to 5% [27].

Our oncological outcomes are also in keeping with existing reports of high volume centers and surgeons. In patients with pathologically localized disease, the rate of PSMs was 9%, while a systematic review revealed a PSM rate of 9% in pT2 cases, ranging from 4% to 23% [28]. Among patients with pT3 disease, the PSM rate was 23%, as compared with a mean of 37% in the literature (range 29–50%) [28].

Functional outcomes represent a promising aspect of this technique. In our cohort, 53.1% of patients presented recovery of potency at 1 mo postoperatively. At 3 and 12 mo, respectively, our rates of potency recovery were 69.9% and 86.7%. This compares with the means of 50% at 3 mo (range 32–68%) and 70% at 12 mo (range 54–90%) found in the literature [29]. Since potency recovery depends highly on patient and disease characteristics, this general comparison precludes definite conclusions about the impact of technique on functional results. Interestingly, the Retzius sparing approach, which preserves part of the anterior structures reported here, has elicited somewhat similar results, ranging from 71% to 81% of potency after 1 yr [26]. However, the patients in our cohort experienced early recovery of potency and were close to the highest rates of potency recovery in the literature. Several characteristics underscore the fact that our cohort was not particularly selected toward lower complexity. Our study population comprised largely overweight (59%) and obese (16%) patients, also presenting frequently with intermediate- (54%) and high-risk (25%) disease, with almost one third of patients having extracapsular extension.

Continence recovery following RARP depends on several factors regarding both patient characteristics and surgical technique [30]. Among preoperative patient characteristics, age [5], BMI, prostate volume [6], and comorbidities [5] have been reported to influence postoperative continence recovery. Several characteristics underscore the fact that our cohort was not particularly selected toward lower complexity. Although characteristics such as comorbidity index and prostate weight were favorable among our patients, the presence of adverse characteristics in our cohort suggests that our excellent results in continence recovery, reaching 97% at 6 mo and 98% at 12 mo, are not merely due to a highly selected sample but due to factors related to the surgical technique.

However, our results have limitations. This is a non-comparative study design; hence, the individual influence of the modified technique cannot be demonstrated. Furthermore, this is a single cohort of individuals undergo-

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ing RARP by a single surgeon with large experience. Longer follow-up for oncological results as well as randomized trials should further elucidate whether this technique provides significant improvement in functional results.

5. Conclusions

The modified approach to RARP with preservation of the DVC and the endopelvic fascia in combination with retrograde release of NVB appears to be a safe and effective, maximizing early functional recovery without compromising oncologic outcomes.

Author contributions: Rafael Ferreira Coelho had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: de Carvalho, Coelho.
Acquisition of data: de Carvalho, Coelho, Barbosa, Guglielmetti.
Analysis and interpretation of data: de Carvalho, Coelho.
Drafting of the manuscript: de Carvalho, Coelho, Barbosa, Cordeiro, Guglielmetti.
Critical revision of the manuscript for important intellectual content: de Carvalho, Coelho, Patel, Nahas, Rocco.
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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.eururo.2018.07.003.

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