ORIGINAL ARTICLE

Do we need the nerve sparing radical prostatectomy techniques (intrafascial vs. interfascial) in men with erectile dysfunction? Results of a single-centre study

Wael Y. Khoder · Raphaela Waidelich · Michael Seitz · Armin J. Becker · Alexander Buchner · Stefan Trittschler · Christian G. Stief

Abstract

Objectives To report effect of different nerve sparing techniques (NS) during radical prostatectomy (RP) (intrafascial-RP vs. interfascial-RP) on post-RP incontinence outcomes (UI) in impotent/erectile dysfunction (ED) men.

Patients and methods A total of 420 impotent/ED patients (International Index of Erectile Function-score <15) with organ-confined prostate cancer were treated with bilateral-NS [intrafascial-RP (239) or interfascial-RP (181)] in our institution. Intrafascial-RP was indicated for biopsy Gleason score ≤6 and PSA ≤10 ng/ml while interfascial-RP for Gleason score ≤7 and higher serum PSA. Seventy-seven patients with bilateral non-NS-RP were taken for comparison. No patient received pre-/postoperative radiation/hormonal therapy or had prostatic enlargement surgery. UI was assessed 3, 12 and 36 months postoperatively by third party. Continence was defined as no pads/day, safety 1 pad/day as separate group, 1–2 pads/day as "mild-incontinence" and >2 pads/day as "incontinence".

Results All groups had comparable perioperative criteria without significant preoperative morbidities. International Prostate Symptom Score showed severe symptoms in 5 % of patients without correlation to UI. UI-recovery increased until 36 months. Full continence was reported from 56 versus 62 and 53 % patients after intrafascial-RP versus interfascial-RP and wide excision at 3 months, respectively ($p = 0.521$). Corresponding figures at 12 months were 70 versus 61 versus 51 % ($p = 0.114$) and at 36 months 85 versus 75 versus 65 % ($p = 0.135$), respectively. After 12 and 36 months, there was tendency to better UI-results in advantage of NS-technique; best results were achieved in intrafascial-RP group. UI-recovery was age-dependant. Advantage was found in NS-group compared with non-NS-group in older patients (>70 years, $p = 0.052$).

Conclusions Impotent/ED patients have higher chances of recovering full continence after NS–RP. NS should be planned independently of preoperative potency status whenever technically and oncologically feasible. Age and lower urinary symptoms are not restrictions. Current data should be considered in preoperative patient counselling.

Keywords Prostate cancer · Radical prostatectomy · Continence results after radical prostatectomy · Impotence

Introduction

Radical prostatectomy (RP) represents the one of the most effective treatments for organ-confined prostate cancer (PCa) compared to conservative managements in respect to cancer-specific survival [1]. It is the most widely performed therapy for patients with organ-confined prostate cancer implicating a high cure rate by surgery alone as well as low surgical morbidity [2].

Thanks to the early detection programs for PCa, including PSA screening, there is a significant shift of the diagnosed PCa towards earlier stages and younger patients [2, 3]. This has increased the interest and awareness about the importance of preserving the postoperative quality of life. Therefore, both post-RP urinary incontinence (UI) and erectile dysfunction (ED) still represent the most important issues for PCa patients [4, 5].

W. Y. Khoder (✉) · R. Waidelich · M. Seitz · A. J. Becker · A. Buchner · S. Trittschler · C. G. Stief
Department of Urology, University Hospital-Grosshadern,
Ludwig-Maximilians-University-Munich, Munich, Germany
e-mail: wael.khoder@med.uni-muenchen.de

Recently, many nerve sparing techniques through different approaches (open, laparoscopic and robotic assisted) have been increasingly used as a therapeutic option for selected patients [6–10]. All these surgical approaches aim to provide optimal cancer control while maintaining the integrity of the surrounding pelvic anatomical structures to preserve postoperative urinary continence and sexual potency [11, 12]. However, certain proportion of patients post-RP still experience UI and ED with subsequent deterioration of their quality of life. This has led some work groups to explore preoperative patient characteristics such as age, preoperative functional status and comorbidities as possible predictors for the postoperative functional outcomes [13].

While several studies have demonstrated a strong correlation between nerve sparing RP and postoperative continence [14], others denied this correlation [15]. However, these studies have examined this association in heterogeneous patient collections and mostly in a retrospective manner. In current study, we have examined the effect of different nerve sparing techniques of RP (intrafascial vs. interfascial) on the postoperative urinary recovery in a group of men with a definitive impotence or ED. The rate of UI and its postoperative recovery over 3-year follow-up were compared with the results of a non-nerve sparing RP control group of impotent patients at a single high volume centre series.

Patients and methods

Current analysis of our prospective database included 420 impotent/ED patients with PCa treated with bilateral neurovascular bundle preservation (NS) either retropubic intrafascial-RP or interfascial-RP with or without pelvic lymph node dissection since 2007 at our institute.

The indication for intrafascial-RP was patients with biopsy Gleason score ≤6 and PSA ≤10 ng/ml with low tumour size, while interfascial-RP was done in patients with Gleason score ≤7 and higher serum PSA. A control group of 77 patients with bilateral wide excision RP was taken for comparison. No patient received pre- or postoperative radiation or hormonal therapy or had any surgery for benign prostatic enlargement. All patients gave consent for surgery after detailed preoperative counselling.

All study data including patients' chronological, clinical and functional data were completed before surgery. Baseline lower urinary symptoms (LUTS), urinary continence and erectile function were assessed 1 day before surgery by the validated International Prostate Symptom Score (IPSS) and International Index of Erectile Function (IIEF-5) questionnaires, respectively. All study population

suffered preoperative impotence/ED defined as IIEF score <15 points as mentioned in the literature [16]. All patients responded negatively to the following questions: IIEF3-"ability to insert your penis into your partner's vagina?" and IIEF4-"Did your erections last long enough to have sexual intercourse?" and were included regardless if they used a phosphodiesterase-5 inhibitor or not.

The NS-techniques were already described in the literature. Intrafascial-RP [7] was used in 239 patients. It involves small incision of the endopelvic fascia only ventrally medial to puboprostatic ligaments which are cut just proximal to prostate opening the intrafascial plan. After control of the plexus santorini, the prostate apex is carefully dissected and catheter is reflected to cut the exposed verumontanum. The prostatic capsule is freed laterally from its thin surrounding fascia (periprostatic fascia) containing small vessels and nerves. Dennonvilier fascia is bluntly dissected from the dorsal surface of the prostate with clipping of perforator vessels. Its last attachment at the prostate base is separated at base of seminal vesicles, then centrally. This maintains all periprostatic fasciae (including endopelvic fascia) intact.

The interfascial-RP [12] was used in 181 patients. This technique involves the incision of endopelvic fascia, incising the levator and prostatic fasciae at high lateral positions over the prostate to developing the plane between the prostatic capsule and prostatic fascia. The neurovascular bundles are preserved using clips. In both techniques, coagulations were avoided.

Postoperative continence recovery was assessed by the patients themselves according to their daily pad usage. All patients underwent 3 weeks of continence rehabilitation in specialised hospitals, which is a standard procedure in Germany. Patients were followed up at 3, 12 and 36 months postoperatively. This was done by a separate hospital unit (third party). Patients not requiring any pads were defined as continent. Those who did require 1 pad for safety were evaluated as separate group. Requirement for 1–2 pads daily during daily physical activities was considered as "mild incontinence" and more than 2 pads daily as "incontinence".

Continuous variables were compared using the Mann–Whitney test. Categorical variables (e.g. continence outcome, PSM) were tested for significance using the chi-square test. p values below 0.05 were regarded as significant. For all calculations, the software STATISTICA 10 (StatSoft, Tulsa, OK) was used.

Results

Perioperative characteristics of patients included in the study are shown in Table 1. There were comparable criteria

Table 1 Perioperative patient characteristics and histological findings for 420 impotent/ED men included in current study. (A) Open complete intrafascial (239 patients) versus interfascial radical prostatectomy (181 patients). (B) Nerve sparing (420 patients) versus wide excision prosta- tectomy (77 patients). (C) Histopathological findings of 420 impotent men included in current study. A total of 241 patients underwent bilat- eral nerve sparing (open complete intrafascial und interfascial radical prostatectomy) versus wide excision prostatectomy (77 patients)

(A)	Intrafascial-RP median (range)	Interfascial median (range)	p value (Mann–Whitney test)
Age (years)	68.0 (48.2–81.9)	68.1 (48.1–80.7)	0.578
BMI (kg/m^2)	26.8 (21.5–36.8)	26.7 (19.4–38.1)	0.477
Initial PSA (ng/ml)	5.9 (0.3–9.9)	8.2 (0.1–95.0)	<0.001
IIEF score before RP	4 (0–15)	0 (0–15)	0.026
Prostate volume (ml)	46 (7–160)	44 (14–148)	0.672
Intraop. blood loss (ml)	100 (50–800)	150 (50–1,300)	0.117
Duration of surgery (min)	65 (40–200)	65 (45–215)	0.032
(B)	Nerve sparing median (range)	Wide excision median (range)	p value (Mann–Whitney test)
Age (years)	68.1 (48.1–81.9)	69.1 (53.6–82.0)	0.042
BMI (kg/m^2)	26.8 (19.4–38.1)	26.8 (19.2–38.5)	0.431
Initial PSA (ng/ml)	6.8 (0.1–95.0)	17.7 (2.8–168.0)	<0.001
IIEF score before RP	2.5 (0–15)	1 (0–15)	0.304
Prostate volume (ml)	45 (7–160)	42 (15–122)	0.449
Intraop. blood loss (ml)	150 (50–1,300)	200 (100–700)	<0.001
Duration of surgery (min)	65 (40–215)	70 (50–225)	<0.001
(C)	Nerve sparing % (n/total)	Wide excision % (n/total)	p value (chi-square test)
pT2	76 (318/420)	17 (13/77)	<0.001
pT3	24 (102/420)	83 (64/77)	
Gleason score			
6	38.8 (163/420)	6.5 (5/77)	<0.001
7	51.4 (216/420)	19.5 (15/77)	
8–10	9.8 (41/420)	74.0 (57/77)	
R0 (in pT2)	88 (280/318)	85 (11/13)	0.710
R1 (in pT2)	12 (38/318)	15 (2/13)	
R0 (in pT3)	48 (49/102)	34 (22/64)	0.083
R1 (in pT3)	52 (53/102)	66 (42/64)	

between all three groups. Significance was only found in the preoperative serum PSA. Further, operative times as well as blood loss were significantly different between nerve sparing techniques and wide excision group. Table 1 C shows the histopathological results of both nerve sparing as well as non-nerve sparing RP groups.

Only patients without severe preoperative morbidi- ties (e.g. heart failure, COPD, brain insults, etc.) were included in the current study. Patients who had inconti- nence due to their comorbidities were excluded. Study patients have documented full continence, and results of IPSS questionnaire revealed mild obstruction (score 0–7) in 55.8 versus 54.5 versus 53.4 % for intrafascial- RP versus interfascial-RP versus wide excision, respec- tively. Corresponding figures for moderate obstruc- tion (score 8–19) were 40.9 versus 40.3 versus 41.1 %, respectively. Severe obstruction (score 20–35) was found in 3.3 versus 5.2 versus 5.5 %, respectively. Results of

continence after 3, 12 and 36 months in relation to pre- operative IPSS score (mild, moderate, severe) and sur- gical technique are listed in Table 2. These differences were not significant.

Complete follow-up data were available from 247 (59 %), 250 (60 %) and 149 (35 %) patients after 3, 12 and 36 months, respectively. The different grades of continence recovery at 3, 12 and 36-month follow-up data are dem- onstrated in Fig. 1. There was gradual continence recov- ery with gradual decrease in incontinence rates (2 or more pads/day) after all techniques over the postoperative time until 36-month evaluations.

Overall, the full continence (0 pads) was reported from 56 versus 62 and 53 % of patients after intra- fascial-RP versus interfascial-RP and wide excision RP at 3 months, respectively. Corresponding figures at 12 months were 70 versus 61 versus 51 % and at 36 months 85 versus 75 versus 65 %, respectively. There

Table 2 Correlation between full continence (0 pads/s) after 3, 12 and 36 months, preoperative symptoms (IPSS score) (mild = 0–7, moderate = 8–19, severe = 20–35) and surgical technique

	Intrafascial % (n/total)	Interfascial % (n/total)	Wide % (n/total)	p value
Mild				
3 months	53 (31/59)	64 (37/58)	52 (12/23)	0.409
12 months	68 (40/59)	68 (40/59)	57 (13/23)	0.580
36 months	90 (36/40)	77 (27/35)	71 (10/14)	0.187
Moderate				
3 months	60 (27/45)	61 (27/44)	50 (5/10)	0.801
12 months	70 (31/44)	54 (22/41)	46 (6/13)	0.155
36 months	77 (24/31)	71 (17/24)	0 (0/2)	0.061
Severe				
3 months	66 (4/6)			
12 months	44 (4/9)			
36 months	0 (0/3)			

No discrimination between surgical techniques in severe cases was possible due to low case number

Note the differences of the total patients' number due to some missing data or incomplete questionnaires

was no significant difference between the three groups at 3 months ($p = 0.521$), 12 months ($p = 0.114$) and 36 months ($p = 0.135$). After 12 and 36 months, there was a tendency to better continence results in advantage of nerve sparing techniques; best results were achieved in the intrafascial-RP group (Fig. 2a). Furthermore, the difference between nerve sparing RP and wide excision was not significant after 12 months ($p = 0.093$) and 36 months ($p = 0.141$).

The continence recovery rate at 1 and 3 years was different according to patients' age. This was 62 versus 59 versus 60 % ($p = 0.925$) and 80 versus 69 versus 80 % ($p = 0.474$) for patients between 60 and 70 years, and 79 versus 64 versus 50 % ($p = 0.154$) and 88 versus 81 versus 50 % ($p = 0.134$) for patients over 70 years after intrafascial-RP versus interfascial-RP versus wide excision RP, respectively (Fig. 2b, c). A big albeit not significant difference was found when comparing nerve sparing with non-nerve sparing groups in older patients (>70 years); among these patients, 70 and 50 % had full continence in the nerve sparing and wide excision group after 12 months ($p = 0.134$); 80 and 65 % had full continence in the nerve sparing and wide excision group after 36 months ($p = 0.052$). It was not possible to compare the results between the three operative techniques for ages <60 years due to the small patient number in the wide excision group (three patients). However, the young group of patients had very good continence results after nerve sparing procedures at 3, 12 and 36 months (73 vs. 82 vs. 95 %, respectively).
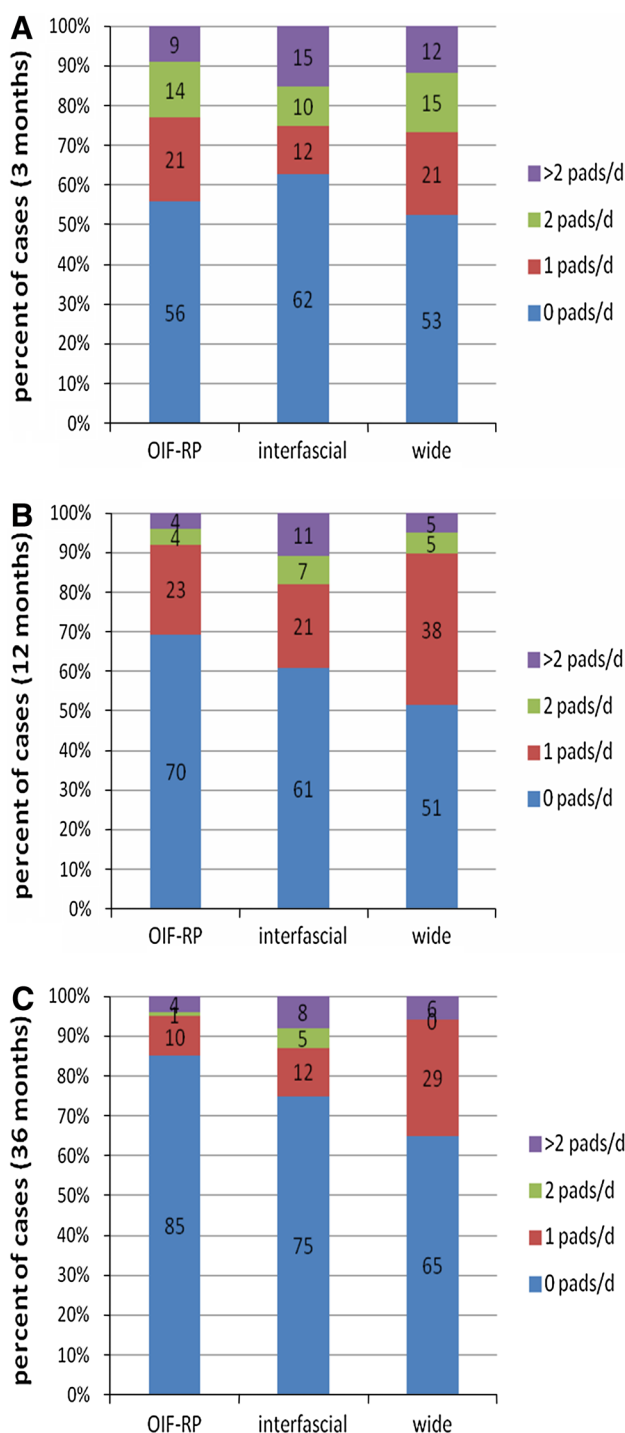

Fig. 1 Continence results of 420 impotent/ED men after open intrafascial, interfascial and wide excision radical prostatectomy after 3 months (**a**), 12 months (**b**) and 36 months (**c**)

Discussion

The most important two functional drawbacks of RP are the postoperative UI and ED. Both conditions have a significantly negative impact on patient quality of life [4].
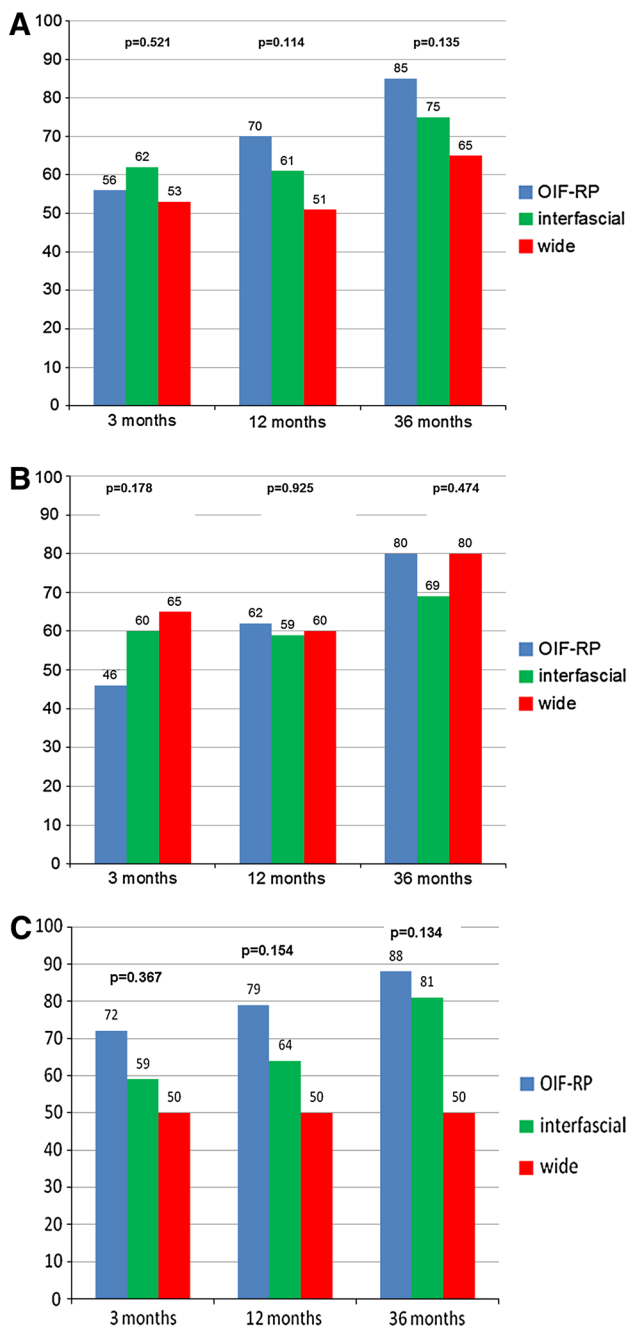
Fig. 2 Results of complete continence (0 pads/day) postopen intrafascial versus interfascial versus non-nerve sparing radical prostatectomy after 3, 12 and 36 months postoperatively. **a** All patients collective (420 patients). **b** For patients ages 61–70 years. **c** For patients ages >70 years

To our knowledge, this is the first time to report the direct association of nerve sparing techniques on postoperative continence in impotent/ED men after controlling all possible effecting factors. In this case, the only measurable postoperative functional result would be the continence recovery. However, there is a significant difference between

the published post-RP studies in reporting the postoperative incontinence rates in potent patients (6.4–20 %) [7–10, 17]. A fact indicating that the recovery of continence after RP is a multifactorial procedure depending on several pre-, intra- and postoperative parameters including the used continence definition, clinical characteristics, surgical techniques and time of evaluation [13–15].

These factors can be divided into none modifiable factors including the known preoperative patient/tumour criteria and modifiable factors that can be controlled during surgery or surgical planning [13]. In addition, various postoperative rehabilitation manoeuvres can help hasten urinary continence [18]. In order to examine the role of nerve sparing on postoperative continence recovery, all these factors were controlled. All patients had comparable preoperative criteria, were impotent and had bilateral nerve sparing surgery by high-volume surgeons. Further, all have the same rehabilitation procedures for continence over 3 weeks after surgery. A control group of comparable patients treated with non-nerve sparing RP done by the same surgeons was recruited for comparison.

The current results show a better postoperative continence recovery in impotent/ED men after nerve sparing techniques. Advantage was shown especially in older age men (>70 years). The observed outcome differences were not significant, which may be due to the number of cases. However, this observed advantage after nerve sparing RP should encourage surgeons to plan bilateral nerve sparing, whenever possible, even in older impotent men, where some clinicians continually discourage nerve sparing to minimise surgical morbidity. Further, there were insignificant better results after intrafascial-RP compared to interfascial-RP. Accordingly, it is advisable to use this technique in selected patients with low tumour volumes whenever feasible.

Some reports with conflicting results were recently published as an effort to identify predictors of urinary recovery after RP. The main concluded factors included erectile function, tumour characteristics [19], age and nerve sparing [17]. These reports were retrospective and included the statistical analysis of heterogeneous patients groups for urinary recovery. This was either using a logistic regression or time-dependent analysis approaches. Other studies denied the association between nerve sparing and better continence based on their continence results at 24 months which was not dependant on whether men regained potency or whether they had a bilateral or unilateral nerve sparing procedure [15]. However, lack of a control group from non-nerve sparing technique as well as the unequal patient groups in respect to nerve sparing techniques (bilateral in 88 % and unilateral in 12 %) could have also supported the opposite of their conclusions. Therefore, the results of previous studies should be interpreted with caution. The

current study provides for the first time a direct comparison between the different nerve sparing techniques and non-nerve sparing RP in impotent/ED men. This supports the results giving robust conclusions.

Several anatomical studies had established the association between the neurovascular bundles and the functional continence results after RP. While sensory and motor pudendal innervations to pelvic region did not change after retropubic NS-RP, an impaired membranous urethral sensitivity as well as its microcirculation seemed to be associated with UI [12, 17, 20]. A fact that confirms the current mentioned concept of discouraging non-nerve sparing RP, whenever possible, to improve the post-RP incontinence results. Moreover, several recently published clinical studies of many technical refinements (e.g. intrafascial technique) through the different approaches (laparoscopic, extraperitoneal endoscopic and robotic assisted) have demonstrated superior postoperative functional results compared to standard interfascial techniques [6–10, 21]. Current results were comparable to mentioned studies. However, we have not founded significant difference between intrafascial-RP and interfascial-RP for continence results in this patients group, denying its regular use in these patients.

Age is already identified as a predictor for continence recurrence [18]. Interestingly, current results show advantage in older impotent patients after nerve sparing RP. Furthermore, potency was associated with postoperative continence recurrence in patients treated with laparoscopic and robotic RP [22, 23]. These data were explained by the impaired pelvic vascular status associated with impotence. Current data do not seem to support this association. We believe that nerve preservation in impotent men is mandatory for continence recovery even in the presence of these expected vascular problems.

Similar to previous results, no association was found between severity of preoperative LUTS and continence recovery after surgery [19]. Further, no patient with preoperative incontinence was included in current study, which was identified as a predictor for postoperative incontinence by some authors [24]. There was lack of association between baseline IPSS and continence recovery; 95 % of the included patients in our study had no/mild/moderate symptoms. Evaluating patients with homogenous LUTS severity distribution had no significant difference on the postoperative results. The preoperative discrimination between storage and voiding symptoms might add another dimension to current analysis. Thus, future studies may be needed to clarify this issue.

Similarly, urinary outcomes were found Significantly Affected by NS-Quality during RP showing an advantage to NS in potent men [25]. This counters some previous studies [15, 17]. The authors address that NS makes sense for better continence outcomes and concludes that the quality of NS significantly influences patient-defined urinary functional convalescence. Current work is a good conjunct to this study but in impotent men. Further, only patients with both sides NS were included to avoid biases.

Despite of the robust data and conclusions of current study, every RP-outcomes study has limitations which should be argued. The patient number is fairly enough for the conclusions but homogenously recruited. The postoperative follow-up questionnaires were sent back from the patients in a complete unsolicited way without any reminder from our unit, albeit these follow-up patients' numbers were sufficient for valid statistic evaluations. Furthermore, these surgeries are standardised in our institution avoiding any potential differences in nerve sparing techniques which support the current conclusions from the provided results. Despite used routinely in our institution, the mentioned patients' selection criteria for each RP-technique could be discussed differently from other surgeons. Current study design has prevented bias as full potency might have induced the surgeons to use more meticulous nerve sparing techniques. Accordingly, this can be fully excluded based on our results. Current impotence definition may be not used by other authors, but we have selected patients, who have not even occasional sexual activity to support the conclusions. Pad weights rather than daily pad numbers may be considered by some surgeons as a better estimation for postoperative incontinence. Accordingly, we have considered continence as no usage of pads to avoid any misleading results. Patients self-assessments could be considered as a drawback, so we have evaluated patients with one safety pad/day as a separate group negating biases. The oncologic differences between groups exist, as they should, and this may affect urinary continence recovery as different cancer states may affect quality of life, though there were an unlikely explanation for the differences noted. Lastly, detailed oncological results were out of the scope of current study.

Despite the aforementioned limitations, the current study represents the first direct comparison of different bilateral nerve sparing techniques in large group of ED men over an intermediate-term follow-up for continence recovery.

Conclusions

Nerve sparing RP should be planned independently of preoperative potency status whenever technically and oncologically feasible. Age at surgery and LUTS are not a restriction for indicating NS–RP. Impotent/ED patients have higher chances of recovering full continence after nerve sparing surgery. Intrafascial-RP could be indicated for selected impotent patients adding some more benefit for the

continence recovery rates. Current data add to the improvement of the preoperative patients counselling regarding postoperative continence recovery.

Conflict of interest The authors declare that they have no conflict of interest that may pose with the publication of the current manuscript.

Ethical standards The study has been approved by the department ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave their informed consent prior to surgery. Statistical evaluations were done anonymously and details that might disclose the identity of the subjects under study were omitted. Current manuscript represents a retrospective evaluation and analysis of our prospective and consecutive RP data bank, which was done by a separate hospital unit (third party).

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