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Validated Prospective Assessment of Quality of Life After Robot-Assisted Laparoscopic Prostatectomy: Beyond Continence and Erections

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Abstract

Continence and erectile function represent major concerns after robot-assisted laparoscopic prostatectomy (RALP), although the analysis of only these results may underestimate the impact of surgery on quality of life (QoL). The aim of the study is to prospectively analyze QoL after RALP according to the validated European Organization for Research and Treatment of Cancer Quality of Life Questionnaire prostate cancer–specific module (EORTC-QLQ-PR25) and C30 and explore risk factors for the deterioration of QoL after surgery.

A total of 584 patients undergoing RALP were prospectively enrolled. QoL was assessed with the validated EORTC-QLQ-PR25 and C30. Differences across QoL items were assessed via Wilcoxon rank-sum test and associations between risk factors and QoL scores were tested via univariate and multivariate linear regression analyses.

All items of the PR25 questionnaire showed a significant deterioration at 1 month after RALP and began to normalize 3 months after surgery. At 24 months follow-up, urinary, bowel, and sexual activity scores were not significantly different from preoperative scores, while incontinence aid, treatment-related symptoms, and sexual functioning remained significantly worse. Preoperative sexual activity was more important in determining 3-month sexual outcomes than preoperative 5-item version of the International Index of Erectile Function (IIEF-5) or nerve-sparing approach. An overall return to preoperative QoL was registered at 3 months after RALP in global and physical QoL, and most important, global, physical, social, and role-functioning QoL scores were improved at 12 and 24 months compared to preoperative scores.

In this prospective study, detailed data on QoL are reported via the EORTC-PR25 and C30 questionnaires. While urinary, bowel, and sexual activity scores return to baseline values 24 months after surgery, incontinence aid, treatment-related symptoms, and sexual functioning may remain significantly deteriorated. Larger studies are needed to validate these findings.

Keywords

prostate cancer, quality of life, robotics

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Prostate cancer (PCa) is a major health concern worldwide (Center et al., 2012). In Belgium, nearly 8,000 new cases are diagnosed each year (Belgian Cancer Registry, s. d.), of which 89% present with stage I–III disease and these patients may be considered candidates for radical local treatment (Belgian Cancer Registry, s. d.). Robot-assisted laparoscopic prostatectomy (RALP) is becoming the new standard of treatment in the local control of

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disease, with comparable oncologic outcomes to the open approach (Mottet et al., 2017). After cancer control, the surgeon's main focus while performing radical prostatectomy is the preservation of urinary continence and, where indicated, of sexual potency. Great effort has been made by the urological community in order to maximize these two functional outcomes. The robotic platform, by increasing dexterity, reducing surgical trauma, magnifying vision, and allowing better preservation of anatomical structures, has indeed determined a shift in radical prostatectomy functional recovery (Park et al., 2013; Sooriakumaran et al., 2018), although controversy remains whether such an advantage is true in the long term and when comparing with highly skilled open surgeons (Ploussard, 2018; Yaxley et al., 2016). Clearly, an element of major bias in most studies exploring erectile function and continence after prostatectomy is the variability in the definitions of "continence" and "potency" (Borregales et al., 2013). Deciding whether surgery was *functionally successful* only by weighing a urinary pad or asking a patient if his erections are adequate is clearly reductive and a poor proxy of good surgery. For example, not wearing a protection pad does not at all exclude a urinary leakage (Lee et al., 2010). A wider analysis of quality of life (QoL) outcomes, tailored to the individual patient and evaluating the overall impact of radical prostatectomy and PCa, is needed and should be implemented when exploring continence and erectile function results, since each individual may experience and suffer incontinence and impotence in a different manner as these are continuous and not categoric phenomena.

The European Organization for Research and Treatment of Cancer (EORTC) has introduced validated questionnaires to explore QoL in oncologic patients (van Andel et al., 2008). These include the EORTC Quality of Life Questionnaire C30 (QLQ-C30; Aaronson et al., 1993), which is the core questionnaire for all cancer patients to evaluate QoL in clinical trials, and the EORTC PR25, specifically designed for men harboring PCa. Although studies exist analyzing QoL modifications after radical prostatectomy (Donovan et al., 2016; van der Poel et al., 2013), these are scarce and the majority of data is extrapolated from open cohorts (Donovan et al., 2016).

The aim of the current study is to analyze functional outcomes and QoL scores after RALP in a prospective series of two Belgian centers (Hopital Erasme and Institut Jules Bordet), evaluating their modifications and exploring potential risk factors for QoL degradation after surgery.

Materials and Methods

After institutional review board approval and ethics committee approval (Be-RALP study, Registre du Cancer Belge, RIZIV/INAMI), beginning in January 2010 until December 2015, all patients undergoing RALP with or without pelvic node dissection in two academic centers in Belgium (Hopital Erasme and Institut Jules Bordet) were prospectively enrolled in the Belgian Cancer Registry, Be-RALP study. Patients signed written informed consent to participate in the study. All patients harbored clinically localized or locally advanced PCa. Exclusion criteria were all men who underwent salvage RALP after failure of any kind of primary treatment for PCa (brachytherapy, radiotherapy, high-intensity focused ultrasound [HIFU]) as well as all patients who had received any form of hormonal treatment for PCa in the 12 months prior to surgery. Patients undergoing cytoreductive prostatectomy for metastatic PCa were excluded.

Questionnaires

Patients were invited to anonymously fill four questionnaires prior to surgery: the 5-item version of the International Index of Erectile Function (IIEF-5), the International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF), the EORTC PR25, and the EORTC QLQ-C30. After surgical planning, the patients received the questionnaires and were asked to answer the questions at home. Questionnaires were then retrieved by a specialized nurse and blindly inserted in the Belgian Cancer Registry via an Internet access program.

The ICIQ-UI Short Form provides a brief and robust measure to assess the impact of the symptoms of incontinence on QoL and outcome of treatment. This short and simple questionnaire is also of use to urologists to obtain a brief yet comprehensive summary of the level, impact, and perceived cause of symptoms of incontinence and to facilitate patient–clinician discussions. Its brevity also makes the ICIQ-UI Short Form an ideal research tool. The questionnaire is scored from 0 to 21, with 0 being the absolute absence of incontinence and 21 being major incontinence.

The IIEF-5 is a widely used, multidimensional questionnaire for the evaluation of male sexual function. It is recommended for the diagnostic evaluation of erectile dysfunction (ED) severity and as the end point for clinical trials. The IIEF-5 score is the sum of the ordinal responses to the five items and allows the categorization of erectile dysfunction. Scores 22–25 are associated with *No erectile dysfunction*; 17–21: *Mild erectile dysfunction*; 12–16: *Mild to moderate erectile dysfunction*; 8–11: *Moderate erectile dysfunction*; and 5–7: *Severe erectile dysfunction*.

Two separated, EORTC-validated questionnaires were given to patients. While the C30 is a questionnaire common to multiple cancers, the PR25 is specifically

designed for PCa patients. The former is divided into 15 items: 6 are functional scales (global, physical, role functioning, emotional functioning, cognitive, and social QoL), for which a higher score means a higher QoL. The 9 items are symptom scales (financial, fatigue, nausea, pain, dyspnea, insomnia, appetite, constipation, and diarrhea), for which a higher score means a poorer QoL. The questionnaire PR25, specific for PCa, is composed of 25 questions and allows a quantification of urinary symptoms, bother related to incontinence aid, bowel symptoms, hormone treatment–related symptoms (hot flushes, gynecomastia, lower extremity edema, weight alterations, and feeling less masculine), sexual activity, and sexual functioning. All scores of EORTC QoL questionnaires are expressed in percentages (0%–100%), following EORTC recommendations (Fayers et al., 2001).

Surgery

Surgery was performed via the robotic platform DaVinci S or SI, according to the hospital. Three experienced surgeons (>200 RALP cases performed prior to study) performed all surgeries. All patients underwent a transperitoneal, anterograde radical prostatectomy. Pelvic node dissection was performed according to preoperative Briganti nomogram. Unilateral or bilateral nerve sparing was performed according to patient–surgeon preoperative discussion and if judged oncologically safe. Patients then responded to the four questionnaires at 1, 3, 12, and 24 months after RALP. Each questionnaire was responded to anonymously by the patient at home right before the follow-up consultation. Regarding adjuvant or salvage radiotherapy and hormone therapy, patients were treated according to clinical, pathologic, and biochemical characteristics and based on multidisciplinary team decision. Patients regularly underwent pelvic floor muscle training beginning at 4 weeks after surgery, until satisfactory continence control was achieved.

Statistical Analysis

Descriptive statistics were used to depict variables across different postoperative phases. All scores of QoL questionnaires (PR25 and Q30) were expressed as percentages. Distributions of QoL scores on various time moments were compared to preoperative values using Wilcoxon signed-rank sum test. Univariate and multivariate linear regressions were performed to assess associations between potential risk factors and PR25 QoL outcomes (continuous, 0–100). Univariate and multivariate linear regression models were then constructed to assess risk factors for postoperative EORTC PR25 QoL scores, on early follow-up (3 months) and late follow-up (24 months). All statistical analyses were performed using Stata 13.1 (StataCorp, College Station, TX). Associations with p value $\leq .05$ were considered statistically significant.

Results

Overall, 584 patients completed ICIQ-SF, IIEF5, and EORTC PR25 questionnaires and were included in the final analysis. Concerning the EORTC QLQ-C30, subanalysis was restricted to 345 patients having completed the questionnaire. Table 1 illustrates global patient characteristics. Of note, 60% (353/584) of the patients underwent bilateral nerve-sparing RALP, 18% (104/584) had unilateral nerve sparing, and 22% (127/584) did not receive a nerve-sparing procedure.

International Consultation on Incontinence Questionnaire Short Form

Regarding preoperative continence status (Table 2), mean ICIQ was 1.9, though it must be underlined that ICIQ was equal to 0 (no leakage at all) in 77% of patients; a nonnegligible number of patients thus presented already urinary leakage in the preoperative setting, with 8% of the cohort having an ICIQ 1–5, 10% an ICIQ score of 6–10, and 5% having an ICIQ of 11–21 (indicating significant leakage). In the immediate postoperative period, a significant ($p < .001$) increase in ICIQ scores was observed, rising to a mean of 10 ± 6 at 1 month after surgery and showing an overall decrease during follow-up to a mean value of 4, 1 and 2 years after RALP, yet significantly higher compared to preoperative values ($p < .001$). Of note, 2 years after surgery 41% (240/584) of patients reported an ICIQ of 0, meaning no leakage whatsoever, 47% (274/584) had an ICIQ 1–10, and 12% (70/584) had a persistent ICIQ >11.

Five-Item Version of the International Index of Erectile Function

At baseline, median IIEF-5 was 16 (5–22), with only 28% (164/584) of patients showing no signs of ED (IIEF-5 ≥22) and 31% (181/584) of the cohort presenting with severe baseline ED (Table 2). IIEF scores at 1 and 3 months after surgery show a major decline in erectile function, with 82%–88% of men unable to obtain rigid erections. On future follow-up, we observed an amelioration of erectile function. These data must be interpreted with caution as they represent the erectile function of the entire cohort, including men with baseline ED and those in whom a non-nerve-sparing procedure was performed; if considering only patients with a

Table 1. General Characteristics of the Cohort.

Age (years)	64 (59–68) 64 ± 7
PSA (ng/ml)	7.1 (4.8–10.2) 9.6 ± 10.9
Family history of PCa	
No	385 (66%)
Yes	38 (7%)
Unknown	161 (27%)
cT	
≤1c	320 (55%)
2a–c	224 (38%)
≥3a	40 (7%)
Pathologic Gleason score	
6 (3 + 3)	265 (45%)
7 (3 + 4)	179 (31%)
7 (4 + 3)	82 (14%)
8	33 (6%)
9–10	25 (4%)
pT	
2a	33 (6%)
2b	36 (6%)
2c	316 (54%)
3a	138 (24%)
3b	60 (10%)
4	1 (0.2%)
pN	
0	220 (38%)
1	29 (5%)
X	335 (57%)
Surgical margins	
Negative	440 (75%)
Positive	144 (25%)
Nerve sparing	
None	127 (22%)
Unilateral	104 (18%)
Bilateral	353 (60%)
EBL (ml)	250 (150–400) 326 ± 294
Radiotherapy	
None	545 (93%)
<3 months	3 (0.5%)
<12 months	27 (5%)
<24 months	9 (1.5%)
Androgen deprivation therapy	
None	568 (97%)
3 months	10
12 months	15
24 months	16

Note. EBL = estimated blood loss; PCa = prostate cancer; PSA = prostate-specific antigen.

preoperative IIEF5 >11 and nerve-sparing procedures, 56% (81/145) of these men had an IIEF >11 at 2-year follow-up after RALP.

Table 2. ICIQ and IIEF Modifications Following RALP.

Preoperative		*p* value[a]
ICIQ	0 (0–0) 1.9 ± 5	—
IIEF	16 (5–22) 14 ± 10	
1 month post-op		
ICIQ	9 (6–14) 10 ± 6	<.001
IIEF	1 (1–4) 3 ± 4	<.001
3 months post-op		
ICIQ	7 (2–11) 7 ± 6	<.001
IIEF	2 (1–6) 5 ± 5	<.001
12 months post-op		
ICIQ	4 (0–7) 4 ± 5	<.001
IIEF	4 (1–13) 7 ± 7	<.001
24 months post-op		
ICIQ	3 (0–7) 4 ± 5	<.001
IIEF	5 (1–16) 8 ± 8	<.001

Note. ICIQ = International Consultation on Incontinence Questionnaire; IIEF = International Index of Erectile Function.
[a]Wilcoxon signed rank sum test compared to pre-op value.

QoL According to EORTC PR25

Figure 1 illustrates the modifications of QoL according to the PR25 questionnaire. Globally, all items were significantly deteriorated ($p \leq .04$) 1 month after surgery on first follow-up, with the greatest difference seen in sexual function (Δ 45%). "Bowel symptoms" were the first item to return to nonsignificantly different values compared to the preoperative status, returning to baseline at 3 months after surgery. For urinary symptoms instead, 12 months were necessary to restore preoperative scores, which at 24 months were even better compared to preoperative values, though this difference appeared nonsignificant (16 vs. 13, $p = .15$). On the other hand, patients who continued to present urinary incontinence referred a deteriorated QoL score concerning "bother from incontinence aid," even 2 years after surgery. Both sexual activity and sexual function items were significantly decreased after surgery. However, sexual activity (which does not necessarily require intercourse) exhibited a steady recovery, returning to values not significantly different from baseline at 24 months ($p = .65$). Sexual function, which analyzes erections, ejaculation, feeling comfortable about sex, and enjoying sex, was dramatically reduced by RALP.

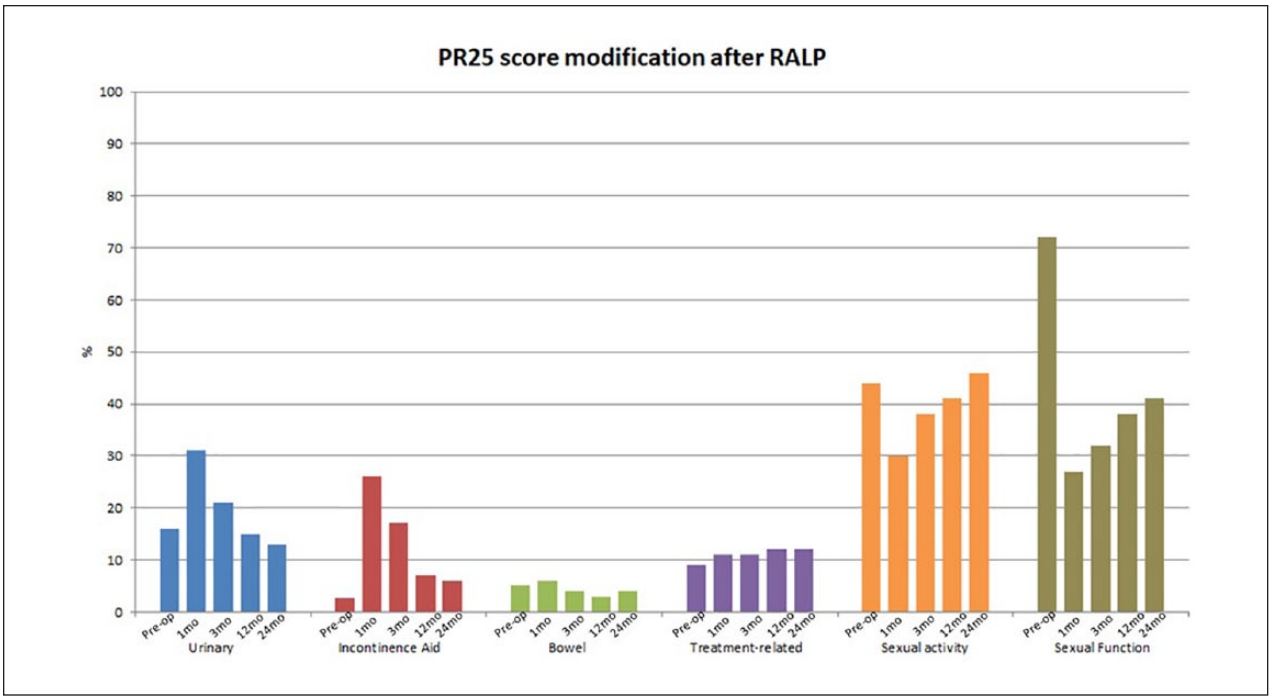

Figure 1. Modifications of QoL scores after RALP according to the EORTCPR25 questionnaire. QoL = quality of life; RALP = robot-assisted laparoscopic prostatectomy; and EORTCPR25 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Prostate Cancer

Although scores did ameliorate with ongoing follow-up, the reported scores 2 years after surgery remained significantly inferior compared to preoperative sexual functioning (72% vs. 41%, $p < .001$).

Risk Factors for QoL Modifications

On univariate and multivariate linear regressions, multiple factors associated with postoperative deterioration of QoL scores were found (Tables 3 and 4). Concerning urinary symptoms, preoperative score was significantly and positively associated with 3- and 24-month scores ($p < .001$). Bowel symptoms appeared to be positively associated both with preoperative scores ($p < .001$) and non-specimen-confined disease (≥pT3b or pN1 or R1). Treatment-related symptoms showed significant association with preoperative scores and non-specimen-confined disease and the strongest association with hormone therapy. These associations remained significant 2 years after RALP. Analyzing sexual activity, on univariate linear regression, age, non-specimen-confined disease, and hormone therapy were inversely associated with such QoL score. Preoperative sexual activity score, preoperative IIEF5, and bilateral nerve sparing, all significantly predicted 3-month and 24-month sexual activity scores. On multivariate analysis only preoperative score (positive association) and early hormone therapy (inverse association) were significant predictors of sexual activity at 3 months, while at 2 years only age (inverse) and preoperative score were significantly associated. Similarly, regarding sexual functioning, multiple risk factors analyzed were significantly associated with 3- and 24-month scores, including age, preoperative sexual functioning, preoperative IIEF5, bilateral nerve sparing, non-specimen-confined disease, and early hormone therapy. Nonetheless, on multivariate analysis, only age (inverse) and preoperative score significantly predicted sexual functioning scores.

QoL According to EORTC QLQ C30

When exploring baseline overall QoL, analyzed by the C30 questionnaire, the cohort presented a high level of overall QoL (Figure 2). Physical, role functioning, and social scores all had a mean value >90%. A reduction of emotional score in the preoperative setting was detected, with a mean value of 75%. In the specific categories of QoL, an increased rate of insomnia was also found, possibly reflecting this stressful phase.

The first 3 months after surgery are characterized by a significant deterioration in QoL scores (Figure 2); although physical and global QoL return to baseline values at 3 months, role functioning and social QoL require more time to adjust. Of note, insomnia, which is

Table 3. Univariate and Multivariate Analysis Exploring Association Between Risk Factors and QoL at 3 Months Post-Op.

	Univariate			Multivariate		
	Coeff	95% CI	*p*	Coeff	95% CI	*p*
Urinary symptoms						
Age	0.07	[–0.14, 0.29]	.48	0.002	[–0.21, 0.22]	.99
Pre-op urinary symptoms	**0.35**	**[0.26, 0.44]**	**<.001**	**0.35**	**[0.26, 0.44]**	**<.001**
Pre-op ICIQ	0.17	[–0.88, 0.42]	.20	−0.04	[–0.29, 0.21]	.73
Non-specimen confined[a]	1.37	[–1.8, 4.6]	.40	0.54	[–2.58, 3.66]	.73
Nerve sparing unilateral	−2.49	[–7.2, 2.25]	.30	−1.13	[–5.69, 3.42]	.62
Nerve sparing bilateral	−2.59	[–6.3, 1.14]	.17	−0.91	[–4.61, 2.80]	.63
Incontinence aid						
Age	0.27	[–0.11, 0.65]	.16	0.39	[–0.06, 0.84]	.09
Pre-op incontinence aid	−0.029	[–0.28, 0.23]	.82	−0.10	[–0.37, 0.17]	.46
Pre-op ICIQ	0.36	[–0.14, 0.86]	.16	0.63	[–0.26, 1.53]	.16
Non-specimen confined[a]	−2.6	[–8.1, 2.97]	.36	−1.64	[–8.04, 4.76]	.62
Nerve sparing unilateral	−1.32	[–9.36, 6.72]	.75	−0.49	[–9.46, 8.47]	.91
Nerve sparing bilateral	−1.12	[–7.47, 5.22]	.73	−0.57	[–7.98, 6.84]	.88
Bowel symptoms						
Age	−0.004	[–0.12, 0.11]	.94	−0.01	[–0.12, 0.10]	.84
Pre-op bowel	**0.19**	**[0.10, 0.28]**	**<.001**	**0.19**	**[0.10, 0.28]**	**<.001**
Non-specimen confined[a]	**1.88**	**[0.28, 3.49]**	**.02**	**1.75**	**[0.16, 3.34]**	**.03**
Treatment-related symptoms						
Age	−0.04	[–0.18, 0.10]	.54	−0.07	[–0.19, 0.05]	.26
Pre-op treatment related	**0.40**	**[0.32, 0.47]**	**<.001**	**0.38**	**[0.30, 0.45]**	**<.001**
Non-specimen confined[a]	**3.27**	**[1.28, 5.25]**	**<.001**	**1.96**	**[0.11, 3.81]**	**.038**
Early hormone therapy	**13.03**	**[5.49, 20.56]**	**<.001**	**7.9**	**[0.85, 14.9]**	**.028**
Sexual activity						
Age	**−0.39**	**[–0.75, –0.02]**	**.04**	0.01	[–0.36, 0.39]	.96
Pre-op sexual activity	**0.32**	**[0.24, 0.41]**	**<.001**	**0.29**	**[0.19, 0.39]**	**<.001**
Pre-op IIEF-5	**0.51**	**[0.26, 0.76]**	**<.001**	0.08	[–0.20, 0.37]	.57
Non-specimen confined[a]	**−5.54**	**[–10.9, –0.17]**	**.04**	−2.4	[–7.7, 2.9]	.37
Nerve sparing unilateral	3.26	[–4.7, –11.19]	.42	−1.7	[–9.5, 6.1]	.67
Nerve sparing bilateral	**8.75**	**[2.50, 15.00]**	**.006**	1.9	[–4.5, 8.3]	.56
Early hormone therapy	**−29.8**	**[–50.2, –9.43]**	**.004**	**−22.97**	**[–42.6, –2.5]**	**.03**
Sexual functioning						
Age	**−1.22**	**[–1.56, –0.87]**	**<.001**	**−1.04**	**[–1.44, –0.65]**	**<.001**
Pre-op sexual functioning	**0.17**	**[0.08, 0.27]**	**<.001**	0.06	[–0.05, 0.17]	.32
Pre-op IIEF-5	**0.77**	**[0.48, 1.04]**	**<.001**	0.25	[–0.14, 0.66]	.21
Non-specimen confined[a]	−0.45	**[–9.92, 0.83]**	.09	−3.6	[–9.17, 2.05]	.21
Nerve sparing unilateral	6.08	[–1.86, 14.01]	.13	4.4	[–3.80, 12.6]	.29
Nerve sparing bilateral	**9.38**	**[3.03, 15.7]**	**.004**	3.6	[–3.2, 10.5]	.30
Early hormone therapy	−20.3	[–46.02, 5.47]	.12	−13.05	[–38.2, 12.1]	.31

Note. Coeff = coefficient; IIEF = 5-item version of the International Index of Erectile Function; ICIQ = International Consultation on Incontinence Questionnaire; QoL = quality of life.
[a]Non-specimen-confined disease ≥pT3b or pN1 or R1.

better, though not statistically significantly, at 1 month (22 vs. 18, $p = .34$), is significantly reduced at 3-month follow-up (22% vs. 14%, $p = <.001$; Figure 2). Similarly, appetite is significantly improved at 3 months (6% vs. 4%, $p < .001$), and so are diarrhea symptoms (8% vs. 6%, $p = .02$). Fatigue and pain, significantly higher 1 month after surgery, returned to baseline at 3 months.

One year after surgery, global, physical, role functioning, emotional, and social QoL were all ameliorated compared to preoperative values (all $p < .01$; Figure 2). Similarly, fatigue, pain, insomnia, appetite, and diarrhea were all significantly improved (all $p < .03$), and no global QoL score was worse than the preoperative status. Globally, these results were maintained at 2-year follow-up.

Table 4. Univariate and Multivariate Analysis Exploring Association Between Risk Factors and QoL at 24 Months Post-Op.

	Univariate			Multivariate		
	Coeff	95% CI	*p*	Coeff	95% CI	*p*
Urinary symptoms						
Age	0.03	[–0.21, 0.26]	.83	−0.02	[–0.25, 0.21]	.84
Pre-op urinary symptoms	**0.29**	**[0.19, 0.38]**	**<.001**	**0.28**	**[0.18, 0.38]**	**<.001**
Pre-op ICIQ	0.08	[–0.14, 0.30]	.49	0.03	[–0.18, 0.24]	.78
Non-specimen confined[a]	1.66	[–1.63, 4.94]	.32	1.06	[–2.2, 4.30]	.51
Nerve sparing unilateral	−1.87	[–6.83, 3.09]	.46	−0.99	[–5.77, 3.80]	.68
Nerve sparing bilateral	−1.97	[–5.96, 2.02]	.33	−0.64	[–4.61, 3.34]	.75
Early RT	**20.14**	**[1.39, 38.9]**	**.035**	**19.43**	**[1.22, 37.6]**	**.037**
Any RT	1.72	[–3.5, 6.98]	.52	−0.08	[–5.77, 5.61]	.98
Incontinence aid						
Age	0.066	[–0.23, 0.36]	.66	−0.22	[–0.66, 0.22]	.32
Pre-op incontinence aid	0.21	[–0.23, 0.65]	.35	0.20	[–0.25, 0.65]	.38
Pre-op ICIQ	−0.08	[0.36, 0.19]	.55	−0.09	[–0.53, 0.34]	.68
[a]Non-specimen confined	−1.85	[–5.97, 2.28]	.38	−3.9	[–10.5, 2.74]	.25
Nerve sparing unilateral	0.0001	[–6.23, 6.23]	.99	1.98	[–6.72, 10.7]	.65
Nerve sparing bilateral	−2.37	[–7.36, 2.61]	.35	−3.26	[–10.70, 4.17]	.39
Early RT	−6.12	[–29.7, 17.49]	.61			
Any RT	−0.13	[–6.73, 6.44]	.97	3.35	[–6.84, 13.5]	.52
Bowel symptoms						
Age	−0.03	[–0.17, 0.10]	.63	−0.04	[–0.18, 0.09]	.52
Pre-op bowel	0.10	[–0.012, 0.21]	.08	0.09	[–0.02, 0.21]	.09
Non-specimen confined[a]	**2.67**	**[0.79, 4.54]**	**.005**	**2.78**	**[0.81, 4.6]**	**.007**
Early RT	0.27	[–10.6, 11.2]	.96	−1.90	[–13.07, 9.26]	.74
Any RT	1.27	[–1.76, 4.31]	.41	−0.23	[–3.55, 14.06]	.89
Treatment-related symptoms						
Age	−0.09	[–0.29, 0.11]	.39	−0.14	[–0.33, 0.05]	.15
Pre-op treatment related	**0.36**	**[0.25, 0.47]**	**<.001**	**0.33**	**[0.22, 0.44]**	**<.001**
Non-specimen confined[a]	**6.05**	**[3.23, 8.87]**	**<.001**	**5.09**	**[2.3, 7.87]**	**<.001**
Hormone therapy at 24 months	**10.06**	**[2.5, 17.61]**	**.009**	3.44	[–3.92, 10.79]	.36
Sexual activity						
Age	**−1.12**	**[–1.62, –0.62]**	**<.001**	**−0.75**	**[–1.25, –0.25]**	**.003**
Pre-op sexual activity	**0.33**	**[0.22, 0.44]**	**<.001**	**0.25**	**[0.12, 0.37]**	**<.001**
Pre-op IIEF-5	**0.60**	**[0.29, 0.92]**	**<.001**	0.13	[–0.20, 0.47]	.43
Non-specimen confined[a]	**−10.39**	**[–17.54, 3.24]**	**.005**	−4.55	[–11.64, 2.53]	.21
Nerve sparing unilateral	**10.88**	**[0.19, 21.56]**	**.046**	3.20	[–7.44, 13.84]	.56
Nerve sparing bilateral	**17.43**	**[8.87, 21.56]**	**<.001**	6.73	[–2.2, 15.68]	.14
Hormone therapy at 24 months	**−33.11**	**[–51.8, −14.4]**	**.001**	−17.56	[–36.77, 1.64]	.07
Sexual functioning						
Age	**−1.44**	**[–1.93, –0.95]**	**<.001**	**−1.11**	**[–1.58, –0.65]**	**<.001**
Pre-op sexual functioning	**0.34**	**[0.22, 0.46]**	**<.001**	**0.36**	**[0.25, 0.48]**	**<.001**
Pre op IIEF-5	**0.59**	**[0.27, 0.89]**	**<.001**	0.06	[–0.24, 0.37]	.69
Non-specimen confined[a]	−6.81	[–14.20, 0.58]	.07	−2.31	[–0.89, 4.32]	.49
Nerve sparing unilateral	10.67	[–0.85, 22.19]	.069	3.83	[–6.8, 14.45]	.48
Nerve sparing bilateral	**17.74**	**[8.17, 27.3]**	**<.001**	8.18	[–0.78, 17.14]	.07
Hormone therapy at 24 months	**−40.90**	**[–73.33, –8.4]**	**.01**	−29.50	[–59.24, 0.24]	.052

Note. Coeff = coefficient; IIEF = 5-item version of the International Index of Erectile Function; ICIQ = International Consultation on Incontinence Questionnaire; QoL = quality of life.
[a]Non-specimen-confined disease ≥pT3b or pN1 or R1.

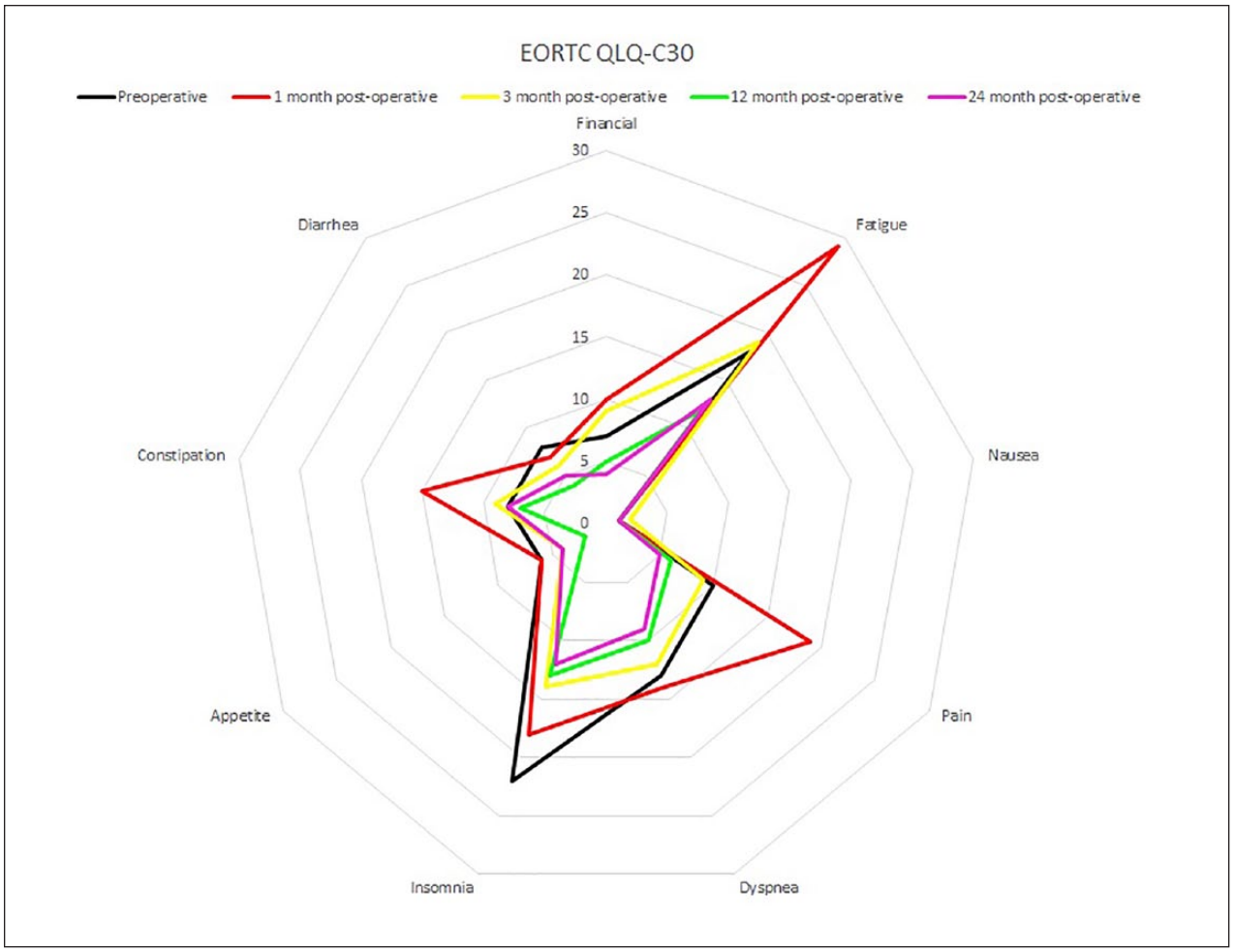

Figure 2. QoL after RALP (black line represents preoperative scores and purple represents 24 month scores). QoL = quality of life; RALP = robot-assisted laparoscopic prostatectomy.

Discussion

QoL is a complex outcome to explore and PCa diagnosis and therapy can significantly alter the perception of life and its quality for a man (Gacci et al., 2017). Across current therapies for localized PCa, radical surgery is currently a mainstay of treatment (Mottet et al., 2017), and in the past 10, years the advent of robotics has changed the face of prostatectomy in Europe. Promising studies reported favorable (Ficarra et al., 2012) and, at times, surprisingly excellent (Galfano et al., 2013) functional outcomes after RALP and, together with company and social marketing, these have raised the expectations of PCa patients regarding surgery results (Schroeck et al., 2012). Although the major impact of continence and sexual function on QoL after RALP is obvious, urologic surgeons may underestimate the impact of other items, such as gastrointestinal morbidity and anxiety, on the overall QoL of patients. While patients may perceive RALP to be the same procedure, no matter the underlying cancer, with increasing use of magnetic resonance imaging (MRI) and the improvement of prostate biopsy techniques, a trend in inverse stage migration of candidates for prostatectomy has been observed, with higher grade and higher risk patients growing in the past years (Albisinni et al., 2017). This translates into a modification of surgical techniques, including the use of wider resection techniques, change in application of nerve-sparing techniques, and lymph node dissection, which can present nonnegligible morbidity (Keskin et al., 2016). The dissection of a bilateral nerve-sparing RALP with no pelvic node dissection for organ-confined Gleason 7 (3 + 4) PCa cannot be considered the same operation as a wide resection of cT3 Gleason 9 (4 + 5) PCa associated with pelvic node dissection, and this translates into a modification of postoperative QoL, as seen in the current study.

The literature on QoL alteration after RALP is scarce and most surgeons advise and consult their patients based mainly on their personal experience rather than on

published reports. The current research reports a large prospective series of patients undergoing RALP in Belgium, reporting modifications in QoL, both overall and specific to PCa, and explores risk factors for degradation in such QoL.

Urinary incontinence represents a source of major stress for patients undergoing radical prostatectomy, with potential significant impact on QoL (Jang et al., 2017). In the present study a significant degradation in ICIQ score 1 month after surgery was found, with gradual recuperation of urinary continence later, in line with current studies (Donovan et al., 2016; Mendiola et al., 2008; Reynolds et al., 2010; Tseng et al., 2006). The modification in ICIQ score was accompanied by a significant increase in urinary-related QoL, measured by urinary symptoms of EORTC PR25 and bother from incontinence aid in the same questionnaire. Of note, at 3 months after surgery the only significant risk factor identified was preoperative urinary symptom score, meaning that patients who were already bothered before surgery were at a higher risk of maintaining a higher score in the early and late postoperative control. These results could be considered quite inevitable, given the impact of all other urinary organs (bladder, urethra, pelvic musculature) except the prostate in the pathophysiology of lower urinary tract symptoms (LUTS). Of note, the urinary symptoms of EORTC PR25 analyze storage symptoms (pollakiuria, nycturia) and pain during urination, rather than voiding symptoms. As the preoperative details of obstructed voiding and the International Prostate Symptom Score (IPSS) score are unknown, the presented data do not allow determining whether radical prostatectomy could potentially alleviate LUTS in patients presenting with obstructive micturition. Regarding bother from urinary incontinence, no significant risk factor was identified.

When comparing QoL measurement across studies, one must bear in mind sociocultural differences across the examined cohort, which may play a significant role in subjective perceptions of symptoms, their interpretation, and QoL expectations after oncologic surgery. Nonetheless, these results are comparable to those of current literature: (Wyler et al., 2007) reported data in 343 patients undergoing laparoscopic radical prostatectomy in a single center. Urinary symptoms were 15.9% at baseline and increased to 41% at 1 month after surgery (16% and 31%, respectively, in the current study). It is interesting to note that in such study the authors did not find a significant difference in QoL outcomes based on surgical experience. Moreover, similarly to this Belgian experience, the authors reported a baseline global QoL score of $77.2 + 18$ (73 ± 21 in the present study), which normalized before 1 year postoperatively and finally increased to a significant higher level. Baseline and follow-up urinary symptom scores were comparable (Wyler et al., 2007). Van den Bergh et al. (2014) compared QoL results across patients undergoing direct RALP and patients who initially were elected for active surveillance and then were shifted to RALP. The authors reported similar postoperative scores, concluding that delaying radical treatment in favor of an initial surveillance did not jeopardize QoL outcomes.

While analyzing sexual QoL, the first important factor to keep in mind is baseline values. Indeed, median IIEF-5 across the present entire cohort was 16; moreover, when examining sexual-related QoL, median value of sexual activity and interest was 50%, with interquartile ranges not passing two thirds of the cohort. These results were comparable to or better than those reported from other countries (Hjälm-Eriksson et al., 2015; van der Poel et al., 2013; Wyler et al., 2007), although age and cultural differences most likely explain observed differences. Whether the recent diagnosis of PCa (and its associated anxiety) had a role in reducing the sexual drive of patients cannot be evaluated with the available data. However, of interest, baseline values were much more significant in the determination of postoperative sexual activity and function than surgical approach and in particular nerve-sparing technique. Globally, from the current analyses, age was the single most important factor in predicting early and late postoperative sexual activity and functioning. No significant association of unilateral nerve sparing with any of our early or late sexual outcomes in terms of QoL was found: As such, patients should be informed that other than increasing the risk of a positive surgical margin (Lavallée et al., 2016), a unilateral nerve sparing may have no effect of postoperative sexual QoL.

Examining the EORTC Q30 questionnaire implies difficult interpretation, given its detailed analysis of QoL domains, no matter the primary organ from which the cancer arises. In the present study however, there are multiple interesting points that emerge. First, all functional scales improve 1 year after surgery: some faster, beginning at 1–3 months, such as the emotional scale (probably reflecting the reduced anxiety after surgery), others more smoothly, such as the role-functioning and the social-functioning scales, given the physiologic time needed for men to regain confidence after RALP. Nonetheless, all scores are significantly improved (all $p < .01$) at 12 months follow-up, apart from cognitive function, which shows no modification as a consequence of surgery. Another item that improved immediately after surgery was insomnia, confirming the positive impact of the reduction of anxiety after the surgical trauma. Furthermore, the present data demonstrate that patients exhibit significant increase of symptoms, including pain, constipation, and fatigue up to 1 month after surgery, and globally it is not until the 3-month control that patients report return to baseline or improvement of these general symptoms. This

information can be of importance when counseling and reassuring for patients before surgery.

This study is not devoid of limitations. First, some parameters including body mass index, membranous urethral length, and comorbidities, which may all potentially play a role in postoperative continence, erectile function, and QoL, were unavailable and could not be incorporated in the multivariate regression models. Second, analyses are not corrected by socioeconomic status, which may also modify perception of QoL (Klein et al., 2017). Third, it is impossible to assess the compliance of patients in pelvic floor muscle training, adding a potential confounding bias. Finally, the variability of surgeon volume and experience may have introduced bias; however, the three surgeons in the present cohort present similar experience in RALP and this could increase the applicability of these results to other realities.

We nonetheless acknowledge that this was a purely prospective trial, thus limiting recall biases. Moreover, this is a cohort composed of European men, with social and cultural differences from U.S. men, adding significant information to the current knowledge on QoL after RALP. Finally, the long follow-up (24 months) allows a vivid representation of functional and QoL results after RALP and of how these results continue to improve and stabilize long after surgery.

Conclusions

In this prospective study, detailed QoL outcomes of men undergoing RALP are reported. After a net reduction immediately after surgery, the vast majority of scores returned to baseline or are improved by 1 year. Preoperative urinary bother was significantly associated with early and late urinary-related QoL, while age was the most significant predictor of sexual-related QoL after surgery.

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