ORIGINAL RESEARCH ARTICLE

Reduction of lower urinary tract symptoms in prostate cancer patients treated with robot assisted laparoscopic prostatectomy

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ABSTRACT

Problem: The aim of this study was to evaluate the change in lower urinary tract symptoms (LUTS) in patients treated with robot assisted laparoscopic prostatectomy (RALP) and to assess factors that may predict a reduction of LUTS after RALP and how this influences quality of life (QoL).

Materials and method: In our institutional prospective research registry, 1,935 patients operated in the period between 2009 and 2021 with baseline- and 12-month EPIC-26 questionnaire were eligible for the study. SF-12 data estimating general QoL were also analyzed. A domain summary score was constructed from the four questions concerning obstructive/irritative voiding symptoms, and transformed linearly to a 0–100 scale with higher scores representing less symptoms. A change of 6 points or more was considered Meaningful Clinical Differences (MCD). Two summary scores were calculated from the SF-12 – a mental component score (MCS-12) and a physical component score (PCS-12). Multi variable regression was used to estimate covariates associated with postoperative change in MCD, MCS-12 and PCS-12.

Results: Mean LUTS-score showed an increase of 4,3 points 12-months post-RALP. A total of 50.4% of patients achieved MCD. In multivariate logistic regression, preoperative LUTS was statistically significant associated with MCD. Reduction of LUTS was associated with improved mean score of MCS-12 and PCS-12.

Discussion and conclusion: Along with information about risk for urinary incontinence after RALP, patients with LUTS at baseline should be informed that these symptoms may be reduced after RALP. In our study, this LUTS reduction was associated with better general QoL.

Introduction

Prostate cancer (PCa) and benign prostatic hyperplasia (BPH) usually occur in men of advanced age and frequently coexist [1]. BPH may cause lower urinary tract symptoms (LUTS) and increase serum PSA levels. LUTS is not associated with an increased risk of PCa [2]. The prevalence of BPH increases with age, reaching 50% – 60% for men in their 60s [3]. Men suffering from LUTS often seek medical advice and undergo PSA testing as part of the clinical evaluation [1, 4, 5]. LUTS often reduce patients' quality of life (QoL) due to storage- (e.g. urgency, nocturia) and/or voiding-symptoms (e.g. intermittency, weak voiding stream) [6, 7] and can even increase the mortality risk [8].

Men with non-metastatic PCa and at least 10 years life expectancy may be offered curative treatment with either radical prostatectomy (RP), external beam radiotherapy (EBRT) or brachytherapy (BT). Neither EBRT nor BT reduce the prostatic obstruction, and moderate/severe LUTS is regarded as a contraindication to BT [9].

Data about changes in LUTS after local PCa treatment, assessed by patient-reported outcome measures, is seldom reported in PCa studies [10]. The impact of changes in urinary function, i.e. LUTS on QoL after robot assisted laparoscopic prostatectomy (RALP) is underreported as well [11]. Preoperative information offered to the patients is mainly focused on the risk of postoperative urinary incontinence and erectile dysfunction. In the present study, we sought to address the impact of RALP on LUTS in PCa patients and assess predictors for reduction of LUTS after RALP. We also wanted to assess the impact of LUTS on general QoL.

Patients and methods

Clinical data are consecutively recorded in our institutional Research Registry of Prostate Cancer. To evaluate patient urinary function after RALP, we used the self-administered questionnaire EPIC 26 (Expanded PCa Index-Composite). It is mailed to the patients before surgery (baseline) and at 3, 12 and 36 months after RALP. EPIC-26 [12, 13] contains 26 items which constitute five domains: Urinary Incontinence, Urinary Obtructive/Irritative, Bowel, Sexual, and Hormonal. Response options for each EPIC item form a Likert scale, and multi-item scores are transformed

linearly to a 0–100 scale, with higher scores representing better QoL. Use of EPIC-26 is the recommended PCa-specific Patient Reported Outcomes Measures (PROMs) instrument in National Cancer Institute-sponsored clinical trials [12] and is recommended by the International Consortium for Health Outcomes Measurement [13]. The Norwegian version of EPIC-26 has shown acceptable reliability and validity for assessment of adverse effects after treatment of non-metastatic PCa [14].

Urinary irritative/obstructive symptoms are described by four questions: *How big a problem, if any, has each of the following been for you during the last 4 weeks?* 1. *Pain or burning on urination? 2. Bleeding with urination? 3. Weak urine stream or incomplete emptying? 4. Need to urinate frequently during the day?*

In analysis 'change of LUTS score' was defined as the LUTS score at 12 months postoperatively minus the LUTS score at baseline. The minimum Meaningful Clinical Differences (MCD) for the urinary irritative-obstructive domain is estimated to a range of 5–7 points [15]. An increase of 6 points or more for change of LUTS score was considered MCD.

Nervesparing (NS) was dichotomized into *no NS* and *NS.* Preoperative risk group stratification was based on the European Association of Urology (EAU) classification [16] and dichotomized into *low/intermediate* and *high risk groups.*

Information about comorbidity was obtained from questions included in the questionnaire about presence in the patient's history of the following diagnoses: diabetes, coronary heart disease, stroke, pulmonary disease, neurological disease, depression and renal disease. Comorbidity was dichotomized into *no comorbidity* and *comorbidity* (one or more of the diagnoses listed above).

Prostate volume (PV) was calculated on preoperative MRI or transrectal ultrasound.

General QOL was assessed by SF-12 (short form health survey), completed by patients between 2009 and 2016. SF-12 is a health survey yielding two summary scores assessing physical component score function (PCS-12) and mental component score well-being (MCS-12) [17]. The Norwegian

population mean PCS-12 and MCS-12 scores were 50,3 and 50,6, respectively [18].

Patients who received adjuvant or salvage radiation therapy or androgen deprivation therapy (ADT) within 12 months after RALP were excluded from the analyses.

Statistics

Patient characteristics are described as mean with standard deviation (SD) and range for continuous data and frequencies for categorical data. Differences between paired total scores were examined by using one-sample *t*-test. A change in the total score of LUTS of at least 6 points from baseline to 12 months is considered as MCD in LUTS. Predictors for reduction of LUTS after RALP were assessed using logistic regression. Association between independent variables of interest and total scores of mental and physical components were studied by performing linear regression analyses. For the analyses of linear regression, the goodness of fit was checked by plotting the predicted values vs standardized residuals and calculating the coefficient of determination (R^2). The R^2 indicates the proportion of variance in the dependent variable associated with the independent variables and ranges between 0 and 1. A large value of R^2 indicates a large variation explained by the model and good fit to the data. For logistic regression analyses, the Hosmer-Lemeshow test and value of Nagelkerke's R^2 were used to check the goodness of fit [19]. A value of $R^2 < 0.01$ from a univariable analysis of regression was considered as independence (i.e. no association) between the outcome and independent variable. Thereby the independent variable was omitted/excluded from further analysis.

P-value less than 0.05 was considered statistically significant. All statistical analyses were performed by using IBM SPSS ver. 22.0 (IBM Co., Armonk, NY, USA).

Results

During the study period, 3,851 patients underwent RALP and were eligible for the study. Of these patients, 2,811 patients (73%) signed informed consent for inclusion in our Research Registry of Prostate Cancer. All of these patients were offered EPIC-26 and 2,230 patients (79%) returned the questionnaire both at baseline and at 12 months follow-up. Within 12 months postoperatively, 295 patients had received postoperative radiation therapy and/or ADT and were excluded from the study. Hence, this study comprised 1,935 patients with characteristics depicted in table 1. We found a mean increase in LUTS score (clinical improvement) of 4,3 points (Table 2, Figure 1), using the 4 items recommended in the original coding instructions for EPIC 26 [15]. About half of the patients (50.4%) achieved a change in LUTS score corresponding with MCD (Figure 2) (P = 0.8).

At 12 months post-RALP, 13% of the patients reported daily use of two pads or more (Table 2). Urinary continence decreased at 12 months post-RALP as shown by a decrease in mean summary urinary incontinence score by 21 points (Table 2, Figure 1).

In univariable logistic regression analyses, the LUTS score at baseline had a Nagelkerke's $R^2 = 0.41$, indicating a strong

Table 1. Characteristics of patients operated between 2009 and 2021 with robot assisted radical prostatectomy.

Variables	Value (n = 1,935)			
	Median	Range	n	%
Age (years), median (range)	66	39–81		
BMI, kg/m² median (range)	27	17–44		
Comorbidity				
No comorbidity N (%)			1,215	62.8
≥1 comorbidities N (%)			703	36.3
Prostate volume (mL), median (range)	36	10–240		
EAU risk group				
Low-/Intermediate risk N (%)			1,352	71
High risk N (%)			545	29
Nerve sparing				
None N (%)			566	30
Unilateral/Bilateral N (%)			1,332	70

BMI: Body mass index; EAU: European Association of Urology.

Table 2. Changes in EPIC 26 urinary domain summary scores and SF-12 scores between baseline and 12 months post-RALP.

EPIC 26	N = 1,935				P
	Mean	SD	n	%	
12 months postoperative LUTS score, mean (SD)	88.9	13			<0.001
Change[a] from baseline, mean (SD)	+4.3	15			
12 months postoperative Urinary Incontinence summary score, mean (SD)	73.3	27			<0.01
Change[a] from baseline, mean (SD)	−20.0	27			
12 months postoperative Use of ≥ 2 pads per day (item 3), N (%)			250	13	
SF-12	n = 911				
12 months postoperative Physical Component Summary (PCS) score, mean (SD)	51.2	8			<0.01
[a]PCS Change from baseline, mean (SD)	+1.7	7			
12 months postoperative Mental Component Summary (MCS) score, mean (SD)	54.4	9			<0.01
[a]MCS change from baseline	−1.5	9			

[a]Score difference between baseline and 12 months after RP: worsening (−); improvement (+). MCS: mental component score; PCS: physical component score; LUTS: lower urinary tract symptoms; RALP: robot assisted laparoscopic prostatectomy.

relationship with MCD at 12 months post-RALP (Table 3). Independent variables such as NS, comorbidity and EAU risk group had Nagelkerke's $R^2 < 0.01$, indicating that very little of the variance in the dependent variable MCD can be explained by these binary independent variables (data not shown). In multivariable logistic regression analyses, LUTS score at baseline and prostate volume retained its statistical significance, whereas age did not (Table 3).

A total of 911 patients returned SF-12 questionnaire both at baseline and 12 month post-RALP. For assessment of general QoL, analyses of SF-12 data showed improvement of MCS-12 score and deterioration of PCS-12 score at 12 months postoperatively (Table 2). Reduced LUTS and less urinary incontinence at 12 months were significantly associated with better mental and physical health 12 months postoperatively (Tables 4 and 5).

Discussion

In this study we have shown that patients undergoing RALP had a reduction of LUTS at 12 months postoperatively, and the reduction was associated with the degree of preoperative LUTS and preoperative prostate volume. Age was not predictive of LUTS reduction. Moreover, the reduction of LUTS symptoms was associated with better general QoL.

We are not aware of other studies of similar sample size using EPIC 26 for evaluating changes in LUTS in patients undergoing RALP. Our study corroborates findings by Leyh-Bannurah [20] in 5,506 RALP patients using International Prostate Symptom Score (IPSS) at baseline and 12 months after
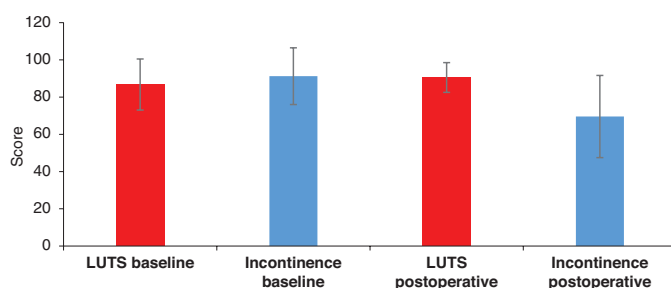
RALP. They reported that a higher preoperative LUTS burden (severe vs. moderate) was independent predictors of LUTS reduction after RALP. In an older study by Masters et al. [21] examining 125 RALP patients with urinary flowmetry and IPSS score at baseline and postoperatively, 38% and 56% of the patients had bladder outlet obstruction (defined by a flow rate of ≤10 mL/s) and moderate/severe symptoms (IPSS ≥ 8) before surgery, respectively. At 20-month follow-up, the median flow rate increased to 24 mL/s and the proportion of patients with IPSS ≥ 8 decreased to 14%.

In our study, the association between PV and MCD was weak, indicated by Nagelkerke's R^2 of 0.02. This finding is in line with the current understanding of LUTS as a disorder often unrelated to prostate enlargement [3].

The findings by SF-12 data showing association between reduction of LUTS and better general QoL have also been shown by others [22]. Our SF-12 data also reveal an association between urinary incontinence and mental- and physical health. When constructing a summary score for urinary function consisting of all 8 questions in the EPIC-26 urinary domains, hence includes both LUTS- and incontinence score, Berge et al. [23] found that better urinary function was associated with better mental health.

Strengths of this study are relatively large patient population with a relatively high response rate to the EPIC-26 questionnaire
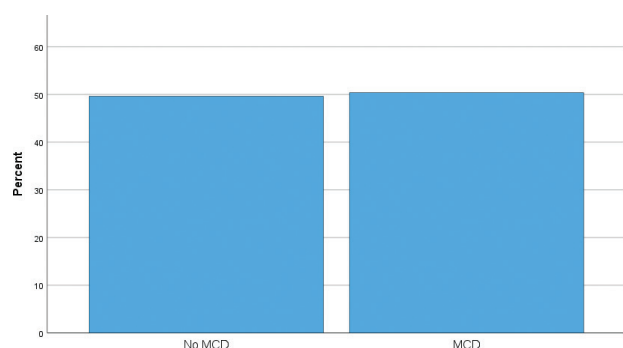

Figure 1. Mean Summary score of LUTS og urinary incontinence score with standard deviation. Higher scores denote less LUTS and incontinence.

Figure 2. Percentage of patients with change of lower urinary tract symptoms (LUTS) score similar or higher than Meaningful Clinical Differences (MCD). Six points improvement of LUTS score were considered the lower limit for MCD.

Table 3. Univariable and multivariable logistic regression.

Variable	Univariate				Multivariate			
	OR	95% CI	P	R^2	OR	95% CI	P	R^2
LUTS score baseline	0.94	0.93, 0.94	<0.001	0.41	0.94	0.86, 0.89	<0.001	0.46
Prostate volume	1.02	1.01, 1.02	<0.001	0.02	1.01	1.00, 1.02	0.01	
Age at RALP	1.03	1.01, 1.04	<0.001	0.01	0.99	0.99, 0.97	0.3	

Baseline covariates associated with meaningful clinical difference (MCD). A reduction of at least 6 points from baseline to 12 months in LUTS score is considered as MCD. OR: odds ratio; CI: confidence interval; R^2: Nagelkerke's R^2; LUTS: lower urinary tract symptoms; RALP: robot assisted laparoscopic prostatectomy.

Table 4. Uni- and multivariable linear regression.

Variable	Univariable				Multivariable			
	Reg coeff	95% CI	R^2	P	Reg coeff	95% CI	R^2	P
LUTS score 12 months postop	0.31	0.16, 0.24	0.09	<0.001	0.25	0.12, 0.21	0.13	<0.001
Urinary in-continence 12 months postop	0.22	0.05, 0.09	0.05	<0.001	0.10	0.01, 0.05		0.007
Age at RALP	0.14	0.10, 0.27	0.02	<0.001	0.16	0.14, 0.30		<0.001
Comorbidity	−0.10	−3.91, −1.65	0.02	<0.001	−0.18	−2.82, −0.61		0.002

Independent variables associated with mental component score (MCS) at 12 months postoperatively (N = 911). Reg coeff: regression coefficient; CI: confidence interval; R^2: coefficient of determination; LUTS: lower urinary tract symptoms; RALP: robot assisted laparoscopic prostatectomy.

Table 5. Uni- and multivariable linear regression.

Variable	Univariable				Multivariable			
	Reg coeff	95% CI	R^2	P	Reg coeff	95% CI	R^2	P
LUTS score 12 months postop	0.33	0.16, 0.23	0.11	<0.001	0.24	0.10, 0.18	0.16	<0.001
Urinary in-continence 12 months postop	0.27	0.06, 0.10	0.07	<0.001	0.12	0.01, 0.05		<0.001
Age at RALP	−0.08	−0.18, −0.02	0.01	0.01	-0.05	−0.14, 0.01		0.08
Comorbidity	−0.24	−5.05, −3.01	0.06	<0.001	-0.18	−3.96, −1.95		<0.001

Independent variables associated with physical component score (PCS) at 12 months postoperatively (N = 911). Reg coeff: regression coefficient; CI: confidence interval; R^2: coefficient of determination; LUTS: lower urinary tract symptoms; RALP: robot assisted laparoscopic prostatectomy.

data at baseline and 12 months post RALP. Complementary clinical data gave the opportunity to analyse relevant predictors. One limitation in our study was the lack of urodynamic examination pre- and postoperatively which is better suited to confirm improvement of urinary flow. Another limitation is that the use of IPSS could have documented more detailed changes in LUTS compared to the more coarse EPIC-26 questionnaire, which also include items not so relevant for LUTS. We were not able to find studies with a comparison between EPIC-26 and IPSS. In a paper by Vertosick et al. [24], the authors concluded that no comparison was possible due to differences in the domains addressed by these questionnaires.

Conclusion

PCa patients experience a reduction in LUTS after RALP. Along with information about the risk for urinary incontinence, patients with LUTS should be informed that these symptoms may be reduced after RALP. In our study, this LUTS reduction was associated with better general QoL.

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