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Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial

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Abstract

Background: Robot-assisted laparoscopic radical prostatectomy (RALP) has become widely used without high-grade evidence of superiority regarding long-term clinical outcomes compared with open retropubic radical prostatectomy (RRP), the gold standard.
Objective: To compare patient-reported urinary incontinence and erectile dysfunction 12 mo after RALP or RRP.
Design, setting, and participants: This was a prospective, controlled, nonrandomised trial of patients undergoing prostatectomy in 14 centres using RALP or RRP. Clinical-record forms and validated patient questionnaires at baseline and 12 mo after surgery were collected.
Outcome measurements and statistical analyses: Odds ratios (ORs) were calculated with logistic regression and adjusted for possible confounders. The primary end point was urinary incontinence (change of pad less than once in 24 h vs one time or more per 24 h) at 12 mo. Secondary end points were erectile dysfunction at 12 mo and positive surgical margins.
Results and limitations: Of 2625 eligible men, 2431 (93%) could be evaluated for the primary end point. At 12 mo after RALP, 366 men (21.3%) were incontinent, as were 144 (20.2%) after RRP. The adjusted OR was 1.08 (95% confidence interval [CI], 0.87–1.34). Erectile dysfunction was observed in 1200 men (70.4%) 12 mo after RALP and 531 (74.7%) after RRP. The adjusted OR was 0.81 (95% CI, 0.66–0.98). The frequency of positive surgical margins did not differ significantly between groups: 21.8% in the RALP group and 20.9% in the RRP group (adjusted OR: 1.09; 95% CI, 0.87–1.35). The non-randomised design is a limitation.

[†] The LAPPRO Steering Committee members are listed in Appendix 1.

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Conclusions: In a Swedish setting, RALP for prostate cancer was modestly beneficial in preserving erectile function compared with RRP, without a statistically significant difference regarding urinary incontinence or surgical margins.
Patient summary: We compared patient-reported urinary incontinence after prostatectomy with two types of surgical technique. There was no statistically significant improvement in the rate of urinary leakage, but there was a small improvement regarding erectile function after robot-assisted operation.

1. Introduction

In prostate cancer (PCa) treatment, the aim of retaining urinary continence and full sexual health after treatment is universal. Surgeons who perform radical prostatectomy (RP) continuously accumulate experience and develop their technical skills, resulting in improved urinary continence and sexual health [1]. The traditional surgical approach is open surgery (retropubic RP [RRP]), on which the evidence for RP as a cure for PCa rests [2]. Over the past 20 yr, laparoscopic methods have been developed; however, reviews of clinical and oncologic outcomes do not favour laparoscopy over RRP [3,4]. Robot-assisted laparoscopic prostatectomy (RALP) was introduced with the aim of improving surgical outcomes, but controlled or randomised studies on the long-term effects are few and present knowledge of effectiveness is based mainly on case series or registry data [4–7].

During RALP, the surgeon has a three-dimensional view of the operating field that should mimic open surgery better than the two-dimensional view with the laparoscopic technique. Performing RRP, the surgeon is guided by the use of external loupes and a headlight; RALP incorporates high-level resolution and enlarged images as well as excellent lighting conditions [8]. In open surgery, the surgeon uses digital palpation of the prostatic contours to identify anatomic landmarks and gain haptic feedback from the tissues, including a direct sense of traction force. These approaches cannot be used in the robot-assisted technique. Consequently, each technique is likely to have technical pros and cons that may reflect on postoperative urinary and sexual function.

We initiated a prospective, controlled, nonrandomised trial in which the intervention was RALP and the control was RRP. The short-term results have been reported with longer operating time, less blood loss during surgery, and shorter length of hospital stay for RALP compared with RRP [9].

In this analysis, the aim was to determine patient-reported urinary incontinence and erectile dysfunction 12 mo after RP performed by RRP or RALP.

2. Patients and methods

Details of patients and methods are shown in Supplement 1.

The Laparoscopic Prostatectomy Robot Open (LAPPRO) study had an open, prospective, controlled, nonrandomised study design and included patients from seven centres performing RALP, at which only 4% of the included radical prostatectomies were RRPs, and seven different centres performing RRP, at which RALP was not performed. To minimise differences between groups, we collected information on risk factors and made adjustments during analysis of the data. The design and data collection have been described previously [9,10].

The LAPPRO trial was registered with the ISRCTN (ISRCTN06393679). The regional ethics review board in Gothenburg, Sweden, approved the study (approval 277-07).

All men diagnosed with PCa and scheduled for RP at 14 participating centres were screened for possible inclusion in the study (Fig. 1). For this analysis, patients had to meet the following inclusion criteria: age <75 yr; ability to read and write Swedish; written informed consent; tumour stage cT1, cT2, or cT3; no signs of distant metastases; and prostate-specific antigen (PSA) concentration <20 ng/ml. To decrease the influence of the initial learning period in this analysis, we included only patients operated on by surgeons with experience of ≥100 procedures [11,12].

The primary end point was urinary incontinence 12 mo after surgery, as reported by the patients, in an attempt to decrease bias owing to patient–surgeon relationships [13–15]. The time point is appropriate, as little change was seen in continence later than 12 mo after surgery [16,17]. The questionnaire used the same clinometric approaches as those used previously [18–22]. The questionnaire included 39 questions about urinary function, most of which have been used before [14,23,24]. For the primary end point, we asked, "How many times do you change pad, diaper, or other sanitary protection during a typical 24 hours?" Answer categories are given in Table 1. For the secondary end point of self-reported erectile dysfunction, we used a Swedish translation of question 3 from the International Index of Erectile Function [25] score: "When you had erections with sexual stimulation, how often was your erection hard enough for penetration during the last 3 months?" Answer categories are given in Table 2. The questionnaire included further questions about urinary leakage (Table 1) [26] and erectile dysfunction (Table 2). The analyses did not include adjustment for treatment of erectile dysfunction.

The secondary end point of positive surgical margin, included in the analysis as a surrogate variable for oncologic safety, was based on the clinical record form alternatives of *no information, negative, focal, extensive*, or *other*. In the analysis, we combined focal and extensive into *positive surgical margin* status.

2.1. Statistical analysis

After interim analysis, group sizes were set at 700 patients in the RRP group and 1400 in the RALP group to yield 80% power to detect an absolute difference of 5%, based on a significance level of 0.05 and a two-sided test, under the assumption that urinary incontinence after RRP would be 10–18%.

The statistical analysis plan defined effect measures, possible confounders and mediators, and certain sensitivity analyses. The primary end point was dichotomised between change of pads less than once per 24 h and one time or more per 24 h.

The choice of possible confounders to urinary continence was based on 17 probable risk factors, and the main effect measure of the primary

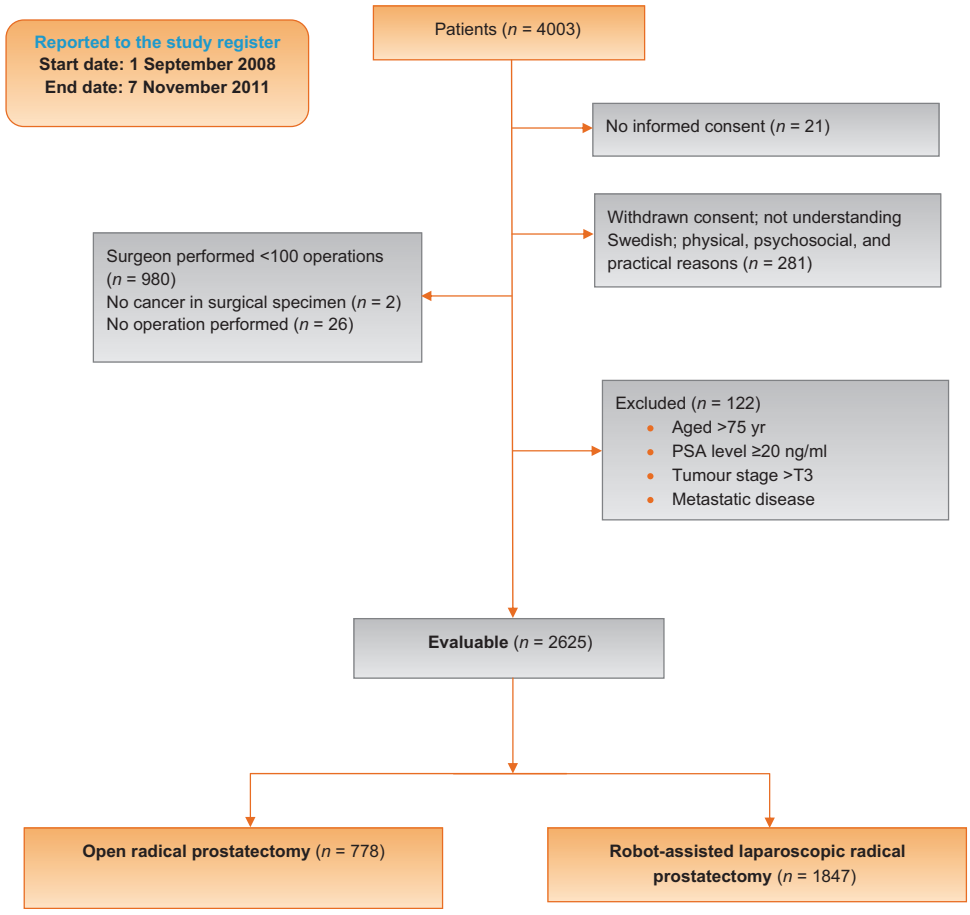

Fig. 1 – Flow diagram. Numbers may not sum properly, as the same participant may have fulfilled more than one exclusion criterion.

end point was based on 50 imputed data sets. The imputation was performed in R, with use of the *Multiple Imputations by Chained Equations* function [27]. With the primary end point as the outcome, we used successive model formation (forward selection) with the level of significance set at 0.20 to obtain a final model of predictors; any variable included in >25 of the 50 imputed models was taken to be a possible confounder (Supplement 1; Supplementary Table 1a). This procedure was repeated for the secondary end point, based on 19 probable risk factors for erectile dysfunction (Supplement 1; Supplementary Table 1b).

As measures of effect, we report unadjusted relative risk ratios (RRs), calculated with log-binomial regression models and, due to lack convergence of log-binomial models, unadjusted and adjusted odds ratios (ORs) calculated with logistic regression models (Supplementary Table 2–4). The effect of possible mediators on the primary end point was analysed in a stepwise fashion adjusting for four factors describing preoperative tumour stage, each considered one at a time and then all four together: PSA concentration, Gleason score at biopsy, clinical tumour stage, length of cancer in biopsy sample, and neurovascular bundle preservation during the operation (Table 1b and 2). We calculated 95% confidence intervals (CIs) for all models. The adjusted ORs were based on a pooled estimate from the 50 imputed data sets. We made the calculations for measures of effect in SAS v.9.3 for Windows (SAS Institute Inc., Cary, NC, USA).

Eight possible confounders were defined and tested in a univariate analysis for the secondary end point reflecting oncologic safety: cancer cells in the surgical margin of specimens reported at pathology examination (Supplementary Table 1c).

3. Results

3.1. Demography

Of 2625 eligible men, 2431 (93%) could be assessed for the primary end point (Fig. 1). Return of the clinical record forms varied from 97% to 99%, and response rate for questionnaires ranged from 89% to 99%.

Preoperative tumour characteristics did not differ significantly between the groups, except that clinical stage T2 tumours were more frequent in the RALP group than in the RRP group, and the total number of biopsies was higher in the RRP group than in the RALP group (Table 3). Patients undergoing RALP had higher educational levels, higher American Society of Anesthesiologists classification scores, and lower body mass index values than patients in the RRP group (Table 3). The skin-to-skin operative time was significantly longer for RALP, as was total time in the operating room. Significantly more patients underwent neurovascular bundle preservation during RALP, and significantly more lymph node dissections were made during RRP. Perioperative bleeding was less and the length of hospital stay was shorter in the RALP group (Table 3). There was no significant difference between groups regarding frequencies of treatment with radiation or endocrine substances at 12 mo after surgery.

3.2. Urinary incontinence

The following variables occurred in ≥34 of the 50 imputed models and were selected as possible confounders: age, diabetes mellitus, mental disorder, history of abdominal surgery, prostate weight, pulmonary disease, and employment status.

When adjusted for possible confounders, no statistically significant difference in ORs was found between groups for any definition of urinary incontinence, as the 95% CIs for all ORs covered unity (Table 1). The adjusted OR of urinary incontinence as defined for the primary analysis (at least one pad changed per 24 h) at 12 mo was 1.21 (95% CI, 0.96–1.54), and the 95% CIs for the ORs comparing any frequency of changing pads covered unity (Table 1a). When the additional questions concerning details of urinary leakage and discomfort were taken into account, the proportions of patients classified as having urinary incontinence ranged from 20% to 56% after RRP and from 21% to 57% after RALP, with the higher frequencies found when we assessed urinary incontinence by a combination of *not pad-free* and *not leakage-free* (Table 1b).

A sensitivity analysis of influence of including centre, calculating unadjusted RRs withdrawing one centre at a time, did not result in any significant difference among centres. The effects of preoperative tumour characteristics on urinary incontinence (Table 1b) resulted in ORs ranging from 1.32 to 0.95, and all 95% CI values covered 1.0, regardless of the definition of urinary incontinence used, indicating that this contrast was not significant. The

Table 1a – Urinary incontinence at 12 mo for comparisons of open and robot-assisted laparoscopic surgery, as reported by patients

	<1 pad [*]	1 pad [*]	2–3 pads [*]	4–5 pads [*]	≥6 pads [*]
Robot-assisted surgery, %	175 (10)	230 (13)	103 (6.0)	19 (1.1)	14 (0.8)
Open surgery, %	96 (13)	85 (12)	40 (5.6)	12 (1.7)	7 (1.0)
Definition of outcome	>0 <1 pad [*]	≥1 ≥1 pad [*]	≥2 ≥2 pads [*]	≥4 ≥4 pads [*]	≥6 ≥6 pads [*]
Adjusted A OR [**] (95% CI)	1.00 (0.82–1.23)	1.21 (0.96–1.54)	1.05 (0.74–1.49)	0.91 (0.48–1.71)	0.99 (0.37–2.65)
Adjusted B OR [†] (95% CI)	1.01 (0.81–1.26)	1.24 (0.96–1.60)	1.17 (0.79–1.74)	1.13 (0.54–2.38)	0.98 (0.33–2.90)

CI = confidence interval; OR = odds ratio.

[*] To determine use of protective measure against urinary leakage (eg, pads), patients were asked, "How many times do you change pad, diaper or other sanitary protection during a typical 24 hours?" The following responses were available: "Not applicable, I do not use pad, diaper or a sanitary protection," "Less than once per 24 hours," "About once per 24 hours," "About two to three times per 24 hours," "About four to five times per 24 hours," or "About six times or more per 24 hours" [24].

[**] Adjusted A: adjusted for age at surgery, inguinal hernia, abdominal surgery, diabetes, pulmonary disease, mental disorder, prostate weight.

[†] Adjusted B: adjusted for same as A plus all four preoperative tumour factors.

Table 1b – Urinary incontinence measured by various definitions as reported by patients 12 mo after surgery

Definition of urinary incontinence	Open surgery, *n* (%)	Robot-assisted surgery, *n* (%)	Adjusted A, OR (95% CI) [*]	Adjusted B, OR (95% CI) [†]	Adjusted C, OR (95% CI) [‡]
Change of pad [§] at least once per 24 h (primary end point)	144 (20)	366 (21)	1.21 (0.96–1.54)	1.24 (0.96–1.60)	1.31 (1.01–1.70)
Not pad free [§] and not leakage free	399 (56)	978 (57)	1.14 (0.94–1.37)	1.18 (0.96–1.44)	1.20 (0.98–1.47)
Urinary leakage daytime	252 (35)	606 (35)	1.13 (0.93–1.38)	1.16 (0.94–1.44)	1.19 (0.96–1.48)
Any urinary leakage daytime	367 (51)	902 (52)	1.14 (0.95–1.38)	1.16 (0.95–1.42)	1.19 (0.97–1.45)
Do you have urinary leakage?	117 (17)	310 (18)	1.28 (0.99–1.65)	1.32 (1.00–1.73)	1.38 (1.05–1.83)
Urinary discomfort	261 (37)	592 (35)	0.96 (0.79–1.17)	0.95 (0.77–1.17)	0.98 (0.79–1.21)

CI = confidence interval; OR = odds ratio.

Information on unadjusted risk and ORs is available in Supplementary Table 2.

[*] Adjusted A: adjusted for age at surgery, inguinal hernia, abdominal surgery, diabetes, pulmonary disease, mental disorder, prostate weight.

[†] Adjusted B: adjusted for same as A plus all four preoperative tumour factors.

[‡] Adjusted C: adjusted for same as A plus B plus degree of neurovascular bundle preservation.

[§] To determine use of protective measure against urinary leakage (eg, pads), patients were asked, "How many times do you change pad, diaper or other sanitary protection during a typical 24 hours?" The following responses were available: "Not applicable, I do not use pad, diaper or a sanitary protection," "Less than once per 24 hours," "About once per 24 hours," "About two to three times per 24 hours," "About four to five times per 24 hours," or "About six times or more per 24 hours" [24].

Table 2 – Erectile dysfunction compared between open and robot-assisted laparoscopic surgery using various definitions and as reported by patients 12 mo after surgery

Definition of erectile dysfunction	Open surgery, *n* (%)	Robot-assisted surgery, *n* (%)	Adjusted A, OR (95% CI) [**]	Adjusted B, OR (95% CI) [†]	Adjusted C, OR (95% CI) [‡]
IIEF score [§]	531 (75)	1200 (70)	0.80 (0.64–1.00)	0.79 (0.63–1.00)	0.73 (0.58–0.93)
IIEF-5 score [#] at 12 mo ≤16	570 (81)	1311 (78)	0.86 (0.68–1.09)	0.75 (0.58–0.96)	0.75 (0.58–0.97)
IIEF-5 score [#] at 12 mo ≤21	654 (93)	1508 (90)	0.71 (0.50–0.99)	0.61 (0.42–0.88)	0.61 (0.42–0.88)
Penile stiffness less than half of the time	574 (81)	1323 (77)	0.81 (0.64–1.03)	0.75 (0.59–0.96)	0.75 (0.58–0.97)
No spontaneous morning erection	664 (93)	1522 (89)	0.59 (0.42–0.82)	0.52 (0.36–0.76)	0.50 (0.35–0.74)
Erectile dysfunction, combined variable [+]	561 (79)	1282 (75)	0.80 (0.64–1.00)	0.74 (0.59–0.95)	0.75 (0.58–0.96)

CI = confidence interval; IIEF = International Index of Erectile Function; OR = odds ratio.
Information on unadjusted risk and ORs is available in Supplementary Table 3.
[**] Adjusted A: adjusted for age at surgery, educational level, smoking, employment, cardiovascular disease.
[†] Adjusted B: adjusted for same as A plus all four preoperative tumour characteristic variables.
[‡] Adjusted C: adjusted for same as A plus B plus degree of neurovascular bundle preservation.
[§] IIEF Questionnaire, question 3: "When you had erections with sexual stimulation, how often was your erection hard enough for penetration during the last 3 months?" with cutoff between response 2 and 3. The following responses were available: "No sexual activity" (0); "Almost never or never" (1); "A few times (much less than half the time)" (2); "Sometimes (about half the time)" (3); "Most times (much more than half the time)" (4); and "Almost always or always" (5).
[#] IIEF Questionnaire modified version with five questions, six answer categories, 0–5 points per question; score ≤16 = erectile dysfunction; score ≤21 = some erectile function.
[+] Erectile dysfunction implies a lack of stiffness at sexual activity or morning erection.

Table 3 – Baseline patient, perioperative, and 12-mo follow-up characteristics

Characteristic	Open retropubic radical prostatectomy [*] (*n* = 778)	Robot-assisted laparoscopic radical prostatectomy [*] (*n* = 1847)	*p* value
Preoperative characteristics			
Age at surgery, yr			
Median (IQR)	63 (59–67)	63 (58–66)	0.03
Preoperative PSA level, ng/ml			
Median (IQR)	6.2 (4.5–9.0)	6.1 (4.5–8.9)	0.73
Not stated	4	5	
Preoperative clinical tumour stage			
cT1	494 (64)	1099 (60)	0.006
cT2	218 (28)	652 (35)	
cT3	27 (3.5)	57 (3.1)	
Not stated	39 (5.0)	39 (2.1)	
Preoperative biopsy Gleason score			
≤7	716 (92)	1732 (94)	0.7
≥8	45 (5.8)	102 (5.5)	
Not stated	17 (2.2)	13 (0.7)	
Total length of cancer in prostate biopsy, mm			
Median (IQR)	7.0 (3.2–15)	7.5 (4.0–16)	0.07
Not stated	74	71	
Cores taken at prostate biopsy, no.			
Median (IQR)	10 (10–11)	10 (9–10)	<0.001
Not stated	36	73	
IPSS score [**]			
Mild 0–7	363 (52)	908 (56)	0.3
Moderate 8–19	265 (38)	597 (37)	
Severe 20–35	49 (7.1)	95 (5.8)	
Not stated	17 (2.4)	30 (1.8)	
Preoperatively continent [†]			
<1	675 (97)	1606 (98)	0.2
≥1	12 (1.7)	17 (1.0)	
Not stated	7 (1.0)	7 (0.4)	
Preoperatively potent			
Yes	489 (71)	1166 (72)	0.8
No	182 (26)	421 (26)	
Not stated	23 (3.3)	43 (2.6)	
Residence			
Urban	566 (82)	1396 (86)	0.05

Table 3 (*Continued*)

Characteristic	Open retropubic radical prostatectomy * (*n* = 778)	Robot-assisted laparoscopic radical prostatectomy * (*n* = 1847)	*p* value
Rural	118 (17)	216 (13)	
Abroad	5 (0.7)	8 (0.5)	
Not stated	5 (0.7)	10 (0.6)	
Level of education			
University/college	246 (36)	691 (42)	0.009
Technical training school	80 (12)	184 (11)	
High school	208 (30)	462 (28)	
Elementary school	143 (21)	254 (16)	
Other	14 (2.0)	30 (1.8)	
Not stated	3 (0.4)	9 (0.6)	
Marital status			
Partner	636 (92)	1467 (90)	0.2
Single	54 (7.8)	153 (9.4)	
Not stated	4 (0.6)	10 (0.6)	
Preoperative BMI, kg/m^2			
Median (IQR)	26.2 (24.5–28.1)	25.9 (24.1–28.0)	0.03
Not stated	12	32	
Preoperative ASA score ‡			
1	508 (67)	1113 (60)	0.005
2	218 (29)	646 (35)	
3	15 (2.0)	43 (2.3)	
Not stated	22 (2.9)	42 (2.3)	
Perioperative characteristics			
Skin-to-skin operating time, min			
Median (IQR)	89 (74–125)	168 (144–201)	<0.001
Not stated	32	310	
Total time in operating room, min			
Median (IQR)	126 (102–186)	236 (210–270)	<0.001
Not stated	158	321	
Neurovascular bundle preservation, no. (%)			
No neurovascular dissection	246 (32)	287 (16)	<0.001
Uni- or bilateral partial dissection	63 (8.3)	244 (13)	
Unilateral inter- or intrafascial dissection	104 (14)	339 (18)	
Bilateral, partial dissection on one side	63 (8.3)	368 (20)	
Bilateral, interfascial dissection on both sides	182 (24)	388 (21)	
One side interfascial, one intrafascial dissection	18 (2.4)	122 (0.7)	
Intrafascial dissection on both sides	84 (11)	93 (5.0)	
Not stated	1 (0.1)	2 (0.1)	
Lymph node dissection			
No	553 (73)	1604 (87)	<0.001
Yes	206 (27)	235 (13)	
Not stated	2 (0.3)	4 (0.2)	
Perioperative bleeding, ml			
Median (IQR)	550 (350–800)	100 (50–200)	<0.001
Not stated	12	127	
Pathology tumour stage			
pT2	562 (74)	1287 (71)	0.2
pT3	190 (25)	511 (28)	
pT4	3 (0.4)	10 (0.6)	
pTX	0 (0.0)	7 (0.4)	
Not stated	7 (0.9)	6 (0.3)	
Surgical margin status			
Negative	585 (77)	1399 (77)	0.15
Positive	154 (20)	399 (22)	
Not stated	23 (3.0)	23 (1.3)	
Prostatectomy specimen Gleason score			
≤7	643 (84)	1657 (91)	0.005
≥8	30 (3.9)	138 (7.6)	
Not stated	89 (12)	26 (1.4)	
Length of hospital stay, d			
Median (IQR)	4 (3–5)	3 (2–4)	<0.001
Not stated	3	1	

ASA = American Society of Anesthesiologists; BMI = body mass index; IPSS = International Prostate Symptom Score; IQR = interquartile range; PSA = prostate-specific antigen.

* Because of rounding, percentages may not total 100.

** Seven questions with six answers each, 0–5 points per question. A high score indicates better erectile function.

† Use of protective measure (eg, pads), described as number of changes per 24 h.

‡ 1 = normal healthy patient, 2 = mild systemic disease, 3 = severe systemic disease.

Table 4 – Comparison of open surgery and robot-assisted laparoscopic surgery concerning positive surgical margins

	Open surgery, *n/N* (%)	Robot-assisted surgery, *n/N* (%)	Adjusted RR * (95% CI)	Adjusted OR (95% CI)
PSMs **	156/748 (21)	395/1812 (22)	1.06 (0.90–1.26)	1.09 (0.87–1.35)

CI = confidence interval; OR = odds ratio; PSM = positive surgical margin; RR = relative risk.
* Relative risk: percentage with outcome in the continent group divided by percentage with outcome in the incontinent group for each possible cutoff.
** Defined as a pathology report of cancer cells present in the surgical margin.

definition used for the primary end point resulted in an OR of 1.31 (95% CI, 1.01–1.70) after adjustment for background factors, tumour characteristics, and neurovascular preservation (Table 1b). The ORs for other definitions of incontinence all had 95% CIs covering 1.0 after adjustment, indicating that there were no statistically significant differences between the two techniques.

3.3. *Erectile dysfunction*

The following confounding variables (occurring in ≥42 of 50 imputed models) were selected as possible: age at surgery, educational level, smoking status, employment status 12 mo after surgery, and history of cardiovascular disease. After adjustment, the OR for any erectile dysfunction was 0.80 (95% CI, 0.64–1.00) (Table 2). Classification of erectile dysfunction by different definitions did not substantially affect the ORs (Table 2). When adjustments were made for the preoperative clinical tumour characteristics, OR was 0.74 (95% CI, 0.59–0.95); the neurovascular preservation OR was 0.75 (95% CI, 0.58–0.96) (Table 2); and adjusting for lymph node dissection resulted in an OR of 0.78 (95% CI, 0.61–1.00).

3.4. *Positive surgical margin*

Of the possible confounders, only prostate weight was carried through to the final analysis. The frequencies of positive surgical margin were 22% and 21% for RALP and RRP, respectively (Table 4), and the unadjusted and adjusted RRs and ORs all had 95% CIs covering 1.0.

4. Discussion

This large, prospective, controlled, nonrandomised trial to evaluate outcomes of RALP in comparison with RRP showed no statistically significant difference regarding the primary end point: patient-reported urinary incontinence 12 mo after surgery. However, for erectile dysfunction 12 mo after the operation, fewer patients were affected after RALP than after RRP. The surgical approach made no difference in the rate of positive surgical margins, a surrogate marker for oncologic outcome.

Hu and coworkers performed a registry-based study of reimbursement claims for urinary incontinence after minimally invasive RP, including RALP [7]. Their propensity model–adjusted figures were 15.9 per 100 person-years for minimally invasive surgery and 12.2 for RRP, which resulted in a ratio of reimbursement claims of 1.30 (95% CI, 1.05–1.61). In contrast, we based our analyses of urinary incontinence on patients' self-reported experiences of urinary incontinence. All procedures in our study were performed by surgeons who had performed ≥100 procedures, whereas Hu and coworkers did not take surgeon experience into account. We found no statistically significant difference regarding incontinence when comparing RALP and RRP. A recent report on learning curve found a surgeon "break-even point" regarding urinary continence of 182 cases [12].

Several reports have been published on single-institution case series [28–30], in which selection-induced problems leading to confounding by indication might compromise the interpretation when comparing two simultaneously performed techniques because of surgeon and/or patient preferences. Patient selection by the surgeon may imply that more complex cases with higher risk of untoward results would not be included, resulting in better outcomes, whereas a selection of treatment modality by the patient may be due to an assumption of results of the chosen procedure, which could influence the patients' perception of outcomes postoperatively. Ahlering et al found no difference in urinary incontinence at 3 mo postoperatively [28], whereas Ficarra et al reported a significantly better continence at 12 mo after RALP compared with RRP [29]. With the design of our trial, unaccounted-for problems induced by selection should be small, and our result—finding no statistically significant difference in urinary incontinence between the two techniques—should accurately reflect practice in Sweden at the time. When Barry et al assessed data from a national registry asking patients about urinary incontinence after RALP or RRP, they found no statistically significant difference in outcomes between techniques [30].

We suggest that in the future, the appropriate definition of urinary incontinence from the patient's perspective should be *not pad-free and not leakage free*, as indicated when taking the patient's bother into account [26].

In our study, RALP resulted in a statistically significantly higher proportion of men (30%) with erectile function 12 mo after surgery than did RRP (25%), but the majority of the men in the two groups experienced negative effects on sexual health. Hu and coworkers reported 26.8 reimbursement claims per 100 person-years for erectile dysfunction after minimally invasive surgery and 19.2 for open surgery, which gives an OR of 1.40 (95% CI, 1.14–1.72) [7]. Their definition of erectile dysfunction is quite different from that used in our study, which is probably an important reflection of the differences in frequencies; the method and

definition we used should reflect the reality more closely. The high level of erectile dysfunction reported in our study is most probably explained by the use of validated questionnaires sent to a third party, the high answering rates, and the population basis for the cohort. In comparison to a recent report from a highly specialised tertiary referral centre [17], the rates of erectile dysfunction in our trial are higher, but there are noteworthy differences in answering rates (at most, 62% vs >90% in our trial), apart from the unknown effect of referral as such. A meta-analysis of six comparative studies reported better return to sexual health after RALP than after RRP at 12 mo, with an OR of 2.84 (95% CI, 1.46–5.43) [31]. We found a small but statistically significant difference in favour of RALP (70%) versus RRP (75%), and that difference persisted after using various definitions of erectile dysfunction and after adjustments. However, the absolute difference of 5% was modest. The health-economic analysis, which is part of our trial protocol and still to be performed, will be of considerable interest.

For valid comparisons among studies, the definitions of urinary incontinence and erectile dysfunction, ideally, should be identical. In our study, we were able to use a number of definitions by asking several questions and found consistent results for comparisons of the two techniques, and we conclude that the results are robust.

Self-reported data can vary in validity depending on whether questionnaires are returned to a neutral third party instead of the centre responsible for the surgery [13,14]. Significant differences regarding urinary incontinence comparing interviews in the clinical setting with questionnaires have been reported [15]. We chose questionnaires and central administration to ensure that contacting, sending, and reminding were uniform and to avoid patient dependency.

The strengths of our study include the prospective controlled design; the sample size; the short inclusion period; the high participation and response rates; the experience of the surgeons; the collection of information before, during, and after surgery; and the use of validated measures. A concern before start of the study was that the lack of randomisation could lead to an imbalance between groups for important risk factors for urinary incontinence. This imbalance was counteracted by collection of information about possible risk factors and use of this information for adjustments during analyses. The modest changes in RRs and ORs after adjustments indicate that the residual confounding effects of lack of randomisation (selection-induced problems) are small, if any, with regard to the assessment of the primary end point. The case volumes of the surgeons and the centres might influence the rates of urinary incontinence and erectile dysfunction at 12 mo. The effect of surgeon experience on outcome in terms of recurrence has been described by Vickers et al [32], and this variable as well as functional outcomes are of interest from a planning perspective in national health care systems and for individual patients. An analysis of this aspect within the framework of this trial, including initial experience, is planned. In this analysis, our aim was to study the mean competence at the time in Sweden for the respective techniques at the experience level of ≥100 operations.

5. Conclusions

Earlier suggestions of improved erectile function, although modest, after RALP were substantiated, whereas improvement of urinary continence was not.

Author contributions: Eva Haglind 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: Haglind, Carlsson, Stranne, Thorsteinsdottir, Lagerkvist, Wiklund, Bjartell, Hugosson, Damber, Steineck, Anderberg, Björholt.
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Supervision: None.
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Appendix 1. The LAPPRO (Laparoscopic Prostatectomy Robot Open) Trial Steering Committee

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Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eururo.2015.02.029.

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