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Long-term functional outcomes after robot-assisted prostatectomy compared to laparoscopic prostatectomy: Results from a national retrospective cluster study

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ABSTRACT

Background: Despite multiple studies evaluating the effectiveness of Robot-Assisted Radical Prostatectomy (RARP), there is no definitive conclusion about the added value of RARP. A retrospective cluster study was conducted to evaluate long-term sexual and urinary functioning after RARP and Laparoscopic Radical Prostatectomy (LRP) based on real-world data from 12 Dutch hospitals.

Methods: Data was collected from patients who underwent surgery between 2010 and 2012. A mixed effect model was used to evaluate differences between groups on urinary and sexual functioning (EPIC-26). Additionally, a regression analysis was conducted to evaluate the relationship between these functional outcomes and, among others, hospital volume.

Results: 1370 (65.1%) patients participated, 907 underwent RARP and 463 LRP, with a median follow-up time of 7.08 years (SD = 0.98). The RARP group showed a statistically and clinically significant better urinary functioning compared to the LRP group ($p = 0.002$). RARP showed also a shorter procedure time ($p=<0.001$), reduced blood loss ($p=<0.001$), and a higher chance of neurovascular bundle preservation (39.8% vs 29.1%; $p=<0.01$).

Conclusion: RARP resulted in better long-term urinary function compared to LRP. Based on the results from this study, guidelines concerning the preferred surgery type and the position on reimbursement may change, especially when RARP proves to be cost-effective.

Background

To guide treatment decisions among prostate cancer patients, knowledge about the impact of treatments on their Health-Related Quality of Life (HRQoL) and their preferences is important [1]. Radical prostatectomy (RP) is known for its negative impact on urinary and sexual functioning [1,2]. The introduction of the Da Vinci® (Intuitive Surgical) robot in prostate cancer care was expected to improve HRQoL and survival by providing better sight and a greater range of motion.

Although no benefits have been proven in recurrence-free survival [3], the introduction of Robot-Assisted RP (RARP) has shown improvements in hospital stay, blood loss, urinary incontinence, and erectile functioning compared to Open (ORP) and Laparoscopic (LRP) RP [4–6]. To date, systematic reviews are still unable to draw definitive conclusions from studies on the efficacy of RARP due to high variability in patient selection, study design, and outcome measurements [7–9].

More recently, population-based studies compared functional outcomes after RARP and ORP [10–12]. Showing better sexual functioning after two years for RARP, but no long-term difference in

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functional outcomes was seen [10,11]. As multiple studies have suggested that hospital volume is associated with better functional outcomes [13,14], hospital volume should be taken into account when evaluating RARP. Note, however, that the previous and other recent observational and randomized studies mainly compared RARP to ORP [15,16]. Therefore, the clinical evidence base to decide on the position of RARP in the current treatment landscape, especially in comparison to LRP, is inconclusive [17].

In this study, we evaluated the long-term (6–9 years) urinary and sexual functioning in 1370 prostate cancer survivors after RARP and LRP based on real-world data from the Netherlands, collected in 12 hospitals.

Material and methods

Study design and patient population

Prostate cancer patients who underwent surgery between 2010 and 2012 were invited to participate in this retrospective cluster study. This timeframe was specifically chosen to involve high volume hospitals that still performed LRP as well as larger hospitals that already adopted RARP and had performed at least 50 RARPs. We selected hospitals with different hospital volumes for both interventions. In total, 12 hospitals participated in our study, eight that performed RARPs, and seven LRPs during our timeframe. Four hospitals provided data for both procedures. From these hospitals, patients were invited when (i) their vital status was known or could be validated with the general practitioner, (ii) they were not part of the first 50 RARPs, (iii) they were living in the Netherlands, and (iiii) they had sufficient command of the Dutch language. General clinical information was collected from deceased patients.

The study was approved by the medical ethical committee of the Netherlands Cancer Institute (NKI-AVL) and the institutional review boards of all recruiting hospitals. All participants gave consent to use and evaluate the sampled data as described in the informed consent.

Procedure

Fig. 1 shows the CONSORT diagram of the study. From the 2626 patients assessed for eligibility, 2117 were invited by their treating physicians to participate between January 2018 and March 2019.

Study measures

Primary outcome measures were the Urinary Incontinence domain and Sexual domain of the Expanded Prostate cancer Index Composite short form (EPIC-26) [18]. Besides, being incontinent and having erectile dysfunction was evaluated by one question per domain: number of pads used (use of $\geq$1 pad) and the quality of the erection (not firm enough for any sexual activities), respectively (Appendix E).

Secondary outcome measures were: Bowel, Hormonal and Urinary irritative/obstructive of the EPIC-26, the Summary score of the EORTC QLQ C30 version 3.0, and utilities measured by EQ5D-5L for overall quality of life. All these questionnaires were incorporated in one survey that was sent to the patients.

Additionally, clinical characteristics were retrieved from the medical record (see Table 1 and Appendix B). Besides, the survey incorporated questions on social-demographics, complications (Clavien Dindo classification [19]), hormonal treatment or radiotherapy within 6 months after treatment with or without PSA rise, and the use of additional care, pharmaceuticals or instruments for complaints related to erectile dysfunction and incontinence. Furthermore, five questions from the EPIC-26 and EORTC-QLQ-PR25 were included in the survey to evaluate the preoperative status of the patients. Baseline continence was defined as no pads used and no unintentional release of urine. Baseline potency was defined as having no problem at all with getting or maintaining an erection. Finally, for patients who deceased between surgery and inclusion, the date of death and cause of death was retrieved from the medical record.

Statistical analysis

The domain scores of the EPIC-26 were calculated according to published scoring algorithms. Some of the questions had to be recoded because an additional answer option was given: “Not applicable (because I was not sexually active)”. The recoding procedure is provided in Appendix A.

To analyse the difference in the primary and secondary outcomes between RARP and LRP a mixed effects modelling approach with random intercept was used. The primary analysis included only patients who were defined as continent and potent at baseline. Clustering based on hospital was included as a random factor. The models were adjusted for possible confounders: age at inclusion, D'Amico risk score [20], receiving radiotherapy, neurovascular bundle preservation, use of pharmaceuticals or instruments for erectile dysfunction, hospital type, and hospital volume. The confounders were added stepwise as fixed factors. Details on the evaluation of the best model were incorporated in Appendix C. The P-value for the overall model effects was set at 0.05. A difference of 6–9 points on the Urinary Incontinence domain and a difference of 10–12 on the Sexual Domain were considered clinically significant [21].

Additionally, the socio-demographic and clinical characteristics of the groups were compared using chi-square tests and independent samples *t*-test. The survival of the total patient population receiving RP was compared with Kaplan Meier curves and a log-rank test. Patients who died after the 1st of March 2018 were excluded from survival analysis because patient recruitment in the first recruiting hospital was then completed.

Finally, regression analyses were conducted using mixed effect models with random intercept and random clustering of hospital to evaluate the influence of hospital volume, age, D'Amico risk score, receiving radiotherapy, and neurovascular bundle preservation on better urinary and sexual functioning.

Results

Study sample

The total set of potential patients was n = 2626. In total 202/2626 patients died before inclusion, of which 164 died before March 1, 2018. Overall mortality in the LRP group (n = 72) was significantly higher than in the total RARP group (n = 92) (8.7%; 5.1% log-rank: 0.003). Prostate cancer-specific mortality was also higher in the LRP group (RARP: N = 17, 0.95%, LRP: N = 12, 1.44%, log-rank 0.326), though not significant.

From the 2117 invited patients, 1378 patients completed the questionnaire showing an overall response rate of 65.1%. Eight patients were removed from the study sample because of various reasons (Fig. 1), resulting in a final sample of 1370 patients. 907 underwent RARP, and 463 LRP.

Patient and hospital characteristics

All patient and clinical characteristics are listed in Table 1. The median age of the study sample at inclusion was 71.5 years (46.6–85.1), and the median time to follow-up was 7.08 years

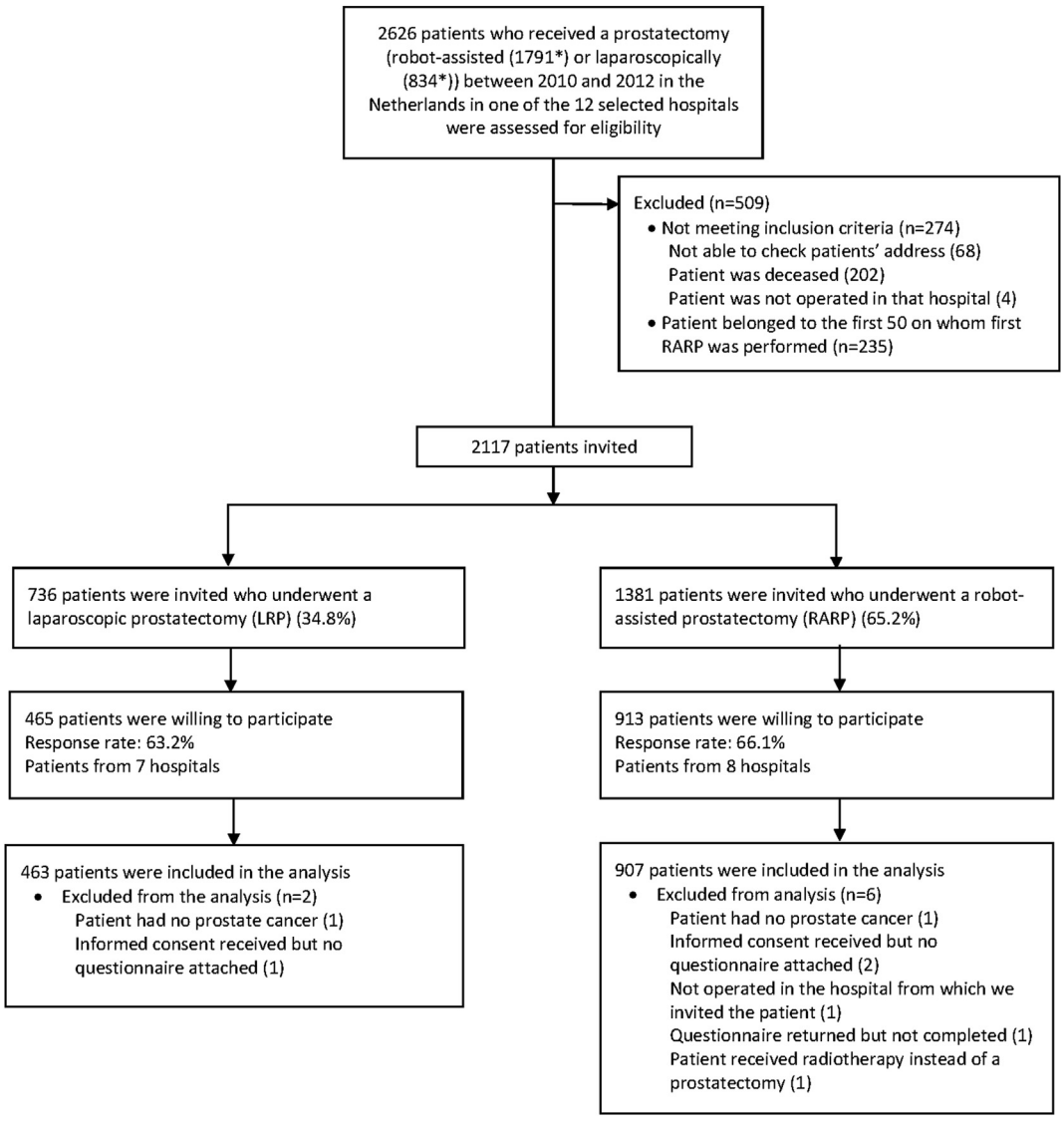

Fig. 1. CONSORT diagram.
Caption: * of one of the eligible patients it was unknown whether he underwent LRP or RARP, eventually this patient did not participate; RARP = Robot-Assisted Radical Prostatectomy, LRP = Laparoscopic Radical Prostatectomy.

(5.27–9.86). At baseline, 3.6% and 18.9% of the patients were considered incontinent and impotent respectively, which did not significantly differ between the groups. In the RARP group, patients were more often operated in high volume ($p < 0.01$) and academic hospitals ($p < 0.001$) compared to the LRP group.

Clinical characteristics and per- and postoperative outcomes

In the RARP group, a higher proportion of patients was classified as clinical high-risk [20] (33.6%; 26.6%, $p = 0.02$). Furthermore, RARP showed a shorter procedure time (159 min; 191 min, p=<0.001), less blood loss (156 ml; 250 ml, p=<0.001), and a higher chance of neurovascular bundle preservation (39.8%; 29.1%, p=<0.01).

Positive surgical margin rate (RARP: 27.3%; LRP: 25.9%, $p = 0.59$) and biochemical recurrence (RARP: 33.6%; LRP: 33.7%, $p = 0.99$) was similar between the groups. Notably, a higher number of LRP patients received hormonal therapy compared to RARP (10.8%; 7.5%, $p = 0.07$).

Follow-up characteristics

Table 2 presents the follow-up characteristics of the study population. The complication rate (RARP: 18.5%; LRP: 16.4%, $p = 0.34$) and the severity of the complications was similar between the groups ($p = 0.49$). The LRP group had more often complaints of incontinence (52.1%; 67.3%, $p < 0.001$) and of the patients experiencing complaints, a higher number of patients in the LRP group received a surgical procedure e.g. male sling (5.5%; 13.7%, $p < 0.01$). The LRP group also had more often complaints of erectile dysfunction directly after surgery (74.4%; 81.2%, $p = 0.02$). Table 2 presents the proportion of patients who used additional care for those complaints.

Primary outcome measurements

The RARP group showed a statistically and clinically significant better urinary function compared to the LRP group (estimated means: 73.34; 64.98, $p = 0.002$) (Table 3). No significant differences

Table 1
Sociodemographics, clinical characteristics and peri-operative measurements of the study population of 1370; other numbers apply when indicated.

	Robot-assisted prostatectomy (n=907)	Laparoscopic prostatectomy (n=463)	P value
Sociodemographics and general characteristics			
Age			
at surgery (median, range)	64.00 (39-79)	64.00 (45-75)	0.51
at filling in questionnaire (median, range)	71.21 (46.6-85.1)	72.08 (51.8-83.7)	0.06
Marital status			
Married or living together with partner	792 (87.7%)	407 (88.3%)	0.90
Missing	4	2	
Highest completed education level			0.32
Primary education	41 (4.6%)	29 (6.4%)	
Secondary education vocational education	523 (58.5%)	253 (56%)	
Higher education	330 (36.9%)	170 (37.6%)	
Volume hospital (number of prostatectomies per year)			<0.01
< 50 patients per year	86 (9.5%)	90 (19.4%)	
50-100 patients per year	113 (12.5%)	243 (52.5%)	
100-150 patients per year	243 (26.8%)	130 (28.1%)	
>150 patients per year	465 (51.3%)	0	
Type of hospital			<0.001
General hospital	407 (44.9%)	337 (72.8%)	
Academic or specialized hospital	500 (55.1%)	126 (27.2%)	
Baseline incontinent (%)	29 (3.2%)	21 (4.6%)	0.21
Missing	7	5	
Baseline impotent (%)	161 (18.2%)	98 (21.7%)	0.12
Missing	20	12	
Clinical characteristics			
Preoperative prostate volume (mL) median, range	41.00 (12-220)	38.00 (0-170)	0.06
Missing	197	235	
Preoperative PSA level (ng/mL) median, range	8.5 (1-254)	9 (0.7-80)	0.36
Missing	18	14	
Clinical stage			<0.01
cT1a-1b	12 (1.4%)	5 (1.1%)	
cT1c	338 (40.6%)	241 (54.5%)	
cT2a	219 (26.3%)	105 (23.8%)	
cT2b	96 (11.5%)	34 (7.7%)	
cT2c	86 (10.3%)	27 (6.1%)	
cT3	81 (9.7%)	30 (6.8%)	
Missing	75	21	
cGleason Score			0.34
≤6	493 (55.4%)	247 (53.8%)	
7	293 (32.9%)	167 (36.4%)	
>7	104 (11.7%)	45 (9.8%)	
Missing	17	4	
D'Amico risk classification			0.02
Low risk	264 (29.5%)	138 (29.8%)	
Intermediate risk	330 (36.9%)	202 (43.6%)	
High risk	300 (33.6%)	123 (26.6%)	
Missing	13	0	
Skin-to-skin procedure time (minutes) median, range	159.00 (70 - 412)	191.00 (72 - 300)	<0.001
Missing	48	151	
Perioperative blood loss (ml), median, range	156.00 (0 - 3200)	250.00 (0 - 3300)	<0.001
Missing	54	15	
Neurovascular bundle preservation			<0.01
Bilateral	356 (39.8%)	133 (29.1%)	
Unilateral	275 (30.8%)	151 (33%)	
None	263 (29.4%)	173 (37.9%)	
Missing	13	6	
Pathologic characteristics			
Pathological T-stage			<0.001
pT0	8 (0.9%)	0	
pT1	8 (0.9%)	1 (0.2%)	
pT2a	95 (10.7%)	121 (26.3%)	
pT2b	63 (7.1%)	13 (2.8%)	
pT2c	439 (49.54%)	162 (35.2%)	
pT3	254 (28.7%)	157 (34.1%)	
pT4	19 (2.1%)	6 (1.3%)	
Missing	21	3	
pGleason Sum			0.11
≤6	317 (35.3%)	151 (32.6%)	
7	436 (48.5%)	251 (54.2%)	
>7	146 (16.2%)	61 (13.2%)	
Missing	8	0	
Prostate volume (g), median, range	55 (5-718)	54 (12-200)	0.33

Table 1 (*continued*)

	Robot-assisted prostatectomy (n=907)	Laparoscopic prostatectomy (n=463)	P value
Missing	90	157	
Positive resection margin (%)	246 (27.3%)	120 (25.9%)	0.59
Missing	5	0	
Lymph node dissection performed (%)	343 (37.9%)	124 (26.8%)	<0.01
Missing	2	1	
Number of lymph nodes removed median, range	9 (1-38)	12 (1-56)	<0.001
Missing	31	45	
Positive lymph nodes (% of patients that received a lymph node dissection)	10.8%	7.0%	0.35
Missing	0	23	

were found in sexual functioning between RARP and LRP (28.89; 24.77, p = 0.12). Based on the number of pads used, RARP patients showed a higher chance to be continent (p = 0.002). Based on the firmness of the erection, the RARP group showed a non-significant higher chance for being potent (p = 0.052) (Appendix E). Appendix D shows the observed scores of the Urinary Incontinence and Sexual domain.

Secondary outcome measurements

On the EPIC domains: Urinary irritative/obstructive and Bowel, both groups showed high and similar scores (Table 3). On the EPIC hormonal domain, a significant better score was seen for RARP, corresponding with the lower number of patients receiving hormonal treatment (RARP: 92.78; LRP: 91.39, p = 0.04). The EORTC-

Table 2

- Postoperative characteristics including the use of care after surgery of the study population of 1370; other numbers apply when indicated. ◦ These questions asked patients whether they had experienced complaints directly after surgery and whether they used additional care for those complaints. $ These percentages represent the number of patients that used a certain type of care of the total number of patients that described to use care or pharmaceuticals for certain complaints. Patients were allowed to choose multiple answers therefore the numbers do not add up.

Characteristics of follow-up	Robot-assisted prostatectomy (n=907)	Laparoscopic prostatectomy (n=463)	P value
Occurrence of BCR when at least 3 years of follow-up data is available (%)	190 (33.6%) n= 565	101 (33.7%) n=300	0.99
Received radiotherapy (%)	188 (20.7%)	97 (21.0%)	0.96
Received hormonal therapy (%)	68 (7.5%)	46 (10.8%)	0.07
Duration of admission (days) median, range	3.0 (2-27)	3.0 (2-27)	0.11
Complications (patient-reported) classified by Clavien-Dindo grading system	168 (18.5%)	76 (16.4%)	0.34
Grade 1	70 (41.7%)	34 (44.7%)	0.49
Grade 2	41 (24.4%)	13 (17.1%)	
Grade 3	46 (27.4%)	21 (27.6%)	
Grade 4	11 (6.5%)	8 (10.5%)	
Patients having incontinence complaints after surgery	461 (52.1%)	307 (67.3%)	<0.001
Missing	22	7	
Among the patients with complaints; patients that used additional care$	399 (86.6%)	285 (92.8%)	<0.01
Physiotherapy	376 (94.2%)	268 (94.2%)	0.912
Number of visits (median, range)	*6.00 (1-60)*	*8.00 (1-60)*	0.015
Visiting the general practitioner	24 (6.0%)	17 (6.0%)	0.98
Number of visits (median, range)	*2.00 (1-20)*	*2.50 (1-40)*	0.31
Surgical procedure (e.g. male sling)	22 (5.5%)	39 (13.7%)	<0.01
Among the patients with complaints; the number of pads used in the previous 4 weeks			0.02
None	205 (44.7%)	103 (34.0%)	
1 per day	154 (33.6%)	115 (38.0%)	
2 per day	60 (13.1%)	44 (14.5%)	
3 or more per day	40 (8.7%)	41 (13.5%)	
Missing	2	4	
Patients having complaints of erectile dysfunction after surgery	653 (74.4%)	362 (81.2%)	0.02
Missing	29	17	
Among the patients with complaints, patients who used additional care$	195 (29.9%)	104 (28.7%)	0.68
Physiotherapy$	29 (14.9%)	17 (16.3%)	0.8
Number of visits (median, range)	8.00 (1-25)	9.00 (2-30)	
Visiting the general practitioner$	45 (23.1%)	14 (13.5%)	0.047
Number of visits (median, range)	2.00 (1-12)	2.00 (1-4)	
Visiting a different specialist$	127 (65.1%)	78 (75.0%)	0.08
Most frequent described specialties: $			
•Urologist or urology department	94 (74.0%)	63 (80.8%)	
•Sexologist or outpatient clinic for sexuality	23 (18.1%)	5 (6.5%)	
Number of visits for all the described specialists (median, range)	3.00 (1-80)	3.00 (1-18)	
Patients who used pharmaceuticals or other medical instruments for complaints of erectile dysfunction in the whole population	326 (36.5%)	146 (32.3%)	0.13
Missing	13	11	
Using a tablet (e.g. Cialis, Viagra, Levitra) $	207 (63.5%)	88 (60.3%)	0.5
Using an intra-urethral injection (e.g. Muse) $	6 (1.8%)	14 (9.6%)	<0.01
Using an intra-cavernous injection (e.g. Androskat) $	116 (35.6%)	55 (37.7%)	0.66
Prothesis$	4 (1.2%)	0 (0%)	0.32
Vacuum constriction device$	51 (15.6%)	32 (21.9%)	0.1

Table 3
Primary and Secondary outcomes. # Reports the sample size included in the model as for some patients information on incorporated confounders was missing, those were left out of the analysis.

A. Primary outcomes				
Outcome measurement	Robot-assisted prostatectomy (907)	Laparoscopic prostatectomy (463)	Absolute difference	P value
EPIC domain: Urinary incontinence (0–100) (SE)	73.34 (1.33) N = 823#	64.98 (1.63) N = 419#	8.35	**0.002**
Being incontinent based on Question 27 from Urinary Incontinence domain (SE) $	41.5% (3.7%) N = 842#	52.9% (4.2%) N = 427#	11.4%	**0.002**
EPIC domain: Sexual (0–100) (SE)	28.89 (1.87) N = 659#	24.77 (2.18) N = 327#	4.12	0.12
Having erectile dysfunction based on Question 59 from Sexual domain (SE) $	67.7% (2.9%) N = 682#	76.2% (3.4%) N = 336#	8.5%	0.052

B. Secondary outcomes			
	Robot-assisted prostatectomy (907)	Laparoscopic prostatectomy (463)	P value
EPIC domains (0–100) (SE)			
• Urinary irritative/obstructive*	95.75 (0.43) N = 868#	95.08 (0.56) N = 451#	0.36
• Bowel~	94.83 (0.55) N = 870#	94.70 (0.65) N = 452#	0.88
• Hormonal~	92.78 (0.47) N = 859#	91.39 (0.61) N = 441#	**0.04**
EORTC summary score (0–100) (SE)*	92.33 (0.39) N = 867#	91.37 (0.50) N = 444#	0.09
EQ5D-5L (0–1) (SE) *	0.918 (0.005) N = 872#	0.914 (0.006) N = 450#	0.54

A. Shows the primary outcomes noted in estimated marginal means returned from the mixed effect model which are controlled for hospital (cluster), age at the time of completing the questionnaire, D'Amico risk score, radiotherapy received at any time during follow-up (both salvage and adjuvant) and neurovascular bundle preservation. In this analysis, patients being incontinent and impotent before surgery were excluded. The analysis on the Urinary Incontinence was also controlled for hospital type and for the Sexual domain we additionally controlled for the use of pharmaceuticals or instruments used when patients had complaints after surgery. The addition of hospital volume depressed the fit of the model in both domain scores and was therefore not included. Incontinence was defined as use of 1 or more pads per day. Having erectile dysfunction was defined as: erection not firm enough for any sexual activity. The observed results from the two separate questions of the EPIC-26 are presented in Appendix E $ The analysis was controlled for cluster, D'Amico risk score, Radiotherapy, nerve-sparing and age.
B. Shows the estimated marginal means of the secondary outcomes. ~ controlled for cluster, D'Amico risk score, and radiotherapy. Age depressed the model fit and was not included. * controlled for cluster, D'Amico risk score, and nerve-sparing. Age depressed the model fit and was not included.

C30 summary score (RARP: 92.33; LRP: 91.37) and the utility values were comparable between the groups (RARP: 0.918; LRP: 0.914).

Factors influencing functional outcome scores

Table 4 presents the results from the regression analysis. Patients in both groups show a statistically and clinically significantly better urinary functioning when not receiving radiotherapy (RARP:+7.55, $p < 0.001$; LRP:+9.39, $p = 0.005$), and when having a nerve-sparing procedure (both groups: $p < 0.05$). Furthermore, a larger hospital volume was a clinically significant predictor of better urinary functioning in the LRP group.

Only for patients undergoing RARP, a statistically significantly better sexual functioning was seen when not receiving radiotherapy (+6.66, $p = 0.007$). Patients in both groups show significantly better sexual functioning when being younger of age (both groups: $p < 0.01$) and when having neurovascular bundle preservation. In the LRP group, a higher hospital volume was predictive of better sexual functioning.

Discussion

To the best of our knowledge, this is the first large cohort study that shows a clear clinical long-term benefit concerning urinary functioning after RARP compared to LRP. Over the years, many studies showed a trend towards short-term better sexual and urinary functioning after RARP [7–12,22,23]. Consistent with the literature, our results indicated that undergoing RARP is associated with shorter procedure time, reduced blood loss, and a higher chance of neurovascular bundle preservation [12,23,24]. Furthermore, RARP could be beneficial for sexual functioning as well, since our data showed that nerve-sparing procedures were closely related to better sexual functioning [25]. Our data do not show significance in better sexual functioning after RARP, although patients seemed to have a lower risk for having erectile dysfunction compared to LRP. This may be explained by aspects other than erectile functioning e.g. partner support and mental health that relate to sexual functioning [26]. Furthermore, age and longer follow-up are likely to affect the valuation of being potent [25]. Finally, it should be mentioned that these conclusions are drawn based on data from the early introduction period of the Da Vinci robot generating a possibly relative negative scenario for RARP as the performance of the Da Vinci robot is closely related with the experience of the surgeon [27].

We also found that irrespective of the type of procedure, being younger, receiving neurovascular bundle preservation, and not receiving adjuvant radiotherapy were associated with having better urinary and sexual functioning. These factors should be discussed with patients to optimally guide their treatment decision since survival between treatment options for localized prostate cancer is comparable [28].

In our study the observed functioning scores in both interventions were lower compared to that of earlier studies with shorter follow up [15]. This can be explained by the fact that our study was executed in different volume hospitals and patients were not excluded based on certain clinical characteristics, possibly more

Table 4
Regression analysis for primary outcome measures: EPIC-26 Urinary Incontinence and Sexual domain by means of a mixed effect model corrected for cluster (hospital). SE: Standard Error.

Urinary Incontinence Domain						
	Robot-assisted radical prostatectomy			Laparoscopic radical prostatectomy		
Parameter	Estimate	SE	P value	Estimate	SE	P value
Intercept	99.03	10.20	.000	54.75	17.73	0.002
D'Amico risk score						
low risk	−2.18	2.32	0.347	5.38	3.87	0.165
intermediate risk	−1.06	2.06	0.605	1.65	3.41	0.628
high risk	0[ref]			0[ref]		
Radiotherapy						
No	7.55	2.13	<0.001	9.39	3.30	0.005
Yes	0[ref]			0[ref]		
Neurovascular bundle preservation						
Bilateral	3.71	2.24	0.098	7.81	3.66	0.034
Unilateral	4.75	2.22	0.033	4.36	3.31	0.189
None	0[ref]			0[ref]		
Hospital volume						
>150 patients	3.70	3.01	0.220	–	–	–
100-150 patients	−5.12	3.18	0.108	10.81	4.07	0.008
50-100 patients	−0.91	3.71	0.807	14.05	3.56	<0.001
0-50 patients	0[ref]			0[ref]		
Age at surgery	−0.49	0.15	0.001	−0.209	0.255	0.412

Sexual domain						
	Robot-assisted radical prostatectomy			Laparoscopic radical prostatectomy		
Parameter	Estimate	SE	P value	Estimate	SE	P value
Intercept	84.67	11.78	<0.001	77.06	15.99	**<0.001**
D'Amico risk score						
low risk	1.86	2.75	0.501	4.62	3.57	0.196
intermediate risk	0.38	2.44	0.876	5.44	3.21	0.091
high risk	0[ref]			0ref		
Radiotherapy						
No	6.66	2.48	0.007	5.38	3.16	0.090
Yes	0[ref]			0[ref]		
Neurovascular bundle preservation						
Bilateral	18.81	2.68	<0.001	11.27	3.34	**0.001**
Unilateral	12.31	2.66	<0.001	11.16	3.01	**<0.001**
None	0[ref]			0[ref]		
Hospital volume						
>150 patients	4.09	3.82	0.285			
100-150 patients	−4.37	3.98	0.273	9.97	3.88	**0.011**
50-100 patients	−0.75	4.56	0.869	2.90	3.27	0.376
0-50 patients	0[ref]			0[ref]		
Age at surgery	−1.09	0.172	.000	−1.125	.227	**<0.001**

closely resembling daily clinical practice. Besides, as functional outcomes are known to worsen over time because of age [29], a longer follow-up period may also be an explanation for these differences. This argument is strengthened by two studies showing comparable domain scores for RARP after 6 and 3 years respectively [11,12]. In accordance with literature, LRP showed lower scores on the Urinary Incontinence and Sexual domains compared to ORP [22], which suggests that functional outcomes after LRP are worse than after ORP.

Our data also showed that higher hospital volume was associated with better functional outcomes after LRP. Such a relationship was not found among patients undergoing RARP. This could be explained by not having an equal distribution of hospital volume among the groups, as RARP was more often performed in high volume hospitals, and using a relatively short learning curve of only 50 procedures, where a minimum of 200 has been suggested [30]. When using a longer learning curve we would have missed a substantial number of patients undergoing RARP in lower-volume hospitals (50–100/year), since the majority of these hospitals shifted within our timeframe. Furthermore, it seems that other hospital-specific characteristics e.g. surgeon experience play an important role since we found that hospitals performing "50–100 procedures/year" in the LRP group showed better urinary functioning compared to hospitals performing "100–150 procedures/year".

The retrospective design of our study has some disadvantages. We had a lack of firm baseline information on incontinence and erectile dysfunction, which could have led to recall bias. We also had more missing data in the RARP group, due to the referral system in the Netherlands. Despite a carefully chosen timeframe, we were unable to include patients from very large-volume hospitals (>150 procedures/year) for the LRP group resulting in a selection bias [11,14]. The latter was controlled for by including a cluster variable for hospital. We lacked information on surgeon expertise as some of the operating surgeons have since retired or currently work in a different hospital. Concerning blood loss, we had no information on more reliable measures such as hemoglobin levels or the number of blood transfusions needed. We also did not have information on comorbidities in both groups. Furthermore, although we did not expect differences in comorbidities between the groups [12,22], a difference in all-cause mortality was found, but which could partly be explained by comorbidities. Finally, a response rate of 65% could have led to selection bias.

A great strength of the present analysis is being the first national

study evaluating long-term functional outcomes after RARP in a large cohort of prostate cancer patients. Further strengths include the incorporation of healthcare usage for incontinence and erectile dysfunction complaints, the inclusion of patients operated within a narrow timeframe evaluating the early introduction phase of the Da Vinci robot, and controlling for cluster effects by using mixed-effect modelling.

In light of recent developments, e.g. centralization of prostate cancer care, comparison with more recent data is necessary to be more conclusive on the relationship between hospital volume or surgeon experience and improved functional outcomes after RARP. Furthermore, a cost-effectiveness analysis is necessary to decide on coverage for RARP, as RARP comes with substantial extra costs [31]. Finally, the findings in overall and prostate-cancer specific mortality are noteworthy but no conclusions can be drawn yet; this aspect merits further study, taking in-depth medical file data and population registry data into account.

Conclusions

We conclude that RARP is preferred over LRP when it comes to perioperative outcomes and long-term urinary functioning. Therefore, guidelines concerning the preferred surgery type may change, and decision-makers have to reconsider their position on coverage, especially when RARP proves to be cost-effective compared to LRP.

CRediT authorship contribution statement

Melanie (M.A.) Lindenberg: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing – original draft, Visualization, Project administration, Funding acquisition. **Valesca (V.P.) Retèl:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Supervision, Funding acquisition. **Jacobien (J.M.) Kieffer:** Methodology, Formal analysis, Writing – review & editing. **Carl (C.) Wijburg:** Writing – review & editing. **Laurent (L.M.C.L) Fossion:** Writing – review & editing. **Henk (H.G.) van der Poel:** Software, Conceptualization, Writing – original draft. **Wim (W.H.) van Harten:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Supervision, Funding acquisition.

Declaration of competing interest

The authors report to have no competing interest. WvH obtained grants from Novartis, Agendia and Intuitive Surgical. VR obtained grants from Agendia.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2021.06.006.

Author contributions

ML conceptualized the research and manuscript together with WvH, VR and HvdP. JK, HvdP, ML, WvH and VR had discussions regarding the methodology and the statistical analysis. The analysis was performed by ML and JK and supervised by WvH, VR and HvdP. Data was collected and curated by ML. The manuscript was written by ML under supervision of WvH, VR, HvdP and JK. The manuscript was reviewed and edited by all authors (WvH, VR, HvdP, JK, CW, LF). Funding for the research was acquired by efforts from ML, VR and WvH.

Ethics approval and consent to participate

The study was checked by the medical ethical committee of the Netherlands Cancer Institute and was judged as a "non-WMO-applicable" research. Patients completed an informed consent form, which explained how their data would be used and reported. The study was performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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List of abbreviations

EPIC-26: expanded prostate cancer index composite short form
HRQoL: Health related quality of life
LRP: Laparoscopic radical prostatectomy
NKI-AVL: Netherlands cancer institute – Antoni van leeuwenhoek hospital
ORP: Open radical prostatectomy
RP: Radical prostatectomy
RARP: robotic radical prostatectomy