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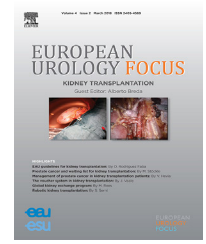
EUROPEAN UROLOGY FOCUS xxx (xxxx) xxx–xxx

available at www.sciencedirect.com
journal homepage: www.europeanurology.com/eufocus



Prostate Cancer

Robotic-assisted Versus Laparoscopic Radical Prostatectomy: 12-month Outcomes of the Multicentre Randomised Controlled LAP-01 Trial

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Article info

Article history:
Accepted February 8, 2022

Associate Editor: Christian Gratzke

Keywords:
Prostate cancer
Prostatectomy
Robotic-assisted prostatectomy
Laparoscopic prostatectomy
Continence
Potency
Multicentre randomised trial

Abstract

Background: Recently, our LAP-01 trial demonstrated superiority of robotic-assisted laparoscopic radical prostatectomy (RARP) over conventional laparoscopic radical prostatectomy (LRP) with respect to continence at 3 mo.
Objective: To compare the continence, potency, and oncological outcomes between RARP and LRP in the 12-mo follow-up.
Design, setting, and participants:: In this multicentre, randomised, patient-blinded controlled trial, patients referred for radical prostatectomy to four hospitals in Germany were randomly assigned (3:1) to undergo either RARP or LRP.
Outcome measurements and statistical analysis:: Continence was assessed as a patient-reported outcome through validated questionnaires. Secondary endpoints included potency and oncological outcomes. Data were statistically analysed by bivariate tests and multivariable models.
Results and limitations:: At 12 mo, follow-up data were available for 701 of 782 patients. Continence at 6 and 12 mo after surgery was better in RARP patients, however no longer statistically significant (p = 0.068 and 0.38, respectively). Patients who were potent at baseline and underwent nerve-sparing surgery reported significantly higher potency after RARP, as defined by the capability to maintain an erection sufficient for intercourse at 3 (p = 0.005), 6 (p = 0.018), and 12 mo (p = 0.013). There were no statistically significant differences in oncological outcomes at 12 mo. It is a limitation that the influence of different anastomotic techniques was not investigated in this study.

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https://doi.org/10.1016/j.euf.2022.02.002

Please cite this article as: Vinodh-Kumar-Adithyaa Arthanareeswaran et al., Robotic-assisted Versus Laparoscopic Radical Prostatectomy: 12-month Outcomes of the Multicentre Randomised Controlled LAP-01 Trial, Eur Urol Focus (2022), https://doi.org/10.1016/j.euf.2022.02.002

Conclusions: Both LRP and RARP offer a high standard of therapy for prostate cancer patients. However, robotic assistance offers better functional outcomes in specific areas such as potency and early continence in patients who are eligible for nerve-sparing RP.
Patient summary: We compared outcomes 12 mo after radical prostatectomy between robotic-assisted and conventional laparoscopy. Both methods were equivalent with respect to oncological outcomes. Better recovery of continence in patients with robotic-assisted surgery, which was observed at 3 mo, blurred up to 12 mo. A benefit of robotic-assisted surgery was also observed in potency.

1. Introduction

Since its introduction in 2000 [1–3], robotic surgical assistance has become the most popular approach to perform radical prostatectomy (RP) in many western countries. However, the dissemination of robotic-assisted radical prostatectomy (RARP) has not been driven by level 1 evidence. Currently, the available guidelines do not highlight any specific approach to be clearly superior. Rather, the guidelines recommend that surgeons apply the technique in which they are most proficient [4–6]. To date, only two randomised controlled trials (RCTs) exist that investigated differences between RARP and conventional laparoscopic RP (LRP). Asimakopoulos et al [7] reported a faster return to potency for the RARP arm and Porpiglia et al [8,9] observed significantly higher rates of continence in RARP patients. However, this evidence has been criticised as insufficient to support and justify the transition from conventional laparoscopic to the robotic-assisted approach. Both trials were limited due to their single-surgeon setting, which might not necessarily reflect daily clinical practice.

In order to provide high-quality evidence, the LAP-01 multicentre, patient-blinded, randomised controlled trial was conducted in Germany between November 2014 and April 2019 [10]. Patients were randomised in a 3:1 ratio to RARP or LRP, and were blinded to the approach until completion of a 3-mo follow-up (FU). Superiority of RARP in terms of recovery of early continence (at 3-mo FU) was reported previously in the group of patients who received a bilateral nerve-sparing (NS) procedure (p = 0.005) [10]. This difference was not observed in the non-NS group (p = 0.90).

There is a general agreement that RP patients continue to recover even after 3 mo, especially with regard to continence and potency. Therefore, 12-mo functional and oncological data are of paramount importance to compare the outcomes of the different surgical approaches. We now report the 12-mo results of the LAP-01 trial.

2. Patients and methods

2.1. *Study design and participants*

This was an investigator-initiated, multicentre, randomised, patient-blinded controlled trial that was conducted at four high-volume urology departments in Germany. The trial was designed to show superiority of RARP over LRP in terms of continence at 3 mo postoperatively. This goal was met, and the corresponding results have been published previously [10].

Between November 2014 and April 2019, participating centres recruited men under 75 yr of age with newly diagnosed prostate cancer who selected RP as their primary treatment. The inclusion and exclusion criteria are described in Supplementary Table 1. In total, 15 surgeons performed the procedures in this trial, with a mean of 51 procedures per surgeon (range 1–198, median 38). With the exception of one surgeon, all surgeons had performed >150 procedures using both approaches. Ethical approval was obtained from the ethical committees of all four participating centres, and written informed consent was obtained from all patients. The LAP-01 trial was registered with the German Clinical Trial registry (Deutsches Register Klinischer Studien; DRKS ID number: DRKS00007138) and the U.S. National Library of Medicine clinical trial registry (clinicaltrials.gov; NCT number: NCT03682146).

2.2. *Sample size calculation*

A 10% difference in continence rates (44% vs 34%) at 3-mo FU, and an error rate of α = 5% and 10% dropouts were assumed. To detect a difference with 80% power by log-rank test, a sample size of N = 782 was calculated. Sample size calculation is explained in detail elsewhere [10].

2.3. *Randomisation and data acquisition*

Patients were randomised in a 3:1 ratio to RARP or LRP 1 d prior to surgery. Randomisation was stratified by scheduled NS procedure (non-NS, unilateral NS, and bilateral NS), age ($\leq$65 or >65 yr), and trial site. Treatment allocation was performed centrally and was computer assisted by the Clinical Trial Center Leipzig using a minimisation procedure with a random component [11]. Study data were extracted from case report forms and medical records.

2.4. *Procedures and postoperative care*

Both RARP and LRP were performed as described previously [10]. All patients were instructed to perform pelvic floor muscle exercises and could choose to attend a 3-wk postoperative rehabilitation programme that is compensated by the German health care system. It is offered between 1 wk and 3 mo after RP, and includes extensive pelvic floor training. The subsequent postoperative care was provided by urologists in private practice. In Germany, the costs for phosphodiesterase type 5 inhibitors are not covered by public health insurance.

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2.5. *Outcomes*

Functional and oncological outcomes were assessed via validated questionnaires at baseline and at 3, 6, and 12 mo postoperatively. During the FU period, participants received their questionnaires by mail and completed them independently at home.

2.6. *Continence*

Data on continence were collected via patient-reported pad diary until 3 mo after RP. After this, data on pad usage were collected using standardised questionnaires. Patients were defined to be continent if they either did not use any pad or used a safety pad without involuntary loss of urine (no use of pads or single safety pad = 0/safety pad criterion). To further assess the continence status, the International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) was used, which consists of three questions. Furthermore, the prostate cancer–specific health-related quality of life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC QLQ-PR25) was used to assess urinary symptoms, which consists of eight questions [12].

2.7. *Potency*

Potency was investigated by means of the International Index of Erectile Function (IIEF) version 5 along with three specific questions and the EORTC QLQ-PR25 sexual activity (two questions) and sexual functioning (four questions, conditional on being sexually active) subscales [12]. Potency was defined as the ability to maintain an erection sufficient for penetration.

2.8. *Oncological outcomes*

Data on biochemical recurrence (BCR) were gathered by contacting the patients' urologists at 3, 6, and 12 mo postoperatively. At the same time points, patients were asked whether they had been diagnosed with recurrence and/or metastases, or whether they had received additional therapies for prostate cancer. BCR was defined as a prostate-specific antigen (PSA) value of $\geq$0.2 ng/ml.

2.9. *Statistical analysis*

2.9.1. *Analysis population*

Three different populations were defined. First, all randomised patients who underwent surgery formed the safety analysis set. Second, the full analysis set consisted of all treated patients with the available primary endpoint. Following the intention-to-treat principle, they were analysed according to the randomised arm. The third population (PbNS) was defined for analysis of potency in a post hoc fashion. It consisted of patients who were potent at baseline and underwent a unilateral or bilateral NS procedure.

To characterise the study cohort, means and standard deviations were calculated for continuous variables, and number and percentages were calculated for categorical data. The skew distributed PSA values preoperatively were summarised by median and quartiles. Frequencies of continent patients were compared in total and separately for the categories of NS by the chi-square test. We compared mean questionnaire scores (IIEF and ICIQ sum, PR-25 scales) by means of *t* test for independent samples. Cohen's D was calculated as an effect measure for continuous characteristics; 95% confidence intervals for proportions and their differences were calculated by the method of Wilson. The measure A, the probability of stochastic superiority following Delaney and Vargha [13], was calculated for ordinal data.

For longitudinal considerations, linear mixed models were calculated, including arm, randomisation strata, and time as fixed factors and a random intercept for patient and centre. The coefficient of the interaction term time $\times$ arm estimates the effect of different changes of the questionnaire scale adjusted by the baseline value. However, terms with negligible effects were removed from the model.

Data preparation and descriptive statistics were done by means of IBM SPSS Statistics, version 26. The analysis of ordinal data as well as generation of graphs was realised by means of R, including the packages *survival*, *binom*, *orddom*, *QoLR*, and *lmerTest* [14,15].

3. Results

We randomised 782 patients into two groups (RARP n = 586 and LRP n = 196). At 12-mo FU, the analysis set consisted of 701 patients (Fig. 1). The baseline characteristics between the trial groups were well balanced and are presented in Supplementary Table 2. Patients who were potent at baseline and received an NS surgery showed similar baseline characteristics and are presented in Supplementary Table 3.

3.1. *Continence*

The study showed a significant difference of 8.7% in continence rates among the RARP patients according to the 0 pads/safety pad definition at 3-mo FU (p = 0.027) [10]. This difference decreased to 7.5% at 6-mo and to 3.2% at 12-mo FU and was no longer significant (p = 0.068 and p = 0.38 respectively; Fig. 2). The difference in continence was more pronounced for patients who had received an NS procedure, but was not significant at 6 and 12 mo FU (Fig. 2). There was only an insignificant difference in the ICIQ sum scores at 6 and 12 mo, as shown in Table 1. In addition, differences between treatment groups in urinary symptoms, as measured by the QLQ-PR25, were negligible (Table 1).

3.2. *Potency*

Potency was compared by analysing data from patients who underwent an NS procedure and were potent at baseline (PbNS post hoc analysis) which included 310 patients (Table 2). RARP patients reported about 15% higher rates of potency during the entire FU period (3 mo: p = 0.005; 6 mo: p = 0.018; 12 mo: p = 0.013). The superiority of RARP in erectile function recovery was also documented by the outcomes of the IIEF questionnaire at 3-mo (p = 0.010) and 12-mo (<0.001) FU. RARP patients also reported higher PR-25 values for sexual activity and functioning at 3, 6, and 12 mo. The difference is low at 3 mo and increases up to 1 yr. However, high variability thwarts significance (Table 2).

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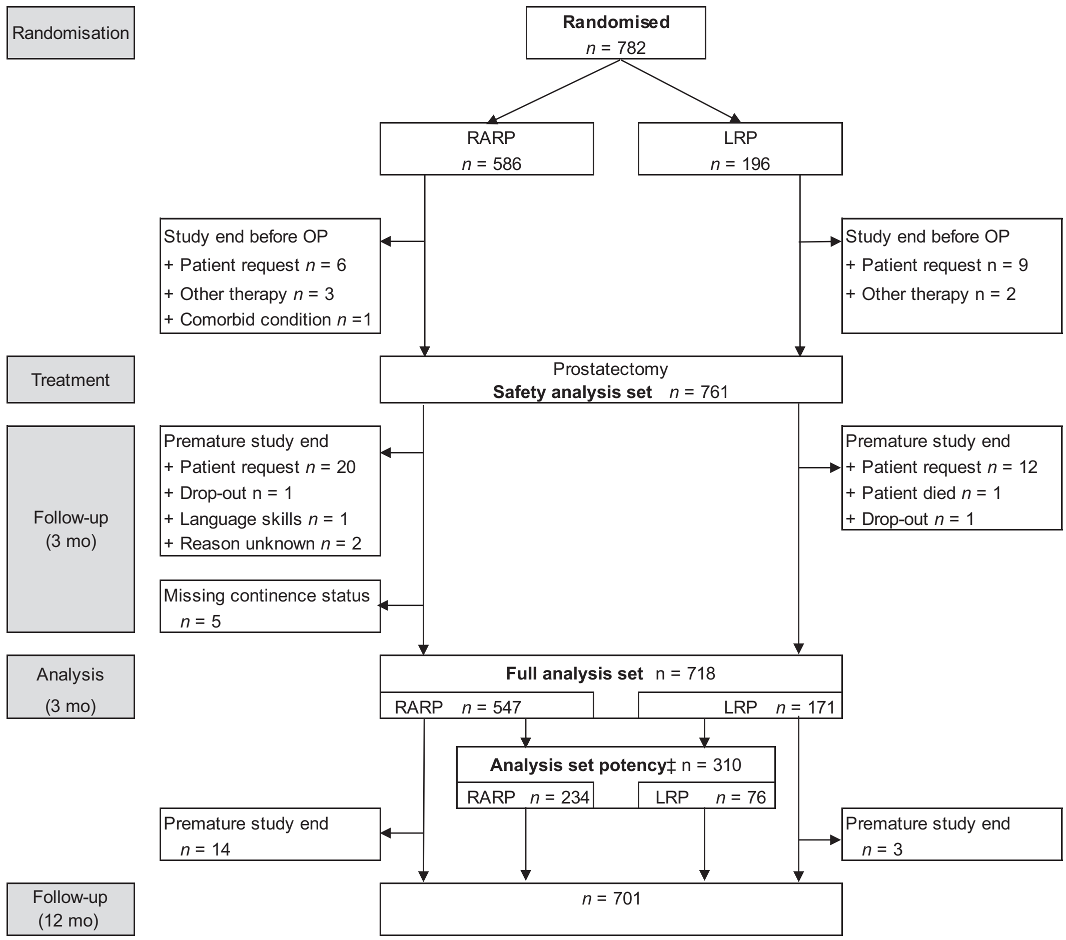

Fig. 1 – Flow chart of the trial. LRP = laparoscopic radical prostatectomy; OP = operation; RARP = robotic-assisted laparoscopic radical prostatectomy.

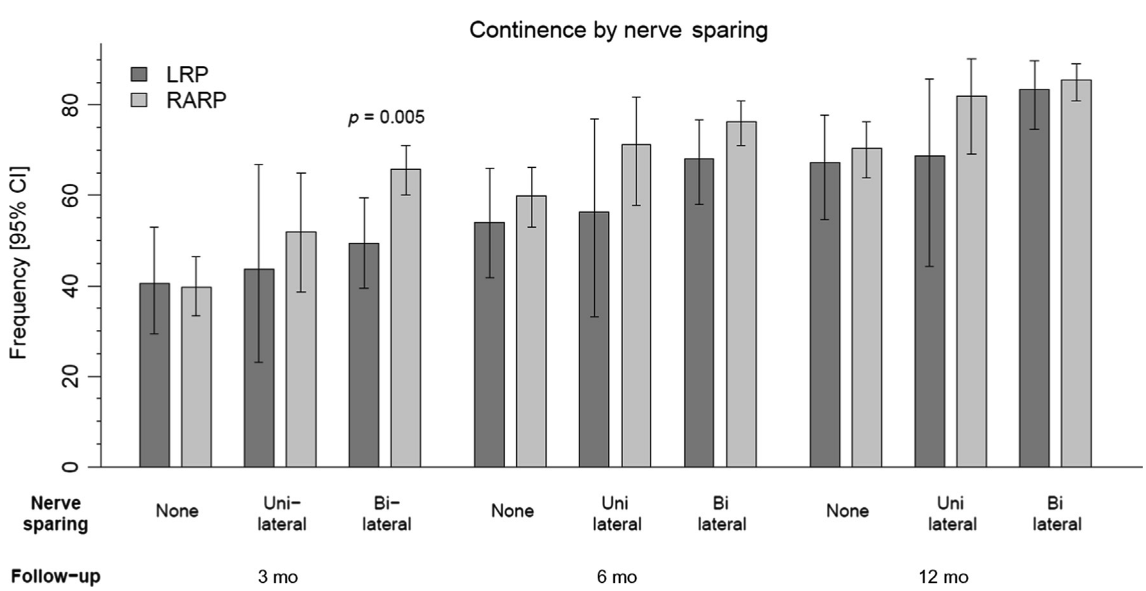

Fig. 2 – Continence by arm and nerve-sparing surgery follow-up at 3, 6, and 12 mo. The diagram shows frequencies including 95% confidence intervals stratified by study arm and category of nerve-sparing surgery. CI = confidence interval; LRP = laparoscopic radical prostatectomy; RARP = robotic-assisted laparoscopic radical prostatectomy.

Table 1 – Continence recovery at 6- and 12-mo FU; descriptive statistics and tests

		ITT: Randomisation arm				*p* value	Effect measure
		RARP (*N* = 547)		LRP (*N* = 171)			
6-mo FU							
ICIQ-SF							Prob. of stoch. superiority [a]
1. How often do you leak urine?	Never	186	36%	42	25%	0.074	56% (51–61%)
	About once per week or less often	123	24%	39	24%		
	2 or 3 times a week	57	119%	17	10%		
	About once daily	45	8.6%	15	9.1%		
	Several times a day	104	20%	50	30%		
	All the time	7	1.3%	2	1.2%		
2. How much urine do you leak?	None	186	36%	46	28%	0.27	53% (48–58%)
	Little	304	59%	107	66%		
	Moderate	22	4.3%	8	4.9%		
	Large	3	0.6%	2	1.2%		
		Mean ± SD		Mean ± SD			Mean difference (95% CI)
3. Overall, how much does leaking urine interfere with your everyday life?		1.8 ± 2.4		1.9 ± 2.3		0.47	−0.1 (−0.2, 0.1)
ICIQ sum		4.7 ± 4.6		5.4 ± 4.6		0.091	−0.7 (−1.5, 0.1)
EORTC QLQ-PR25 urinary symptoms		22.5 (21, 24)		23.3 (20.7, 25.9)			−0.07 (−0.24, 0.11)
12-mo FU							
ICIQ-SF							Prob. of stoch. Superiority [a]
1. How often do you leak urine?	Never	230	45%	62	38%	0.51	53% (48–57%)
	About once per week or less often	122	24%	39	24%		
	2 or 3 times a week	42	8.2%	20	12%		
	About once daily	35	6.8%	11	6.7%		
	Several times a day	81	16%	30	18%		
	All the time	5	1.0%	1	0.6		
2. How much urine do you leak?	None	233	46%	63	39%	0.26	53% (48 to 58%)
	Little	270	53%	92	57%		
	Moderate	7	1.4%	4	2.5%		
	Large	2	0.4%	2	1.2%		
		Mean ± SD		Mean ± SD			Mean difference (95%CI)
3. Overall, how much does leaking urine interfere with your everyday life?		1.4 ± 2.2		1.6 ± 2.5		0.28	−0.1 (−0.3, 0.1)
ICIQ sum		3.9 ± 4.3		4.4 ± 4.6		0.17	−0.5 (−1.4, 0.3)
EORTC QLQ-PR25 urinary symptoms		19.2 (17.7, 20.7)		20.2 (17.5, 22.8)			−0.08 (−0.25, 0.10)

CI = confidence interval; EORTC QLQ-PR25 = prostate cancer–specific health-related quality of life questionnaire of the European Organization for Research and Treatment of Cancer; FU = follow-up; ICIQ-SF = International Consultation on Incontinence Questionnaire Short Form; ITT = intention to treat; LRP = laparoscopic radical prostatectomy; RARP = robotic-assisted radical prostatectomy; SD = standard deviation.
[a] Effect measure A: probability of stochastic superiority, especially appropriate for ordinal variables [12]. It means, for example, for the first question (6 mo): in pairwise comparison, patients of the RARP arm have a lower (better) category with probability 56%.

3.3. *Oncological outcomes*

The data concerning oncological outcomes are presented in Table 3. There were only insignificant differences in BCR rates and postoperative radiotherapy rates between RARP and LRP groups in all tumour stages (pT2, pT3, and pT4).

4. Discussion

RARP is increasingly being utilised around the world since its inception in 2001 in spite of insufficient high-quality evidence to support its superiority. Unfortunately, the available literature is based on either observational studies or monocentric studies with limited numbers of patients. In order to close this gap, we conducted the first multicentre, randomised, patient-blinded study worldwide to compare RARP and LRP in terms of functional and oncological outcomes. It is also the largest study carried out till date on this topic, with 782 randomised and 718 primarily evaluated patients.

Incontinence following RP is one of the most bothersome postoperative complications that has a significant impact on patient's quality of life [16–20]. A recent meta-analysis by Carbonara et al [21] that included previous prospective and observational studies showed that the urinary incontinence rate after 12 mo was significantly lower in the RARP group. It should be noted that the reported continence rates are strongly influenced by differing definitions used to assess urinary continence and vary widely across the published studies. A similar problem was observed in studies comparing RARP and the open approach. A recent RCT involving 326 men did not show significant difference in the continence rates at 6, 12, and 24 mo between open RP and RARP using the Expanded Prostate Cancer Index Composite (EPIC) questionnaire [22,23]. A prospective trial by Porpiglia et al [9] randomised 120 prostate cancer patients to either RARP or LRP, and showed statistically significant differences in continence 12 mo after surgery in favour of RARP. In another randomised comparison of RARP versus LRP, Asimakopoulos et al [7] assessed 128 patients sched-

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uled to undergo RP with bilateral NS. Their trial did not observe a statistically significant difference in continence. Recently, early functional outcomes of our trial that showed significantly higher continence rates at 3-mo FU in the RARP group ($p = 0.027$) were published. However, the result was influenced, to a large extent, by the patients who underwent NS surgery. It is noteworthy that this difference in continence rate diminishes at the 12-mo FU in our trial.

In terms of potency, a meta-analysis showed that the recovery rate of erectile functioning was higher for RARP than for LRP at 12-mo ($p = 0.007$) FU, with potency being defined as an IIEF-5 score of >17 [21]. Our trial showed significantly better potency rates throughout the FU period (from 3 to 12 mo). Thus, patients who are eligible for an NS surgery benefit from the use of robotic-assisted surgery. Patel et al [24] have previously introduced the concept of the "pentafecta" outcome, which includes the achievement of potency, continence, BCR-free survival rates, negative surgical margins, and no postoperative complications after RARP. Although erectile dysfunction was considered to be the most common reason for the failure of pentafecta achievement, the recovery of erectile function after RP is a difficult outcome to compare. Different definitions for potency recovery, differences in postsurgery rehabilitation, and characteristics of the surgical techniques (with or without NS) influence reports on potency outcomes in studies. Furthermore, new techniques have been published recently on potency-preserving techniques for robotic platforms, such as real-time penile oxygen monitoring and cavernous nerve mapping [25,26]. Two monocentric RCTs demonstrated significantly better potency recovery in the RARP group after 12-mo and 5-yr FU. Both the return to baseline for IIEF-5 score and that to IIEF-5 >17 were significantly higher in the RARP group [7]. Whereas a cumulative analysis by Ficarra et al [27] did not observe a significant difference between the two methods. These findings, however, must be interpreted with caution as study type, differences in patient inclusion criteria, surgical techniques, and learning curves could have influenced the results. A subgroup analysis of our trial involving only patients who were potent at baseline and who underwent an NS procedure clearly showed a significant advantage of RARP over LRP in terms of potency throughout the FU period. This result highlights the fact that RARP can be recommended to patients who are primarily potent and in whom the tumour status permits NS surgery.

A possible explanation for the advantage of RARP over LRP is the improved manoeuvrability in robotic-assisted surgery, which can enable improved dissection of the prostatic plexus and the neurovascular bundle. This could be an explanation why patients who are candidates for an NS procedure have an advantage in functional outcomes. The nerves of the neurovascular bundle partly innervate the external urethral sphincter and transport the parasympa-

Table 2 – Potency

Analysis of the PbNS ($N = 310$) (Patients who were potent at baseline and underwent nerve sparing surgery)	Randomisation arm: RARP ($N = 234$)	Randomisation arm: LRP ($N = 76$)	p value	Effect measure
3 mo				
In the last 3 mo:				Frequency difference
1. Has the urologist offered erectility supporting treatment?	121 (54%)	37 (49%)	0.46	10% (−8.1%, 18%)
2. Did you have an erection hard enough for sexual intercourse?	52 (23%)	6 (8.2%)	0.005	15% (6.6%, 23%)
3. Did you use erectility supporting aids?	112 (51%)	33 (44%)	0.30	6.9% (−6.1%, 20%)
				Adjusted mean difference
IIEF Sum	7.1 (6.3, 7.9) [a]	5.3 (3.9, 6.7)	0.010 [b]	2.1 (0.46, 3.7) [c]
EORTC QLQ-PR25 sexual activity	47.1 (43.6, 50.5)	44.4 (38.5, 50.4)	0.18	4.5 (−2.2, 11.2)
EORTC QLQ-PR25 sexual functioning	47.7 (45.3, 50.1)	46.9 (42.4, 51.4)	0.55	1.7 (−4.0, 7.4)
6 mo				
In the last half year:				Frequency difference
1. Has the urologist offered erectility supporting treatment?	125 (55%)	35 (48%)	0.29	7.2% (−6.0%, 20%)
2. Did you have an erection hard enough for sexual intercourse?	69 (31%)	12 (16%)	0.018	14% (3.8%, 25%)
3. Did you use erectility supporting aids?	121 (53%)	37 (51%)	0.15	2.6% (−11%, 16%)
				Adjusted mean difference
IIEF sum	7.9 (7.1, 8.7)	6.7 (5.3, 8.1)	0.069	1.5 (−0.15, 3.1)
EORTC QLQ-PR25 sexual activity	50.4 (47.0, 53.8)	45.9 (39.9, 51.9)	0.056	6.4 (−0.3, 13.1)
EORTC QLQ-PR25 sexual functioning	50.8 (48.4, 53.1)	51.0 (46.6, 55.4)	0.82	0.6 (−5.0, 6.3)
12 mo				
In the last half year:				Frequency difference
1. Has the urologist offered erectility supporting treatment?	117 (52%)	40 (56%)	0.62	−3.3% (−16%, 9.9%)
2. Did you have an erection hard enough for sexual intercourse?	89 (40%)	17 (24%)	0.013	16% (4.4%, 28%)
3. Did you use erectility supporting aids?	120 (55%)	44 (60%)	0.41	−5.5% (−18%, 7.5%)
				Adjusted mean difference
IIEF sum	9.4 (8.6, 10.1)	6.8 (5.4, 8.2)	<0.001	2.8 (1.2, 4.4)
EORTC QLQ-PR25 sexual activity	53.1 (49.6, 56.5)	49.2 (43.2, 55.2)	0.089	5.7 (−1.0, 12.4)
EORTC QLQ-PR25 sexual functioning	52.6 (50.3, 55.0)	48.7 (44.5, 52.8)	0.078	4.8 (−0.6, 10.3)

EORTC QLQ-PR25 = prostate cancer–specific health-related quality of life questionnaire of the European Organization for Research and Treatment of Cancer; IIEF = International Index of Erectile Function; LRP = laparoscopic radical prostatectomy; RARP = robotic-assisted radical prostatectomy.
[a] 95% confidence intervals.
[b] p value from the interaction term in the mixed linear model.
[c] Estimated difference adjusted by baseline means.

Table 3 – Oncological outcomes at 12 mo

	RARP (*N* = 562)	LRP (*N* = 199)	*p* value
pT2			
PSA <0.2, no radiotherapy	323 (91%)	111 (93%)	0.33
Radiotherapy without PSA recurrence	7 (2.0%)	2 (1.7%)	
PSA recurrence without radiotherapy	15 (4.2%)	1 (0.8%)	
PSA recurrence with radiotherapy	11 (3.1%)	5 (4.2%)	
Total	356 (100%)	119 (100%)	
pT3			
PSA <0.2, no radiotherapy	106 (53%)	44 (57%)	0.78
Radiotherapy without PSA recurrence	50 (25%)	20 (26%)	
PSA recurrence without radiotherapy	10 (5.0%)	2 (2.6%)	
PSA recurrence with radiotherapy	33 (17%)	11 (14%)	
Total	199 (100%)	77 (100 %)	
pT4			
PSA <0.2, no radiotherapy	0 (0%)	1 (50%)	0.60
PSA recurrence without radiotherapy	3 (75%)	1 (50%)	
PSA recurrence with radiotherapy	1 (25%)	0 (0%)	
Total	4 (100%)	2 (100%)	

LRP = laparoscopic radical prostatectomy; PSA = prostate-specific antigen; RARP = robotic-assisted radical prostatectomy.

thetic fibres that enable an influx of blood into the corpora cavernosa [28]. The external urethral sphincter is further innervated by the pudendal nerves that spring from the S2 to S4 nerve roots [29]. This dual innervation of the external sphincter could explain the short-term differences in continence between the two groups, as the damage caused to the neurovascular bundle during RP leads to deterioration of the continence apparatus. After an initial phase of incontinence due to diminished innervation of the external sphincter, fibres of the pudendal nerves might compensate the function of the damaged neurovascular nerves. Herein, better nerve preservation and more careful dissection facilitated by the robotic-assisted approach could lead to a better short-term recovery of continence. Over time, urinary continence may improve further as fibres of the pudendal nerves compensate for the damaged fibres of the neurovascular bundle. This dual innervation could explain the reduction of difference between the two approaches as time passes. Similarly, persistent differences in potency between the two groups may be due to the fact that the corpora cavernosa are predominantly innervated by the neurovascular bundle, and therefore other nerves cannot compensate for the loss of innervation.

There is a paucity of high-quality studies that compare data on BCR in this regard. Furthermore, different definitions for BCR, and inclusion of patients from different tumour stages and those who underwent adjuvant radiotherapy further complicate the situation. Two monocentric RCTs did not show significant difference in the BCR rates at 12-mo FU ($p = 0.2$ and $p = 0.19$) [7,8]. The trials, however, included only patients with clinical stage up to T2. On the contrary, we included a wider spectrum of clinical tumour stages that better reflects everyday clinical practice. A subgroup analysis of BCR rates based on pathological tumour stage and adjuvant radiotherapy status revealed comparable outcomes between both techniques at 12-mo FU. This highlights the fact that both LRP and RARP are equally effective with regard to oncological outcomes.

Our study results that are based on a multicentre randomised design, rigorous 3-mo patient blinding, large sample size, and robust and well-defined outcomes may have future implications on the outlook of minimally invasive prostatectomy. Robotic-assisted surgery is here to stay, and as more companies introduce new robots to the market, the competition may lead to a cost reduction. Furthermore, robotic surgical systems offer the prospect of standardised and structured mentoring programmes for the trainees [29]. The master-slave console systems allow for better options to guide the trainees than conventional laparoscopic systems. This may result in a shorter learning curve [30]. However, it should be noted that we did not examine the learning curve of the procedures as participating surgeons were already skilled in the examined procedures.

4.1. *Limitations*

It is a limitation that the influence of different anastomotic techniques was not investigated in this study. Furthermore, the setting in the German health-care system could limit the transferability of the data to other health care systems. Additionally, a limitation of the currently presented data includes a possibly remaining, but not detected, difference in terms of continence between the two groups. This stems from the sample size calculation that was originally performed to show a difference at 3-mo FU. Therefore, a difference in continence rates might remain undetected due to a sample size originally calculated for a different time point.

5. Conclusions

In conclusion, both LRP and RARP offer a high standard of therapy for prostate cancer patients. Patients with low- and intermediate-risk prostate cancer who are eligible for an NS approach will likely benefit from the use of robotic-assisted surgery for NS RP. This benefit will be a higher rate of early continence and likely a sustained higher rate of postoperative potency. Patients with high-risk prostate cancer who are not eligible for an NS approach will likely not profit from a robotic-assisted approach and may undergo conventional laparoscopic surgery without a higher risk of postoperative incontinence.

***Author contributions*:** Jens-Uwe Stolzenburg 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.

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Acquisition of data: Holze, Neuhaus.
Analysis and interpretation of data: Mende, Holze, Stolzenburg.
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Statistical analysis: Mende, Holze.
Obtaining funding: Holze, Stolzenburg.
Administrative, technical, or material support: Neuhaus.
Supervision: Stolzenburg, Holze.
Other: None.

Financial disclosures: Jens-Uwe Stolzenburg certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** This study was funded by Deutsche Krebshilfe (German Cancer Aid, grant number 110462). The funding agency had no part in study conception, design and decision to publish the results.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euf.2022.02.002.

References

[1] Binder J, Kramer W. Robotically-assisted laparoscopic radical prostatectomy. BJU Int 2001;87:408–10.
[2] Pasticier G, Rietbergen JB, Guillonneau B, Fromont G, Menon M, Vallancien G. Robotically assisted laparoscopic radical prostatectomy: feasibility study in men. Eur Urol 2001;40:70–4.
[3] Rassweiler J, Frede T, Seemann O, Stock C, Sentker L. Telesurgical laparoscopic radical prostatectomy. Initial experience. Eur Urol 2001;40:75–83.
[4] Leow JJ, Chang SL, Meyer CP, et al. Robot-assisted versus open radical prostatectomy: a contemporary analysis of an all-payer discharge database. Eur Urol 2016;70:837–45.
[5] Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer—2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2021;79:243–62.
[6] Sanda MG, Cadeddu JA, Kirkby E, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. Part II: recommended approaches and details of specific care options. J Urol 2018;199:990–7.
[7] Asimakopoulos AD, Pereira Fraga CT, Annino F, Pasqualetti P, Calado AA, Mugnier C. Randomized comparison between laparoscopic and robot-assisted nerve-sparing radical prostatectomy. J Sex Med 2011;8:1503–12.
[8] Porpiglia F, Fiori C, Bertolo R, et al. Five-year outcomes for a prospective randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. Eur Urol Focus 2018;4:80–6.
[9] Porpiglia F, Morra I, Lucci Chiarissi M, et al. Randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. Eur Urol 2013;63:606–14.
[10] Stolzenburg JU, Holze S, Neuhaus P, et al. Robotic-assisted versus laparoscopic surgery: outcomes from the first multicentre, randomised, patient-blinded controlled trial in radical prostatectomy (LAP-01). Eur Urol 2021;79:750–9.
[11] Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics 1975;31:103–15.
[12] van Andel G, Bottomley A, Fossa SD, et al. An international field study of the EORTC QLQ-PR25: a questionnaire for assessing the health-related quality of life of patients with prostate cancer. Eur J Cancer 2008;44:2418–24.
[13] Delaney HD, Vargha A. Comparing several robust tests of stochastic equality with ordinally scaled variables and small to moderate sized samples. Psychol Methods 2002;7:485–503.
[14] Team RC. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing.
[15] Anota ASM, Bascoul-Mollevi C, Bonnetain F. QoLR: an R package for the longitudinal analysis of health-related quality of life in oncology. J Stat Softw 2017;77:1–30.
[16] Chung JW, Kim SW, Kang HW, et al. Efficacy of modified radical prostatectomy technique for recovery of urinary incontinence in high-grade prostate cancer. Minerva Urol Nefrol 2020;72:605–14.
[17] Palisaar JR, Roghmann F, Brock M, Loppenberg B, Noldus J, von Bodman C. Predictors of short-term recovery of urinary continence after radical prostatectomy. World J Urol 2015;33:771–9.
[18] Penson DF, Feng Z, Kuniyuki A, et al. General quality of life 2 years following treatment for prostate cancer: what influences outcomes? Results from the prostate cancer outcomes study. J Clin Oncol 2003;21:1147–54.
[19] Wallerstedt A, Nyberg T, Carlsson S, et al. Quality of life after open radical prostatectomy compared with robot-assisted radical prostatectomy. Eur Urol Focus 2019;5:389–98.
[20] Donovan JL, Hamdy FC, Lane JA, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. N Engl J Med 2016;375:1425–37.
[21] Carbonara U, Srinath M, Crocerossa F, et al. Robot-assisted radical prostatectomy versus standard laparoscopic radical prostatectomy: an evidence-based analysis of comparative outcomes. World J Urol 2021;39:3721–32.
[22] Coughlin GD, Yaxley JW, Chambers SK, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: 24-month outcomes from a randomised controlled study. Lancet Oncol 2018;19:1051–60.
[23] Yaxley JW, Coughlin GD, Chambers SK, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. Lancet 2016;388:1057–66.
[24] Patel VR, Sivaraman A, Coelho RF, et al. Pentafecta: a new concept for reporting outcomes of robot-assisted laparoscopic radical prostatectomy. Eur Urol 2011;59:702–7.
[25] Tewari A, Srivastava A, Sooriakumaran P, Grover S, Dorsey P, Leung R. Technique of traction-free nerve-sparing robotic prostatectomy: delicate tissue handling by real-time penile oxygen monitoring. Int J Impot Res 2012;24:11–9.
[26] Klotz L, Heaton J, Jewett M, et al. A randomized phase 3 study of intraoperative cavernous nerve stimulation with penile tumescence monitoring to improve nerve sparing during radical prostatectomy. J Urol 2000;164:1573–8.
[27] Ficarra V, Novara G, Rosen RC, et al. Systematic review and meta-analysis of studies reporting urinary continence recovery after robot-assisted radical prostatectomy. Eur Urol 2012;62:405–17.
[28] Stolzenburg JU, Schwalenberg T, Horn LC, Neuhaus J, Constantinides C, Liatsikos EN. Anatomical landmarks of radical prostatectomy. Eur Urol 2007;51:629–39.
[29] Walz J, Burnett AL, Costello AJ, et al. A critical analysis of the current knowledge of surgical anatomy related to optimization of cancer control and preservation of continence and erection in candidates for radical prostatectomy. Eur Urol 2010;57:179–92.
[30] Smith AL, Krivak TC, Scott EM, et al. Dual-console robotic surgery compared to laparoscopic surgery with respect to surgical outcomes in a gynecologic oncology fellowship program. Gynecol Oncol 2012;126:432–6.