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Robot-assisted radical prostatectomy has lower biochemical recurrence than laparoscopic radical prostatectomy: Systematic review and meta-analysis

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Purpose: To assess the effectiveness and safety of robot-assisted radical prostatectomy (RARP) versus laparoscopic radical prostatectomy (LRP) in the treatment of prostate cancer.

Materials and Methods: Existing systematic reviews were updated to investigate the effectiveness and safety of RARP. Electronic databases, including Ovid MEDLINE, Ovid Embase, the Cochrane Library, KoreaMed, Kmbase, and others, were searched through July 2014. The quality of the selected systematic reviews was assessed by using the revised assessment of multiple systematic reviews (R-Amstar) and the Cochrane Risk of Bias tool. Meta-analysis was performed by using Revman 5.2 (Cochrane Community) and Comprehensive Meta-Analysis 2.0 (CMA; Biostat). Cochrane Q and I2 statistics were used to assess heterogeneity.

Results: Two systematic reviews and 16 additional studies were selected from a search performed of existing systematic reviews. These included 2 randomized controlled clinical trials and 28 nonrandomized comparative studies. The risk of complications, such as injury to organs by the Clavien-Dindo classification, was lower with RARP than with LRP (relative risk [RR], 0.44; 95% confidence interval [CI], 1.23–0.85; p=0.01). The risk of urinary incontinence was lower (RR, 0.43; 95% CI, 0.31–0.60; p<0.000001) and the potency rate was significantly higher with RARP than with LRP (RR, 1.38; 95% CI, 1.11–1.70; I^2=78%; p=0.003). Regarding positive surgical margins, no significant difference in risk between the 2 groups was observed; however, the biochemical recurrence rate was lower after RARP than after LRP (RR, 0.59; 95% CI, 0.48–0.73; I^2=21%; p<0.00001).

Conclusions: RARP appears to be a safe and effective technique compared with LRP with a lower complication rate, better potency, a higher continence rate, and a decreased rate of biochemical recurrence.

Keywords: Laparoscopy; Meta-analysis; Prostatic neoplasms; Prostatectomy; Robotics

INTRODUCTION

Radical prostatectomy has historically been the preferred treatment option for patients with localized prostate cancer. However, surgical innovations to reduce blood loss and hasten the recovery rate have led to the introduction of

laparoscopic radical prostatectomy (LRP) followed by robot-assisted radical prostatectomy (RARP) as alternatives to open surgery [1,2]. RARP was introduced to decrease the difficulty in performing complex laparoscopic procedures such as urethral anastomosis. The robotic platform provided several advantages over LRP, such as seven degrees of freedom, tremor filtration, a three-dimensional magnified view, and preferred ergonomics [3]. Therefore, robot-assisted surgery has become popular in Korea, the United States, and Europe [1,4]. However, this trend has occurred despite a lack of high-quality evidence supporting improvement in outcomes.

Randomized controlled trials comparing the safety and effectiveness of RARP and LRP are limited. Therefore, high-level evidence is a requisite for clinicians needing recent evidence on the treatment of prostate cancer. The primary objective of this study was to determine whether RARP is more effective than LRP in the treatment of prostate cancer in terms of functional, oncological, and perioperative outcomes.

MATERIALS AND METHODS

1. Inclusion criteria

Eligible studies included randomized controlled trials and prospective and retrospective cohort studies comparing RARP and LRP. A study was excluded if it did not report any outcomes of interest or functional and oncological outcomes.

2. Search strategy

We searched electronic databases for reviews published through July 2014, including Ovid MEDLINE (Ovid, New York, NY, USA), Ovid EMBASE (Ovid), the Cochrane Library (London, United Kingdom), KoreaMed (KAMJE, Seoul, Korea), Kmbase (MedRIC, Chungbuk, Korea), KISS (Korean Studies Information Co, Paju, Korea), RISS (KERIS, Daegu, Korea), and KisTi (KISTI, Daejeon, Korea). Patient-related search terms (prostatic neoplasm, prostatic cancer, prostatic carcinoma, prostatic tumor), and intervention-related search terms (robotics, computer-assisted surgery, telerobot, remote operation, remote surgery, da Vinci) were combined.

3. Data synthesis and analysis

Two independent reviewers selected the studies, extracted data, and performed quality assessments. The authors assessed the relevance and quality of the selected systematic reviews related to the research question through the revised assessment of multiple systematic reviews (R-Amstar). For the prospective randomized controlled clinical studies, the Cochrane Collaboration's tool for assessing risk of bias was used to perform the quality evaluations. For the nonrandomized studies on the final selected literature, a revised risk of bias was used to perform the quality
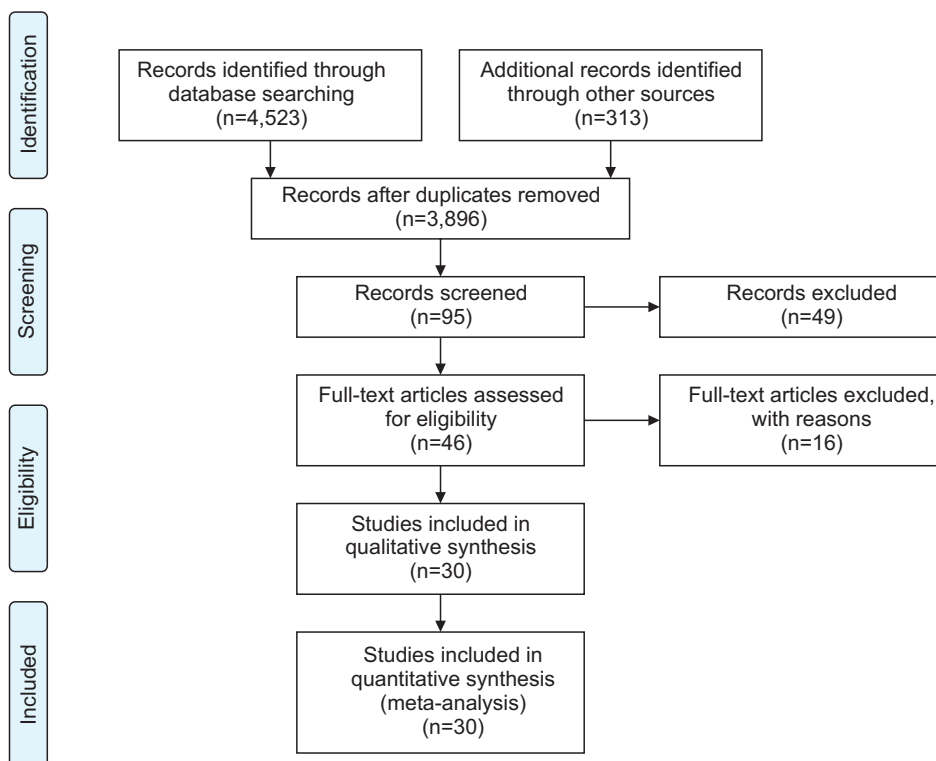

Fig. 1. Flow diagram of the study selection process.

evaluations. Functional and oncologic outcomes, as well as postoperative complications and perioperative results (operation duration, length of stay), were calculated and compared between the groups.

4. Statistical analysis

Meta-analysis was conducted by using RevMan 5.2 (Cochrane Community, London, United Kingdom) and Comprehensive Meta-Analysis 2.0 (CMA; Biostat, Englewood, NJ, USA). The Cochrane Q and I2 statistics were used to assess statistical heterogeneity. The results were expressed as weighted means and standardized mean differences for continuous outcomes and as relative risk (RR) and 95% confidence intervals (CIs) for dichotomous variables. For dichotomous variables, the random effect model of Mantel-Haenszel was used, and for continuous data, the random effect model of the inverse-variance method was used. Publication bias was tested by using a funnel plot and Egger's test. The statistical analyses were reviewed by a statistician with previous meta-analysis experience.

5. Details of included studies

The studies selected are outlined in Fig. 1. Thirty articles were evaluated. There were 2 randomized controlled clinical trials (RCTs) and 28 nonrandomized comparative studies (Table 1).

6. Quality assessment

For the RCTs, there was a low risk of bias in sequence generation, blinding, selective report, and other biases. However, the allocation of concealment was uncertain, and incomplete outcome data were at a high risk of bias. In the cohort studies, sequence generation and allocation of concealment, which are important factors in the quality assessment of therapeutic publications, were at a high risk of bias.

RESULTS

1. Postoperative complications

The risk of complications, such as bladder neck contracture (RR, 0.40; 95% CI, 0.17–0.92; p=0.03), organ injury (RR, 0.23; 95% CI, 0.11–0.49; p=0.0002), and other major complications (Clavien-Dindo III–V) according to the Clavien-Dindo classification (RR, 0.44; 95% CI, 0.23–0.85; p=0.01), was lower for RARP than for LRP. Anastomosis site leakage (RR, 0.67; 95% CI, 0.42–1.08; p=0.10) and the rates of infection (RR, 1.21; 95% CI, 0.84–1.76; p=0.31), ileus (RR, 0.73; 95% CI, 0.38–1.40; p=0.34), and pulmonary embolism (RR, 1.20; 95% CI, 0.22–6.51;

p=0.83) were not significantly different between the groups (Fig. 2). No significant difference in the conversion rate (RR, 0.70; 95% CI, 0.25–1.95; p=0.50) was observed. RARP carried a lower risk of transfusion than LRP (RR, 0.70; 95% CI, 0.54–0.91; I2=44%; p=0.007).

2. Perioperative data

The operation time for RARP was shorter than that for LRP (RR, -18.74; 95% CI, -32.15 to -5.33; p=0.006), but the statistical heterogeneity was high (χ^2=527.29, df=22, p<0.00001, I2=96%). The hospital stay following RARP was 1.53 days shorter than that following LRP. The results of the subgroup analysis according to region showed a mean difference of -1.13 (95% CI, 2.93–0.67; p=0.22) in the Asia Pacific region, -0.56 (95% CI, 1.14–0.02; p=0.06) in the United States, and 0.32 (95% CI, 0.88–0.25; p=0.28) in Europe. However, the overall statistical heterogeneity was high (I2=94%).

3. Functional outcomes

The functional outcomes were improved in a comparison between RARP and LRP (Fig. 3). The urinary incontinence rate at 12 months was lower for RARP than for LRP (RR, 0.43; 95% CI, 0.31–0.60; p<0.000001), and statistical heterogeneity was low (I2=0%). The potency recovery rate was higher for RARP than for LRP at postoperative 12 months (RR, 1.38; 95% CI, 1.11–1.70; I2=78%; p=0.003). Potency recovery was defined as an International Index of Erectile Function 5 (IIEF-5)>17.

4. Oncologic outcomes

The overall positive surgical margin (PSM) results were investigated in 7 studies. When analyzing PSM rates in the pT2 group, the RARP and LRP series had PSM rates of 14.2% (123 of 864 cases) and 11.3% (97 of 860 cases) with an RR of 1.22 (95% CI, 0.98–1.54; p=0.11). In the pT3 group, the PSM rates for RARP and LRP were 43.1% (116 of 269 cases) and 34.4% (72 of 209 cases) with an RR of 1.26 (95% CI, 1.00–1.58; p=0.05) (Fig. 4).

The biochemical recurrence (BCR) rate was significantly lower for RARP than for LRP (RR, 0.59; 95% CI, 0.48–0.73; I2=0%; p<0.00001) (Fig. 4). Five studies used prostate-specific antigen (PSA)≥0.2 ng/mL to indicate BCR, 1 study used PSA≥0.4 ng/mL, and 2 studies did not define the cutoff used. The follow-up period ranged from 3 months to 60 months. The overall BCR rates for RARP and LRP were 8.6% (162 of 1,885 cases) and 13.7% (314 of 2,288 cases).

Table 1. The characteristics of the included studies

Study	Study design	Country	Sample size			Participants (mean/median age years, mean/median PSA ng/mL, clinical/pathologic T stage)			Intervention (surgical technique)		Follow-up (mo)
			Total	RARP	LRP	RARP	LRP	p-value	RARP	LRP	
Asimakopoulos 2011 [9]	RCT	Italy	112	52	60	61.1±5.1 7.37 (1.5–9.15) cT1: 25, cT2: 35	59.6±5.4 8.9 (5.8–9.2) cT1: 14, cT2: 38	0.13 0.3 0.1	Transperitoneal, ante-grade nerve-sparing intrafascial technique	Transperitoneal, ante-grade nerve-sparing intrafascial technique	12
Durand 2008 [24]	Retrospective cohort study	France	57	34	23				Transperitoneal approach	Transperitoneal approach	
Hakimi 2009 [25]	Prospective cohort study	USA	150	75	75	59.8 (42–71) 8.4 pT2: 64, pT3: 11	59.6 (43–72) 7.5 pT2: 71, pT3: 4	0.88 0.217 0.099	Nerve-sparing technique	23% performed in extraperitoneal fashion	12
Ball 2006 [26]	Prospective cohort study	USA	206	82	124	60±7 6±2.4 cT1:66, cT2: 15, cT3: 1	61±7 7.2±7.1 cT1: 100, cT2: 24, cT3: 0		Bladder neck preservation	Transperitoneal combining anterograde and retrograde approach	36
Bolenz 2010 [23]	Retrospective cohort study	USA	473	262	211	61 (57–66) 5.3 (4.2–7)	59 (54–63) 5 (4.1–6.5)	0.001 0.29			
Drouin 2009 [27]	Retrospective cohort study	France	156	71	85	60.4 (46–70) 7.8 (3–24) cT1:50, cT1: 21	61.8 (39–73) 8.9 (3.4–37) cT1: 55, cT2: 30	>0.05	Transperitoneal approach	Transperitoneal approach	48.4
Gosseine 2009 [28]	Prospective cohort study	France	247	122	125			>0.05			
Hu 2006 [29]	Retrospective cohort study	USA	680	322	358	62.1 (41–84) cT1:269, cT2: 86, cT3: 3	63.7 (40–83) cT1: 232, cT2: 77, cT3: 1	>0.05	Transperitoneal approach of Montsouris technique	Transperitoneal approach of Montsouris technique	
Joseph 2005 [30]	Retrospective cohort study	France/USA	100	50	50	59.6±1.6 7.3±1.26 pT2: 44, pT3: 6	61.8±1.6 6.0±0.83 pT2: 40, pT3: 9	0.06 0.06	Extraperitoneal approach	Extraperitoneal approach	5.3
Rozet 2007 [31]	Retrospective cohort study	France	266	133	133	62 (49–76) 7.6 (0.9–38) cT1:76, cT2: 57	62.5 (47–74) 7.8 (3.2–19) cT1: 91, cT2: 41, cT3: 1	0.46 0.81	Extraperitoneal approach	Extraperitoneal approach	
Trabulsi 2008 [32]	Retrospective cohort study	USA	240	50	190			>0.05	Transperitoneal approach	Transperitoneal approach	
Cho 2009 [33]	Retrospective cohort study	South Korea	120	60	60	66.3 (50–77) 9.98 (2.91–26.3) cT2: 51, cT3: 9	66.5 (57–75) 11.04 (2.72–36.6) cT2: 42, cT3: 18	0.45 0.28 0.12	Transperitoneal approach	Extraperitoneal approach	16.8 (RARP), 51.2 (LRP)
Kasraeian 2011 [34]	Retrospective cohort study	France	400	200	200	60.8 (44–73) 6.4 (2.1–19.8) cT1:134, cT2:66	61.9 (45–75) 6.8 (2.7–48.8) cT1: 131, cT2: 68	0.067 <0.001 0.752 0.833	Extraperitoneal interfascial technique	Extraperitoneal interfascial technique	
Kermarrec 2010 [35]	Retrospective cohort study	France	397	221	176	60.6 7.48 cT1:129, cT2: 92	61.84 7.86 cT1: 104, cT2: 72	0.16 0.33 0.90			

Table 1. Continued

Study	Study design	Country	Sample size			Participants (mean/median age years, mean/median PSA ng/mL, clinical/pathologic T stage)			Intervention (surgical technique)		Follow-up (mo)
			Total	RARP	LRP	RARP	LRP	p-value	RARP	LRP	
Kermarrec 2010 [35]	Retrospective cohort study	France	397	221	176	60.6 7.48 cT1:129, cT2:92	61.84 7.86 cT1:104, cT2:72	0.16 0.33 0.90		Transperitoneal Montsouris technique	
Koutlidis 2012 [36]	Prospective cohort study	France	410	234	176	60.9±5.8 7.5±4.5 cT1:137, cT2:97	61.9±6.6 7.9±4.9 cT1:102, cT2:74	0.08 0.5 0.9	Transperitoneal Montsouris technique	Transperitoneal Montsouris technique	
Lee 2009 [37]	Retrospective cohort study	South Korea	52	21	31	64.6±6.79 8.1±7.01 cT1:3, cT2:12, cT3:6	63±8.52 11.7±13.72 cT1:5, cT2: 19, cT3:7	0.612 0.211 0.506	Transperitoneal approach	Transperitoneal approach	2.7 (RARP) 4.4 (LRP)
Magheli 2011 [38]	Retrospective cohort study	USA	1,044	522	522	58.3±6.3 5.4±3.2 cT1:417, cT2:105	58.4±6.4 5.4±2.7 cT1:414, cT2:108	0.496 0.929 0.778			30 (RARP) 17 (LRP)
Nakamura 2011 [39]	Retrospective cohort study	USA	10	5	5	65 (59–73) 4.8 (2–6.5)	66.4 (59–71) 5.3 (4.3–6.3)	0.852 0.373	Transperitoneal approach	Transperitoneal approach	
Park 2013 [40]	Retrospective cohort study	South Korea	327	183	144	63 (44–75) 4.98 (0.05–51.4) cT1:54, cT2: 79, cT3: 50	67 (38–77) 5.84 (0.08–41.2) cT1:50, cT2: 52, cT3: 42	<0.001 0.634 0.593	Transperitoneal approach Periurethral suspension Rocco stitch	Transperitoneal approach Periurethral suspension Rocco stitch	13 (RARP) 19 (LRP)
Ploussard 2014 [41]	Prospective cohort study	France	2,386	1,009	1,377	62.7 9.2 cT1:81.8%, >cT1: 18.2%	62.7 9.8 cT1:81%, >cT1: 19%	1.00 0.123 0.764	Extraperitoneal approach	Extraperitoneal approach	15.4 (RARP) 39 (LRP)
Porpiglia 2013 [18]	RCT	Italy	120	60	60	63.9±6.7 6.9±4.2 cT1–T2:60	64.7±5.9 8.3±6.5 cT1–T2: 60	0.595 0.115	Transperitoneal anterograde approach Rocco stitch	Transperitoneal anterograde approach Rocco stitch	12
Berge 2013 [1]	Prospective cohort study	USA	420	210	210	61.7 (40–76) 9.0 (2.3–40) pT2: 146, pT3: 63	61.7 (42–76) 8.6 (2.3–28) pT2: 132, pT3: 77	0.9 0.4 0.1	Montsouris transperitoneal approach	Bladder neck dissection initially thereafter Montsouris approach	36
Stolzenburg 2013 [42]	Prospective cohort study	German	200	100	100	61.21±7.7 8.75±7.1 pT2:77, pT3: 20, pT4: 3	61.33±7.4 10.7±11.49 pT2: 67, pT3: 33		Extraperitoneal intrafascial approach	Extraperitoneal intrafascial approach	
Willis 2012 [43]	Prospective cohort study	USA	282	121	161	58.1±6.3 5±2.2 cT1:99, cT2: 22	58±6.7 5.7±2.9 cT1:128, cT2: 33	0.86 0.72 0.19	Montsouris retrovesical approach with bilateral pelvic lymphadenectomy	Montsouris retrovesical approach with bilateral pelvic lymphadenectomy	12
Wolanski 2012 [44]	Retrospective cohort study	Australia	160	73	87	61.4±7.2 6.0 (2.9)	61.3±6.5 6.4 (2.8)	0.921 0.324	Extraperitoneal, antegrade, athermal approach	Transperitoneal approach with routine posterior rhabdosphincter reconstruction	3

PSA, prostate-specific antigen; RARP, robot-assisted radical prostatectomy; LRP, laparoscopic radical prostatectomy; RCT, randomized controlled clinical trial.

A Clavien-dindo classification

	RARP		LRP			Risk ratio		Risk ratio
Study or subgroup	Events	Total	Events	Total	Weight (%)	M-H, random, 95% CI	Year	M-H, random, 95% CI
1.9.1 Minor complications								
Menon 2002	1	40	2	40	3.3	0.50 [0.05, 5.30]	2002	
Sundaram 2004	1	10	1	10	2.9	1.00 [0.07, 13.87]	2004	
Hu 2006	62	322	102	358	9.8	0.68 [0.51, 0.89]	2006	
Joseph 2007	34	754	195	800	9.6	0.18 [0.13, 0.26]	2007	
Rozet 2007	33	133	14	133	9.0	2.36 [1.32, 4.20]	2007	
Drouin 2009	10	71	5	85	7.3	2.39 [0.86, 6.68]	2009	
Gosseine 2009	4	122	8	125	6.7	0.51 [0.16, 1.66]	2009	
Bolenz 2010	12	262	4	211	6.9	2.42 [0.79, 7.38]	2010	
Philippe 2012	8	73	18	87	8.3	0.53 [0.24, 1.15]	2012	
Ploussard 2014	43	1,009	51	1,377	9.5	1.15 [0.77, 1.71]	2014	
Subtotal (95% CI)		**2,796**		**3,226**	**73.1**	**0.87 [0.46, 1.64]**		
Total events	208		400					

Heterogeneity: Tau^2=0.79; Chi^2=90.07, df=9 (p<0.00001); I^2=90%
Test for overall effect: Z=0.44 (p=0.66)

	RARP		LRP			Risk ratio		
1.9.2 Major complications								
Menon 2002	0	40	2	40	2.3	0.20 [0.01, 4.04]	2002	
Hu 2006	6	322	30	358	7.9	0.22 [0.09, 0.53]	2006	
Rozet 2007	1	133	1	133	2.7	1.00 [0.06, 15.82]	2007	
Drouin 2009	0	71	1	85	2.1	0.40 [0.02, 9.62]	2009	
Philippe 2012	4	73	7	87	6.6	0.68 [0.21, 2.24]	2012	
Ploussard 2014	3	1,009	3	1,377	5.2	1.36 [0.28, 6.75]	2014	
Subtotal (95% CI)		**1,648**		**2,080**	**26.9**	**0.44 [0.23, 0.85]**		
Total events	14		44					

Heterogeneity: Tau^2=0.07; Chi^2=5.50, df=5 (p=0.36); I^2=9%
Test for overall effect: Z=2.43 (p=0.01)

	RARP		LRP			Risk ratio		
Total (95% CI)		**4,444**		**5,306**	**100.0**	**0.75 [0.44, 1.26]**		
Total events	222		444					

Heterogeneity: Tau^2=0.72; Chi^2=97.53, df=15 (p<0.00001); I^2=85%
Test for overall effect: Z=1.09 (p=0.28)
Test for subaroup differences: Chi^2=2.09, df=1 (p=0.15); I^2=52.2%

(0.01 0.1 1 10) Favours RARP Favours LRP

B Organ injury

	RARP		LRP			Risk ratio		Risk ratio
Study or subgroup	Events	Total	Events	Total	Weight (%)	M-H, fixed, 95% CI	Year	M-H, fixed, 95% CI
Hu 2006	3	322	23	358	60.2	0.15 [0.04, 0.48]	2006	
Lee 2009	0	21	1	31	3.4	0.48 [0.02, 11.36]	2009	
Cho 2009	0	60	2	60	6.9	0.20 [0.01, 4.08]	2009	
Drouin 2009	0	71	1	85	3.8	0.40 [0.02, 9.62]	2009	
Stolzenburg 2013	0	100	0	100		Not estimable	2013	
Ploussard 2014	3	1,009	11	1,377	25.7	0.37 [0.10, 1.33]	2014	
Total (95% CI)		**1,583**		**2,011**	**100.0**	**0.23 [0.11, 0.49]**		
Total events	6		38					

Heterogeneity: Chi^2=1.46, df=4 (p=0.83); I^2=0%
Test for overall effect: Z=3.77 (p=0.0002)

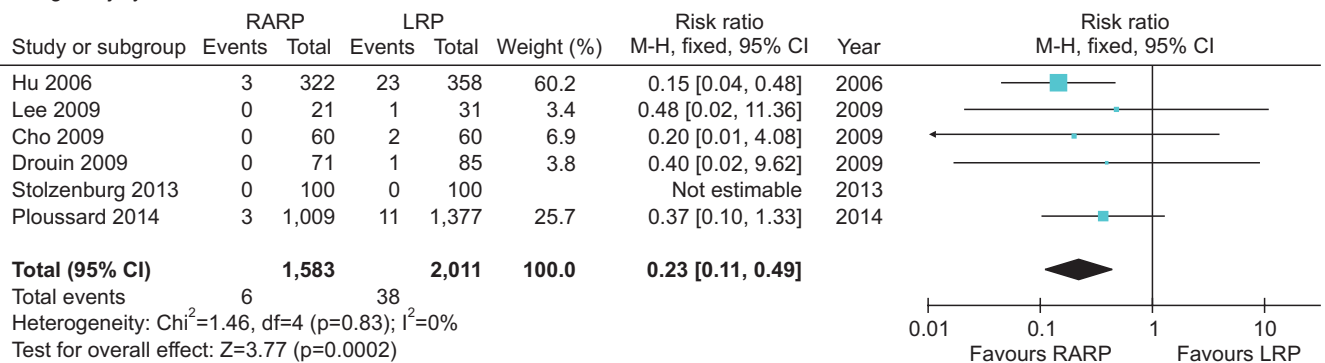(0.01 0.1 1 10) Favours RARP Favours LRP

Fig. 2. Cumulative analyses of robot-assisted radical prostatectomy comparing laparoscopic radical prostatectomy in postoperative complication (A: Clavien-dindo classification, B: Organ injury). RARP, robot-assisted radical prostatectomy; LRP, laparoscopic radical prostatectomy; M-H, Mantel Haenszel; CI, confidence interval; df, degrees of freedom.

5. Publication bias

A funnel plot analysis for organ injury, blood transfusion rate, length of stay, potency, and overall BCR revealed a symmetrical funnel plot, indicating no publication bias (Fig. 5) (p=0.53, p=0.47, p=0.26, p=0.10, and p=0.70, respectively, Egger test). However, operative time revealed asymmetry on the funnel plot (p=0.01, Egger test).

DISCUSSION

Our study revealed three important findings: (1) the risk of complications after RARP was significantly lower than

A Urinary incontinence rate

Study or subgroup	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year	Risk ratio M-H, fixed, 95% CI
Trabulsi 2008	12	205	8	45	13.2	0.33 [0.14, 0.76]	2008	
Cho 2009	4	60	17	60	17.0	0.24 [0.08, 0.66]	2009	
Hakimi 2009	5	75	8	75	8.0	0.63 [0.21, 1.82]	2009	
Asimakopoulos 2011	3	52	10	60	9.3	0.35 [0.10, 1.19]	2011	
Park 2013	23	183	32	144	35.9	0.57 [0.35, 0.92]	2013	
Porpiglia 2013	6	50	17	53	16.6	0.37 [0.16, 0.87]	2013	
Total (95% CI)		**625**		**437**	**100.0**	**0.43 [0.31, 0.60]**		
Total events	53		92					

Heterogeneity: Chi^2=3.61, df=5 (p=0.61); I^2=0%
Test for overall effect: Z=5.09 (p<0.00001)

0.01　0.1　1　10
Favours RARP　　Favours LRP

B Sexual function recovery rate

Study or subgroup	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, random, 95% CI	Year	Risk ratio M-H, random, 95% CI
Hakimi 2009	43	58	36	55	14.6	1.13 [0.89, 1.45]	2009	
Cho 2009	16	53	13	41	7.2	0.95 [0.52, 1.75]	2009	
Asimakopoulos 2011	40	62	19	60	10.6	2.04 [1.35, 3.09]	2011	
Willis 2012	21	24	38	57	14.7	1.31 [1.03, 1.66]	2011	
Park 2013	64	183	33	144	11.9	1.53 [1.07, 2.18]	2013	
Berge 2013	24	58	38	81	11.3	0.88 [0.60, 1.30]	2013	
Porpiglia 2013	28	35	19	35	12.2	1.47 [1.04, 2.08]	2013	
Ploussard 2014	582	1,009	435	1,377	17.5	1.83 [1.66, 2.01]	2014	
Total (95% CI)		**1,482**		**1,850**	**100.0**	**1.38 [1.11, 1.70]**		
Total events	818		631					

Heterogeneity: Tau^2=0.06; Chi^2=32.16, df=7 (p<0.00001); I^2=78%
Test for overall effect: Z=2.97 (p=0.003)

0.01　0.1　1　10
Favours RARP　　Favours LRP

Fig. 3. Cumulative analyses of robot-assisted radical prostatectomy comparing laparoscopic radical prostatectomy in functional outcome (A: Urinary incontinence rate, B: Sexual function recovery rate). RARP, robot-assisted radical prostatectomy; LRP, laparoscopic radical prostatectomy; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom.
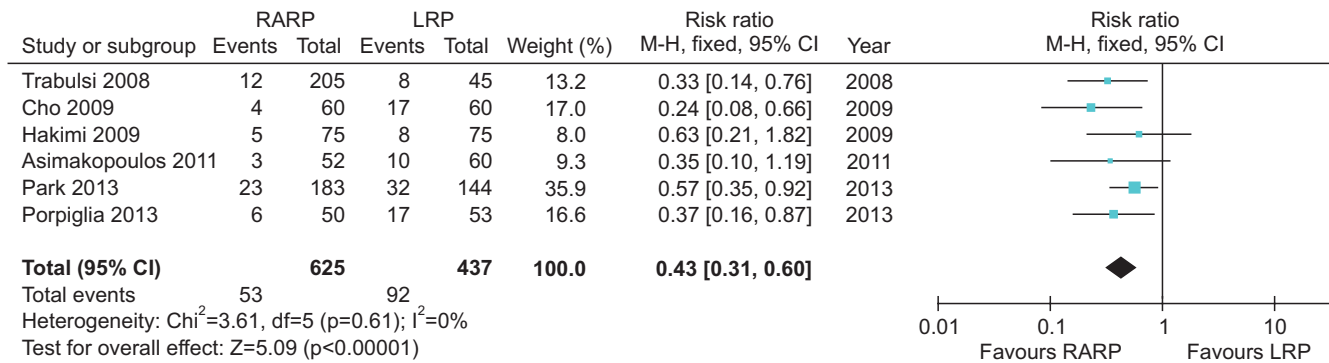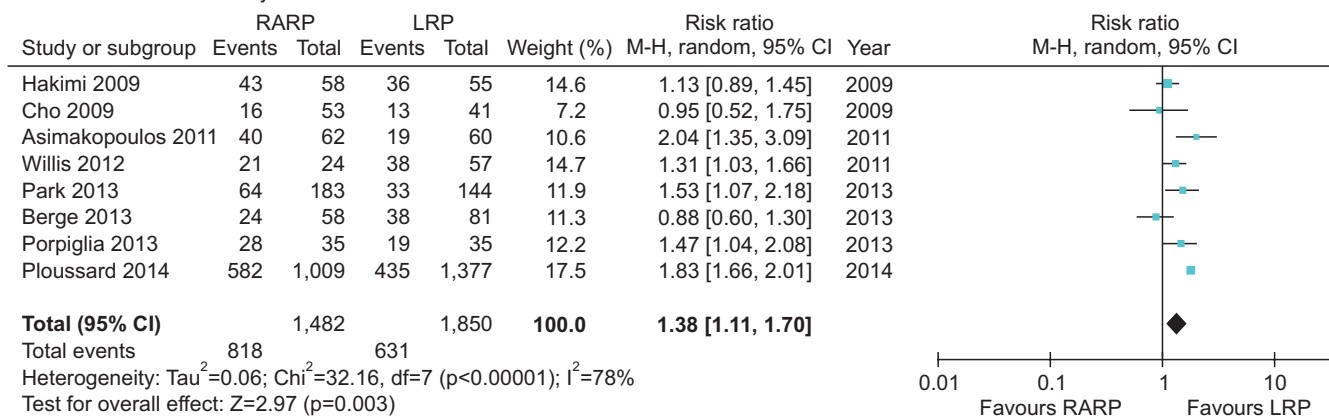
after LRP; (2) in comparison with LRP, the risk of urinary incontinence at 12 months was significantly lower and the potency rate was higher with RARP; (3) the BCR rate was significantly lower after RARP than after LRP.

The major findings of this meta-analysis showed significant differences in complications such as organ injury and other major complications according to the Clavien-Dindo (III–V) classification. The major complication rate was significantly lower for RARP than for LRP. Although both laparoscopic and robotic surgeries are regarded as minimally invasive techniques, the main advantages of RARP, such as seven degrees of freedom in robotic arm movement and magnified 3D vision of the robotic platform, result in decreased postoperative complications.
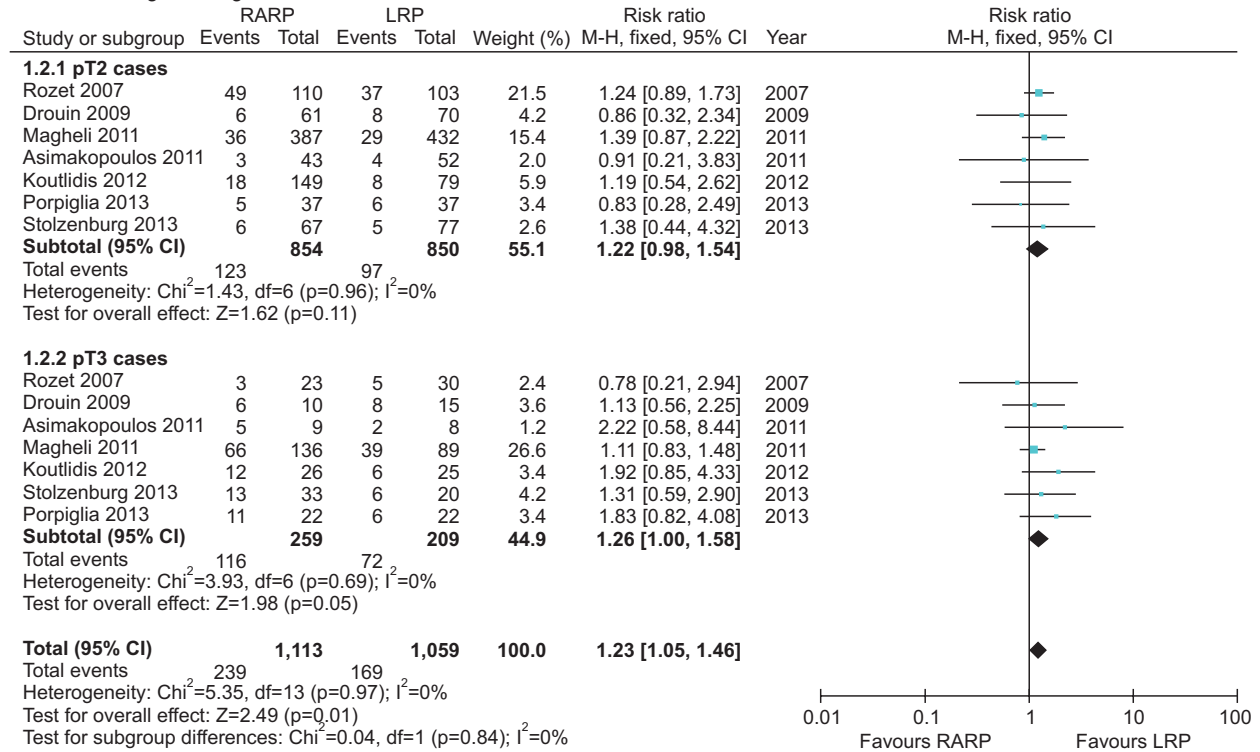
Incontinence is another complication of prostatectomy that greatly affects quality of life [5]. The urinary incontinence rate is influenced by the definition of incontinence. Thus, as reported previously, any systematic review is difficult to accomplish owing to the varying definitions used for urinary incontinence, such as involuntary urine loss [6], needing zero or 1 pad [7], and also those in the International

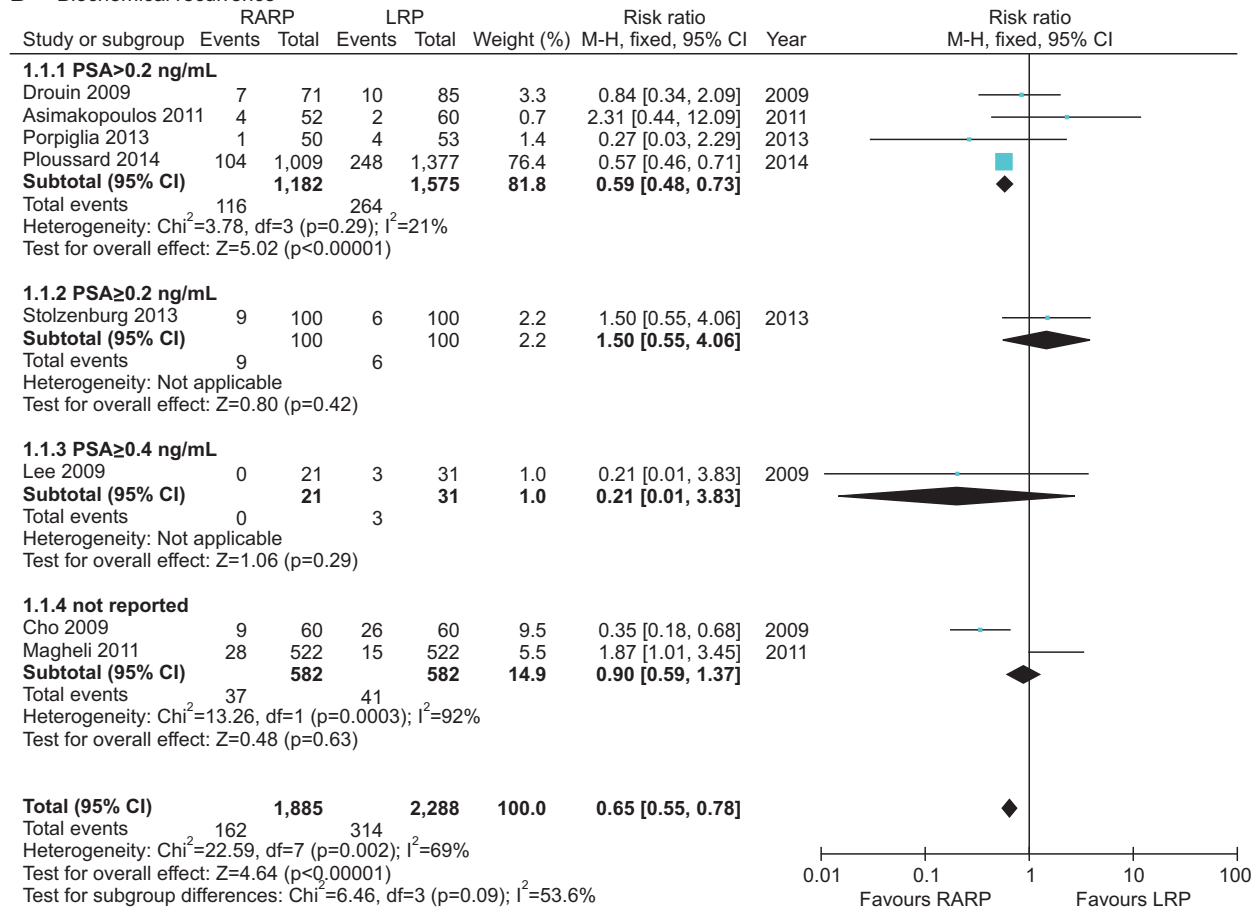Consultation on Incontinence Questionnaire-Short Form survey [8].

The urinary incontinence rate after 12 months was significantly lower with RARP than with LRP in this meta-analysis and in other randomized controlled trials, in which the rates for RARP and LRP were 6% and 17%, respectively, but without statistical significance owing to the limited study population [9]. Many modifications have been suggested in the field of robotics to improve the continence rate. Patel et al. [10] reported a peri-urethral suspension suture technique to improve the rate (92.8% vs. 83%; p=0.013 over 3 months). A modified posterior reconstruction that increased the continence rate by 4 weeks was reported by Coelho et al. [11]. In 2011, Asimakopoulos et al. [9] suggested a pubovesical-complex-sparing technique, in which a ventral plane was developed between the detrusor apron and the prostate. Owing to the technical feasibility of robotic assistance, reconstruction procedures have additionally improved the continence rate.

The potency recovery rate is another major concern for patients undergoing prostatectomy. The most common reason
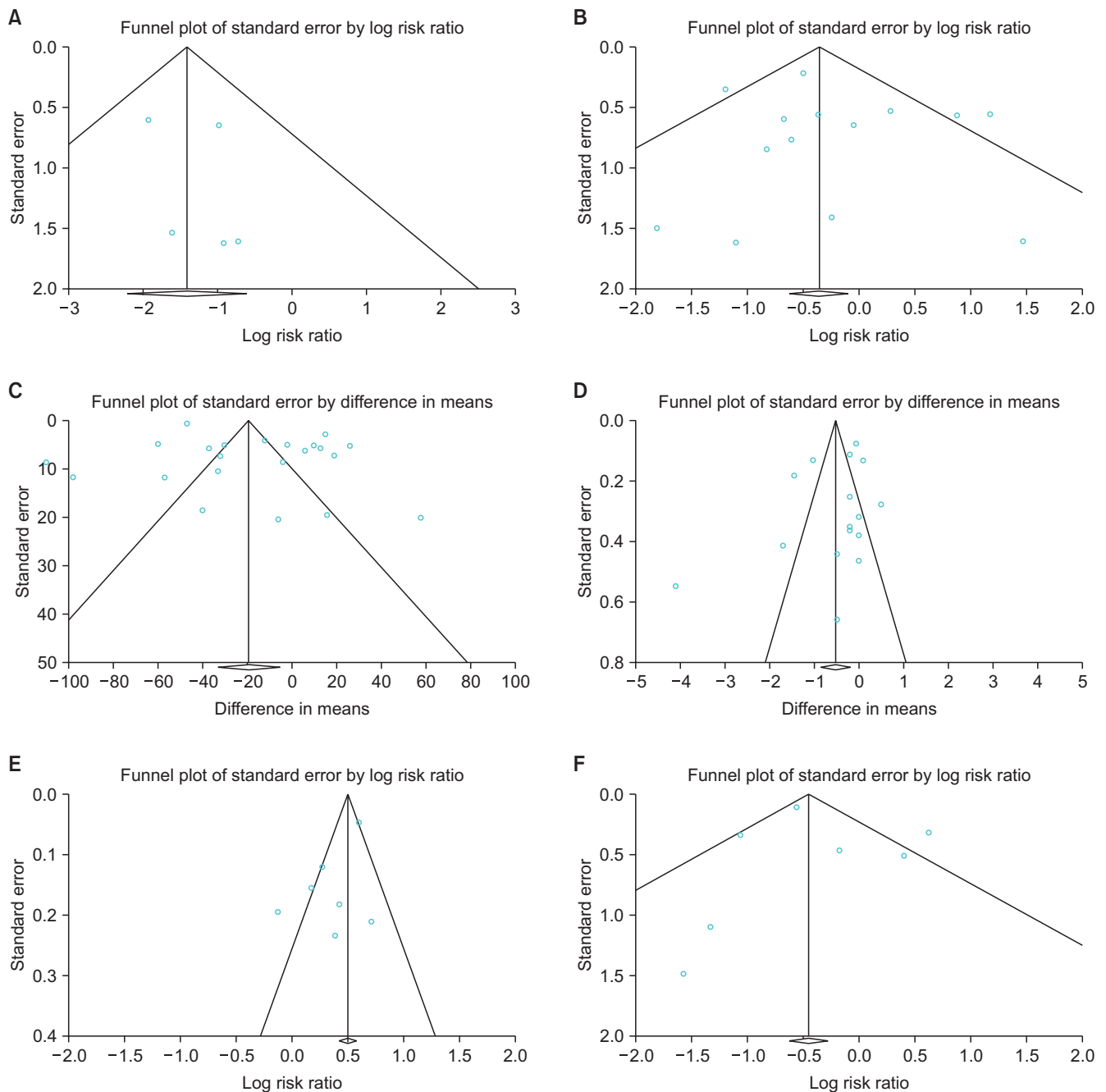
A Positive surgical margin

Study or subgroup	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.2.1 pT2 cases							
Rozet 2007	49	110	37	103	21.5	1.24 [0.89, 1.73]	2007
Drouin 2009	6	61	8	70	4.2	0.86 [0.32, 2.34]	2009
Magheli 2011	36	387	29	432	15.4	1.39 [0.87, 2.22]	2011
Asimakopoulos 2011	3	43	4	52	2.0	0.91 [0.21, 3.83]	2011
Koutlidis 2012	18	149	8	79	5.9	1.19 [0.54, 2.62]	2012
Porpiglia 2013	5	37	6	37	3.4	0.83 [0.28, 2.49]	2013
Stolzenburg 2013	6	67	5	77	2.6	1.38 [0.44, 4.32]	2013
Subtotal (95% CI)		**854**		**850**	**55.1**	**1.22 [0.98, 1.54]**	
Total events	123		97				

Heterogeneity: Chi^2=1.43, df=6 (p=0.96); I^2=0%
Test for overall effect: Z=1.62 (p=0.11)

	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.2.2 pT3 cases							
Rozet 2007	3	23	5	30	2.4	0.78 [0.21, 2.94]	2007
Drouin 2009	6	10	8	15	3.6	1.13 [0.56, 2.25]	2009
Asimakopoulos 2011	5	9	2	8	1.2	2.22 [0.58, 8.44]	2011
Magheli 2011	66	136	39	89	26.6	1.11 [0.83, 1.48]	2011
Koutlidis 2012	12	26	6	25	3.4	1.92 [0.85, 4.33]	2012
Stolzenburg 2013	13	33	6	20	4.2	1.31 [0.59, 2.90]	2013
Porpiglia 2013	11	22	6	22	3.4	1.83 [0.82, 4.08]	2013
Subtotal (95% CI)		**259**		**209**	**44.9**	**1.26 [1.00, 1.58]**	
Total events	116		72				

Heterogeneity: Chi^2=3.93, df=6 (p=0.69); I^2=0%
Test for overall effect: Z=1.98 (p=0.05)

	RARP	Total	LRP	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
Total (95% CI)		**1,113**		**1,059**	**100.0**	**1.23 [1.05, 1.46]**	
Total events	239		169				

Heterogeneity: Chi^2=5.35, df=13 (p=0.97); I^2=0%
Test for overall effect: Z=2.49 (p=0.01)
Test for subgroup differences: Chi^2=0.04, df=1 (p=0.84); I^2=0%

0.01 0.1 1 10 100
Favours RARP   Favours LRP

B Biochemical recurrence

Study or subgroup	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.1.1 PSA>0.2 ng/mL							
Drouin 2009	7	71	10	85	3.3	0.84 [0.34, 2.09]	2009
Asimakopoulos 2011	4	52	2	60	0.7	2.31 [0.44, 12.09]	2011
Porpiglia 2013	1	50	4	53	1.4	0.27 [0.03, 2.29]	2013
Ploussard 2014	104	1,009	248	1,377	76.4	0.57 [0.46, 0.71]	2014
Subtotal (95% CI)		**1,182**		**1,575**	**81.8**	**0.59 [0.48, 0.73]**	
Total events	116		264				

Heterogeneity: Chi^2=3.78, df=3 (p=0.29); I^2=21%
Test for overall effect: Z=5.02 (p<0.00001)

	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.1.2 PSA≥0.2 ng/mL							
Stolzenburg 2013	9	100	6	100	2.2	1.50 [0.55, 4.06]	2013
Subtotal (95% CI)		**100**		**100**	**2.2**	**1.50 [0.55, 4.06]**	
Total events	9		6				

Heterogeneity: Not applicable
Test for overall effect: Z=0.80 (p=0.42)

	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.1.3 PSA≥0.4 ng/mL							
Lee 2009	0	21	3	31	1.0	0.21 [0.01, 3.83]	2009
Subtotal (95% CI)		**21**		**31**	**1.0**	**0.21 [0.01, 3.83]**	
Total events	0		3				

Heterogeneity: Not applicable
Test for overall effect: Z=1.06 (p=0.29)

	RARP Events	Total	LRP Events	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
1.1.4 not reported							
Cho 2009	9	60	26	60	9.5	0.35 [0.18, 0.68]	2009
Magheli 2011	28	522	15	522	5.5	1.87 [1.01, 3.45]	2011
Subtotal (95% CI)		**582**		**582**	**14.9**	**0.90 [0.59, 1.37]**	
Total events	37		41				

Heterogeneity: Chi^2=13.26, df=1 (p=0.0003); I^2=92%
Test for overall effect: Z=0.48 (p=0.63)

	RARP	Total	LRP	Total	Weight (%)	Risk ratio M-H, fixed, 95% CI	Year
Total (95% CI)		**1,885**		**2,288**	**100.0**	**0.65 [0.55, 0.78]**	
Total events	162		314				

Heterogeneity: Chi^2=22.59, df=7 (p=0.002); I^2=69%
Test for overall effect: Z=4.64 (p<0.00001)
Test for subgroup differences: Chi^2=6.46, df=3 (p=0.09); I^2=53.6%

0.01 0.1 1 10 100
Favours RARP   Favours LRP

Fig. 4. Cumulative analyses of robot-assisted radical prostatectomy comparing laparoscopic radical prostatectomy in oncologic outcome (A: Positive surgical margin, B: Biochemical recurrence). RARP, robot-assisted radical prostatectomy; LRP, laparoscopic radical prostatectomy; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom.

Fig. 5. Funnel plot of the studies of organ injury (A), blood transfusion rate (B), operative time (C), length of stay (D), potency (E) and overall biochemical recurrence (F) used in the meta-analysis.

for failure to reach pentafecta is erectile dysfunction (35%) [12]. Our findings differed from those previously reported by NETSCC (2012), which showed no difference in the potency rate between RARP and LRP at 12 months postoperatively. In our meta-analysis, the potency rate of RARP at 12 months was significantly higher than that for LRP. Different potency recovery rates could be due to several factors, including different definitions of erectile dysfunction, various characteristics of the surgery, and differences in postsurgical rehabilitation [13]. Potency recovery was

measured by using several methods, including the IIEF-5 and the Sexual Health Inventory for Men score. Various techniques for preserving potency have been developed on the robotic platform, including cavernous nerve preservation. Several nerve-sparing techniques were developed in previous studies. For example, Ahlering et al. [4] evaluated the adverse effects of electrocautery on dissection of the prostate and the superiority of cautery-free nerve-sparing techniques on the recovery of potency. Menon et al. [14] evaluated the "Veil of Aphrodite" technique in which the inter-fascial plane

was extended towards the apex and laterally towards the prostatic pedicle. At 6 to 18 months postoperatively, 94% of men who attempted sexual intercourse after undergoing this technique reported success, with a median SHIM score of 18 out of 25. Following recent discoveries of the periprostatic fascial anatomy, extrafascial, interfascial, and intrafascial approaches have been developed. Comparing inter-fascial and extrafascial approaches, Shikanov et al. [15] reported a significantly improved potency rate (p=0.03) using the inter-fascial approach.

Three-dimensional magnified visualization of the robotic platform has enabled meticulous dissection of the periprostatic fascia layer and the neurovascular bundle. Further insights into the multilayered structure of the periprostatic fascia and the course of the cavernous nerves have supported the development of intra- or interfascial surgical planes, which have enabled improved functional outcomes in urinary incontinence and potency. A PSA level>0.2 ng/mL was selected as the important criterion, based on recommendations of clinical practice guidelines [16]. In an oncological RARP study, Menon et al. [17] reported biochemical-free survival rates of 95.1%, 90.6%, 86.6%, and 81.0% after 1, 3, 5, and 7 years, respectively. Few studies have reported BCR rates after RARP and LRP. Recently, Porpiglia et al. [18] reported BCR-free survival rates of 98% for a RARP group and 92.5% for an LRP group (p=0.190).

The oncologic outcome in the current study was noteworthy because of the statistically significant differences in BCR rates between the two groups. Ficarra et al. [13] demonstrated that BCR was significantly influenced by surgical experience, clinical tumor size, and anatomic tumor characteristics. Kim et al. [19] analyzed the preoperative predictors of BCR using multivariable analysis, which suggested that PSA, pathologic stage, pathologic Gleason score, and PSM were independently associated with BCR. In a Japanese study, the predictive factors of BCR following RARP were serum PSA levels, the percentage of positive cores, and the Gleason score. PSA density was also a strong predictor of advanced pathological features and BCR [20]. In our systematic review, the oncologic results for BCR showed a statistically significantly improved BCR in the RARP group relative to the LRP group, although the propensity score matching was similar between the groups. The PSM patients in the intermediate- and high-risk disease groups had higher rates of BCR than did those who were marginal or negative. However, the PSM in the low-risk disease group was not associated with disease progression [21]. After adjustment for differences in clinical and pathological features, the presence of a base margin was

significantly associated with a shorter time to recurrence for intermediate- and high-risk disease. The apex margin also was associated with the time to recurrence, but not statistically so for intermediate-risk disease. Thus, the similar PSM rate did not indicate a similar BCR rate. The length of the PSM was also independently predictive of BCR. Patients with a PSM <1 mm appeared to have similar outcomes compared with those with negative surgical margins [22]. Patients with a PSM <1 mm did not differ from those with a negative margin, and as the length of the positive margin increased so did the risk of BCR. Interestingly, the risk of BCR did not differ between patients with a negative surgical margin and those with a PSM <1 mm.

The current study had several limitations. First, because this is a relatively new procedure, data were lacking on long-term oncologic results following RARP, such as the cancer-specific survival rate. Second, significant heterogeneity was evident in terms of surgical experience and definition of functional outcomes. Third, some of recently published articles had far larger cohorts, which strongly influenced the meta-analysis. Fourth, there was an era bias in several centers in that RARP was performed after LRP.

CONCLUSIONS

In conclusion, RARP showed favorable results compared with LRP. However, few long-term, high-quality studies are available comparing RARP and LRP. Although further studies are needed, our results revealed that RARP had an improved BCR rate, potency rate, and continence rate with fewer complications than LRP. Further high-quality studies that minimize confounding and selection biases with long-term follow-up are needed to further clarify the clinical efficacy and safety of RARP.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGMENTS

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