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Research Article

Clinical outcomes and costs of robotic surgery in prostate cancer: a multiinstitutional study in Korea

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ABSTRACT

Background: This study compared the surgical, functional, and oncologic outcomes of robot-assisted laparoscopic radical prostatectomy (RALP), laparoscopic radical prostatectomy (LRP), and retropubic radical prostatectomy (RRP) in Korean men.

Methods: The study population included 864 patients who underwent radical prostatectomy for prostate cancer in the departments of urology of five tertiary hospitals between 2010 and 2011. RALP, LRP, and RRP perioperative, oncological, and functional outcomes as well as complications were assessed. Medical cost data were analyzed for 682 of 864 patients.

Results: No significant differences were found among the three groups regarding the length of stay, biochemical recurrence, complications, and metastasis. The RALP group had a significantly higher rate of pelvic lymph node dissection (64.6% vs. 35.3% or 53.3%, *P value* <0.0001) and bilateral nerve-sparing procedures (15.7% vs. 10.0% or 8.9%, *P value* <0.0001) and less blood loss (median 250 mL vs. 300 mL or 700 mL, *P value* <0.0001) than the LRP and RRP groups. The 12-month continence recovery rate was higher in the RALP group (92.1%) than in the LRP (86.5%) and RRP (84.4%) groups (*P value* <0.0001). Medical costs for RALP were approximately twofold to threefold higher than those for LRP or RRP.

Conclusions: Our findings suggest that surgical and functional outcomes are better with robot-assisted surgery than with laparoscopic or open surgery in terms of estimated blood loss and urinary continence; however, no differences were found among groups in terms of biochemical recurrence and the rate of complications.

1. Background

Prostate cancer is the second most common cancer affecting men worldwide. A total of 14,828 new prostate cancer cases and 1,840 prostate cancer deaths were expected to occur in Korea in 2015. The national crude incidence rate of prostate cancer will likely reach 58.3 per 100,000 men, and the age-standardized incidence rate, 38.1.[1]

Laparoscopic radical prostatectomy (LRP), which was implemented in the early 1990s, not only has an overall success rate that is comparable to retropubic radical prostatectomy (RRP) but also is a minimally invasive procedure that shortens the length of

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; EBL, estimated blood loss; PLND, pelvic lymph node dissection; PSA, prostate-specific antigen; RALP, robot-assisted laparoscopic radical prostatectomy; LRP, laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.

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postoperative hospitalization owing to reduced estimated blood loss and fast recovery. In addition, the oncological outcomes of LRP are equivalent to those of RRP in terms of positive margin rates. However, the uncomfortable postures adopted by the surgeon, the reliance on the two-dimensional imaging, and the steep learning curve due to the procedure's high degree of difficulty are some limitations of LRP.[2] On the other hand, robot-assisted laparoscopic radical prostatectomy (RALP) introduced in 2001 allows a comfortably seated surgeon on a console, simultaneous use of at least two surgical instruments offering high degrees of freedom of motion, and a three-dimensional stereoscopic camera, replicating the steps of an RRP. However, the lack of tactile sense and high cost are among its disadvantages.

Most studies comparing clinical outcomes between RALP and other techniques have been conducted in white populations. According to a systematic literature review, RALP showed better functional outcomes than LRP or RRP in terms of improved sexual function and recovery of continence.[3] Many previous studies have reported not only better functional outcomes but also improved immediate postoperative outcomes through reductions in the length of hospitalization and estimated blood loss,[4–7] although other studies have not reported significant differences in outcomes among different surgical techniques.[8,9] This study compared the clinical outcomes and cost of RALP versus LRP and RRP in Korean prostate cancer patients.

2. Methods

2.1. Patients

A total of 1,228 patients who underwent radical prostatectomy for prostate cancer in the departments of urology of five tertiary hospitals of South Korea from January 2010 to December 2011 were included in this retrospective study. All five hospitals were the tertiary general hospitals in Seoul. The study population included patients who (1) underwent RALP, LRP, or RRP for the treatment of prostate cancer and (2) had no prior history of prostate cancer. The exclusion criteria were (1) history of prostate, urethra, or bladder-related surgery; (2) absence of T1–T3 or missing clinical stage; (3) prostate-specific antigen (PSA) > 20 ng/mL; (4) Gleason biopsy score <6; (5) history of neoadjuvant chemotherapy, neoadjuvant hormonal therapy, or radiotherapeutics; (6) foreign patients; and/or (7) clinical trial participants. The final study population consisted of 864 Korean men. Of these 864 patients, 559 underwent RALP, 170 underwent LRP, and 135 underwent RRP.

2.2. Data collection

RALP, LRP, and RRP perioperative, oncological, and functional outcomes, as well as complications and costs, were compared among groups. Operative time was defined as the period from the first incision to the final closure of the wound. The oncological outcomes were assessed by positive surgical margin (PSM) status and biochemical recurrence (BCR) rates. BCR was defined as PSA measurements ≥0.2 ng/mL. The functional outcome was continence; urinary continence was defined as the absence of any urinary leakage or the use of only one safety pad. Urinary incontinence was confirmed through electronic medical record data. Complications were at least one of the following: anastomotic leakage, bladder neck contracture, wound infection, organ injuries, ileus, thromboembolism, inguinal hernia, urinary retention, lymphocele.

Total medical cost data were analyzed for 682 of 864 patients. These data were collected by reviewing the medical chart to estimate total medical costs, including amounts covered by National Health Insurance. The medical costs of radical prostatectomy procedures included costs of not only the operation but also 1 year of postoperative management. The medical costs incurred by the selected patients were determined from medical hospitalization and outpatient receipts from diagnosis of disease to 1 year thereafter. The health-care receipts were separated as covered, non-covered, and selective costs. Personal identification keys were used

Table 1
Preoperative characteristics of the patients.

	RALP ($n = 559$)		LRP ($n = 170$)		RRP ($n = 135$)		P
	N	%	N	%	N	%	
Age, years	68 (63–73)		71 (67–74)		73 (68–77)		<0.0001
50–59	86	15.4	15	8.8	5	3.7	<0.0001
60–69	257	46.0	69	40.6	48	35.6	
70–79	216	38.6	86	50.6	82	60.7	
BMI, kg/m^2	24.3 (22.7–26.2)		24.4 (22.6–26.1)		24.3 (22.5–26.5)		0.9826
<25	359	64.2	103	60.6	78	57.8	0.3236
≥25	200	35.8	67	39.4	57	42.2	
ASA classification							
1	272	48.7	46	27.1	30	22.2	<0.0001
2	274	49.0	118	69.4	98	72.6	
3	13	2.3	6	3.5	7	5.2	
Prostate volume	31.7 (25.5–41)		31 (23.8–41)		36.4 (26–45)		0.0141
PSA level, ng/mL	6.0 (4.4–9)		6.5 (4.5–9.4)		6.2 (4.5–9.7)		0.5051
Gleason score	7 (6, 7)		7 (6, 7)		7 (6, 7)		0.2894
6	272	48.7	83	48.8	59	43.7	0.8673
7	188	33.6	59	34.7	43	31.9	
8–9	99	17.7	28	16.5	33	24.4	
Clinical stage							
Tx	5	0.9	17	10	12	8.9	<0.0001
T1	177	31.7	29	17.1	60	44.4	
T2	272	48.7	99	58.2	55	40.7	
T3	105	18.8	25	14.7	8	5.9	

Data are expressed as median (interquartile range) or percent.
ASA, American Society of Anesthesiologists; BMI, body mass index; LRP, laparoscopic radical prostatectomy; PSA, prostate-specific antigen; RALP, robot-assisted laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.

to block verification of personal patient information. Costs were measured in 2011 in US dollars (USD) and are outlined.

2.3. Statistical analysis

Baseline characteristics and clinical outcomes of RALP, LRP, and RRP were evaluated and compared using a Chi-square test for categorical variables and an analysis of variance for continuous variables. Fisher's exact test was used to compare proportion of complication and metastasis. Because the health-care cost distribution curve was skewed to the right, median, minimum, and maximum values are presented instead of mean values. All analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Reported statistical significance levels were all two sided, and the threshold of statistical significance was $P < 0.05$.

2.4. Ethics statements

The Institutional Review Board (IRB) of the National Evidence-based Healthcare Collaborating Agency (IRB No. NECAIRB14-002) and each participating hospital approved this study. Because this study was conducted retrospectively, the IRB waived the requirement for documentation of the patient's written informed consent.

3. Results

The preoperative characteristics of the patient's cohort according to the surgical approach are shown in Table 1. The RALP, LRP, and RRP groups were comparable in terms of body mass index, PSA, and Gleason score. The mean age was significantly lower in the RALP group than in the LRP or RRP group (68 years vs. 70 years or 71 years, respectively). Low-grade prostate cancers of American Society of Anesthesiologists classification were more frequently reported in the RALP group ($P < 0.0001$).

Table 2 shows a comparison of perioperative parameters by surgical approach. Operation time was the shortest with RRP, and blood loss was significantly lower with RALP (250 mL) than with LRP (300 mL) and RRP (700 mL). Pelvic lymphadenectomy and nerve-sparing techniques were more frequent in the RALP group than in the LRP or RRP group. Length of hospital stay did not differ among groups ($P = 0.6985$). The number of lymph node dissections was the lowest with LRP. Nerve-sparing techniques were more frequently used during RALP. The rate of early complications (<30 days) was the lowest with RALP and highest with LRP.

The oncological outcomes are shown in Table 3. The pT3 rate was higher in the RALP group (32.6%) than in the LRP (29.4%) or RRP (29.6%) group. pT2a and pT2b rates were higher in the RALP group than in the LRP and RRP groups. The lowest pT2c rate was found in the RALP group. The PSM rate was the lowest in the LRP group (20.6%) and highest in the RRP group. The anterior surgical margin was the lowest in the RALP group, whereas the apex surgical

Table 3
Oncological outcomes in the robot-assisted laparoscopic radical prostatectomy, laparoscopic radical prostatectomy, and retropubic radical prostatectomy groups.

	RALP ($n = 559$)		LRP ($n = 170$)		RRP ($n = 135$)		*P*
	N	%	N	%	N	%	
Pathologic stage							
T2a	119	21.3	25	14.7	17	12.6	0.0029
T2b	46	8.2	6	3.5	5	3.7	
T2c	209	37.4	89	52.4	72	53.3	
T3a	130	23.3	40	23.5	28	20.7	
T3b	52	9.3	10	5.9	12	8.9	
NA	3	0.5	0	—	1	0.7	
Positive surgical margins							
Overall	160	28.6	35	20.6	47	34.8	0.0051
pT2	73	13.1	17	10.0	24	17.8	
pT3	87	15.6	18	10.6	23	17.0	
Positive margin sites	160	28.6	35	20.6	47	34.8	—
Apex	82	14.7	20	11.8	22	16.3	
Posterior	35	6.3	15	8.8	9	6.7	
Anterior	24	4.3	17	10.0	14	10.4	
Bladder	6	1.1	0	—	2	1.5	
Other	77	13.8	11	6.4	20	14.8	
Biochemical recurrence							
12 months	90	16.1	31	18.2	29	21.5	0.3031
24 months	107	19.1	34	20.0	30	22.2	0.7030
36 months	117	20.9	34	20.0	31	23.0	0.7937

LRP, laparoscopic radical prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.

Table 4
Complications, metastasis, and mortality rate in the robot-assisted laparoscopic radical prostatectomy, laparoscopic radical prostatectomy, and retropubic radical prostatectomy groups.

	RALP ($n = 559$)		LRP ($n = 170$)		RRP ($n = 135$)		*P*
	N	%	N	%	N	%	
Complications							
<90 days	9	1.6	3	1.8	3	2.2	0.8621[a)]
<12 months	38	6.8	15	8.8	9	6.7	0.6399
<24 months	58	10.4	20	11.8	14	10.4	0.8705
Metastasis							
<90 days	2	0.4	0	—	0	—	—
<12 months	4	0.7	1	0.6	3	2.2	0.2248[a)]
<24 months	9	1.6	3	1.8	5	3.7	0.2946[a)]
Death							
<90 days	0	—	0	—	0	—	—
<12 months	1	0.2	0	—	0	—	—
<24 months	3	0.5	0	—	0	—	—

LRP, laparoscopic radical prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.
[a)] Fisher's exact test.

Table 2
Perioperative parameters in the robot-assisted laparoscopic radical prostatectomy, laparoscopic radical prostatectomy, and retropubic radical prostatectomy groups.

	RALP ($n = 559$)	LRP ($n = 170$)	RRP ($n = 135$)	*P*
Operative time, min (IQR)	199.5 (167–249)	242.5 (212.5–272.5)	120 (101–160)	<0.0001
Hospital stay, day (IQR)	7 (5–8)	6.5 (5–8)	6 (5–9)	0.6985
EBL, mL (IQR)	250 (150–400)	300 (150–500)	700 (600–900)	<0.0001
PLND, yes (%)	361 (64.6)	60 (35.3)	72 (53.3)	<0.0001
Nerve sparing, yes (%)	450 (80.5)	67 (39.4)	82 (60.7)	<0.0001
Unilateral	354 (63.3)	47 (27.6)	62 (45.9)	
Bilateral	88 (15.7)	17 (10.0)	12 (8.9)	
Complications [<30 days (%)]	28 (5.0)	29 (17.1)	13 (9.6)	0.0006

EBL, estimated blood loss; LRP, laparoscopic radical prostatectomy; PLND, pelvic lymph node dissection; RALP, robot-assisted laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.

Table 5
Medical costs in the robot-assisted laparoscopic radical prostatectomy, laparoscopic radical prostatectomy, and retropubic radical prostatectomy groups (Unit: USD).

	RALP ($n = 421$)			LRP ($n = 141$)			RRP ($n = 120$)		
	Median	Min	Max	Median	Min	Max	Median	Min	Max
Overall									
Total cost	20,206	10,721	69,179	9,460	6,266	55,263	6,959	3,842	35,606
Covered	3,439	1,043	19,784	5,282	4,153	23,073	4,735	2,682	26,318
Noncovered	16,239	8,978	64,693	3,348	1,878	32,190	2,197	1,089	15,736
Hospitalization									
Total cost	18,312	10,483	64,537	7,414	5,627	51,152	4,775	1,534	16,931
Covered	2,318	217	9,405	4,386	3,648	19,826	3,125	956	11,656
Noncovered	15,826	8,970	61,631	2,784	1,664	31,325	1,437	578	15,553
Outpatient									
Total cost	2,286	11,152	21,643	1,673	186	9,094	2,112	485	30,918
Covered	1,290	7,226	17,742	904	167	8,706	1,477	352	23,418
Noncovered	499	3,926	12,716	387	19	3,454	605	56	7,498
Surgery cost	14,253	8,055	36,616	4,073	1,797	29,869	1,599	1,336	29,245

LRP, laparoscopic radical prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy; RRP, retropubic radical prostatectomy.

margin was higher in the RALP and RRP groups than in the LRP group. There were no significant differences in BCR according to the surgical approach.

Safety outcomes among groups are listed in Table 4. The overall 3-year complication rates were 10.4%, 11.8%, and 10.4% in the RALP, LRP, and RRP groups, respectively. The most common complications included bladder neck contracture, infection, and inguinal hernia. The rate of long-term complications was similar among groups and follow-up periods. Because few metastases or mortalities occurred, comparison of these outcomes among surgical approaches was not possible.

The cost of radical prostatectomy procedures, including the operation itself and the 1-year postoperative management period, was the highest for RALP (median 20,206 USD), followed by LRP (median 9,460 USD) and RRP (median 6,959 USD) (Table 5). The cost of RALP was twofold and threefold higher than that of LRP and RRP, respectively. The cost of surgery accounted for the majority of the medical expenses incurred in the first year after RALP, and no other significant differences in cost were found among groups. National Health Insurance did not cover the majority of expenses of RALP, which had the highest proportion of uncovered costs (85.0%), followed by LRP and RRP.

In terms of functional outcome, RALP showed the highest urinary continence recovery rate, with 89.4% and 95.0% of patients showing complete continence recovery at the 3-month and 3-year follow-up assessments, respectively. Continence rates for LRP and RRP were 80.6% and 81.5% at the 3-month assessment and 89.2% and 89.8% at the 3-year assessment, respectively (Fig. 1). The trend for urinary continence recovery according to the surgical approach did not differ between follow-up periods.

4. Discussion

Results of the present multiinstitutional study suggest that RALP has a higher continence recovery rate than LRP or RRP and is safer, with less estimated blood loss and lower complication rates within 30 days of surgery, resulting in improved postoperative outcomes. However, contrary to previous studies, no statistically significant differences were found among surgical techniques in terms of length of hospitalization and biochemical relapse. Moreover, the total 1-year health-care cost associated with RALP was twofold to threefold higher than that of LRP or RRP.

Although previous studies have used slightly different definitions for urinary continence, recovery of continence after prostatectomy is generally defined as using just one or no pad per day. Urinary incontinence is frequently reported to occur after radical prostatectomy, and its reported prevalence varies greatly (from 4% to 31%) according to the definition of incontinence used (no pad vs. safety pad).[3,10] The reported rate of continence recovery also varies depending on the surgical technique used, but the continence recovery rate is generally higher with RALP than with LRP or RRP, which is consistent with the findings of this study. Previous reports have shown a continence recovery rate of more than 95% among patients who had received RALP,[11,12] and Stolzenburg et al reported continence scores of 83.8% at 6 months and 92% at 1 year in 700 patients who underwent LRP via a peritoneal approach.[13] However, other studies have reported that RRP has a higher continence recovery rate than RALP.[14,15] As suggested by Ficarra et al, a standardized classification that distinguishes between not using pads and using a safety pad should be considered in future studies.[3]

No statistically significant differences among surgical techniques were found for BCR rates at 12, 24, and 36 months. Our BCR rates were similar to those reported in a systematic review and several comparative studies.[4,16–17]

According to previous studies, the rates of surgery-related complications for RRP, LRP, and RALP are 6.6–19.1%, 3.6–17.1%, and 4–5%, respectively,[18–20] whereas other complications, such as transfusion and rectal or ureteral injury, were reported to be approximately 1–4%.[21,22] One systematic review reported that the mean of overall complication rate after robot-assisted radical prostatectomy was 9%.[4] The overall complication rates were similar for LRP and RALP, and only the transfusion rate was significantly lower with RALP in that report. In our study, in terms of safety outcomes, RALP group had the lowest incidence of complications within 90 days, but this difference was not significant. Because metastasis and mortality rates were very low in all three the groups, a direct comparison of these outcomes was difficult.

In our study, the PSM rate was the lowest in the LRP group, followed by RALP and RRP. A previous meta-analysis also demonstrated that PSM rates were higher with LRP than with RALP group but similar to RRP.[23] In another study, the PSM rate was significantly lower for RALP than RRP.[24] Koutlidis et al reported no significant differences between RALP and LRP.[25] In a systematic review, PSM rates were similar for all analyses comparing RALP versus RRP and RALP versus LRP.[4]

The total health-care cost within 1 year after the procedure was approximately 20,206 USD per person for RALP, which was more than double the cost of LRP or RRP. For prostate cancer, RALP provides three-dimensional stereoscopic images, offers outstanding operational functionality, and is minimally invasive. As the patient's demand for RALP increases, its use is also expected to increase, and in various countries such as Japan, Hong Kong, and Denmark, RALP

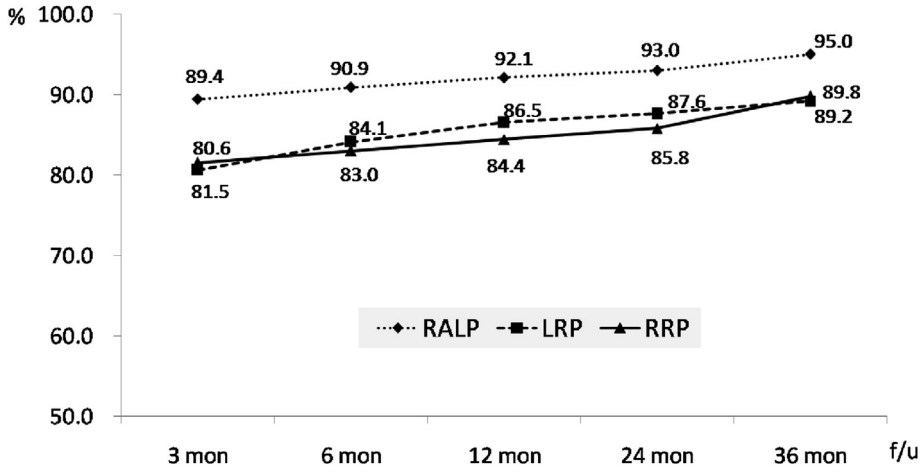

Fig. 1. The figure shows the recovery rate of urinary continence in the robot-assisted laparoscopic radical prostatectomy (RALP), laparoscopic radical prostatectomy (LRP), and retropubic radical prostatectomy groups (RRP).

is being converted to benefit coverage.[26] Because public health-care systems differ among countries, future evaluations of cost-effectiveness using in-country data will be necessary.

Our findings are significant from the perspective that this study used patient data from multiple institutions in Korea to analyze the safety, effectiveness, and costs associated with RALP for prostate cancer. However, because our study was limited by a retrospective design and short follow-up observation period, our findings do not fully reflect the clinical situation in Korea and cannot be generalized to all prostate cancer patients. This study has two main limitations. First, the number of subjects enrolled was insufficient to make comparisons of results based on the different radical prostatectomy techniques used. The subjects included in this study consisted of those who received RALP (more than half, 65%), and the percentages of patients undergoing RRP or LRP were low (15% and 20%, respectively). Because baseline conditions of radical prostatectomy were different among techniques, a subgroup analysis was performed for patients with localized prostate cancer (below clinical stage T2), which is a major indication for radical prostatectomy, to secure the possibility of comparison; however, differences in baseline conditions among techniques still existed. To compensate for this, attempts were made to compare surgical outcomes after matching the variable that could affect outcome, but the subject dropout rate after matching was high. Because there were virtually no adverse events recorded, such as metastasis or mortality, comparisons among surgical techniques were still not possible for those variables. Second, improvement in sexual function, which is an important functional outcome variable of radical prostatectomy, could not be verified using medical records. Improvement in sexual function is a very subjective indicator that requires data collection through a survey instrument with proven validity, but because this study was retrospective in design, assessing an improvement in sexual function among patients who received radical prostatectomy was not possible. In the future, verification of improvement in sexual function through a prospective study design and oncological outcomes through long-term observations is needed.

5. Conclusion

The results are the first to report in Korea that robot-assisted surgery are superior to laparoscopic or open surgery in terms of blood loss and urinary continence. No significant differences in BCR and overall complications were found among surgical techniques. Further prospective studies with longer follow-up duration are needed.

Availability of data and materials

The data sets supporting the conclusions of this article are available in the National Evidence-based Healthcare Collaborating Agency (NECA) data base repository. In addition, the data sets analyzed during the present study are available from the NECA management committee on reasonable request.

Authors' contributions

Yun JE and Lee SH contributed to conception and coordination of the study. Lee NR, Kwak C, Rha KH, Seo SI, Hong SH, Lee YG, and Kim CS contributed to data acquisition. Yun JE, Lee NR, and Park DA reviewed and analyzed data. Yun JE, Lee NR, Kwak C, Rha KH, Seo SI, Hong SH, and Lee YG prepared the manuscript. Lee SH and Kim CS contributed to the critical review of the manuscript. All authors approved the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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