Comparison of the Outcomes between Laparoscopic Radical Prostatectomy and Robotic-Assisted Laparoscopic Radical Prostatectomy: A 4-Year Single and High Volume Center Experience

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Background: Prostate cancer is one of the most common cancers in men. The standard surgical approaches in localized prostate cancer are open, laparoscopic and robotic-assisted laparoscopic radical prostatectomy (RARP). Recently, RARP has been introduced as an alternative approach to standard laparoscopic radical prostatectomy (LRP). In the present study, we aimed to compare the outcomes between LRP and RARP during a 4-year period in Ramathibodi Hospital.

Objective: Compare the outcomes between LRP and RARP during a 4-year period in Ramathibodi Hospital.

Materials and Methods: The study was a retrospective observational study. We included patients with localized and locally advanced prostate cancer (stage T1-T3) receiving LRP or RARP in Ramathibodi Hospital during January 2013 and October 2016. Demographic data, baseline laboratory data, tumor staging and perioperative parameters were obtained from electronic medical records. The primary outcome was the comparison of free surgical margin and functional outcomes including incontinence rates and erectile dysfunction between LRP and RARP. The secondary outcomes were differences in perioperative parameters.

Results: Two-hundred and forty-five patients were included; 103 in the LRP group and 142 in the RARP group. Baseline characteristics were similar between two groups, except higher pathological stage 3 and prostate volume in the RARP group. The rate of free surgical margins was 56.3% in LRP group vs. 63.3% in RARP group (p=0.24). The rate of the patients who had incontinence was 19.4% in LRP vs. 30.3% in RARP (p=0.48) and erectile dysfunction was 21.4% in LRP vs. 28.9% in RARP (p=0.12). The operative time was similar in both groups. Biochemical recurrence and other perioperative parameters did not differ between the two groups.

Conclusion: LRP and RARP provide similar outcomes in terms of oncological and functional results in a 4-year experience of our center. RARP may provide the better results in margin status compared to LRP. We encourage urologists in our Asian community to perform randomized studies to confirm these outcomes.

Keywords: Prostate cancer, Laparoscopic radical prostatectomy, Robot-assisted laparoscopic radical prostatectomy

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Radical prostatectomy has been recognized as the preferred standard treatment option for localized prostate cancer. Currently, minimally invasive approaches including laparoscopic and robotic surgery are considered the alternative standard treatment to open surgical approach.

Robotic assisted radical prostatectomy (RARP) has become popular around the world especially in USA and

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Europe⁽¹⁻³⁾. It provides several benefits over standard laparoscopic radical prostatectomy (LRP) such as 3-dimension laparoscopic view, better ergonomics, decreasing the difficulty of suturing at the urethral anastomosis, and shortening the learning curve of surgeons. However, the cost of robotic surgery is the major limitation for widespread use of this technology, especially in developing countries. In Asia, the data regarding the safety and effectiveness of RARP and LRP is also limited. Therefore, high quality evidence in this issue is needed to help urologists to select the proper treatment of localized prostate cancer. Our primary objective of this study was to determine whether RARP provides more advantages than LRP in the treatment of prostate cancer by experienced laparoscopic and robotic surgeons in terms of oncological, functional and perioperative outcomes.

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Materials and Methods

This study was approved by the Ethics Committee of Ramathibodi Hospital. A retrospective review of consecutive patients with localized and locally advanced prostate cancer (stage T1-T3N0M0) receiving LRP or RARP in Ramathibodi hospital during January 2013 and October 2016 was done. All data were obtained from electronic medical records. All procedures were performed by two experienced surgeons using the same defined protocol. Demographic data, baseline laboratory data, and tumor staging (Gleason score) were collected. Operative parameters including skin-to-score operative time, blood loss, hospital stay, and analgesic use were obtained.

The primary outcome is the difference between free surgical margins and functional outcomes between two surgical techniques. Secondary outcomes are differences in perioperative parameters including operative time, blood loss, length of hospital stay, pain score, use of analgesia, and biochemical recurrence (BCR) at 12 months after surgery. Free surgical margin is defined as no residual tumor by tissue pathology. Incontinence is defined as persisting symptoms after 12 months of surgery and regular pad use. Erectile dysfunction is defined as persisting symptoms after 12 months of surgery with or without the use of phosphodiesterase type 5 (PDE-5) inhibitors. BCR was defined as PSA >0.2 ug/L for at least 2 times over a period of at least 1 week.

Surgical technique

${\it Robotic-assisted\ laparoscopic\ radical\ prostatectomy\ (RARP)}$

The RARP was performed using the Si da Vinci Robotic System (Intuitive Surgical, Sunnyvale, CA). First, the patient was positioned supine in low lithotomy in a 15 to 30° Trendelenburg position. All cases were performed by transperitoneal approach and using the six-port technique as described by Patel⁽⁴⁾. The posterior approach starting from seminal vesicle identification was used. The anterior bladder part was dropped and the dorsal venous complex was isolated and ligated by PDS 1-0. Bladder neck dissection was then performed with the precise excision technique to preserve the bladder neck and to remove all prostate tissue. The pedicle was controlled. The nerve preservation was attempted in all cases if the clinical staging of the disease was allowed. The apex dissection was carefully performed to preserve the sphincter and the maximum length of the urethra. Finally, the running vesicourethral anastomosis was performed with V-LocTM 3-0 suture. The watertight anastomosis has been confirmed in all cases.

Laparoscopic radical prostatectomy (LRP)

Standard laparoscopic approach was performed with standard five to six port configuration. The extraperitoneal or intraperitoneal approach was selected which depended on each surgeon's preference. The patient was placed in supine lithotomy and Trendelenburg position. The surgical steps were applied similarly as described

previously in the robotic approach.

Statistical analysis

Statistical analyses were performed using SPSS Software (IBM® SPSS® Statistics21; SPSS, Inc., Chicago, IL, USA). The significance level was defined at 0.05 with a 95% confidence interval. Normally distributed data was presented as means and standard deviation and compared using unpaired t-test. Non-normally distributed data was presented using median and interquartile range (IQR) and compared using Mann Whitney U test. Categorical data were presented in numbers and percentages and compared using Chi-square or Fisher-exact test.

Results

Demographic and perioperative outcomes

There were 103 patients in the LRP group and 142 patients in the RARP group. The two groups were comparable in terms of demographic data, baseline laboratory data, pre-operative PSA, total pathological Gleason score (Table 1). The mean age was 66.6 ± 7.09 years old. The median PSA in the LRP group was 10.10 ng/mL (IQR 7.85 to 17.90) compared with 11.55 ng/mL (IQR 7.25 to 22.50) in the RARP group (p = 0.59). The mean pathological Gleason score was also comparable between the two groups, 6.92±1.19 in the LRP group and 6.76±0.90 in the RARP group, respectively (p = 0.14). However, patients in the RARP group had significantly higher pathologic stage 3 (68.9%) compared with the LRP group (31.3%); p = 0.01. The prostate volume was also significantly higher in the RARP group than the LRP group (43.59±25.37 gm vs. 33.84 ± 18.6 gm; p = 0.009).

For perioperative data, the operative time was comparable including the time required for robot docking in the RARP group (Table 2). Estimated blood loss and required morphine for analgesia were also not different between two groups. However, the length of hospital stay was slightly longer in the RARP group than LRP group (8 days, IQR 6,9 vs. 7 days, IQR 5,8; p = 0.02).

Functional and oncological outcomes

There was comparable proportion of patients with free surgical margins between LRP and RARP group (56.3% vs. 63.4%, p=0.24) (Table 3). The incontinence rate at 12 months was non-significantly higher in the RARP group compared with LRP (30.3% vs. 19.4%; p=0.48). The erectile dysfunction rate was comparable between the two groups (21.4% in the LRP group vs. 28.9% in the RARP; p=0.12). The rate of BCR within the first year after surgery for LRP also did not differ from RARP (2% vs. 4.9%; p=0.32).

Subgroup analysis of the primary outcome during 2014 to 2016

Considering the time required for learning curve for robotic procedure, the authors chose to perform subgroup analysis of the primary outcome since 2014 (Table 4). There

Table 1. Demographic data between the laparoscopic radical prostatectomy and robotic-assisted laparoscopic radical prostatectomy

Variable	Types of operation		<i>p</i> -value
	Laparoscopic (n = 103)	Robotic (n = 142)	
Age (years), mean ± SD	66.78±6.97	66.44 <u>+</u> 7.20	0.62
Weight (kg), mean <u>+</u> SD	67.33 <u>+</u> 11.36	68.97 <u>+</u> 10.40	0.12
Body mass index (kg/m²), mean ± SD Underlying diseases	24.73 <u>+</u> 3.79	25.00 <u>+</u> 3.31	0.28
Diabetes	25 (24.27)	38 (26.76)	0.69
Hypertension	70 (67.96)	92 (64.79)	0.46
Chronic kidney disease	1 (0.97)	4 (2.82)	0.31
Hepatitis B infection	1 (0.97)	3 (2.11)	0.45
Dyslipidemia	40 (38.83)	63 (44.37)	0.46
Coronary artery disease	1 (0.97)	10 (7.04)	0.06
Hemoglobin (g/dL), mean ± SD	13.54 <u>+</u> 2.01	13.74±1.56	0.19
Hematocrit (%), mean <u>+</u> SD	40.46 <u>+</u> 3.87	40.79 <u>+</u> 4.03	0.26
Platelet counts (mm³), mean ± SD	231.17 <u>+</u> 53.89	225.44 <u>+</u> 56.82	0.22
Blood urea nitrogen (mg/dL), mean ± SD	15.17±4.62	14.40 ± 4.07	0.10
Creatinine (mg/dL), mean <u>+</u> SD	1.07 <u>+</u> 0.37	1.06 <u>+</u> 0.27	0.41
Preoperative PSA (ng/mL), median (IQR; Q1 to Q3)	10.10 (7.85 to 17.90)	11.55 (7.25 to 22.50)	0.59
Total pathological gleason score, mean ± SD	6.92 <u>+</u> 1.19	6.76 <u>+</u> 0.90	0.14
Prostate volume (gm), mean ± SD	33.84 <u>+</u> 18.6	43.59 <u>+</u> 25.37	0.009
Pathological stage, n (%)*			0.01
Stage: T1	9 (60%)	6 (40%)	
Stage: T2	69 (46.31%)	80 (53.69%)	
Stage: T3	25 (31.25%)	55 (68.85%)	

^{*} Pathological staging is not available in 1/142 of RARP group

Table 2. Perioperative outcomes between the LRP and RARP group

Parameters	Types of operation		<i>p</i> -value
	Laparoscopic (n = 103)	Robotic (n = 142)	
Operative time, median (IQR; Q1 to Q3)	185 (160 to 230)	180 (150 to 240)	0.64
Length of hospital stay, median (IQR; Q1 to Q3)	6 (5 to 8)	7 (6 to 9)	0.02
Estimated blood loss, median (IQR; Q1 to Q3)	350 (250 to 580)	400 (300 to 500)	0.35
Morphine required, n (%)	90 (87.38)	133 (93.66)	0.50

 $\textbf{Table 3.} \ \ \textbf{Functional and oncological outcomes between the LRP and RARP group}$

Variable	Types of operation		<i>p</i> -value
	Laparoscopic (n = 103)	Robotic (n = 142)	
Free surgical margin, n (%)	58 (56.31)	90 (63.38)	0.24
Erectile dysfunction, n (%)	22 (21.36)	41 (28.87)	0.12
Incontinence, n (%)	20 (19.42)	43 (30.28)	0.48
Biochemical recurrence, n (%)	5 (2.04)	12 (4.90)	0.32

were a total of 139 cases; 61 patients in the LRP group and 78 in the RARP group. Baseline characteristics including tumor staging were not different (data not shown here). The RARP group had significantly higher proportions of patients

with free surgical margin than the LRP group (45.3% vs. 28.8%; p=0.04). The incontinence rates and erectile dysfunction incidence were comparable between the two groups.

Table 4. Subgroup analysis of outcomes between LRP and RARP during 2014 to 2016

Variable	Types of operation		<i>p</i> -value
	Laparoscopic (n = 61)	Robotic (n = 78)	
Free surgical margin, n (%)	40 (28.78)	63 (45.32)	0.04
Erectile dysfunction, n (%)	16 (11.51)	27 (19.42)	0.36
Incontinence, n (%)	10 (7.19)	10 (7.19)	0.55

Discussion

Our research is one of the few articles in which was compared the large group of the patients with localized prostate cancer between LRP and RARP in Southeast Asia. LRP may not be of interest in US or Europe anymore. The high cost of robotic surgery is well-recognized; therefore, LRP is still needed for the treatment of prostate cancer with a significant number of the patients in our region.

LRP has been done for more than 10 years at Ramathibodi Hospital and the outcomes were comparable with open surgery in terms of oncological and functional outcomes. It provides less morbidity compared to open surgical approach. We have performed RARP in our center since 2013 and have had very good outcomes using the robotic approach. Currently, our center considers LRP or RARP to be the alternative standard for the treatment of localized prostate cancer.

RARP provides better ergonomics, visualization and reduces the learning curve of surgeons compared to laparoscopic surgery. However, there were a significant number of the patients who may not be able to afford the cost of the robotic approach. Therefore, we still have to perform LRP in those patients.

Our results demonstrated comparable outcomes between LRP and RARP regarding oncological (margin status) and functional outcomes (incontinence and potency). The demographic data were comparable in both groups except for the staging of the disease. The robotic group had higher pathological staging especially for pT3 disease. The margin status was comparable for the whole series in both groups; however, the margin status was better in RARP group when we compared the data since 2014. This can be explained by the learning curve of the surgeons in RARP during the first year of the operation. RARP provides the benefit of margin status compared to LRP because the margin status was comparable even RARP had higher disease staging. Our data revealed similar outcomes as in an earlier systematic review regarding positive surgical margins. The authors have demonstrated no significant differences in positive margins between the 2 groups. The positive margin (PSM) rates were 14.2% (RARP) and 11.3% (LRP) with a relative risk (RR) of 1.22 (95% CI, 0.98 to 1.54; p = 0.11) in the pT2 disease. The PSM rates were 43.1% (RARP) and 34.4% (LRP) with a RR of 1.26 (95% CI, 1.00 to 1.58; p = 0.05) in the pT3 disease. However, the biochemical recurrence rate was lower in RARP group than LRP group (RR, 0.59; 95% CI, 0.48 to 0.73; I2 = 21%; $p < 0.00001)^{(5)}$.

The functional outcomes including continence and potency were also comparable in both groups in our series. However, most of the studies showed more favorable data in the RARP group for the functional outcomes⁽⁵⁻⁸⁾. For continence, one of the explanations is that LRP has been done by experienced surgeons, therefore, the urethral and sphincter preservation have been done very well in both techniques. Potency also depends on several factors including staging of the disease (higher rate of pT3 in the robotic group), age of the patients, and potency status before surgery. We unfortunately did not use the International Index of Erection Function (IIEF-5 score) for potency evaluation, therefore, it is quite hard to draw the conclusion.

The perioperative outcomes were comparable in both groups. The bleeding and operative time was similar. The patients in robotic group stayed in the hospital 1 day longer than laparoscopic group. This can maybe explained by higher socioeconomic status in the robotic group. The cost of the hospital stay was not their primary concern. Basically, they could be discharged from the hospital earlier, but they chose to stay until urinary catheters were removed.

The present study has several limitations. First, the number of the patients in this study seems to be high in the Southeast Asia region. However, it may be considered to be low volume number when compared to the US or European series. Second, we may have a selection bias to use robotic approach in the difficult and higher disease staging cases. Third, we already mentioned that we did not use IIEF-5 to evaluate the potency. Fourth, it is difficult to compare the data during the beginning of robotic surgery in year 2013 or early 2014 to the data of laparoscopic approach. During that period, it was the beginning of robotic surgery but the surgeons had done LRP for 10 years starting from 2004. Therefore, the outcomes of year 2013 to 2014 may not reflect the true outcomes because of bias in comparison.

Conclusion

LRP and RARP provide the similar outcomes in term of oncological and functional results. When the learning curve has passed, RARP may provide the better results in margin status compared to LRP. We encourage urologists in our Asian community to perform randomized studies to confirm these outcomes. This data can guide us to select the proper treatment for localized prostate cancer.

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What is already known on this topic?

LRP and RARP provide excellent alternative methods for localized prostate cancer treatment in developed countries. However, in developing countries, few studies have explored the safety and effectiveness between LRP and RARP.

What this study adds?

Our study has demonstrated comparable efficacy between the LRP and RARP techniques in terms of oncological and functional outcomes. In the latter years, RARP yields significantly better free margins than LRP. This should encourage more urologists to employ RARP in the treatment strategy of localized prostate cancer and conduct randomized controlled trials to further verify these outcomes.

Potential conflicts of interest

The authors declare no conflict of interest.

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