The Efficiency and Safety of Transperitoneal Versus Extraperitoneal Robotic-Assisted Radical Prostatectomy for Patients with Prostate Cancer: A Single Center Experience with 1-year Follow-up

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Purpose: Several studies have compared the short-term outcomes of extraperitoneal robot-assisted laparoscopic radical prostatectomy (EP-RALP) and transperitoneal RALP (TP-RALP). The study was designed to evaluate the long-term outcomes of the two methods.

Materials and Methods: A prospective, non-randomized study was conceived. The demographics and operative outcomes of patients with prostate cancer undergoing RALP from September 2016 to January 2017 at our center were included.

Results: A total of eighty-six patients were enrolled. Thirty-seven patients underwent EP-RALP, and forty-nine patients received TP-RALP. No significant difference was observed in age, body mass index, pathological T stage, pathological N stage, M stage, 2014 International Society of Urological Pathology group, comorbidities or American Society of Anesthesiologists score. A lower preoperative prostate-specific antigen (PSA) was detected in the EP-RALP group. No significant differences were observed in overall operation time, robotic console time, surgical margin status, postoperative hospitalization time, drop of hemoglobin and complications, except that patients with EP-RALP had a shorter time to first exsufflation after surgery than those with TP-RALP (41.35 vs. 51.80 h, $P < .001$). Postoperative PSA until 12 months was deemed comparable in both groups. Complete continence until 12 months after surgery was desirable but not significantly different between two groups (75.0% in EP- RALP vs. 86.7%. in TP-RALP, $P = .179$).

Conclusion: The long-term outcomes of EP-RALP were analogous to those of TP-RALP. Therefore, EP-RALP is an alternative approach for patients with localized prostate cancer.

Keywords: prostate cancer; robot-assisted prostatectomy; extraperitoneal approach; transperitoneal approach; enhanced recovery after surgery

INTRODUCTION

Robot-assisted laparoscopic radical prostatectomy (RALP) is a minimally-invasive approach for patients with localized prostate cancer, and it has been commonly performed worldwide.(1) Compared with laparoscopic radical prostatectomy (LRP), the robot system could provide a clearer version of pelvic structures and more flexible instruments.(2) Transperitoneal (TP) approach has been predominant since it was performed by Binder et al.(3) Gettman et al first reported extraperitoneal RALP (EP-RALP) in 2003.(4) Then, several studies compared perioperative outcomes between EP-RALP and TP-RALP.(5-11) A systematic review by Lee et al. concluded that operation time and length of stay were shorter with EP-RALP than with TP-RALP.(12) On the other hand, the difference in the surgical margin status between the two groups was not statistically significant.(12) Although EP-RALP seemed superior to TP-RALP in some aspects, the number of studies was limited. The TP approach still makes up a majority of RALP. Thus, we attempted to evaluate the long-term outcomes of the TP-RALP and EP-RALP methods.

MATERIALS AND METHODS

A prospective, non-randomized study was conceived and has been approved by Biomedical Ethics Committee of West China Hospital, Sichuan University. The ethical approval number is 201752. Patients with prostate cancer undergoing RALP from September 2016 to January 2017 at our center were included. All patients had been diagnosed with prostate cancer by histological examinations, including prostate biopsy, or transurethral resection of prostate (TURP) and were initially diagnosed with benign prostate hyperplasia (BPH). Prostate-specific antigen (PSA), magnetic resonance imaging (MRI) and bone scans were also completed before surgery to evaluate the clinical stage.

Patient demographics included age, preoperative PSA,

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Table 1. Patient demographics.

	EP-RALP (N = 37)	TP-RALP (N = 49)	*P*-value
Age, year; mean ± SD (range)	67.40 ± 7.96 (46-79)	67.43 ± 7.88 (48-87)	.989
BMI, kg/m2; mean ± SD (range)	24.99 ± 3.23 (17.30-32.66)	24.40 ± 2.63 (18.13-31.51)	.351
Preoperative PSA, ng/mL; median (IQR)	12.26 (14.06)	18.06 (30.35)	.011
pT, n (%)			.073
T1	1 (2.7)	0	
T2	21 (56.8)	20 (40.8)	
T3	15 (40.5)	29 (59.2)	
Lymphadenectomy, n (%)	7 (18.9)	4 (8.2)	.195
pN, n (%)			.576
N0	5 (71.4)	2 (50)	
N1	2 (28.6)	2 (50)	
M, n (%)			.430
M0	36 (97.3)	49 (100)	
M1b	1 (2.7)	0	
Nerve-sparing technique, n (%)	12 (32.4)	14 (28.6)	.813
2014 ISUP grade, n (%)[a]	(available n = 32)		.203
1	2 (5.9)	1 (2.0)	
2	9 (26.5)	12 (26.5)	
3	13 (38.2)	22 (44.9)	
4	4 (11.8)	4 (8.2)	
5	4 (11.8)	10 (20.4)	
NHT, n (%)	5 (13.5)	0	.013
Co-morbidity, n (%)[b]			
Totally, n (%)	31 (83.8)	34 (69.4)	.138
For detail, n (%)			.898
Hypertension	14 (37.8)	15 (30.6)	
Diabetes mellitus	8 (21.6)	9 (18.4)	
Other cancer	2 (5.4)	3 (6.1)	
CNS diseases	1 (2.7)	2 (4.1)	
COPD	1 (2.7)	2 (4.1)	
Cardiac diseases	3 (8.1)	3 (6.1)	
Other diseases	2 (5.4)	0	
ASA score, n (%)			.629
2	26 (70.3)	37 (75.5)	
3	11 (29.7)	12 (24.5)	

[a]Gleason score was not available among 5 patients received NHT.
[b]patients may had more than one co-morbidity.
EP-RALP, extraperitoneal robotic-assisted laparoscopic radical prostatectomy; TP-RALP transperitoneal robotic-assisted laparoscopic radical prostatectomy; BMI, body mass index; SD, standard deviation; IQR, interquartile range; PSA, prostate specific antigen; T, tumor; N, node; M, metastasis; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; ISUP, International Society of Urological Pathology; NHT, neoadjuvant hormornal therapy; ASA, American society of Anesthesiologists.

American Society of Anesthesiologists (ASA) score, TNM staging, 2014 International Society of Urological Pathology (ISUP) grade[1-5] and comorbidities. Efficiency parameters for evaluation included overall operative time, robotic console time, surgical margin status, postoperative PSA and complete continence. Patients undergoing TP-RALP were regularly required to take sodium phosphate oral saline the day before surgery for bowel preparation, while patients with EP-RALP were not. Complete urinary continence was defined as no use of pad all day. Safety parameters including complication rates, postoperative hospitalization time, drop in hemoglobin and time to first exsufflation were assessed. The complications were classified using the Clavien-Dindo classification system.

TP-RALP technique

The patients were placed supine with a 30° to 40° inclined Trendelenburg position after general anesthesia was administered. A sterile 22 French Foley catheter was inserted. A paraumbilical incision of 3 cm was made. Then successive dissections to the peritoneum were performed. Next, a 12-mm trocar was inserted into the peritoneal cavity. After pneumoperitoneum was established at 12 to 15 mmHg, the camera was placed through this port. The other three robotic ports and one assistant port were placed under vision as described in the book by Smith et al.[13]

First, median umbilical ligaments on both sides were incised in a reversed “U” manner. Then, the endopelvic fascia could be exposed and incised. Next, the dorsal vein complex was sutured with 2-0 Vicryl. With the help of the No.3 robotic arm, bladder neck dissection was performed. After the catheter was removed, seminal vesicles were dissected, and the deferens were cut off. On the superficial Denonvilliers fascia, the dissection of the prostate apex should be made carefully to avoid injuring rectum. The prostate could be totally dissected after the junction of prostate and proximal urethra was incised. Finally, drainage was placed in the pelvis. It was usually removed on the 2nd or 3rd day after surgery.

EP-RALP technique

The patients were placed supine with a 15° to 20° inclined Trendelenburg position. After the catheter was inserted, a 3 cm paraumbilical incision was made. Then successive dissections were performed until the posterior rectus sheath. The middle finger was introduced behind the rectus muscles. Thus, an extraperitoneal space was established by blunt digital dissection and balloon dilation. A camera was placed through the paraumbilical incision with a 12-mm trocar. Pneumoperitoneum was then established that in the TP approach.

Table 2. Perioperative outcomes.

	EP-RALP (N = 37)	TP-RALP (N = 49)	*P*-value
Preoperative bowel preparation, n (%)	0	45 (91.8)	< 0.001
Overall operation time, min; mean ± SD (range)	150.27 ± 16.75 (110-180)	155.41±15.44 (120-180)	.144
Robotic console time, min; mean ± SD (range)	106.49 ± 15.81 (70-130)	112.04 ± 13.30 (75-135)	.089
Surgical margin status, n (%)			1.000
Positive	9 (24.3)	12 (24.4)	
Negative	28 (75.7)	37 (75.6)	
Positive margin location, n			
Apex	5	7	
Bladder neck	3	4	
Other	2	5	
Time to first exsufflation, h; mean ± SD (range)	41.35 ± 9.18 (24-60)	51.80 ± 10.23 (26-72)	< 0.001
Postoperative hospitalization time, d; mean ± SD (range)	5.62 ± 2.18 (4-15)	5.78 ± 2.38 (4-16)	.759
Drop of hemoglobin, g/L; mean ± SD (range)	22.11 ± 10.51 (5-48)	22.63 ± 11.62 (3-47)	.827
Transfusion rate, n	0	0	-
Complications, n (%)			.847
I	3 (8.1)	4 (8.2)	
II	1 (2.7)	0	
III-V	0	0	

EP-RALP, extraperitoneal robotic-assisted laparoscopic radical prostatectomy. TP-RALP, transperitoneal robotic-assisted laparoscopic radical prostatectomy. SD, standard deviation; PSA, prostate specific antigen.

Next, two 5-mm robotic ports were placed under vision with a distance of 8 cm to the camera port and inferior to the camera port level of approximately 2 cm. After the left iliac fossa was identified and dissected, another robotic port was placed. Likewise, a 12-mm port was positioned for the assistant on the patient's right side. Thus, five trocars (one for camera, three for arms and one for assistant) were established. The placement of these ports might require further mobilization under vision. The procedures of prostatectomy were similar to those of the TP approach.

Statistical Analysis

SPSS 19.0 software was used for all data analyses. The continuous variables were presented as the mean ± standard deviation or median with interquartile range (IQR), and evaluated using the independent samples t test or Wilcoxon rank-sum test. The categorical variables were presented by number and frequency (%), and the significant differences were evaluated using the chi-square test or Fisher's exact test. Mann Whitney-U test was used for analysis of multiple ranked variables. A $P < .05$ was considered as statistically significant.

RESULTS

Eight-six consecutive patients with prostate cancer who underwent RALP were included in our study. Thirty-seven patients underwent EP-RALP, while forty-nine underwent TP-RALP. The decision to perform which approach mostly depended on the surgeon's preference. The patient demographics are listed in **Table 1**. No significant difference was observed in age, BMI, pathological T stage, pathological N stage, M stage, 2014 ISUP group, and comorbidities or ASA score. However, five patients received neoadjuvant hormonal therapy (NHT) in the EP-RALP group, while no patients in TP-RALP group did ($P = .013$).

Operative and postoperative outcomes are presented in **Table 2**. No significant differences were observed in overall operation time, robotic console time, surgical margin status, postoperative hospitalization time, drop in hemoglobin or complications between the two groups. The proportions of patients who underwent lymphadenectomy between two groups was not significantly different (presented in **Table 1**). However, we found that patients in the EP-RALP group had a shorter time to first exsufflation after surgery than those in the TP-RALP group (41.35 vs. 51.80 h, $P < .001$). Furthermore, positive margin status was 11.6% (5/43) in patients with pT ≤ 2, which was lower than that in patients with pT3 (16/44) ($P = .007$, data not shown in table).

The most common postoperative complications were edema of lower extremity and scrotum. None of the patients had class III-V complications (e.g. ileus, deep vein thrombosis, pulmonary embolism, or death). Specifically, in the EP-RALP group, two patients suffered edema of the lower extremity (one underwent lymphadenectomy), and one who had epididymitis before surgery suffered edema in the scrotum. One patient with atrial fibrillation and hypertension suffered mild congestive heart failure but did not require a visit to the intensive care unit (ICU). This patient was finally managed. In the TP-RALP group, fat liquefaction occurred in one patient. Two patients undergoing lymphadenec-

Table 3. Postoperative PSA level (median, ng/mL).

	EP-RALP	TP-RALP	*P*-value
At 1 months	.073 (n = 32)	.142 (n = 38)	.055
At 3 months	.003 (n = 25)	.095 (n = 31)	< 0.001
At 6 months	.004 (n = 21)	.033 (n = 24)	.065
At 9 months	.004 (n = 17)	.067 (n = 15)	.118
At 12 months	.003 (n = 12)	.025 (n = 10)	.021

EP-RALP, extraperitoneal robotic-assisted laparoscopic radical prostatectomy. TP-RALP, transperitoneal robotic-assisted laparoscopic radical prostatectomy.

Table 4. Complete continence rate.

	EP-RALP	TP-RALP	*P*-value
At 1 months	13/36 (36.1%)	18/47 (38.3%)	.838
At 3 months	23/36 (63.9%)	31/47 (66.0%)	.845
At 6 months	26/36 (72.2%)	35/47 (74.5%)	.818
At 12 months	27/36 (75.0%)	39/45 (86.7%)	.179

EP-RALP, extraperitoneal robotic-assisted laparoscopic radical prostatectomy. TP-RALP, transperitoneal robotic-assisted laparoscopic radical prostatectomy.

tomy had edema of the lower extremities. One patient suffered diarrhea. All patients were relieved by appropriate treatment.

The postoperative PSA levels are presented in **Table 3**. At 1 month (n = 70), 6 months (n = 45) and 9 months (n = 32) after surgery, the PSA levels were not significantly different between the two groups. They were lower in the EP-RALP group at 3 months (n = 56) and 12 months (n = 22). It seemed that patients in the EP-RALP group had a lower postoperative PSA level, which may be due to a relatively lower baseline, moreover, five patients in the EP-RALP group had received NHT.

The urinary continence rate was comparable between the EP-RALP and TP-RALP groups. At 12 months after surgery, although the continence rate of the TP-RALP group seemed obviously higher than that of the EP-RALP group (86.7% vs. 75.0%), this difference was not statistically significant (**Table 4**).

DISCUSSION

Radical prostatectomy (RP) is recommended for localized prostate cancer.[1] In addition, patients with locally advanced prostate cancer can also benefit from RP combined with other therapies.[14] In the present study, five patients in EP-RALP group had received NHT for 3 months. Thus, RP plays an important role in the management of prostate cancer.

As a minimally invasive procedure, LRP is the most common approach used around the world. However, RALP is becoming a new gold standard approach for RP. The robotic system not only offers three-dimensional vision and flexible wrists, but also provides surgeons with more comfort during surgery. As a result, thousands of patients have benefited from the robotic system.

The TP approach for prostate cancer has been predominant in RALP and LRP for decades. However, the EP approach is commonly used in open RP (ORP), also known as retropubic RP. Gettman et al. performed EP-RALP on four patients, and it turned out to be practical [4]. Atug et al. first conducted a study to compare operative the outcomes of TP-RALP (n = 40) and EP-RALP (n = 40).[5] In this study, the operation time, complication rate, estimated blood loss (EBL) and length of stay (LOS) were not significantly different between the two groups.[5] A randomized controlled trial (RCT) by Capello et al. also demonstrated that both accesses were sufficiently effective and safe.[6] A recent RCT by Akand et al. found that the time to oral diet was shorter among patients who underwent EP-RALP than among those who underwent TP-RALP, which was consistent with the findings of our study.[10] A study by Sugi et al. demonstrated that an enhanced recovery after surgery (ERAS) protocol was successfully applied in patients who underwent TP-RALP.[15] The median time to first defecation was 3.0 d and 2.6 d in the conventional group and ERAS group, respectively ($P = .0061$).[14] In view of the surgical approach, EP-RALP could be a desirable management for ERAS.

The patient demographics were not significantly different between the EP-RALP and TP-RALP groups, except the preoperative PSA and proportion of patients who received NHT. We analyzed preoperative PSA between patients with and without NHT, and the difference was statistically significant (0.421 vs. 25.92 ng/ml, $P < .001$, not presented in tables). Thus, a higher proportion of NHT in the EP-RALP group resulted in a lower preoperative PSA level than that in the TP-RALP group. In addition, the postoperative PSA level seemed to be the same, but the limited sample in both groups and data variability in the TP-RALP group should be noticed. In addition, we compared the histological patterns by the 2014 ISUP grading system instead of the traditional Gleason score system because the 2014 ISUP grading group system is closely related to patient prognosis and was accepted by the World Health Organization in 2016.[16]

The complication rates were similar in the two groups. None of the patients had severe complications (class III-V). This finding was consistent with those of four studies.[5-7,10] However, two studies demonstrated a higher complication rate in the TP-RALP group than that in the EP-RALP group.[8,11] Cheung et al. found that 7/105 (6.7%) patients undergoing the TP approach suffered from ileus, while none of the patients in the EP-RALP group did.[8] Although the surgeon's practice played an important role, a lower complication of bowels in patients who underwent EP approach may have resulted from fewer intraoperative procedures on bowels.

Most of previous studies demonstrated no significant difference in EBL between EP-RALP and TP-RALP groups. However, Akand et al. found less EBL in the EP-RALP group than in the TP-RALP group.[10] In the present study, we calculated the drop in hemoglobin to assess blood loss by subtracting the postoperative hemoglobin value from the preoperative hemoglobin value because intraoperative and postoperative blood loss was difficult to evaluate. As a result, no significant difference was observed between the two groups ($P = .827$). In addition, no patients in either group were converted to open surgery.

Positive surgical margin rates were similar between the two groups in our study. According to previous studies, positive surgical margin rates were 3.2% to 30.0% and 0% to 33.3% in the EP-RALP and TP-RALP groups, respectively.(5-9, 11) Patients with pT $\geq$ 3 had a higher positive margin rate.[5,8] In the present study, a total of 19 patients had positive margins in total. Fourteen patients (73.7%) had pT3, while 5 patients had pT2. Most of positive margins were located at the prostate apex and bladder neck. This finding was in accordance with that of the study by Atug et al.[5] Thus, surgeons should be more careful during surgery when dissecting apex and bladder neck.

The assessment of urinary continence is important for patients undergoing prostatectomy. Most patients were followed up. At 1 month after surgery, complete continence was 36.1% and 38.3% in the EP-RALP and TP-RALP groups, respectively. At 12 months, 75.0 % and 86.7% of patients in the two groups had complete urinary continence. These outcomes seemed favorable. Unfortunately, we did not investigate the incontinence questionnaire score. Although Chung et al. found that the continence rates at 6 and 12 months were not significantly different between the EP-RALP and TP-RALP groups, they demonstrated a faster postoperative continence recovery in EP-RALP group.[8] The study by Akand et al. also led to a similar outcome of continence in both groups, which was in line with the findings of present study.[10] Surgical techniques for preventing of urinary incontinence have been explored. Totally, the preservation of sphincter complex and pelvic floor were regarded as main procedures to preventing postoperative incontinence during radical prostatectomy.[17] A study also showed that shorter resected membranous urethra might indicate better urinary continence. For patients who were incontinent at 3 weeks after the removal of the catheter, solifenacin was proven to be effective.[18] Furthermore, numerous studies recommended that artificial urinary sphincter was effective for severe urinary incontinence after radical prostatectomy.[19] However, no additional interventions were required for patients with severe urinary incontinence in the present study.

There were some limitations in the present study. First, it was not a randomized controlled study. Surgeon preference played a key role in decision making to perform which approach. The preoperative PSA level at baseline was not equal between the two groups because five patients had received NHT prior to EP-RALP. In fact, this study was based on a real-world pattern. In addition, erectile function was not evaluated in our study, because aged patients in China usually care more about oncologic outcomes than sexual function. In the study by Akand et al., postoperative erectile function rates at six months after surgery were similar in both groups.[10] However, postoperative erectile function was less influenced by the surgical approach, and more related to preoperative sexual function and whether the neurovascular bundle (NVB) had been preserved.

CONCLUSIONS

Compared with TP-RALP, patients undergoing EP-RALP had a shorter time to exsufflation after surgery. In addition, no significant differences were observed in postoperative complications, overall operation time, robotic console time, positive margin rate or long-term urinary continence between the two groups. Thus, EP-RALP is a desirable approach for patients with localized prostate cancer.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to disclose.

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