ORIGINAL RESEARCH

Laparoscopic Radical Prostatectomy After Robotic Radical Prostatectomy Training: A Matched Pair Analysis of a Single Surgeon Experience

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Objective: The authors compared the perioperative, oncological, and functional outcomes of a single surgeon's prior experience with robot assisted laparoscopic prostatectomy (RALP) to those of laparoscopic radical prostatectomy (LRP) which he performed later after RALP.
Methods: This was a retrospective study on patients who underwent LRP and RALP by a single surgeon who performed a similar antegrade approach to the prostate. Patients' clinical characteristics were collected— then a 1:1 pairing on LRP to RALP patients with the same preoperative profile. Paired t-test with a level of significance was set at $p<0.05$ using MedCalc.
Results: One hundred cases were done from April 2011 to March 2020. Out of eighty-four with sufficient data, twelve pairs were matched with no significant difference on age (p=0.13), BMI (p=0.26), clinical stage (p=1.0), prostate size (p=0.46), PSA (p=0.40) and Gleason score (p=1.0). Significant difference was noted on lymph node dissection (p=0.003), number of isolated lymph nodes (p=0.038), duration of procedure (p=0.0263), and surgical margin (p=0.0069). No significant difference on lymph node yield (p=0.67), blood loss (p=0.95), hospital stay duration (p=0.71), perineural invasion (p=0.894), lymphovascular invasion (p=0.4783), extracapsular extension (p=0.843), seminal vesicle involvement (p=0.4783), follow-up PSA (p=1.000) for two years, complications (p=0.09), return of continence (p=0.287) and erectile dysfunction (p=1.0).
Conclusion: A trained robotic surgeon can perform laparoscopic radical prostatectomy with comparable perioperative, oncologic, and functional outcomes.

Key words: Radical prostatectomy, laparoscopy, robotics, matched-pair analysis

Introduction

Radical prostatectomy is the standard of treatment for localized and locally advanced prostate cancer. Treatment options have evolved from doing open radical prostatectomy to robotic surgery to achieve the best oncologic outcome for the patients.[1-3] In the current era, both laparoscopy and robot-assisted surgery have been the trend due to overwhelming evidence of the decreased intraoperative time of conduct, shorter postoperative convalescence, and better oncologic outcomes.[1,2,4]

Some countries, however, favored robotic-assisted surgery due to the minimal number of procedures to achieve the learning curve.[4] It has the advantage of stable 3D vision, wristed instruments, filtration of hand tremors, and robust instrument movements.[1,5] In contrast, laparoscopic surgery has a steep learning curve and is daunting, especially for the laparoscopically naïve surgeon.[4] It needs good hand-eye coordination and requires the capacity

to operate on limited tactile feedback on a non-3D vision.[5] The main rate-limiting factor in LRP is the required technical dexterity of the surgeon during the urethrovesical anastomosis. This is the main stumbling block that dissuades the surgeon from resorting back to LRP after he has learned RALP. For these reasons, most surgeons who are robot trained shy away from conventional laparoscopy. Meanwhile, in developing countries where robot use is not fully available and economically impractical to patients, surgeons who are robot trained resort to laparoscopy. The surgeon, recognizing all the advantages of minimally invasive surgery, offers LRP to patients who cannot afford RALP. This decision was made despite the technical challenges inherent to it.

The aim of this study was to determine whether there are comparable perioperative, oncological, and functional outcomes of a single surgeon's prior experience with robot assisted laparoscopic prostatectomy (RALP) to those of laparoscopic radical prostatectomy (LRP) which he performed later after RALP.

Methods

This retrospective study was approved by the institutional ethics and review board in accordance to the Helsinki Declaration of 1975, as revised in 1983. The authors reviewed the charts (admission and out-patient) and histopathologic reports of prostate cancer patients who underwent LRP and RALP using similar anterior approach by a trained robotic surgeon who initially did twenty-seven RALP cases before performing LRP between April 2011 to March 2020.

Clinical characteristics of patients were collected. They included age, body mass index (BMI), clinical-stage, prostate size, prostate-specific antigen (PSA), Gleason score, evaluation of surgical margin, presence of perineural invasion, presence of lymphovascular invasion, presence of extracapsular extension, seminal vesicle involvement, and lymph node isolated, duration of the procedure, blood loss, duration of hospital stay, follow-up PSA for two years (considered undetectable levels was <0.10 ng/mL), continence (considered continent if using 0-1 pad) and erection evaluation (using SHIM score), and complications. To control patient variability patients from each treatment arms: Group 1, RALP, and Group 2, LRP were match-paired so that their demographical and clinical characteristics were similar. Match pairing was done using MedCalc with level of significance set at $p<0.05$ using the following preoperative clinical characteristics: age, BMI, clinical-stage, prostate size, PSA, and Gleason score. From a pool of 100 cases done, only 84 patients had sufficient data (30 LRP and 54 RALP). A total of 12 patients for each group of LRP and RALP were match-paired. Preoperative profile between LRP and RALP groups showed no significant difference (i.e. age, BMI, clinical-stage, prostate size, PSA, and Gleason score). The aurhors then looked into differences between groups.

The perioperative, oncological, and functional outcomes between the two groups were then compared using paired t-test with a level of significance set at $p<0.05$ on MedCalc. Student t-test was used for age, BMI, prostate size, PSA, mean hospital days, mean months before continence, duration and blood loss based on mean. While Fisher's Exact/Chi Square test was used for clinical stage, Gleason score. Mann Whitney U test was used for duration, blood loss, based on median hospital days, median erectile dysfunction. Fisher's Exact Test was used for the lymph node dissection, complications and surgical margin, and erectile dysfunction. Categorized data were summarized in tabular form using frequency, percentages, mean/median, and standard deviation.

Results

Preoperative Profile

The two groups have the same profile in terms of age ($p=0.1266$), PSA ($p=0.4008$), clinical-stage ($p=1.00$), and Gleason score ($p=1.00$). Additionally, results showed that the mean prostate size was statistically similar ($p=0.4576$). The average age of patients under LRP was 63 years old, while the average age for RALP was 66 years old. The BMI of patients in LRP was in the upper limit of normal to overweight (24.5 ± 2.6) while RALP patients were mostly overweight to obese (26.3 ± 4.9), however

statistically insignificant (p=0.2662). The mean PSA was 9.4 and 11.1, respectively.

Intraoperative Outcome

Table 2 showed that lymph node dissection was mostly done for patients under the RALP group (83.3%) compared to only 16.7% for the LRP group (p=0.0033). In conjunction, lymph node isolation was significantly higher for patients who underwent RALP, where a typical patient can yield to around 24 lymph nodes with one out of three (0.3) nodes turned positive (p=0.0385).

Table 1. Preoperative patient profile.

	LRP (n=12)	RALP (n=12)	p-value
Age, mean ± SD	63.3 ± 4.2	66.3 ± 5.0	0.1266
BMI (kg/m^2), mean ± SD	24.5 ± 2.6	26.3 ± 4.9	0.2662
Clinical stage, n, %			
T1			
T1a	0 (0.0)	0 (0.0)	
T1b	0 (0.0)	0 (0.0)	
T1c	7 (58.3)	7 (58.3)	1.0000
T2			
T2a	3 (25.0)	4 (33.3)	
T2b	1 (8.3)	1 (8.3)	
T2c	1 (8.3)	0 (0.0)	
Prostate size (grams), mean ± SD	35.2 ± 10.6	39.0 ± 13.7	0.4576
PSA (ng/dl), mean ± SD	9.4 ± 5.4	11.1 ± 4.4	0.4008
Gleason score, n, %			
6 (3+3)	6 (50.0)	6 (50.0)	
7 (3+4)	5 (41.7)	5 (41.7)	1.0000
8 (4+4)	1 (8.3)	1 (8.3)	

SD Standard Deviation

Table 2. Intraoperative outcome.

	LRP (n=12)	RALP (n=12)	p-value
Lymphadenectomy			
No	10 (83.3)	2 (16.7)	0.0033*
Yes	2 (16.7)	10 (83.3)	
Lymph node yield (Positive)			
Mean ± SD	0.0	0.3 to 0.9	0.6761
Lymph node yield (Isolated)			
Mean ± SD	5.0	24.0 ± 10.8	0.0385*
Duration of procedure (minutes)			
Mean ± SD	240.5 ± 53.2	300.3 ± 68.6	0.0263*
Blood loss (cc)			
Mean ± SD	390.8 ± 366.9	300.3 ± 68.7	0.2909

* Significant
SD Standard Deviation

The mean duration of the procedure was significantly longer for RALP with an average of 300 minutes or almost 5 hours, as compared to around 240 minutes for LRP or 4 hours (p=0.0263). The shortest duration for LRP was 180 minutes, while the longest recorded was 355 minutes. The range for RALP was 194 to 402 minutes

However, in terms of blood loss, no significant difference existed between the two groups having a mean blood loss of 319 mL in LRP while 300 mL for RALP (p=0.2909). The most significant blood loss for LRP was 1 liter, while the most significant blood loss for RALP was 600 milliliters.

Postoperative and Oncologic Outcome

Table 3 shows no significant difference in mean hospital stay between the two groups (p=0.7100). The average was around 4 to 5 days. The longest admission was six days, while the shortest was two days. Complications were noted in 33% of RALP patients and none in patients under LRP (p=0.0932). A negative surgical margin was more prevalent in LRP (100%) than in RALP (50%) (p=0.0069). On the other hand, results showed no significant difference in positive perineural invasion (p=0.0894), lymphovascular invasion (p=0.4783), extracapsular extension (p=0.0843), and seminal vesicle involvement (p=0.4783).

Table 3. Post-operative and oncologic outcome.

	LRP	RALP	p-value
Hospital Days			
Mean ± SD	4.4 ± 1.3	4.6± 0.8	0.7100
Complications, n, %			
Yes	0 (0.0)	4 (33.3)	0.0932
No	12 (100.0)	8 (66.7)	
Surgical margin, n, %			
Positive	0 (0.0)	6 (50.0)	0.0069*
Negative	12 (100.0)	6 (50.0)	
Perineural invasion			
Positive	2 (16.7)	7 (58.3)	0.0894
Negative	10 (83.3)	5 (41.7)	
Lymphovascular extension			
Positive	0 (0.0)	2 (16.7)	0.4783
Negative	12 (100.0)	10 (83.3)	
Extracapsular extension			
Positive	1 (8.3)	5 (41.7)	0.0843
Negative	11 (91.7)	7 (58.3)	
Seminal vesicle involvement			
Positive	0 (0.0)	2 (16.7)	0.4783
Negative	12 (100.0)	10 (83.3)	
Follow-up PSA			
Detectable	1 (8.3)	1 (8.3)	1.0000
Undetectable	11 (91.7)	11 (91.7)	

* Significant
SD Standard Deviation

Functional Outcome

As shown in Table 4, no patient in both groups became incontinent. The duration of continence return was not significantly different between the two groups (p=0.2874). Specifically, patients under LRP returned their continence with a mean of 90.4 days or three months. The most extended return of continence was 300 days. On the other hand, the mean return of continence for RALP was 55.1 days, where the most extended continence return was 180 days or six months. Prevalence of erectile dysfunction turned out to be not significant as 66.7% of patients of LRP had erectile dysfunction, just slightly lower than 75% for RALP (p=1.000). Undetectable PSA was achieved similarly in both groups with a mean follow-up of 12 months for the LRP group and 13 months for the RALP group. Although in the RALP group, two patients with positive surgical margins underwent adjuvant therapy, one of which had PSA recurrence while the other still had undetectable PSA at 18 months follow-up.

Discussion

In many countries, RALP has become the standard treatment for prostate cancer.[6-7] Due to the advantages of robotic-assisted surgery, most surgeons who have performed the robotic approach shy away from conventional laparoscopy.[5] The authors determined the perioperative, oncological and functional outcomes of a single surgeon who performed RALP first prior to LRP cases. The surgeon in this study was fellowship-trained in a high-volume training center in robotics surgery certified by the Endourological Society.

Both techniques of prostatectomy made use of the anterior approach. The basis for selecting which technique the surgeon will perform – either LRP or RALP, is mainly the patient's choice. Patients clearly understood the advantages of RALP, however some deferred to LRP because it is economical.

A high lymph node yield was noted in the RALP than in LRP group. During the early cases, the surgeon initially did an extended lymphadenectomy removing node-bearing tissues to both groups with predicted lymph node metastasis of >2% (by Briganti nomogram), which was bounded by the external iliac vein anteriorly, pelvic sidewall laterally, bladder wall medially, pelvic floor posteriorly, Cooper's ligament distally and internal iliac proximally. Then later, a standard lymphadenectomy was done, removing only the obturator fossa and external iliac artery lymph nodes. The difference can be explained by two factors. First, it appears that the surgeon, when it was clinically indicated, shifted to standard pelvic lymph node dissection (sPLND) from extended dissection as he did more cases. Hence, since he initially did RALP, more RALP patients underwent extended PLND compared to more recent LRP cases. He did not perform any type of PLND since pre-operative PSMA-PET scan did not show any lymph node metastases. Other differences in lymph node yield could also be due to dependency on several factors: patient and tumor characteristics, the experience of the urologist at the time of operation, size of the lymph node packets removed, the pathologist's experience and expertise, and

Table 4. Functional outcome.

	LRP	RARP	p-value
Incontinent , n, %	0 (0.0)	0 (0.0)	-
Return of continence (days)			
Mean ± SD	90.4 ± 97.76	55.1 ± 55.42	0.2874
Erectile dysfunction			
Yes	8 (66.7)	9 (75.0)	1.0000
No	4 (33.3)	3 (25.0)	

SD Standard Deviation

the method of processing and blocking in the laboratory.[8]

In terms of duration, LRP procedures were faster than RALP. In this study, total operative duration was accounted as the skin-to-skin time of the procedure similar to the retrospective analysis by Wolanski, et al.[9] The variance in duration was due to the difference in docking time and extent of lymphadenectomy for the RALP group. The paired RALP cases with a long duration of the procedure were performed in the infancy of doing RALP. On the other hand, some of the paired LRP patients with a short duration of the procedure were done in recent times by the surgeon who probably already obtained proficiency for the procedure. In short, the differences transpire due to the surgeon's level of experience over time.[2]

Initially, RALP indirectly improves and potentiates the surgeon's skills in doing LRP since RALP holds the inherent and unique potential for superior ergonomics for the primary surgeon with shorter learning curve as compared to LRP. The disadvantage of having limited instrumentation in RALP was eliminated during LRP. Hence, operative time for the surgeon through time as he performed LRP was faster compared to RALP.

In terms of blood loss, there was no significant difference between groups. Factors that decrease blood loss include the tamponade effect by pneumoperitoneum, early identification, and precise ligation of vessels.[11] Meanwhile, factors that increase blood loss include a prolonged operative time, some patients who are obese predisposing to a higher risk of bleeding due to disorders of coagulation and hemostasis, positional compensation by exaggerated Trendelenburg due to excessive intraperitoneal contents falling into the pelvis, which might aggravate cardiorespiratory functional compromise and cause resulting vasodilatation from elevated CO_2 concentration which is adverse for hemostasis, and technical difficulty by the surgeon during the infancy of the learning curve process.[10]

There was no significant difference in hospital stay between both groups. Some of the adverse pathologic findings on both groups (i.e., perineural invasion, lymphovascular extension, extracapsular extension, seminal vesicle involvement) were not significant. However, there was prevalence in positive surgical margins and complications in the RALP group. The positive surgical margins were in the apical portion. Those differences was probably due to acquired awareness of the technique by the surgeon's extensive training either as a first assistant or the primary surgeon in RALP before performing the LRP.[6] Other possible factors such as incomplete excision, inadvertent capsular tear during surgery, sticky cell phenomenon, and artifacts associated with handling from removal up to the specimen processing were considered. Since the authors used a similar approach for prostatectomy, they assumed that the surgeon already acquired some proficiency while performing LRP.

The authors also determined the time post-prostatectomy PSA results achieved undetectable levels (i.e., <0.10 ng/mL) starting from the initial post-prostatectomy PSA measurement, which is six weeks. Each group had one patient who never achieved undetectable levels. They underwent androgen deprivation therapy. However, this incidence among groups was not statistically significant. Having such a difference in the RALP group can be correlated to the high number of patients with positive surgical margins, as previously discussed. Seo, et al. mentioned several causes of elevated PSA in post-prostatectomy patients with a positive surgical margin. Higher preoperative PSA levels, greater BMI, high Gleason score, large tumor volume, and advanced pathologic stage were cited.[12] Looking back to this pool of patients, the authors noted that those who had positive surgical margins and detectable PSA levels had some of these factors.

Early RALP cases done by the surgeon had Clavien-Dindo II and III complications (i.e., lymphocele, bladder neck contracture, and transfusion). One RALP patient who had bladder neck contracture underwent transurethral incision of bladder neck while the other RALP patient who had lymphocele underwent aspiration. Both patients had no further complications thereafter. No complications were observed in the LRP cases. Statistically, there was no significant difference between groups.

Erectile function (using the SHIM score) and return of continence (no. of pads) were also not statistically significant. Hence, the functional outcome between RALP and LRP by the same

surgeon was similar. The advantage of improved vision and ergonomics in RALP enabled the application of meticulous apical dissection and nerve-sparing technique to LRP, which provided sufficient urethral stump length for early recovery continence.[4] RALP replicates laparoscopy techniques using a robot to easy performance; hence the transition from RALP to LRP is feasible.[9]

This paper had several limitations: 1) Variables such as the learning curve, performance of lymphadenectomy, technical variations, and preoperative erectile function were uncontrollable and not considered; 2) The matched pairing did not consider the time frame at which these patients were done (i.e., whether they were done in the early learning curve of RALP or LRP or later in the surgeon's experience); 3) The matched pairing was limited to the removal of dissimilarities between LRP and RALP, causing the sample size to decrease to only 12 pairs (24 cases out of 100), leaving a significant amount of cases unanalyzed. It would have been better if the entire group of 100 cases were analyzed.

Conclusion

A trained robotic surgeon can perform laparoscopic radical prostatectomy with comparable perioperative, oncologic, and functional outcomes. Performing the robotic approach first seemed to facilitate the proficiency for the laparoscopic approach to achieve similar outcomes. Thus, doing LRP after RALP training, in terms of intraoperative outcome, was somewhat comparable. A critical understanding of key anatomic landmarks and adhering to a similar technical approach is paramount to achieve such results. Further studies with a higher volume of cases are needed to validate these findings.

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