

Laparoscopic Extraperitoneal Radical Prostatectomy: Impact of the Learning Curve on Perioperative Outcomes and Margin Status

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ABSTRACT

Objective: After improved technical modifications that followed the original reports by pioneering laparoscopic surgeons, the impact of the learning curve has not been objectively assessed for laparoscopic extraperitoneal radical prostatectomy (LERP). In this study, we assessed the impact of the learning curve on operative and oncologic outcomes at a high surgical volume institution.

Methods and Material: We prospectively analyzed 400 consecutive patients with localized prostate cancer treated with LERP between January 2004 and July 2006. Patients were divided into 4 equal groups (1–100, 101–200, 201–300, and 301–400). Kruskal-Wallis test was performed to determine whether all the preoperative variables were comparable among groups. Fisher's exact test was performed to determine the association of margin status with pathological stage. Chi-square test was performed to determine whether margin status was associated with groups (1 vs. 2, 3, & 4). Wilcoxon rank-sum test was used to determine whether operative time was statistically different in group 1 (1–100) compared with groups 2, 3, and 4.

Results: All groups were comparable with respect to preoperative data. Positive margin rate significantly decreased after the first 200 cases for patients with pT2a-c disease (28.4% to 31.9% vs. 11.6% to 11.5%). Margin status was significantly associated with groups (Group 1 & 3: $P=0.0044$ and group 1 & 4: $P=0.0021$). Operative time significantly decreased after the first 100 cases (350 min vs. 218 min, 192 min, and 223 min) ($P<0.0001$).

Conclusions: In a tertiary care academic institution, the

operative and pathologic outcomes improved significantly with increased surgical experience. At our institution, the operative and pathologic outcomes improved after 100 and 200 cases, respectively.

Key Words: Laparoscopic prostatectomy, Prostate, Prostatic neoplasms, Prostatectomy, Robotic-assisted radical prostatectomy, Robotic prostatectomy.

INTRODUCTION

Although open radical prostatectomy (ORP) is an established surgical treatment modality for localized prostate cancer,¹ laparoscopy is increasingly being offered as an alternative to open surgery. Pure or robotic-assisted laparoscopic radical prostatectomy is becoming the preferred surgical approach in many centers around the world.^{2–8} The main advantages compared with ORP include the excellent magnified view of the pelvic anatomy, a shorter catheterization time, and low intra- and postoperative blood loss and transfusion rates.^{2–8}

Currently, the procedural complexity necessitating considerable learning experience is being discussed as a challenging part of the pure laparoscopic approach. Thus, many urological centers have opted for robotic-assisted radical prostatectomy (RARP) due to the reported less steep learning curve.^{9,10} However, the pure laparoscopic extraperitoneal radical prostatectomy (LERP) learning curve has not been assessed, especially after improved technical modifications that followed the original reports by pioneering laparoscopic surgeons.^{2–5,11}

In this study, we evaluated the operative and pathologic outcomes of pure laparoscopic extraperitoneal radical prostatectomy in the first 400 cases performed at our institution.

MATERIALS AND METHODS

From January of 2004 to July 2006, 400 patients diagnosed with localized prostate cancer underwent LERP by a single surgeon (JMPS) assisted by training residents, or a urologic oncology fellow (ARR). Following institutional re-

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view board approval, perioperative and pathologic data were obtained from our prospectively collected surgical database.

Patient Selection and Staging Prior to LERP

All patients had a preoperative Gleason biopsy sum <8, and a DRE indicating a clinical stage <T3. Patients with a PSA >10ng/mL had a bone scan and computerized tomogram (CT) or MRI to exclude bone and lymphatic metastases. All patients had an LERP, with an attempt to preserve both nerve bundles, regardless of clinical stage.

LERP Technique

The standard LERP at our institution has been described previously.¹² Briefly, we use an extraperitoneal 4- to 5-port antegrade approach, and use a double needle running suture for the vesico-urethral anastomosis.

Postoperative Care

Patients are hospitalized for a minimum of 1 day and are discharged when they are able to take oral feedings and ambulate. A cystogram is routinely ordered 2 weeks after surgery. When the cystogram shows absent extravasation, the Foley catheter is removed.

Data Analyzed

The perioperative and pathologic data for each patient were analyzed and included age, PSA, biopsy Gleason score, DRE clinical stage, pathologic stage, specimen Gleason score, percentage of tumor in the specimen, prostate weight, margin (positive or negative), BMI, EBL, OR time, transfusion rate, hospital stay, JP drainage, and Foley drainage.

Complications were tabulated into a classification system:

- Intraoperative Grade I: Deviation from expected threshold, (passing from extraperitoneal to intraperitoneal access, and others) Grade II: Additional intervention (transfusion, surgical maneuver to control injury to other organs, and others.) Grade III: ICU/Critical care
- Immediate Postoperative Grade I: Deviation from expected threshold (fever, ileus, and others) Grade II: Non-invasive intervention (prolonged JP drainage, prolonged Foley catheter time, and others) Grade III: Invasive intervention (replacing catheter due to urinary retention, urinoma drainage, ureteral stent due to obstruction, and others)

- Late Postoperative >30 days (Grade I: Deviation from expected threshold (perineal pain, urinary tract infection), Grade II: Noninvasive intervention (self-resolved hematuria) Grade III: Invasive intervention (bladder neck contracture interventions) Grade IV: death.

Patient Grouping

Patients were divided into the following groups: Group I (case 1 to 100), Group II (101 to 200), Group III (201 to 300), and Group IV (301 to 400). The groups were evaluated for differences in preoperative (age, BMI, PSA) and pathologic parameters (biopsy Gleason score) and to see whether they were comparable. The groups were compared for intraoperative and postoperative outcomes as well as margin status to search for differences.

OR Time

Cases were divided into those that took ≤4 hours (subgroup 1) and those that took >4 hours (subgroup 2). The percentage of cases with <4 hours was compared consecutively in each 100 case group to find any significant difference.

Blood Loss

Cases were divided into those having ≤250 mL of EBL (subgroup 1) and >250 mL of EBL (subgroup 2). The percentage of cases with <250 mL of EBL was compared consecutively in each 100 case group to find any significant difference.

Statistical Analysis and Methods Used

All statistical analyses were performed using SAS (version 9.1.3; SAS Institute; Cary, NC). Descriptive statistics were generated for continuous (mean, standard deviation, range, median) and categorical variables (frequency, percent). The data were divided into 4 equal groups (1 to 100; 101 to 200; 201 to 300; and 301 to 400) prior to performing the analyses. Kruskal-Wallis test was performed to determine whether all the preoperative variables were comparable in each group. We looked at the distribution of continuous variables in each group. Fisher's exact test was performed to determine the association of margin status with pathologic stage. The 2 were found to be statistically significantly associated (P=0.0073). Statistical significance was based on a 2-sided significance level of 0.05. Chi-square test was performed to determine whether margin status was associated with group 1 vs. 2, 3, & 4. Wilcoxon rank-sum test was used to see whether operative time

was statistically different in group 1 (1 to -100) compared with groups 2, 3, and 4. We also looked at the distribution of margin status by pathologic stage within each group. The operative time was categorized into 2 subgroups: ≤ 4 hours and > 4 hours, and its distribution was determined in each group. Similarly, estimated blood loss was categorized into 2 subgroups: ≤ 250 mL and > 250 mL, and we looked at its distribution in each group. We also plotted the operative time and estimated blood loss against the chronological order of patients, which was indicative of increasing experience.

RESULTS

The mean age, BMI, and PSA of the patients was 59 years (range, 37 to 78), 28 (range, 14 to 50), and 5.7ng/mL (range, 0.2 to 49), respectively. The mean OR time and EBL for the whole population of patients was 246 minutes (range, 95 to 671) and 514 ML (range, 50 to 5000), respectively. The mean total number of units transfused was 0.35

units (range, 0 to 10). The mean preoperative and postoperative hemoglobin was 13.7 (range, 9 to 17.5) and 11 (range, 7 to 15). The mean hospitalization time, Foley catheter and JP drainage was 2 days (range, 1 to 40), 16 (range, 3 to 41), and 2 (range, 1 to 20), respectively. The mean specimen weight and percentage of tumor in the specimen was 49 grams (range, 12 to 196) and 13% (range, 1% to 85%), respectively. None of the patients had a Gleason score of 8 or above on the biopsy specimen.

The whole series of cases was divided into 4 consecutive groups of 100 cases. Age, PSA, biopsy Gleason score, specimen size, and BMI were comparable. The perioperative outcome of each group is presented in **Table 1**.

The overall number of cases that took < 4 hours to perform was 250 (63.2%). When the groups were compared for cases that took ≤ 4 hours to operate vs. those that took > 4 hours, the results were the following: Group I: 14 (14.1%) vs. 85 (85.9%); Group II: 74 (74.0%) vs. 26

Table 1.
Patient Demographics and Perioperative Outcome of Cases Divided Into 4 Groups

	Age	PSA	Specimen (g)	BMI	OR Time (min)	EBL	Units Transfused	Hosp Days	Foley Days	JP Days
Group 1 (N=100)										
Mean	58.30	6.15	43.68	27.61	350.01	547.98	0.56	2.53	18.59	3.09
STD	7.57	4.50	16.49	4.03	101.04	507.25	1.45	1.80	6.67	2.50
Median	58.00	5.10	41.70	27.28	330.00	400.00	0.00	2.00	19.00	2.00
Group 2 (N=100)										
Mean	59.32	5.84	51.86	29.14	217.85	515.50	0.31	2.28	17.19	2.53
STD	7.84	5.24	24.59	5.17	59.90	367.88	0.88	0.96	5.88	1.18
Median	60.00	5.00	46.25	27.75	210.00	400.00	0.00	2.00	15.50	2.0
Group 3 (N=100)										
Mean	59.62	5.40	48.16	28.17	191.51	426.28	0.15	2.19	16.00	1.91
STD	7.42	2.76	20.34	4.63	52.33	282.40	1.04	3.94	6.28	0.95
Median	60	4.95	43.50	27.45	180.00	400.00	0.00	2.00	14.00	2.00
Group 4 (N=100)										
Mean	59.87	5.66	53.31	28.63	222.58	563.50	0.38	2.55	15.64	2.67
STD	7.81	4.11	27.90	4.04	60.80	651.22	1.54	1.81	6.13	3.08
Median	61.00	5.00	45.00	28.23	215.00	400.00	0.00	2.00	14.00	2.00

(26.0%); Group III: 90 (91.8%) vs. 8 (8.2%); Group IV: 73 (73.0%) vs. 27 (27.0%).

The overall number of patients with an EBL <250 mL was 99 (24.9%). When the groups were compared for patients who had ≤250 mL of blood loss vs. those that had >250 mL blood loss, the results were the following: Group I: 21 (21.2%) vs. 78 (78.8%); Group II: 20 (20.0%) vs. 80 (80.0%); Group III: 26 (26.5%) vs. 72 (73.5%); Group IV: 32 (32.0%) vs. 68 (68.0%).

Operative time decreased after 100 cases (350 min vs. 218 min, 192 min, and 223 min) (**Figure 1**), and EBL remained constant at a mean of 500 mL (median, 400 mL) with no significant variation when comparing groups of 100 cases (**Figure 2**). The mean operative time decreased significantly in groups 2, 3, and 4 compared with group 1 (P<0.0001).

The pathologic stage and percentage of positive margin (M+) for the whole series was the following: 5 cases with pT0Nx/N0Mx (0% M+), 59 with pT2aNx/N0Mx (6.8% M+), 4 with pT2bNx/N0Mx (25% M+), 290 with pT2cNx/

N0Mx (23.8% M+), 33 with pT3aNx/N0Mx (33% M+), and 10 with pT3bNx/N0Mx (40% M+).

Positive margin rates significantly decreased after 200 cases for patients with pT2a-c disease (28.4–31.9% vs. 11.6%–11.5%) (**Table 2**). Margin status was significantly associated with groups (Group 1 & 3: P=0.0044 and Group 1 & 4: P=0.0021).

The majority of the perioperative complications were either Grade I or II (**Table 3**). In our series, 6 patients were admitted to ICU (intraoperative Grade III complication) due to cardiac arrest at the moment of closure of port sites (1), pulmonary embolism followed by compartment syndrome (1), prolonged surgical time and severe intraperitoneal urinary leak (1), prolonged surgical time and intraoperative blood loss (1), pneumopericardium (1), prolonged surgical time, epigastric bleeding, and severe retroperitoneal hematoma(1)

In the immediate postoperative period, 16.7% of the cases had a grade II complication (urinary leak evidenced at the

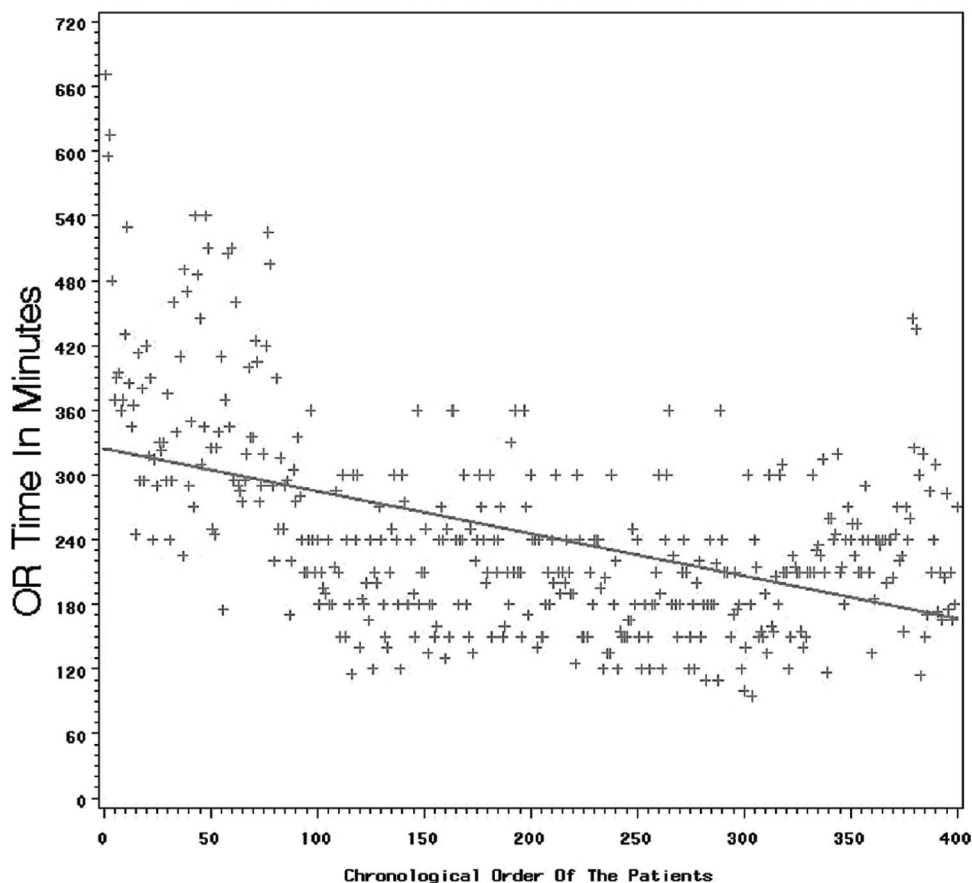


Figure 1. Operating room time.

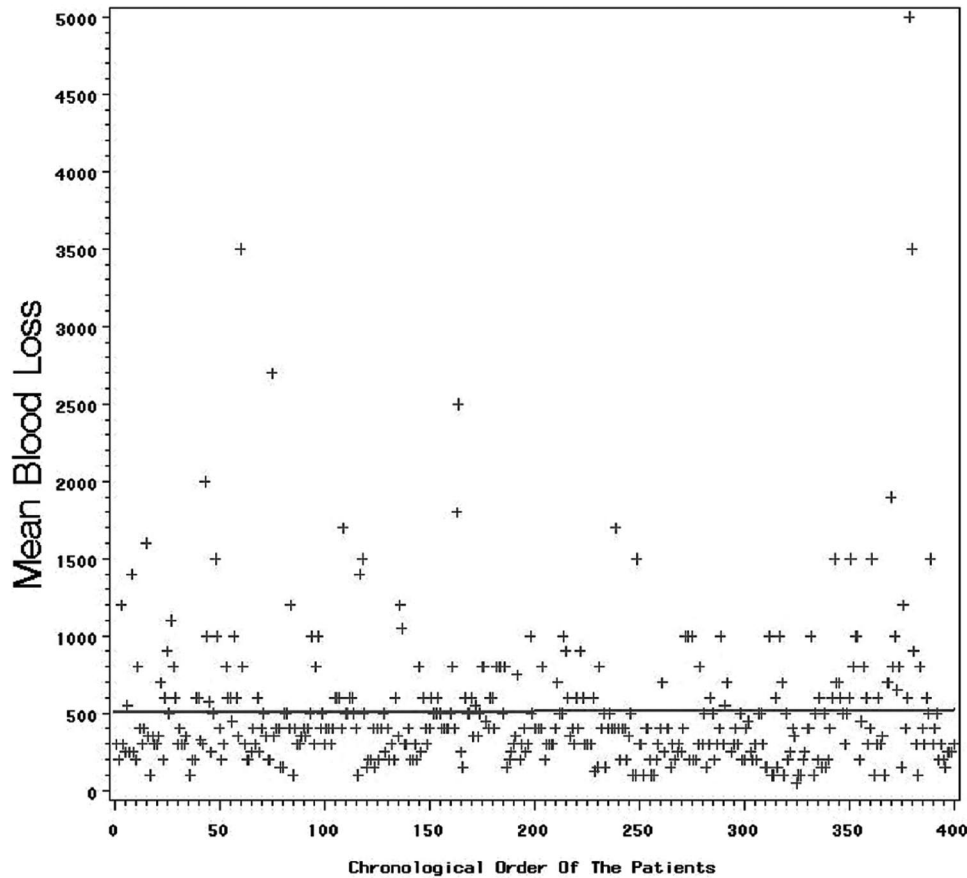


Figure 2. Blood loss.

Table 2.
Decrease in Margin Positivity With Increasing Number of Cases Performed

	pT2a-cNx/N0Mx		pT3a-bNx/N0Mx		Total	
	# Margin+ / # Cases	%	# Margin+ / # Cases	%	# Margin+ / # Cases	%
Overall	74/352	21.0	15/43	34.9	89/395	22.5
Group I	25/88	28.4	7/12	58.3	32/100	32
Group 2	29/91	31.9	1/8	12.5	30/99	30.3
Group 3	10/86	11.6	4/12	33.3	14/98	14.2
Group 4	10/87	11.5	3/11	27.3	13/98	13.3

cystogram ordered 2 weeks after surgery). The majority of these patients required prolonged catheterization time (>14 days). We only considered a perfect cystogram as a condition to DC the Foley catheter in the postoperative period, and the first cystogram, per protocol, was always around 2

weeks. Grade II complications, such as this one, decreased significantly in our series after 100 cases (**Figure 3**).

At 12 months of follow-up, 95% of our patients reported using 0 to 1 pad (as a protection pad only) a day. At 12

Table 3.

Grade and Time of Complications in the Whole Series

Grade and Time of Complication	Laparoscopic Extraperitoneal Radical Prostatectomy (400 Cases)
Intraoperative	
I	5 (1.3%)
II	14 (3.5%)
III	6 (1.5%)
Immediate Postoperative	
I	17 (4.3%)
II	67 (16.7%)
III	10 (2.5%)
Late Postoperative	
I	5 (1.3%)
II	1 (0.2%)
III	7 (1.7%)

months, 75% of the patients that were having sexual intercourse before surgery reported having erections. All of these patients received penile rehabilitation with PDE-5 inhibitors, beginning on the day of discharge.

DISCUSSION

The majority of studies regarding the learning curve for laparoscopic radical prostatectomy have been reported by pioneering surgeons, taking into account their initial experiences, and before the laparoscopic surgical technique had matured.¹³ Some advocate that it takes around 60 cases to surpass the learning curve in experienced laparoscopic hands, 80 to 100 cases for surgeons with no laparoscopic experience, and that operative times continued to improve even after 300 cases.¹⁴⁻¹⁶

On the other hand, reports are contradictory regarding the learning curve for RARP. Some advocate 25 cases and others 150 to 250 cases.^{10,17,18} Finally, no objective report is available on the learning curve for laparoscopic extraperitoneal radical prostatectomy, especially after the pioneering era.

No accepted standard exists for either a definition or measurement of the learning curve. Typically, it is the self-declared point at which a surgeon states he or she has become comfortable performing the procedure. Thus, the

learning curve could vary considerably, depending on a number of surgeon-related factors. Some surgeons may be slower to learn the procedure, and others simply may require greater experience before they feel comfortable with the operation. In our study, we have taken into account objective parameters, such as perioperative and pathologic outcomes to assess the learning curve.

We noticed that a significant difference existed in the mean operative time after 100 cases (**Figure 1**). The first group had a mean of 350 minutes compared with 218 minutes for the second group. More importantly, the percentage of cases that took <4 hours significantly increased from 14% in the first group to 74% in the second group.

Our results clearly trace a difference in margin status after 200 cases for patients having pT2a-c disease. Positive margin rate decreased from 28.4% to 31.9% in the first 200 patients to 11.6% to 11.5% in the next 200 patients (**Table 2**).

Despite the fact that our institution is an academic one with training of residents and fellows, the operative time and margin rates improved. However, this could have influenced the results of EBL, which did not show dramatic variation with increased experience.

Blood loss was around a mean of 500 mL from the beginning of the series of cases, and this mean was not altered significantly with increasing experience (**Figure 2**). Another explanation for this finding may be the laparoscopic influence on blood loss since the beginning. Increased intracavitary pressures may cause constant venous bleeding to decrease during a surgery that involves a highly vascular organ, such as the prostate. When we searched for a difference in percentage of patients having an EBL <250 mL, we noticed a tendency toward an increasing percentage of patients having <250 mL of EBL, with the increasing number of cases performed.

The other perioperative outcomes, such as Foley removal, drain removal, and hospitalization time, were not influenced by the increasing number of cases performed. Of note, all patients had a cystogram 2 weeks after surgery, and the Foley catheter was removed only if there was no extravasation demonstrated on the cystogram. It is for this reason that our mean catheterization time was 16 days, and there was no variation with consecutive cases performed. We now feel that a cystogram is not necessary when the bladder is filled at the end of the procedure, and the anastomosis is proved to be watertight.

In 2006, Tooher et al¹³ reported a systematic review of laparoscopic radical prostatectomy for localized prostate

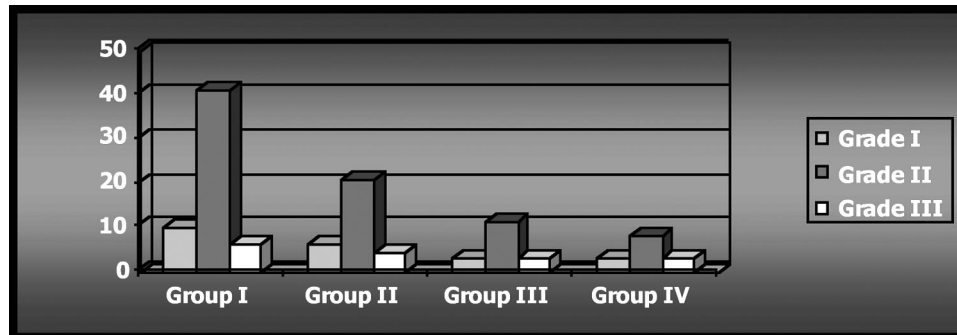


Figure 3. Number of intraoperative and immediate-operative complications (Groups of 100 cases).

cancer and only found 6 studies reporting outcomes in such a way that the effect of increasing experience with laparoscopic approaches could be tracked. Operative time decreased with increasing experience in 5 of 5 studies. In 2 of 3 studies, blood loss tended to decrease with increasing experience. Transfusion rates decreased with increasing experience in 3 of 3 studies. Increasing experience did not affect margin rates in 2 studies, and only 2 other studies demonstrated more positive margins in early experience. With respect to length of stay (2 studies) and catheterization (2 studies), there was no difference with increasing experience.

Recently, in a risk-adjusted analysis of positive surgical margins following laparoscopic and retropubic radical prostatectomy, Touijer et al¹⁹ demonstrated that the positive surgical margin rate in the open procedure remained unchanged, reflecting a mature and well-established technique, while that of laparoscopic radical prostatectomy achieved a significant decrease with time, demonstrating that the procedure and therefore the results continue to evolve. In their study, the learning curves for positive surgical margins (for pT2 disease) in the laparoscopic group matched the open group after 200 cases, which is comparable to our results.¹⁹

Our study reflects the effect of increasing experience in a high volume academic cancer institution on perioperative and pathologic outcomes of patients with localized prostate cancer treated exclusively with LERP. It is important to underline that this study was designed when the surgical technique of LERP was fully standardized worldwide (after the pioneering era), and as such it is the first study to identify multiple learning curves and give approximately the number of cases that it takes to surpass them, with special consideration to an oncologic end point specific to radical prostatectomy, such as positive surgical margins. According to our results, LERP in our institution continues to evolve.

Open nerve-sparing radical prostatectomy is a mature technique for more than 20 years; however, the lack of series in the literature reporting on learning curves for open nerve-sparing radical prostatectomy does not allow for objective comparisons. Only the series of Vickers et al²⁰ clearly identifies that the learning curve to decrease prostate cancer recurrence after open radical prostatectomy was significant and did not start to plateau until a surgeon had completed approximately 250 operations.

Finally, robotic-assisted laparoscopic radical prostatectomy has been adopted by many centers around the world for the treatment of localized prostate cancer. The technique is now mature in both the intraperitoneal and extraperitoneal approach. However, real learning curves based on objective parameters for the extraperitoneal approach are lacking and should be analyzed.

CONCLUSION

This study may serve as a reference to academic institutions involved in residency and fellowship training that are starting to perform laparoscopic extraperitoneal radical prostatectomy. There are multiple learning curves that involve the improvement of operative and oncological outcomes. At our institution, the operative and pathologic outcomes improved after 100 and 200 cases, respectively. The learning curve to reach optimal quality of life outcomes for pure LERP should be analyzed.

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