The Learning Curve Does Not Affect Positive Surgical Margin Status in Robot-Assisted Laparoscopic Prostatectomy

Ekrem Islamoglu[1]*, Kaan Karamık[1], Cagatay Ozsoy[1], Husnu Tokgoz[1], Mutlu Ates[1], Murat Savas[1]

Purpose: To assess the oncologic results of our robot-assisted laparoscopic prostatectomy (RALP) cases and investigate whether the learning curve (LC) affects the oncological outcomes.

Materials and Methods: Between March 2015 and September 2017, 111 patients underwent RALP by a single surgeon in our clinic. The learning curve was analyzed using the moving average method. We compared the rate of positive surgical margins(PSM) and oncological outcomes, operation times, hematocrit changes and duration of hospitalization among the patients during and after the LC. Complications were also noted according to Clavien system.

Result: LC analysis using the moving average method showed that the LC stabilized between cases 51–60. So, patients were classified into two groups; 1-50 cases (Group 1) and 51-111 cases (Group 2). PSM rates were 36% for group 1 and 18% for group 2, and statistically different ($p = 0,032$). Extracapsular invasion (ECI) was significantly higher in group 1 (56,5%) than in group 2 (29,5%) ($P = 0.005$). Multiple logistic regression analysis revealed that presence of ECI was an independent factor for PSM associated with the groups (OR: 2.512; 95% CI: 1.055-5.979). Both operation time and duration of postoperative hospitalization were significantly reduced from group 1 to group 2. A total of 11 patients (10%) had complications and one of them (0.9%) required surgical intervention.

Conclusion: We can conclude that at least 50 RALP cases are needed to gain proficiency even for an experienced surgeon in laparoscopic radical prostatectomy. Our study demonstrates that surgeons experience can affect the perioperative variables but the LC does not affect PSM status in RALP.

Keywords: learning curve; positive surgical margin; robot-assisted prostatectomy

INTRODUCTION

Prostate cancer (PCa) is the most commonly diagnosed cancer in men and it's also second-ranked cancer that results in death in the United States.[1] According to the cancer statistics collected in Turkey, it is the second most common type of cancer in 11.8% of men, in all age groups.[2] Currently, radical prostatectomy is the only surgical treatment of localized PCa. In 1980, Walsh et al. described retropubic radical prostatectomy (RRP) and this procedure remained the gold standard for a long time.[3] In 1992, Schuessler et al. performed the first laparoscopic radical prostatectomy (LRP) as an alternative to RRP.[4] Despite the development of laparoscopic technique in the following years, the LRP continued to be a long and complex surgery with a steep learning curve and even surgeons with high laparoscopy skills required a series of 40-100 cases to gain mastery.[5] The difficulties of the LRP brought along different quests and after the introduction of the da Vinci robotic surgery system, Binder et al. performed the first robot-assisted laparoscopic radical prostatectomy (RALP) in May 2000.[6] With its three-dimensional magnified vision, enhanced ergonomics, computer filtration of tremors and scaled-down movement with the use of an endo-wrist instrument with seven degrees of freedom of range in motion, robotic surgery has initiated a new era of radical prostatectomy. As a matter of fact, 85% of radical prostatectomies in the US have become robot-assisted, less than a decade after its introduction.[7] Of course, robotic surgery has some disadvantages; high costs, inability to understand the tissue or suture tension due to lack of tactile sensation and collision of robotic arms with each other or assistant port are the major ones.[8]

We assessed the results of our RALP cases performed by a single surgeon in our clinic and investigated whether the learning curve affects the oncological outcomes.

PATIENTS AND METHODS

Our robotic team consists of a console surgeon, one assistant surgeon, one surgical nurse, one surgical technician and one circulating nurse. Before the robotic prostate surgery, the console surgeon and the assistant surgeon had gained experience in open RRP and LRP cases.

Between March 2015 and September 2017, 111 patients who underwent RALP by a single surgeon in our clinic, were enrolled in the study. Preoperative clinical data; including age, serum prostate-specific antigen (PSA), biopsy Gleason score and number of cores positive, were collected. The preoperative risk was determined by D'Amico risk stratification and patients were classified as low, intermediate and high risk.[9] We performed

[1]University of Health Sciences, Antalya Training and Research Hospital, Antalya, Turkey.
*Correspondence: University of Health Sciences, Antalya Training and Research Hospital, Antalya, Turkey.
Orcid id: 0000-0003-0693-0666. Phone: (+90)05327115759. Fax: +90 242 2494487. E-mail: meislamoglu@gmail.com.
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Table 1. Comparison of demographic and clinical characteristics of both groups

		Group 1(1-50)	Group 2 (51-111)	*p*-value
Age, mean±SD		63.5 ± 6.4	64.7 ± 6.9	0.331
PSA, median(min-max)		7.8 (3.1-53.4)	6.5 (0.3-40)	0.406
Number of cores positive, median(min-max)		3 (1-10)	3 (1-11)	0.144
Biopsy Gleason score, n(%)	4-6	32 (64)	38 (62.3)	0.981
	7	15 (30)	19(31.1)	
	8-10	3(6)	4 (6.6)	
Risk group, n(%)	Low	18 (45)	28 (45.9)	0.932
	Intermediate	15 (37.5)	24 (39.3)	
	High	7 (17.5)	9 (14.8)	

all RALP procedures via transperitoneal approach, using 6 trocar ports of a conventional 4-arm da Vinci XI robotic system, beginning with initial dissection of the seminal vesicles and the prostate in a posterior fashion as described by Zorn et al.[10] Subsequently, returning to the anterior aspect of the prostate and separating the dorsal vein complex. The neurovascular bundle (NVB) was completely released and the prostate is dissected from the bladder neck. Urethrovesical anastomosis was done continuously, using two 15 cm 3-0 V-lock sutures and 18 French Foley catheter with 10 ml balloon was inserted.

Bilateral pelvic lymphadenectomy (BPLND) was performed in all high risk and selected intermediate-risk patients according to Briganti nomogram.[11] None of the patients received neoadjuvant hormonal therapy. Perioperative parameters were recorded such as operation time, intraoperative complications and whether BPLND or NVB preservation was done. Operation time was defined as skin to skin time in minutes and includes the docking and undocking time. Postoperative parameters including hematocrit change, duration of hospitalization and catheter removal date were noted. Pathological outcomes included pathological Gleason score; positive surgical margin (PSM) status; extracapsular, lymphovascular, perineural and seminal vesicle invasion; as well as lymph node positivity. In order to classify the complications after surgery, the Clavien system, which provides standardization in the literature, was used.[12]

Patient data were prospectively registered in a specific database that was accessible only to authorized people. The patients who provided a written informed consent document were assured regarding the confidentiality of their data. The data were analyzed in a retrospective way to evaluate the clinical and pathological outcomes. Our study was in accordance with the Helsinki Declaration and did not gain ethics committee permission as it included retrospective data.

Statistical analysis

The learning curve evaluation parameter was operation time. The learning curve was analyzed using the moving average method.[13] We decided to use the 10-case moving average as the moving averages for less than 10 cases that exhibited excessive variation. Trends in the operation time can be unclear because of differences between individual cases. With the moving average method, using the mean operation times, the individual changes are removed, and trends are clarified. The patients were divided into two groups, one inside and one after the learning curve.

Between two groups; statistical analysis was made using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY). Fisher's exact test and Pearson chi-square analysis performed for categorical variables. The normality assumptions were controlled by the Shapiro-Wilk test. The differences between two groups were evaluated with Student's t-test for normally distributed data or Mann-Whitney U test for non-normally distributed data. Data are expressed as n(%),

Table 2. Comparison of clinical and pathological outcomes of both groups

		Group 1(1-50)	Group 2(51-111)	*p*-value
Surgical margin status, n(%)	Negative	32 (64)	50 (82)	0.032
	Positive	18 (36)	11(18)	
Extracapsular invasion, n(%)	Yes	28 (56)	18 (29.5)	0.005
	No	22 (44)	43 (70.5)	
Lymphovascular invasion, n(%)	Yes	15 (30)	11(18)	0.139
	No	35 (70)	50 (82)	
Perineural invasion, n(%)	Yes	39 (78)	45 (73.8)	0.605
	No	11(22)	16 (26.2)	
Seminal vesicle invasion, n(%)	Yes	10 (20)	11(18)	0.792
	No	40 (80)	50 (82)	
Pathological Gleason score, n(%)	4-6	19 (38)	22 (36.1)	0.922
	7	27 (54)	35 (57.4)	
	8-10	4 (8)	4 (6.6)	
Lymph node positive, n(%)	Yes	5 (25)	2 (13)	0.240
	No	15 (75)	13 (87)	
Pathological stage, n(%)	pT2	27 (54)	39 (64)	0.262
	pT3	23 (46)	22 (36)	
	pT3	13/23(56%)	6/22 (27%)	
Biochemical recurrence, n(%)	Yes	6 (12)	4 (6.6)	0.999
	No	44 (88)	57 (93.4)	
Duration of follow-up, months		15 (12-33)	6 (3-12)	< 0.001
Additional treatment, n(%)		11(22)	6 (9.8)	0.153

Table 3. Multiple logistic regression analysis for the effect of ECI on surgical margin status

	Wald	*p*-value	Odds Ratio (95%CI)
Surgical margin status	0.972	0.324	1.635(0.615-4.344
Extracapsular invasion	4.331	0.037	2.512(1.055-5.979)

mean ± standard deviation(SD) or median (min-max), as appropriate. *P* values < 0.05 were considered statistically significant. Multivariate analysis was performed using logistic regression.

RESULTS

As shown in **Figure 1**, learning curve analysis using the moving average method showed that the learning curve stabilized between cases 51–60. So, we divided the patients into two groups, Group 1 (cases 1-50) and Group 2 (cases 51-111).

Preoperative clinical characteristics of both groups are shown in **Table 1** and two groups were similar to each other as seen. The entire cohort aged 64 years on median (range 44-75), with a median PSA of 7.1 ng/ml. According to D'amico risk classification and biopsy Gleason scores, there was no difference between the two groups before surgery (*P* > 0.05).

Pathological outcomes and clinical follow-up are shown in **Table 2**. PSM rates were 36% for group1 and 18% for group 2, and statistically different (*P* = 0.032). Additionally, extracapsular invasion (ECI) was significantly higher in group 1 (56.5%) than in group 2 (29.5%) (*P* = 0.005). There was no difference between the two groups in terms of pathologic Gleason score; lymphovascular, perineural, seminal vesicle invasion and pathologic T stage (*P* > .05). Multivariate analysis was performed to define whether ECI affected PSM, using logistic regression. As seen in **Table 3**, multiple logistic regression analysis revealed that presence of ECI was an independent factor for PSM associated with the groups (OR: 2.512; 95% CI: 1.055-5.979).

A total of 35 patients underwent extended BPLND during RALP, 20 patients in group 1 (40%) and 15 patients in group 2 (24%). Although lymph node positivity was higher in group 1(25% and 13%, respectively), there was no statistically significant difference between two groups (*P* = 0.24). The median follow-up of entire patients was 11 months and biochemical recurrence (BCR) rates were 12% and 6,6% in group 1 and 2, respectively (*p* = 0.99). A total of 7 patients with positive lymph nodes received early hormone therapy and 10 patients with BCR directed to radiotherapy. Although patients in group 1 needed more additional treatment (22% and 9,8%, respectively), there was no statistically significant difference between two groups (*P* = 0.153).

Patients with PSM are analyzed in subgroups and relationship between PSM and pT stage, lymphovascular, perineural, extracapsular invasion are shown in **Table 4**.

Operative parameters are shown in **Table 5**. Both operation time (skin to skin time, as defined) and duration of postoperative hospitalization were significantly reduced from group 1 to group 2 (*P* < 0.001). A factor that could affect the operation time is whether BPLND is performed or not. Since the BPLND performed patients were equally distributed in two groups, the effects on the operation time were evaluated as being equal. Hematocrit decrease on the first postoperative day did not show a significant difference between two groups (*P* = 0.587).

The complications were classified using the Clavien system (from 1 to 4) and shown in **Table 6**.[14] A total of 11 patients (10%) (each one suffering single event) had complications and one of them (0.9%) required surgical intervention. This patient had adhesions due to previous peritonitis surgery, and ileal perforation was detected when he was explored due to the acute abdomen on the 2nd postoperative day. The ileum was repaired as primary and patient was discharged on the postoperative 9th day. Two patients with urethra-vesical anastomosis stenosis and one patient with urethral stricture were treated with endoscopic intervention.

DISCUSSION

Radical prostatectomy is a complex surgery combined of extraction and reconstruction of tissues. Robotic surgery has the advantage to simplify this complex procedure with its excellent three-dimensional vision and high motion range endo-wrist instruments. After the introduction of RALP, there has been a rapid increase in daily practice and interest in robotic surgery. But it should be kept in mind that, as with any new surgical technique RALP also have a learning curve. There is no consensus regarding the optimal way of detecting the learning curve of a surgical procedure but traditionally, the operative time has been widely used to assess this. Zorn et al. suggested that 120 RALP cases are needed to achieve a skin-to-skin operation time under 4 hours.[15] Ou et al. reported that the console time becomes gradually shorter with every 50 cases experience in their study.[16] In our study; operation time, described as

Table 4. Comparison of pathological parameters in patients with PSM between two groups

PSM (n:29)		Group 1(1-50)	Group 2 (51-111)	*p*-value
Lymphovascular invasion, n(%)	No	10(55.6)	9(81.8)	0.234
	Yes	8(44.4)	2(18.2)	
Perineural invasion, n(%)	No	2(11.1)	3(27.3)	0.339
	Yes	16(88.9)	8(72.7)	
Extracapsular invasion, n(%)	Yes	0(0)	6(54.5)	0.001
	No	18(100)	5(45.5)	
Pathological Stage n(%)	T2	5(27.8)	5(45.5)	*
	T3A	6(33.3)	4(36.4)	
	T3B	7(38.9)	2(18.2)	

Table 5. Comparison of operative parameters of both groups

	Group 1(1-50)	Group 2 (51-111)	*p*-value
Operation time, (mean ± SD) min	257.1 ± 32.7	174.4 ± 41.3	< 0.001
Duration of hospitization (min-max)	4 (2-9)	3 (2-8)	< 0.001
Hematocrit decrease median (min-max)	4.5 (0.7-10.9)	3.3 (0.5-14.5)	0.587
BPLND, n(%)	20 (40)	15 (24)	0.376
NVB preservation, n(%)	18 (36)	29 (47)	0.403

skin-to-skin time, was used to detect the learning curve. We used the moving average method to find the cut-off point for a learning curve in RALP, as used in the literature before.[17,18] We found that at least 50 RALP cases are needed to gain proficiency even for an experienced surgeon in laparoscopic radical prostatectomy. To our understanding, reducing docking time with the more rapid determination of trocar positions and placement affected the operation time as well as improvements in surgical technique.
The independent risk factors for disease recurrence and progression after radical prostatectomy are the presence of PSM, preoperative PSA, pathologic Gleason score and seminal vesicle involvement.[19] Among these, PSM is the only factor dependant on surgical experience. The main purpose of any urologist performing radical prostatectomy should be to reduce PSM rate and prevent disease recurrence. In the most extensive literature review, Novara et al. reported a 15% mean rate of PSMs in RALRP series published between 2008 and 2011 (each including >100 cases), with a range of 6.5–32% and concluded that PSM rate is higher in men with a more advanced pathologic stage.[20] Our study included a single surgeon with open and laparoscopic surgical background in radical prostatectomy and yielded that PSM rate has decreased dramatically from 36% to 18% after first 50 patients. But the higher rate of ECI in group 1 directed us to make a multivariate analysis to find out the effect of ECI on PSM. In this analysis, we found that the presence of extracapsular invasion was an independent factor for PSM and affected the PSM rates in both groups. From this point of view, we feel that the learning curve does not play a significant role in pathologic outcomes of RALP.
We performed video documentation in all RALPs and reviewed our records in correlation with pathological reports to improve our technique. According to discussions with pathologists we made minor modifications in our technique after 40 patients. After dissecting seminal vesicles from a posterior approach we continued dissection until neurovascular bundle and apex appear, then turned in anterior approach and completed NVB dissection, dorsal venous complex ligation, and urethral incision in a traditional way. In Tewari's series, this retroapical technique decreased the authors' rate of PSMs from 4.4% to 1.4% and we believe that this modification had an effect in our lower PSM rate in the second group.[21]
Although positive margins in prostate cancer are considered an adverse oncologic outcome, their long-term impact on survival is highly variable and largely influenced by other risk modifiers.[22] BCR rates for RALP differs with follow-up time in different series. Propiglia et al. and Asimakopoulos et al. reported their BCR rates as 2,0% and 4,4% respectively, with a 12 months follow-up.[23,24] Park et al. and Ploussard et al. found BCR rates as 13,1% within 19 months and 10,3% within 15 months follow-up, respectively.[25,26] In our study, we had a BCR rate as 12% in Group 1 with 15 months of follow-up and 6,6% in Group 2 with a 6 months follow-up. The rates of need for additional therapy were 22% and 6,6% (p = 0,153) in Group 1-2, respectively. Although follow-up period was short these findings were consistent with the literature.
We classified our complications using Clavien system and our 10% complication rate is within average when compared with newer series ranging from 5,08% to 19,6%.[16,27] In Patel's series with 2500 cases, a single surgeon had low complication rates of 5,08% in a large volume center and demonstrated a tendency to decrease with increasing experience of the surgeon.[28]
This study has some limitations. Although it was based on a prospective database the study was retrospective. Also, the follow-up period is relatively short and oncological outcomes such as BCR require further observation. Lastly, the cohort was small with 111 cases and a study with larger sample size could demonstrate the effect of learning curve on PSM better.

Table 6. Classification of complications occurred in entire patients using Clavien system

	Number (by event)	Detail
Clavien 1	5	Lymphocele(2), urine leakage(1), intraoperative tachycardia(1), umblical wound infection(1),
Clavien 2	2	Blood transfusion(2)
Clavien 3	3	Urethral stricture(1), urethra-vesical anastomosis stenosis (2)
Clavien 4	1	Ileum perforation(1)

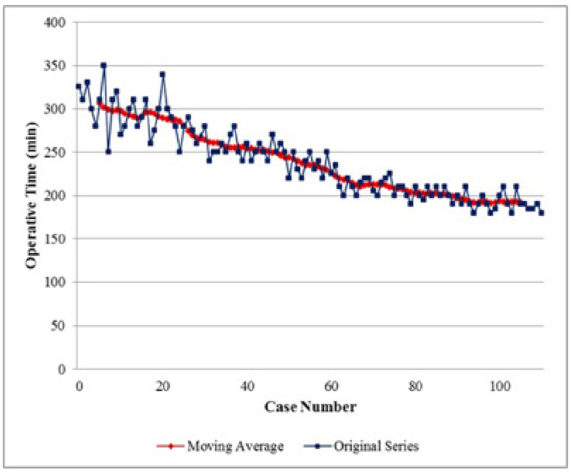

Figure 1. Time taken to perform RALP in each case. Moving average curve of RALP.

CONCLUSIONS

We can conclude that at least 50 RALP cases are needed to gain proficiency even for an experienced surgeon in laparoscopic radical prostatectomy. Our study demonstrates that surgeons experience can affect the perioperative variables but the learning curve does not affect PSM status in RALP.

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CONFLICT OF INTEREST

No competing financial interests exist.

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