# LEARNING CURVE OF ROBOTIC RADICAL PROSTATECTOMY

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# ABSTRACT

Introduction: Prostate cancer (PrC) is the fifth most common malignancy worldwide and the second most common malignancy in men. Currently, robotic-assisted laparoscopic radical prostatectomy (RARP) has become a popular treatment for localised PrC treatment worldwide. We aimed to assess the learning curve of RARP in our institution.

Methods: A total of 391 patients who underwent RARP in our clinic between February 2009 and April 2013 were included in the study. We retrospectively evaluated patient data that were recorded prospectively. The demographic, perioperative, postoperative functional, and oncological results of six surgeons' patient groups (n=72, n=110, n=103, n=38, n=36, and n=32) and three consecutive series formed by dividing the patient groups of the three surgeons with the highest volume of cases were analysed.

Results: There was no significant difference between patient groups with regard to age, American Society of Anesthesiologists score, preoperative International Prostate Symptom Score, International Index of Erectile Function (IIEF) score, number of previously performed operations, prostate-specific antigen levels, clinical stage, biopsy pathology, pathological stage, positive surgical margin (PSM) rate, biochemical recurrence (BCR) rate, potency, and continence rate at postoperative Month 12. When we assessed the three consecutive series of the three highest-volume surgeons we found that, over time, operation time (OT) decreased significantly (p<0.001), blood transfusion rate decreased significantly (p=0.015), estimated blood loss (EBL) decreased (p>0.05), and median IIEF score at 12 months improved significantly (p<0.001) in the series of Surgeon 1; OT decreased significantly (p<0.001), EBL decreased (p>0.05), and median IIEF scores at 12 months improved significantly (p<0.001), and PSM rate decreased and median IIEF scores at 12 months improved (p>0.05 for both) in the series of Surgeon 3. The overall complication rate was 2%. The overall PSM rate was 20.4% (9.3% for pT2 tumours and 44% for pT3 tumours). The overall rate of BCR was 9.4%.

Conclusion: In our clinical experience, OT, EBL, and blood transfusion rate seem to decrease during the learning curve of RARP.

<u>Keywords:</u> Prostate cancer, robotic-assisted laparoscopic radical prostatectomy (RARP), prostate-specific antigen (PSA), positive surgical margin (PSM) rate.

### INTRODUCTION

Prostate cancer (PrC) is the fifth most common malignancy worldwide and the second most common malignancy in men.<sup>1</sup> In Turkey, PrC is the second most common type of cancer following lung cancer.<sup>2</sup> In men with localised PrC and a life expectancy >10 years, the 'gold standard' treatment option is radical prostatectomy (RP). Currently, minimally invasive techniques are improving and are becoming more preferable for surgeons, as well as for patients. Laparoscopic radical prostatectomy (LRP) and, subsequently, roboticassisted laparoscopic radical prostatectomy (RARP) have become attractive treatment modalities for urologists and patients in Europe and the USA. RARP was first performed by Binder and Kramer in 2000.<sup>3</sup> Currently, it is the most common technique for RP in the USA and the numbers are growing in Europe.<sup>4</sup>

We have been performing RARP in our hospital since February 2009. The learning curve is an important factor in surgical procedures that have many variables. Patel et al.<sup>5</sup> reported the learning curve of RARP as 25 cases. In this study we evaluated the learning curve of RARP in our institution.

### **METHODS**

Overall, 391 patients who underwent RARP in our clinic between February 2009 and April 2013 were included in the study. Patients with missing data, those lost to follow-up, and data from surgeons who had performed <5 procedures were excluded.

We retrospectively analysed the data that were prospectively recorded. There were six surgeons and the patients were divided into six groups according to the surgeon (Group 1: n=72, Group 2: n=110, Group 3: n=103, Group 4: n=38, Group 5: n=36, Group 6: n=32). Surgeons 1, 2, and 3 performed the highest volume of procedures and their cases were also examined as three consecutive series in order to evaluate improvement over time. Surgeon 1's three series each included 24 patients, Surgeon 2's three series included 37, 37, and 36 patients, and Surgeon 3's three series included 35, 34, and 34 patients. Demographic, perioperative, postoperative functional, and oncological results were analysed.

PrC was diagnosed by transrectal ultrasoundguided needle biopsy following transurethral prostatectomy and open prostatectomy. Perioperative and short-term post-operative data were recorded. Preoperative data included patient age, body mass index (BMI), serum prostatespecific antigen (PSA) level, Gleason score (GS), clinical stage, American Society of Anesthesiologists (ASA) score, International Prostate Symptom Score (IPSS), and International Index of Erectile Function (IIEF) score. Perioperative data included operation time (OT), anastomosis time, estimated blood loss (EBL), blood transfusions, and complications. Postoperative data included complications and pathological results including margin status, biochemical recurrence (BCR), continence, and potency status. For potency, Questions 1-5 and 15 of the IIEF questionnaire were used. We considered the use of 0-1 pads as continent, 2 pads as mild incontinence, and >2 pads as severe incontinence. Clinical staging was performed according to the 2002 TNM classification.

All operations were performed using the transperitoneal five-port technique. We used the da Vinci S<sup>™</sup> surgical robot (Intuitive Surgical, Inc., Sunnyvale, California, USA) in our operations. Nerve sparing was applied to all patients with clinical stage T1-T2a and GS <7, as well as selected patients with clinical stage T2b-T2c and GS >8.

#### **Statistical Analysis**

Statistical analysis was performed using the SPSS program for Windows 11.5 (SPSS, Chicago, Illinois, USA) and by applying the one-way ANOVA, Kruskal-Wallis test, post-hoc Tukey's test, Conover's practical nonparametric statistics, Pearson's chi-squared test, and Fisher's exact test. A p value <0.05 was considered statistically significant.

#### RESULTS

The clinical characteristics of the patients are summarised in Table 1. Patient age, total/free PSA levels, and ASA scores were similar between the different surgeon groups. Mean BMI was significantly higher in Surgeon 1's group compared with Surgeon 3's group (p=0.041), and patients in Surgeon 1's group displayed a significantly lower median prostate weight than those in the groups of Surgeons 2, 3, 5, and 6. Patients in Surgeon 4's group displayed a significantly lower mean prostate weight than those in the groups of Surgeons 2, 5, and 6 (p=0.007).

Preoperative GSs were similar between surgeon groups (p=0.906). Most of the patients had GS

3+3 PrC, with the proportion of these patients in each of surgeon groups 1-6 being 67.6%, 66.4%, 65%, 68.4%, 65.7%, and 58.1%, respectively. There was no statistically significant difference between surgeon groups in terms of clinical stage (p=0.243). Most of the patients displayed a clinical stage of T1c, with the proportion of these patients in each of surgeon groups 1-6 being 61.1%, 59.1%, 50.5%, 57.9%, 52.8%, and 40.6%, respectively. Preoperative IIEF scores and IPSS scores were also similar between the surgeon groups (p=0.350 and p=0.203, respectively).

The OT, EBL, and blood transfusion rates were compared between the surgeon groups and between the three consecutive series from the three surgeons with the highest volume of procedures. The median OTs in surgeon groups 1-6 were 215 mins (range: 90-360), 142.5 mins (range: 115-300), 137.5 mins (range: 95-275), 130 mins (range: 125-135), 110 mins (range: 95-115), and 125 mins (range: 95-145), respectively. The median EBLs in surgeon groups 1-6 were 150 cc (range: 40-1500), 100 cc (range: 30-1100), 100 cc (range:

20-500), 100 cc (range: 50 400), 100 cc (range: 50-800), and 100 cc (range: 20-400), respectively. The rates of blood transfusion in surgeon groups 1-6 were 8.3%, 0.9%, 0%, 0%, 2.8%, and 0%, respectively.

The rates of complications in surgeon groups 1-6 were 20.8%, 16.4%, 8.7%, 2.6%, 5.6%, and 3.1%, respectively. The overall complication rate was 11.7%. 34% of the complications were major and 66% of them were minor ones. Postoperative GS and positive surgical margin (PSM) rates were similar between surgeon groups (p=0.133 and p=0.177, respectively). The rates of BCR in surgeon groups 1-6 were 6.9%, 14.5%, 7.8%, 5.3%, 8.3%, and 9.4%, respectively, with no statistically significant difference (p=0.439). The 12-month continence rates of surgeon groups 1-6 were 94.4%, 99.1%, 96.1%, 97.3%, 91.7%, and 93.5%, respectively, with no statistical significant difference (p>0.05). The overall potency rate at 12 months was 53.4% and the overall continence rates at 3 months and 12 months were 60% and 94.8%, respectively.

Patient group	Age, years	BMI	t-PSA	f-PSA	Prostate weight, g	ASA 1/2/3
Surgeon 1 (n=72)	62.4±6.3	27.3±3.4ª	6.5 (1.4-32.0)	1.06 (0.07-6.40)	48.5 (18-100) <sup>a,b,c,d</sup>	4/63/5
Surgeon 2 (n=110)	61.0±6.8	26.5±1.9	7.6 (1.1-78.0)	1.09 (0.03-14.30)	55 (20-112) <sup>b,e</sup>	9/101/0
Surgeon 3 (n=103)	61.6±5.6	26.3±1.4ª	6.9 (1.2-170.0)	1.02 (0.04-5.98)	52 (30-140)ª	12/91/0
Surgeon 4 (n=38)	60.9±6.8	26.5±1.4	6.6 (0.4-21.0)	1.00 (0.10-7.36)	46 (25-115) <sup>e,f,g</sup>	1/36/1
Surgeon 5 (n=36)	62.8±7.1	26.8±1.5	5.8 (2.2-30.0)	0.97 (0.62-5.20)	60 (22-105) <sup>c,f</sup>	5/31/0
Surgeon 6 (n=32)	62.7±5.8	26.8±1.2	10.0 (0.3-45.0)	1.26 (0.57-4.26)	60 (27-130) <sup>d,g</sup>	3/29/0
p value	0.460*	0.041*	0.051**	0.150**	0.007**	0.051**

Table 1: Patient characteristics according to surgeon groups.

\*One-way ANOVA; \*\*Kruskal-Wallis test; aStatistically significant difference between Surgeon 1 and Surgeon 3 groups (p<0.05); bStatistically significant difference between Surgeon 1 and Surgeon 2 groups (p=0.005); cStatistically significant difference between Surgeon 1 and Surgeon 5 groups (p=0.006); dStatistically significant difference between Surgeon 1 and Surgeon 6 groups (p=0.004); eStatistically significant difference between Surgeon 2 and Surgeon 4 groups (p=0.046); fStatistically significant difference between 5 groups (p=0.028); gStatistically significant difference between 5 groups (p=0.028); gStatistically significant difference between 5 groups (p=0.018).

BMI: body mass index; t-PSA: total prostate-specific antigen; f-PSA: free prostate-specific antigen; ASA: American Society of Anesthesiologists score.

#### Table 2: Perioperative outcomes and PSM rates of the three surgeons with the highest surgical volume.

Outcome	Series 1	Series 2	Series 3	p value
OT				
Surgeon 1	227.5 (90-380)ª	215 (130-320) <sup>b</sup>	122.5 (100-280) <sup>a,b</sup>	<0.001*
Surgeon 2	155 (115-300) <sup>a,c</sup>	120 (95-176)°	120 (95-155)ª	<0.001*
Surgeon 3	120 (105-275)ª	131 (100-172) <sup>b</sup>	110 (95-165) <sup>a,b</sup>	<0.001*
EBL				
Surgeon 1	215 (40-1000)	125 (40-400)	150 (50-1500)	0.260*
Surgeon 2	150 (30-500)	100 (50-1100)	100 (50-1000)	0.596*
Surgeon 3	150 (50-500) <sup>a,c</sup>	100 (50-300) <sup>b,c</sup>	50 (20-500) <sup>a,b</sup>	<0.001*
Blood transfusion				
Surgeon 1	5 (20.8%)°	O (0.0%) <sup>c</sup>	1 (4.2%)	0.015**
Surgeon 2	0 (0.0%)	0 (0.0%)	1 (2.8%)	0.324**
Surgeon 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
PSM		İ		
Surgeon 1	3 (12.5%)	5 (20.8%)	3 (12.5%)	0.662**
Surgeon 2	10 (27.0%)	8 (21.6%)	12 (33.3%)	0.532†
Surgeon 3	7 (20.0%)	7 (21.2%)	5 (14.7%)	0.766†
pT2 – PSM				
Surgeon 1	0 (0.0%)	0 (0.0%)	1 (4.2%)	0.329**
Surgeon 2	5 (13.5%)	5 (13.5%)	1 (2.8%)	0.152**
Surgeon 3	3 (8.6%)	0 (0.0%)	2 (5.9%)	0.121**
pT3 – PSM				
Surgeon 1	3 (12.5%)	5 (20.8%)	2 (8.3%)	0.448**
Surgeon 2	5 (13.5%)	3 (8.1%) <sup>b</sup>	11 (30.6%) <sup>b</sup>	0.033†
Surgeon 3	4 (11.4%)	6 (18.2%)	3 (8.8%)	0.505**

\*Kruskal-Wallis test; \*\*Likelihood-ratio test; <sup>+</sup>Pearson's chi-squared test; <sup>a</sup>Difference between Series 1 and Series 3 is statistically significant (p<0.01); <sup>b</sup>Difference between Series 2 and Series 3 is statistically significant (p<0.05); <sup>c</sup>Difference between Series 1 and Series 2 is statistically significant (p<0.05). OT: operation time; EBL: estimated blood loss; PSM: positive surgical margin.

The three consecutive series of the surgeons with the highest volume of cases (Surgeons 1, 2, and 3) were compared with regard to OT, EBL, blood transfusion rate, and PSM rate (Table 2). In the three series of Surgeon 1, OT decreased significantly between consecutive series (p<0.001). In the three series of Surgeon 2, OT decreased significantly between the first and second series, although not between the second and third series (p<0.001). In the three series of Surgeon 3, OT decreased significantly between the second and third series. EBL decreased significantly in each consecutive series of Surgeon 3 (p<0.001), whereas EBL in the consecutive series of Surgeons 1 and 2 displayed a trend towards being lower in the second and third series compared with the first series, although this failed to reach statistical significance (p>0.05). The blood transfusion rate was significantly higher in Surgeons 1's first series compared with the second and third series (p=0.015). Overall, PSM rates did not change significantly in any of the three surgeons' series, although the rate in Surgeon 2's third series was significantly higher than in the second series with regard to pT3 stage tumours.

The median IIEF scores of Surgeon 1's group at 12 months were 13 (range: 6-26) for the first series, 6 (range: 6-24) for the second series, and 21 (range: 6-25) for the third series, which showed a significant improvement in the third series (p<0.001). The median IIEF scores of Surgeon 2's group at 12 months were 6 (range: 6-26) for the first series, 18 (range: 6-26) for the second series, and 18 (range: 6-28) for the third series, which showed a significant improvement in both the second and third series (p=0.01). The median IIEF scores of Surgeon 3's group at 12 months were 19 (range: 6-26) for the first series, 16 (range: 6-25) for the second series, and 20 (range: 6-28) for the third series, which showed no statistically significant difference between series (p>0.05). The continence rates for Surgeon 1's group at 12 months were 95.8%, 83.3%, and 100% for the first, second, and third series, respectively. The continence rates for Surgeon 2's group at 12 months were 100%, 97.3%, and 100% for the first, second, and third series, respectively. The continence rates of Surgeon 3's group at 12 months were 91.4%, 100%, and 97% for the first, second, and third series, respectively. The 12-month continence rate of Surgeon 1's group was significantly lower in the second series than in the first and third series (p=0.017), but there was no significant difference in the series of Surgeon 1 and Surgeon 2 (p>0.05).

# DISCUSSION

RARP has become a frequently applied surgical modality in the treatment of localised PrC. RARP is both a well-tolerated and quick-to-learn procedure relative to LRP.<sup>6</sup> Patel et al.<sup>5</sup> reported that 25 cases are required in order to complete the learning curve of RARP. In fact, every individual has his/her own learning curve and the number of cases needed to become proficient varies.

In our study, BMI was significantly higher in Surgeon 1's patient group than Surgeon 2's group. Agarwal et al.<sup>7</sup> and Gumus et al.<sup>8</sup> reported BMI values similar to those in our study. Prostate weight was significantly different between the surgeon groups in our study. The patient groups of Surgeon 1 and Surgeon 4 had significantly lower prostate weights compared with the other groups. Median prostate weight ranged between 46-60 g when considering all the surgeons' patient groups. Agarwal et al.<sup>7</sup> and Sharma et al.<sup>9</sup> reported similar mean prostate weights in their studies.

In our study, we divided the three surgeon groups with the highest number of cases into three consecutive series in order to evaluate parameters related to the learning curve. The OT, EBL, and blood transfusion and PSM rates were compared between the three consecutive series in each of these three surgeon groups. The OT decreased significantly in the third series of Surgeon 1 (after 48 cases), in the second series of Surgeon 2 (after 74 cases), and in the third series of Surgeon 3 (after 69 cases).

Doumerc et al.<sup>10</sup> reported that a surgeon with experience of 2,000 open RP procedures had to perform 110 RARP procedures in order to be able to complete it in <3 hours. On the other hand, Gumus et al.<sup>7</sup> reached 168 minutes after the first 40 cases. Therefore, our results seem to be similar with these previous studies. EBL is another important parameter in the evaluation of the learning curve. Stolzenburg et al.<sup>11</sup> reported EBL as 254 cc during their learning curve. In our study, EBL was 150 cc in Surgeon 1's series and 100 cc in both the other surgeons' series. We did not detect a significant decrease in EBL, except in Surgeon 3's consecutive series. The blood transfusion rate has been reported by other groups as being 17%<sup>12</sup> and 2.2%.<sup>7</sup> The blood transfusion rate in our study was 2%. Surgeon 1's group had a higher blood transfusion rate compared with the groups of Surgeon 2 and Surgeon 3. Overall, EBL and blood transfusion rates in our study were in accordance with the published literature. Furthermore, our total complication rate of 11.7% was similar to those reported in larger studies.<sup>7</sup>

The primary goal of all RP techniques is to eradicate the disease. Therefore, the PSM rate is also very important. Even during the learning curve, the PSM rate should be at least 'acceptable'. Villamil et al.<sup>13</sup> reported an overall PSM rate of 21% in their series of 300 patients (16.6% in pT2 and 27.7% in pT3 disease); dividing these patients into three groups of 100 gave chronological PSM rates of 28%, 20%, and 16%. Our overall PSM rate was 20.4%, with a rate of 9.3% in pT2 patients and a rate of 44% in pT3 patients. Although we did not detect a significant decrease in the three series, there was an increase in Surgeon 2's series. We think this may be because our surgeons are still on the learning curve in terms of PSM, and some researchers suggest that the 'tipping point' for reducing PSM rates takes longer than for other parameters.<sup>10,14</sup> Another important parameter for disease-free survival is BCR. Our BCR rate was 9.4%, which is similar to previous studies.<sup>7-15</sup>

Although curative treatment is important in PrC surgery, maintenance of quality of life and patient satisfaction in terms of preserving potency and

continence are also important. Tholomier et al.<sup>16</sup> reported that the potency rate for all 722 men in their study was 52% at 12 months. In another study that reports their learning curve, the potency rate at 18 months was 70.7%.<sup>17</sup> Our overall potency rate at 12 months was 53.4%, which was comparable to previous studies. Finally, median IIEF scores at 12 months were significantly improved in the third series of Surgeon 1 and Surgeon 2. In previous studies, continence rates at 3 months were 59.7-65% and were 59-92.5% at 12 months.<sup>7,9,11,18</sup> Our overall continence rates at 3 months and 12 months were 60% and 94.8%, respectively, which are comparable to previously published studies.

# CONCLUSION

There were significant improvements in OT, EBL, and blood transfusion rates with increasing surgeon experience. There was not a significant change in PSM rates. The OT, EBL, blood transfusion rates, overall complication rates, PSM rates, BCR rates, continence, and potency rates were all similar to previously published studies of RARP. Therefore, RARP can be performed relatively safely even in the learning curve period and the outcomes improve with experience.

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