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The Impact of Experience on the Risk of Surgical Margins and Biochemical Recurrence after Robot-Assisted Radical Prostatectomy: A Learning Curve Study

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Abbreviations and Acronyms

BCR = biochemical recurrence

ISUP = International Society of Urological Pathology

PSA = prostate specific antigen

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Purpose: Improved cancer control with increasing surgical experience (the learning curve) has been demonstrated for open and laparoscopic prostatectomy. We assessed the relationship between surgical experience and oncologic outcomes of robot-assisted radical prostatectomy.

Materials and Methods: We analyzed the records of 1,827 patients in whom prostate cancer was treated with robot-assisted radical prostatectomy. Surgical experience was coded as the total number of robotic prostatectomies performed by the surgeon before the patient operation. We evaluated the relationship of prior surgeon experience to the probability of positive margins and biochemical recurrence in regression models adjusting for stage, grade and prostate specific antigen.

Results: After adjusting for case mix, greater surgeon experience was associated with a lower probability of positive surgical margins ($p = 0.035$). The risk of positive margins decreased from 16.7% to 9.6% in patients treated by a surgeon with 10 and 250 prior procedures, respectively (risk difference 7.1%, 95% CI 1.7–12.2). In patients with nonorgan confined disease the predicted probability of positive margins was 38.4% in those treated by surgeons with 10 prior operations and 24.9% in those treated by surgeons with 250 prior operations (absolute risk reduction 13.5%, 95% CI −3.4–22.5). The relationship between surgical experience and the risk of biochemical recurrence after surgery was not significant ($p = 0.8$).

Conclusions: Specific techniques used by experienced surgeons which are associated with improved margin rates need further research. The impact of experience on cancer control after robotic prostatectomy differed from that in the prior literature on open and laparoscopic radical prostatectomy, and should be investigated in larger multi-institutional studies.

Key Words: prostatic neoplasms, prostatectomy, robotic surgical procedures, margins of excision, learning curve

It is widely acknowledged that the outcome of surgery is related to surgeon experience, which is commonly referred to as the learning curve. The learning curve pertains to the general surgical technique and the mastery of specific operating procedures. Studies on the learning curve in urology have become widespread in recent years.[1]

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The relationship between experience and radical prostatectomy outcomes has been previously evaluated.[2] Although it has commonly been shown that surgeon results improve with experience, most learning curve studies have focused on technical aspects such as transfusion and operative time.[3–5] These outcomes are undoubtedly important, particularly with respect to understanding how surgeons master the surgical techniques, but they are less relevant to patients than the main goal of oncologic surgery, which is cancer control.

The impact of experience on the oncologic efficacy of radical prostatectomy has been assessed in open[6] and laparoscopic[7] series. Although the improvement in outcomes was slower for laparoscopy than for the open approach, in those studies a learning curve was found for cancer control. It is notable that the studies included many surgeons from several institutions. In contrast, evidence of the learning curve of robotic prostatectomy is limited. In one of the few studies in the literature the association between experience and recurrence risk was assessed for a single surgeon who converted from open to robotic surgery.[8] Other investigators assessed the learning curve of minimally invasive radical prostatectomy performed by 9 surgeons.[9] However, instead of calculating a learning curve, the authors divided patients into different categories of experience, which is a demonstrably suboptimal method.[10]

Accordingly, we used individual data from our institutional database to assess how the prior experience of a surgeon is related to the oncologic efficacy of robotic radical prostatectomy.

MATERIALS AND METHODS

Our study population consisted of 2,857 patients with clinically localized prostate cancer who were treated with robot-assisted radical prostatectomy between 2006 and 2017 at San Raffaele Hospital, Milan, Italy. We excluded from analysis 275 patients who received neoadjuvant or adjuvant therapy, 269 with missing data on the covariates and 82 treated by surgeons with a total experience of fewer than 50 procedures at the time that the last patient was included in study, leaving 2,231 patients eligible for analysis. Eligible patients were treated at our institution by 1 of 9 surgeons, of whom all but 1 performed their first robotic procedure at our hospital. The surgeon with previous robotic experience reported having done 50 procedures before moving to our institution.

Surgery was performed using a conventional surgical approach to robot-assisted radical prostatectomy.[11] Extended pelvic lymph node dissection was done in patients at greater than 5% preoperative risk for nodal involvement.[12] A nerve sparing technique was offered based on patient and cancer characteristics at diagnosis. All patients underwent preoperative abdominal computerized tomography and bone scintigraphy with preoperative prostate magnetic resonance indicated according to physician preference. The most updated ISUP grading system[13] and TNM classification[14] at the time of evaluation were used. Margin status was defined as a tumor involving the inked resection margin in the surgical specimen.

Followup consisted of serum PSA measurement every 3 months during year 1 after surgery, every 6 months during year 2 and annually thereafter. Biochemical recurrence was defined as PSA greater than 0.2 ng/ml on 2 consecutive measurements.

Surgical experience was coded as the number of prior robotic prostatectomies performed by the surgeon at the time of the index patient operation, including procedures performed in patients ineligible for analysis as well as those done elsewhere. There is evidence that the learning curve for surgical margins and the risk of BCR in the first case of a surgeon did not differ when compared between fellowship and nonfellowship trained surgeons.[15] Thus, procedures in which the surgeon was not documented as having primary responsibility (for example during training) were not included as part of the surgeon prior experience. This also allowed us to be consistent with our previous studies on the learning curve.[6,7]

During our preliminary analysis we found that 1 surgeon had almost twice the number of cases as the next most experienced surgeon. Since this could have distorted the estimation of the learning curve,[10] we curtailed surgical experience at 500 procedures. After removing these 404 cases our final cohort for analysis consisted of 1,827 records.

Our analysis consisted of 3 main steps. 1) We performed multivariable logistic regression to assess the association between positive margin status and surgical experience (continuous variable). The model included the covariates total preoperative PSA, pathological ISUP grade (1 vs 2 vs 3 vs 4-5), seminal vesicle involvement, extraprostatic extension, nodal status (pN1 vs pN0 vs pNx) and at least 50 open radical prostatectomies prior to the first robotic case (yes/no). We included robotic surgical experience as a nonlinear term using restricted cubic splines with knots at the quartiles. Since data on different patients treated by the same surgeon correlated, we incorporated surgeon clustering in our analysis using the cluster option in Stata®. To visualize our findings, we calculated the probability of positive surgical margins and the 95% CI of each level of surgical experience by setting variables at the mean.

2) We assessed the relationship between surgical experience and BCR. Since BCR data were available on only 1,283 patients (71%), we investigated whether patients with available or missing BCR data had similar disease characteristics using the Wilcoxon rank sum and chi-square tests.

3) Finally, we performed multivariable Cox regression to evaluate the association between surgeon robotic experience and recurrence after radical prostatectomy. The identified covariates were the same as those described. Similarly we included restricted cubic splines to model the effects of surgical experience on BCR and the cluster option. We then calculated the 5-year probability

of freedom from BCR and the corresponding CIs, and used that likelihood to produce a learning curve according to surgical experience.

RESULTS

Table 1 shows the distribution of surgeons by the total number of procedures performed per surgeon and by the median annual caseload. Although many surgeons had an annual caseload of fewer than 30 procedures, approximately half of the patients were treated by a high volume surgeon with high volume defined as 80 procedures or more per year. Table 2 lists the clinical and pathological characteristics of our cohort according to different levels of surgical experience. Although differences between the groups were statistically significant in some cases, differences between the groups were small.

Our multivariable model to predict positive surgical margins revealed a significant nonlinear association with surgical experience ($p = 0.035$). Figure 1 shows the surgical margin learning curve. The rate of positive surgical margins decreased with increasing surgical experience up to the 250th procedure. Although the risk of positive margins appeared to increase thereafter, the increase was well within the CI and, therefore, consistent with random variation around a constant rate of positive margins. The risk of positive margins for a surgeon with 10 and 250 prior operations was 16.7% and 9.6%, respectively (absolute difference 7.1%, 95% CI 1.7–12.2). When stratified by pathological stage T2 vs T3, the curve of extraprostatic disease was steeper. The risk of positive margins in a patient with extraprostatic disease treated by a surgeon with 10 vs 250 prior operations was 38.4% and 24.9%, respectively (absolute risk reduction 13.5%, 95% CI −3.4–22.5). Interestingly prior open experience did not significantly affect the positive margin rate ($p = 0.4$).

We performed a number of sensitivity analyses. Because the threshold of the number of prior open procedures which should count as sufficient prior open surgery experience is subject to disagreement, we repeated our analyses using thresholds of 100 and 250. For similar reasons we repeated our analyses using different cutoffs of the minimum number of robotic procedures performed by a surgeon to be included in our study (more than 10 and separately more than 25).

The supplementary table (https://www.jurology.com) shows the results. Briefly, although results were above the conventional level of statistical significance in a few cases, our results were not importantly affected with all estimates close to that of our main analysis. Our findings were similarly unaffected when we restricted analysis to patients whose surgeon had performed at least 200 total procedures. The decrease in the positive margin risk was smaller but still present at from 9.6% to 8.1% for a surgeon with 10 and 250 prior procedures, respectively (absolute reduction 1.5%, 95% CI −3.2–7.2). Finally, when we restricted analysis to 447 patients treated by surgeons who had performed fewer than a total of 200 procedures, greater prior experience was still associated with a lower risk of positive margins ($p < 0.0001$).

BCR data were available on 1,283 patients (71%). When compared with patients lost to followup, the group with available BCR data had slightly lower preoperative PSA (median 5.9 vs 6.2 ng/ml, $p = 0.02$) and a lower rate of ISUP grade 2-3 tumors (58% vs 67%, $p = 0.001$). There were 118 BCRs with 3 and 5-year BCR-free probabilities of 92% (95% CI 90–93) and 85% (95% CI 82–88), respectively. A total of 496 and 172 patients who did not experience BCR had available 3 and 5-year followup data, respectively. Median followup in patients without BCR was 32 months (IQR 16–50).

Figure 2 shows the Kaplan-Meier estimates of recurrence-free probability up to 5 years after surgery according to different levels of surgical experience. On multivariable Cox regression the relationship between surgical experience and BCR was not significant ($p = 0.8$). Figure 3 shows the 5-year BCR-free probability after robotic prostatectomy according to increasing surgical experience. Although we did not find an association between experience and recurrence, a clinically relevant reduction in the recurrence rate with increasing experience could not be excluded when considering the 95% CI.

Table 1. *Surgeons and patients by total lifetime and annual number of robotic procedures performed per surgeon*

No. Robotic Prostatectomies	No. Surgeons (%)	No. Pts (%)
Total lifetime:	9 (100)	1,827 (100)
50–149	4 (44)	312 (17)
150–299	2 (23)	288 (16)
300+	3 (33)	1,227 (67)
Annual:	9 (100)	1,827 (100)
Fewer than 30	3 (33)	294 (16)
30–79	4 (44)	718 (39)
80 or More	2 (23)	815 (45)

DISCUSSION

We documented a learning curve for surgical margins after robotic radical prostatectomy. We also found that surgical experience and BCR after robotic prostatectomy were not significantly associated. Thus, increasing experience is not associated with better cancer control after robotic prostatectomy.

Our results showed that prior experience with open surgery was not associated with the risk of

Table 2. *Study cohort clinical and pathological characteristics by surgeon experience at time of index patient operation*

	No. Surgeon Prior Surgeries						
	0–99		100–249		250+		p Value
No. pts (%)	685	(37)	564	(31)	578	(32)	—
Mean ng/ml total PSA (95% CI)	6.0 (4.7–8.2)		6.1 (4.8–8.2)		5.9 (4.6–8.0)		0.5
No. seminal vesicle involvement (%)	18	(3)	22	(4)	20	(4)	0.4
No. extracapsular extension (%)	155	(23)	134	(24)	121	(21)	0.5
No. pathological ISUP grade (%):							
1	226	(33)	168	(30)	210	(36)	0.006
2/3	412	(60)	356	(63)	350	(61)	
Greater than 3	47	(7)	40	(7)	18	(3)	
No. nodal status (%):							
pN0	412	(60)	398	(71)	489	(85)	<0.0001
pN1	13	(2)	15	(2)	10	(1)	
pNx	260	(38)	151	(27)	79	(14)	

positive margins during robotic prostatectomy. It is plausible that absent haptic feedback or a different surgical anatomy entailed by magnified vision[16,17] may limit the translation of important skills from open surgery. A previous laparoscopic series demonstrated similar results,[7] supporting our finding that experience is relatively independent for each surgical approach.

We found no statistically significant association between surgical experience and BCR. This is in contrast to the prior literature on open[6] and laparoscopic[7] radical prostatectomy. A possible explanation of this difference may be the relatively limited number of surgeons in our series, which was 9. Conversely, previous evidence of a learning curve for laparoscopic and open prostatectomy was identified in a much greater number of patients and surgeons.[6,7]

However, it is also plausible that aspects of the robotic technique affect cancer control differently than other surgical approaches. For example, the high dexterity provided by robotic surgery may ease prostate dissection or facilitate the surgeon in thoroughly removing the lymph nodes. Thus, it is possible that robotic prostatectomy ensures proper cancer excision during the early procedures with oncologic efficacy even for less experienced surgeons.

Such a hypothesis seems to contradict our finding of a learning curve for surgical margins. However, the magnitude of the relationship between margin status and recurrence is still debatable.[18] Although positive margins are associated with a higher risk of recurrence,[19] an improved rate for experienced surgeons does not necessarily translate to a lower risk of BCR. Therefore, the learning process for surgical margins might be partially independent of the oncologic efficacy of robotic surgery.

In contrast to our findings, others observed a learning curve for BCR after robotic prostatectomy. For example, Thompson et al described improved

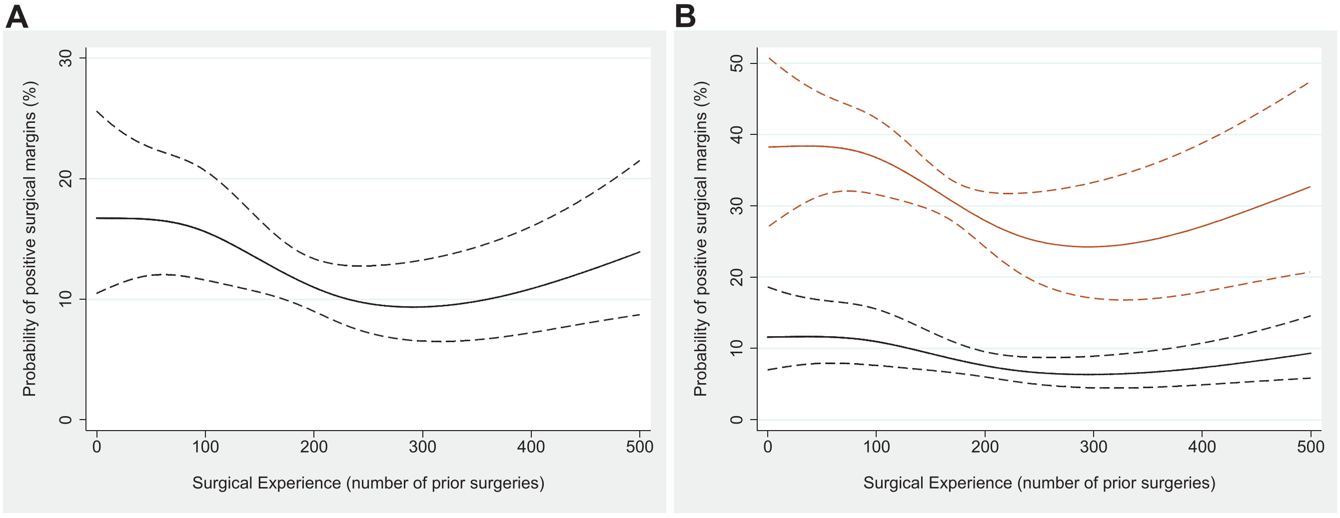
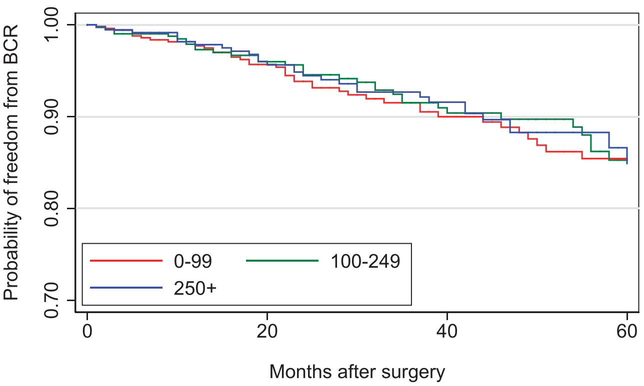


Figure 1. Surgical margin learning curves in patients with typical cancer severity. Predicted probability of positive surgical margins (solid curves) and 95% CI (dashed curves) by increasing surgical experience in entire cohort (*A*) and stratified by organ confined (black curves) or extraprostatic (brown curves) disease (*B*). Dashed curves indicate 95% CI.



Number at risk				
0-99	508	326	167	104
100-249	413	278	159	83
250+	363	252	160	50

Figure 2. Probability of freedom from BCR after robotic radical prostatectomy stratified by number of prior surgeon procedures at time of surgery.

cancer control for a single surgeon after approximately 200 procedures.[8] However, since the learning curve may vary among surgeons, such a study cannot be considered to describe the impact of surgical experience on cancer control for an average surgeon.

A learning curve for BCR was also described in a series of 9 surgeons.[9] Of the 1,701 robotic prostatectomies analyzed the risk of recurrence decreased with increasing experience, which ranged from 0 to more than 1,000 prior procedures. If a surgeon had performed more than 1,000 operations, the obvious corollary is that that surgeon was the only contributor to the right hand tail of the learning curve. As previously described,[10] this may influence the results of learning curve studies. Moreover, the authors assumed a linear relationship between surgical experience and BCR. In contrast, including cubic splines would have allowed for a nonlinear association and, thus, might have affected the results.

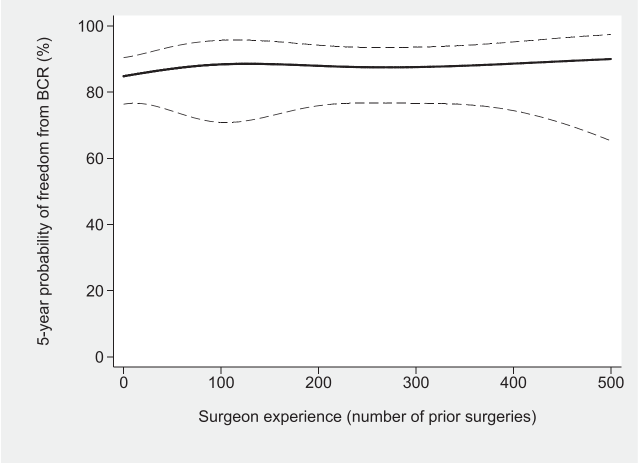


Figure 3. Predicted probability (solid curve) of freedom from BCR after robotic prostatectomy by increasing surgical experience. Dashed curves indicate 95% CI.

Our study has several limitations. Our cohort did not have complete recurrence data available. However, the comparison of patients with available and missing data on BCR showed only small differences. The relatively limited number of surgeons at a single institution may have limited the validity of our findings. Although the single center nature of our study mitigated differences in the surgical technique, disease management (eg the indication for lymphadenectomy) or the definition of biochemical recurrence used,[20] the surgical learning curve of robotic prostatectomy should be further investigated in larger multi-institutional studies. Finally, since rising PSA does not always translate to a higher risk of death from prostate cancer,[21] using BCR as an oncologic surrogate may be problematic. However, BCR invariably precedes stronger oncologic end points such as metastasis and it often triggers postoperative treatments which may be associated with side effects. Thus, it is of direct clinical interest for patients.

Our findings have implications for surgical practice. For example, empirical research should be done to determine how more experienced robotic surgeons avoid positive margins. In this context surgical videos may facilitate the comparison between the techniques of more and less experienced surgeons for delicate steps of surgical dissection, for example at the apex.[22] With respect to research the magnitude of the association between margin status and BCR is currently unclear. Although our results reinforce prior evidence that such outcomes are weakly related,[18] additional research is needed to draw definite conclusions on the reliability of margin status as an oncologic surrogate.

Moreover, future studies should be done to examine the effect of experience on cancer control after robotic prostatectomy. It seems counterintuitive that surgeon results would not improve with experience. However, the relationship between experience and oncologic efficacy may differ for the robotic technique compared to other approaches. Potential reasons may include case selection[23] (do patients treated robotically have better baseline characteristics?), procedure complexity[24] (is the robotic technique easier than other approaches?) and surgical education[25–27] (does robotic surgery allow for better surgical training?). Accordingly more attention should be given to the whole process of learning to improve the surgical quality of robotic radical prostatectomy.

CONCLUSIONS

Increasing prior experience is associated with a lower rate of positive margins during robotic prostatectomy. The impact of experience on BCR after robotic prostatectomy differed from that in the prior literature on open and laparoscopic radical prostatectomy, and should be investigated in larger multi-institutional studies.

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