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Published Version:
Bravi, C.A., Dell'Oglio, P., Mazzone, E., Moschovas, M.C., Falagario, U., Piazza, P., et al. (2023). The Surgical Learning Curve for Biochemical Recurrence After Robot-assisted Radical Prostatectomy. EUROPEAN UROLOGY ONCOLOGY, 6(4), 414-421 [10.1016/j.euo.2022.06.010].

Availability:
This version is available at: https://hdl.handle.net/11585/906094 since: 2022-11-23

Published:
DOI: http://doi.org/10.1016/j.euo.2022.06.010

HHS Public Access
Author manuscript
Eur Urol Oncol. Author manuscript; available in PMC 2024 August 01.

Published in final edited form as:
Eur Urol Oncol. 2023 August ; 6(4): 414–421. doi:10.1016/j.euo.2022.06.010.

The Surgical Learning Curve for Biochemical Recurrence After Robot-assisted Radical Prostatectomy

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Critical revision of the manuscript for important intellectual content: Galosi, Galfano, Schiavina, Suardi, Terrone, Autorino, Carrieri, Briganti, Montorsi, Patel, Mottrie.
Statistical analysis: Bravi, Sjoberg.
Obtaining funding: Vickers.
Administrative, technical, or material support: None.
Supervision: Galosi, Galfano, Schiavina, Suardi, Terrone, Autorino, Carrieri, Briganti, Montorsi, Patel, Mottrie.
Other: None.

Financial disclosures: Carlo A. Bravi certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

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Abstract

Background: Improved cancer control with increasing surgical experience—the learning curve—was demonstrated for open and laparoscopic prostatectomy. In a prior single–center study, we found that this might not be the case for robot-assisted radical prostatectomy (RARP).

Objective: To investigate the relationship between prior experience of a surgeon and biochemical recurrence (BCR) after RARP.

Design, setting, and participants: We retrospectively analyzed the data of 8101 patients with prostate cancer treated with RARP by 46 surgeons at nine institutions between 2003 and 2021. Surgical experience was coded as the total number of robotic prostatectomies performed by the surgeon before the patient operation.

Outcome measurements and statistical analysis: We evaluated the relationship of prior surgeon experience with the probability of BCR adjusting for preoperative prostate-specific antigen, pathologic stage, grade, lymph-node involvement, and year of surgery.

Results and limitations: Overall, 1047 patients had BCR. The median follow-up for patients without BCR was 33 mo (interquartile range: 14, 61). After adjusting for case mix, the relationship between surgical experience and the risk of BCR after surgery was not statistically significant ($p = 0.2$). The 5-yr BCR-free survival rates for a patient treated by a surgeon with prior ten, 250, and 1000 procedures performed were, respectively, 82.0%, 82.7%, and 84.8% (absolute difference between ten and 1000 prior procedures: 1.6% [95% confidence interval: 0.4%, 3.3%). The results were robust to a number of sensitivity analyses.

Conclusions: These findings suggest that, as opposed to open and laparoscopic radical prostatectomy, surgeons performing RARP achieve adequate cancer control in the early phase of their career. Further research should explore why the learning curve for robotic surgery differs from prior findings for open and laparoscopic radical prostatectomy. We hypothesize that surgical education, including simulation training and the adoption of objective performance metrics, is an important mechanism for flattening the learning curve.

Patient summary: We investigated the relationship between biochemical recurrence after robot-assisted radical prostatectomy and surgeon's experience. Surgeons at an early stage of their career had similar outcomes to those of more experienced surgeons, and we hypothesized that surgical education in robotics might be an important determinant of such a finding.

Keywords

Prostate cancer; Radical prostatectomy; Biochemical recurrence; Robot-assisted surgery; Learning curve; Surgical experience

1. Introduction

Surgeon experience is a widely recognized determinant of surgical outcomes [1]. The relationship between surgical experience of the operating surgeon and outcomes, commonly referred to as the learning curve, pertains to the general surgical technique and the mastery of specific operating procedures [2]. Most learning curve studies [3] have focused on technical aspects such as transfusion and operative time [4], and have demonstrated that surgeon performance improves with experience. While important for understanding how surgeons master surgical procedures, such studies are less valuable than those that have the main goal of oncologic surgery, which is cancer control, as an endpoint.

The impact of experience on the oncologic efficacy of radical prostatectomy has been investigated in open [5] and laparoscopic [6] series. These multicenter studies included 72 and 29 surgeons and 7765 and 4792 patients, respectively. There was a large and highly significant difference in the absolute risk of recurrence, about 8%, with the learning curve being slower for the laparoscopic approach.

In contrast, evidence on the learning curve for cancer control after robot-assisted radical prostatectomy (RARP) is limited. In one of the few available studies on this topic, the association between experience and recurrence risk was assessed for a single surgeon who converted from open to robotic surgery [7]. Other investigators assessed the learning curve of minimally invasive radical prostatectomy performed by nine surgeons [8]. However, instead of calculating a learning curve, the authors divided patients into different categories of experience, a demonstrably suboptimal method [9], underestimating the number of the procedures needed to reach the potential plateau of the learning curve. Previously, we assessed the relationship between surgeon's experience and the risk of biochemical recurrence (BCR) after RARP in a single-institution, multisurgeon series [10]. The probability of freedom from recurrence did not change as a function of surgeon experience. However, this may be due to the relatively limited number of cases, single-center experience, and limited number of surgeons included in the analyses.

For these reasons, we built a multi-institutional collaboration to investigate whether prior experience of a surgeon is related to oncologic outcomes after RARP.

2. Patients and methods

2.1. Patient population

We retrospectively analyzed the data of 10 227 patients treated with RARP at nine participating institutions between 2003 and 2021 (Supplementary Table 1). Patients who received adjuvant therapy ($n = 666$; adjuvant therapy defined as additional treatments received within 6 mo from surgery), had missing data for BCR ($n = 1106$), or were treated by a surgeon with a lifetime caseload of fewer than 20 robotic radical prostatectomies (n = 110) were excluded, leaving 8345 patients with complete clinical, pathologic, and follow-up data eligible for analysis. No patient received neoadjuvant therapy. All information was obtained with appropriate ethics committee or institutional review board waivers, and data were made anonymous before analysis.

Eligible patients were treated by one of 46 surgeons. Surgeons who had previously performed RARP before their first robotic procedure on a patient in the study cohort were asked to provide details of their previous caseload. Most surgeons performed their cases at the same institution, whereas two surgeons reported having moved between two institutions included in the study. One surgeon reported having performed the first 1500 cases on nonstudy patients, and the lifetime caseload was calculated accordingly for that surgeon.

2.2. Surgical technique and follow-up

Surgery was performed using a conventional surgical approach to RARP [11]. The indication for pelvic lymph node dissection was based on the preoperative risk for nodal involvement calculated with the most updated nomogram available at the time of surgery [12–15]. A nerve-sparing technique was offered based on patient and cancer characteristics at diagnosis. All patients underwent preoperative abdomen computerized tomography and bone scintigraphy with preoperative prostate magnetic resonance indicated according to physician preference. The most updated International Society of Urological Pathology (ISUP) grading system [16] and TNM classification at the time of evaluation were used. Patients were evaluated 2 mo after discharge and then at least every 4 mo for the 1st year, semiannually for the 2nd year, and annually thereafter [17]. Follow-up visits consisted of a physical examination, serum chemistry evaluation, and diagnostic imaging if necessary.

2.3. Outcome definition

Our primary goal was to investigate the association between surgical experience and cancer control after RARP, namely, BCR after surgery. BCR was defined as a prostate-specific antigen (PSA) level of ≥0.2 ng/ml on two consecutive measurements [17]. Positive surgical margins were defined as a tumor involving the inked resection margin in the surgical specimen. For BCR after surgery, patients were censored on the date of last evidence of freedom from BCR.

2.4. Statistical analyses

Our statistical analyses involved several steps [18]. According to prior methodology [5,6,10], surgeon experience was coded as the number of RARPs done by the surgeon before the index patient's operation [10,19–21]. Surgeon experience was entered as a continuous variable, using restricted cubic splines with knots at the tertiles to allow a nonlinear relationship between experience and recurrence. If a surgeon had performed an open or a laparoscopic radical prostatectomy before his/her first robotic patient, this was recorded, but open and laparoscopic procedures were not counted toward robotic surgical experience. During our preliminary analyses, we found that only one surgeon had carried out >2250 robotic prostatectomies in our dataset. Since this could distort the estimation of the learning curve [9,10], we curtailed surgical experience at 2250 procedures. After removing these 244 cases, our final cohort for analysis consisted of 8101 records.

We assessed the association between surgeon's robotic experience and BCR after surgery using a multivariable Cox regression model. The adjustment for case mix included the following covariates, selected a priori: preoperative PSA, extraprostatic extension at final pathology (no vs yes), seminal vesicle invasion at final pathology (no vs yes), lymph-node involvement at final pathology (pN0 vs pN1 vs pNx), and pathologic ISUP grade (1 vs 2 vs 3 vs 4 vs 5). Moreover, since we found evidence of a stage migration toward more aggressive disease over the period of study (Supplementary Table 2), we included the year of surgery in our model as a continuous variable. Within-surgeon clustering was incorporated into our analyses using the *cluster* option in Stata statistical software. There was no clustering by institution, as there is no plausible mechanism by which an institution could affect the learning curve, given that, with two exceptions, no surgeons moved between institutions. To produce a learning curve, we calculated the 5-yr BCR-free probability predicted by the model for each level of surgical experience, using the mean value for covariates.

We performed a number of sensitivity analyses to assess the robustness of our findings. Since patients treated at one institution received a Retzius-sparing radical prostatectomy, and some authors argued that this surgical technique might affect margin rates [22], we excluded men receiving surgery at this institution. In separate analyses, we repeated our analyses after excluding patients treated at San Raffaele Hospital, as they were part of our prior series [10]. We also repeated the analyses after excluding surgeons who moved between Institutions and the surgeon whose data on initial cases were not available for the analyses. Since the year of surgery might be correlated with surgical experience, we repeated analyses after excluding this covariate. Similarly, we run sensitivity analyses after excluding nodal status at final pathology, a feature that might be influenced by the surgeon's experience. Finally, we assessed the hypothesis that the association between surgical experience and BCR after surgery might differ for those surgeons who have achieved certain technical skills as a result of a large number of cases performed in their career, by excluding patients treated by surgeons who had done >500 procedures.

All statistical analyses were performed using Stata version 14.0 (StataCorp LP, College Station, TX, USA).

3. Results

The distribution of surgeons by the total number of lifetime operations is shown in Table 1. Although around half of the surgeons had performed fewer than 100 RARPs in their career, 15 (33%) surgeons had carried out >100 procedures and five (10%) have performed >500 RARPs.

Clinical and pathologic information of patients is shown in Table 2, stratified by surgeon experience. A total of 2286 (28%) patients were seen by a surgeon who had performed fewer than 100 previous procedures, while slightly more than one-third (38%, $n = 3042$) were seen by a surgeon with experience of >500 previous procedures at the time of their operation. We saw evidence of an association between experience and risk, with patients treated by more experienced surgeons having higher rates of seminal vesicle invasion, higher rates of ISUP group ≥3 tumors, and lymph-node involvement.

3.1. Surgical learning curve for BCR after RARP

There were 1047 cases of BCR, and the median follow-up for patients without BCR was 33 mo (interquartile range: 14, 61). A total of 3326 and 1981 patients who did not experience BCR had, respectively, 3- and 5-yr follow-up data available. The probabilities of freedom from BCR after 3, 5, and 10 yr of surgery were 88% (95% confidence interval [CI]: 87%, 89%), 83% (95% CI: 82%, 84%), and 74% (95% CI: 72%, 75%), respectively.

Figure 1 shows the Kaplan-Meier estimates of recurrence-free probability up to 10 yr after surgery according to different levels of surgical experience. These initial descriptive analyses suggested that there was no association between the probability of recurrence and surgeon's experience. On multivariable Cox regression, the relationship between surgical experience and BCR after RARP was not statistically significant ($p = 0.2$).

As shown in Figure 2, we did not find evidence of an association between the probability of freedom from BCR after 5 yr from RARP and increasing surgical experience. The 5-yr BCR-free survival rates for a patient treated by a surgeon with prior experience of performing ten, 250, and 1000 procedures were 82.5%, 82.7%, and 84.1%, respectively (absolute difference between ten and 1000 prior procedures: 1.6%; 95% CI: 0.4%, 3.3%).

3.2. Sensitivity analyses

We conducted a number of sensitivity analyses (Table 3). We repeated the analyses after excluding patients treated at Niguarda Hospital who received a Retzius-sparing RARP, a technique that might affect surgical outcomes. Similarly, since most of the patients operated at San Raffaele Hospital were included in our prior study [10], we repeated the analyses after excluding these men. Moreover, we excluded patients operated by two surgeons who moved between institutions and, in separate analyses, men treated by the surgeon whose initial cases were not available in our dataset. As shown in Table 3, the relationship between surgeon experience and outcome did not reach the conventional level of statistical significance in all cases.

To focus specifically on the earliest phase of surgical learning, we restricted the analyses to patients operated by surgeons with no more than 500 prior procedures performed at index patient operation. Similar to our main analyses, the relationship between surgical experience and BCR did not reach statistical significance ($p = 1$; risk difference for ten vs 250 previous surgeries of <1.5%). Finally, our results did not change after the exclusion of certain covariates that might be correlated with surgical experience (ie, year of surgery and pathologic nodal status; both $p = 0.2$).

4. Discussion

In contrast to the learning curves previously described for open and laparoscopic radical prostatectomy [5,6], we did not find evidence of improved cancer control after RARP as the experience of the operating surgeon increased.

There are several possible explanations for our findings. First, RARP may be inherently easier to learn than laparoscopic and/or open techniques [23,24]. For instance, laparoscopy requires learning how to operate with instruments that have limited haptic feedback and minimal flexibility, and thus, tissue manipulation may be challenging especially for inexperienced surgeons. Moreover, in a procedure such as radical prostatectomy with a delicate reconstructive phase requiring suturing and knotting skills, this may translate into slower learning for surgeons who start with this technique, reaching surgical proficiency only after a certain number of cases. Instead, other aspects may be problematic for surgeons starting with open surgery. The small pelvis is a challenging surgical field, not easily accessible and with difficult anatomy, requiring high dexterity to perform quality surgery, especially for surgeons in training. Appropriate training for open surgeons may also be limited by the fact that, as compared with minimally invasive techniques, it is more problematic to record high-quality videos of open procedures, which are therefore less reproducible for educational purposes. In this regard, since the operative view during robotic surgery is controlled by the surgeon and thus always focused on the surgical field, educational videos may provide more valuable information for robotic trainees. Among other potential advantages as compared with open surgery, robotics offers a three-dimensional magnified vision, articulating instruments, and lack of hand tremor; all these factors may contribute to improved surgical performance. With respect to laparoscopic surgery, enhanced manipulation of robotic instruments allows surgeons to operate with more precise and fluent movements as compared with traditional laparoscopy. For these reasons, it is plausible that surgeons starting with RARP might be comfortable and efficient in performing surgery from the initial cases.

Another possible explanation for our findings concerns surgical education. If less experienced surgeons had similar outcomes to those of more experienced ones, it is plausible that education in robotic surgery may provide surgeons with better skills, allowing them to perform surgery in their initial cases as good as more experienced surgeons. In recent years, there have been several calls for improvement in how surgeons are trained [25]. Traditional, classroom-based surgical education was usually blamed for suboptimal outcomes of the trainees, and a transition toward more practical training was usually recommended in order to improve surgical education and, in turn, optimize clinical outcomes. With respect to a well-established surgical procedure such as radical prostatectomy, structured training including surgical simulation has already been described for laparoscopic radical prostatectomy [26]. However, whether these programs are actually part of the surgical community remains at least questionable [25]. In addition, the technical challenges of laparoscopy and the growing interest toward robotic surgery opened the discussion of whether robot-assisted surgery might shorten the learning curve of new surgeons approaching radical prostatectomy. In this regard, prior evidence showed that robot-assisted surgery allowed an open surgeon to achieve and overcome outcomes that he/she had with open surgery after a long learning curve [7]. Still, whether this might apply to an average surgeon remained a matter of debate. We here provided evidence that not only robotic assistance might shorten the process of learning, but this may also be possible for the average surgeon. As compared with open and laparoscopic training, robotics allows for more structured, more widely available training programs and surgical curricula [27–30]. Simulation technologies, video review, and, in general, more practical training [31] may be the reason why robotic surgeons in the early phase of their career seem to have outcomes comparable with those of more experienced surgeons. In addition, the development of objective performance metrics [32] as well as the increasing adoption of proficiency-based progression training methodology in robotic surgery [33] may be reasons to explain our findings.

Our findings have implications for empirical research. It seems counterintuitive that surgeon results would not improve with experience. In this regard, it is possible that the surgeons included in our study were not good at learning, barely improving their skills during their career. Although this might explain why more experienced surgeons had recurrence rates similar to those of novices, it may also be a consequence of external modifiers influencing the process of learning. For instance, prior evidence showed that surgeons without fellowship training never improved their rates after open radical prostatectomy [34]. Whether this might be the case for RARP should be investigated in future studies. We also have to acknowledge that, despite our findings, RARP might still allow for a learning curve that we simply failed to detect. In fact, the confidence interval around our learning curve is relatively wide, and it is consistent with a reduction of recurrence rates with higher experience. This is also consistent with a possible learning curve for only a subgroup of patients. Prior research showed a very different learning process for organ- versus non–organ-confined disease [35]. When we replicated these analyses, we found that the relationship between surgeon experience and outcomes was statistically significant only in men with organ-confined disease ($p = 0.0001$; data not shown). In this regard, future research is required to understand what it is that less experienced surgeons are doing that leads to recurrence in organ-confined disease. Other relevant points of attention for empirical research concern the outcomes of interest. If increasing surgical experience does not affect BCR after surgery, whether other aspects of RARP (eg, functional outcomes) might be influenced by surgeon experience remains an open question. We reported that this was the case in our prior single-center study, but further, multi-institutional collaborations should focus on this specific hypothesis. Moreover, our multi-institutional data collection did not include perioperative data. Since these outcomes are demonstrably relevant to patients [36] and institutional health policies, future investigations are awaited to test this research hypotheses.

Our study is not devoid of limitations. First, 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 (Supplementary Table 3). Similarly, the median follow-up for BCR in our cohort was relatively short. That said, we described 5-yr recurrence rates to allow for an adequate number of patients at risk for the estimation. Moreover, prior series on open [5] and laparoscopic [6] radical prostatectomy had similar follow-up length and found a learning curve for BCR. Therefore, we are confident that our findings are not a result of the short follow-up after surgery. Another potential limitation concerns the multi-institutional nature of our dataset. The inclusion of a number of institutions from different regions and health care systems may have resulted in different surgical techniques/practices (eg, patient selection and/or nerve-sparing indications) across centers, the details that might not have been captured in our dataset. For similar reasons, and owing to the retrospective design, we cannot exclude residual confounding from known and unknown variables. For instance, the multi-institutional data collection did not account for central specimen review, a feature that might influence results and outcomes after surgery [37,38]. Similarly, information on how surgeons were trained was not available. However, our results are consistent with prior evidence [10] and were robust to a number of sensitivity analyses. Therefore, we are positive that our findings were not a result of unmeasured confounding. It can also be hypothesized that, since rising PSA does not always translate to a higher risk of death from prostate cancer [39], using BCR as an oncologic surrogate may be problematic. However, BCR invariably precedes stronger oncologic endpoints such as metastasis, and it often triggers postoperative treatments that may be associated with side effects. Thus, it is of direct clinical interest for patients. Furthermore, whether or not we consider BCR to be a strong surrogate for clinically relevant endpoints, it remains an excellent assay of surgical technique. Finally, we have to acknowledge that other metrics of surgical competence—for example, perioperative outcomes, complications, and functional outcomes—might be of interest for surgeons and patients. Although these metrics were not the focus of the present study, we plan to investigate them in future studies.

5. Conclusions

We found that the probability of BCR after RARP seems to be independent of the experience of the operating surgeon. As opposed to the open and laparoscopic approaches, which have a documented learning curve, the absolute risk difference of BCR between experienced and inexperienced surgeons was of no clear clinical relevance in our study. Since patient characteristics and long-term recurrence risk of our cohort are similar to those of prior series, our findings might be taken to suggest that adequate cancer control after RARP is feasible also in the early phase of a surgeon' career. Further research should explore why the learning curve for robotic surgery differs from prior findings for open and laparoscopic radical prostatectomy. We hypothesize that surgical education, including simulation training and the adoption of objective performance metrics, is an important mechanism for flattening the learning curve.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding/Support and role of the sponsor:

This work was supported in part by the National Institutes of Health/National Cancer Institute (NIH/NCI) with a Cancer Center Support Grant to Memorial Sloan Kettering Cancer Center (P30 CA008748), a SPORE grant in Prostate Cancer to Dr. H. Scher (P50-CA92629), and the Sidney Kimmel Center for Prostate and Urologic Cancers.

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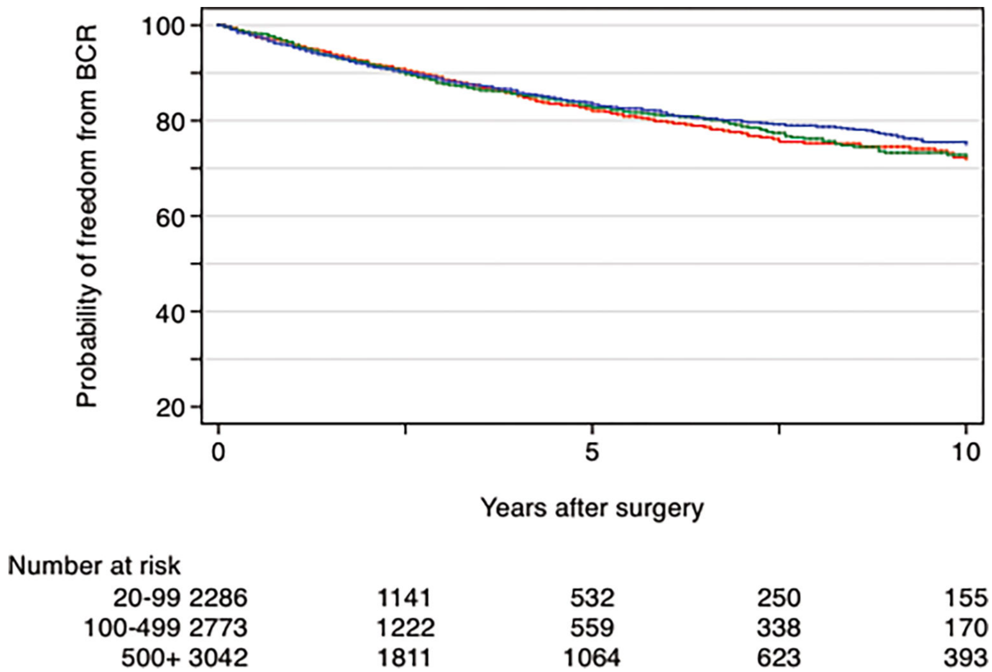

Fig. 1 –.

Kaplan-Meier curves depicting biochemical recurrence–free survival after robot-assisted radical prostatectomy, by lifetime surgical experience of the surgeon. Red line indicates 20–99 procedures, green line 100–499 procedures, and blue line >500 procedures. BCR = biochemical recurrence.

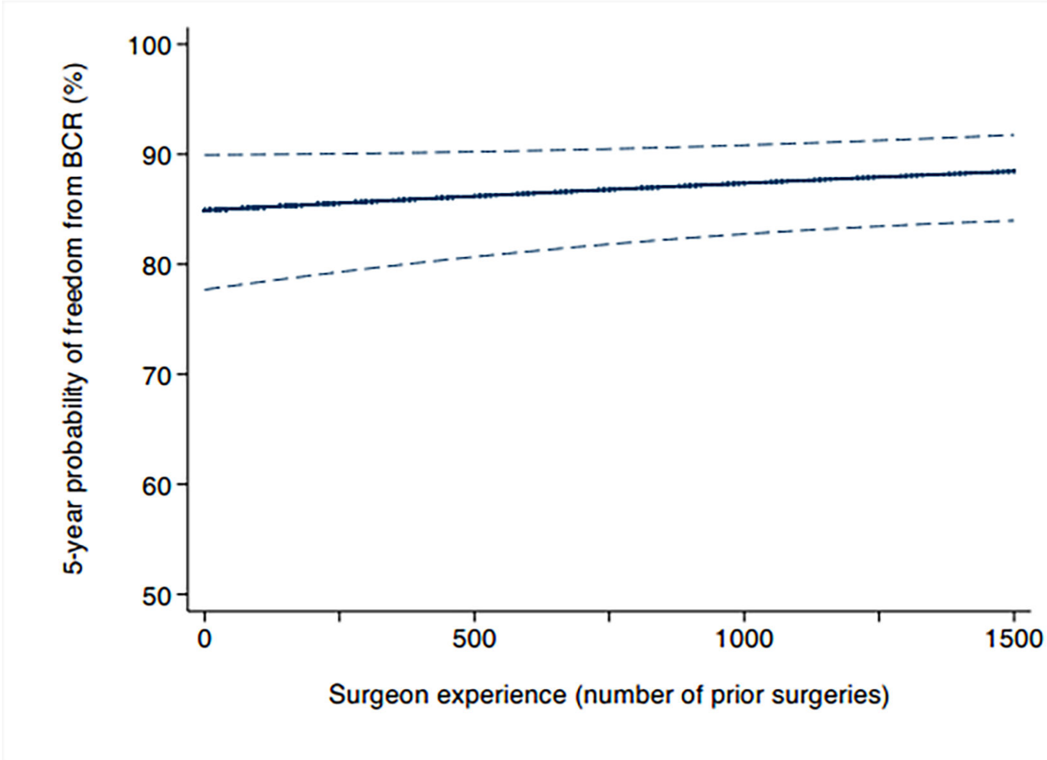

Fig. 2 –.

Probability of freedom from biochemical recurrence 5 yr after robot-assisted radical prostatectomy over surgical experience for a patient with typical cancer severity. Dashed lines indicate 95% confidence interval. BCR = biochemical recurrence.

Table 1 –

Distribution of surgeons and number of patients according to total lifetime number of robotic procedures and median caseload per year per surgeon

	Number of surgeons (%)	Number of patients (%)
Total lifetime number of robotic prostatectomies performed		
20–99	21 (45)	634 (8)
100–299	15 (33)	1753 (22)
300–499	5 (12)	1395 (17)
500–1500	3 (6)	1958 (24)
≥1500	2 (4)	2361 (29)
Total	46 (100)	8101 (100)
Annual number of robotic prostatectomies performed		
≤25	18 (39)	495 (6)
26–49	17 (37)	1937 (24)
50–99	5 (12)	1081 (13)
100–149	4 (8)	3157 (39)
≥150	2 (4)	1431 (18)
Total	46 (100)	8101 (100)

Table 2 –

Clinical and pathologic characteristic of the study cohort by level of experience (prior surgeries) of the surgeon at the time of the index patient's operation

	0–99 (*N* = 2286; 28%)	**100–499 (*N* = 2773; 34%)**	**500+ (*N* = 3042; 38%)**	***p* value**
Preoperative PSA level (ng/ml)	6.4 (4.9, 8.8)	6.4 (4.9, 9.0)	6.3 (4.6, 9.2)	0.6
Extracapsular extension, *n* (%)	688 (30)	815 (29)	920 (30)	0.8
Seminal vesicles invasion, *n* (%)	97 (4)	148 (5)	224 (7)	<0.0001
Pathologic ISUP group, *n* (%)				
1	618 (27)	727 (26)	730 (24)	0.002
2	989 (43)	1201 (43)	1305 (43)	
3	443 (20)	616 (22)	690 (23)	
4–5	236 (10)	229 (9)	317 (10)	
Nodal status at final pathology, *n* (%)				
pN0	1111 (49)	1696 (61)	1148 (38)	<0.0001
pN1	40 (1)	73 (3)	141 (4)	
pNx	1135 (50)	1004 (36)	1753 (58)	
Positive surgical margins, *n* (%)	522 (23)	558 (20) [a]	508 (17) [b]	<0.0001
Patients with pT2	338 (19)	338 (16) [a]	363 (14) [b]	<0.0001
Patients with pT3	185 (35)	221 (35)	145 (30)	0.2

ISUP = International Society of Urological Pathology; PSA = prostate-specific antigen.

[a]Missing in two patients.

[b]Missing in one patient.

Table 3 –

Sensitivity analyses

Analysis	Adjusted *p* value for surgeon experience [a]	Adjusted 5-yr probability of freedom from BCR (%)	
		10 prior RARPs	1000 prior RARPs
Main analysis	0.2	82.0	84.8
Exclude patients treated at specific centers			
Niguarda Hospital (Retzius-sparing technique)	0.2	83.9	85.0
San Raffaele Hospital (included in prior paper)	0.11	83.3	85.6
Exclude two surgeons who moved between institutions	0.13	83.0	85.7
Exclude surgeons whose initial cases were not available	0.6	83.9	82.7
Patients whose surgeon completed ≤500 prior RARPs	1	83.2	81.9 [b]
Exclude covariates			
Year of surgery	0.2	82.7	85.6
Pathologic nodal status	0.2	81.5	83.0

BCR = biochemical recurrence; RARP = robot-assisted radical prostatectomy.

Probabilities are for a patient with typical cancer severity (mean prostate-specific antigen level, pathologic stage and grade, nodal status, and year of surgery).

[a]Test for the association between experience and outcome in the multivariable model (two-sided *p* value).

[b]Calculated for a surgeon who performed 250 prior RARPs.