Positive surgical margin rates during the robot-assisted laparoscopic radical prostatectomy learning curve of an experienced laparoscopic surgeon

Anthony F. Adili, MBBCH; Julia Di Giovanni, MBBCH; Emma Kolesar; Nathan C. Wong, MD; Jen Hoogenes; Shawn Dason, MD, FRCSC; Bobby Shayegan, MD, FRCSC

Division of Urology, McMaster University, Hamilton, ON, Canada

Cite as: *Can Urol Assoc J* 2017;11(11):E409-13 http://dx.doi.org/10.5489/cuaj.4588

Published online November 1, 2017

Abstract

Introduction: Since its introduction, robot-assisted laparoscopic radical prostatectomy (RARP) has gained widespread popularity, but is associated with a variable learning curve. Herein, we report the positive surgical margin (PSM) rates during the RARP learning curve of a single surgeon with significant previous laparoscopic radical prostatectomy (LRP) experience.

Methods: We performed a prospective cohort study of the first 400 men with prostate cancer treated with RARP by a single surgeon (BS) with significant LRP experience. Our primary outcome was the impact of case timing in the learning curve on margin status. Our analysis was conducted by dividing the case numbers into quartiles (Q1–Q4) and determining if a case falling into an earlier quartile had an impact on margin status relative to the most recent quartile (Q4).

Results: The Q1 cases had an odds ratio for margin positivity of 1.74 compared to Q4 ($p=0.1$). Multivariate logistic regression did not demonstrate case number to be a significant predictor of PSM. The mean Q1 operative time was 207.4 minutes, decreasing to 179.2 by Q4 ($p<0.0001$). The mean Q1 estimated blood loss was 255.1 ml, decreasing to 213.6 by Q4 ($p=0.0064$). There was no change in length of hospitalization within the study period.

Conclusions: Even when controlling for copredictors, a statistically significant learning curve for PSM rate of a surgeon with significant previous LRP experience was not detected during the first 400 RARP cases. We hypothesize that previous LRP experience may reduce the RARP PSM learning curve.

Introduction

Robot-assisted laparoscopic radical prostatectomy (RARP) has been widely adopted over the last decade. Estimates from the U.S. suggest that 67% of patients undergoing radical prostatectomy had RARP in 2010, compared to only 8% in 2004.[1] The adoption of any novel surgical techniques is associated with a learning curve that may affect surgical quality. With progression along the RARP learning curve, improvements may be seen in various domains, including operative time, estimated blood loss, positive surgical margin rate, urethrovesical anastomosis time, complications, length of hospital stay, transfusion rate, early continence, potency, and conversion rate.[2]

Positive surgical margin (PSM) rates after RARP range from 6.5–32% and serve as an important marker of surgical quality.[3] A PSM after RARP is independently associated with an increased risk of biochemical recurrence.[3] Patients with a PSM after RARP will also be more likely to receive adjuvant or salvage radiation therapy.[4] An extremely variable learning curve has been documented for PSM rates after RARP — with prior series estimating a plateau in PSM rates after 20 to 1600 cases.[2] It is likely that many factors, including prior experience with non-robotic or pure laparoscopic radical prostatectomy (LRP), may impact the RARP learning curve. In this study, we report the PSM rates during the RARP learning curve of a single surgeon with significant previous LRP experience.

Methods

Study design

Participants were enrolled in this study if they underwent RARP at St. Joseph's Healthcare Hamilton (SJHH) by a single surgeon (BS). Consecutive participants were enrolled in this study from March 2012 to April 2015 after institutional review board approval was obtained. This was a cohort study in which outcomes were prospectively collected. Participants were excluded if they had an aborted procedure, had a conversion to an open surgical approach, were undergoing salvage RARP for radio-recurrent prostate cancer, had suspected stage T4 disease preoperatively, had received a course of neoadjuvant androgen-deprivation therapy, had no malignancy found on the RARP specimen, or were undergoing cytoreductive RARP for oligometastatic disease.

Perioperative management

Participants were diagnosed with prostate cancer by transrectal ultrasound-guided prostatic biopsy. Participants received a preoperative anesthetic consultation and basic laboratory panel. Participants on anticoagulation had a preoperative thrombosis consultation and were bridged as necessary. Participants were permitted to be on low-dose antiplatelets (acetylsalicylic acid 81 mg) if felt necessary by thrombosis physicians. Participants with high-risk disease (prostate-specific antigen [PSA]>20 ng/ml or Gleason 8–10) were staged with a bone scan and computed tomographic (CT) scan of the abdomen and pelvis. Participants with suspected locally advanced disease based on rectal examination or CT scan also underwent preoperative magnetic resonance imaging (MRI). The postoperative course after RARP followed a standardized institutional clinical pathway. Participants routinely did not have a drain placed and went home with a urethral catheter on postoperative Day 1.

Operative technique

All RARP procedures were performed by a single surgeon (BS) using the da Vinci Si surgical system (Intuitive Surgical Inc., Sunnyvale, CA, U.S.). RARP was performed via a transperitoneal approach. Our RARP dissection begins with a limited posterior dissection to identify the seminal vesicles and vasa deferentia, followed sequentially by release of the bladder and development of the retropubic space, bilateral extended pelvic lymphadenectomy, resection of preprostatic fat and nodal tissue, endopelvic fascial incision, bladder neck dissection, an antegrade approach to pedicle division and nerve-sparing, ligation and division of the dorsal venous complex, division of the prostatic apex and urethra, specimen removal, and vesicourethral anastomosis. No significant changes in the RARP technique were made during the study period. Because patients with a low risk of lymph node metastases generally undergo active surveillance at our centre, bilateral obturator fossa lymphadenectomy is routinely performed and submitted with preprostatic nodal tissue for nodal staging. Participants had nerve-sparing when possible, with partial (interfascial or extrafascial) ipsilateral neurovascular bundle sparing for cases of high-volume and/or high-grade disease. Wide neurovascular bundle excision was performed for cases of ipsilateral high-volume and/or high-grade disease with suspected extracapsular extension based on clinical stage, visual inspection, tissue reaction, or MRI findings. Trainees are involved as bedside assistants for the RARP procedure and perform certain steps of the RARP procedure on a trainee console. Despite this, all the dissection during steps relevant to margin status (apical dissection, intrafascial nerve-sparing, bladder neck in extensive tumours) was performed by the operating surgeon (BS).

Prior to performing RARP, the operating surgeon (BS) had performed 600 LRP procedures in independent practice. The technique employed during LRP was transperitoneal and followed a similar approach as that of the RARP procedure. Criteria for preoperative staging, lymphadenectomy, and nerve-sparing were the same for LRP as RARP.

Pathological details

Staging was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC) staging system.[5] A dedicated genitourinary pathologist analyzed each specimen for margin status. Margin positivity was analyzed according to the International Society of Urological Pathology (ISUP) Working Group 5 Consensus.[6] Margins were considered positive if there was tumour located at the inked prostatic margin. The location of margin positivity was recorded. Although comments were made on the extent of margin positivity in certain cases, this was not routinely quantified. Whole-mount sectioning was not performed.

Statistical analysis

The primary outcome of this study was the impact of case timing in the learning curve on margin status. This analysis was conducted by dividing the case numbers into quartiles (Q1–Q4) and determining if a case falling into an earlier quartile had an impact on margin status relative to the most recent quartile (Q4). This was assessed with an odds ratio, with the most recent quartile (Q4) used as a reference. Logistic regression of case number as a continuous variable predictor of margin status was also performed. Copredictors used in the logistic regression model were derived from previous series and included T3 vs. T2 stage, body mass index (BMI), prostate weight, and PSA.[7] Secondary outcomes included the impact of case quartile on operative time, estimated blood loss, and length of hospital stay. Subgroup analysis was conducted to determine the effect of quartile on T2 and T3 PSM rates. Statistical analysis was performed with Medcalc Version 14.8 (Medcalc Software). Odds ratios and their statistical significance were computed in the methods previously described by Altman[8] and Sheskin,[9] respectively. Student's t-testing was used to compare mean values where appropriate. Differences were considered statistically significant when the two-tailed p value was less than 0.05. Where appropriate, the most recent quartile was used as the reference standard, with statistical testing performed in relation to this.

Results

A total of 400 participants met study inclusion criteria. No participants met exclusion criteria, and so this study was an analysis of the first 400 RARP cases performed by the operating surgeon (Table 1). The mean time elapsed during each quartile was 306.8 days, during which a mean of 2.6 cases were performed each week. Median patient age was 63.8 years and median PSA was 6.9 ng/ml.

Overall mean operative duration was 187.2 minutes and mean estimated blood loss was 240.9 ml (Table 2). Bilateral nerve-sparing was performed in 241/400 patients (60.3%). A total of 157/400 (39.3%) patients had pT3 disease and 39/400 (9.8%) had Gleason 8–10 disease on final pathology (Table 3). There were 82 positive margins, of which 53 (64.6%) arose from those with pT3 disease and 29 (35.4%) from those with pT2 disease. Of the 82 positive margins, 43 (52.4%) were positive apical margins.

The first quartile of cases had an odds ratio for margin positivity of 1.74 (95% confidence interval [CI] 0.90–3.36; p=0.1) relative to the most recent quartile (Table 4). The odds ratio for pT2 positive margins was 1.69 (95% CI 0.62–4.58; p=0.30). The odds ratio for pT3 positive margins was 1.45 (95% CI 0.62–3.41; p=0.39). When looking at the second or third quartiles relative to the most recent quartile, no significant differences were noted. Multivariate logistic regression did not demonstrate case number to be a significant predictor of PSM (Exp[B] 0.998; 95% CI 0.994–1.002; p=0.329).

The first quartile operative time was a mean of 207.4 minutes, decreasing to 179.2 by quartile 4 (p<0.0001). The first quartile estimated blood loss was a mean of 255.1 ml and this decreased to 213.6 ml by quartile 4 (p=0.0064). There was no change in length of hospitalization within the study period. Again, there were no differences noted in operative time or estimated blood loss when quartiles 2 and 3 were compared to quartile 4.

Table 1. Baseline characteristics of study participants

Property	Q1	Q2	Q3	Q4	Overall
Case number (n)	1–100	101–200	201–300	301–400	1–400
Start date	3/2012	4/2013	12/2013	9/2014	
Days (n)	384	249	283	210	1126
Cases/week	1.8	2.8	2.5	3.3	2.6
Median age (years)	63.1	64.4	63.4	64.2	63.8
Median ASA	3	2	3	3	3
Median BMI (kg/m^2)	28.7	28.1	30.0	30.0	29.4
Median gland volume (mL)	32.0	33.5	35.0	34.5	34.0
Mean cores positive (n)	4.8	2.8	3.3	3.3	3.6
Median PSA (ng/mL)	6.9	6.9	7.7	6.5	6.9

No statistically significant differences between quartile were noted. ASA: American Society of Anesthesiologists Score; BMI: body mass index: PSA: prostate-specific antigen.

Discussion

In this series of 400 consecutive RARP performed by an experienced LRP surgeon, no learning curve was detected for PSM rates in all cases or in subgroup analysis of pT2 cases or pT3 cases. The learning curve in adopting RARP for surgeons with significant LRP experience is not well-documented. Our literature search has uncovered only a limited number of learning curve series of surgeons with explicitly stated LRP experience (Table 5). Several other authors have also reported that they did not detect a learning curve in PSM rates during their initial experience with RARP, although this was not universal. Comparing these series directly proves difficult due to differing methodology — some authors compare their early RARP outcomes to their most recent LRP outcomes, while others divide their RARP outcomes into groups based on case number.

Abboudi et al[2] have previously suggested in their systematic review that RARP may have a PSM learning curve ranging from 20–1000 or more cases. The generalizability of this finding to our study is limited, as this is based primarily on data from surgeons that had limited laparoscopic experience or limited to no experience with LRP. While RARP and LRP differ in their technical approach, these operations are fundamentally similar in their conceptual and anatomic approach. We hypothesize that this similarity may hasten the RARP learning curve and explain the difficulty in detecting a significant PSM learning curve when adopting RARP after significant LRP experience. Alternate hypotheses as to why a learning curve was not detected in PSM rates during this study include the fact that the learning curve likely occurs within the first 100 cases; subtle differences over time are not reflected statistically; the operating surgeon is still early in the learning curve, with gains occurring later after more than 400 cases; or that more challenging cases were pursued with time that were not reflected by the reported clinicopathological parameters. Ultimately, further followup and perpetual

Table 2. Operative characteristics of study participants

Property	Q1	Q2	Q3	Q4	Overall
Mean OR time (minutes)	207.4*	184.4	177.6	179.2	187.2
Mean estimated blood loss (mL)	255.1*	246.4	248.6	213.6	240.9
Number of transfusions (n)	1	0	1	1	1
No nerve-sparing (n)	23	28	39	24	28.5
Unilateral nerve-sparing (n)	13	9	6	6	8.5
Bilateral nerve-sparing (n)	64	63	50	64	60.3
Length of stay (days)	2	2	2	2	2

*Statistically significant difference relative to most recent quartile (Q4). OR: operating room.

Table 3. Pathological characteristics of study participants

Property	Q1	Q2	Q3	Q4	Overall
Gleason 6 (n)	23	19	19	15	19
Gleason 7 (n)	67	70	65	68	67.5
Gleason 8–10 (n)	7	9	11	12	9.8
ECE (n)	39	29	44	41	38.3
SVI (n)	11	8	17	10	11.5
N1 disease (n)	4	2	4	2	3
Prostate weight (g)	48.4	52.8	52.5	55.1	52.2
Positive margins (n)	29	15	19	19	20.5
T3 positive margins (n)	17	8	16	12	13.3
T2 positive margins (n)	12	7	3	7	7.3
Apical margins (n)	18	10	8	7	10.8

No statistically significant differences were noted between quartiles. ECE: extracapsular extension; SVI: seminal vesicle invasion.

Table 4. All-stage, T3, and T2 margin rates compared between quartile 1 and the most recent quartile (Q4)

Property	All-stage	T3	T2
Q1 positive margins	29	17	12
Q4 positive margins	19	12	7
Odds ratio	1.74	1.45	1.69
95% confidence interval	0.90–3.40	0.62–3.40	0.62–4.60
p	0.1	0.3	0.3

analysis of our outcomes will be necessary to determine whether the PSM rate has actually reached a plateau.

In contrast to our findings with PSM rates, we did detect a reduction in estimate blood loss and operative time with increasing case quartile. These findings are consistent with most previous studies reporting a reduction in operative time and blood loss with increasing experience (Table 5).[2] While these measures do not necessarily reflect surgical quality, they do reflect improved efficiency resulting from familiarity with the procedure and technology.

Limitations of this study include the use of PSM rates as a primary outcome, which is only a surrogate of a clinically meaningful oncological outcome — cancer-specific mortality (CSM). A PSM after RARP has been shown to be independently associated with an increased risk of biochemical recurrence and patients with a PSM after RARP will also be more likely to receive adjuvant or salvage radiation therapy.[3,4] While relevant, the translation of these findings into CSM is unclear.

Additionally, our prospective data collection did not include certain data that would have contributed to this study. Study outcomes (PSM rate, estimated blood loss, and operative time) were not being collected during the LRP era, which may have served as a control group. Finally, functional outcomes were not assessed in this study. Previous studies have suggested that improvements in functional outcomes occur during the RARP learning curve.[2] Given the high survival rates of many patients with localized prostate cancer regardless of margin status, these are important clinical outcomes. Additionally, we could have considered other confounders on the learning curve that have been previously described, such as days between cases.[17]

The study of the RARP learning curve is important because of its relevance in credentialing robotic surgeons. In their recent review, Lee et al have advocated for an increased emphasis on proficiency with basic robotic skills and procedural tasks rather than number of completed cases in robotic surgery credentialing.[18] This fits intuitively with a learning curve whose extent and method of measurement are uncertain. In keeping with this, Lovegrove et al have validated a RARP Assessment Score to assess competency at high-risk steps of RARP.[19] The RARP Assessment Score divides the procedure into 41 steps, which are then rated by a mentor on each case from 0–5. These authors did demonstrate a learning curve in multiple steps and found that the study participants rated the assessment tool acceptable, feasible,

Table 5. Series reporting the robotically assisted laparoscopic radical prostatectomy learning curve of investigators with previous laparoscopic radical prostatectomy experience

Author	Previous experience	Reported learning curve
Jaffe et al 2009[10]	3091 LRP (535 before RARP era), unspecified number of surgeons	189 cases for OR time and PSM rate
Wolanski et al 2012[11]	200–300 each (2 surgeons)	None detected in T2 or T3 PSM rate, 3-month PSA recurrence, OR time – 20 cases
Barret et al 2011[12]	>300 LRPs (2 surgeons)	100 for pT2 PSM
Stolzenburg et al 2013[13]	1000 LRP each (2 surgeons)	Not detected for PSM rate or 3-month detectable PSA value EBL and OR time – not reached in 100 cases
Di Pierro et al 2014[14]	>50 LRP (1 surgeon)	PSM rate not reported, 175 cases for complication rate, OR time declined after first 59 cases
Ku and Ha 2015[15]	369 LRP (1 surgeon)	None detected T2 PSM rate, 3-month intercourse or pad use rate OR time – 20 cases
Wagenhoffer et al 2015[16]	86 LRP (1 surgeon)	Not detected for PSM rate, increased OR time compared to LRP in first 100 cases, less blood loss in first 100 cases

EBL: estimated blood loss; LRP: laparoscopic radical prostatectomy; OR: operating room; PSM: positive surgical margin; RARP: robot-assisted laparoscopic radical prostatectomy.

and having educational impact. This tool, however, is limited by its uncertain translation to relevant oncological or functional outcomes.

Ultimately, credentialing a RARP surgeon will need to integrate an assessment of technical skill, oncological outcomes, functional outcomes, and efficiency-related outcomes. Proficiency will need to be judged based on outcomes, not solely based on surgical volume. Understanding factors that affect the learning curve, such as prior LRP experience, will be important in establishing credentialing standards.

Conclusion

Even when controlling for copredictors, a statistically significant learning curve for PSM rate of a surgeon with significant previous LRP experience was not detected during RARP in this prospective cohort study. We hypothesize that previous LRP experience may reduce the RARP PSM learning curve.

Competing interests: The authors report no competing personal or financial interests.

This paper has been peer-reviewed.

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Correspondence: Dr. Nathan C. Wong, Division of Urology, McMaster University, Hamilton, ON, Canada; nathan.wong@medportal.ca