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Cancer Control, Continence, and Potency After Laparoscopic Radical Prostatectomy Beyond the Learning and Discovery Curves

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Abstract

Purpose: To investigate the results of laparoscopic radical prostatectomy (LRP) beyond the learning and discovery curves of 700 patients previously reported by the authors for potency.
Patients and Methods: Five hundred consecutive patients underwent LRP during a 28-month period with a minimum follow-up of 12 months. Median age (with range) = 61.0 (33–76) years; prostate-specific antigen level = 7.0 (1–37); biopsy Gleason sum = 7 (4–10). Clinical stage was T_1 in 41.0%, T_2 in 54.2%, and T_3 in 4.8%. Nerve preservation (NP) was performed bilaterally in 57.9%, unilaterally in 15.3%, and on neither side in 26.8%.
Results: Median operative time was 157 (91–331) minutes, with no conversions or intraoperative blood transfusions; 0.4% of patients received a transfusion postoperatively, and 4.2% had complications. There were no rectal injuries. The overall positive margin rate was 13.0% and correlated with pathologic parameters. At a minimum of 1 year follow-up (mean = 13.5 (12–36) mos), overall survival was 100%, and biochemical disease-free survival was 98.8%. The pad-free rate was 97.4%. Potency (International Index of Erectile Function-5 score ≥ 17) at a mean follow-up of 13.5 months in previously potent men in their 4th, 5th, 6th, and 7th decades after bilateral NP was 100.0%, 91.8%, 82.9%, and 60.0% and after unilateral NP was 100%, 66.7%, 50.1%, and 0.0%. Overall potency after bilateral neurovascular bundle NVB preservation was 86.9%.
Conclusion: LRP is capable of matching or exceeding the best results for open radical prostatectomy and robot-assisted radical prostatectomy when performed by an experienced surgeon in a high-volume setting. These results suggest that the method used to perform radical prostatectomy is a less important determinant of success than surgical experience.

Introduction

Much has been written on the subject of surgical "learning curve" (LC) for radical prostatectomy (RP): ie, the number of cases that a surgeon needs to complete before inexperience no longer affects results. Importantly, the LC is also lengthened early in the use of a new technique by the development process during which the steps are modified according to patient outcomes. This is the discovery curve (DC).[1] For the results of a novel procedure to be accurately interpretable, both the LC and the DC need to have been overcome by the surgeon who is reporting results.

The LC for open radical prostatectomy (ORP) has been estimated by Vickers and colleagues[2] at 250 cases and that of laparoscopic radical prostatectomy (LRP) at 750 cases.[3] In a previous publication, the authors demonstrated separate learning curves for the different outcome parameters that were measured during and after LRP, reflecting the different degree of technical difficulty of individual components of the procedure.[4] For preservation of potency, which the authors consider to be the most technically challenging facet of RP, the LC plateaued at 700 patients. The LC for the more recently developed technique of robot-assisted RP (RARP) has been estimated as being as short as 8 to 12 cases,[5] but most experienced radical prostatectomists agree that the best possible results for RP appear only to be attained after several hundred cases have been completed, regardless of which technique is used.[6]

Interestingly, the transition for experienced practitioners of ORP to LRP or RARP may not necessarily be easier than for their less experienced colleagues, probably because of the different perspective encountered during minimal access RP (MARP) and the different order of the operative steps. Secin and associates[7] demonstrated that previous open RP experience does not shorten the learning curve for LRP, and Jaffe

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and coworkers[8] showed that previous LRP experience does not shortened the RARP learning curve.

The aim of this article is to investigate the short- and intermediate-term performance of LRP beyond the authors' LC and DC.

Patients and Methods

Five hundred appropriately counselled, consecutive, and consenting patients with $cT_{1–3}$ adenocarcinoma of the prostate who opted for surgery underwent LRP during a 28-month period from 2006 to 2008 (Table 1). This cohort immediately followed the authors' initial experience of 700 cases.[4]

All cases were performed or supervised by a single surgeon (CGE). A five-port, open-access extraperitoneal antegrade laparoscopic approach, as previously described by the authors,[9] was used in low-risk[10] patients, who did not have pelvic lymph node dissection (PLND) performed. Extended PLND was performed in high-risk patients until April 2008 and after that in intermediate- and high-risk patients using a transperitoneal technique previously described by the authors.[11]

Intrafascial nerve preservation, including preservation of the lateral prostatic fascia (LPF), was used for patients with low- and intermediate-risk disease, and an interfascial technique, incising the LPF just above the neurovascular bundle (NVB), was used in high-risk, previously potent patients in whom potency preservation was a priority.

The bladder neck was reconstructed using a posterior "racket-handle" technique after mucosal eversion. The urethrovesical anastomosis was fashioned using five or six interrupted 3/0 Polysorb™ sutures on a 27-mm 5/8 circle needle over a 16F silicone catheter.

The drain was removed when drainage was <100 mL/24 h. Patients were discharged to home when comfortable. Catheters were removed at 8 to14 days, depending on the availability of a member of the operating team to supervise a trial of voiding, all without previous cystography, except after salvage surgery (n = 4) when cystography was performed after 3 weeks. Patients were routinely given ciprofloxacin 500 mg twice daily for 7 days after catheter removal, pending the result of their catheter urine microbiologic evaluation.

Table 1. Patient Demographics

N	500
Age (years)	61.0 (33–76)
Weight (kg)	82.5 (51–123)
BMI (kg/m^2)	26.0 (19–40)
PSA (μg/L)	7.0 (1–37)
Gleason sum	7 (4–10)
Clinical stage	
T_{1a}	0 (0.0%)
T_{1b}	3 (0.6%)
T_{1c}	202 (40.4%)
T_{2a}	193 (38.6%)
T_{2b}	13 (2.6%)
T_{2c}	65 (13.0%)
T_{3a}	23 (4.6%)
T_{3b}	1 (0.2%)

Values are patients or median plus range, except Gleason sum.
BMI = body mass index; PSA = prostate-specific antigen.

Prostate specimens were fully fixed in formalin before their surface was inked, and they were serially sliced from apex to bases at 5-mm intervals. Whole-mount slices were all processed to paraffin wax, embedded, and sections were cut, stained with hematoxylin and eosin, and mounted before microscopic examination by a consultant pathologist.

Continence was defined as freedom from the use of any form of protection (pad or liner). Potency was defined as an International Index of Erectile Function-5 score of ≥ 17 with or without oral phosphodiesterase type 5 inhibitors. Data were patient reported during their outpatient attendance at the hospital using a questionnaire at 3-month intervals during the first year and 6-month intervals thereafter until 5 years. Data were entered by any of the authors into a prospective database using Microsoft Access software (Microsoft Corporation, Redmond, WA) and analyzed using Microsoft Excel 2007 and Analyse-it version 2.08 software (Analyse-it Software Ltd, Leeds, England).

Results

Inpatient results are summarized in Table 2 and outpatient results in Table 3. Perioperative datasets were complete in 100% of patients. Follow-up data were missing in 12 (2.4%) patients, who had chosen to be followed up by their referring urologist and for whom no feedback had been received. Twenty-seven percent of patients had preexisting erectile dysfunction (ED), and 3.8% had commenced neoadjuvant hormonal manipulation by their referring physician. Four percent of patients had a history of transurethral resection of the prostate, and 0.2% of patients had previously had a bladder neck incision.

Previous abdominal surgery had been performed in 19.6% of patients, including open groin herniorrhaphy in 4.4%, laparoscopic mesh herniorrhaphy in 2.0%, appendectomy in 7.6%, and bowel surgery in 1.8%. A trainee performed at least one step of the procedure in 120 s (24%) cases under the supervision of the senior surgeon.

Median operative time was 157 (91–331) minutes, with no conversions or intraoperative blood transfusions; 0.4% of patients received a transfusion postoperatively. Nerve preservation (NP) was performed bilaterally in 57.9%, unilaterally in 15.3%, and on neither side in 26.8%. Pelvic lymphadenectomy was performed in 27.1%. The median catheterization time was 9 (3–42) days, and postoperative hospital stay was 3 (2-7) days.

The authors agree with Coelho and colleagues[12] that a standardized system of reporting complications after RP should be adopted to allow comparison of surgical series, and complications were therefore categorized according to the Clavien system.[13] There were 21 (4.2%) complications and no rectal injuries (Table 2). Minor complications (grades I and II), including transfusion, occurred in 0.4%, complications necessitating intervention without anesthesia (grade IIIa) in 2.2%, complications necessitating operative intervention (IIIb) in 1.6%. There were no life-threatening complications or deaths (grades IV and V).

Small bowel injury, which was unrecognized at the time of LRP, occurred in a patient with a multiply-operated abdomen (sigmoid colectomy with colostomy, closure of colostomy, and two operations to repair a midline incisional hernia, the latter with mesh) and was caused by insertion of the right paramedian port through the mesh and adherent small bowel.

Table 2. Inpatient Results

Conversion to open surgery	0
Operative time (min)	157 (91–331)
Blood loss (mL)	200 (10–1200)
Patients transfused	2 (0.4%)
Lymphadenectomy	135 (27%)
Neurovascular bundle preservation	None = 150 (30%) Unilateral = 90 (18%) Bilateral = 260 (52%)
Postoperative hospitalization (nights)	3.0 (2–7)
Catheterization time (days)	9.0 (3–42) d
Complications by Clavien grade	

	n	%
I & II		0.4%
Transfusion	2	
IIIa		2.2%
Ulnar nerve neuropraxia	1	
Obturator nerve neuropraxia	1	
Paralytic ileus	1	
Postoperative myocardial infarction	2	
Wound infection	1	
Septicemia after catheter removal	1	
Urinary retention causing renal failure	1	
Pulmonary embolus	2	
Symptomatic lymphocele drained	1	
IIIb		1.6%
Small bowel injury	1	
Laparoscopy for hemostasis	2	
Symptomatic lymphocele deroofed	1	
Bladder neck stenosis	4	
IV		0.0%
V		0.0%
Total	21	4.2%

Values are patients or median plus range.

Table 3. Outpatient Results

A. Histology: Positive Margins and Lymph Node Involvement

pT	*Positive margins*	*Positive nodes*
pT_{2a} (46/500 = 9.2%)	0 (0%)	0 (0%)
pT_{2b} (14/500 = 2.8%)	0 (0%)	0 (0%)
pT_{2c} (343/500 = 68.6%)	28 (8.2%)	4 (1.5%)
pT_{3a} (70/500 = 14.0%)	25 (35.3%)	1 (1.5%)
pT_{3b} (27/500 = 5.4%)	12 (45.5%)	1 (3.7%)
Overall	65 (13.0%)	6 (1.2%)

Lymph node count = 11.0 (2–26).

B. Histology: Pathologic Stage and Grade Correction

	Up	*Down*
Stage ($T_{2/3}$)	65/271 = 24.0%	8/24 = 33.3%
Grade	140/500 = 28.0%	58/500 = 11.6%

Prostate-specific antigen

- The first postoperative prostate-specific antigen level was $\leq 0.1\ \mu g/L$ in 496 (99.2%) patients.
- At a mean follow-up of 13.5 (12–36) months, overall survival was 100% and 494 (98.8%) of patients were free of biochemical recurrence.

Continence

- The pad-free rate was 487/500 = 97.4%.

C. Potency by Neurovascular Bundles Preserved and Patient age

NVBs preserved	*40–49 y*	*50–59 y*	*60–69 y*	*70–76 y*
2 (n = 260)	18/18 = 100%	112/122 = 91.8%	87/105 = 82.9%	9/15 = 60.0%
1 (n = 90)	5/5 = 100%	18/27 = 66.7%	27/53 = 50.1%	0/5 = 0.0%

Overall potency after bilateral NVB preservation = 226/260 = 86.9%.
NVB = neurovascular bundle.

Values are numbers of patients or median plus range.

It was treated by open resection and anastomosis 24 hours after surgery and was followed by abdominal wall sepsis necessitating debridement and subsequent removal of infected mesh. Two patients were returned to the operating theater within 24 hours of surgery for laparoscopic aspiration of pelvic blood clot and hemostasis. Of the two patients in whom symptomatic lymphoceles developed after standard PLND, one had it drained percutaneously and the other opted for the more definitive procedure of laparoscopic fenestration 10 days after LRP, both with no long-term sequelae.

The overall positive surgical margin (PSM) rate was 13.0% and correlated with the pathologic T stage (Table 3). The location of the positive margin was at the apex in 36.5%, base in 7.5%, posterior in 22.4%, anterior in 7.1%, and >1 location in 26.5%. The significant up- (24.0%) and down- (33.3%) staging and grading (28.0% and 11.6%) seen in this and other contemporary RP series is a reminder of the relative inaccuracy of clinical staging and grading of prostate cancer and should serve as a brake to the wider dissemination of active surveillance until better biomarkers are available to predict future tumor behavior.

An initial prostate-specific antigen (PSA) level of $\leq 0.1\ \mu g/L$ was achieved in 99.2% of patients. All patients with a recordable initial PSA level (measured at 3 months) had pT_3 disease. The median lymph node count was 11.0 (2–26). Lymph node positivity (Table 3) correlated with pathologic stage. At a mean follow-up of 13.5 (12–36) months, overall survival was 100% and biochemical disease-free survival was 98.8%.

The overall pad-free rate was 97.4%. Potency in previously potent men correlated with patient age and with the number of NVBs preserved and ranged from 60% to 100% when both NVBs were preserved and 0% to 100% when only one NVB was preserved (Table 3). The overall potency rate after bilateral NVB preservation was 86.9%.

Discussion

All patients who stayed in hospital beyond 3 days did so because of complications, but comparison of postoperative hospitalization between series is confounded by the

differences in culture, patient expectations, hospital reimbursement, and support services outside the hospital seen in different countries.

Comparison of RP series is also confounded by a number of other variables, including (but not limited to): differences in surgical ability and experience; variations in the cancer parameters of the patients being treated; and a lack of consistency in defining and reporting results. One of the other major confounders, however, which is not usually accorded an appropriate level of importance, is the negative impact of the LC on surgical results, often producing results that are subject to misinterpretation or impossible to place in context.[14] It is only by comparison of large series of RP by surgeons who are beyond the LC and DC that conclusions can be drawn regarding the relative performance of their chosen surgical technique.

The DC for preservation of potency during the authors' initial 700 cases, which was initially based on the original description by Guillonneau and Vallancien,[15] incorporated the following refinements in chronological order: the abandonment of bipolar diathermy on NVBs; the use of bipolar diathermy during vas and seminal vesicle (SV) dissection; the preservation of SV tips; preservation of aberrant pudendal arteries; preservation of the lateral prostatic fascia; and the adoption of an intrafascial technique (except in patients with a primary Gleason score of ≥ 4). Potency rates in this series are likely to have been suppressed by relatively short follow-up as well as NP in men with ED performed to improve early continence rates.

The changes made to improve continence during the DC were, in chronological order: avoiding overdissection of the urethra; division of the urethra last; reconstitution of the prostate "pillars"; and NP in men with ED but who were at low-risk of recurrence. The authors have not found that the Rocco suture[16] or dorsal suspension of the dorsal vein complex/urethral complex[17] to be helpful in improving continence.

The results obtained in this series compare favorably with the best published results for ORP and RARP from high-volume centers, which have achieved continence and potency rates of up to 93.0% and 86.0%[18] for ORP, respectively, and 98%[19] and 87%[20] for RARP, respectively. They surpass the authors' results for their first 1000 cases[4] and also compare favorably with those found in the 1,000 patient open radical retropubic prostatectomy series by Lepor and associates[21] published in 2001 held up as the "high standard for those advocating laparoscopic radical prostatectomy." The higher PSM rate for pT_2 that was disease seen in this series compared with that of Hoznek and coworkers[22] (8.2% *vs* 2.3%) is offset by the higher potency rate (86.9% *vs* 56.0%) and lower overall PSM rate (13.0% *vs* 16.0%) seen in this series, reflecting the potentially reciprocal relationship between potency preservation and cancer control. The fact that Patel and associates[23] managed to produce a better compromise between PSM and potency rates (2.5% for pT_2 disease and 78.0% overall potency, respectively) than the authors of this series (5.8% for pT_2 disease and 86.9% overall potency, respectively) may be explained by the higher proportion of cT_1 patients in most North American (but unstated in theirs) compared with European series as a result of more widespread screening for prostate cancer using PSA.

The continence and potency rates in this series at least match the best reported for ORP and RARP,[18–23] lending further support to the current evidence that it is surgical ability and experience that dictate outcomes after RP and not the technique used.[24,25] Despite this conclusion, the authors predict an ongoing decline in the use of ORP because of the effect of marketing of RARP on patient "demand." The authors also predict a peak in the number of centers offering RARP as poor results from low-volume centers[26,27] drive patients toward surgeons who achieve better results. In addition, the authors acknowledge that RARP is probably easier to learn than LRP for those urologists who do not already have significant laparoscopic skills and is therefore likely to continue to be seen as the more attractive option to surgeons who want to offer their patients MARP in the Western world despite its much greater cost. The consistent attainment of the best possible results in patients undergoing RP, however, will most likely continue to remain a challenge that only surgeons in high-volume practices are likely to be capable of meeting.

This study has limitations, which include the lack of data collection by a third party, its retrospective nature, and limited follow-up period. Its results, which are those of a single surgeon, might not be predictive of others. The authors also accept the limitations of comparing results between series because of potential differences in data collection and reporting standards.

Conclusion

LRP is capable of matching the best published results for RP in respect to morbidity, and oncologic and functional outcomes when performed by an experienced surgeon in a high-volume setting. However, the literature suggests, however, that it is these two factors that are the key to success, rather than the method used to perform RP.

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Disclosure Statement

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Abbreviations Used

DC = discovery curve
ED = erectile dysfunction
LC = learning curve
LPF = lateral prostatic fascia
LRP = laparoscopic radical prostatectomy
MARP = minimal access radical prostatectomy
NP = nerve preservation
NVB = neurovascular bundle
ORP = open radical prostatectomy
PLND = pelvic lymph node dissection
PSA = prostate-specific antigen
PSM = positive surgical margin
RARP = robot-assisted radical prostatectomy
RP = radical prostatectomy
SV = seminal vesicle