Minimally Invasive Approaches to Prostate Cancer
A Review of the Current Literature

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Introduction: While radical retropubic prostatectomy has been the gold standard surgical approach, the explosion of minimally invasive methods has led to the search for less invasive treatment options. We offer an overview of the evolution of laparoscopic radical prostatectomy (LRP) and robot-assisted laparoscopic prostatectomy (RALP) in terms of the landmark publications and recent head-to-head comparisons, and we review our own experience.

Materials and Methods: A Medline search was performed using the keywords *prostate cancer, prostatectomy, laparoscopic, and robotic.* All pertinent articles concerning localized prostate cancer were reviewed. The Montefiore experience consisted of a retrospective review of a prospectively maintained confidential database.

Results: Several laparoscopic and robotic series were identified including review articles of each modality as well as studies directly comparing the two. Both LRP and RALP compare very favorably with conventional open surgery in terms of safety and oncologic efficacy. Both minimally invasive approaches offer decreased blood loss, transfusion rate, and length of hospital stay when contrasted with open surgery. When compared directly, LRP and RALP offer similar surgical, oncologic, and functional outcomes. However, RALP likely requires a shorter learning curve.

Conclusion: The use of minimally invasive techniques has revolutionized the surgical treatment of prostate cancer. Pure LRP has been shown to be feasible and reproducible. However, it has a steep learning curve and is difficult to learn. In contrast, RALP is easier to learn and is now the surgical treatment of choice in most centers of excellence in the United States. The superior optics with respect to visualization and magnification translates into a procedure that is equivalent, if not superior, with respect to perioperative parameters, oncologic outcomes, and functional outcomes to its open counterpart.

Keywords: prostatic neoplasms, surgical procedures, laparoscopy, robotics

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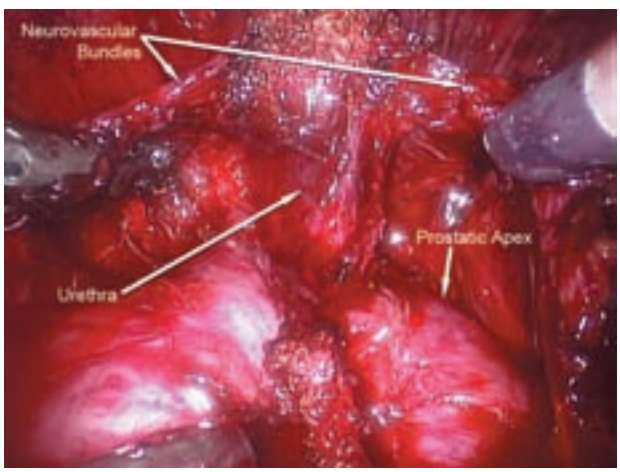
INTRODUCTION

Prostate cancer is the second most common diagnosed cancer in men in the United States trailing only nonmelanoma skin cancer. It is also the second leading cause of cancer-related mortality after lung cancer.[1] The two mainstays of treatment for localized prostate cancer are radiation and surgical excision. Radical retropubic prostatectomy (RRP) has been the gold standard for the surgical approach, although the perineal approach has been shown to be equally efficacious surgical option.[2] The explosion of minimally invasive surgery and the inherent morbidity associated with conventional open radical prostatectomy has led to the search for less invasive treatment options.

Schuessler and colleagues[3] attempted

the first laparoscopic radical prostatectomy (LRP) in 1992 and published a series comprised of 9 prostatectomies. The operation was cumbersome and difficult with unacceptably prolonged operative time. The authors concluded that the procedure offered no advantage compared to RRP. After substantially improving the techniques at Montsouris in France, Guillonneau and associates published their series demonstrating substantial improvements in postoperative convalescence.[4] The operation was shown to be feasible, but more importantly, reproducible. The expansion of LRP in the United State has been limited, however, secondary to the steep learning curve.[5,6]

Recently, robot-assisted laparoscopic prostatectomy (RALP) has introduced several new theoretical advantages to accelerate learning for the laparoscopically naive surgeon. The *Da Vinci* surgical system's (Intuitive Surgical, Sunnyvale, California, USA) magnified 3-dimensional view and intuitive surgical capabilities has allowed surgeons to master the laparoscopic extirpation of the prostate with optimal visualization and dexterity (Figure). Additionally, it has been hypothesized that the development of robotic laparoscopic equipment with 6 degrees of freedom has shortened the LRP learning curve. In 2000, Menon and colleagues spear-headed and described the technique of robotic prostatectomy at Henry Ford Hospital.[7] Since then, numerous studies have evaluated RALP in terms of its learning curve as well as direct comparisons of surgical and oncologic outcomes to both the open and pure laparoscopic approaches. Herein, we offer an overview of evolution of LRP and RALP in terms of the landmark publications and recent head-to-head comparisons.



Magnified view of the prostatic apex after a bilateral nerve-sparing robotic prostatectomy prior to urethral transection.

LAPAROSCOPIC RADICAL PROSTATECTOMY

Laparoscopy was introduced to urology in the early 1990s,[8] with the first series of LRP reported by Schuessler and colleagues in 1991.[3] Guillonneau and colleagues described their early experience in published in 1997.[4] Several large subsequent studies have evaluated the risks and benefits of LRP. The driving force has been an attempt to minimize the patient's overall pain, length of hospital stay, and hasten return to normal activities, while at the same time, duplicate the overall surgical and oncologic outcomes of RRP. Laparoscopic radical prostatectomy has been shown to offer improved visualization of the pelvic anatomy, thereby optimizing preservation of anatomical structures, namely the neurovascular bundles and the external striated sphincter, which could lead to improvements in potency and urinary continence. Guillonneau and colleagues' early data, along with numerous other series have consistently described lower blood loss and decreased postoperative need for analgesia, while achieving comparable negative surgical margins and disease-free follow up.[4,9,10]

Operative Results

Most studies indicate longer operative time for LRP when compared to RRP, but LRP seems to offer consistently more significant decrease in estimated blood loss (EBL), and transfusion rates. Rassweiler and coworkers found a more significant reduction in postoperative pain following the LRP compared to the RRP.[9] In this study, 55% of patients undergoing RRP still required analgesics compared to only 9% in the LRP group. In their excellent recent review of 10 LRP series, Tooher and colleagues[10] found the mean operative time of 288 minutes for LRP versus 168 minutes for RRP. The EBL decreased from a mean of 1400 mL to 800 mL and the transfusion rate, from 26% to 2%. The length of hospital stay varied significantly in terms of countries of origin (European versus United States), but seemed to be significantly less for LRP.[11,12] At our institution, a single surgeon (RG) has performed over 300 pure laparoscopic prostatectomies. A review of our last

135 patients, which comprises our experience well after the learning curve was overcome, revealed comparable outcomes. The average operative time was 280 minutes, EBL was 298 mL, and the average length of hospital stay was 2.6 days.

Complications

The incidence of conversion of LRP to an open procedure ranges in the literature from zero to 14% in several studies.[13-15] Most studies cite similar complication rates between RRP and LRP.[9],[10] Rassweiler and colleagues[9] found that the complication rate significantly improved when trending their experience of LRP over time. In their group of 438 patients, the first third had a similar complication rate to that of RRP, but the last third a significantly decreased rate. They also found differences in the types of complications. In the early laparoscopic group there were more rectal injuries compared to those in the late laparoscopic and open groups (3.2% versus 1.8% and 1.8%, respectively) and more urinary leakages (2.3% versus 0.5% and 0.9%, respectively). On the other hand, compared to early and late laparoscopic groups, the incidences of lymphocele (6.9% versus zero and zero), wound infection (2.3% versus 0.5% and zero), and embolism/pneumonia (2.3% versus 0.5% and 0.5%) were higher after open surgery.

Oncologic Outcomes

In the 5 studies reviewed by Tooher and colleagues, the positive margin rates for LRP and RRP were similar.[13-17] Importantly, stage for stage, there did not appear to be any differences in the positive margin rate between laparoscopic and open prostatectomy. Biochemical recurrence-free survival, defined as prostate-specific antigen greater than 0.2 ng/mL on more than 1 occasion, was poorly reported, but it did not appear to differ between laparoscopic and open approaches in 4 studies.[14,15,18,19]

Quality-of-Life Outcomes

The two major factors that directly impact quality of life are urinary incontinence and erectile dysfunction. The definition of continence and potency are variable in the literature and therefore, there is great variability in their reporting noted in the literature. Rassweiler and coworkers reviewed the literature concerning continence range at 12 months for both RRP and LRP.[9] Both rates were similar (81% to 92% for RRP and 84% to 97%) for LRP. Rogers and colleagues looked at age and return continence and potency after LRP using the Expanded Prostate Cancer Index Composite.[20] They found that younger men (less than 50 years) treated with nerve-sparing laparoscopic radical prostatectomy regain urinary control and potency earlier than older men. However, validated questionnaire subscale analyses demonstrated that the return to preoperative baseline urinary continence and sexual function was similar in all age groups (< 59, 50 to 59, and > 60 years) by the end of the first postoperative year. Jacobsen and associates found no differences in continence 1 year after open radical retropubic prostatectomy or laparoscopic radical prostatectomy.[21] Urinary incontinence was found to affect a similar proportion of patients who underwent open (13%) and laparoscopic (17%) radical prostatectomies 12 months postoperatively.

Learning Curve

Tooher and colleagues cited 6 studies dealing with the learning curve in LRP. They found that most clinical parameters improved with time, including estimated blood loss, length of procedure, and complications.[10] Of note, length of catheter time and hospital stay did not seem to improve. Our experience at Montefiore Medical Center with respect to the learning curve showed that the use of intensive laparoscopic skills training at a minimally invasive surgery center helped overcome the steep learning curve.[22] More importantly, all operations were video recorded. By reviewing operative footage, the surgeon was able to assess outcomes by comparing cases in which the optimal outcome was not achieved to cases in which it was indeed achieved to modify his surgical technique. Using these criteria, the operative aspects of the learning curve were reasonably overcome by the 35th case.

We have published our experience comparing pure LRP and RRP performed by a single surgeon (RG).[23] A total of 70 LRP patients operated on between 2001 and 2002 with at least 18 months of follow-up were compared with a matched cohort of 70 patients who had undergone RRP from 1999 to 2001. The baseline patient characteristics, perioperative and histologic parameters, recovery time, complications,

and 18-month functional data were compared. No significant differences were found in the preoperative characteristics. The mean operative time was 181.8 ± 18.7 minutes for RRP and 246.4 ± 46.1 minutes for LRP ($P < .001$). The mean estimated blood loss was 563.2 mL for RRP and 275.8 mL for LRP ($P < .001$). The positive margin rates were not significantly different between the RRP and LRP groups (20% and 15.7%, respectively). The mean pain score on the postoperative day 1 was 4.5 in the LRP group and 7.8 in the RRP group on an analog pain score of zero to 10 ($P = .02$). Full recovery was achieved at 33 ± 17 days and 45 ± 20 days for the LRP and RRP groups, respectively ($P < .001$). The total perioperative complication rates for LRP and RRP were comparable at 18.5% and 15.7%, respectively. The diurnal continence rate (no pads) for the LRP and RRP groups was 70.0%, 90.0%, and 92.8% and 71.4%, 87.6%, and 92.0% at 6, 12, and 18 months, respectively. The potency rate after bilateral neurovascular preservation with or without sildenafil for the LRP and RRP group was 55.0%, 72.6%, and 79.5% and 43.0%, 58.0%, and 72.4% at 6, 12, and 18 months, respectively, with no significant differences. We concluded that LRP is well tolerated and provides short-term oncologic and functional results comparable to those of RRP.

At our institution we have performed over 300 pure laparoscopic prostatectomies. A review of 135 patients was conducted towards the end of our experience in whom complete data and follow-up was available. This comprised our experience well after the learning curve was overcome and has revealed comparable outcomes. The average operative time was 280 minutes, EBL was 298 mL and the average length of stay was 2.6 days in this cohort. This compares well with our previous experience and with other reports in the literature[4,10] (Table 1).

ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY

The use of a robotic technology offers many advantages over conventional LRP, including 3-dimensional visualization, magnification, increased degrees of freedom, absence of the fulcrum effect, and robotic-wrist instrumentation. The hypothesis is that RALP can successfully reduce the learning curve that even experienced surgeons face while performing LRP. The steep learning curve for LRP is often cited as a major impediment for the widespread implementation of LRP. Any improvement that is gained by the use of robotic technology would help circumvent this issue and favor the use of a laparoscopic approach compared to the traditional open technique. Menon, Guillonneau, and Vallancien at Henry Ford Hospital developed the robotic prostatectomy in 2000.[24] Since that time, an explosion of case series have surfaced in the literature looking at the surgical and oncologic outcomes. We have currently performed over 160 robotic prostatectomies. Our learning curve for this procedure has been low due to our relatively adequate and prior experience with pure LRP. We believe there are inherent advantages to the robotic technique. Herein, we review the different aspects of RALP by citing appropriate references and present our current experience with each parameter discussed.

Operative Results

As with any new surgical procedure, the initial reports of operative time with RALP varied greatly. In a recent review of the literature, Patel and coworkers found the operative time to range from 141 minutes to 540 minutes.[25] However, most published reports from major centers find a marked decrease in time with Patel and associates reporting operative time of approximately 90 minutes after a series of 1000 patients.[25] Aherling and colleagues

Table 1. Outcomes of Laparoscopic Radical Prostatectomy at Our Center and in the Literature

Outcome	Large Series (Guillonneau et al[4]; n = 550)*	Review of Series (Tooher et al[10])†	Montefiore Experience (n = 135)*
Operative time, min	200	288 (180 to 400)	280
Estimated blood loss, mL	380	800 (317 to 1100)	298
Length of hospital stay, d	4.2	5 (2 to 12)	2.6
Positive margin rate, %	16.7	23 (11 to 50)	17.0
Overall complication rate, %	3.6	17 (0 to 25)	17.0

*Values for the first 3 rows are means.
†Values for the first 3 rows are medians (ranges).

reported a direct comparison of their experience with open and robotic approaches and found no significant difference in operative time between the two modalities.[26] In a subsequent study, the same authors showed that the conversion of skills from RRP can be successfully transferred to laparoscopy using a robotic interface with the Da Vinci surgical system.[27] A retrospective study by Hu and coworkers comparing RALP to LRP showed a mean operative time of 4.1 hours and 3.1 hours, respectively, using a sample size of over 300 cases for each group.[28]

With respect to blood loss, many reported series report transfusion rate approaching nil.[24] Tewari and colleagues described a 67% transfusion rate in RRP compared to zero in RALP.[29] Hu and colleagues also reported a decrease in the EBL for RALP, 200 mL compared to 250 mL in RRP.[28] Other studies have shown even lower values for EBL in their RALP case series, such as Patel and associates[30] who report an EBL of 75 mL (with an average of only 43 mL in the last 100 patients), and Ahlering and colleagues who report an average EBL of 145 mL.[27] Our mean EBL in our initial 131 patients was 242 mL.

Complications

Hu and colleagues reviewed the intraoperative complication rates in their and Menon's series of 1100 patients.[28,31] Both series had a major intraoperative complications rate of less than 1% including ureteral, rectal, and epigastric vessel injury. In a recent review of the literature, Ficarra and associates cited an overall postoperative complication rate ranging from 1.5% to 17%, with the major complications consisting of rectal and ureteral injuries, ileus, and urinary leakage.[32] Our overall complication rate was 13% for our initial 131 patients.

Oncologic Outcomes

The literature has a wide range of positive margin rates, largely correlating with clinical and pathologic stage. Ficarra and colleagues' review article[32] stratified the literature on pathologic stage and found the positive surgical margin rate to vary from 5.7% to 27% in stage T2 disease to 26% to 40% in T3a and 27% to 67% in T3b. The overall positive margin rate varied from 2% to 36%. With regards to positive margins, most series report a lower positive margin rate in pathologic T2 disease as opposed to pathologic T3 disease, with T2 positive margin rate quoted as low as 5% in some series. The most common positive margin site in our experience is the apex, even though visualization and dissection are greatly aided and enhanced by the robotic optics. The prostate-specific antigen recurrence rates are still premature with the majority of studies, as it is in our experience.

Functional Outcomes

In terms of continence, the range is from 76% to 95% of patients who are fully continent, defined as the use of no pads at 3 months time.[25,29] Patel and colleagues,[30] who have the longest period of follow-up, report that all patients were continent at 18 months after surgery. These values are similar to those seen in both RRP and LRP.

Data are sparse regarding potency following RALP. In a recent series, a 78% potency rate was reported at one 1 year with or without the use of oral medications, with only 15% of patients being unable to sustain erections sufficient for intercourse, and another 7% requiring injection therapy.[30] Tewari and colleagues[29] reported 82% of preoperatively potent patients younger than 60 years returned to some sexual activity and 64% having sexual intercourse at 6 months. In patients older than 60 years, 75% had some return of sexual activity and 38% having intercourse at 6 months postoperative.

Learning Curve

The greatest advantage of RALP compared to LRP may lie in the significantly decreased learning curve. A laparoscopically naive surgeon may require as many as 80 to 100 cases before reaching the peak the leaning curve for LRP. In a prospective study of 200 patients in a community setting, Patel and colleagues reported a learning curve of 20 to 25 cases using RALP. A second study performed by Ahlering and coworkers[27] reported even shorter learning curve of only 8 to 12 cases, although this series only included 45 patients. This study also delineated the individual steps of the operation. The surgeon was laparoscopically naive and only received a 1-day training course, in addition to performing 2 cadaveric cases, prior to the 45 cases in the series. This is in contrast to Patel and colleagues' study where the surgeon was a fellowship-trained laparoscopist.[30]

Table 2. Outcomes of Robot-Assisted Laparoscopic Prostatectomy at Our Center and in the Literature*

Outcome	Large Series (Joseph et al[36]; n = 325)	Review of Series (Ficarra et al[32])	Montefiore Experience (n = 131)
Operative time, min	130	168 (130 to 250)	191
Estimated blood loss, mL	196	174 (75 to 500)	242
Length of hospital stay, d	1	1.8 (1.2 to 5)	1.8
Positive margin rate, %	13.0	15.1 (2 to 59)	15.2
Overall complication rate, %	9.6	11.3 (1.5 to 17.2)	13.0

*Values for the first 3 rows are means (ranges).

Our learning curve with the RALP was abbreviated due to our prior LRP experience. This is only with regard to perioperative parameters such as blood loss, operative time, and anastomosis time. There are different definitions of learning curve. Just being able to complete the robotic operation fast does not translate into proficiency and overcoming the learning curve. Proficiency has to be defined also by the return of functional outcomes after surgery. The learning curve continues to evolve and continues well into one's experience. This has been shown with RRP and is most probably true for RALP as well.[33]

Costs

The overall costs of these new technologies complicate their recommendation for widespread use, despite favorable surgical outcomes compared to conventional RRP. Using an economic model with data from several peer-reviewed articles, Lotan and associates evaluated the current cost components for RRP, LRP, and RALP.[34] They reported that RRP remains the most cost-effective approach and has a cost advantage of US$ 487 and US$ 1726 over LRP and RALP, respectively. This study mentioned that the main factors responsible for the increased cost burden for RALP are the purchase and maintenance costs of the robot (US$ 857 per case) and the equipment costs (US$ 1705). Even if the robot (approximate cost US$ 1 200 000) was donated through philanthropic efforts, there is still a US$ 1155 added cost for RALP versus RRP. Equipment costs for LRP (US$ 533 per case) accounts for the major cost burden over RRP. This is the case since cost advantage for the shorter length of hospital stay in LRP cases is mitigated by the longer operative time. Of note, Lotan and colleagues mentioned that at current costs for the Da Vinci robot, no single-factor change could make RALP cost equivalent to RRP.[34] The robotic equipments costs would have to decrease to US$ 550 per case for a donated robot to reach economic equivalence. Conversely, the robot cost would have to decrease to US$ 500 000, the maintenance contract to US$ 34 000 per year, and the equipment cost to US$ 500 per case for RALP to have an advantage to RRP. On the other hand, Menon and coworkers estimated that an institution must perform 75 cases per year with an average operative time of 3 hours per case to be cost-effective in the United States.[35]

Table 2 details our initial experience with RALP in 131 patients along with comparisons to the current literature.[32,36]

LAPAROSCOPIC RADICAL PROSTATECTOMY

VERSUS ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY

A few recent papers have reviewed direct comparisons between the two modalities. Rozet and colleagues[37] from France reviewed their series consisting of 4 surgeons. The RALP series was matched to a retrospective series of equivalent LRP patients. The authors found no statistical differences regarding operative time, EBL, hospital stay, or bladder catheterization between the two groups. The overall rate of complications was higher in the RALP group (9.1% versus 19.4%), but the overall rate of major complications was not significantly different (6.0% versus 6.8%). The positive margin rate was 26% and 21% for the RALP and LRP cases, respectively, across all pathological stages ($P = .42$). Both Menon and colleagues[35] and Joseph and colleagues[36] did find significant decrease in blood loss when comparing the to groups in favor of RALP. Our comparative experience can be seen in Table 3. The most striking difference in our experience is the operative time that is significantly decreased with RALP as opposed to LRP. The EBL

Table 3. Laparoscopic Versus Robotic Prostatectomy at Montefiore Center*

Demographics	Laparoscopy	Robotic Surgery	*P*
Patients	135	131	
Age, y	60.3 ± 7.0	60.1 ± 6.9	.78
Positive/negative margins	23/109	20/97	.19
PSA, ng/mL	7.68 ± 5.01	8.36 ± 6.19	.33
Specimen weight, g	48.27 ± 24.05	53.62 ± 23.74	.07
Postoperative Gleason	6.4 ± 0.6	6.5 ± 0.9	.36
Length of hospital stay, d	2.6 ± 1.6	1.8 ± 1.2	< .001
Estimated blood loss, mL	298.33 ± 114.69	242.33 ± 227.98	.01
Operative time, min†	279.2 ± 62.6	191.3 ± 43.7	< .001
Complication rate, %	17	13	.49

*Values of continues variables are shown as mean ± standard deviation.
†Operative time was determined as the total operative room time, from time in to time out of room.

which is significantly less with LRP as compared to RRP, based on our previous report, is even further reduced in RALP. Of course there are other variables that are difficult to assess and prove with regard to ergonomics and surgeon fatigue, but our anecdotal experience is that robotics does significantly enhance the surgeon's ability to perform a precise and accurate operation that is much less taxing and ergonomically easier than pure laparoscopy.

CONCLUSION

The use of minimally invasive techniques has revolutionized the surgical treatment of prostate cancer. Pure LRP has been shown to be feasible and reproducible. However, it has a steep learning curve and is difficult to learn. In contrast, RALP is easier to learn and is now the surgical treatment of choice in most centers of excellence in the United States. Traditional RRP has set the bar very high for the surgical treatment of prostate cancer. Experiencing the robotic capabilities, it is not difficult to envision why it is a superb modality for prostate cancer surgery. The superior optics with respect to visualization and magnification translates into a procedure that is equivalent, if not superior, with respect to perioperative parameters, oncologic outcomes, and functional outcomes to its open counterpart.

CONFLICT OF INTEREST

None declared.

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