ORIGINAL RESEARCH

Clinical and Pathological Outcomes of Laparoscopic Radical Prostatectomy in a Large Volume Center in the Philippines: A Ten-year Experience

Noel T. Borromeo III, MD; Jose Benito A. Abraham, MD, FPUA and Ernesto L. Gerial Jr., MD, FPUA

Department of Urology, National Kidney and Transplant Institute

Introduction: Currently, there are limited studies on laparoscopic radical prostatectomy (LRP) in the country. The authors report the clinical and oncological outcomes of LRP over a 10-year experience in a large volume center in the Philippines.
Methods: This retrospective study included 101 patients treated consecutively with LRP from 2008 to 2017. Patient demographics, preoperative prostate features, perioperative data and complications were summarized to determine surgical outcomes. Histopathological results were analyzed to determine oncological efficacy.
Results: The mean age was 64.8-7.1 years (R:46-84), BMI was 25.3±3.0 kg/m^2 (R:18.7-34.1), prostate volume was 41.1±21.2g (R:7.9-133) and preoperative PSA was 21.5±19.9 ng/mL (R:2.0-100). Operative time was 276.1±70.0 mins. (R:165-475) and estimated blood loss was 604.7±478.4 mL (R: 100-3700). Five (5%) required conversion to open. Time to oral intake was 1.3±0.7 days (R:1-5). Bowel function returned in 2.0±0.9 days (R: 1-4). The drain was removed after 3.7±1.2 days (R:0-9) in 89 patients while 12 patients were discharged with the surgical drain. The length of stay was 4.5±1.8 days (R: 3-14). Pathologically, 26 (25.7%) had extracapsular extension and 14 (13.8%) had seminal vesicle involvement. Three out of 44 (6.8%) who had pelvic lymphadenectomy had nodal metastasis. Thirty (29.7%) had positive surgical margins, the most common site being the apex (17, 56.6%). Thirty-one (30.6%) had Grade I to III complications. There was no mortality.
Conclusion: Laparoscopic radical prostatectomy continues to be a feasible minimally invasive alternative treatment for localized prostate cancer with an acceptable safety profile and high oncological efficiency.

Key words: laparoscopic radical prostatectomy, prostate cancer, oncological outcomes

Introduction

Prostate cancer is the second most common malignancy in men worldwide, representing 7.1% of all cancers diagnosed in men.[1] Historically, the gold standard for the treatment of localized prostate cancer is open radical retropubic prostatectomy.[2] The first laparoscopic radical prostatectomy (LRP) performed by Schussler, et al. to provide a minimally invasive alternative to open surgery, but it did gain much popularity among urologists because of the technical challenges encountered during the prostate

dissection and urethrovesical anastomosis, and the lack of haptic feedback which resulted to prolonged operative times.[3]

The da Vinci robotic system was later introduced to circumvent these limitations of LRP. It offered superior benefits to LRP such as binocular vision, higher magnification, wristed movement of the instruments (Endo-wrist technology) and microsurgical precision.[4] These features made it easier for surgeons to do LRP, and thus, it eventually emerged as the new global gold standard for the treatment of localized prostate cancer in progressive nations.[5]

In spite of its expansive worldwide application however, the restrictive cost of robotic-assisted technology has limited its availability to areas such as the Philippines. In fact, only three centers in the Philippines have a da Vinci robotic system. Therefore, in the local setting such as the National Kidney and Transplant Institute (NKTI), the laparoscopic urologist feels the need to hone his minimally invasive surgical skills in order to perform LRP where robotic-assisted surgery is still unavailable.

The main objective of this study was to determine the perioperative and oncological outcomes of patients who underwent LRP in NKTI over a ten-year period from January 2007 to December 2017.

Methods

This descriptive study has been approved by the Hospital Ethics Review Board, in accordance with the Helsinki Declaration of 1975, as revised in 1983. The authors analyzed the data on all patients who were treated consecutively with LRP at the NKTI from over a ten-year period between January 2007 to December 2017. They reported their initial experience of 10 cases of LRP in 2006 and compared it to a similar group of open radical prostatectomy (ORP) cases and demonstrated that LRP had less transfusions and shorter hospital stay as compared to ORP. They excluded this from the present study because it formed part of the early experience.[6]

A chart review was done to gather demographic data related to the patient's age, body mass index (BMI), co-morbidities and previous surgeries. Tumor characteristics were characterized using prostate volume, prostate specific antigen (PSA) and Gleason score (GS).

The clinical outcome measures included intraoperative and postoperative factors: estimated blood loss (EBL), blood transfusion requirements, operative time, conversion to open surgery and length of hospital stay. The postoperative complications were summarized based on the Clavien-Dindo classification. Oncological outcomes were based on the histopathological analysis of the prostate, positive margin rates and quality of lymph nodes. They were unable to include functional outcomes related to continence and erectile function because of these data were incomplete and some were unavailable.

A total of 5 surgeons, who are all experienced in laparoscopic urological procedures, performed LRP within the same institution. The technique which was used was either a transperitoneal anterior or posterior dissection of the seminal vesicles. An anterior approach utilizes initial downward reflection of the bladder and early dissection of the prostate and the bladder neck followed by dissection of the seminal vesicles.[7] On the other hand, a posterior approach to the dissection of the seminal vesicles prior to downward reflection of the urinary bladder, and anterior prostate dissection.[8]

The patient's data were entered into an MS Excel file for computation of means and standard deviations for each of the quantitative clinical parameters while the qualitative variables were summarized in frequencies and percentages.

Results

Preoperative Data

A total of 101 patients underwent LRP from January 2007 to December 2017 in the National Kidney and Transplant Institute. Forty-four patients underwent bilateral pelvic lymph node dissection because of the following clinical indications: an elevated PSA>10 and Gleason Score >7, and radiographic evidence of enlarged pelvic lymph nodes.

The patients' clinical demographics are summarized in Table 1. The mean age was 64.8±7.1 years (R: 46-84). The mean BMI was 25.3±3.0 kg/m^2 (R: 18.7-34.1). Eighty-five (84.2%)

patients had co-morbidities, in which hypertension was the most common [77(76.2%)], followed by Diabetes Mellitus [35(34.7%)]. Seventeen (16.8%) patients had previous abdominal surgery. Table 2 summarizes the pre-operative prostate features. The mean prostate volume of 41.1±21.2 grams (R: 7.9-133) and mean preoperative prostate specific antigen (PSA) of 21.5±19.9 ng/mL (R: 2.0-100). Majority of patients (n=69) (68.3%) had early stage prostate cancer.

Table 1. Patient demographics

Patient Characteristics	Summary
Age (years)	64.8 ± 7.1
BMI	25.3 ± 3.0
Comorbidities	
Hypertension	77 (76.2%)
Diabetes Mellitus	35 (34.7%)
Coronary Artery Disease (CAD)	5 (5.0%)
Cardiovascular Disease (CVD)	5 (5.0%)
BA	5 (5.0%)
PTB	5 (5.0%)
Dyslipidemia	4 (4.0%)
Arthritis	2 (2.0%)
Myocardial Infarction (MI)	2 (2.0%)
Aneurysm	1 (1.0%)
Asthma	1 (1.0%)
Chronic Kidney Disease (CKD)	1 (1.0%)
CTURP	1 (1.0%)
COPD	1 (1.0%)
CABG	1 (1.0%)
ESRD	1 (1.0%)
Previous Abdominal Surgery	17 (16.8%)

Values expressed as mean ± SD or counts (%).

Table 2. Preoperative parameters

Preoperative Parameters	Summary
Prostate volume (cm^3)	41.1 ± 21.2
PSA (ng/mL)	21.5 ± 19.9
Pathologic T stage	
IIIb	14 (13.8%)
IIIa	18 (17.8%)
II	69 (68.3%)

Values expressed as mean ± SD or counts (%).

Intraoperative Outcomes

Table 3 summarizes the intraoperative clinical parameters. The mean operative time was 276.1±70.0 minutes (R=165-475; median 263 minutes). The mean blood loss was 604.7±478.4 mL (R= 100-3700; median 500 ml). Ninety-one patients (90%) had blood loss less than 1000 ml. Moreover, fifty-four patients (53.4%) had blood loss less than 500 ml. Only nine patients (8%) received blood transfusion.

Table 3. Intraoperative parameters

Intraoperative parameters	Summary
Operative time (min)	276.1 ± 70.0
Blood loss (mL)	604.7 ± 478.4
Converted to open surgery	5 (4.9%)
Transfusion	9 (8.9%)

Values expressed as mean ± SD or counts (%).

Five patients required conversion to open surgery, four due to dense periprostatic adhesions and one due to bleeding. Two were done during 2008, the other two on 2010 and one on 2011. One of the five patients had a previous abdominal surgery, which was radical right nephrectomy (2001) for malignancy. Four of the patients had a Gleason score of 7 and one had a Gleason score of 8.

Postoperative Recovery

The mean number of days before oral intake is 1.3±0.7 days (range, 1 to 5), 79 (78%) patients were started on oral feeding on post-operative day 1. The mean number of days to return to bowel function is 2.0±0.9 days (range, 1 to 4). The surgical drain was removed after a mean of 3.7 ± 1.2 days (range, 0 to 9) from 89 patients while 12 patients were discharged with the surgical drain. The mean length of hospital stay was 4.5±1.8 days (R=3-14). All patients were discharged with an indwelling Foley catheter, which was removed on follow-up for an average of 7-10days.

Table 4. Postoperative parameters of patients undergoing LRP between 2007-2017

Postoperative parameters	Mean ± SD
Days to oral intake	1.3 ± 0.7
Return of bowel function, days	2.0 ± 0.9
Hospital stay, days	4.6 ± 1.8
Surgical drain duration (days)	3.7 ± 1.2

Oncological Outcomes

Table 5 summarizes the histopathological analysis of these patients who underwent LRP. Thirty-nine (38.6%) of the 101 patients had locally advanced disease (with extracapsular extension and seminal vesicle involvement). Twenty-six (25.7%) patients had extracapsular extension and 14 (13.8%) patients had seminal vesicle involvement. Three (6.8%) of the 44 patients whose nodes were dissected had microscopic nodal involvement. Thirty (29.7%) patients had positive surgical margins, the most common site being the apex (17, 56.6%) followed by the basal margin (13, 43.3%). Sixty-eight (67.4%)of the 101 patients had organ-confined disease.

Complications

There were thirty-one (30.6%) patients developed complications. A total of 19 (18.8%) patients were classified with Grade I, 10 (9.9%) patients with Grade II and 2 (1.9%) patients with grade III classification. There were no grade IV or V complications. Seventy (69.3%) patients had no complications. Table 6 shows the complications categorized based on the Clavien-Dindo classification.

Two patients developed Grade IIIb complications. One developed decreased urine output with persistently heavily soaked drains, and on postoperative day 3. He was brought back to the operating room and underwent cystoscopically guided urethral catheter reinsertion and suprapubic tube cystostomy. On postoperative day 7, the penrose drains were removed, and the patient was discharged with indwelling urethral catheter and clamped suprapubic catheter. All urine leakage eventually stopped and both catheters were removed a week later without further eventualities. Another patient had burning epigastric discomfort on postoperative day 3, followed by with coffee ground aspirate after via the nasogastric tube. He underwent esophagoduodenoscopy on postoperative day 4, which showed gastroduodenitis, gastric ulcers and esophageal candidiasis. The patient was treated with proton pump inhibitors, antifungal medicine and was discharged recovered on postoperative day 7.

Ten patients had grade II complications. Among these, 9(9%)patients had postoperative anemia requiring blood transfusions. One (1%) patient developed atrial fibrillation on postoperative day 3, which was managed easily with amiodarone protocol and the patient was discharged improved on postoperative day 8.

Discussion

The first LRP, described by Schuessler, et al. in 1997, demonstrated the feasibility of a laparoscopic

Table 5. Pathological analysis

Pathological analysis	Summary
Gleason score	
3+3	15 (14.8%)
3+4	24 (23.7%)
4+3	29 (28.7%)
4+4	9 (8.9%)
4+5	19 (18.8%)
5+4	5 (4.9%)
Lymphadenectomy	44
Lymph nodes positivity, %	3 (6.8%)
Perineural invasion	46 (45.5%)
Extracapsular extension	26 (25.7%)
Seminal vesicle involvement	14 (13.8%)
Positive surgical margin	30 (29.7%)
apex	17
peripheral	8
basal	13
mid	6
urethral	2
posterior	3
bladder neck	2

Values expressed as mean ± SD or counts (%)

Table 6. Clavien-Dindo classification, complications ad treatments

Category	Event	Management	Summary
III			2 (1.9 %)
	Gastroduodenitis, Gastric ulcers, esophageal candidiasis	s/p esophagoduodenoscopy (day 4 post op) PPI, anti-fungal	
	Decreased urine output per urethral catheter and heavily soaked penrose drains (1 patient)	s/p Cystoscopically guided urethral catheter insertion and suprapubic catheter insertion (day 3 post op)	
II			10 (9.9 %)
	Anemia (9 patients)	Blood transfusion	
	Atrial fibrillation (1 patient)	Cardiac monitor Amiodarone protocol	
I			19 (18.8 %)
	Fever (10 patients)	Anti- pyretic	
	Ileus (3 patients)	NGT	
	Clot retention (2 patients)	Tranexamic acid and urethral catheter flushing	
	Vomiting (2 patients)	Anti-emetic	
	Pleural effusion bilateral (1 patient)	Observation	
	Left flank hematoma (1 patient)	Observation	
	No complications		70 (69.3%)

approach to prostate cancer in nine patients. The mean operative time was 9.4 hours.[3] There were three complications: cholecystitis, thrombophlebitis associated with a pulmonary embolism, and a small bowel hernia into a trocar site. While surgery was completed successfully in all patients, the authors stated that it had limited advantages over open surgery with regard to tumor removal, continence, potency, length of stay, convalescence, and cosmetic result. However, in this early period, LRP did not become very popular because of difficult dissection and the highly technical skills that are required to do intracorporeal knot tying for urethrovesical anastomoses.

Later on, the procedure was revisited by European surgeons who applied several modifications known as the Montsouris technique, popularized by Guilloneau and Vallencien.[8] This standardized method of performing LRP allowed the surgeons to decrease the operative time significantly, averaging about 180 minutes. It also made the surgery reproducible, and ultimately replaced the open surgical method. Later, Curto, et al. also improved on the technique by describing a nerve-sparing LRP which was intended to preserve erectile function among these patients.[9]

Years later, the robotic platform to prostate cancer was introduced by Binder to circumvent the technical difficulties inherent to LRP.[4] The unique features of a three-dimensional, binocular image, high definition video system and Endowrist technology allowed the surgeon to perform the surgery with more ease and facility even among laparoscopically-naïve surgeons. Indeed, a recent review showed that robotic prostatectomy has now emerged as the new gold standard for the extirpation of localized prostate cancer.[5]

However, this technology is not readily available because of its restrictive costs. In this situation therefore, the laparoscopic surgeon has to adapt and acquire special skills to perform LRP without the use of the robotic technology. By doing so, he can offer this less costly, minimally invasive approach to patients with localized prostate cancer. Refinements in the technique were developed by Guillonneau, et al., resulting further to a standardization of LRP technique.[10] This has led to a more detailed dissection of the prostate, decreased venous bleeding in the surgical field, accurate prostate dissection and preservation of the neurovascular bundles. These advantages also translated to a low positive surgical

margin rate, low morbidity profile, and favorable postoperative quality of life outcomes.

The authors reported their first case of LRP in 2006.[11] This was on a 63-year-old male patient with lower urinary tract symptoms, prostate volume of 61gm and PSA of 11ng/ml. Transrectal biopsy revealed adenocarcinoma of the prostate with a Gleason Score of 6, and a negative metastatic work-up. Operative time reached 300 mins with an estimated blood loss of 1000cc. However, the patient did well postoperatively and the histopathological analysis showed adenocarcinoma of the prostate occupying only 5% of the prostate, with negative margins.

Since then, the authors applied the standard technique of LRP as described by Guilloneau and Vallencien to their patients diagnosed with early stage prostate cancer. They also compared their early series of LRP to their series of open radical prostatectomy (ORP) and found shorter hospitalization time, quicker recovery and lesser blood loss in favor of LRP.[6] This is consistent with the findings of the experience of other reports.[12] In this report, the authors experienced very modest blood loss averaging about 600cc. They believe that this has resulted from their familiarity with the dissection and the early control of the dorsal venous complex. They have also excluded the cases in their early experience in order to limit the effect of the learning curve to the clinical outcome. The numbers remain modest compared to other higher volume centers worldwide. However, by increasing the case load, they hopefully would also increase their clinical efficiency.

The foremost goal of radical prostatectomy, regardless of the surgical approach, is adequate and safe eradication of prostate cancer. This is reflected in the adequacy of surgical excision and negative margins. The present study demonstrated a surgical margin rate of 29.7%. This is slightly higher compared to the 16% to 27% positive surgical margin rates of cases performed by surgeons who have done more than 100 LRPS.[12] In the present series, most patients had positive margins at the apex, consistent with those reported in other literature. This is attributable to the conservatism with apical dissection, which is usually observed by most surgeons as they avoid injury to the external sphincter. The heterogeneity in the surgical skills may have negatively impacted on the tissue margin rates. In this particular series, there were multiple surgeons and therefore each one had varied LRP experiences. The case rate per surgeon is also lower than those reported internationally. Only half of the patients underwent laparoscopic pelvic lymphadenectomy, as indicated by a high PSA > 10 and Gleason score > 7 and radiographic evidence of enlarged lymph nodes. Among these patients, only 6.8% yielded metastasis. However, given the retrospective nature of this study, the authors cannot determine whether a template lymphadenectomy was performed in all cases. Therefore, they cannot ascertain the number and extent of the lymph nodes that were harvested for analysis.

The present study had a 4.9% conversion rate. Its threshold for conversion was high, because the authors were determined to improve their surgical technique in order to increase their experience. In those cases where conversion was needed, strict indications were present. These were for patients with very adherent periprostatic fibrosis where progression of the surgical dissection utilizing laparoscopic methods were not possible. The complication rate in this series is 30.6%. However, majority are of low grade based on the Clavien-Dindo Classification.

To date, this is the largest long-term study in the Philippines describing LRP experience. The subject population, however, is still low compared to other studies worldwide. At the same time, multiple surgeons were included and evidently, these have variability in surgical technique, expertise and learning curves. Some cases used anterior vs. posterior dissection of the seminal vesicles vis-à-vis the prostatectomy. The differences between these two approaches were not accounted for in this study.

The threefold goals of radical prostatectomy, regardless of the surgical approach (open, laparoscopic or robotic) also referred to as the trifecta, include: a) complete surgical excision with negative surgical margins, b) maintenance of urinary continence and c) preservation of erectile function.[13] Given the retrospective nature of the study, the authors were unable to evaluate the functional outcomes of urinary continence and erectile function because data were not available. NKTI as a referral center also obliged the authors to send back these patients to their respective referring urologists for long term

follow-up. In this case, they are no longer able to monitor these outcomes.

The authors were unable to determine the differences in outcomes between anterior and posterior approaches to the seminal vesicles. As of this writing, laparoscopic surgeons have transitioned to an exclusively posterior approach.

Long-term follow up is missing related to biochemical failure, disease progression, metastatic rates, and survival outcomes. A real-time electronic database which includes prospective data gathering at the initiation of the study is a better option in order to minimize lost information related to these factors.

Conclusion

The authors' limited experience was able to demonstrate that laparoscopic radical prostatectomy (LRP) is a considerable viable minimally invasive option for the treatment of localized prostate cancer. In the absence of a robotic platform, they believe that they can continue to offer this technique to their patients so that they may gain the benefits of a minimally invasive approach while attaining a cure for their disease condition.

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