Original Article

Laparoscopic radical prostatectomy: Oncological outcome analysis from a single-center Indian experience of 6 years

Shashikant Mishra, Vikas Agrawal, Naushad Khatri, Rajan Sharma, Abraham Kurien, Arvind Ganpule, V. Muthu, Ravindra B. Sabnis, Mahesh R. Desai

Department of Urology, Muljibhai Patel Urological Hospital, Nadaid, Gujarat, India

ABSTRACT

Background: There is a lack of published data on laparoscopic radical prostatectomy (LRP) in India. Although the published short-term oncologic outcomes after LRP are encouraging, intermediate and long-term data are lacking.
Objective: We analyzed the oncological outcome after LRP based on 6 years of experience and compared it with the other single-center published literature.
Materials and Methods: Of the 90 patients who underwent LRP for a clinical T2 localized disease, 73 patients with at least a follow up of one year were analyzed. Patients were classified as low-, intermediate-, and high-risk D'Amico groups in 22 (30%), 26 (36%), and 25 (34%) of the patient population, respectively. Progression of disease was defined as a PSA of 0.4ng/ml with a confirmatory rise. We used Kaplan-Meier product limit estimates to calculate actuarial 5-year probabilities of biochemical progression-free survival. Univariate analysis of risk factors for biochemical recurrence (BCR) was done.
Results: The mean age of the patients was 63.3 ± 6.6 years. The average follow-up for patients was 22 (12-72) months. There was no prostatic cancer-specific mortality. Fourteen patients had BCR. The 5-year progression-free probability for men with low-, intermediate-, and high-risk prostate cancers was 91%, 82%, and 58%, respectively. High-risk group, Gleason sum more than 8, extracapsular extension, and positive surgical margin were significantly associated with biochemical progression.
Conclusions: LRP provided a similar level of oncological success as reported by the other contemporary single-center published literature

Key words: Biochemical recurrence, Indian experience, laparoscopic radical prostatectomy, oncological outcome

INTRODUCTION

Schuessler *et al.* performed the first laparoscopic radical prostatectomy (LRP) in 1997.[1] Since then, LRP has been widely reported and has become an increasingly important treatment armamentarium for prostate cancer treatment with worldwide acceptance. The assumed advantage of laparoscopic approach for prostate cancer has been greater patient satisfaction and a higher quality of life. Shorter convalescence with a more rapid return to normal activity and shorter catheter duration are attractive goals to be achieved by LRP. Additional potential benefits of LRP are decreased blood loss and magnification of the operative field. The ×10 magnification afforded by laparoscopy also allows more precise visualization of intraoperative details, which is particularly valuable for creating the vesicourethral anastomosis.[2]

There is a lack of Indian data on long-term oncological efficacy results of LRP. Unlike western population, where screening has resulted in stage migration, the same is perhaps not true for Indian population. The treatment for a clinical T2 disease and its oncological outcome may therefore be different than western population. Hence, before using western data to extrapolate their finding in rationalizing the treatment pattern in Indian men, an Indian experience is mandated. In this paper, we report a detailed analysis of oncological outcomes based on 6 years of experience of LRP.

For correspondence: Dr. Mahesh R Desai, Muljibhai Patel urological Hospital,Nadiad, Gujarat, India.
E-mail: mrdesai@mpuh.org

Access this article online

Quick Response Code:

Website: www.indianjurol.com

DOI: 10.4103/0970-1591.94953

MATERIALS AND METHODS

Between January 2005 and December 2010, 90 consecutive patients with clinical T2 stage prostate cancer were treated by LRP at our institute. We performed a retrospective study of the patients who had undergone LRP. Five patients whose clinically relevant details were missing in the record sheets and initial six cases that were performed by a mentor were excluded from the study, leaving 79 eligible for analysis. Of these 79, case records of 73 patients with at least one-year oncological follow-up were included for efficacy analysis. Preoperative clinical parameters analyzed were patient's age, comorbidity, serum prostate-specific antigen (PSA), transrectal ultrasound-guided (TRUS) biopsies, and clinical TNM stage. TRUS, CT scan abdomen, and bone scan were done as part of staging the disease. All surgically fit patients with clinical T2 stage were offered LRP after prior counseling.

The transperitoneal, anterior surgical approach as described by Gill and Zippe was followed.[3] A single surgeon (MRD) performed all the cases. Before delivering the specimen out, a frozen section of the bladder neck and the urethral margin were done. If the report was positive, additional resection of the margin was done or else urethrovesical anastomosis completed. Water tightness was confirmed by inflating the bladder with saline. At the end of the procedure, 14 Fr Romovac drain was placed in the retropubic space. The prostate with the attached seminal vesicles was entrapped in an extraction bag and positioned at the level between the spermatic cord and lateral abdominal wall. The prostate was removed through the umbilical port. Lymph node dissection was not performed as a part of staging value in the entire cohort.

The radical prostatectomy (RP) specimen was coated with India ink to delineate the surgical margins and then fixed in 10% formalin. A whole-mount specimen was first made. Prostate and seminal vesicles were step-sectioned transversely at 5 mm intervals [Figure 1]. Specimens were examined for the following variables: Gleason grade and sum, pathologic stage, seminal vesicle invasion, bladder neck invasion, and extra prostatic extension. A positive surgical margin (PSM) was defined as the presence of cancer at the inked margin of resection in the RP specimen. The bladder neck margin was coned from the RP specimen. Bladder neck involvement was defined as the presence of neoplastic cells within thick smooth muscle bundles of the coned bladder neck in the absence of intermixed benign prostatic glandular tissue on the corresponding slide.

Postoperatively, the planned PSA-monitoring schedule consisted of a measurement at 1 and 3 months, 3-monthly till 2 years, and yearly afterwards. Biochemical recurrence (BCR) was defined as a PSA of 0.4ng/ml with confirmatory rise. Patients were stratified as low, intermediate, or high risk based on the pretreatment prostate cancer nomogram progression-free probability of >90%, 89–71%, and <70%, respectively. Local recurrence was detected by digital rectal examination and imaging studies. TRUS and prostatic fossa biopsy were used to assess tumor status in the resection bed. Bone scan was done to detect disseminated disease in select high-risk patients. On the basis of negative biopsies, bone scan, initial pathological stage, and pattern of PSA rise, local recurrence was assumed. Patients with confirmed BCR were offered salvage local radiotherapy in the absence of documented systemic relapse. Concurrent hormonal therapy was given along with radiotherapy. These groups of patients were further followed up with similar PSA assessment. Patients with BCR were analyzed to identify the factors affecting recurrence with univariate analysis. Factors studied to identify risk factors for BCR were as follows: age, PSA, TRUS biopsy Gleason score, TRUS biopsy Gleason grade, clinical stage as per D'Amico risk stratification, and histopathological findings. The histopathological variables were organ confinement, focal extra capsular extension, seminal vesicle involvement, surgical margin status, and Gleason score of the surgical specimen. The significance of the factors was carried out by Fishers exact *t* test using SPSS software 15. *P* value less than 0.04 was considered statistically significant. The probability of freedom from recurrence following LRP was estimated using the Kaplan-Meier product limit estimates.

RESULTS

The demography profile and functional outcome of the patients is as in Table 1.

The mean operation time was 246 ± 84 minutes. There was one conversion to open radical prostatectomy (ORP) due to bleeding from external iliac vein. Rest of the cases could be completed without problem. The PSM rate was 17.8% (13). Urethral margin positivity was seen in 13 cases, whereas multifocal margin positivity was in two cases. Pathological upstaging, from cT1 to pT2, cT2 to pT3, and cT1 to pT3, were seen in 59%, 54%, and 40% cases, respectively. Peri-neural invasion was seen in 76%. Final histopathological specimen revealed pT3 disease in 40 patients (focal extra capsular extension in 37 and seminal vesicle involvement in three). The median follow-up for patients was 26.8 (12-72) months. There was no prostate cancer-specific mortality. Among the 73 patients, 14 (19.2%) patients had BCR of which there were 12 local recurrences and two distant metastases. All patients with local recurrence, except two, received radiotherapy, whereas two patients with distant metastases received hormonal treatment. In the BCR cohort, eight and six patients were in the high-risk and intermediate-risk group, respectively. The 5-year biochemical progression-free probability for men with low-, intermediate-, and high-risk prostate cancers was 91%, 82%, and 58%, respectively [Figure 2]. The overall 5-year BCR-free survival was 68% [Figure 3]. Preoperative variables associated with increased

Table 1: Demography of the patients

Number of patients	90
Age (mean ± SD), years	62.8 ± 7.4
Comorbidity	
Diabetes	31
Hypertension	43
COPD	12
PSA ng/ml (Mean ± SD), range	13.9 ± 9.8 (4.6 to 59)
D'Amico risk stratification	
Low risk	25
Intermediate risk	32
High risk	33
Gleason score (Mean ± SD)	6.81 ± 0.86
OR duration (minutes) (Mean ± SD)	246 ± 84
Nerve sparing	
Unilateral	66
Bilateral	14
No nerve sparing	10
Catheter duration (days) (Mean ± SD)	8.4 ± 3.5
Hospital stay (days)	8.2 ± 3.1
Continence* (%)	
3 months	84%
6 months	92%
2 months	94%
Potency**	
6 months	26%
12 months	53.8%
Gleason score (Mean ± SD)	6.81 ± 0.86

*Continence was defined as requirement of no pads. **Potency was defined as erection sufficient enough for penetrative intercourse with or without aid of support medications oral or intra cavernosal.

Table 2: Mono-variate analysis of factors affecting biochemical recurrence

Parameter	Biochemical recurrence	No recurrence	*P* value
Age			
>60	9	30	0.392
≤60	5	29	
S. PSA			
>20	7	7	0.004
≤20	7	52	
D'Amico risk group			
High risk	7	5	0.001
Low/Intermediate risk	7	54	
TRUS Gleason Grade (Biopsy)			
≥4	9	3	<0.001
<4	5	56	
TRUS Gleason Score (Biopsy)			
>8	6	7	0.014
≤8	8	52	
Surgical margin	6	7	0.014
Positive	8	52	
Negative			
Perineural invasion			
Present	12	44	0.497
Absent	2	15	
Extracapsular extension			
Present	13	24	0.004
Absent	1	25	
Lymphovascular invasion			
Present	8	50	0.032
Absent	6	9	
Seminal vesicle infiltration			
Present	2	1	0.09
Absent	12	58	
Pathological stage			
pT2	3	30	<0.001
pT3	15	25	
Gleason score (specimen)			
>8	7	6	0.002
≤8	7	53	

TRUS - Transrectal ultrasound-guided

incidence of BCRs were high-risk group localized disease, s. PSA more than 20ng/ml, and TRUS Gleason score of ≥8 or grade ≥4 [Table 2]. Similarly, histopathological variables associated were extra prostatic extension, specimen Gleason score of ≥ 8, and PSM [Table 2].

DISCUSSION

The primary goal of prostate cancer surgery is to provide satisfactory oncologic outcomes. BCR and PSM are the two commonly used indices to assess oncologic outcomes following RP. The advocates of laparoscopy assume that it offers better visualization and access to the tight confines of the male human pelvis, eventually translating into better oncological, functional, and morbidity outcome. There is still a lack of scientific evidence to prove that it meets quality control. Prospective comparative studies of ORP and LRP have however demonstrated equivalency of oncologic results with regard to BCR and PSM.[4-8] The end point of the present report is not a comparison of oncological efficacy of LRP other approaches or treatment modalities, but rather a description of oncologic results of 6 year of experience with LRP across all risk groups.

Although ORP provides long-term oncologic control for up to 15 years, limited follow-up data are available for the LRP. The reported contemporary data discussed in this manuscript are to provide perspective and should by no means be used for a comparative analysis, since the methodology, time frame of the study, and end-point definitions vary greatly from one study to another. At our institution, midterm cancer control data are now available and show that LRP effectively controlled the disease in 68% of men with prostate cancer at 5 years after surgery. This is comparable with single institution LRP series reported worldwide [Table 3].

We expect the overall midterm oncologic results obtained by preoperative risk stratification with 95% confidence intervals. Prostate cancer is known for its heterogeneity, with cancers ranging from totally indolent to rapidly lethal. Therefore, reporting of results based on risk groups can be more informative. In our study, 40 patients (54.8%) were found

Table 3: Other published single centre reports on laparoscopic radical prostatectomy

Author	Center	Number of patients	% Positive surgical margin	% Biochemical recurrence
Chan[9]	Hong Kong	125	22	26
Mirandolino[10]	Brazil	730	19.5	10.3
Turk[11]	Germany	125	26.4	Not reported
Hozneck[12]	Creteil	134	24.5	11.4
Bollens[13]	Brussels	50	22	Not reported
Farouk[14]	Cleiveland Clinic	100	Not reported	Not reported
Hara[15]	Kobe	26	Not reported	Not reported
Guillonneau[16]	Montsouris	1000	19.2	90.5 at 3 years
Eden[17]	UK	100	16%	Not reported
Rassweiler[18]	Germany	500	19	27
Stoltenberg[19]	Leipzig	700	19.8	
Current study	India	73	17.8	32

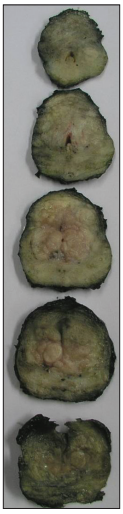

Figure 1: Step sectioned whole-mounted radical prostatectomy specimen

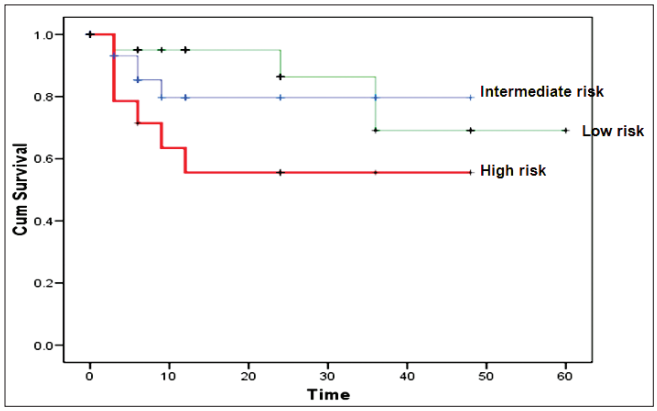

Figure 2: Biochemical recurrence free progression probability in the risk stratified localized carcinoma prostate

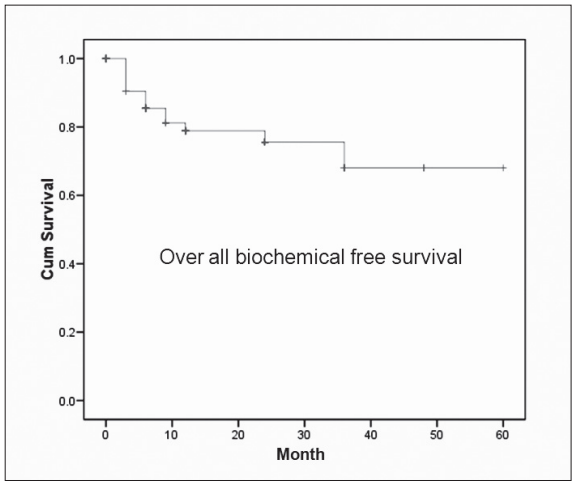

Figure 3: Overall biochemical recurrence free progression for localized carcinoma prostate

to have pT3 disease on final histopathologic evaluation. There was focal extra capsular extension in 37 patients. This means that unlike west, where many patients have a pathological T2 group detected by aggressive screening of prostate cancer, the same was not seen in our patients. Majority of these patients were still in the high-risk group. When stratified by risk of disease progression according to Kattan's nomogram, LRP was effective in controlling cancer at 5-year postoperatively in 53% of men with high-risk prostate cancer. In the ORP western published literature, Hull *et al.* and Kupelian *et al.* reported 65% and 37% 5-year freedom from progression in the high-risk group, respectively.[20,21] Many definitions of BCR are currently used in literature. However, in a study by Cronin *et al.*, groups using different definitions will come to similar conclusions on prognostic factors.[22] At our institute, the agreed upon definition of BCR is 0.4ng/ml, confirmed by a subsequent rising PSA level.

Consistent with other contemporary RP series, the author's data demonstrate that higher grade and risk group results in biochemical progression. We also analyzed Gleason grade and score on needle biopsy as one of the factors having prognostic significance. Our data suggest that the Gleason score of the needle biopsy adds additional prognostic value to the RP specimen Gleason score in a manner that may be applicable to strategies of risk stratification and patient

counseling before surgery. One factor that we did not study was the impact of learning curve of the surgeon on BCR. The author was already well conversant with ORP and had performed more than 500 laparoscopic procedures before starting LRP. Once the procedure was started, over the period of time only the operative time decreased and proficiency increased. There was one conversion in the early learning curve. Cancer control after RP improves with increasing surgeon experience, irrespective of the patient risk. To admit the down side of the learning curve on the oncological efficacy, seven patients of low-/intermediate-risk prostate cancer experienced recurrence. This could undermine the excellent rates of cancer control in patients with low-risk disease by most experienced surgeons. Salvage treatment after BCR also differed at different centers and varied according to the disease severity, center's expertise, and year of BCR. We offered salvage local radiotherapy at 3 months to patients having a higher grade of disease and PSM. Though limited by a short number of patients, no prostate cancer-specific mortality was found in the current study.

Margin status is an important independent predictor of disease recurrence after RP and, therefore, a measure of treatment efficacy. The PSM rate was 20% for ORP *vs* 16.7% for Robotic-assisted radical prostatectomy (RALRP) in a study by Ahlering *et al*.[23] Smith *et al*. retrospectively reviewed 200 procedures from each approach. The overall incidence of PSM was significantly lower among the RALRP cohort compared with ORP cases (15% *vs* 35%, $P<0.001$). [24] Surgeons reporting more than 100 LRPs showed PSM rates that ranged from 16 to 27% [Table 3]. Based on such published results, PSM rate LRP may be perceived to be comparable with ORP.

CONCLUSIONS

LRP provides optimal cancer control. Traditional clinicopathological parameters correlate with the treatment results. The 5-year progression-free probability for men with low-, intermediate-, and high-risk prostate cancers was 91%, 82%, and 58%, respectively. Overall LRP provided 5-year biochemical recurrence-free survival in 68% of patients with clinically localized prostate cancer.

REFERENCES

1. Schuessler WW, Kavoussi LR, Clayman RV. Laparoscopic radical prostatectomy: Initial case report. J Urol 1992;147:246.
2. Trabulsi EJ, Guillonneau B. Laparoscopic radical prostatectomy. J Urol 2005;173:1072-9.
3. Gill IS, Zippe CD. Laparoscopic radical prostatectomy: Technique. Urol Clin North Am 2001;28:423-36.
4. Touijer K, Eastham JA, Secin FP, Romero Otero J, Serio A, Stasi J, *et al*. Comprehensive prospective comparative analysis of outcomes between open and laparoscopic radical prostatectomy conducted in 2003 to 2005. J Urol 2008;179:1811-7.
5. Khedis M, Huyghe E, Soulie M, Seguin P, Mouly P, Plante P. Comparison of carcinological results between laparoscopic and retropubic radical prostatectomy. BJU Int. 2004;94:222.
6. Salomon L, Sebe P, De la Taille A, Vordos D, Hoznek A, Yiou R, *et al*. Open versus laparoscopic radical prostatectomy (part I). BJU Int. 2004;94:238.
7. Rassweiler J, Seemann O, Schulze M, Teber D, Hatzinger M, Frede T. Laparoscopic versus open radical prostatectomy (a comparative study at a single institution). J Urol 2003;169:1689-93.
8. Roumeguere T, Bollens R, Vanden Bossche M, Rochet D, Bialek D, Hoffman P, *et al*. Radical prostatectomy (a prospective comparison of oncological and functional results between open and laparoscopic approaches). World J Urol 2003;20:360-6.
9. Chan SW, Lam KM, Kwok SC, Yu C, Au WH, Yung YP, *et al*. Laparoscopic radical prostatectomy: single centre experience after 5 year. Hong Kong Med J 2008;14:192-7.
10. Mariano MB, Tefilli MV, Fonseca GN, Goldraich IH. Laparoscopic radical prostatectomy: 10 years experience. Int Braz J Urol 2009;35:565-71.
11. Turk I, Deger S, Winkelmann B, Schonberger B, Loening SA. Laparoscopic radical prostatectomy. Technical aspects and experience with 125 cases. Eur Urol 2001;40:46-52.
12. Hoznek A, Salomon L, Olsson LE, Antiphon P, Saint F, Cicco A, *et al*. Laparoscopic radical prostatectomy. The Creteil experience. Eur Urol 2001;40:38-45.
13. Bollens R, Vanden Bossche M, Roumeguere T, Damoun A, Ekane S, Hoffmann P, *et al*. Extraperitoneal laparoscopic radical prostatectomy. Results after 50 cases. Eur Urol 2001;40:65-9.
14. Farouk A, Gill I, Kaouk J. 100 laparoscopic radical prostatectomy (LRP): learning curve in the United States. J Endourol 2002;16:33.
15. Hara I, Kawabata G, Miyake H, Hara S, Fujisawa M, Okada H, *et al*. Feasibility and usefulness of laparoscopic radical prostatectomy: Kobe University experience. Int J Urol 2002;9:635-40.
16. Guillonneau B, El-Fettouh H, Baumert H, Cathelineau X, Doublet JD, Fromont G, *et al*. Laparoscopic radical prostatectomy: Oncological evaluation after 1,000 cases a Montsouris Institute. J Urol 2003;169:1261-6.
17. Eden CG, Cahill D, Vass JA, Adams TH, Dauleh MI. Laparoscopic radical prostatectomy: the initial UK series. BJU Int 2002;90:876-82.
18. Rassweiler J, Schulze M, Teber D, Marrero R, Seemann O, Rumpelt J, *et al*. Laparoscopic radical prostatectomy with the Heilbronn technique: oncological results in the first 500 patients. J Urol 2005;173:761-4.
19. Stolzenburg JU, Rabenalt R, DO M, Ho K, Dorschner W, Waldkirch E, *et al*. Endoscopic extra-peritoneal radical prostatectomy: Oncological and functional results after 700 procedures. J Urol 2005;174:1271-5.
20. Hull GW, Rabbani F, Abbas F, Wheeler TM, Kattan MW, Scardino PT. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. J Urol 2002;167:528-34.
21. Kupelian P, Katcher J, Levin H, Zippe C, Suh J, Macklis R, *et al*. External beam radiotherapy versus radical prostatectomy for clinical stage T1-2 prostate cancer: therapeutic implications of stratification by pretreatment PSA levels and biopsy Gleason scores. Cancer J Sci Am 1997;3:78-87.
22. Cronin AM, Godoy G, Vickers AJ. Definition of biochemical recurrence after radical prostatectomy does not substantially impact prognostic factor estimates. J Urol 2010;183:984-9.
23. Ahlering TE, Woo D, Eichel L, Lee DI, Edwards R, Skarecky DW. Robot-assisted versus open radical prostatectomy (a comparison of one surgeon's outcomes). Urology 2004;63:819-22.
24. Smith JA Jr, Chan RC, Chang SS, Herrell SD, Clark PE, Baumgartner R, *et al*. A comparison of the incidence and location of positive surgical margins in robotic assisted laparoscopic radical prostatectomy and open retropubic radical prostatectomy. J Urol 2007;178:2385-90.

How to cite this article: Mishra S, Agrawal V, Khatri N, Sharma R, Kurien A, Ganpule A, *et al*. Laparoscopic radical prostatectomy: Oncological outcome analysis from a single-center Indian experience of 6 years. Indian J Urol 2012;28:32-6.

Source of Support: Nil, **Conflict of Interest:** None declared.