



Laparoscopic Radical Prostatectomy in Oligometastatic Carcinomaprostate: Single Institute Experience

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I. INTRODUCTION

Oligometastatic cancer is a term first described in 1995 by Hellman and Weichselbaum as early tumours in which metastasize is limited in number at an intermediate state between locally confined cancer and widespread systemic metastasis. Although many literatures propose various definitions of oligometastatic PCa, most of which are generally defined as less than or equal to four extra pelvic metastatic sites.

More recently, there is a new emerging concept about the role of RP for the treatment of Oligometastatic PCa. One of the most important concepts to identify feasibility of LRP in patients with mPCa is whether or not the complications of aggressive local surgery are outweighed by benefits. At this time, there is no clear consensus on the definition of oligometastatic and it is unclear who will benefit from surgery. To avoid equivocation over the meaning of disease-free after RP, using undetectable PSA and no castrate testosterone level as a screening at end point is reasonable.

The laparoscopic approach is the by far the most daunting approach to radical prostatectomy. It is associated with less bleeding, better visualization, less post operative pain and shorter convalescence and hospital stay than the open counterpart. The first laparoscopic radical prostatectomy (LRP) was performed in 1997 by Schussler et al. Since then, LRP has been reported widely and it has become increasingly important as a treatment for localized carcinoma prostate.

II. MATERIALS AND METHODS

A retrospective study of 20 patients with age less than 80 years with newly diagnosed case of oligometastatic locally resectable prostatic carcinoma, having good general physical and performance status were included and underwent laparoscopic prostatectomy with or without

neoadjuvant hormonal therapy in form of orchidectomy/LHRH Agonist (Triptorelin 11.25mg) from September 2018 to December 2020.

Eight patients were post-orchidectomy in other Centre and were fit for the Laparoscopic Radical Prostatectomy, were selected for the study while other twelve patients underwent Laparoscopic Radical Prostatectomy as primary therapy. While another 15 patients with metastatic carcinoma prostate (Group II) having poor general physical and performance status underwent bilateral sub capsular orchidectomy/medical castration and kept under serial S.PSA level measurement and observation of disease progression. Patients with Poor performance Status, prior radiotherapy or chemotherapy and having more than 3 skeletal metastasis or any visceral metastasis were excluded from this study.

Those patients who underwent LRP had first follow up at one month. Then three monthly for one year, six monthly for second year and yearly for third, fourth and fifth year with S.PSA and S. testosterone level at every visit. Patients of group with only ADT had regular follow up three monthly for one year, six monthly for second year and yearly for third, fourth and fifth year with S.PSA and S. Testosterone level at every visit.

We aimed to study the effect of laparoscopic radical prostatectomy on overall treatment outcome and impact of laparoscopic radical prostatectomy on disease progression, morbidity and survival in patients with oligometastatic Prostate cancer.

III. RESULTS AND OBSERVATIONS

Chronological age is not an exclusion criterion in our series as we have performed laparoscopic radical prostatectomy in patients as old as 80 years as long as the patient is having life expectancy of at least 10 years. Most of the patients in our series (9 cases) are in age group of 61 to 70



years, Five patients in the age group of >70 years and six patients in the age group of 50-60 years.

The size of the prostate varied widely from 20-60cc. We have performed laparoscopic radical prostatectomy in 12 cases where the PSA level was more than 50ng/ml with average pre-

operative S.PSA 68.09 (18.02-->150 ng). A total of 20 patients in group I who operated as laparoscopic radical prostatectomy were having Gleason Score ranging from 6-9 with eight patients having more than seven Gleason's score

Table: Patient's Profile for group I and II

	GroupI	GroupII
No.ofPatients	20	15
PatientsAgeRange years	55-80years	64-94years
GleasonRange	6-9	7-9
ProstaticVolume(gm)	20-70gm	30-60gm
Pre-OperativeS.PSA	68.09(18.02-150 ng).	83.22ng(62.01-150 ng)

The mean operative time for group I was 4.1 minutes (3.7-4.6 hours). The median blood loss was 300ml, however the average Transfusion requirement (allogenic) was 1.46 (0-4). There were conversion to open surgery into two cases out of 20 cases(10%), one for rectal injury and another for dense adhesion. The hospital stay of the patients were about 2-4 days. Patients were kept in the hospital till patients were ambulatory and felt fit enough to go home. Continence was evaluated at 1, 3, 6 and 12 months with a median follow up of 3-26 months. 15 of 20 (75%) patients were continent. Of the 9 patients who were potent preoperatively 5 remained potent (55.5%) after the surgery.

Of the twenty patients in group I, three patients (15%) had biochemical recurrence in the form of raised PSA (6.1ng/ml, 4.6ng/ml and 2.8ng/ml) at 6- month follow up and underwent B/L sub capsular orchidectomy for the same. Four patients had expired in this series one in post-operative period due to massive myocardial ischemic attack, two because of progression of

aggressive disease another because of reason other than prostatic cancer in follow up.

Patients in LRP group were in cT2 stage in 13 % of cases and cT3 were 87% of cases, all cases in group 2 were in T3 stage. 55 % of group 1 patient were N0 while all cases in group 2 were N1. Median lymph node harvested was 21 (18-24). Urinary tract complications secondary to disease progression were more in ADT group 13.3 % underwent TURP, 6.6 % underwent suprapubic cystostomy, 6.6 % underwent PCN insertion and 13.3 % underwent cystoscopy clot evacuation.

Cancer specific survival

In the entire concert 8 patients died in FU, out of these 8 patients only two patients in LRP group died due to CA prostate and 5 patients died due to Ca prostate in ADT group and one patient died in LRP group in immediate postoperative period due to MI so median CSS was not reached in LRP group while median CSS in ADT group is 40 months.

Table: Univariate and multivariate analyses of factors associated with cancer- specific survival

Variable	Univariate		Multivariate	
	HR(95%CI)	pvalue	HR(95%CI)	pvalue
Age,years	1.056 (1.010-1.103)	0.015	1.031 (0.984-1.080)	0.202
PSA,ng/ml	0.998 (0.993-1.004)	0.557	0.996 (0.990-1.002)	0.164



Biopsy Gleason score				
≤8	Ref	0.067	Ref	0.232
≥9	2.145 (0.949–4.848)		1.785(0.709–4.494)	
Clinical T stage				
≤cT2	Ref	0.344	Ref	0.744
≥cT3	2.630 (0.354–19.516)		1.414 (0.177–11.265)	
Clinical N stage				
cN0	Ref	0.545	Ref	0.797
cN1	1.291 (0.564–2.954)		0.890 (0.364–2.171)	
Treatment				
ADT	Ref	0.004	Ref	0.004
LRP	0.267 (0.109–0.654)		0.264 (0.107–0.650)	

PROGRESSION FREE SURVIVAL

16 patients developed radiological progression in form of new metastasis out of which 10 (66.6%) patients were ADT group and 7 (35%) from LRP group Kaplan Meier analysis shows that

progression free survival was longer in patient with LRP group p value is = 0.008 which is significant median progression free survival was 62 months in LRP group vs 28 months in ADT group.

Table: Univariate and multivariate analyses of factors associated With progression-free survival

Variable	Univariate		Multivariate	
	HR(95%CI)	pvalue	HR(95%CI)	pvalue
Age, years	1.033 (0.998–1.070)	0.066	1.025 (0.980–1.071)	0.28
PSA,ng/ml	0.996 (0.992–1.001)	0.091	0.996 (0.992–1.001)	0.097
Biopsy Gleason score		0.007		0.003
≤8	Ref		Ref	
≥9	2.301 (1.255–4.221)		2.548(1.362–4.767)	
Clinical T stage		0.565		0.922
≤cT2	Ref		Ref	
≥cT3	1.353 (0.483–3.788)		0.948 (0.328–2.739)	



Clinical N stage				
cN0	Ref	0.051	Ref	0.198
cN1	1.856 (0.996–3.456)		1.523 (0.802–2.893)	
Treatment				
LRP	Ref	0.01	Ref	0.003
ADT	0.448 (0.242–0.826)		0.388 (0.206–0.731)	

IV. DISCUSSION

Certainly the most novel concept for surgical treatment of the primary tumor in prostate cancer would be its application in the presence of metastatic disease. Overall it is an interesting concept that removing the prostate gland may favorably improve the response to systemic therapy (androgen ablation) in cases of metastatic disease.

OPERATIVE TIME:

Mean operative time for Group I in whom laparoscopic radical prostatectomy done was 4.1 hours. More over the slight increase in duration in this group maybe due to the learning curve and also increased incidence of rectal injury in Group I (5%). Guillonnet et al in their series of 350 patients has an operative time averaging 3.6 hour, Hoznek et al in their series of 200 cases 3.5 hour, Bollens et al in their series of 50 cases 5.3 hour, Turk et al in their series of 125 cases 4.4 hour.^{9,7}

CONVERSION TO OPEN:

Conversion to open surgery was 10% (2/20) in Group I in our series of 20 cases. The reason for open conversion were rectal injury and bleeding in two cases. Bollens et al in their series of 50 cases had a conversion rate 2 percent. Rassweiller et al in their group of 100 cases had an conversion rate 5 percent, Gill et al required open conversion in 2.5 percent, Dahl et al required conversion in 1.4 percent of cases.

RECTAL INJURY:

Incidence of rectal injury was in one Patient 5% (1/20) and there was no incidence of rectal injury in last 10 cases. Abbou et al had rectal injury in 2.2 percent cases, Rassweiller et al in percent, Lein et al 4.2 percent, Guillonnet et al in 1.92 percent, Chang et al in 0.9 percent, Rozet et al observed rectal injury in 0.7 percent in their series of 600 cases.

PERIOPERATIVE COMPLICATION:

In our series we had other major and minor complication in the form of open conversion, excessive blood loss, transfusion requirement, rectal injury, excessive drain output, wound complication, post-operative fever, transient paralytic ileus, chest infection etc in 20 percent of the cases. Guillonnet et al in their series of 350 patients had total perioperative complications in 17 percent of the cases. Hoznek et al in their series of 200 cases had total perioperative complications in 11.9 percent of the cases and Bollens et al in their series of 50 cases had total perioperative complications in 34 percent of the cases. Total perioperative complication rate in our series is comparable to the one observed by Salomon et al who observed perioperative complications of 18 percent in their series and Guillonnet et al in their series of 350 patients, had total perioperative complications in 17 percent of the cases.

HOSPITAL STAY:

Patients were kept in the hospital till patients were ambulatory and felt fit enough to go home. In Group I the average hospital stay was 3 days with patient of rectal injury staying upto 12 days due to sub-acute intestinal obstruction. Steinberg et al in their series of 150 cases had average hospital stay of 2.3 days in their later 50 cases. Hoznek et al had average hospital stays of 6.2 days, Gill et al 1.6 days; Eden et al 4.2 days, Goemen et al had average hospital stays of 4.6 days in their series.

MARGIN POSITIVITY STATUS:

Although tumour extension to the surgical margin is clearly an adverse finding after radical prostatectomy, Smith J A opined that almost half of the patients with positive surgical margin remain tumour free with long term follow up. Catalona et al in their series of 1870 cases of RRP found that most of the positive surgical margin occurs at the



prostatic apex or posterolaterally along the course of the neurovascular bundle. Guillonnet et al in their series of 350 patients had positive margin in 17 percent of the cases, Hoznek et al in their series of 200 cases had positive margin in 25 percent of the cases, Gill et al found positive margin in 23 percent of their cases.

CONTINENCE RATE:

The causes of urinary incontinence after radical prostatectomy are likely multifactorial and include both functional and anatomical changes related to removal of prostate gland and alteration in the pelvic floor musculature and the urinary sphincter complex. Walsh PC concluded that though the physiologic mechanism of male urinary incontinence is poorly understood meticulous haemostasis, precise anatomical dissection of the prostatic apex, providing structural support to the posterior urethra and creating a water tight anastomosis are the key surgical steps in ensuring excellent continence outcome.

Our observations of preserving a long urethral stump for vesicourethral anastomosis resulting in reduced incidence of PPI were supported by many published series. Coakley et al used an endorectal MRI to measure the length of posterior urethra preoperatively and correlate that with PPI outcome in 211 patients and showed that a longer posterior urethra was associated with significantly more rapid recovery of urinary continence after radical prostatectomy. Continence was evaluated at 1, 3, 6 and 12 months.

At 6 months 15 of 20 patients (75%) in Group I were continent. Hoznek et al in their series of 200 cases had continence rate of 78.4 percent at 12 months post operatively, Rassweiler et al in their group of 100 cases had continence rate of 78 percent at 6-month post operatively, Turk et al in their series of 125 cases had continence rate of 86 percent at 6 month post operatively, Steinberg et al in their series of 150 cases had continence rate of 94 percent at 6 month post operatively.

CANCER CONTROL:

Of the fifteen patients in group I, three patients (15%) had biochemical recurrence in the form of raised PSA (6.1ng/ml, 4.6ng/ml and 2.8ng/ml) at 6- month follow up and underwent B/L sub capsular orchidectomy for the same. Another three patients had got further progression in form of multiple skeleton metastases with long bone fracture with metastatic lung and brain lesions both of these patients were having S.PSA more than 100. Three patients had expired in this study one in post-operative period due to massive myocardial ischemic attack, two because of

progression of aggressive prostatic cancer in follow up.

Of the fifteen patients in group II, three patients (20%) had biochemical recurrence in the form of raised PSA at 6-month follow up. Another five patients had got further progression in form of multiple skeleton metastases with long bone fracture with metastatic lung and brain lesions. Five patients had expired in this study because of progression of aggressive prostatic cancer in follow up. One was lost to follow-up.

There is compelling possibility that removing the prostate in men with metastatic prostate cancer might result in a more complete and durable response. Currently men with metastatic disease for which hormone therapy fails are destined to die of the disease. While they can respond to subsequent chemotherapy, those responses are transient. Clearly men with metastatic prostate cancer would benefit from a more durable response to hormonal therapy, which may be attainable by removing the prostate.

V. CONCLUSION

Laparoscopic radical prostatectomy is becoming the procedure of choice in the surgical management of early prostate cancer. But in selected cases of patient having androgen resistance metastatic prostate cancer, Laparoscopic radical prostatectomy is a viable option for patients, particularly in view of excellent local control rates and low morbidity.

- It appears that patients with node positive and possibly minimal distal metastatic (absence of multiple metastases in skull, ribs, long bones, and non nodal soft tissue) prostate cancer have a better response to surgical removal of the gland with or without androgen ablation.
- Surgical cytoreduction of cancer in a case of metastatic prostate cancer results in a more favorable and durable response to systemic therapy increasing patient longevity or improving the patient's health-related quality of life.
- It is reasonable to explore aggressive surgical therapy for advanced prostate cancer having androgen resistance in selected cases that having good general physical and performance status, but Oncological efficacy of this technique will require a large and longer study follow up data.
- There is improved cancer specific survival and progression free survival in the patient who have undergone laparoscopic radical prostatectomy in oligometastatic prostate cancer. The patients who have undergone LRP enter into CRPC state later as compare to those who took only ADT.



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