Journal of Clinical and Medical Images

Research Article

ISSN: 2640-9615 | Volume 6

Salvage Laparoscopic Radical Prostatectomy in Nonmetastatic Castration- Resistant Prostate Cancer: 2 Years Follow-Up and Current Evidence

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Received: 26 May 2022
Accepted: 07 Jun 2022
Published: 13 Jun 2022
J Short Name: JCMI

Citation:

Lopez Fontana G, Salvage Laparoscopic Radical Prostatectomy in Nonmetastatic Castration- Resistant Prostate Cancer: 2 Years Follow-Up and Current Evidence.
J Clin Med Img. 2022; V6(12): 1-4

Keywords:

Prostate cancer, salvage radical prostatectomy, radiotherapy, castration-resistant prostate cancer.

1. Abstract

1.1. Objective: To analyze the perioperatory and short-oncological outcomes in 5 cases with castration recurrent prostate pancer without metastasis [CRPC M0] developed after prostatic radiotherapy [pRT] and androgenic deprivation therapy [ADT] who underwent salvage laparoscopic RP [sLRP] with two years follow-up and review the current evidence.

1.2. Material and Methods: Perioperatory and oncological outcomes were prospectively analyzed. Inclusion criteria were patients that had received pRT and ADT with posteriorly presented as a CRPC M0 in standard imagines and positron emission tomography coline [PET]. Evidence was reviewed in PUBMED database.

1.3. Results: No surgical complications and blood transfusion were reported. Two patients required an endoscopic urethrotomy due to bladder neck contracture [Clavien IIIb]. Final pathological findings were pT3 or more, multifocal with 3 positive surgical margins. Four patients reach undetectable PSA after surgery except one that continuous under ADT without disease progression. After 24 months follow-up, 4 patients persist with undetectable PSA and one with stable disease under ADT. Current evidence demonstrated that CRPC M0 treated with open, laparoscopic, or robotic RP a biochemical recurrence of 68.7% as a hormone- sensitive PC; however, 17.4% were disease-free after 4 years of follow-up.

1.4. Conclusion: Our serie, sLRP is safety and feasible with 4 cases disease free after 24 months follow-up. Current evidence is a retrospective and multicenter experience with few cases and intermediate oncological follow-up. More cases with longer follow-up and better evidence are required to opt for this treatment as a first line.

2. Introduction

Prostate cancer [PC] is the most common cancer and the second leading cause of cancer death in United States [1]. Although PC screening with prostatic specific antigen [PSA] and digital rectal examination is controversial, nowadays most tumors are diagnosed in a nonmetastatic stage [2]. Primary treatment options such as radical prostatectomy [RP] or primary radiotherapy [pRT] in association or not with androgenic deprivation therapy [ADT] are the most common options, nevertheless, biochemical recurrence [BCR] may reach 30-40% [3,4]. Treatment options for BCR after RP vary including radiotherapy, hormonal therapies, early chemohormonal approaches, or a combination of these [5]. However, after primary RT, salvage radical prostatectomy [sRP] or ADT are the only opportunities for cancer control. sRP may lead to poor functional outcomes and complications [6] while ADT provides temporary control until PC develops an antiandrogenic resistance representing the next step in PC natural history [7].

ADT has been the only treatment option for M0 Castration- resistant PC [CRPC M0]. However, two phase 3 randomized controlled trials published in 2018 demonstrated that adding androgenic receptor blockage with apalutamide or enzalutamide to ADT improved metastasis-free survival and cancer specific survival [8, 9]. The main concern is that these options do not yield a definitive cure and their impact on overall survival is still unclear.

The introduction of new molecular imaging techniques like choline and more recently PSMA PET/CT in the re- staging of recurrent PC has allowed more accuracy the site of recurrence, even more, when the primary treatment had been radiotherapy [10]. Therefore, in CRPC M0 after radiotherapy sRP may be an option

in order to control PC and even more a possibility of cure.

Currently, there is little evidence about surgery in this setting; therefore, the aim of this study was to analyze the short-oncological outcomes in 5 cases with CRPC M0 that underwent salvage laparoscopic RP [sLRP] and review the literature.

3. Material and Methods

The database was prospectively performed from all patients diagnosed with CRPC M0 that underwent sRP after having received 76 Gy 3D primary radiotherapy for PC. All underwent surgery with curative intent only. Inclusion criteria were patient with CRPC defined as three consecutive rises in PSA one week apart resulting in two 50% increases over the nadir, and PSA > 2 ng/mL despite castrate levels of serum testosterone and no evidence of bone metastases and/or retroperitoneal disease at bone scan, computed tomography [CT] and positron emission tomography PET/MRI coline. Also, patients were divided if were at high risk for develop metastasis using a PSA double time [PSADT] less or more than 10 months [11]. Undetectable PSA was defined as a value of 0.1 ng/ml or less. Every patient underwent transperitoneal sLRP with extended lymphadenectomy by two laparoscopic surgeons [GLF, JMG] as described previously by Guillonneau and Vallencien [12] without neurovascular bundels preservation in these cases, prior informed consent. This approach is always elective for every RP in our center. All patients had discontinued ADT one month before surgery and the final histopathological findings was examined by the same genitourinary pathologist based on the protocol form the American College of Pathologists [13]. Positive surgical margins [PSM] were defined as the presence of tumor cells at the inked margin. Perioperatory outcomes such as surgical time, estimated blood loss and hospital stay were analyzed as well as oncological outcomes by PSA every 3 months at the same laboratory. Complications were evaluated using Dindo-Clavien classification [14]. Finally, urinary continence was also assessed by the number of pads needed per day.

4. Results

After data base analyzed from all laparoscopic radical prostatectomy, five patients were included. Perioperatory and oncological outcomes are detailed in [Tables 1,2 and 3]. Whole patients had received 3D RT with 76 Gy as a primary

treatment except one that was added ADT for 6 months. No perioperative complications were reported without blood transfusion and surgical conversion. All patients were discharged the day after surgery and the urinary catheter was removed on the tenth day. As a complication, two patients required an endoscopic urethrotomy due to bladder neck contracture [Clavien IIIb]. Pathological staging was equal or more than pT3a at the final histological findings, multifocal and 3 patients presented PSM. Four cases reach undetectable PSA at four to six weeks after surgery except one that the PSA was 0.98 ng/ml. Despite this, the patient continuous under ADT without disease progression due to stable PSA meaning that the remaining PC cells are hormone-sensitive. An interesting fact was that this case presented with pattern 4 at the surgical margin and PSADT was less than 10 months. During a 24-month follow-up, 4 patients persist with undetectable PSA and one with the stable disease under ADT. Finally, all patients are urinary continent without pads needed at twelve months after surgery. Erectile dysfunction was presented in all cases even with phosphodiesterase-5 inhibitors.

Table 1: Perioperatory outcomes of our serie

EBL: Estimated Blood Loss

Cases	Age	Surgical Time(min).	EBL (ml)	Hospital Stay (Days)	Complications
1	69	300	500	1.5	Clavien IIIb
2	66	350	400	1.5	Calvien IIIb
3	65	240	600	1.5	No
4	60	240	300	1.5	No
5	64	310	250	1.5	No

Table 2: Oncological Characteristics and outcomes

GS: Gleason Score

Cases	Diagnosis Age	Year	Biopsy	cT Stage	PSA (ng/ml)	Risk Classification	ISUP
1	61	2009	GS 7(4+3)	cT2b	12	Intermediate	2
2	57	2011	GS 8(3+5)	cT2b	17	High	4
3	58	2012	GS 7(3+4)	cT2a	43	High	2
4	54	2014	GS 6(3+3)	cT2c	8	Intermediate	1
5	58	2011	GS 7(4+3)	cT2a	9	Intermediate	3

Table 3: PSA value from the serie

Case 2 never reach undetectable PSA (orange)

Cases	RT Treatment (Year)	Type RT	Time to BCR (Years)	ADT	PET/MRI	DT PSA (Months)	Presurgical PSA (ng/ml)
1	2010	3D	7	Againest LHRH	Right lobe	12.3	3.95
2	2012	3D	7	Againest LHRH	Right lobe	8.9	4.3
3	2012	3D+ ADT 6 months	7	Againest LHRH	Right base and apical	11.8	3.15
4	2012	3D	5	Againest LHRH	Left Base	14.8	3.6
5	2012	3D	6	Againest LHRH	Bilateral	11.4	3.7

Cases	Final Histopathological Findings	Margins	Margins Pattern	Stage
1	Gleason 7(4+3) [65% pattern 4; 30% pattern 3 and 5% pattern 5]; multifocal	Positive	3	pT3a N0
2	Gleason 9(4+5) [90% pattern 4 and 10% pattern 5]; multifocal	Positive	4	pT3b N0
3	Gleason 8 (4+4); multifocal	Negative		pT3a N0
4	Gleason 7(3+4) [90% pattern 3 and 10% pattern 4]; multifocal	Positive	3	pT3b N +(2/16)
5	Gleason 7(4+3) [80% pattern 4, 15% pattern 3 and 5% pattern 5]; multifocal	Negative		pT3a N0

RT: Radiotherapy; BCR: Biochemical Recurrence; ADT: Androgenic Deprivation Therapy; DT PSA: Double Time PSA

Months/Cases	1	2	3	4	5	PSA ng/ml (value)
1	<0.03	0.98	<0.008	<0.01	<0.01	
3	0.1	0.28	<0.008	<0.02	<0.01	
6	0.05	1.88	0.01	<0.02	<0.01	
9	0.02	0.8	0.008	<0.02	<0.01	
12	0.1	0.9	0.008	<0.02	<0.01	
15	0.02	1.2	0.008	<0.02	0.01	
18	<0.01	2.9	<0.008	<0.02	0.02	
24	0.08	3.1	<0.008	<0.03	0.04	

5. Discussion

PC recurrence after primary radiotherapy [RT] is treated using ADT in approximately 90% of cases. The development of CRPC represents the next step in PC natural history [7]. The increased accuracy of new technologies and molecules allows to detect PC sites of metastasis compared to standard staging imagines [10]. Among patients who developed CRPC without metastasis [M0], approximately one in three and one in five will develop metastases or die of the disease within 2 years; respectively [15]. New therapies have shown an increased metastasis-free survival [8,9]; nevertheless, do not yield a definitive cure being surgery a reasonable strategy that may provide an alternative treatment in selected cases. The first experience was reported by Gontero et al. in 12 cases showing that sRP is feasible in CRPC M0 with a higher complication rate compared to sRP in hormone-naïve PC probably due to the more aggressive nature of the hormone-refractory disease [16]. Six years later, the same author published a retrospective multicenter experience including open, laparoscopic and robotic approaches adding eleven patients being currently the only report in the literature with a total of 23 cases [17]. Histopathological findings demonstrated that most of the patients had PSM, extraprostatic disease [≥pT3], 30% lymph node involvement and the Gleason score was ≥8 in 65%. Despite these aggressive features, almost 70% reached undetectable PSA after surgery without ADT. Only seven patients had persistence PSA hormone-sensitive and 6 CRPC persistence. Biochemical recurrence occurred in 68,7% in hormone-sensitive PC and in 58,8% in CRPC at a median of 11 and 31 months from surgery; respectively. At median 4 years of follow-up, 17.4% were disease- free and 34.4% had died from PC.

Our preliminary report adds 5 cases to the literature being 28 patients altogether with a minimum of 24 months of follow-up. Final histopathological findings demonstrated the aggressive disease of this cases being ≥pT3 in all cases and one with lymph node involvement. Three patients had PSM; however, and despite this, all patients except one could reach undetectable post-operatory PSA and remained for more than 24 months. The case with persistence

detectable PSA continues with ADT without disease progression and stable PSA less than 1 ng/ml establishing as hormone- sensitive PC. The interesting features, in this case, were that pattern at PSM was 4 and PSADT less than 10 months. In Argentina there is not approval PET/TC PSMA yet; therefore, this patient still under ADT only. Finally, all patients were continent at 12 months without erectile function even with phosphodiesterase-5 inhibitors.

The main limitations of these publications are that PET/TC or PET/MRI are not indicated in patients under ADT enabling a bias at the results, the retrospective analysis, different surgeons in the analysis from Gontero et al. [17] knowing that oncological outcomes depend on surgeon experience when RP is performed, different approaches and lymph node dissections, no standard surgical technique, and a few cases.

6. Conclusion

Current evidence demonstrated that sRP in CRPC M0 even laparoscopic, robotic or conventional approach is feasible with more surgical complications probably due to the aggressive PC features. Regarding oncological outcomes, PC can be cured up to 17% of the patients in an intermediate follow-up allowing an alternative to new therapies in these patients, and a significant proportion experience prolonged BCR and CRPC-free status delaying a systemic therapy. However, the evidence is not enough to propose surgery in CRPC M0 instead of medical treatment. It is necessary prospective, comparative, randomized and controlled trials with more cases and identify different features that could allow which patients will be benefited from surgery instead of medical treatment. Our serie, sLRP was safety, feasible and after 24 months follow-up and four cases were disease free survival. Strikingly, pattern 4 at PSM and PSADT less than 10 months were two characteristics of adverse oncological outcomes.

References

1. US Cancer Society. Prostate at a glance. Estimated new cases, 2021.
2. Drazer MW, Dezheng H, Eggener SE. National Prostate Cancer Screening Rates After the 2012 US Preventive Services Task Force Recommendation Discouraging Prostate- Specific Antigen-Based Screening. J Clin Oncol. 2015; 33(22): 2416-2423.
3. Simmons MN, Stephenson AJ, Klein EA. Natural history of biochemical recurrence after radical prostatectomy: risk assessment for secondary therapy. Eur Urol. 2007; 51:1175-1184.
4. Boorjian SA, Thompson RH, Tollefson MK, Rangel LJ, Bergstralh EJ, Blute ML et al. Long-term risk of clinical progression after biochemical recurrence following radical prostatectomy: the impact of time from surgery to recurrence. Eur Urol. 2011; 59: 893-899.
5. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, Van der Kwast T et al. EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration- resistant prostate cancer. Eur Urol. 2014; 65(2): 467-479.
6. Gontero P, Marra G, Alessio P, Filippini C, Oderda M , Munoz F et al. Salvage radical prostatectomy for recurrent prostate cancer: morbidity and functional outcomes from a large multicenter series of open versus robotic approaches. J Urol. 2019; 202: 725-731.
7. Loriot Y, Supiot S, Beauval JP, Schluurmann F, Pasticier G, Sargos P, et al. Management of non-metastatic castrate-resistant prostate cancer: a systematic review. Cancer Treat Rev. 2018; 70: 223-231.
8. Smith MR, Saad F, Chowdhury S, Oudard S, Hadaschik BA, Graff JN, et al. Apalutamide treatment and metastasis-free survival in prostate cancer. N Engl J Med. 2018; 378:1408-1418.
9. Hussain M, Fizazi K, Saad F, Rathenborg P, Shore N, Ferreira U, et al. Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. N Engl J Med. 2018; 378: 2465-2474.
10. Afshar-Oromieh A, Zechmann CM, Malcher A, Eder M, Eisenhut M, Linhart HG et al. Comparison of PET imaging with a (68) Ga-labelled PSMA ligand and (18) choline- based PET/CT for the diagnosis of recurrent prostate cancer. Eur J Nucl Med Mol Imaging. 2014; 41(1): 11-20.
11. Memorial Sloan Kettering Cancer Center, PSA Doubling time.
12. Guillonneau B, Vallancien G. Laparoscopic radical prostatectomy: the Montsouris technique. J Urol. 2000; 163(6): 1643-1649.
13. https://documents.cap.org/protocols/cp-malegenital-prostate-radicalprostatectomy-20- 4101.pdf.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240(2): 205.
15. Smith MR, Kabbinavar F, Saad F, Hussain A, Gittelman MC, Bilhartz DL, et al. Natural history of rising serum prostate-specific antigen in men with castrate nonmetastatic prostate cancer. J Clin Oncol. 2005; 23(13): 2918-2925.
16. Gontero P, Spahn M, Marchioro G, Karnes JR, Briganti A, Frea B, et al. Salvage radical prostatectomy in nonmetastatic castration-resistant prostate cancer patients who received previous radiotherapy: a feasibility study. Eur Urol. 2014; 65(1): 254-255.
17. Marra G, Calleris G, Alessio P, Oderda M, Palou J, Joniau S, et al. Outcomes of Salvage Radical Prostatectomy for M0 Castration-resistant Recurrent Prostate Cancer: A Reasonable Option in the Era of New Antiandrogen Therapies? Eur Urol Focus. 2021; 7(4): 807-811.