

ORIGINAL ARTICLE

3D laparoscopic salvage radical prostatectomy: mini-series report and review of the literature

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Summary

Purpose: Salvage therapy represents a rescue therapy, given after the first line of treatment had failed. The purpose of this study was to review the outcomes of patients who underwent salvage laparoscopic radical prostatectomy (sLRP) in our department and to review current published studies.

Methods: Our mini-series consisted of 6 patients with recurrent prostate cancer (PCa) after non-surgical primary treatment. All interventions were performed by a single surgeon from the Oncological Institute "Prof. Dr. Ion Chiricuță" Cluj Napoca, Romania. A literature review was carried out in June 2020 using the PubMed and MEDLINE databases to identify relevant studies published in the literature between 2000 and 2020. Six papers were selected for our review. We reviewed the oncological and functional outcomes of patients that underwent sLRP.

Results: Extraperitoneal sLRP was performed in 6 patients.

Biochemical failure after primary treatment developed between one and five years. Mean operative time was 135.5 min, mean blood loss was 328 ml. No intraoperative complications occurred and no conversions to open surgery. RO was achieved in 5 out of the 6 patients (83.5%). Out of the 6 patients 2 are incontinent.

Conclusions: SLRP remains an underused procedure and a missed therapeutic opportunity for selected patients. From published data and personal experience, we conclude that in experienced hands sLRP for localized prostate cancer is a feasible, safe and efficient method to treat recurrent PCa. Short-term oncological outcomes are optimistic but further studies need to be made to observe the long-term outcomes.

Key words: 3D laparoscopy, prostate cancer, salvage prostatectomy, salvage therapy

Introduction

Prostate cancer (PCa) is the second most commonly diagnosed cancer in men accounting for 13.5% of all cancers diagnosed according to the Global Cancer Observatory produced by the International Agency for Research on Cancer, with a total of 1.276.106 new diagnosed cases worldwide in 2018[1]. In localised disease a life expectancy of at least 10 years [2] is considered mandatory for any benefit from local treatment. In cases with

low-risk PCa and organ-confined disease active surveillance can be offered. Treatment options range from radical prostatectomy, radiotherapy, hormonal therapy. Other modalities have emerged as potential therapeutic options such as cryotherapy and high-intensity focused ultrasound (HIFU) which are categorized as experimental local treatments in the EAU guidelines. Recurrence of PCa after primary treatment is a significant and common con-

dition in clinical practice. The rates of recurrence range from 15% and can go up to 60% depending on the primary treatment that was chosen and the length of the follow-up [3], thus a form of salvage therapy must be considered in these cases.

Salvage therapy represents a rescue therapy, given after the first line of treatment had failed. It is considered a final attempt in patients with recurrence of different pathologies, especially cancer. Treatment options for patients with PCa include salvage radical prostatectomy (sRP), salvage radiotherapy, life-long androgen deprivation therapy, which is not curative and is associated with a plethora of adverse effects, cryotherapy and HIFU [4]. The overall utilization of salvage local treatment options as potentially curative has increased in recent years. This trend is not applicable for the salvage radical prostatectomy which is still rarely performed despite evidence of oncological efficacy and improved safety in recent studies. There is yet no universally accepted approach for the management of PCa recurrence [3,5].

After a proper selection of the cases, sRP can be offered to patients with a long-life expectancy (greater than 10 years) [2] and high risk for cancer-specific mortality. It can provide intermediate-term cancer control in cases with recurrent disease confined to the prostate or periprostatic tissue. The peri-operative complications are similar to those of standard RP with a higher risk of rectal injury due to the modified structures after primary treatment [4]. A major problem in patients with recurrent PCa is that usually the cancer is already advanced by the time the patient sees a specialist [5].

The evolution of surgical settings with 3D and 4K laparoscopic cameras and robotic surgical systems in the high-volume oncological centers, that allow a more detailed view of the structures and cleavage planes, have been important factors in the improvement of the minimal invasive surgical technique.

The aim of this study was to review the outcomes of our patients who underwent salvage laparoscopic radical prostatectomy (sLRP) in our department, emphasizing the evolution in the surgical technique and dexterity, thus checking the feasibility of this procedure and at the same time the improvement of postoperative morbidity.

Methods

Our mini-series consisted of 6 patients with recurrent PCa after non-surgical primary treatment, one after cryotherapy, one after HIFU and in 4 patients after external radiotherapy. All the interventions were performed by a single surgeon from the Oncological Institute "Prof. Dr. Ion Chiricuta" Cluj Napoca, Romania. All patients

underwent physical examination, completed IIEF 5, IPSS and urinary incontinence questionnaires, blood tests, serum PSA measurement, computerized tomography (CT) and bone scan to exclude metastatic disease. All recurrences were confirmed histologically by means of transrectal ultrasound guided biopsies. Hospital charts were evaluated to collect patients' information regarding previous treatment, initial PSA before the primary treatment and specimen staging.

The surgical technique for salvage laparoscopic 3D radical prostatectomy (sLRP) does not significantly depart from that of standard laparoscopic radical prostatectomy. We used the five-port extraperitoneal approach for both standard sLRP and LRP. The patient was placed in dorsal decubitus position and the arms are tucked and padded with maximum waist extension by operating table flexion and steep Trendelenburg. The ports were placed in the standard configuration, with a 10 mm under-umbilical trocar and two 10 mm trocars on each side. Sharp dissection was required because of intense periprostatic fibrosis, 5mm Ligasure and metal clips were used as sealing devices and lymph node dissection was performed in all patients. The urethro-vesical anastomosis was carried out in a continuous suture, with 2.0 polydioxanone thread and a 26.2 mm round ½ c needle.

A literature review was carried out in June 2020 using the PubMed and MEDLINE databases to identify relevant studies published in the literature, using the search terms "salvage radical prostatectomy" and "laparoscopy", published between 2000 and 2020. Papers regarding robotic or open approaches were excluded. A total of 23 papers were identified, from which 6 were selected for our review. The excluding criteria were ar-

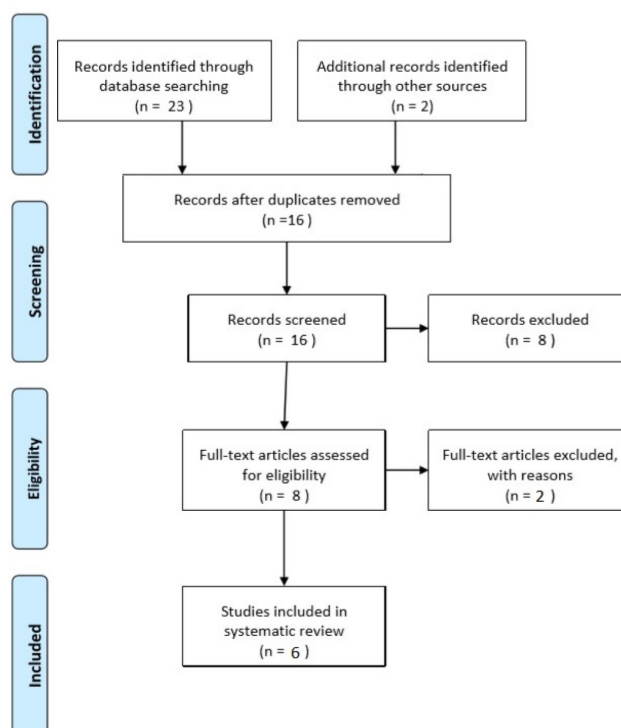


Figure 1. Prisma flow diagram.

ticles concerning only open or robotic salvage prostatectomy and articles published before 2000. Prospective and retrospective articles published in English that analysed the results after laparoscopic salvage radical prostatectomy were included. The literature review was conducted according to PRISMA guidelines (Figure 1). We collected the information from these papers (Figure 3) and compared them to our peri-operative results.

Results

Extraperitoneal laparoscopic salvage prostatectomy was performed in 6 patients. Initial PSA before the primary treatment was 16.31 ng/mL (range 8 to 38). Biochemical failure after primary treatment developed between one and five years. Patients did not have a history of previous operations. Mean operative time was 135.5 min (87 to 166), with a mean blood loss of 328 ml (150 to 500). No intraoperative complications occurred

and no conversions to open surgery. We placed a single drain tube which we suppressed in the 4th postoperative day. Postoperative hospital stay was between 5 and 14 days (mean 8.7). The histopathological reports after the sLRP revealed 5 patients with ypT3b and one patient with ypT2c, 2 patients with Gleason score of 8, 3 with 7(4+3) and one with 7(3+4). R0 could be achieved in 5 out of the 6 cases of salvage prostatectomy –83.5%. With the structures being severely modified after the failed primary treatment, nerve sparing and functional outcomes were not priorities for the interventions, with the best oncological outcome being the main goal. Bladder catheter was suppressed after an average of 15.5 days (14 to 19) due to slower tissue healing. Mean follow up was 14.8 months, presented in Table 1. Out of the 6 patients that underwent sLRP, 2 are incontinent. No patient had postoperative lymphocele or urethral

Table 1. Perioperative data for sLRP patients (n=6)

Case number	1	2	3	4	5	6
Age, years	73	65	61	72	74	64
Initial PSA (ng/ml)	8	12,4	38	7,5	22	10
Primary treatment	RT+HT	RT+HT	RT+HT	CT	RT+HT	HIFU
Recurrence (years)	3	5	2	1	1	1.5
Preoperative PSA (ng/ml)	6	1.44	9.4	5	0.8	2.2
Operating time (min)	87	150	160	166	120	130
Blood loss (ml)	170	450	500	500	150	200
Intraoperative complications	0	0	0	0	0	0
Catheterisation time (days)	15	14	15	16	19	14
Hospital stay (days)	14	5	11	7	7	8
ypT	3b	2c	3b	3b	3b	3b
Gleason score	7(3+4)	8(4+4)	7(4+3)	8(4+4)	7(4+3)	7(4+3)
Lymph node dissected	12 (1+)	4	15 (3+)	6	11	10
Continenace	0	1	1	0	1	1
Biochemical recurrence	0.06	1.88	0.003	0.137	0.003	0.003
Follow-up (months)	24	19	8	15	11	12
Positive surgical margins	-	-	-	-	+	-

Table 2. Functional outcomes

Case number	1	2	3	4	5	6
IIEF-before surgery	5	2	21	18	19	18
IIEF-after surgery	0	1	1	1	0	0
IPSS-before surgery	10	0	27	4	0	6
IPSS-after surgery	2	1	0	8	7	1
ICIQ-before surgery	7	0	0	0	0	0
ICIQ-after surgery	15	9	8	20	3	2
Pads after surgery	3	1	1	4	control	control

IIEF: International index of erectile function, IPSS: International Prostate Symptom Score, ICIQ: The International Consultation on Incontinence Questionnaires

stenosis. Preoperatively 4 patients were potent (IIEF=18-21), postoperatively all 6 patients were impotent (IIEF=0-1)(Table 2). At follow-up 5 patients were free of disease with PSA levels lower than 0.2ng/ml. Patient 2 had biochemical recurrence at 6 months after surgery (PSA=0.225 ng/ml) [20] because according to EAU guidelines PSA recurrence is considered >0.21 with the last PSA 1.88 ng/ml. The histopathological findings after prostatectomy described prostate adenocarcinoma ypT2cN0Mx with a Gleason score of 8(4+4) and no positive surgical margins. The patient underwent adjuvant radiotherapy after the biochemical recurrence was diagnosed [20,21].

Discussion

Salvage radical prostatectomy represents a technically challenging procedure regardless if it is done open, laparoscopic or robotic. This is related to the changes that occur in the tissue after the primary treatment, thus a higher risk of complications is present. Because the learning curve for laparoscopic and robotic interventions is larger than for open surgery, these two can be performed only in specialized high-volume centers by experienced surgeons. The introduction of 3D systems in the laparoscopic setting has had a strong impact on the evolution of the efficiency of this procedure. Studies are showing a significant difference between 2D and 3D laparoscopic settings regarding the efficiency, total operative time, blood loss, dissection and suturing [7,8]. This could be supported by the improvement in depth of perception, leading to better visibility, which is important for these complex urological operations. A study on 20 surgeons divided in experts, surgeons with intermediate experience and novices have concluded that the robot can be helpful for novices, but well-trained laparoscopic surgeons may not really benefit from 3D robot systems if 3D laparoscopy is available [9,10].

Another important factor to have in mind are the costs related to the surgical intervention. The robotic system represents the most expensive option due to purchase of the robot itself, the maintenance and cost of the disposable robotic instruments [11]. For medical institutions from developing countries (low and middle-income countries) or hospitals that can't afford the robotic procedure, the 3D laparoscopic system is the best option, having the video quality, the depth of perception, spatial resolution and the visibility of the camera from the robot setting, but with the more affordable price of the setting and instruments.

A review of the literature by Matei et al that included 27 single-center or multicenter retro-

Table 3. Literature review (n=6)

	n	Duration of surgery (hours)	Mean pre-operative PSA (ng/ml)	Pre-operative potency n (%)	Intra-operative complications	Mean hospital stay	Incontinence %	Erectile dysfunction %	PSM %	Catheterization time (mean days)	Anastomosis stricture	Post-operative complications	Biochemical recurrence
Vallencien et al.	7	3.1	0.68	2 (28.57)	0	6.4	28.50	100	28.50	13	0	2	2
Stoltzenburg et al.	9	2.5	12.64	3 (33.33)	0	N/A	22.20	100	22.20	6	0	1	1
Nunez-Mora et al.	9	2.8	9.1	5 (55.55)	0	4	33.30	80	22.20	24	0	2	2
Leonardo et al.	13	3.7	3.31	8 (61.53)	0	8	30.76	100	15.38	N/A	2	2	1
Liatsikos et al.	12	2.5	12.7	3 (25)	0	N/A	16.66	100	25	7	0	1	1
Ahallaal Y et al.	15	4	3.49	5 (33.33)	1	2	53.33	93.33	13.33	15	0	5	4

PSA: prostate specific antigen, PSM: positive surgical margin

spective open, laparoscopic and robotic sRP case series, underlined the rates of postoperative complication that ranged from 0-11% for laparoscopic procedures and 0-33% for robotic procedures. The incontinence rates ranged were 22-33% for the laparoscopic approach and 20-100% for the robotic approach [12]. Erectile dysfunction (ED) was evaluated as well with a preoperative ED ranging from 10-91% and a post-op ED from 72-100%. This shows the difficulty of nerve sparing in these patients with changed structures after the primary treatment (Table 3).

Publications regarding sLRP consider the procedure as a feasible option that provides good functional and oncological outcomes and may present less morbidity compared to the open procedure. This can be related to the better image and angles provided by the endoscopic camera. We included 6 publications after our literature review (Figure 1). As intraoperative complications Ahallal et al described one patient who had a rectal injury that was primarily sutured and was protected by a diverting colostomy, reversed 3 months later. No other intraoperative complications were described. Regarding anastomotic stenosis after sLRP, Leonardo et al reported 2 patients with anastomotic stenosis (Clavien IIIa) at 3 months that required internal urethrotomy. The incontinence rate ranged from 16.66% to 53.33% with a mean of 30.79%. This percentage is slightly higher than the one from standard RP [5] and underlines the effect of the primary treatment on the prostate and periprostatic structures. Urinary incontinence is more frequent in post radiotherapy surgery than in primary surgery, ranging between 10% and 73% in open surgery. Erectile dysfunction after primary treatment ranged from 38.47% to 75% with a postoperative erectile dysfunction of 100% in 4 studies [8,9,16,17]. Nunez-Mora et al and Ahallal et al reported one patient each with erectile dysfunction after surgery in their studies [15,18]. These results underline the primary focus on the oncological outcomes and not on the functional ones (Table 3).

Because the recurrence of PCa after primary treatment occurs in patients with radioresistance or aggressive cancers [6], positive surgical margins (PSM) and biochemical recurrence after sLRP are important factors and key aspects to pay attention to. In the publications included in our literature review, the PSM ranged from 13.33% to 28.50% with a mean of 21.10% which is in the limit of PSM after standard RP (6-22%) [19] and in accordance with our results (83.5%). There was a mean 18.71% of patients with biochemical recurrence after sLRP. In our mini-series one out of 6 patients had biochemical recurrence which stands for 16.67 %, (Table 3).

Stephenson et al concluded that the PSA progression free probability after 5-years following salvage RP is 77% for patients with organ-confined disease (stage II), 71% for isolated extracapsular extension (stage III) and 24% for seminal vesicle invasion and/or lymph node metastases (stage IV) [5].

sLRP remains an underused procedure and also a missed therapeutic opportunity for selected patients with long life-expectancy and high-risk cancer-specific mortality. The oncological outcomes of this mini-series and also from other articles published were satisfactory, technological evolution and their implementation in high-volume oncological centers having a great impact on these results. We therefore conclude that in experienced hands sLRP for localized PCa is a feasible, safe and efficient method to treat recurrent PCa after failed primary treatment. Short-term oncological outcomes are optimistic but further studies need to be made to underline the efficacy of these interventions and the long-term outcomes so that experienced surgeons will take them into consideration.

Conflict of interests

The authors declare no conflict of interests.

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