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Pilot study of salvage laparoscopic prostatectomy for the treatment of recurrent prostate cancer

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Abstract

OBJECTIVE—To evaluate feasibility, safety and oncological efficacy of salvage laparoscopic radical prostatectomy for pathology-proven biochemical recurrence after primary radiation therapy or cryotherapy for prostate cancer.

MATERIALS AND METHODS—This retrospective pilot study examined 15 patients from 2004 to 2010 with biochemical recurrence after external beam radiation therapy (n = 8), brachytherapy (n = 6) or cryotherapy (n = 1). Patients were treated with salvage laparoscopic radical prostatectomy (11 conventional, four robotic-assisted) with bilateral pelvic dissection.

RESULTS—Median duration of surgery was 235 min. None of the following occurred: conversion to open surgery, transfusion, urethrovesical stenosis or perioperative or postoperative mortality. One patient presented with a rectal injury, repaired using uninterrupted sutures and a colostomy. One patient had anastomotic leak treated with prolonged Foley catheterization. Pathological stage was pT2a in three, pT2b in three, pT3a in four, pT3b in three and pT4 in two patients; two patients had nodal metastasis. Within an 8-month median follow-up, 11 patients were disease-free and three had persistent postoperative prostate-specific antigen (PSA) elevation; the remaining patient experienced PSA recurrence after 21 months. Seven patients achieved continence (no pads) by 8.4 months (median), one patient manifested severe incontinence corrected by implanting an artificial sphincter, and seven patients with a 12.6-month mean follow-up continued to need one or two pads per day. Erectile dysfunction was present in five patients before surgery and in 14 patients after surgery.

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Conflict of interest
None declared.

CONCLUSIONS—Salvage laparoscopic radical prostatectomy seems to offer a safe therapeutic alternative for patients failing primary radiation or cryotherapy. However, larger studies with longer-term data are required.

Keywords

cryotherapy; laparoscopic prostatectomy; prostatic neoplasms; radiotherapy; salvage therapy

Introduction

After primary radiation therapy or cryotherapy for prostate adenocarcinoma, a biochemical-only recurrence (defined as PSA rise with a negative metastatic evaluation) poses a diagnostic and therapeutic dilemma for clinicians and patients alike. Open radical prostatectomy (ORP) represents the most effective curative treatment option for these patients [1].

In the primary cancer setting, we have shown that laparoscopic radical prostatectomy (LRP) is safe and has equivalent functional and oncological outcomes to ORP [2]. Several small series have assessed the early morbidity and efficacy of conventional and robotic-assisted LRP in the salvage setting [3–6]. The primary aim of the current study was to test the feasibility and safety of salvage LRP (sLRP) for recurrent prostate cancer. Before enrolling more patients into our institution's sLRP programme, we analysed our data to assess whether the morbidity of sLRP was comparable to historical controls at our centre (i.e. salvage ORP (sORP)). We also assessed the early functional and oncological outcomes of our sLRP patients.

Materials and methods

After approval by the institutional review board, we retrospectively identified 15 patients in the Memorial Sloan-Kettering Cancer Center radical prostatectomy database who underwent sLRP between 2004 and 2010 for biopsy-proven local recurrence after cryotherapy or radiation therapy for localized prostate cancer. All patients underwent prostate biopsy for biochemical recurrence (BCR) according to Phoenix criteria [7]. Median age at time of sLRP was 62.3 years (interquartile range (IQR) 57.4–71.4).

The primary treatment was external beam radiation therapy (EBRT) in eight patients, brachytherapy in six patients and cryotherapy in one patient. The median serum PSA before primary therapy was 5.5 ng/mL (IQR 4.4–7.8). Clinical stage before primary therapy was known in 13 patients: T1c in 11 patients, T2a in one patient and T3b in one patient. Biopsy Gleason score before primary therapy was 6 (3 + 3) in five patients, 7 (3 + 4) in six, 8 (4 + 4) in two and 9 (4 + 5) in two. The median EBRT dosage was 72 Gy (IQR 66–81). The median interval from primary therapy to BCR was 46 months (range 6–144, IQR 29–59). The median serum PSA nadir after primary therapy was 1.33 ng/mL (IQR 0.9–1.5).

At the time of surgery, median serum PSA level was 3.49 ng/mL (IQR 2.9–6.0). Imaging studies such as bone scan and CT of the abdomen and pelvis were negative for metastatic disease. All patients underwent extended pelvic lymph node dissection and radical

prostatectomy either by conventional (n = 11) or robotic-assisted (n = 4) transperitoneal laparoscopy.

Patient, tumour and treatment characteristics were prospectively recorded for each patient and retrospectively analysed. Complications were prospectively recorded and graded according to the Clavien scale [8]. Urinary function was assessed using the urinary questionnaire validated at the Memorial Sloan-Kettering Cancer Center and the IPSS. Sexual function was assessed using the Sexual Health Inventory for Men score.

The prostatectomy specimens were analysed by the whole-mount step-section technique. Postoperatively, patients were followed with serial serum PSA determinations and digital rectal examinations every 3 months for the first two years and annually thereafter. Disease recurrence after sLRP was defined as a serum PSA level of 0.1 ng/mL or higher with a confirmatory rise.

Results

Perioperative data and complications

Perioperative data are shown in Table 1. There was no perioperative mortality. No conversion to open surgery was necessary, and median operation time was 235 min (IQR 210–285). Median blood loss was 200 mL (IQR 150–275) and none of the patients received any transfusion.

One patient had an intra-operative rectal injury that was primarily repaired using uninterrupted sutures and protected by a diverting colostomy that was reversed 3 months later without any other sequela. This patient had pT3a stage, negative surgical margins and no lymph node invasion.

There were five minor medical complications (three grade 1 and two grade 2), and there was no grade 3 or higher complication. Three patients had gross haematuria during the first postoperative week and were treated with intermittent bladder irrigation. One patient presented an asymptomatic urinary tract infection 4 days after the surgery which was managed successfully with antimicrobial therapy. One patient had an anastomotic leak treated with prolonged Foley catheterization (30 days). There were no cases of urethrovesical stenosis.

Length of hospital stay was 2–8 days (median 2 days; IQR 1–4). All patients underwent a cystogram prior to catheter removal. Average length of urethral catheterization was 15 days (SD 2.6 days).

Oncological outcomes

Three patients had pT2a disease, three pT2b, four pT3a, three pT3b and two pT4. Both pT4 patients had a positive surgical margin at the bladder neck; the remaining 13 patients had negative surgical margins. Pathological Gleason score was 6 (3 + 3) in one patient, 7 in seven patients (4 + 3 in four patients), 8 (4 + 4) in four patients, and 9 (4 + 5) in another three.

The median number of lymph nodes removed was 16 (IQR 13–21). Two patients had metastasis to regional lymph nodes: one patient had one positive node out of 14 and the second had four positive nodes out of 21.

Median follow-up on the remaining 13 patients without such metastasis was 8 months (IQR 2–17). Eleven patients remained disease-free. Three patients had persistent postoperative elevation of PSA (nadirs of 0.7, 1.9 and 0.15 ng/mL after 1.5, 1.9 and 2 months, respectively). These three patients experienced subsequent PSA rise and were followed up by medical oncologists according to our protocol. One had positive lymph node invasion, the second had an extracapsular extension and the third had positive surgical margins (pT4 N0 with bladder involvement). The remaining patient experienced PSA recurrence after 21 months.

Functional outcomes

Seven patients achieved continence (no pads) within a median time of 8.4 months (IQR 2.0–24.5). One patient had severe incontinence and underwent a successful implantation of an artificial sphincter 13 months after sLRP. Seven patients continued to need one to two pads per day at a mean follow-up of 12.6 months (SD 10.0). None of the patients complained of obstructive LUTS. The median IPSS score at 6 months was 14 (IQR 5–15). Erectile dysfunction was present in five patients before surgery and only one patient had an erection postoperatively.

Discussion

The non-extirpative local therapies EBRT, brachytherapy and cryotherapy have comparable local tissue effect, and the same rules are followed for diagnosis and management of recurrence after these therapies [9]. It is estimated that approximately one-third of the patients found to have clinically localized prostate cancer undergo treatment with radiotherapy [10], with a BCR rate after 5 years ranging roughly between 25% and 50% [11]. There is controversy as to the best treatment for patients experiencing biochemical failure after treatment with full-dose local radiotherapy or cryotherapy. Salvage cryotherapy carries the disadvantages of limited efficacy and non-negligible complications [12,13]. Similarly, acute morbidity such as vesicorectal fistulas and a high percentage of incontinence is still a major concern for patients considering sORP [14,15], but sORP has the highest efficacy rate and a morbidity profile which is improving over time [1].

We confirmed that sLRP is a feasible and safe minimally invasive procedure. After a median postoperative stay of 2 days, patients were discharged with oral pain medication. There were no perioperative or postoperative deaths and no readmissions. One patient had a rectal injury and a colostomy that was reversed within 3 months. This patient had pT3a stage, negative surgical margins and no lymph node invasion.

We found sLRP to result in expected local disease control in patients with local recurrence after primary therapy with non-extirpative instrumental therapies. Three of the 15 patients had persistent PSA elevation: one had positive lymph node invasion, the second had an extracapsular extension, and the third had positive surgical margins (pT4 N0 with bladder

involvement). One other N0 patient experienced PSA recurrence after 21 months. It is presumed that, at time of sLRP, these four patients had micrometastatic disease. The rate of positive surgical margins (2 of 15) and the number of lymph nodes retrieved were within the range reported at our centre for sORP with extended lymphadenectomy (i.e. removal of obturator, external iliac, hypogastric with or without presacral and common iliac nodes) [1,2]. As the median number of lymph nodes removed was 16, we think that the loco-regional staging should be accurate [16]. Nevertheless, long-term follow-up and survival data are needed before conclusions can be drawn about the oncological efficacy of sLRP.

To our knowledge, there are only three publications [4–6] that have reported their conventional (non-robotic) sLRP experience – see Table 2 [3–6,16–21]. Vallancien *et al*. [6], Stolzenburg *et al*. [5] and more recently Nuñez-Mora *et al*. [4] report BCR-free rates of 71%, 89% and 55.5% at 11.2, 12 and 27 months, respectively. In our series, 11 out of 15 patients were BCR-free with a median follow-up of 8 months, showing sLRP's oncological control to be similar to that of sORP [17–19,22].

Kaouk *et al*. [3] evaluated four patients who underwent salvage robotic-assisted laparoscopic prostatectomy. At a mean follow-up of 1 month three patients were continent, and at a mean follow-up of 5 months one patient had BCR. Eandi *et al*. [18] recently reported data on 18 patients who underwent salvage robotic-assisted laparoscopic prostatectomy. With a median follow-up of 18 months, 33% of patients experienced BCR while only 33% were continent.

We found sLRP to result in urinary control comparable to that seen in historic series. The rate of urinary incontinence ranges from 10% to 73% in the open procedure (sORP) [16,17,19–22], whereas in sLRP it oscillates between 22% and 67% [4–6] with an incontinence rate in our series of seven in 15 (since we defined continence rate as no pads used). No patient in this sLRP series experienced urethrovesical stenosis. We did not use flowmetry in our patients' follow-up; nevertheless, none of them complained of obstructive LUTS and those who underwent cystoscopy (n = 6; for haematuria in one patient, LUTS in one patient, and urinary incontinence in four other patients) did not demonstrate an anastomotic stricture. Furthermore, their IPSS questionnaires did not reveal any evidence of obstruction.

Erectile dysfunction is a very common sequela in sLRP [4–6,18]. Except for two patients (one in the Nuñez-Mora series and one in ours) who were found to have maintained their erections, no other patient in any of the sLRP series was reported to preserve sexual erectile function postoperatively [3–6,18].

Several limitations in our study should be acknowledged. First, this study is a retrospective observation of a small series of patients with short follow-up. It was performed as a quality of care control to assess whether we should continue offering sLRP to our patients. While longer follow-up is necessary before more definite conclusions can be made, these data show that sLRP is feasible, and the early morbidity of the sLRP procedure seems similar to that of sORP, the standard of care for this disease.

In addition, there may have been a selection bias through the referral pattern. Moreover, this study was performed at a tertiary referral centre and its results may not be applicable to the general population of patients with PSA recurrence after non-extirpative instrumental prostate cancer therapy.

Conclusions

sLRP is a feasible method to treat locally recurrent prostate cancer. Our limited experience features an acceptable morbidity with no bladder neck contracture. Longer follow-up is needed before definitive conclusions can be made as to its oncological efficacy and functional outcomes. These data support the expansion of our sLRP programme.

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Abbreviations

ORP	open radical prostatectomy
LRP	laparoscopic radical prostatectomy
sLRP	salvage laparoscopic radical prostatectomy
sORP	salvage open radical prostatectomy
BCR	biochemical recurrence
IQR	interquartile range
EBRT	external beam radiation therapy

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TABLE 1

Perioperative data for sLRP patients (n = 15)

Median age (years)	62.3	IQR 57.4–71.4
Median preoperative PSA (ng/mL)	3.49	IQR 2.90–5.99
Median operating time (min)	235	IQR 210–285
Median estimated blood loss (mL)	200	IQR 150–275
Transfusion rate	0	
Conversion rate to open surgery	0	
Mortality	0	
Rectal injuries	1	
Median length of hospital stay (days)	2	IQR 1–4
Anastomosis stenosis	0	
Continence rate	7/15	
Potency rate	1/15	

TABLE 2

Morbidity from salvage radical prostatectomy: review of the literature, with comparison to series described in this paper

	Number of patients	Mean duration, min	Rectal injury, %	Anastomosis stenosis, %	Positive surgical margins, %	Mean follow-up, months	Incontinence, %
sORP							
Rainwater and Zincke [20]	30	216	0	17	NR	80	10
Link and Freiha [16]	14	185*	0	7	43	18*	73
Amling *et al.* [17]	108	NR	6	21	36	NR	51
Heidenreich *et al.* [19]	21	150	0	12	NR	12.5	24
Stephenson *et al*. [21]	100	240	7	30	21	58*	61
sLRP/sRALP							
Vallancien *et al*. [6]	7	190	0	0	29	11	29
Stolzenburg *et al*. [5]	9	148	0	0	NR	12	22
Nuñez-Mora *et al*. [4]	9	170	0	0	22	27	67
Kaouk *et al*. (sRALP) [3]	4	125	0	0	50	1	25†
Eandi *et al*. (sRALP) [18]	18	156	0	17	28	18*	67
Our series (11 sLRP, 4 sRALP)	15	240	1	0	20	8*	46

NR, not reported.

*Median.

†In this study, ‘incontinence’ did not include patients who used one pad per day but rarely needed them.