

Salvage Radical Prostatectomy: An Alternative Treatment for Local Recurrence of Radioresistant Cancer

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ABSTRACT

Objectives: The treatment of recurrent prostate cancer after radiotherapy or brachytherapy through radical prostatectomy has been little indicated due to the concern over the procedure's morbidity. We present the experience of our service with postradiotherapy radical prostatectomy.

Materials and Methods: Between 1996 and 2002, 9 patients submitted to radiotherapy due to prostate cancer were treated with salvage surgery for locally recurrent disease. All patients had a biopsy of the prostate confirming the tumor recurrence, increase in the PSA levels and staging without evidence of a systemic disease. We have assessed the morbidity and the recurrence-free survival rate after salvage radical prostatectomy.

Results: Preradiotherapy PSA varied from 6.2 to 50 ng/mL (mean 17.3) and clinical staging T1, T2 and T3 in 33.3%, 44.4% and 22.2% of the patients respectively. The interval for the biopsy after conforming external beam radiotherapy or brachytherapy varied from 8 to 108 months (median: 36). Four patients received antiandrogenic therapy neoadjuvant to the surgery with a mean of 7 months (1-48) after radiotherapy. From the six patients potent before the surgery, three have presented erectile dysfunction. Urinary incontinence as well as bladder neck sclerosis occurred in two patients (22.2%). Biochemical recurrence occurred in two individuals (22.2%) 12 months after the surgery. Biochemical recurrence-free survival rate was 77.8% with median follow-up time of 30 months (8-102).

Conclusion: Salvage radical prostatectomy is a safe and effective alternative for the treatment of locally recurrent prostate cancer after radiotherapy and brachytherapy.

Key words: *prostatic neoplasms; radiotherapy; recurrence; salvage therapy; prostatectomy*

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INTRODUCTION

The various forms of treatment for prostate cancer (PCa) include observation, external-beam radiotherapy, brachytherapy, cryotherapy, hormonal therapy and surgery, however, the decision of the ideal therapy should be individualized (1,2). Radical pros-

tatectomy (RP) presents a biochemical recurrence rate of 17 to 33% (3,4), while brachytherapy and external-beam radiotherapy 25 to 40% (5,6). The individuals that present an increase in their PSA level after radiation therapy and that are possible candidates to salvage radical prostatectomy (SRP) should be submitted to a new staging of the disease, since the in-

crease can indicate local recurrence, either systemic or both (2). Prostatic biopsy is positive in 80 to 100% of the cases (2,7), being fundamental the confirmation of the tumor for the therapeutic decision. Salvage procedures such as antiandrogenic therapy, radical prostatectomy and cryotherapy are options for patients with primary treatment failure. SRP has been efficient in the control of the disease in a period of time, with interesting results, reaching 82% disease-free survival rate in five years (8,9). However, SRP has not been getting more acceptance due to technical challenges of the procedure and significant morbidity, occurring urinary incontinence in 23 to 60%, rectal lesion in 15% and ureter lesion in 5% of the patients operated (8,10), with post-operative bladder neck sclerosis in up to 30% of the cases (10,11).

We have presented the results of SRP for radiotherapy recurring PCa treated in our institution.

MATERIALS AND METHODS

Nine men with mean age of 59 years (50-75), with biopsies confirming locally recurrent prostate cancer after conforming external beam radiotherapy (XRT) or brachytherapy (BT) were submitted to SRP between 1996 and 2002. Patients were considered candidates for salvage surgery when they presented a biopsy confirming the presence of a tu-

mor, increase in the PSA levels and absence of systemic disease, confirmed by bone scintigraphy, thorax radiography, tomography or magnetic resonance of the abdomen or pelvis with digital prostate examination at the physical exam. From the nine irradiated individuals, four received BT, four XRT and one was treated with both. Data regarding perioperative characteristics were assessed such as operative time, transoperative bleeding, blood transfusion and hospital stay. In the postoperative follow-up, the erectile function was analyzed by the penetration capacity with or without oral medication, urinary incontinence (> 1 pad/day) and bladder neck sclerosis in all individuals.

RESULTS

Mean follow-up was 30 months (8-102). Demographic data of the studied group are represented on Table-1 with preoperative and pathological Gleason score on Figure-1. Pathological stage was pT2N0 and pT3N0 in four and five patients respectively. Time interval after primary therapy (XRT or BT) for the beginning of antiandrogenic therapy was 1 to 48 months (median: 7 months) performed in four patients and the time to perform the prostate biopsy had a median of 36 months (8-108) after prostatic irradiation.

Table 1 – Demographic characteristics of treated patients with salvage radical prostatectomy.

Patients	Age (years)	Initial PSA (ng/mL)	Biopsy Gleason	Clinical Stage	Primary Treatment	ADT	Gleason in Specimen
AEB	59	6.2	8	T3b	BT	No	8
JFM	50	8.9	6	T1c	BT and XRT	Yes	6
OLM	63	50	5	T3a	XRT	Yes	8
JMN	65	24	5	T2a	XRT	Yes	7
RG	52	22	7	T2a	XRT	Yes	7
AGFR	62	10	7	T2a	BT	No	7
JDR	52	14	4	T1c	BT	No	8
JRLP	54	8.1	4	T2b	BT	No	7
SOL	75	12.6	6	T1c	XRT	No	9

ADT = antiandrogenic therapy neoadjuvant to surgery; BT = brachytherapy; XRT = external beam radiotherapy.

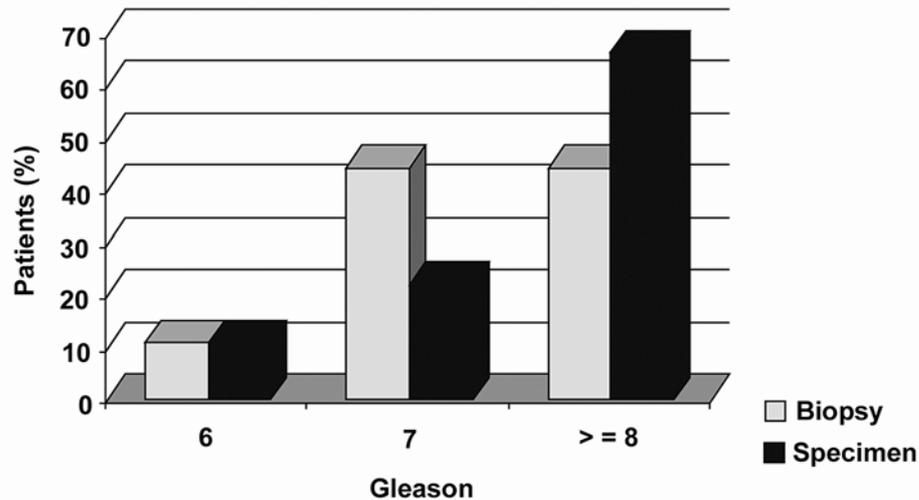


Figure 1 – Correlation between Gleason score at the biopsy and of the specimen.

SRP occurred normally, as Table-2 shows. Pathological staging revealed an organ-confined disease in four patients (44%), extra-prostatic extension occurred in five individuals (56%) and invasion of the seminal vesicles in three (33%). From the four patients that had organ-confined disease, three (75%) had biopsy Gleason score ≤ 7 . All three patients with compromised seminal vesicle presented biopsy Gleason score 7 or 8, while 60% of the patients with periprostatic extension presented a Gleason score 8. Organ-confined disease occurred in 75% of the patients with pre-radiotherapy PSA ≤ 10 ng/mL, with the compromise of the seminal vesicles occurred in all patients with PSA level above 20 ng/mL before radiotherapy.

From the nine analyzed patients, seven (78%) kept urinary continence, two presented bladder neck sclerosis (22%) two months after the surgery, and erectile dysfunction occurred in half of the patients (Table-3). Two individuals presented urinary incontinence after SRP, being one of them, after internal urethrotomy due to bladder neck sclerosis. Both were treated with artificial sphincter AMS 800. On Table-4, those results are compared to other series. After the SRP, biochemical recurrence occurred in two cases (22%) after a median time of 15 months requiring the introduction of antiandrogenic hormonal therapy.

Seven patients (78%) had the PSA less than 0.4 ng/mL, without any evidence of the disease, from which five (56%) without hormonal therapy. One patient with pre-XRT PSA levels of 50 ng/mL, clinical stage T3c, presented a recurrence in retroperitoneal lymph nodes, being submitted to cytotoxic chemotherapy followed by radiotherapy in the areas of compromised lymph nodes. All patients are alive after a median follow-up time of 30 months (8 to 102 months).

Table 2 – Transoperatory parameters and hospital stay.

Parameters	Mean (variation)
Operative time (minutes)	168 (120 - 240)
Bleeding estimation (mL)	433 (380 - 510)
Blood transfusion	-
Hospital stay (days)	4.8 (4-7)

Table 3 – Postoperative complications.

	N (%)
Sexual impotence	4 (50)
Bladder neck sclerosis	2 (22)
Urinary incontinence	2 (22)

DISCUSSION

In this series from the nine patients treated with radical prostatectomy for locally recurrent cancer after primary radiotherapy 78% had disease control, 22% urinary incontinence and 50% erectile dysfunction. Five patients (56%) had no adjuvant treatment without evidence of the disease. SRP was performed without transoperative complications, without the need for blood transfusion and presenting a cancer specific survival rate of 100% in the median follow-up time of 8 years (8-102 months).

SRP, even though associated to a larger control of the prostate cancer locally recurrent after radiotherapy, has received limited attention in the urologic field due to technical challenges during surgery and the potential risk of complications such as urinary incontinence, impotency, bladder neck sclerosis and both rectal and ureteral lesions (8,9). Urinary incontinence after SRP has been much more frequent than in conventional radical prostatectomy that varies between 5 and 31% (12), representing a limiting factor for salvage surgery, since the urinary incontinence in this study was 22%, similar to other series with a variation of 16 to 45% (9,10,12). The insertion of the artificial sphincter AMS 800 in the cases of persisting urinary incontinence has offered good results in most of the cases (13), this resource was used in two cases resolving urinary leaks.

This study demonstrates an acceptable complication rate making the results similar to a conventional radical prostatectomy. Mean operative time was of 168 minutes and bleeding mean of 433 mL, with

mean hospital stay of 4.8 days, similar to other series (9,10). Vaidya & Soloway reported a mean hospital stay of three days (9). Rectal lesion did not occur in our initial SRP experience, being in agreement with the reports of up to 0.6% during conventional radical prostatectomy (14). By analyzing the SRP series the rectal lesion may occur between 2 to 15% and ureteral lesion 5% of the cases, respectively (8,10).

The risk of bladder neck sclerosis is substantially high after the SRP (2), the rate of 22% of the study is similar to those observed by other authors as Table-4 (8,10,11,15) shows. According to the results obtained in other studies, bladder neck sclerosis after conventional radical prostatectomy carries between 1 to 4% (16,17), however, Touma et al. reported an incidence of 17.5% after SRP (12). Bladder neck sclerosis after radiotherapy can be a problem of difficult solution, sometimes requiring more complex procedures for an adequate correction such as appendicovesicostomy or ileovesicostomy as described by Pisters et al. (18).

Erectile dysfunction is considered an inevitable consequence of the SRP, even though preservation of cavernous nerves is possible. When it is possible to preserve neurovascular bundles bilaterally, up to 70% of the patients recuperate their sexual function (10,17) and urinary continence (10). In this work the erectile function was preserved in half of the patients previously potent before the surgery.

Clinical stage of post-radiotherapy recurrent prostate cancer is a predictive factor for disease free survival rate (2,12,15), even though Rogers et al. (8) have not observed this correlation (8). In our series,

Table 4 – Associated morbidity with salvage radical prostatectomy.

References	N	Urinary Incontinence (%)	Bladder Neck Sclerosis (%)	Rectal Lesion (%)	Biochemical Recurrence (%)
Rogers et al. (8)	40	58	27	15	18
Amling et al. (11)	108	51	21	6	43
Stephenson et al. (10)	100	23	30	2	34
Vaidya (9)	6	16	0	0	16
Gheiler et al. (14)	40	50	16	3	53
Present study	9	22	22	0	22

44% of the cases of the disease were organ-confined and the involvement of seminal vesicles occurred in 33% of the individuals. In similar studies those findings occurred in 39% and 30% of the cases, respectively (15). Preoperative PSA levels inferior to 10 ng/mL have a strong correlation to organ-confined disease and higher progression-free survival rate. (2,8,11,12).

Cryotherapy is a viable alternative in the treatment of radioresistant prostate cancer, however, urinary incontinence and bladder neck sclerosis rates are 73% and 44% respectively. Besides, pelvic pain, dysuria, hematuria, bladder neck sclerosis and urethral fistula are other potential complications of cryotherapy (19). Another discouraging factor is the reduced control of cancer in relation to SRP (2,12,19).

In this study 55.5% of the individuals were recurrence-free. SRP is a viable and safe alternative to the treatment of radioresistant cancer, however the selection of cases with PSA < 15 ng/mL and Gleason score ≤ 7 offer better results without the need of associated androgenic blockage.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Walsh PC: Radical prostatectomy for localized prostate cancer provides durable cancer control with excellent quality of life: a structured debate. *J Urol.* 2000; 163: 1802-7.
- Pisters LL: Salvage radical prostatectomy: refinement of an effective procedure. *Semin Radiat Oncol.* 2003; 13: 166-74.
- Han M, Partin AW, Zahurak M, Piantadosi S, Epstein JI, Walsh PC: Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localized prostate cancer. *J Urol.* 2003; 169: 517-23.
- Ward JF, Blute ML, Slezak J, Bergstralh EJ, Zincke H: The long-term clinical impact of biochemical recurrence of prostate cancer 5 or more years after radical prostatectomy. *J Urol.* 2003; 170: 1872-6.
- Joseph J, Al-Qaisieh B, Ash D, Bottomley D, Carey B: Prostate-specific antigen relapse-free survival in patients with localized prostate cancer treated by brachytherapy. *BJU Int.* 2004; 94: 1235-8.
- Kuban DA, Thames HD, Levy LB, Horwitz EM, Kupelian PA, Martinez AA, et al.: Long-term multi-institutional analysis of stage T1-T2 prostate cancer treated with radiotherapy in the PSA era. *Int J Radiat Oncol Biol Phys.* 2003; 57: 915-28.
- Levi AW, Epstein JI: Pseudohyperplastic prostatic adenocarcinoma on needle biopsy and simple prostatectomy. *Am J Surg Pathol.* 2000; 24: 1039-46.
- Rogers E, Otori M, Kassabian VS, Wheeler TM, Scardino PT: Salvage radical prostatectomy: outcome measured by serum prostate specific antigen levels. *J Urol.* 1995; 153: 104-10.
- Vaidya A, Soloway MS: Salvage radical prostatectomy for radiorecurrent prostate cancer: morbidity revisited. *J Urol.* 2000; 164: 1998-2001.
- Stephenson AJ, Scardino PT, Bianco FJ Jr, DiBlasio CJ, Fearn PA, Eastham JA: Morbidity and functional outcomes of salvage radical prostatectomy for locally recurrent prostate cancer after radiation therapy. *J Urol.* 2004; 172: 2239-43.
- Amling CL, Lerner SE, Martin SK, Slezak JM, Blute ML, Zincke H: Deoxyribonucleic acid ploidy and serum prostate specific antigen predict outcome following salvage prostatectomy for radiation refractory prostate cancer. *J Urol.* 1999; 161: 857-62; discussion 862-3.
- Touma NJ, Izawa JI, Chin JL: Current status of local salvage therapies following radiation failure for prostate cancer. *J Urol.* 2005; 173: 373-9.
- Elliott DS, Boone TB: Combined stent and artificial urinary sphincter for management of severe recurrent bladder neck contracture and stress incontinence after prostatectomy: a long-term evaluation. *J Urol.* 2001; 165: 413-5.
- Dillioglulugil O, Leibman BD, Leibman NS, Kattan MW, Rosas AL, Scardino PT: Risk factors for complications and morbidity after radical retropubic prostatectomy. *J Urol.* 1997; 157: 1760-7.
- Gheiler EL, Tefilli MV, Tiguert R, Grignon D, Cher ML, Sakr W, et al.: Predictors for maximal outcome in patients undergoing salvage surgery for radio-recurrent prostate cancer. *Urology.* 1998; 51: 789-95.
- Lepor H, Nieder AM, Ferrandino MN: Intraoperative and postoperative complications of radical retropubic prostatectomy in a consecutive series of 1,000 cases. *J Urol.* 2001; 166: 1729-33.

17. Catalona WJ, Carvalhal GF, Mager DE, Smith DS: Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies. *J Urol.* 1999; 162: 433-8.
18. Pisters LL, English SF, Scott SM, Westney OL, Dinney CP, McGuire EJ: Salvage prostatectomy with continent catheterizable urinary reconstruction: a novel approach to recurrent prostate cancer after radiation therapy. *J Urol.* 2000; 163: 1771-4.
19. Pisters LL, von Eschenbach AC, Scott SM, Swanson DA, Dinney CP, Pettaway CA, et al.: The efficacy and complications of salvage cryotherapy of the prostate. *J Urol.* 1997; 157: 921-5.

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EDITORIAL COMMENT

The authors report on excellent results with post-radiotherapy salvage radical prostatectomy in nine patients. Some considerations can be done, regarding the results obtained herein.

First, one remarkable aspect of the study is the young age range of the patients submitted to salvage radical prostatectomies in this series. Of the nine men, five were under 60 years of age at the time of salvage surgery. Considering that the median time from initial treatment to the establishment of therapeutic failure was 36 months, we can conclude that most patients were really young when receiving the initial radiation treatment. May be that the best window for cure was lost then for these men.

A second intriguing finding is the very low complication rate associated to salvage surgery in the published series, which is considerably lower than that of historical series of greater patient volumes. Urinary incontinence, which approaches 60% in historic series, was observed in only 22% in this study.

Rectal injuries, also reported in larger series (around 10% at Wayne State), (1) were absent here. Besides, the authors reported excellent potency rates, something unexpected in this kind of surgery. This may indicate one of two things: either a low generation of fibrosis by the radiation treatments received or an exceptional surgical technique. This is also confirmed by the lack of transfusions and by the reduced operative time (mean 168 minutes).

Recent data suggest that salvage radical prostatectomy may be a very good option to patients with biochemical failure after initial radiation treatment. This year, the group from Mayo Clinic reported on the results of 138 patients submitted salvage radical prostatectomy, with 65% cancer-specific survival rates (2). Approximately 70% of patients remained continent or in need of one pad/day; transfusion rates were 36%, rectal injuries occurred in 4%, and bladder neck sclerosis in 22%. The conclusions of the authors were that results improved with time, and that

salvage surgery should be offered to Young men with at least 10-year life expectancy and organ-confined disease.

In a setting in which the media easily distorts scientific truth, we have observed growing numbers of non-surgical options for the initial treatment of younger men with clinically localized prostate cancer. In this situation, the favorable results of salvage surgery are welcome. However, we do not know yet whether the results of this Brazilian study (with small numbers, in fact) or the results of the Mayo Clinic are really reproducible by all our urologic surgeons. Probably, our best strategy concerning this subject

would be to inform our urologists that, as we see in muscle-invasive bladder cancer, surgery is still the best initial chance of cure for young men with biologically aggressive prostate cancer.

REFERENCES

1. Pontes JE, Montie J, Klein E, Huben R: Salvage surgery for radiation failure in prostate cancer. *Cancer*. 1993; 71: 976-80.
2. Ward JF, Sebo TJ, Blute ML, Zincke H: Salvage surgery for radiorecurrent prostate cancer: contemporary outcomes. *J Urol*. 2005; 173: 1156-60.

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