Salvage Radical Prostatectomy: Quality of Life Outcomes and Long-Term Oncological Control of Radiorecurrent Prostate Cancer

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Purpose: We review our 20-year experience with salvage radical prostatectomy to determine prognostic variables predictive of oncological control of radiorecurrent prostate cancer. Using a standardized questionnaire we also evaluate outcome data regarding the long-term sexual and urinary effects of salvage radical prostatectomy.

Materials and Methods: Between 1983 and 2002 salvage radical prostatectomy was performed in 51 patients with locally recurrent prostate cancer following definitive radiotherapy. Clinical information was obtained from a prospective database. Quality of life data were collected using the UCLA Prostate Cancer Index, a validated, patient administered instrument.

Results: At 5 years 47% of patients were progression-free without androgen deprivation therapy. Among patients with pT2 disease 100% were progression-free at 5 years, compared with 35% of patients with pT3N0 disease or higher and 0% of patients with node positive (pTxN+) disease ($p < 0.001$). Preoperative PSA 5.0 ng/ml or less was predictive of organ confined disease, and strongly associated with prolonged progression-free and overall survival ($p < 0.001$ and 0.01, respectively). Mean urinary function scores for patients with or without an artificial urinary sphincter compared favorably with scores reported after standard, nonsalvage prostatectomy. Sexual dysfunction was nearly uniform in patients undergoing standard salvage radical prostatectomy but implantation of a penile prosthesis was associated with a clinically significant improvement in sexual function.

Conclusions: When initiated early in the course of recurrent disease, salvage radical prostatectomy provides excellent oncological control of radiorecurrent prostate cancer without the need for androgen ablation. Implantation of an artificial urinary sphincter and inflatable penile prosthesis devices in patients with postoperative urinary incontinence or erectile dysfunction results in significantly improved quality of life parameters.

Key Words: prostatectomy, prostatic neoplasms, salvage therapy, radiotherapy, quality of life

Recurrence after definitive treatment of clinically localized prostate cancer with RT is common, occurring in up to 50% of patients.[1–3] Nearly 90% of these men will receive palliative treatment with chemical or surgical castration as the means of cancer management.[4] Despite reports of durable cancer specific survival following salvRP exceeding 10 years among patients with good prognostic factors, and approximating outcomes achieved following primary radical prostatectomy,[5–8] this potentially curative intervention has been slow to gain acceptance, with fewer than 2% of patients with radiorecurrent prostate cancer treated with salvage prostatectomy.[4] The reluctance to recommend salvRP as an alternative to ADT in healthy, younger men is likely related to concern about the long-term morbidities often associated with salvage therapy, particularly urinary incontinence and sexual dysfunction. Although extensive investigations into QOL outcomes following primary prostate cancer therapies have been performed using standardized and validated questionnaires,[9–16] there is a paucity of reliable QOL outcome data for the salvRP population. The goal of this study was to assess long-term cancer control and patient centered outcomes in a series of 51 consecutive patients who underwent salvRP. It should be noted that QOL outcomes were assessed using a well-known validated disease specific health related instrument. As a secondary goal of the study we identified prognostic factors associated with prolonged overall and progression-free survival (OS and PFS, respectively) following salvRP.

MATERIALS AND METHODS

Of 2,739 patients who underwent radical prostatectomy at the University of Southern California/Norris Cancer Center between 1983 and 2002, we identified 51 patients (1.9%) with clinically localized prostate cancer who underwent salvage radical retropubic prostatectomy for biopsy proven rrCAP. Clinical information regarding pre-RT clinical features, RT regimen and disease course following RT were extracted from our prospectively maintained database. The selection criteria for salvRP included life expectancy of more than 10 years and absence of systemic disease. Specimens were evaluated by a uropathologist using the Gleason grading system and the 1997 American Joint Committee on Cancer TNM staging system.

After obtaining approval from the University of Southern California Institutional Review Board, packets containing

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an informed consent and patient questionnaire were mailed to the 33 patients alive at the time of the study. Telephone reminders were used for all patients who did not respond within 4 weeks. All 33 patients participated in the study.

Study Outcomes

The primary cancer end points analyzed in this study were PFS and OS following salvRP. Serum PSA measurements were obtained preoperatively and on at least an annual basis after surgery. Patients were considered to have progression following salvage prostatectomy if they had a serum PSA of 0.4 ng/ml or greater, radiographic/histological evidence of systemic recurrence, or had postoperative chemical or surgical castration. Patients who underwent bilateral orchiectomy at the time of or within 30 days of salvage prostatectomy were considered to have recurrence at the time of salvRP and, therefore, were included in the OS but not the PFS analyses.

The UCLA PCI was used to assess disease specific QOL outcomes. The function scales of the urinary and sexual domains target difficulties with continence and erections, respectively, while the bother scales focus on how much the patient is troubled by each dysfunction. All scores are on a scale from 0 to 100, with higher scores indicating better outcomes. The UCLA PCI has been shown to be reliable and valid in men with or without prostate cancer, and differences of at least 10 points are considered clinically meaningful.[9,17]

Statistical Analysis

PFS was calculated from the date of salvRP to the date of first documented progression or initiation of ADT. OS was calculated from the date of salvRP to the date of death from all causes. Patients who were alive (for OS) or progression-free (for PFS) were censored at the date of last followup. PSA was assessed as a nominal variable (PSA 5.0 or less, 5.1 to 10.0 and 10.1 ng/ml or greater). Pathological stage was categorically assessed as organ confined (pT2N0), extraprostatic (pT3N0 or pT4N0) or lymph node positive (any pTN+). If a lymph node dissection was not completed the nodal status was considered negative.

Kaplan-Meier plots were used to estimate the probabilities of OS and PFS, and Greenwood's formula was used to estimate the standard errors. The log rank test (overall and stratified) was used to compare the differences in OS or PFS in subgroups. The p values were derived by comparison of all groups simultaneously. All reported p values are 2-sided. Pearson's chi-square tests were used to examine the association between important categorical demographic and clinical variables.

RESULTS

Prior definitive radiation was in the form of EBRT (29), interstitial RT (12), combination of interstitial and EBRT (8), combination of cryotherapy and EBRT (1), and proton beam RT (1). The median interval from RT to salvRP was 5.2 years (range 6 months to 18.7 years). The median EBRT dose, available for 26 of the 38 patients who received EBRT as part of RT, was 6,560 Gy (range 3,400 to 8,000). Before definitive RT 13 men had undergone staging pelvic LND and disease was pN0 at that time.

Median followup after salvRP was 7.2 years (range 9 months to 20.2 years) and median age at surgery was 65 years (range 51 to 77). Preoperative PSA was not available for 6 patients treated before the introduction of PSA testing. Median preoperative PSA before initiation of any preoperative ADT in the remaining 45 patients was 8.0 ng/ml (range 0.8 to 48). Some form of neoadjuvant hormonal manipulation, including luteinizing hormone releasing hormone agonist and antiandrogens, was used in 18% of patients. Simple bilateral orchiectomy was performed at the time of or within 30 days of radical prostatectomy in 16% (8 of 51) of the cohort. Following salvRP, ADT was initiated at the discretion of the primary physician in another 19 patients at a median of 2.2 years (±1.8) following salvRP. Information regarding treatment with ADT was not available for 2 patients. Overall some form of ADT was initiated in 55% (27 of 49) of the cohort, either immediate (within 30 days) or delayed, following salvage surgery.

Poorly differentiated cancer (Gleason 8 or greater) was identified in 43% of the surgical specimens and 61% had a primary Gleason grade of 4 or 5. Extraprostatic and/or LN+ disease was present in 75% of the cohort. Pelvic LND was performed at the time of salvRP in 76% (29 of 38) of the men who had not undergone LND before RT, of whom 28% (8 of 29) were found to have lymphatic metastases (table 1).

Overall Survival

Median OS following salvRP was 12.9 years (95% CI 7.6–19.1), and the estimated chance of surviving 5 and 10 years was 85% ± 5% and 65% ± 8%, respectively. Preoperative PSA was predictive of overall survival ($p = 0.01$). None of the remaining variables were associated with OS (table 2).

Progression-Free Survival

Median PFS following salvRP was 4.8 years (95% CI 2.0–18.1). At 5 years following salvRP 47% ± 8% of the cohort

TABLE 1. *Demographics*

	No. Pts (%)
RT:	
EBRT	29 (57)
Interstitial RT	12 (23)
Interstitial RT + EBRT	8 (16)
Interstitial RT + cryoablation	1 (2)
Proton beam	1 (2)
Lymphadenectomy:	
Pre-RT PLND	13 (25)
PLND at salvRP	29 (57)
LN + found on PLND (29)	8 (28)
Preop PSA (ng/ml)	
5.0 or Less	16 (36)
5.1–10.0	13 (28)
10.1 or Greater	16 (36)
Final total Gleason score:	
6 or Less	10 (20)
7	18 (36)
8 or Greater	22 (44)
Final primary Gleason score:	
2	1 (2)
3	18 (36)
4	19 (38)
5	12 (24)
Pathological stage:	
Organ confined (pT2, N0)	13 (25)
Extraprostatic (pT3 or pT4, N0)	30 (59)
LN+ (any pT, N+)	8 (16)
Margin status:	
Neg	33 (64)
Pos	18 (36)