Impact of Prior Prostate Radiation on Complications After Radical Prostatectomy

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Abbreviations and Acronyms

ASA = American Society of Anesthesiologists Physical Status
BCR = biochemical recurrence
BNC = bladder neck contracture
BNS = bilateral nerve sparing
CLPC = clinically localized prostate cancer
EBL = estimated blood loss
EF = erectile function
ER = emergency room
HIFU = high intensity focused ultrasound
PSA = prostate specific antigen
RP = radical prostatectomy
SP = salvage prostatectomy
UTI = urinary tract infection

Submitted for publication November 17, 2009.
Study received institutional review board approval.
Supported by the Sidney Kimmel Center for Prostate and Urologic Cancers.
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Purpose: Salvage radical prostatectomy is associated with a higher complication rate than radical prostatectomy without prior radiotherapy but the magnitude of the increase is not well delineated.
Materials and Methods: A total of 3,458 consecutive patients underwent open radical prostatectomy and 98 underwent open salvage radical prostatectomy from January 1999 to June 2007. Data were collected from prospective surgical and institutional morbidity databases, and retrospectively from billing records and medical records. Medical and surgical complications were captured, graded by the modified Clavien classification and classified by time of onset.
Results: Median followup after salvage radical prostatectomy and radical prostatectomy was 34.5 and 45.5 months, respectively. Patients with salvage had significantly higher median age, modified Charlson comorbidity score, clinical and pathological stage, and Gleason score. They were less likely to have organ confined disease and more likely to have seminal vesicle invasion and nodal metastasis. There was no significant difference in median operative time, blood loss or transfusion rate. The salvage group had a higher adjusted probability of medical and surgical complications, including urinary tract infection, bladder neck contracture, urinary retention, urinary fistula, abscess and rectal injury. Only 1 of 4 potent patients with salvage prostatectomy who underwent bilateral nerve sparing recovered erection adequate for intercourse. The 3-year actuarial recovery of continence was 30% (95% CI 19–41).
Conclusions: Medical and surgical complications of prostatectomy are significantly increased in the setting of prior radiotherapy. Understanding the magnitude of this increased risk is important for patient counseling.

Key Words: prostate, prostatic neoplasms, salvage therapy, prostatectomy, complications

Radiotherapy in various forms, including external beam radiation and brachytherapy alone or in combination, is increasingly done as primary treatment for CLPC. A recent analysis of the Surveillance, Epidemiology and End Results program showed that more than a third of men undergoing treatment for CLPC received radiotherapy.[1] BCR has been observed in up to 30% to 50% of cases[2,3] with local recurrence in as many as 13% to 35% at 10 years.[4] Increasingly radiotherapy is done as primary treatment in younger men, who are at higher risk for long-term BCR.[5] In select groups with biopsy proven local recurrence after radiotherapy SP can

0022-5347/10/1841-0136/0
THE JOURNAL OF UROLOGY®

Vol. 184, 136-142, July 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.03.031

provide long-term local control and improve progression-free and cancer specific survival.[6–8]

It is widely accepted that SP has a higher complication rate than de novo RP. Recently there has been increased demand for standardization of reporting surgical complications in the literature to facilitate comparisons among centers and techniques.[9] Hence, comprehensive grading schemes have been established to ensure consistency and clarity.[10]

Patients are commonly counseled that SP remains an option after primary radiotherapy failure. However, without knowing the true complication rates of SP and de novo RP appropriately counseling patients on primary treatment and salvage options remains a challenge.

MATERIALS AND METHODS

Patient Population

We reviewed the records of 3,458 consecutive patients who underwent de novo open RP, as done by 1 of 13 surgeons, and 98 who underwent open SP, as done by 1 of 5 surgeons, for CLPC at our institution from January 1999 to June 2007. During that time there was no significant change in surgical technique. Data were gathered from prospective surgical and institutional morbidity databases. We also retrospectively reviewed billing records and medical records. We obtained institutional review board approval for this study.

All medical and surgical complications were captured for the inpatient and outpatient settings, and classified as early—30 or less, intermediate—31 to 90 or late—greater than 90 days based on date of onset. All complications were graded according to the modified Clavien classification.[10]

Definitions

Individual complications were defined as previously reported.[11] EF was assessed using a 5-point scale for erection, including 1—full, 2—decreased but routinely sufficient for intercourse, 3—partial and occasionally satisfactory for intercourse, 4—partial and unsatisfactory for intercourse, and 5—none. Potency levels 1 and 2 were considered preoperative potency. Continence was defined as no leakage requiring pads.

Statistical Analysis

We analyzed differences in medians, means and proportions for statistical significance using the median, Kruskal-Wallis and chi-square or Fisher exact test, respectively. Multivariate logistic regression was done to generate adjusted probabilities and the corresponding 95% CI for the various RP and SP complications, controlling for age, ethnicity, body mass index, preoperative prostate specific antigen, clinical stage, biopsy Gleason score (6 or less vs 7 vs 8 or greater), organ confined status, surgical margin status, various comorbidities, modified Charlson comorbidity index,[12] preoperative ASA, specimen weight, operative time, EBL, transfusion requirement, change in hemoglobin during hospitalization, surgeon, surgeon experience coded as case number and number of lymph nodes retrieved. Curves for the recovery of potency and continence were generated using the Kaplan-Meier method. Statistical analysis was done with SPSS®.

RESULTS

Patient Population

Compared to patients undergoing RP, those undergoing SP were older, and had lower preoperative prostate specific antigen, higher clinical stage, biopsy Gleason score, ASA and modified Charlson comorbidity score, and a higher incidence of dyslipidemia, and coronary artery, cardiac, vascular and endocrine disease. Prior treatment in men with RP consisted of prior chemotherapy in 44 and hormonal therapy in 190, and in those with SP it consisted of prior radiation in 98, chemotherapy in 6 and hormonal therapy in 36. In the SP group median time from radiotherapy to surgery was 5 years (IQR 3–7). The SP group included 64 patients (65%) with prior external beam radiotherapy, 21 (21%) with prior brachytherapy and 13 (13%) with a history of combination therapy with prior radiation spanning 1989 to 2005 at various institutions. There was no statistically significant difference in operative time, EBL, blood transfusion requirement or length of stay between the SP and RP groups.

Since the catheter was routinely left indwelling for 3 weeks after SP to allow healing of irradiated tissue, median catheterization duration was 22 vs 13 days for SP vs RP ($p < 0.001$). Routine postoperative cystography was done more often in patients with SP (36% vs 2%, $p < 0.001$). Drain fluid was sent for creatinine measurement in 17% of SP vs 14% of RP cases ($p = 0.3$). Cancer was pathologically organ confined in 43 men with SP (44%) and in 2,395 (69%) with RP ($p < 0.001$). Positive lymph nodes were present in 16 men (16%) with SP and in 171 (5%) with RP ($p < 0.001$). Seminal vesicle invasion was present in 31 men (32%) with SP vs 260 (8%) with RP ($p < 0.001$). Pathological Gleason score was higher in patients with SP ($p < 0.001$).

Postoperative Course

Intensive care unit admission was required in 7 men (0.2%) who underwent RP but in none who underwent SP. During initial hospitalization 27 men (0.8%) with RP required reoperation compared to none with SP. Of those with RP 25 (0.7%) and none with SP required reoperation other than BNC/stricture incision after discharge home. Median followup after surgery was 34.5 (IQR 19–56) vs 45.5 months (IQR 24–68) for SP vs RP. There were a total of 454 emergency room visits (13%) by men with RP and 33 (34%) by those with SP ($p < 0.001$). In men with RP vs SP there were 154 (4%) vs 13 rehospitalizations