ELSEVIER

Urologic Oncology: Seminars and Original Investigations 32 (2014) 38.e1–38.e7

UROLOGIC ONCOLOGY

Original article

Treatment outcomes and morbidity following definitive brachytherapy with or without external beam radiation for the treatment of localized prostate cancer: 20-Year experience at Mount Sinai Medical Center

Richard A. Marshall, B.A.[a], Michael Buckstein, M.D., Ph.D.[a], Nelson N. Stone, M.D.[b], Richard Stock, M.D.[a,*]

[a] *Department of Radiation Oncology, The Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY*
[b] *Department of Urology, The Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY*

Received 16 January 2013; received in revised form 16 March 2013; accepted 16 March 2013

Abstract

Objectives: To present our treatment algorithm and 20-year experience in treating prostate cancer with brachytherapy since 1990, with focus on cancer-control outcomes and treatment-related morbidity.

Methods and materials: We selected patients treated for localized prostate cancer with brachytherapy, combination therapy with external beam radiotherapy, and adjuvant androgen deprivation therapy as prescribed by our Mount Sinai risk stratification and treatment algorithm. Outcomes were analyzed with respect to biochemical failure, distant metastases, prostate cancer-specific survival, and overall survival. Morbidity was assessed with respect to urinary, sexual, and rectal outcomes.

Results: In total, 2,495 patients met inclusion criteria. The 12-year actuarial freedom from biochemical failure was 83% (low risk: 90%, intermediate risk: 84%, and high risk: 64%); freedom from distant metastasis was 95%; prostate cancer-specific survival was 95%; and overall survival was 70%. On multivariate analysis, significant associations were found between cancer control and risk group, total biologically effective dose, and androgen deprivation therapy. With regard to morbidity, potency was preserved in 61%, and urinary symptoms improved in 35%. The 12-year actuarial freedom from urinary retention events was 90% and from severe rectal bleed was 93%.

Conclusions: Brachytherapy, as administered via the Mount Sinai algorithm, remains an efficacious and benign treatment option for patients with localized prostate cancer of all risk groups.

Keywords: Prostate cancer; Brachytherapy; Radiation; Biochemical control; Survival; Morbidity

1. Introduction

As more long-term data have become available, brachytherapy has established its role as a well-tolerated and effective treatment modality for localized prostate cancer. When initially developed, prostate brachytherapy was used predominantly for the treatment of low-risk disease. Improvements in implant quality, design, and intraoperative dosimetric optimization have yielded excellent long-term outcomes across the spectrum of disease [1–4]. These systemic developments, alongside advancements specific to the treatment of higher-risk disease with dose escalation techniques and adjuvant hormone therapy, have yielded a current treatment landscape including brachytherapy as an alternative in all risk groups. Brachytherapy can be used in low-risk patients as monotherapy or in higher-risk patients as a component of bimodal or trimodal therapy with external beam radiation therapy (EBRT) or androgen deprivation therapy (ADT) or both.

Brachytherapy remains just one of an increasing number of therapeutic alternatives available for the treatment of prostate cancer, and the optimal modality for each individual remains a point of discussion. Factors considered prominently by both physicians and patients in treatment selection are cure rates, treatment-related toxicity, and overall posttreatment quality of life. Using our treatment algorithm, as developed and refined over our 20-year experience at the Mount Sinai Medical Center, we have achieved excellent cancer-control rates, while simultaneously reducing toxicity and preserving long-term quality of life. Given the importance of these factors to treatment

* Corresponding author. Tel.: +1-212-241-7502.
E-mail address: richard.stock@mountsinai.org (R. Stock).

1078-1439/$ – see front matter
http://dx.doi.org/10.1016/j.urolonc.2013.03.004

selection, we present outcomes based on our treatment algorithm incorporating brachytherapy for the treatment of prostate cancer with focus on long-term treatment outcomes and morbidity.

2. Materials and methods

2.1. Patient population and treatment

Patients treated with brachytherapy for biopsy-proven prostate adenocarcinoma at the Mount Sinai Medical Center between June 1990 and December 2009 were selected from our database. Patients who had previously been treated with radiation after surgical treatment, salvage therapy, or EBRT were excluded. The Mount Sinai treatment algorithm, with risk stratification as per the National Comprehensive Cancer Network guidelines, is as follows: patients with low-risk disease, defined as Gleason score ≤ 6, prostate specific antigen (PSA) ≤ 10 ng/ml, and clinical stage T2a or less, were treated with implant alone with ^{125}I or ^{103}Pd. Intermediate risk, defined as Gleason score of 7 or PSA 10 to 20 ng/ml or cT2b or less, were treated with ADT and a full dose implant or a partial ^{103}Pd implant followed by external beam radiation to 45 Gy. High-risk patients, defined as Gleason score 8 to 10, PSA ≥ 20 ng/ml, or $\geq$cT2c or 2 or more intermediate-risk factors, were treated with trimodal therapy including ADT, partial ^{103}Pd implant, and 45 Gy of EBRT.

Seed implantation was performed using the real-time transrectal ultrasound-guided technique as described previously [5]. ^{125}I implants were generally prescribed to 160 Gy, full ^{103}Pd implants to 124 Gy, and partial ^{103}Pd implant to 100 Gy. EBRT was delivered with 3D conformal radiation before 2003 and intensity-modulated radiation therapy or image guided radiation therapy with gold fiducials thereafter as described previously [4]. Postimplant dosimetry was performed for all patients using computed tomography-based dosimetric analysis. Doses were converted from postplan D_{90} to biologically effective dose (BED) using an α/β of 2 Gy. Adjuvant treatment with EBRT targeted the prostate and seminal vesicles and additionally, the pelvic nodes only when node positive on laparoscopic node dissection or radiographic imaging. ADT consisted of a gonadotropin-releasing hormone agonist with or without an antiandrogen. For intermediate-risk patients, ADT was generally given for 6 months duration, 3 months of which was given neoadjuvantly. For high-risk patients, ADT was given for the duration between 9 months and 2 years with most patients treated for 9 months.

2.2. Follow-up and treatment end points

After treatment, patients were followed at least every 6 months prospectively. Treatment outcomes were followed with respect to freedom from biochemical failure (FBF), freedom from distant metastases (FDM), overall survival (OS), and prostate cancer specific survival (PCSS). Biochemical failure was determined using the American Society of Radiation Oncology "Phoenix" definition. Distant metastases were defined as pathologic or radiographic evidence of extrapelvic disease. PCSS was defined as death in the presence of metastatic disease.

In addition, toxicity and quality of life outcomes were assessed at every follow-up. Erectile function was measured with the physician-assessed Mount Sinai Erectile Function Score (MSEFS), which has been shown to correlate with the International Index of Erectile Function-5 [6]. A MSEFS of 2 to 3 was considered potent with or without the use of a phosphodiesterase inhibitor. Urinary symptoms were assessed using the International Prostate Symptom Score (IPSS). Rectal bleeding was assessed using Radiation Therapy Oncology Group (RTOG) late toxicity criteria. Only $\geq$grade 2 events were included in this analysis.

2.3. Statistical analysis

Statistics were analyzed using IBM SPSS statistical software (version 20; SPSS, Inc. Chicago, IL). Survival functions were determined using Kaplan-Meier analysis, and multivariate analyses were performed with Cox regression for cancer-control outcomes and logistic regression for morbidities ($P < 0.05$; 2 sided). In the multivariate analyses, age was treated as a continuous variable and risk group, hormone therapy, and total BED were treated as categorical variables. Pretreatment IPSS (continuous) and erectile function (categorical) were included for morbidities.

3. Results

A total of 2,495 patients met inclusion criteria with a median follow-up of 6 years (range, 2–19 years). The median age was 66 years (range, 39–88); 44% of patients were low risk, 39% intermediate risk, and 17% high risk. Patient, cancer, and treatment characteristics are summarized in Table 1.

Biochemical failure occurred in 251 patients with an overall 12-year actuarial FBF of 83%. Significant differences in biochemical control were found between risk groups with 90%, 84%, and 64% FBF for low-, intermediate-, and high-risk patients, respectively ($P < 0.001$) (Fig. 1A). On multivariate analysis, controlling for age, risk group, and adjuvant therapy with ADT, the rate of biochemical failure was increased associated with increasing risk group ($P < 0.001$) and was decreased associated with increasing total BED ($P < 0.001$) and the use of ADT ($P < 0.001$) (Table 2). Low-dose implants (BED: ≤ 150 Gy_2) were found to independently predict higher rates of biochemical failure than both intermediate-dose implants (BED: 150–200 Gy_2; hazard ratio [HR] = 0.379; 95%