ELSEVIER

Urologic Oncology: Seminars and Original Investigations 24 (2006) 384–390

UROLOGIC ONCOLOGY

Original article

Treatment of intermediate-risk prostate cancer with brachytherapy without supplemental pelvic radiotherapy: A review of the H. Lee Moffitt Cancer Center experience☆

Javier F. Torres-Roca, M.D.[a,*], Alan B. Cantor, Ph.D.[a], Sonia Shukla,[a], Michael E. Montejo, B.S.[a], Jay Friedland, M.D.[a], John D. Seigne, M.B.[b], Randy Heysek, M.D.[a], Julio Pow-Sang, M.D.[a]

[a] *Department of Interdisciplinary Oncology, University of South Florida College of Medicine and H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL 33612, USA*

[b] *Section of Urology, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, USA*

Received 27 June 2005; received in revised form 16 December 2005; accepted 22 December 2005

Abstract

Purpose: To determine the biochemical outcomes of patients with intermediate-risk prostate cancer treated at the H. Lee Moffitt Cancer Center with an I-125 permanent seed implant without supplemental pelvic radiotherapy.

Methods and Materials: Under an institutional review board approved protocol, the charts of 88 patients with intermediate-risk prostate cancer and a minimum follow-up of 36 months treated with brachytherapy without supplemental pelvic radiotherapy were reviewed. Median follow-up for the whole cohort was 57 months (range 37–121). Biochemical failure was defined using the American Society for Therapeutic Radiology and Oncology definition.

Results: The 5-year biochemical failure-free survival for the cohort was 83%. Patients with perineural invasion had a worse biochemical outcome, which was statistically significant (perineural invasion vs. no perineural invasion, 5-year biochemical failure-free survival 64% vs. 89%, $P = 0.004$). None of the following factors were found significant in this subset of patients: Gleason scores 6 versus 7, primary Gleason grades 3 versus 4, percentage of core positive $<20\%$ versus $>20\%$, number of cores positive <2 versus 2 versus >2, hormonal therapy versus no hormonal therapy, T1 versus T2, prostate-specific antigen <10 versus >10, or ≥ 2 intermediate risk factors versus 1 intermediate risk factor.

Conclusions: Our data suggest that patients with intermediate-risk prostate cancer may be treated effectively with brachytherapy without supplemental pelvic radiotherapy. However, because of the limited nature of our study, we cannot exclude that patients with intermediate-risk prostate cancer may benefit from supplemental external beam radiotherapy.

Keywords: Prostate cancer; Brachytherapy monotherapy; Perineural invasion

1. Introduction

The role of brachytherapy in the treatment of intermediate-risk prostate cancer is controversial [1]. In general, these patients are at a higher risk for microscopic extracapsular and seminal vesicle extension than favorable risk patients [2]. Therefore, in theory, brachytherapy monotherapy may risk undertreating the disease that has extended beyond the confines of the prostate. For this reason, a number of institutions have adopted the policy of adding a course of supplemental pelvic irradiation (45 Gy) that precedes or follows the implant [3–6]. In contrast, studies have shown that most extracapsular extension is within 5 mm of the prostate capsule and that high quality brachytherapy without supplemental pelvic radiotherapy can treat this area effectively [7,8]. However, there is no clear consensus as to whether brachytherapy monotherapy with a permanent seed implant is sufficient treatment for these patients.

☆ J.F.T.-R. is supported by a K08 CA108926-01 award from the NCI.

Presented at the 46th Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, October 3–7, 2004.

* Corresponding author. Tel.: +1-813-972-8424; fax: +1-813-979-7231.

E-mail address: torresjf@moffitt.usf.edu (J.F. Torres-Roca).

1078-1439/06/$ – see front matter
doi:10.1016/j.urolonc.2005.12.003

To this end, the Radiation Therapy Oncology Group (RTOG 02–32) has initiated a prospective Phase III trial that randomizes patients with intermediate-risk disease between brachytherapy alone versus external beam radiotherapy (EBXRT) (45 Gy), followed by a brachytherapy boost. The importance of this question is several-fold because combining 2 modalities of radiation therapy may increase the likelihood of complications and decrease quality of life (QOL) scores [9]. A recent prospective analysis has shown that sexual QOL scores are most affected by combination EBXRT and brachytherapy when compared with patients treated with EBXRT or brachytherapy alone [10]. However, this difference was only statistically significant 1 year after therapy as with subsequent follow-up, sexual QOL scores became similar between patients treated with brachytherapy plus or minus EBXRT. Furthermore, to our knowledge, no prospective randomized trial has been conducted to determine whether there are differences in QOL after therapy with either brachytherapy monotherapy or combination therapy (EBXRT + brachytherapy).

Finally, combination therapy is perhaps the most expensive of all forms of treatment for localized prostate cancer. On average, Medicare patients incur costs of approximately $24,407 when undergoing combination therapy. In contrast, costs are significantly less for Medicare patients undergoing brachytherapy monotherapy, EBXRT or radical prostatectomy, averaging approximately $15,301, $15,937, and $19,019, respectively [11].

In July of 1993, a permanent seed brachytherapy program was established at the H. Lee Moffitt Cancer Center. The favored policy until 2001 at our institution was to treat all patients with intermediate-risk cancer with brachytherapy without supplemental pelvic radiotherapy. We have reviewed our experience to determine the clinical outcome of these patients treated with brachytherapy without supplemental pelvic radiotherapy. We were interested in establishing whether there was a subset of patients that could be effectively treated with brachytherapy without supplemental pelvic radiotherapy. Finally, we wanted to identify whether markers of low-volume disease (number of positive cores, percentage of cores positive, etc.) were prognostic factors within this risk group.

2. Methods and materials

2.1. Patients

Between July 1993 and June 1999, a total of 466 patients were treated with a permanent seed implant at our institution. Under an institutional review board approved protocol, we reviewed the charts of all 466 patients and identified those with intermediate-risk cancer. Patients who had been referred from an outside institution had their pathology slides re-reviewed at Moffitt Cancer Center. We defined intermediate-risk prostate cancer as: Gleason score 7 and/or prostate-specific antigen (PSA) $\geq$10 but $<$20 ng/ml, and/or clinical stage $>$T2a but $<$T3a. Patients with more than 1 risk factor were still considered as having intermediate-risk cancer and, thus, eligible for the study.

A total of 129 patients with intermediate-risk cancer were identified. Of 129, 17 patients were treated with combination therapy (EBRT + brachytherapy) and were excluded from the analysis. There were 88 patients treated with brachytherapy without supplemental pelvic radiotherapy with a minimum follow-up of 36 months who became the study population. Median and mean follow-up for this cohort were 57 and 56 months, respectively (range 37–121). Biochemical failure was determine using the American Society for Therapeutic Radiology and Oncology (ASTRO) definition [12]. The AJCC Cancer Staging Manual [13] was used to determine clinical staging.

2.2. Treatment

All patients were treated with an iodine-125 transperineal permanent seed implant using RAPIDStrand (Amersham, Plymouth Meeting, PA), except for 3 patients treated with loose seeds. A single radiation oncologist (J.F.) treated all patients. A total dose of 160 Gy (pre-TG-43) was delivered to the prostate. Computerized tomography (CT) after implant was performed on all patients. Before June 1998, the generated isodose curves were overlaid on CT images. After June 1998, a new planning system was initiated that enabled dose volume histogram calculations.

2.3. Statistical analysis

Biochemical failure rates over time were estimated using the Kaplan and Meier method [14] with estimated standard errors computed using the Greenwood formula [15]. Patients who had no failure, according to the ASTRO definition, when these analysis were performed were considered right-censored regarding biochemical failure as of the date of their last visit (i.e., the analysis treated their failure times as exceeding the time that they were observed). The log-rank test was used to compare groups based on disease characteristics or treatment regarding biochemical failure with time [16]. Two-sided significance levels of 0.05 were used. All statistical analyses were performed using SAS® statistical software (version 9.1; SAS Institute Inc., Cary, NC). The SAS procedure, Proc Lifetest, was used to compute estimates of failure-free probabilities with time and the standard errors of those estimates, and to compare groups regarding freedom from biochemical failure with time.

3. Results

Table 1 shows the distribution of clinical characteristics in our population. Most patients were eligible by having 1 intermediate risk factor, either a Gleason score of 7 or PSA