ELSEVIER

Brachytherapy 13 (2014) 46–52

BRACHYTHERAPY

Decline in acute urinary toxicity: A long-term study in 2011 patients with prostate brachytherapy within a provincial institution

Elisa K. Chan, Mira Keyes*, Tom Pickles, Vincent Lapointe, Ingrid Spadinger, Michael McKenzie, W. James Morris

Department of Radiation Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada

ABSTRACT

PURPOSE: To determine whether acute urinary toxicity rates improve with the overall experience of a large prostate brachytherapy program.

METHODS AND MATERIALS: From 1998 to 2009, 2937 patients were treated with prostate brachytherapy at the British Columbia Cancer Agency. Baseline patient, treatment, and implant factors were recorded prospectively. Acute urinary toxicity data were prospectively recorded at baseline and each follow-up visit. Patients with ≥2 years of follow-up data were grouped into cohorts of 500 for analysis.

RESULTS: Two thousand eleven patients met the above criteria. Acute urinary retention (AUR) in the acute period (within 6 months of implant) occurred in 9.1% of patients overall and was prolonged (catheterization >20 days) in 3.4%. Both overall AUR and prolonged AUR decreased across implant cohorts ($p \leq 0.001$ in both cases). Overall acute Radiation Therapy Oncology Group (RTOG) Grades 0 and 1 urinary toxicity rate was 57.5% and RTOG Grades 2 and 3 urinary toxicity rates were 34.3% and 8.1%, respectively. Acute toxicity improved over time for both RTOG Grades ≥2 and ≥3 toxicity ($p < 0.0001$). International prostate symptom score resolution to baseline was achieved in 80.5% of patients with a median time of 12.2 months.

CONCLUSIONS: Acute AUR and RTOG urinary toxicity rates continue to decline with the increasing experience of our provincial prostate brachytherapy program, despite its expansion to new centers and addition of members. This is likely due to better patient selection, refinement in treatment planning and implantation technique, and mentorship and training process.

Keywords: Prostate brachytherapy; Acute urinary toxicity; Learning curve

Introduction

The British Columbia Cancer Agency (BCCA) established the Provincial Prostate Brachytherapy Program in 1997. As of July 2013, close to 5000 patients have received permanent low-dose-rate prostate brachytherapy implants. The program has expanded throughout the province from a single center with 4 physicians performing implants to currently four cancer centers and 16 physicians.

Prostate brachytherapy is a safe and effective treatment modality for men with low- or intermediate-risk prostate cancer (1). As radiotherapy centers in the province have expanded to include prostate brachytherapy services, ensuring that overall treatment outcomes (2) and side effects (in particular urinary toxicity) are minimized remains an important goal.

Since the inception of the program, a prospective database has been established to record baseline patient, treatment, and implant characteristics on all implanted patients. Information is prospectively collected at each follow-up visit, including prostate-specific antigen (PSA) and testosterone levels and treatment toxicity (genitourinary, gastrointestinal, and sexual function).

Received 11 July 2013; received in revised form 26 August 2013; accepted 15 October 2013.

Presented at the World Congress of Brachytherapy, Barcelona, Spain, May 10–12, 2012, the 26th Annual Scientific Meeting of the Canadian Association of Radiation Oncology, Ottawa, ON, Canada, September 12–15, 2012, and at the British Columbia Cancer Agency Annual Cancer Conference, Vancouver, BC, Canada November 29 to December 1, 2012.

* Corresponding author. Department of Radiation Oncology, British Columbia Cancer Agency, 600 West 10th Avenue, Vancouver, BC, Canada V5Z 4E6. Tel.: +604-877-6000; fax: +604-877-0505.

E-mail address: mkeyes@bccancer.bc.ca (M. Keyes).

1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2013.10.005

The effect of a learning curve in a brachytherapy program has been described previously in the literature, mainly demonstrating the occurrence of technical improvements, such as decreased rate of seed migration (3) or improved dosimetric coverage (4–7). Zelefsky *et al.* (8) have demonstrated that real-time intraoperative evaluation has improved postoperative dose distributions and decreased urinary toxicity at their institution. However, very little has been described regarding the effect of a learning curve in a brachytherapy program on treatment morbidities, such as urinary toxicity.

Initial evaluation of our program has suggested that there was a learning curve effect on urinary toxicity, with an improvement in acute urinary retention (AUR) among our first 800 patients, with a minimum follow-up of 15.6 months at the time of analysis (9). AUR rates were 17% in the first 200 patients vs. only 6.3% in the more recently treated 200 patients.

The purpose of this study was to update the acute urinary toxicity rates for patients within our large cohort who had a minimum of 2 years follow-up and determine if there is a continuing institutional learning curve effect. This evaluation was in part done as an ongoing BCCA Provincial Brachytherapy Program Quality Assurance evaluation process.

Methods and materials

This study was reviewed and approved by the BCCA's review ethics board. Two thousand nine hundred thirty-four consecutive patients were implanted between July 1998 and December 2009 at the BCCA. From this group of patients, those who received ^{125}I permanent seed prostate implants as monotherapy and who had a minimum follow-up of 24 months with the BCCA were included in this study. Patients residing outside of British Columbia were excluded as they received follow-up care in their home province.

The patient population included men with low-risk prostate cancer (clinical stage, ≤T2a; initial PSA [iPSA], ≤10.0 ng/mL; and Gleason score (GS), ≤6) and "low tier" intermediate-risk patients (≤T2c and iPSA, 10–15 ng/mL with GS ≤ 6 or GS = 7 with iPSA <10 ng/mL) (9). Patients with low-risk disease and a prostate volume of ≤50 cc (≤40 cc in the first year) were treated with prostate brachytherapy alone (volume restriction was removed as program gained the experience). Until February 2005, patients with GS 7, iPSA 10–15 ng/mL, or prostate volumes >50cc received 3 months of neoadjuvant and 3 months of concomitant hormone therapy by protocol (luteinizing hormone–releasing hormone agonist, with a minimum of 4 weeks nonsteroidal antiandrogen) together with prostate brachytherapy. After February 1, 2005, the use of androgen deprivation therapy (ADT) was no longer mandatory for any patient subgroup.

Details regarding transrectal ultrasound volume study, brachytherapy, and dosimetry have been described previously (9). All patients were treated with 0.424 U (NIST99) ^{125}I sources (model 6711; Oncura, a Unit of GE Healthcare, Chalfont, St. Giles, UK) prescribed to 144 Gy as a minimum peripheral dose and implanted using preplanning techniques based on an in-house planning algorithm. RAPIDStrand (Oncura) was used for all but the first 325 implants, which were performed with loose seeds. Prostate dosimetry was calculated using postimplant CT. The default timing of the CT was Postoperative Day 28 before May 2006 when a policy change made Day 0 the default timing.

Outcome measurements

The routine follow-up schedule at our institution is as follows: 6 weeks after implant, then every 6 months for 4–5 years, and then annually thereafter. Independent of the frequency of follow-up, all patients were supposed to have a PSA and testosterone values measured every 6 months.

Genitourinary toxicity was evaluated for each patient at each follow-up visit using three different methods. Information regarding any catheterization since the last follow-up visit and the duration of catheterization was recorded. Catheterization duration of more than 20 days was scored as "prolonged" catheterization, consistent with our previous definition (9). Catheterizations that occurred within the first 6 months of implantation were recorded as an acute event, whereas those that occurred after 6 months were recorded as a late event. Discrepant entries were individually reviewed using the patients' electronic medical records. Physicians graded the current genitourinary toxicity at each follow-up visit using the Radiation Therapy Oncology Group (RTOG) scale (10). Patients completed the international prostate symptom score (IPSS) at baseline (before neoadjuvant androgen deprivation and brachytherapy implantation) and each follow-up visit. IPSS resolution was defined as a return of the total IPSS to within 2 points of the baseline score (10).

Statistical analysis

Patients were grouped into cohorts of 500 by implant order for analysis. Baseline characteristics were tested for differences between cohorts and for trends across cohorts. Age, PSA, baseline IPSS, planning ultrasound-determined target volume (PUTV), and number of needles were tested using analysis of variance and Pearson correlation. Clinical tumor stage was tested using the Kruskal–Wallis test and Spearman correlation. Androgen suppression and GSs (≤6 and 7–8) were tested using chi-square and Cochrane–Armitage trend tests.

Differences in outcomes over time were examined by implant cohort as a categorical factor and by implant order number as a continuous factor. Factors associated with acute AUR rates and acute RTOG Levels ≥2 and ≥3 were examined using logistic regression and time to IPSS resolution using the Kaplan–Meier method and log-rank test.