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Shifting brachytherapy monotherapy case mix toward intermediate-risk prostate cancer

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ABSTRACT

PURPOSE: The relative use of brachytherapy (BT) for prostate cancer has declined in recent years. In this setting, we sought to determine whether the case mix of BT monotherapy–treated men has changed over time in terms of risk group composition.

METHODS AND MATERIALS: The Surveillance, Epidemiology, and End Results database was used to identify 30,939 patients diagnosed with prostate adenocarcinoma between 2004 and 2011 who received BT monotherapy. The case mix of BT monotherapy patients was calculated by patient risk group and year of diagnosis.

RESULTS: Between 2004 and 2011, the use of BT monotherapy declined overall. The relative percentage of men undergoing BT with low-risk disease declined by 4.5%, whereas the relative percentage of patients with intermediate-risk disease increased by 4.7%. Non-white patients and those from poorer counties did not show shifts in the risk group makeup of BT monotherapy patients, whereas white patients and those from wealthier counties did.

CONCLUSIONS: Although fewer patients with prostate cancer are undergoing BT monotherapy, men with intermediate-risk disease comprised a significantly larger portion of the BT case mix in 2011 compared with 2004. Future research efforts by brachytherapists should be directed toward improving BT technique, optimizing radiation doses, and obtaining long-term followup data for patients with intermediate-risk prostate cancer.

Keywords: Prostate cancer; Intermediate-risk prostate cancer; Prostate brachytherapy

Introduction

Prostate cancer is the most commonly diagnosed noncutaneous malignancy among men in the United States (1). Local therapy is most commonly surgery or radiation, which includes external beam radiation therapy (EBRT) and brachytherapy (BT). The American Brachytherapy Society 2012 consensus guidelines suggest that low-risk prostate cancer may be appropriately treated with permanent BT without supplemental EBRT or androgen-deprivation therapy (ADT) (2). In the same publication, the American Brachytherapy Society recommends that BT monotherapy be used judiciously among patients with intermediate-risk disease until long-term followup of randomized controlled trials is available. The organization does not recommend BT monotherapy for high-risk prostate cancer, although combination therapy with EBRT and/or ADT was deemed appropriate. The 2015 National Comprehensive Cancer Network guidelines also adopt BT monotherapy for select patients with intermediate-risk disease, such as those with low-volume disease (3).

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Recently, others have shown that the rates of BT and BT monotherapy (used in this article to refer to BT without EBRT or surgery) have declined (4). In this setting, we examined whether the constitution of BT monotherapy patients in terms of risk groups has changed over time to elucidate trends in the practice of prostate BT.

Methods and materials

Patient population

The Surveillance, Epidemiology, and End Results (SEER) database is a population-based cancer registry that collects cancer diagnostic, treatment, and survival data along with patient demographic characteristics (5). We used the SEER*Stat 8.1.5 software (Information Management Services, Calverton, MD) to extract cases from the SEER database. Patients were included if they were diagnosed with prostate adenocarcinoma between 2004 and 2011. These years were chosen because of limitations in the SEER database before 2004, including a lack of information about prognostic information such as Gleason score and prostate-specific antigen (PSA). In total, our approach identified 443,877 men, of whom 30,939 received BT monotherapy. We collected information from SEER on patient age, year of diagnosis, marital status, race, county-wide median family income according to the 2007–2011 American Community Survey, T stage, PSA before diagnosis, Gleason grading at diagnosis or prostatectomy, number of cores biopsied, number of cores positive for cancer, and treatment information, including receipt of surgery, EBRT, or BT. Based on limitations in the SEER database, we were not able to collect information on the use of ADT or exact timing of BT relative to diagnosis. This study was approved by the institutional review board.

Statistical analysis

Stata/MP 13.1 (StataCorp LP, College Station, TX) was used for all statistical analyses. National Comprehensive Cancer Network risk groups were assigned according to the following criteria: low-risk patients have T1c–T2a disease, Gleason score of ≤6, and PSA of ≤10 ng/mL; intermediate-risk patients have T2b or T2c disease, Gleason score of 7, or PSA >10 ng/mL and ≤20 ng/mL; and high-risk patients have T3a disease, Gleason score of ≥8, or PSA >20 ng/mL. Intermediate-risk disease was classified to be favorable or unfavorable based on the definitions described by Zumsteg *et al*. (6). However, we deviated from the previously described definitions by not incorporating percentage of cores positive because that data were only available from 2010 to 2011 in the SEER database. Therefore, patients were deemed to have unfavorable intermediate-risk disease if they had more than one intermediate-risk factor (out of T2b–T2c disease, Gleason score of 7, or PSA 10–20 ng/mL) or primary Gleason pattern of 4; otherwise, intermediate-risk disease was considered to be favorable. The proportion of patients undergoing BT monotherapy was determined by risk group. Where relevant, comparisons were performed using a t test on proportions and reported as significant at the level of $\alpha = 0.05$ following correction for multiple comparisons using the Bonferroni method (7). Specifically, we used $\alpha = 0.05/3 = 0.0167$ for the changes in the three risk groups from 2004 to 2011. Medians were compared using the Wilcoxon–Mann–Whitney U test.

Results

Patient characteristics

Of the 30,939 patients who received BT monotherapy, 57.0% had low-risk disease, 35.2% had intermediate-risk disease, and 7.8% had high-risk disease. Men who were diagnosed with low-risk disease tended to be younger than men with intermediate-risk disease, and men who were diagnosed with high-risk disease tended to be older ($p < 0.001$). As expected, median PSA was higher among men with intermediate- and high-risk disease compared with those with low-risk disease ($p < 0.001$). Other baseline patient characteristics are described in Table 1.

Decline in BT use over time

We first confirmed that the use of BT monotherapy for prostate cancer has declined in recent years, as others have previously reported (4). We found that among all prostate cancer patients, the percentage of patients undergoing BT monotherapy (BT without EBRT or surgery) declined from 10.7% in 2004 to 5.4% in 2011 (Fig. 1a; $p < 0.001$). Among patients with low-risk disease, 23.7% of patients underwent BT monotherapy in 2004,

Table 1
Baseline patient characteristics

Characteristics	Whole cohort	Low risk	Intermediate risk	High risk
N (%)	30,781	17,559 (57.0)	10,819 (35.2)	2403 (7.8)
% White	83.2	83.0	82.5	80.1
% Black	12.6	12.9	12.8	15.0
% Other race	4.2	4.1	4.7	4.9
Median age (year)	66	65	68	69
% Married	78.5	79.4	77.4	75.8
County-wide median family income ($)	69,480	70,260	68,950	67,530
Median PSA (ng/mL)	5.7	5.3	6.5	20.9
% T1c	68.9	92.3	60.9	60.0
% T2	29.6	7.7	39.1	37.7
% T3a	0.15	—	—	2.25
% T3b	0.12	—	—	—
% Gleason 6	70.1	97.5	24.0	25.2
% Gleason 7	23.9	—	75.1	16.0
% Gleason 8–10	4.1	—	—	58.2

PSA, prostate-specific antigen.