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Original Article

Characteristics and national trends of patients receiving treatment of the primary tumor for metastatic prostate cancer☆

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ABSTRACT

Background: We sought to determine temporal trends in the receipt of prostatectomy or locoregional radiation to the prostate for patients with metastatic prostate cancer and to identify predictors of receipt of local treatment.

Methods: We identified 39,976 patients with metastatic prostate cancer diagnosed in 2004–2012 using the National Cancer Database (NCDB). We used logistic multivariable regression to determine trends in the receipt of prostate and/or pelvic radiation or radical prostatectomy after adjusting for demographic and clinical factors.

Results: Patients with metastatic disease were less likely to receive locoregional treatment over time [7.88% in 2004 vs. 5.53% in 2012, adjusted odds ratio (AOR) = 0.97 per year, 95% confidence interval (CI) = 0.95–0.98; $P < 0.001$]. Cofactors associated with decreased likelihood for locoregional treatment included older age (AOR = 0.96 per year, 95% CI = 0.96–0.96, $P < 0.001$) and increased comorbidity level (1 comorbidity: AOR = 0.82, 95% CI = 0.73–0.93, $P = 0.001$; two or more comorbidities: AOR = 0.49, 95% CI = 0.39–0.61, $P < 0.001$). Decreasing utilization of both radiation and surgery of the primary site contributed to this trend. More specifically, patients with metastatic disease were less likely to receive radiation to the prostate and/or pelvis over time (5.9% in 2004 vs. 4.2% in 2012, AOR = 0.97 per year, 95% CI = 0.95–0.99, $P < 0.001$). Similarly, there was a trend toward decreased use of radical prostatectomy (2.17% in 2004 compared to 1.31% in 2012, AOR = 0.96 per year, 95% CI 0.93–0.99, $P = 0.01$).

Conclusion: Despite recent evidence of the possible benefit for locoregional treatment of prostate cancer in the setting of metastatic disease, rates of prostate radiation and radical prostatectomy among this population have actually declined over the 8-year period between 2004 and 2012, suggesting slow adoption of this novel treatment paradigm.

1. Introduction

Prostate cancer remains the second most frequently diagnosed cancer in men and the leading cause of cancer death after lung cancer.[1] With the advent of improved awareness and screening programs, more cases are diagnosed at the early stages of prostate cancer. Still, <5% of patients will present with metastasis at diagnosis,[2] and up to 40% of patients will experience recurrence of disease after conventional radical therapy.[3] Although the 5-year cause-specific survival rate for men who present without metastasis is nearly 100%, patients who present with metastasis have only 28% survival expectancy.[4] Appropriate treatment for this group of patients therefore remains an active area of interest.

Current guidelines recommend immediate or deferred hormone therapy [androgen deprivation therapy (ADT)] as palliative therapy for metastatic prostate cancer.[5] This treatment modality offers improvement of disease-related symptoms, delayed tumor progression, and increased survival.[3] Recent studies suggest that the use of local treatment of the primary tumor may improve outcomes for metastatic patients.[6–11] Similar work in breast cancer,[12] colon cancer,[13] and ovarian cancer[14] has suggested a survival benefit from local surgery or radiation.

☆ Previous work: an abstract based on similar work was presented at the ASTRO 2016 meeting.

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Although data supporting local treatment of metastatic prostate cancer have accumulated in recent years, the retrospective nature of these studies has limited a more widespread adoption of the treatment paradigm. We sought to assess how trends in the treatment of metastatic prostate cancer have evolved in light of the shifting evidence for and against local treatment. Reflecting on current clinical practice patterns may inform future directions for study in these challenging patients.

2. Methods

2.1. Data acquisition

Patient information was obtained from the National Cancer Database (NCDB) after approval from the Dana–Farber/Harvard Cancer Center Institutional Review Board. The NCDB is a national oncology database overseen by the Commission on Cancer and the American Cancer Society. Collectively, the database encompasses 70% of all newly diagnosed cases of cancer in the United States. For our purposes, patients with a diagnosis of prostate cancer were selected ($n = 1{,}802{,}596$). We used a subset of patients with metastatic disease at the time of diagnosis based on the variable coded by the Collaborative Stage Data Collection System. The study was limited to patients diagnosed after 2004, when the variable was first introduced to the database ($n = 39{,}976$). Patients for whom treatment data were unavailable were excluded.

2.2. Statistical analysis

Patient information was entered into STATA software (StataCorp LP, College Station, Texas, version 14.1) for data analysis. Demographic information was calculated according to coded variables in the NCDB database. Comparison of categorical variables was made using the chi-square test, whereas continuous variables were compared with Student *t* test. Logistic regression was performed in STATA for the treatment modalities of interest using year of diagnosis as a covariate and controlling for potential confounding factors such as age, race, income, education level, and comorbidity level (based on Charlson–Deyo Score). We used a two-sided *P* value of < 0.05 as the criterion for statistical significance.

3. Results

3.1. Patient demographics

Based on review, 39,976 patients with metastatic prostate cancer diagnosed from 2004 to 2012 were identified. Patients were classified as those receiving definitive locoregional treatment (surgery or radiation of the primary tumor, $n = 2{,}752$) or no locoregional treatment ($n = 37{,}224$). From surgical cases, we did not count as definitive any patients who received only local destruction of tumor or local excision, or subtotal prostatectomy, or unspecified surgical procedures. Population characteristics are presented in Table 1 comparing no locoregional treatment to patients receiving locoregional treatment. Notable differences included increased age, higher rates of comorbidities, and higher rates of elevated prostate-specific antigen (PSA) among patients who did not receive locoregional therapy. Patients receiving locoregional therapy were more likely to have been treated at an academic institution.

Table 1
Patient demographics.

	No LTx ($n = 37{,}224$)	LTx ($n = 2{,}752$)	*P*
Median age (IQR)	72 (63–81)	66 (59–74)	0.0001
Race (%)			0.001
White	28,106 (75.5)	2,156 (78.3)	
African American	7,530 (20.2)	483 (17.6)	
Other	701 (1.9)	51 (1.9)	
Unknown	887 (2.4)	62 (2.3)	
Education level[a)]			<0.001
Bottom quartile	7,610 (20.4)	488 (17.7)	
Second quartile	8,583 (23.1)	616 (22.4)	
Third quartile	8,119 (21.8)	600 (21.8)	
Top quartile	11,348 (30.5)	945 (34.3)	
Unknown	1,564 (4.2)	103 (3.7)	
Income level[b)]			
Bottom quartile	6,345 (17.0)	393 (14.3)	
Second quartile	6,791 (18.2)	463 (16.8)	
Third quartile	10,032 (27.0)	730 (26.5)	
Top quartile	12,497 (33.6)	1,064 (38.7)	
Unknown	1,559 (4.2)	102 (3.7)	
Comorbidities (Charlson–Deyo Score)			<0.001
None	28,476 (76.5)	2,316 (84.2)	
One	5,973 (16.0)	346 (12.6)	
Two or more	2,775 (7.5)	90 (3.3)	
PSA, ng/mL (%)			<0.001
<10	3,942 (10.6)	876 (31.8)	
10–19	3,844 (10.3)	456 (16.6)	
20–30	2,355 (6.3)	200 (7.3)	
>30	26,535 (71.3)	1,181 (42.9)	
Unknown	548 (1.5)	39 (1.4)	
Treatment center type			<0.001
Nonacademic	24,603 (66.1)	1,688 (61.3)	
Academic	12,596 (33.8)	1,061 (38.6)	
Unknown	25 (0.1)	3 (0.1)	

IQR, interquartile range; LTx, locoregional treatment; PSA, prostate-specific antigen.
[a)] Education level is determined by proportion of residents in the patient's area code who have achieved a minimum high school degree with the bottom quartile ranking as areas with the lowest degree rates.
[b)] Income level is determined by average income of patients provided by zip code.

3.2. Trends in time show decreasing utilization of locoregional treatment

Multivariable logistic regression showed that from 2004 to 2012, patients were less likely to receive locoregional treatment for metastatic prostate cancer [7.88% in 2004 vs. 5.53% in 2012, adjusted odds ratio (AOR) = 0.97 per year, 95% confidence interval (CI) = 0.95–0.98, $P < 0.001$] (Fig. 1). Cofactors associated with decreased likelihood for locoregional treatment included older age (AOR = 0.96, 95% CI = 0.96–0.96, $P < 0.001$) and increased comorbidity level (1 comorbidity: AOR = 0.82, 95% CI = 0.73–0.93, $P = 0.001$; 2 or more comorbidities: AOR = 0.49, 95% CI = 0.39–0.61, $P < 0.001$). Patients in the top income quartile assessed by zip code were found to be more likely to receive locoregional treatment (AOR = 1.25 per year, 95% CI = 1.06–1.48, $P = 0.007$). Race, education, and income level did not otherwise predict receipt of locoregional treatment (Table 2).

3.3. Trends in locoregional therapy are contributed to by decreased use of both radiation and surgery

Trends in utilization of locoregional therapy were subdivided into treatment with radiation to the prostate and/or pelvis or surgery of the primary site for further analysis. Radiation therapy included the use of external beam and brachytherapy or combined modality treatment. Multivariable logistic regression again showed that patients were less likely to receive locoregional radiation (5.9% in 2004 to 4.2% in 2012, AOR = 0.97 per year, 95% CI = 0.95–0.99, $P < 0.001$) (Table 3). Treatment with radiation was also stratified by PSA (recorded as the highest PSA documented prior to diagnostic biopsy) to see if trends were different in patients with low PSA as a

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