Characterizations of Clinical and Therapeutic Histories for Men With Prostate Cancer-Specific Mortality

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Abstract

Careful examination of the clinical course in prostate cancer-specific mortality is scant in nontrial settings. The present study describes the characteristics, timelines, and treatment histories from the initial presentation to death in a cohort of men who died unequivocally from metastatic, castrate-resistant prostate cancer (mCRPC). Special attention was given to the sequence and prevalence of the use of therapeutic agents after the development of mCRPC.

Background: Careful descriptions of men with prostate cancer (PCa)-specific mortality are scant in nontrial settings. The present retrospective review describes the clinical characteristics, timelines, and treatment histories from initial presentation to death in a cohort of men with metastatic, castrate-resistant PCa (mCRPC). Unique to the present study is the unequivocal attribution of PCa death by a single experienced clinician. **Patients and Methods:** A total of 119 patients who had been treated at Tulane Cancer Center and had died of mCRPC from 2008 to 2015 were studied through a retrospective review of the medical records. **Results:** The median age at diagnosis was 65 years (range, 40-85 years), and 34.4% of the patients presented with metastatic disease (stage M1). Of these patients, 56% had received definitive primary therapy, all had received androgen-deprivation therapy, and 52% had received docetaxel. The patients had received a median of 7 (1-14) systemic therapies before death. Most were secondary hormonal manipulations after the diagnosis of mCRPC (median, 4; range, 0-9). The median survival was 69 months (range, 5-270 months) after diagnosis, and the median age at death was 73 years (range, 47-95 years). The presence of metastases at diagnosis was a significant predictor of early death (hazard ratio, 4.33; $P < .001$), and definitive primary therapy was a significant predictor of longer survival ($P < .001$). The median survival for patients presenting with metastases was 39 months (range, 5-235 months) compared with 100 months (range, 6-270 months) for those with localized disease ($P < .001$). The median age at diagnosis between the docetaxel- and non–docetaxel-treated patients was significantly different at 62 and 71 years, respectively ($P = .002$). **Conclusion:** The present retrospective analysis provides initial views clarifying the clinical characteristics of men dying of mCRPC and the therapies they received before death. Additional data are needed in multi-institutional settings to confirm these findings.

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Introduction

In 2014, prostate cancer (PCa) will have accounted for 27% of non–skin cancer diagnoses for men in the United States. With screening and early detection, PCa is often considered a curable disease; however, it remains the second leading cause of cancer-related mortality among men in the United States.[1] Analyses of

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the natural history of disease for patients with PCa-specific mortality are scant in the published data outside of clinical trial settings. The present retrospective, single-institution study examined disease progression and the systemic therapies administered from diagnosis to the death of 119 men dying of castrate-resistant PCa (CRPC). Attribution of PCa-specific mortality was performed by a single, experienced clinician. Unequivocal assessment of the cause of death is critical for a categorical evaluation of this disease, because the vast majority of men diagnosed with PCa in the United States die of non–PCa-related causes.

Several phase III trials (TAX 327, Southwest Oncology Group 99-16) have demonstrated a survival benefit with docetaxel for patients with metastatic CRPC (mCRPC). Although the prevalence of docetaxel in such a setting has been described in population-based studies[2,3] in both Canada and the United Kingdom (37% and 22%, respectively), few data have been published about the US experience. As such, we hoped, in the present study, to characterize the usage and timing of docetaxel, in addition to other systemic therapies, within a single institution's population.

Prognostic modeling was also performed to better understand the major clinical variables predictive of overall survival in these patients. Although the limitations of a single-institution experience are readily apparent, these analyses can be viewed heuristically and validated in the future using larger multi-institutional cohorts.

Patients and Methods

Study Cohort and Variable Definition

Patients who died of PCa at Tulane Cancer Center from 2008 to 2015 (n = 119) were identified and their characteristics studied in a retrospective, single-institution analysis. The patients' medical data were accessed through the hospital electronic medical records. A vast majority of patients were referred from other practices; thus, some information regarding patients' initial diagnoses was not available. Data collection included demographic data, age at diagnosis and death, Gleason score, initial stage, complete therapeutic history, time to developing CRPC, and prostate-specific antigen (PSA) levels. For the purposes of our study, the disease characteristics included tumor grade (low [Gleason score < 7] and high [Gleason score ≥ 7]) and tumor stage (localized vs. metastatic). Definitive therapy was defined as either radical prostatectomy or primary locoregional radiation therapy; these groups were mutually exclusive and only pertinent for those men with localized disease at diagnosis. A single physician (O.S.) performed the attribution of the cause of death for all men included in the analyses.

Statistical Analysis

The median and range were reported for all continuous variables. The percentages were reported for all categorical variables. The χ^2 and t tests were used to test for any statistically significant differences, as appropriate. Univariate regression analysis (defined by the F statistic, with significance at $P < .05$) was conducted to assess the effects of each individual covariate on overall survival (OS; calculated as the time from diagnosis to death). Significant variables were then confirmed and fitted into a prognostic model using Cox multivariate regression analysis. The Cox analyses were performed both with and without the docetaxel stratification, after accounting for potential confounders and interactions. All P values were corrected for multiple testing.

Results

Baseline Characteristics of Deceased Cohort

Overall, 119 patients who had died of CRPC were identified (Table 1). The median age at diagnosis was 65 years (range, 40-85

Table 1 Deceased Cohort Characteristics (n = 119)

Characteristic	n (%)
Race	
White	98 (82)
African American	18 (15)
Unknown	3 (3)
Age (years)	
At diagnosis	
Median	65
Range	40-85
At death	
Median	73
Range	47-95
Gleason score at diagnosis	
High (≥7)	87 (73)
Low (<7)	8 (7)
Unknown	24 (20)
Definitive, primary, local therapy	
Yes	67 (56)
No	50 (42)
Unknown	2 (2)
Radical prostatectomy	
Yes	44 (37)
No	75 (63)
Unknown	0 (0)
Radiotherapy (primary)	
Yes	23 (19)
No	94 (79)
Unknown	2 (2)
Stage	
High (T3-T4)	29 (24.5)
Low (T1-T2)	17 (14)
Unknown	73 (61.5)
Metastases at diagnosis (stage M1)	
Yes	41 (34.4)
No	76 (63.8)
Unknown	2 (1.8)
Lines of therapy before death (n)	
Median	7
Range	1-14
Family history	
Yes	27 (23)
No	66 (55)
Unknown	26 (22)

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