Use of Hormonal Therapy in Men With Metastatic Prostate Cancer

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Purpose: Bilateral orchiectomy or luteinizing hormone releasing hormone agonists represent the standard of care for metastatic prostate cancer. In this population based study we assessed the use rates of these therapies in men who died of prostate cancer.

Material and Methods: A total of 9,110 men 65 years or older who died of prostate cancer in 1991 to 2000 were identified through the population based Surveillance, Epidemiology and End Results, and Medicare linked database to determine hormonal therapy use rates. A modified Poisson regression model was used to estimate the adjusted effects of various factors associated with hormone use.

Results: Approximately 38% of black and 25% of white men did not receive hormonal therapy before dying of prostate cancer. After adjusting for cancer status at diagnosis and other potential confounding factors black race and residence in low income areas were associated with lower hormonal therapy use (relative risk 0.73, 95% CI 0.67 to 0.80 and 0.91, 95% CI 0.85 to 0.98, respectively). Hormonal therapy use was most comprehensive in the Northeast.

Conclusions: A substantial number of men who die as a consequence of prostate cancer never receive hormonal therapy. The use of hormonal therapy varies significantly. Further studies are warranted to determine factors that may be associated with the incomplete use of hormonal therapy for metastatic prostate cancer.

Key Words: prostate; prostatic neoplasms; Medicare; SEER program; antineoplastic agents, hormonal

Prostate cancer is the most common nonskin cancer and the second most common cause of cancer death in men. In men with metastatic disease hormonal therapy, ie DES, orchiectomy or LHRH agonist, has been the mainstay of treatment since recognition of its effectiveness in studies for which Huggins was ultimately awarded the 1966 Nobel Prize in Medicine. Indeed, almost every contemporary textbook, review or clinical guideline recognizes hormonal therapy as the standard of care in men with metastatic disease.[1]

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Study received Institutional Review Board approval from the University of Medicine and Dentistry of New Jersey, SEER program, and Center for Medicare and Medicaid Services.

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The performance and design of this study was reviewed and approved by the National Cancer Institute, and Center for Medicare and Medicaid Services.

This study used the Linked SEER-Medicare Database. The interpretation and reporting of these data are the sole responsibility of the authors. The content of the information does not necessarily reflect the position or the policy of the Government, and no official endorsement should be inferred.

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Remarkably and despite this a modern phase III trial that compared early vs delayed hormonal therapy showed that in practice many patients randomized to delayed treatment never received the prescribed hormonal therapy.[2] It has generally been assumed that these results are not reflective of current practice in the United States and almost all patients with metastatic disease receive hormonal therapy before dying of prostate cancer.[3] However, empirical data to support this assumption have been limited.

We performed a population based study to assess the use of hormonal therapy in men who ultimately died of prostate cancer, a population in which hormonal therapy is indicated. We also examined potential factors associated with failure to administer hormonal therapy in these men.

MATERIALS AND METHODS

Data Sources

The SEER program database was linked with Medicare files to obtain data for this study. Demographics, cancer status at diagnosis and cause of death were obtained from SEER data. Treatment information was obtained from Medicare claims. SEER regions encompass approximately 14% of the population in the United States. The Medicare database covers approximately 97% of individuals in the United States who are 65 years or older and linkage to the SEER database was complete in approximately 94% of the patients.[4]

Study Participants

The study cohort consisted of men who were residents of SEER regions and who died of prostate cancer in 1991 to

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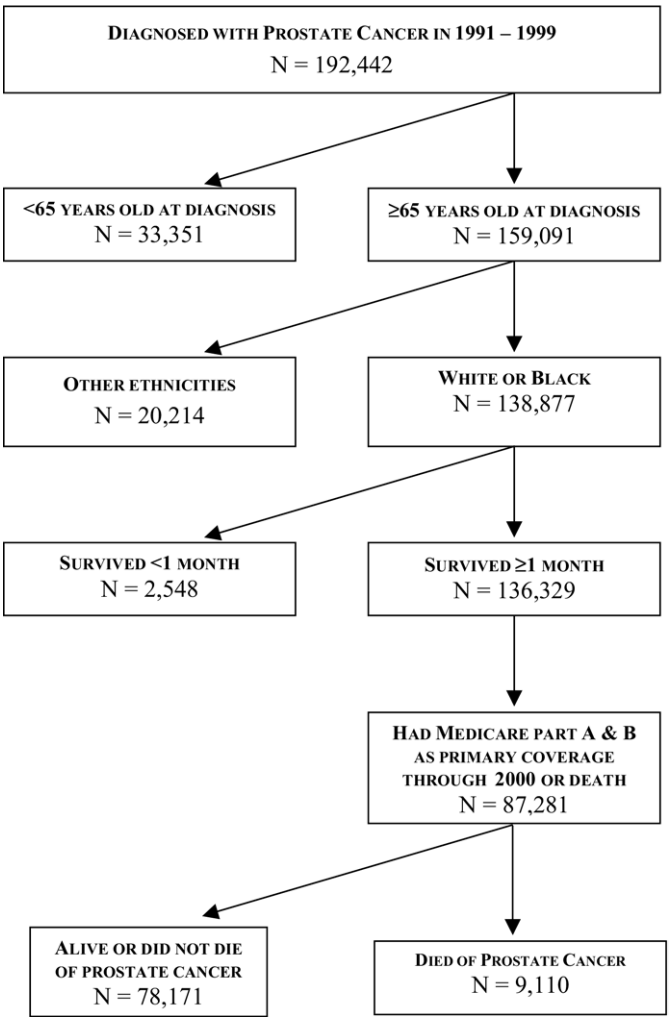
2000. Men who died of competing causes were excluded because it could be acceptable to omit or delay treatment in a population that died of a cause other than prostate cancer. Although the clinician may not be able to predict who is going to die of a competing cause, excluding these patients was a conservative approach and biased against our hypothesis. Including patients who died of competing causes resulted in even lower use rates.

The figure shows assembly of the study population. Patients younger than 65 years were excluded since Medicare did not cover them and, therefore, data on hormonal therapy use were not available. Patients who died of prostate cancer within 1 month of diagnosis were excluded since they may not have had a reasonable opportunity to receive hormonal therapy. To ensure that claims data provided a complete representation of patient care patients had to have Medicare Part A (hospitalization) and Part B coverage (physician services, laboratory and x-ray services, durable medical equipment, and outpatient and other services) as their primary health insurance coverage during the period between cancer diagnosis and the end of followup. Patients covered by a health maintenance organization or the Veterans Administration system were excluded since their Medicare data would not present a complete record of all of their medical treatments. The study received Institutional Review Board approval from the University of Medicine and Dentistry of New Jersey, the SEER program, and the Center for Medicare and Medicaid Services.



Cohort used in this study

Use of Hormonal Therapy

Using a previously described algorithm[5] Medicare physician, inpatient and outpatient claims were used to identify orchiectomy (Healthcare Common Procedure Coding System codes 54520, 54521, 54522, 54530 or 54535, or International Classification of Diseases, version 9 codes 623 and 624) and use of LHRH agonists (Healthcare Common Procedure Coding System codes J1950, J9202, J9217, J9218, J9219).

End Point Validation

A subset of patients in this study had previously been randomly chosen to participate in PCOS.[6] As part of PCOS, medical personnel reviewed the medical records of these patients, and abstracted information about hormonal therapy use and other treatments.[6] For each patient the medical records examined included those from hospitals, radiological or surgical centers and physician offices. Data obtained from the actual medical records as part of the PCOS study were linked with our data using encrypted identifiers. The results of the claims based hormonal therapy use algorithm were then compared with the results of the medical records review.

Other Variables for Risk Adjustment

Median income in 2000 in the ZIP code area of the patient residence was used to assess socioeconomic status since it has been shown to correlate well with self-reported income. Medicare Provider Analysis and Review claims were used to calculate the Charlson index score, a validated measure of comorbidity.[7]

Statistical Analyses

The relative risk of hormonal therapy use by race for each level of risk factors was determined by fitting each model with hormonal therapy use as the outcome variable and race as a predictor. Since hormone therapy use is not rare, the OR is not a good approximation of relative risk.[8] Thus, we used a modified Poisson regression model[8] rather than logistic regression to estimate the adjusted effect of the factors on hormone therapy use. The SAS® system, version 9.1 was used for statistical analysis and assumptions of all statistical models were verified.

RESULTS

Baseline Characteristics in Men Who Died of Prostate Cancer

Table 1 lists baseline characteristics in 9,110 patients who died of prostate cancer during 1991 to 2000. Of patients who died of prostate cancer 60% were diagnosed at age 75 or older, 36% were diagnosed with distant stage disease and 44% had a Gleason score of 8–10 at diagnosis. Compared with white men higher proportions of black men did not receive hormonal therapy ($p < 0.001$), had distant disease ($p < 0.001$), were younger ($p < 0.001$) and were unmarried at diagnosis ($p < 0.001$).