Variation in Use of Active Surveillance among Men Undergoing Expectant Treatment for Early Stage Prostate Cancer

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Purpose: We examined variation in active surveillance use in Medicare eligible men undergoing expectant treatment for early stage prostate cancer.

Materials and Methods: Using SEER (Surveillance, Epidemiology and End Results) and Medicare data we identified 49,192 men diagnosed with localized prostate cancer from 2004 through 2007. Of 7,347 patients who did not receive treatment (ie expectant management) within 12 months of diagnosis we assessed the prevalence of active surveillance (ie repeat prostate biopsy and prostate specific antigen measurement) vs watchful waiting across health care markets. We fit multivariable logistic regression models to examine associations of active surveillance with patient demographics, cancer severity and health care market characteristics.

Results: During the study interval use of active surveillance vs watchful waiting increased significantly in patients treated expectantly from 9.7% in 2004 to 15.3% in 2007 ($p < 0.001$). Active surveillance was less common in older patients, those with high risk tumors and those with more comorbidities (each $p < 0.001$). Patients who were white and had higher socioeconomic status were more likely to receive active surveillance (each $p < 0.05$). After adjusting for patient and tumor characteristics significant differences in the predicted probability of active surveillance persisted across health care markets (range 2.4% to 30.1%). No significant variation in active surveillance use was associated with specific health care market characteristics, including intensity of end of life care, Medicare reimbursement or provider density.

Conclusions: Active surveillance has been relatively uncommon in Medicare beneficiaries with localized prostate cancer. Its use relative to watchful waiting varies based on patient demographics, tumor severity and geographic location.

Key Words: prostate, prostatic neoplasms, SEER program, Medicare, physician's practice patterns

Abbreviations and Acronyms

AS = active surveillance

HMO = health maintenance organization

HRR = hospital referral region

PSA = prostate specific antigen

SEER = Surveillance, Epidemiology and End Results

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ALTHOUGH randomized trials demonstrated benefits of treatment in some men with localized prostate cancer,[1] many men with low risk tumors are unlikely to die of this disease.[2] Thus, some groups contend that many patients with prostate cancer are overtreated, that is exposed to the potential risks of therapy when the benefits of treatment are less apparent.[3] Given these concerns, groups at some centers have established AS protocols to distinguish between indolent and clinically

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significant tumors, and determine when to intervene in patients with evidence of cancer progression.[4] This is in contrast to watchful waiting, an expectant approach reserved for patients with shorter life expectancy in whom treatment is unlikely to impart any survival or quality of life benefit.

Implementation of AS protocols at a population level remains poorly understood. 1) Use may not be optimized since before 2007 fewer than 10% of men with low risk prostate tumors proceeded to AS.[5] 2) Current guidelines offer limited criteria for selecting patients for surveillance.[6] 3) There is no standard protocol for AS because established regimens vary with respect to inclusion criteria and surveillance intensity.[4]

Due to this uncertainty there is likely considerable regional variation in the application of AS in men followed expectantly for localized prostate cancer. If present, such variation can be associated with considerable clinical and economic ramifications.[7] In this context we examined geographic differences in AS use in Medicare beneficiaries treated expectantly for localized prostate cancer as well as potential patient and health care market factors underlying such variation.

METHODS

Data Source

We used data from the NCI (National Cancer Institute) SEER program linked with Medicare claims to identify men 66 years old or older diagnosed with localized prostate cancer. The 15 SEER registries in this study include more than a quarter of the population of the United States and are representative of the entire population.[8] For each case reported to SEER data are collected on patient demographics, cancer directed treatments, tumor characteristics and mortality. Data on demographics and cancer directed treatments are linked to Medicare claims more than 94% of the time.[9] Linkage with claims data is not possible for the remaining 6% of patients in SEER registries whose primary health care insurance is not provided by traditional Medicare but rather by Medicare HMOs, the VHA (Veterans Health Administration) or other payers.

Study Population

We identified men diagnosed with localized prostate cancer from 2004 through 2007. We limited this cohort to patients with at least 1 year of Medicare eligibility before diagnosis to allow for measurement of comorbid conditions. We then excluded patients who 1) were enrolled in a HMO at diagnosis, 2) had less than 6 months of Medicare eligibility after diagnosis, 3) had a diagnosis of a second malignancy and/or 4) died within 12 months of diagnosis. If a patient enrolled in a HMO at any point after diagnosis, we defined the date of enrollment as the end of followup for that patient.

Using these steps our initial cohort comprised 49,193 Medicare eligible men 66 years old or older with localized prostate cancer. We identified the subset of 9,562 men who received expectant management by excluding all who underwent radical prostatectomy, radiation therapy, cryotherapy and/or androgen deprivation therapy within 12 months of diagnosis (supplementary Appendix 1, http://jurology.com/). We also excluded patients without Medicare claims for 12 months after diagnosis (897) and/or evidence of treatment from the SEER PEDSF (Patient Entitlement and Diagnosis Summary File) (1,725). After applying these exclusion criteria our final expectant management cohort comprised 7,347 patients.

In this group we defined receipt of AS based on claims for 1 or more PSA tests and 1 or more prostate biopsies within the first 2 years after prostate cancer diagnosis (supplementary Appendix 2, http://jurology.com/). All other patients in the expectant management group were defined as having received watchful waiting. We excluded 30 men (0.4% of the cohort) who underwent repeat prostate biopsy without repeat PSA testing. The median number of repeat biopsies and PSA tests in the AS cohort was 1 (range 1 to 6) and 5 (range 1 to 29), respectively.

Diagnosis year, age and race were abstracted from SEER data. We measured patient comorbidity using Medicare claims for the 12 months before prostate cancer diagnosis.[10] We assigned socioeconomic status terciles based on residence ZIP Code.[11] Patients were classified with low, intermediate or high risk cancer based on D'Amico criteria using PSA, Gleason grade and clinical stage data in the SEER database.[12]

We selected health care markets defined by HRRs as our unit of analysis. As described previously,[13] HRRs represent individual health care markets for tertiary care. Our analysis was limited to 63 of 306 HRRs with at least 50% of the geographic area in a SEER registry and at least 30 expectant management cases each.[14]

We also ascertained health care market characteristics.[15] Factors related to intensity of care included those related to end of life cancer care (intensive care unit admission during the last month of life, chemotherapy during the last 2 weeks of life and hospice use during the last 6 months of life) and Medicare reimbursements per male enrollee as well as provider density, ie urologists and radiation oncologists.

Statistical Analysis

Associations of patient and tumor characteristics with AS vs watchful waiting were assessed by the Mantel-Haenszel chi-square test. We fit multivariable logistic regression models to characterize relationships between AS and factors of interest. The first model included patient age, diagnosis year, race, comorbidity, patient level socioeconomic status, cancer risk and a HRR indicator to assess for regional variation. We fit a second model that added health care market level factors of interest to the first model, ie end of life cancer care, Medicare reimbursement and provider density. From these data we estimated the predicted probability and/or OR of AS vs watchful waiting based on included covariates. Because practice patterns may be similar in health care markets, we used established methods (robust Huber-White sandwich estimators) to adjust the SE in our models to decrease the risk of a type I statistical error.[16,17]