CLINICAL RESEARCH STUDY

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Who Bears the Greatest Burden of Aggressive Treatment of Indolent Prostate Cancer?

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ABSTRACT

PURPOSE: The long-term prostate cancer-specific survival for patients initially managed with active surveillance for low-risk prostate cancer ranges from 97% to 100%. We characterized factors that are associated with aggressive treatment with radical prostatectomy or radiation for indolent prostate cancer (defined as screening-detected, low-risk disease).

METHODS: The Surveillance, Epidemiology, and End Results Program was used to extract a cohort of 39,803 men diagnosed with prostate-specific antigen–detected, low-risk prostate cancer (clinical category T1c, Gleason score $\leq$6, and prostate-specific antigen $<$10) from 2004 to 2010. After socioeconomic profiles were generated from county-linked education and income data, multivariable logistic regression was used to determine whether there were any factors associated with high rates of aggressive treatment.

RESULTS: The rate of aggressive treatment among all men with indolent prostate cancer was 64.3%. Greater rates of aggressive treatment were experienced by men with high socioeconomic status, Caucasian men, and married men ($P < .001$ for all cases). The increased adjusted odds for receipt of aggressive therapy were 1.25 (95% confidence interval [CI], 1.17-1.32; $P < .001$), 1.26 (95% CI, 1.21-1.32; $P < .001$), and 1.88 (95% CI, 1.80-1.97; $P < .001$) for men with high socioeconomic status, Caucasian men, and married men, respectively, compared with men with low socioeconomic status, non-Caucasian men, and unmarried men, respectively.

CONCLUSIONS: Although men with high socioeconomic status, Caucasian men, and married men often receive the highest quality health care and have the best outcomes for many cancers, it seems that they are most at risk for the avoidable potential harms of aggressive treatment of indolent prostate cancer. Future policy should encourage more stringent guidelines for deferred treatment and culturally and sociodemographically competent counseling of active surveillance.

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Prostate cancer represents the most common noncutaneous malignancy in developed nations, with 650,000 new diagnoses and 136,500 deaths due to disease in 2008.[1] Although prostate-specific antigen screening reduces prostate cancer-specific mortality, overuse and misuse of prostate-specific antigen screening could lead to diagnoses of indolent low-risk tumors that would have otherwise not become life threatening.[2] An increasing proportion of prostate cancer diagnoses are characterized as nonpalpable clinical T1c disease with ongoing trends toward low-risk features at presentation.[2] Overdiagnosis of prostate-specific antigen-detected low-risk disease has led to high rates of overtreatment, resulting in many unnecessary side effects and detriments in quality of life, attenuating the aggregate benefits of prostate-specific antigen-based screening.[3,4]

Deferred treatment with watchful waiting or active surveillance represents an important alternative to definitive therapy for indolent disease that may minimize the burden of overdiagnosis and harms of overtreatment.[5,6] Several studies have reported less than 3% prostate cancer-specific mortality at up to 10 years among men who undergo active surveillance as initial management for localized prostate cancer.[7-9] Although the use of surveillance is increasing in developed nations, treatment of prostate-specific antigen-detected low-risk disease still occurs at high rates, and overtreatment of clinically indolent prostate cancer remains a global concern.[4,5,8,10] Although interventions targeting groups that are susceptible to overtreatment may be effective in reducing rates of unnecessary treatment for low-risk disease, there is little literature that characterizes the patients most likely to be treated aggressively for indolent disease.[10-13]

The aim of this study was to determine whether sociodemographic factors, such as socioeconomic status, marital status, and race, are associated with aggressive treatment among men with indolent, prostate-specific antigen-detected low-risk prostate cancer using the national US Surveillance, Epidemiology, and End Results (SEER) database.[14]

CLINICAL SIGNIFICANCE

- Despite 97% to 100% long-term prostate cancer-specific survival for patients managed with active surveillance, the rate of aggressive treatment among men with indolent prostate cancer remains high.
- Although men with high socioeconomic status, Caucasian men, and married men often receive the highest quality health care, they are the most at risk groups for overtreatment of indolent prostate cancer.
- Policy should encourage more stringent guidelines for deferred treatment and culturally and sociodemographically competent counseling of active surveillance.

MATERIALS AND METHODS

Patient Population and Study Design

Sponsored by the National Cancer Institute, the SEER program collects and publishes cancer incidence, survival, and treatment data from population-based cancer registries; the 17 tumor registries encompass approximately 28% of the US population and capture approximately 97% of incident cancers.[14] The SEER program was used to identify 39,803 men diagnosed with prostate-specific antigen-detected, low-risk prostate (clinical category T1c, Gleason score $\leq$6, and prostate-specific antigen $<$10)[15] from 2004 to 2010. The inclusion period was limited to 2004 to 2010, because 2004 represents the year that SEER initiated collection of prostate-specific antigen data and 2010 represents the most recent year for which full information is available. As provided by SEER, Gleason scores represent the highest Gleason score identified at surgery or at biopsy for nonsurgically managed patients, whereas stage was determined using the American Joint Committee on Cancer 6th edition.[14] Of note, the number of cores obtained at biopsy and prostate-specific antigen density are not recorded by the registries.

Patient composite socioeconomic status was evaluated using income (computed as median household income) and educational status (computed as the percentage of residents aged $\geq$25 years with at least a high school education), which were both determined at the county level by linking to the 2000 US Census.[16] Specifically, socioeconomic status profiles were generated from income and educational status data to analyze treatment trends by socioeconomic strata. This was done by separately stratifying income and educational status into quartiles and assigning the following values to each quartile: first quartile = 1; second quartile = 2; third quartile = 3; and fourth quartile = 4. These values were subsequently added across income and education quartiles creating a composite (income + educational status) socioeconomic score ranging from 2 to 8. These scores were then translated into the following socioeconomic status profiles: income + educational status scores of 2 to 3 represented low socioeconomic status, 4 to 6 represented middle socioeconomic status, and 7 to 8 represented high socioeconomic status.

Residence type (urban vs rural) also was determined at the county level by linking to the 2003 US Department of Agriculture rural-urban continuum codes.[17] The demographics of race and marital status were classified as Caucasian vs other race (African American, Spanish/Hispanic/Latino, Asian or Pacific Islander, Native American) and married vs unmarried, respectively. Last, initial management was defined as aggressive treatment vs nonaggressive management. Aggressive treatment consisted of