Sociodemographic and Clinical Predictors of Switching to Active Treatment among a Large, Ethnically Diverse Cohort of Men with Low Risk Prostate Cancer on Observational Management

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Abbreviations and Acronyms

ADT = androgen deprivation therapy
AS = active surveillance
AT = active treatment
KPNC = Kaiser Permanente Northern California
PCa = prostate cancer
PSA = prostate specific antigen
RP = radical prostatectomy
RT = radiation therapy
WW = watchful waiting

Purpose: We determined the clinical and sociodemographic predictors of beginning active treatment in an ethnically diverse population of men with low risk prostate cancer initially on observational treatment.

Materials and Methods: We retrospectively studied men diagnosed with low risk prostate cancer between 2004 and 2012 at Kaiser Permanente Northern California who did not receive any treatment within the first year of diagnosis and had at least 2 years of followup. We used Cox proportional hazards regression models to determine factors associated with time from diagnosis to active treatment.

Results: We identified 2,228 eligible men who were initially on observation, of whom 27% began active treatment during followup at a median of 2.9 years. NonHispanic black men were marginally more likely to begin active treatment than nonHispanic white men independent of baseline and followup clinical measures (HR 1.3, 95% CI 1.0–1.7). Among men who remained on observation nonHispanic black men were rebiopsied within 24 months of diagnosis at a slightly lower rate than nonHispanic white men (HR 0.70, 95% CI 0.6–1.0). Gleason grade progression (HR 3.3, 95% CI 2.7–4.1) and PSA doubling time less than 48 months (HR 2.9, 95% CI 2.3–3.7) were associated with initiation of active treatment independent of race.

Conclusions: Sociodemographic factors such as ethnicity and education may independently influence the patient decision to pursue active treatment and serial biopsies during active surveillance. These factors are important for further studies of prostate cancer treatment decision making.

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THE use of AS as a management strategy for low risk PCa has been increasing during the last decade.[1] Current United States guidelines recommend observational management, AS or WW, as strategies for men at low risk for disease progression.[2–4] This avoids active treatment unless clinical measures indicate disease progression or the patient requests active treatment.[5,6] Results of PSA testing and repeat biopsies are used to determine PCa progression and prompt the cessation of observational management.[7] Recent systematic reviews advocated serial prostate biopsies to accurately detect disease progression[6] because PSA kinetics are not effective as the only clinical trigger to prompt a switch to active treatment.[8]

Younger age and anxiety are associated with men changing from observation to more aggressive treatment.[9,10] However, few studies have been done to examine nonclinical factors that influence surveillance and followup protocols in a sociodemographically diverse population. In addition, there is limited evidence on whether race/ethnicity and sociodemographic factors influence the initiation of more aggressive treatments in equal access integrated health care systems with salaried providers.[11]

We assessed the impact of sociodemographic and clinical factors on predicting whether men began active treatment after initially choosing observational treatment among an ethnically diverse population of patients with low risk PCa receiving care in an integrated health care system.

METHODS

Study Design and Population

The study population included men seen at KPNC, an integrated health care delivery system. The KPNC health system has comprehensive information on inpatient and outpatient diagnoses, clinical encounters, laboratory test values and tumor related characteristics. We identified men from the KPNC Cancer Registry diagnosed with low risk PCa from January 1, 2004 to December 31, 2012. Low risk PCa was defined using D'Amico/AUA (American Urological Association) criteria,[12] including clinical stage T2a or less, PSA less than 10 ng/ml and Gleason score 6 or less. Men on observational treatment, AS or WW, were those who had not received active treatment within 12 months of diagnosis and who were followed at least 2 years after diagnosis. End of followup for the cohort was December 31, 2014. Active treatment was defined as RP, RT or ADT.

We defined observational management as any use of AS or WW that included evidence of regular PSA monitoring (1 or more PSA measurements per year) or repeat biopsies as there was no uniform surveillance protocol implemented at KPNC during the study period. KPNC provided care in 1 of 12 KPNC service areas in the greater San Francisco Bay Area and the Central Valley of California. The study was approved by the Kaiser Foundation Research Institute and Georgetown University internal/institutional review boards.

Characteristics

Demographic. We obtained age at diagnosis, race/ethnicity, date of diagnosis, census tract educational attainment (percent of the population 25 years old or older with at least a college education who lived in the same census area as the individual) and KPNC service area.

Clinical. The Elixhauser comorbidity index was calculated for 30 individual health conditions diagnosed between 2 years before PCa diagnosis and up to 90 days after PCa diagnosis. We required an inpatient diagnosis and/or at least 2 outpatient diagnosis codes at least 30 days apart to minimize false-positive findings from rule-out diagnoses. We obtained the Gleason score from the first biopsy leading to the PCa diagnosis. There was no central pathological review. Since 2005, Gleason grading had been performed by various pathologists using the ISUP (International Society of Urological Pathology) modified Gleason system (supplementary table 1, http://jurology.com/). However, due to the volume of new cases per year at KPNC (greater than 2,000), pathologists have a robust practice in urological cancer.

Diagnostic biopsies were performed under the general practice guidelines of the period, including 6 core biopsies in the earlier part with a transition to 12 core biopsies in the latter part of the study period. Baseline PSA was defined as serum PSA in ng/ml measured within 6 months prior to diagnosis and examined using categorical (less than 4, 4 to 5, 6 to 7 and 8 to 10 ng/ml) and age specific PSA cutoffs based on AUA criteria.[13] We obtained followup PSA test results and derived certain variables, including PSA slope,[14] PSA doubling time (less than 48 vs 48 months or greater)[15] and followup PSA intermediate risk PCa status, that is any followup PSA greater than 10 ng/ml (yes/no).[16] The supplementary material (http://jurology.com/) shows more detailed methodology.

Analytical Cohort

Of the 6,632 men diagnosed with PCa from January 1, 2004 to December 31, 2012 we identified 2,228 diagnosed with clinically localized low risk PCa who had not received any treatment within 12 months of diagnosis and were followed at least 2 full years after diagnosis. Fewer than 2.6% of men were lost to followup through 2014.