How Active is Active Surveillance? Intensity of Followup during Active Surveillance for Prostate Cancer in the United States

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Purpose: While major prostate cancer active surveillance programs recommend repeat testing such as prostate specific antigen and prostate biopsy, to our knowledge compliance with such testing is unknown. We determined whether men in the community receive the same intensity of active surveillance testing as in prospective active surveillance protocols.

Materials and Methods: We performed a retrospective cohort study of men 66 years old or older in the SEER (Surveillance, Epidemiology and End Results)-Medicare database. These men were diagnosed with prostate cancer from 2001 to 2009, did not receive curative therapy in the year after diagnosis and underwent 1 or more post-diagnosis prostate biopsies. We used multivariable adjusted Poisson regression to determine the association of the frequency of active surveillance testing with patient demographics and clinical features. In 1,349 men with 5 years of followup we determined the proportion who underwent testing as intense as that recommended by the Sunnybrook Health Sciences Centre and PRIAS (Prostate Cancer Research International Active Surveillance) programs, including 14 or more PSA tests and 2 or more biopsies, and The Johns Hopkins program, including 10 or more prostate specific antigen tests and 4 or more biopsies.

Results: Among 5,192 patients undergoing active surveillance greater than 80% had 1 or more prostate specific antigen tests per year but fewer than 13% underwent biopsy beyond the first 2 years. Magnetic resonance imaging was rarely done during the study period. On multivariable analysis recent diagnosis and higher income were associated with a higher frequency of surveillance biopsy while older age and greater comorbidity were associated with fewer biopsies. African American men underwent fewer prostate specific antigen tests but a similar number of biopsies. During 5 years of active surveillance only 11.1% and 5.0% of patients met the testing standards of the Sunnybrook/PRIAS and The Johns Hopkins programs, respectively.

Conclusions: In the community few elderly men receive the intensity of active surveillance testing recommended in major prospective active surveillance programs.

Key Words: prostatic neoplasms, aged, standard of care, watchful waiting, SEER program

Abbreviations and Acronyms

AS = active surveillance

MRI = magnetic resonance imaging

PCa = prostate cancer

PSA = prostate specific antigen

WW = watchful waiting

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Overtreatment of PCa is a significant public health concern and many men with favorable risk PCa may be treated with AS. This approach decreases treatment related morbidity without affecting oncologic outcomes and it is recommended by several professional societies.[1]

While AS use is increasing,[2–5] there is little consensus about what AS actually entails. There is significant variation among published AS protocols, which offer starkly different implications for the patient burden and health care resource use. For example, The Johns Hopkins program recommends PSA checks every 6 months, annual prostate biopsies until age 75 years and recently MRI in men with PSA greater than 10 ng/ml.[6] In contrast, the Sunnybrook Health Sciences Centre AS program in Toronto includes PSA measurements every 3 months for 2 years and every 6 months thereafter.[7] Confirmatory biopsy is recommended within 1 year of enrollment with subsequent biopsy every 3 to 4 years. Finally, the PRIAS protocol includes PSA every 3 months for 2 years and then every 6 months with biopsies at years 1, 4 and 7.[8]

Previous studies have shown that most men on AS remain treatment free at 5 and 10 years when adhering to one of these regimens. Actual adherence and AS effectiveness are important for men with significant life expectancy, given the persistent hazard of PCa progression even at 20 years.[7] Conversely, excessive and invasive surveillance testing may unnecessarily increase morbidity in elderly men with significant comorbidity who are at low risk for PCa death. There is a knowledge gap regarding AS patterns of care in the community and whether they conform to widely accepted regimens.

Our objective was to determine whether real world practice patterns in a nationally representative sample of patients with PCa in the United States conform to the intensity of surveillance in published prospective protocols. We hypothesized that men on AS would undergo 2 or more PSA tests per year and 2 biopsies during a 5-year period, representing the minimum frequency of testing in prospective surveillance cohorts.

METHODS

We performed a retrospective cohort study of men with localized PCa who were deferring initial curative therapy. Using the SEER-Medicare linked database with hospital, outpatient and physician claims we identified 427,592 men diagnosed with prostate adenocarcinoma from 2001 to 2009. SEER is a collection of population based cancer registries encompassing approximately 30% of the American population.[9] We excluded from study men with advanced/metastatic PCa (T3 or greater), those younger than 66 years and those missing the diagnosis month and year. We also excluded men without continuous Medicare Parts A and B coverage, those diagnosed at autopsy and those who died within 3 months of diagnosis. Using ICD-9-CM codes we excluded men treated with received radical prostatectomy, radiation, cryotherapy or androgen deprivation therapy less than 1 year after diagnosis (supplementary table 1, http://jurology.com/).[10]

Thus, 74,992 men undergoing conservative management of PCa were considered for analysis, from whom we excluded 69,800 without repeat prostate biopsy during 2 years after diagnosis, leaving a final study population of 5,192 undergoing AS (supplementary figure, http://jurology.com/). Compared to all conservatively treated men, the study population that met our definition for AS was significantly younger and diagnosed more recently. Men were censored at the time of treatment if they received any treatment (prostatectomy, radiation therapy, cryotherapy or hormonal therapy), at death or otherwise as of December 31, 2011. Mean followup was 46.5 months (median 37.5, range 12.2 to 133.9).

Our primary end point was the proportion of men who underwent the testing intensity recommended by the Sunnybrook Health Sciences Centre,[7] PRIAS[8] and The Johns Hopkins[6] programs. We also examined MRI use during AS (supplementary table 1, http://jurology.com/) and determined the proportion of men who exceeded 10 PSA tests or 5 biopsies within 5 years, which is the maximum intensity recommended by NCCN Guidelines®.[11]

Independent variables of interest were diagnosis year, age, race (white, black and other), Elixhauser comorbidity index with the Klabunde modification (0 vs 1+),[12] marital status (single/divorced/widowed vs married), median income in the patient home ZIP Code™ (above vs below median), biopsy Gleason score (6 or less vs greater than 6) and clinical stage (T2a or less vs greater than T2a). Because PSA data are currently unavailable in SEER, they were not included in risk classification or analysis.[13]

Statistical Analysis

All statistical analyses were performed with SAS®, version 9.3. We used multivariable adjusted Poisson regression, clustering patients by SEER registry, to determine the association between the frequency of surveillance biopsies and independent variables. Natural log of the number of followup months was used to offset the varying duration of followup per patient. This analysis was repeated in the subset of 1,391 men with low risk features (cT2a or less and Gleason 6 or less) who were diagnosed during the last 5 years of the study (2004 to 2009). Those men are more similar to contemporary patients on AS.

Subset analysis was also performed in men with 5 or more years of followup to determine the total number of tests performed and how many fulfilled the testing combination recommended by major AS protocols with data censored at exactly 5 years. For example, during 5 years the Sunnybrook[7] and PRIAS[8] protocols require 14 PSA tests and 2 followup biopsies while The Johns Hopkins protocol requires 10 PSA tests and 4 or more biopsies.[6] We performed subset analysis of men diagnosed at ages less than 70 years since The Johns Hopkins program discontinues biopsies at age 75 years.[14] These calculations were repeated in men at low risk diagnosed during the last 5 years of the study.