Active Surveillance is an Appropriate Management Strategy for a Proportion of Men Diagnosed with Prostate Cancer by Prostate Specific Antigen Testing

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Abbreviations and Acronyms

AS = active surveillance

PSA = prostate specific antigen

SABOR = San Antonio Center of Biomarkers of Risk for Prostate Cancer

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Purpose: The purpose of this study was to determine the fraction of men who would qualify for active surveillance in a population based cohort diagnosed with prostate cancer. In those who qualified and subsequently underwent primary treatment with radical prostatectomy, we assessed the rate of upgrading and up staging.

Materials and Methods: SABOR is a Clinical and Epidemiologic Center of the EDRN (Early Detection Research Network), NCI (National Cancer Institute), with 3,828 men enrolled at the time of review. Of these men 320 were diagnosed with prostate cancer, of whom 281 had sufficient data for review. These 281 cases were reviewed to determine suitability for active surveillance using 2 sets of criteria. Criteria 1 were prostate specific antigen density less than 15%, 2 or fewer cores involved with cancer, Gleason score 6 or less and cancer involving 50% or less of biopsy volume. Criteria 2 were 4 or fewer cores with Gleason 3 + 3 cancer and only 1 core of Gleason 3 + 4 cancer with up to 15% of core involved with Gleason 3 + 4 disease. For those undergoing radical prostatectomy, we examined rates of up staging and upgrading.

Results: Of the 281 patients, 187 (67%) qualified for active surveillance under criteria 1 and/or 2. Treatment data were available on 178 patients, and 74 underwent radical prostatectomy. Using the initial biopsy, 14 men (33.1%) who met criteria 1 and 9 (25%) who met criteria 2 were upgraded and/or up staged on final pathological review. By comparison, 38% of those who did not qualify for active surveillance were upgraded and/or up staged.

Conclusions: In a population based cohort, two-thirds of men diagnosed with prostate cancer qualify for active surveillance. Less restricted criteria for surveillance may be appropriate based on similar rates of upgrading/up staging at radical prostatectomy.

Key Words: prostatic neoplasms, biopsy, prostate-specific antigen, prostatectomy, watchful waiting

Prostate cancer will be diagnosed in 1 of every 6 men in the United States.[1] With respect to treatment, an increased interest in an AS strategy has developed due to the evolving understanding of complications and

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decrements in quality of life with definitive treatment (eg surgery and radiation) as well as the low disease specific mortality with AS. The use of AS has been supported by specialty and decision making organizations in treatment guidelines.[2–5] Despite the high disease specific survival with AS, national data show a slower rate of adoption of this management strategy. In a large collection of practices in the CaPSURE™ program, only 8% of the 4,833 very low risk prostate cancer patients, that is those with a CAPRA (Cancer of the Prostate Risk Assessment) score of 0 to 2, were treated with AS.[6]

An important question to address this issue is what fraction of the men who are undergoing regular PSA testing and who are then found to have prostate cancer would be eligible for AS? A secondary question is, given the known risk of undersampling the prostate during routine prostate biopsy, what is the extent of higher cancer grade in such a population based group of men found to have lower risk prostate cancer? The answers to these 2 questions would provide estimates of what could be appropriate national rates of AS for men diagnosed with prostate cancer through PSA testing. In order to address these 2 questions, we reviewed the risk strata and rates of cancer upgrading in a large, population based study.

PATIENTS AND METHODS

Subjects

SABOR is a Clinical and Epidemiologic Center of the EDRN, supported by the NCI. SABOR is an institutional review board approved study that enrolls men 35 years old or older, with a recommended age of 50 years or greater, with no prior history of prostate cancer, into a community based cohort from the catchment area of the Cancer Therapy and Research Center (the NCI designated Cancer Center), which includes 38 counties of South Texas. Participants must be able to understand English or Spanish sufficiently well to be able to provide informed consent. Since 2000, this study has enrolled and maintained followup data on 3,828 men from this multiethnic South Texas population to evaluate demographic, behavioral, genetic and other markers/measures of risk for prostate cancer. Of these 3,828 men, 320 were diagnosed with prostate cancer, of whom 281 had sufficient data for review.

Treatment of subjects from this cohort diagnosed with prostate cancer between 2000 to 2012 was based on community practice at that time. Patients had a broad range of physician providers throughout South Texas. As would be expected, patterns of treatment during this period changed along with national practices.

Study Design

SABOR participants diagnosed with prostate cancer were evaluated to determine if they would be candidates for AS, based on published criteria.[7–16] The first set of criteria were based on other series but were purposely restricted to include only the lowest risk prostate cancer patients. These criteria included PSA density greater than 15%, 2 or fewer cores involved with cancer, Gleason score 6 or less and cancer involving 50% or less of any single biopsy core. The second group of higher risk patients included 4 or fewer cores with Gleason 3 + 3 cancer and only 1 core of Gleason 3 + 4 cancer with only up to 15% of core involved with Gleason 3 + 4 disease. By using the narrow and more expanded sets of criteria, the subjects eligible for surveillance were assessed from the SABOR cohort. For those subjects who opted for radical prostatectomy, upgrading was defined any increase in pathological grade from biopsy.

Statistical Methods

To compare differences in age and PSA by study groups, appropriate parametric (Student 2-sample t-test) or nonparametric (Wilcoxon rank sum) tests were used depending on whether the data were or were not normally distributed. Differences in proportions were tested using the chi-square or Fisher exact test. Statistical significance was considered at $p < 0.05$ and all tests were 2-sided. All statistical tests were performed using SAS®, version 9.4.

RESULTS

Table 1 displays the characteristics of the entire SABOR cohort and the subjects diagnosed with prostate cancer. Subjects with prostate cancer had higher PSA and were older, and more than a third had a prior history of an abnormal digital rectal examination. Of the 281 patients with sufficient

Table 1. *Baseline characteristics of SABOR cohort by cancer diagnosis*

	No Ca	Ca	p Value
No. pts	3,505	320	—
Mean age (range)	55.9 (22—90)	61.4 (39—84)	<0.0001 (Student 2-sample t-test)
% Race/ethnicity:			0.0002 (chi-square test)
White nonHispanic	49.4	60.1	
White Hispanic	37.2	27.8	
Black nonHispanic	13.4	14.2	
Mean ng/ml PSA (range)	0.9 (0.1—75.6)	2.5 (0.1—766)	<0.0001 (Wilcoxon rank sum test)
% Prostate Ca 1st degree family history	18.7	33.9	<0.0001 (chi-square test)
% Abnormal digital rectal examination history	5.5	34.3	<0.0001 (chi-square test)