Prospective Quality of Life in Men Choosing Active Surveillance Compared to Those Biopsied but not Diagnosed with Prostate Cancer

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Abbreviations and Acronyms

AS = active surveillance

CPDR = Center for Prostate Disease Research

EPIC = Expanded Prostate Cancer Index Composite

HRQoL = health related quality of life

PCa = prostate cancer

PNB = prostate needle biopsy

PSA = prostate specific antigen

SF-36 = RAND Medical Outcomes Study Short Form

WW = watchful waiting

Purpose: Active surveillance is an important alternative to definitive therapy for men with low risk prostate cancer. However, the impact of active surveillance on health related quality of life compared to that in men without cancer remains unknown. In this study we evaluated health related quality of life outcomes in men on active surveillance compared to men followed after negative prostate needle biopsy.

Materials and Methods: A prospective study was conducted on men who were enrolled into the Center for Prostate Disease Research Multicenter National Database and underwent prostate needle biopsy for suspicion of prostate cancer between 2007 and 2014. Health related quality of life was assessed at biopsy (baseline) and annually for up to 3 years using SF-36 and EPIC questionnaires. Health related quality of life scores were modeled using generalized estimating equations, adjusting for baseline health related quality of life, and demographic and clinical characteristics.

Results: Of the 1,204 men who met the initial eligibility criteria 420 had a negative prostate needle biopsy (noncancer comparison group). Among the 411 men diagnosed with low risk prostate cancer 89 were on active surveillance. Longitudinal analysis revealed that for most health related quality of life subscales there were no significant differences between the groups in adjusted health related quality of life score trends over time.

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Conclusions: In this study most health related quality of life outcomes in patients with low risk prostate cancer on active surveillance did not differ significantly from those of men without prostate cancer. A comparison group of men with a similar risk of prostate cancer detection is critical to clarify the psychological and physical impact of active surveillance.

Key Words: watchful waiting, prostatic neoplasms, quality of life, survival rate, image-guided biopsy

THE lifetime risk of prostate cancer is approximately 1 in 6. However, the lifetime risk of death from PCa is 1 in 30.[1] The majority of men diagnosed with PCa are expected to have organ confined low risk disease.[2] Consequently, the successful management of low risk PCa hinges on the ability of clinicians to select appropriate candidates for conservative disease management. Prospective studies have demonstrated that the use of active surveillance in men with low risk PCa is feasible and safe.[3] However, in the U.S. most men with low risk disease still undergo definitive therapy.[4] Definitive treatments for PCa adversely affect heath related quality of life in some manner, including decrements in urinary, sexual and bowel function and/or bother.[5–9]

Missing from the armamentarium for informed PCa treatment decision making is a clear characterization of the downstream HRQoL outcomes directly related to AS. Specifically, it is poorly understood how the HRQoL of patients who select AS compares over time to the HRQoL of men at similar risk but without PCa.[10–12] Without an appropriate nonPCa control group, it could be argued that the burden of diagnosed but untreated disease on HRQoL outweighs the benefit of delaying definitive therapy.[10] To address this question, which was also posed by Bergman and Litwin in a recent review,[10] this prospective study evaluated HRQoL outcomes in men who underwent prostate needle biopsy for suspicion of PCa in a racially diverse, multiinstitutional cohort. By comparing men with low risk PCa on AS to men with a negative PNB, this study aimed to compare HRQoL outcomes during a 3-year period in men with similar risks of PCa.

METHODS

Study Population

The CPDR Multicenter National Database was the source of patients for this study. Demographic, clinical, treatment and outcomes data were collected as part of routine followup on all enrollees. Informed consent was obtained at PNB for suspicion of PCa, as described previously.[13] Since 2007 the prospective collection of HRQoL information has been approved by the institutional review board of each CPDR participating center. These centers include Madigan Army Medical Center, Tacoma, Washington; Naval Medical Center, San Diego, California; Virginia Mason, Seattle, Washington; Tripler Army Medical Center, Honolulu, Hawaii and Walter Reed National Military Medical Center, Bethesda, Maryland. The CPDR Multicenter National Database patient enrollment and data collection activities were approved by each institutional review board, with second tier institutional review board approval by the Uniformed Services University of the Health Sciences.

Survey Instruments

Patient reported HRQoL was captured using 2 questionnaires with established validity and reliability, namely 1) EPIC, a prostate cancer specific instrument and 2) SF-36, a general health assessment instrument.[14,15] The EPIC measures 4 paired subscales evaluating urinary, sexual, bowel, and hormonal function and bother. The SF-36 measures 8 subscales that can be combined into physical component summary and mental component summary scores. For both instruments the subscale scores range from 0 to 100, with higher scores indicating better HRQoL. For the SF-36 summary measures the scores are standardized to the general U.S. population to have a mean of 50 and a standard deviation of 10. HRQoL surveys were administered before or after biopsy (baseline), and at 3, 6, 9, 12, 18, 24, 30 and 36 months after a positive biopsy or 12, 24 and 36 months after a negative biopsy. Only baseline surveys and those from the 12, 24 and 36-month points were included in this analysis.

Study eligibility criteria included completion of a baseline HRQoL survey plus at least 1 followup HRQoL survey and age at biopsy of 75 years or less (fig. 1). The study sample was further restricted to the 2 comparison groups of 1) noncancer (subjects who received a negative PNB result) and 2) patients diagnosed with National Comprehensive Cancer Network® low risk PCa (clinical stage T1-T2a, biopsy Gleason score 6 or less and PSA less than 10 ng/ml), who initially underwent AS. Patients on AS were defined as those who received no definitive treatment in the first 12 months after diagnosis and had AS noted as the management strategy in their medical records or at least 1 PSA or repeat biopsy within 18 months of diagnosis. Treatments received after initial AS were considered secondary treatments. The presence of 8 comorbid conditions was assessed, including prostatitis, renal insufficiency, lung disease, heart disease, hypertension, cerebral vascular accident, diabetes and elevated cholesterol.

Statistical Analysis

Patient demographics, clinical characteristics and baseline HRQoL scores were compared between the noncancer and AS groups using Welch's t-tests assuming unequal variance for continuous variables, the chi-square and Fisher's exact tests for categorical variables, and Cochran-Armitage trend tests for ordinal variables.