Outcomes of Active Surveillance after Initial Surveillance Prostate Biopsy

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Abbreviations and Acronyms

AS = active surveillance
BCR = biochemical recurrence
CBx = confirmatory biopsy
iSPBx = initial surveillance prostate biopsy
mpMRI = multiparametric magnetic resonance imaging
NCCN® = National Comprehensive Cancer Network®
PCa = prostate cancer
PSA = prostate specific antigen
RP = radical prostatectomy
SPBx = surveillance prostate biopsy

Purpose: We analyzed the rates of disease reclassification at initial and subsequent surveillance prostate biopsy as well as the treatment outcomes of deferred therapy among men on active surveillance for prostate cancer.

Materials and Methods: From a prospective database we identified 300 men on active surveillance who had undergone initial surveillance prostate biopsy, with or without confirmatory biopsy, within 1 year of diagnosis. Of these men 261 (87%) were classified as having NCCN very low or low risk disease at diagnosis. Disease reclassification on active surveillance was defined as the presence of 50% or more positive cores and/or surveillance prostate biopsy Gleason score upgrading. Patients with type I disease reclassification included those with any surveillance prostate biopsy Gleason score upgrading, while patients with type II reclassification had to have primary Gleason pattern 4-5 disease on surveillance prostate biopsy. Outcomes after initial surveillance prostate biopsy were evaluated using actuarial analyses.

Results: At the time of initial surveillance prostate biopsy 49 (16%) and 19 (6%) patients had type I and type II disease reclassification, respectively. Those who underwent confirmatory biopsy had significantly reduced rates of type I (9% vs 23%, p=0.001) and type II (3% vs 9%, p=0.01) reclassification at initial surveillance prostate biopsy. For the 251 patients without disease reclassification at initial surveillance prostate biopsy the 2-year rates of subsequent type I and II reclassification were 17% (95% CI 0–24) and 3% (95% CI 0.1–7), respectively. For the 93 patients who received deferred therapy the 5-year biochemical progression-free probability was 89% (95% CI 79–98), including 95%, 82% and 70% among those without, and those with type I and type II disease reclassification, respectively.

Conclusions: Patients on active surveillance with stable disease at the time of initial surveillance prostate biopsy may be appropriate candidates for less intensive surveillance prostate biopsy schedules.

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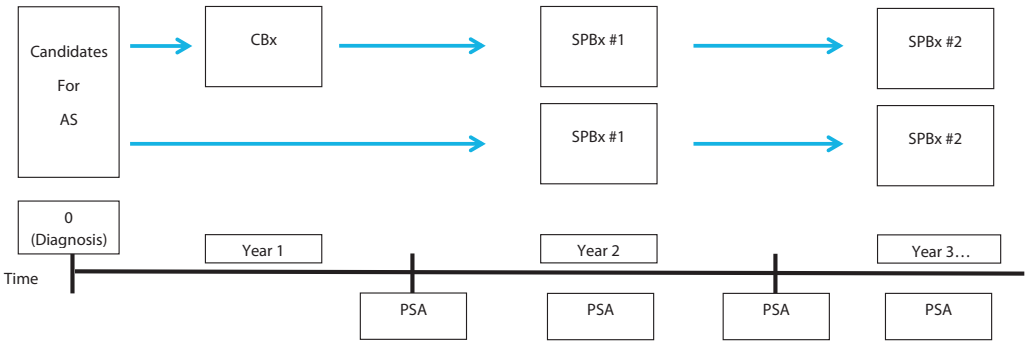
In recent years active surveillance has gained acceptance as a viable management strategy for men with NCCN very low, low and select intermediate risk PCa,[1] which is reflected in current treatment guidelines.[2] While there is growing consensus that multiparametric magnetic resonance imaging or genomic tests have the potential to accurately determine the probability of disease upgrading or up staging, confirmatory biopsy and surveillance prostate biopsy are currently regarded as the most reliable means of identifying patients with favorable disease parameters who are candidates for AS and for determining important disease reclassification necessitating the pursuit of curative therapy while on AS. To our knowledge there is no consensus regarding the appropriate timing of SPBx and annual biopsies are recommended in the protocols used at some institutions.[3] Given the broadening of inclusion criteria for AS to patients with a long life expectancy and/or those with intermediate risk features, and given the substantial heterogeneity of disease among the NCCN risk groups, we surmised that select patient groups may be candidates for a less intensive SPBx schedule based on their baseline features and clinical course on AS.

There is currently a paucity of literature reporting on the prognostic value of the initial SPBx for subsequent disease reclassification and treatment intervention for men on AS. Patients with stable disease at iSPBx may be at low risk for adverse disease reclassification during short-term intervals, for whom a less intensive SPBx schedule may be considered. Prostate biopsy is associated with a low but defined risk of important complications, patient discomfort and cost.[4–8] Thus, reducing the frequency of SPBx may increase the appeal of AS among patients and clinicians, given its relative underuse in the United States.[9–11] Therefore, we endeavored to analyze the rates of disease reclassification on iSPBx, identify clinical factors associated with a low risk of disease reclassification by SPBx, and identify the prognostic value of iSPBx by analyzing subsequent outcomes to determine the need for and safety of intensive SPBx.

PATIENTS AND METHODS

From an institutional review board approved prospective database of 19,548 patients who underwent prostate biopsy at our institution between 1993 and 2015, we identified 514 men who had a positive biopsy for PCa who underwent a subsequent biopsy. Of these men we excluded patients due to lack of Gleason score information on 1 or more prostate biopsies performed elsewhere (174); prior treatment with external beam radiotherapy, brachytherapy and/or cryotherapy (39); or patients who underwent CBx only (1). In total we identified 300 patients who fulfilled our criteria for AS in which 522 surveillance prostate biopsies were recorded after diagnostic or confirmatory biopsy.

In general, AS was restricted to patients with very low and low risk PCa, with or without a CBx. For the purposes of this study a confirmatory biopsy was defined as a biopsy performed within 1 year of a diagnostic biopsy, while SPBx was defined as a biopsy performed 1 or more years after diagnostic biopsy, with or without prior confirmatory biopsy. In recent years select patients with favorable intermediate risk features have also been considered for AS. The surveillance protocol was not standardized, but consisted of periodic PSA testing and clinical assessment at 3 to 6-month intervals and SPBx at 1 to 3-year intervals (see figure). Of the 522 surveillance prostate biopsies in the database, a standard (8 to 14 cores) and saturation (20 or more cores) SPBx was used in 354 (68%) and 164 (31%) cases, respectively (the number of cores could not be reliably ascertained in 4 cases). mpMRI and targeted biopsy (cognitive or ultrasound fusion) were not routinely used



Graphic representation of AS protocol