Pathological Outcome following Radical Prostatectomy in Men with Prostate Specific Antigen Greater than 10 ng/ml and Histologically Favorable Risk Prostate Cancer

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Abbreviations and Acronyms

AS = active surveillance
BCR = biochemical recurrence
BMI = body mass index
GS = Gleason score
HP = high PSA
IP = intermediate PSA
LP = low PSA
PCa = prostate cancer
PSA = prostate specific antigen
PSAD = PSA density

Purpose: Active surveillance is now the treatment of choice in men with low risk prostate cancer. Although there is no consensus on which patients are eligible for active surveillance, prostate specific antigen above 10 ng/ml is generally excluded. In an attempt to determine the validity of using a prostate specific antigen cutoff of 10 ng/ml to counsel men considering active surveillance we analyzed a multi-institution database to determine the pathological outcome in men with prostate specific antigen greater than 10 ng/ml but histologically favorable risk prostate cancer.

Materials and Methods: We queried a prospectively maintained database of men with histologically favorable risk prostate cancer who underwent radical prostatectomy between 2003 and 2015. The cohort was categorized into 3 groups based on prostate specific antigen level, including low—less than 10 ng/ml, intermediate—10 or greater to less than 20 and high—20 or greater. Associations of prostate specific antigen group with adverse pathological and oncologic outcomes were analyzed.

Results: Of 2,125 patients 1,327 were categorized with histologically favorable risk disease. However on multivariate analyses the rates of up staging and upgrading were similar between the intermediate and low prostate specific antigen groups. In contrast compared to the intermediate prostate specific antigen group the high group had higher incidences of up staging ($p = 0.02$) and upgrading to 4 + 3 or greater disease ($p = 0.046$). Biochemical recurrence-free survival rates revealed no pairwise intergroup differences except between the low and high groups.

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Conclusions: Patients with preoperatively elevated prostate specific antigen between 10 and less than 20 ng/ml who otherwise had histologically favorable risk prostate cancer were not at higher risk for adverse pathological outcomes than men with prostate specific antigen less than 10 ng/ml.

Key Words: prostatic neoplasms, prostate-specific antigen, watchful waiting, risk, outcome assessment (health care)

WHILE the advent of PSA has revolutionized the detection of PCa, its predictive ability has decreased in recent years.[1] As a result the over diagnosis of clinically insignificant PCa has led to overtreatment and associated complications, including erectile dysfunction and urinary incontinence.[2,3] With the understanding that many of these cancers have an indolent course AS has emerged as the favored choice in men with lower risk PCa.[4] In patients who elect AS quality of life has been shown to be significantly better than that of men who underwent definitive treatment.[5]

Despite these advantages of AS there are no universally accepted inclusion and exclusion criteria. However establishing AS eligibility criteria remains a clinically complex process. Under lenient criteria patients harboring high risk features may progress during AS and miss the therapeutic window of treatment.[6] Conversely overly stringent criteria may exclude patients based on an isolated finding that is not entirely representative of the tumor characteristics, subjecting them to potentially unnecessary treatment. Therefore multiple investigators have made efforts to refine the eligibility criteria for AS using various clinical parameters, including biopsy GS, clinical stage, preoperative PSA, PSAD and estimated measures of tumor burden (number of positive cores and tumor involvement in each core).

Of the mentioned parameters PSA remains a nonspecific biomarker that may not correlate with disease severity.[7] Moreover although PSA less than 10 ng/ml is a frequently required condition under which many AS protocols operate,[8–11] the current guideline may predispose patients at lower risk with incongruently elevated PSA to aggressive and potentially unnecessary therapies. Specifically urologists infrequently encounter patients with PSA greater than 10 ng/ml but in whom biopsy demonstrates relatively lower risk PCa. Therefore we hypothesized that AS may be a viable option in some men with histologically favorable risk PCa and serum PSA greater than 10 ng/ml.

To answer this question we investigated the rate of adverse oncologic features, specifically upgrading, up staging and biochemical recurrence, in men with serum PSA greater than 10 ng/ml but with biopsy findings consistent with indolent disease. In particular the aim of our study was to assess the risks of poor oncologic outcomes in men with serum PSA between 10 and 20 ng/ml by comparing them to risks in men with lower PSA (less than 10 ng/ml) and higher PSA (20 ng/ml or greater).

MATERIALS AND METHODS

Study Cohort

Under institutional review board approval we reviewed prospectively maintained databases of patients who underwent radical prostatectomy for localized PCa between November 2003 and January 2015 at 3 participating institutions, including Rutgers Cancer Institute of New Jersey, New Jersey, and Samsung Medical Center, Seoul and Seoul National University Bundang Hospital, Bundang, Republic of Korea. Men with histologically favorable risk PCa were categorized into 3 groups using the PSA cutoff values 10 and 20 ng/ml, including LP—less than 10 ng/ml, IP—10 or greater to less than 20 and LP—20 or greater.[12]

Definitions

Histologically favorable risk PCa was defined as 1) biopsy GS 6 or less, 2) 3 or fewer positive cores, 3) 50% or less cancer involvement in each core and 4) clinical stage T2a or less. This definition coincides with our institutional inclusion criteria for AS with the absence of PSA requirement. The terms very low risk and low risk were not used as it may interfere with the formal definition provided by NCCN® (National Comprehensive Cancer Network®).[13]

Up staging was defined as any change from clinical stage T2a or less to pathological stage T3-T4. Upgrading was defined as any increase in GS from biopsy to pathological specimen. Upgrading was divided into 2 groups, including any upgrading (GS 3 + 4 or higher) and stricter upgrading (GS 4 + 3 or higher).[14,15] BCR was defined as rising PSA on 2 consecutive measurements with the last one greater than 0.2 ng/ml. PSAD was calculated in 683 patients using known pathological prostate weights with adjustment using the formula, (preoperative serum PSA/[pathological prostate weight in gm − 7 gm for seminal vesicles]) as a proxy for volume measured by transrectal ultrasound.[16,17] A PSAD threshold of 0.15 ng/ml/gm was used for risk stratification.[13]

Clinicopathological Parameters

Patient demographics (age, race, height and weight), preoperative parameters (serum PSA, derived PSA density, biopsy GS, number of positive cores, maximum percent of cancer in core and clinical stage) and postoperative parameters (pathological stage, pathological