Are Repeat Prostate Biopsies Safe? A Cohort Analysis From the SEARCH Database

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Abbreviations and Acronyms

BCR = biochemical recurrence

PSA = prostate specific antigen

RP = radical prostatectomy

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Purpose: Patients question whether multiple biopsy sessions cause worse prostate cancer outcomes. Therefore, we investigated whether there is an association between the number of prior biopsy sessions and biochemical recurrence after radical prostatectomy.

Materials and Methods: Men in the SEARCH (Shared Equal Access Regional Cancer Hospital) database who underwent radical prostatectomy between 1988 and 2010 after a known number of prior biopsies were included in the analysis. Number of biopsy sessions (range 1 to 8) was examined as a continuous and categorical (1, 2 and 3 to 8) variable. Biochemical recurrence was defined as a prostate specific antigen greater than 0.2 ng/ml, 2 values at 0.2 ng/ml or secondary treatment for an increased prostate specific antigen. The association between number of prior biopsy sessions and biochemical recurrence was analyzed using the Cox proportional hazards model. Kaplan-Meier estimates of freedom from biochemical recurrence were compared among the groups.

Results: Of the 2,739 men in the SEARCH database who met the inclusion criteria 2,251 (82%) had only 1 biopsy, 365(13%) had 2 biopsies and 123 (5%) had 3 or more biopsies. More biopsy sessions were associated with higher prostate specific antigen ($p < 0.001$), greater prostate weight ($p < 0.001$), lower biopsy Gleason sum ($p = 0.01$) and more organ confined (pT2) disease ($p = 0.017$). The Cox proportional hazards model demonstrated no association between number of biopsy sessions as a continuous or categorical variable and biochemical recurrence. Kaplan-Meier estimates of freedom from biochemical recurrence were similar across biopsy groups (log rank $p = 0.211$).

Conclusions: Multiple biopsy sessions are not associated with an increased risk of biochemical recurrence in men undergoing radical prostatectomy. Multiple biopsy sessions appear to select for a low risk cohort.

Key Words: biopsy, prostatic neoplasms, prostatectomy, recurrence, diagnosis

Since the introduction of PSA testing there has been a significant stage migration in prostate cancer.[1] Whereas before the PSA era biopsies were usually performed because of abnormal findings on digital rectal examination,

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in the current era biopsy is most commonly performed because of an abnormal serum PSA.[2] In addition, many men with an abnormal serum PSA and a negative biopsy result are followed carefully, and undergo repeat biopsy because of an increasing PSA or subtle changes detected by digital rectal examination. In addition, diagnoses that may require another biopsy are common, such as high grade prostatic intraepithelial neoplasia and atypia or atypical small acinar proliferation.[3–5] These factors have contributed to an increasing number of men undergoing single as well as multiple prostate biopsies.[6]

Prostate biopsy is the current standard for the diagnosis of prostate cancer and assignment of Gleason grade. In the absence of other reliable diagnostic methods such as accurate and precise prostate imaging, a number of men will undergo multiple biopsy sessions. Patients are often concerned about the potential risks of multiple biopsies. There are theoretical risks of cancer spreading via needle biopsy and of the initiation of inflammatory processes. These might increase the technical difficulty of a subsequent operation and possibly result in higher positive margin rates or directly influence tumor pathology.[7] It has not been fully elucidated if there is an association between multiple prostate biopsies and localized prostate cancer recurrence or adverse outcomes after RP. Therefore, we addressed whether the number of prostate biopsies affects the risk of biochemical recurrence after RP.

METHODS

Study Population

This is an institutional review board approved analysis of the SEARCH database of men who underwent RP between 1988 and 2010, and who were treated at Veterans Affairs medical centers in West Los Angeles and Palo Alto, California; Augusta, Georgia; and Asheville and Durham, North Carolina.[8] The analysis included men who had a known number of prior biopsy sessions. We excluded patients who underwent primary treatment with androgen deprivation or radiation therapy. We also excluded men if time between biopsy and surgery was more than 365 days (152), suggesting an initial active surveillance treatment strategy. The cohort was analyzed in groups based on the number of prior biopsy sessions required to diagnose cancer (1, 2 and 3 to 8). The primary outcome was BCR, which was defined as PSA greater than 0.2 ng/ml, 2 values at 0.2 ng/ml or secondary treatment for an increased PSA.

Statistical Analysis

We evaluated the association between the number of prior biopsy sessions (range 1 to 8) and clinical and pathological characteristics using Kruskal-Wallis and chi-square analyses. Number of biopsy sessions was examined as a categorical variable (1, 2 and 3 to 8), as were Gleason sum, clinical stage, center and pathological stage. PSA, age, year of surgery and prostate weight were examined as continuous variables. We analyzed the association between number of prior biopsy sessions and BCR using Cox proportional hazards models, which adjusted for demographic, clinical and pathological characteristics from the surgical specimen. This analysis included biopsy sessions as a categorical (1, 2 and 3 to 8) and continuous (range 1 to 8) variable. Information on the number of cores on the diagnostic biopsy was missing for 415 men (15%). We were concerned that including this variable in our multivariate models would lead to loss of power. Therefore, we explored whether including the number of cores obtained in our multivariate models would influence the results. We noted that the number of cores obtained was not related to BCR, and inclusion (or exclusion) of this variable in our models did not alter the hazard ratio or p values for the association between number of biopsy sessions and BCR. Therefore, the number of cores was not included in our final multivariate models. Freedom from BCR was plotted using Kaplan-Meier analysis. We evaluated a possible association between the number of biopsies and freedom from BCR using the log rank test. All statistical analyses were performed using STATA® 9.1 and R version 2.11.1.

RESULTS

Patient Characteristics

Of the 2,739 men who met the inclusion criteria 2,251 (82%) had only 1 biopsy, 365 (13%) had 2 biopsies and 123 (5%) 3 or more biopsies to diagnose cancer. Preoperative cohort characteristics are shown in table 1. A larger number of biopsy sessions was associated with older age ($p = 0.017$), higher median PSA (1 biopsy—6.3 ng/ml, 2 biopsies—7.7 ng/ml, 3 or more biopsies—8.1 ng/ml, $p < 0.001$) and greater median prostate weight (1 biopsy—38 gm, 2 biopsies—43 gm, 3 or more biopsies—50 gm, $p < 0.001$). Men who underwent more biopsies had a lower clinical stage biopsy Gleason sum ($p = 0.010$) and were more likely to have organ confined (pT2) disease ($p = 0.017$).

Biochemical Recurrence

After adjusting for clinically and statistically significant variables including pathological features, we found no association between BCR and number of biopsy sessions when analyzed as a continuous (HR 1.04, 95% CI 0.92–1.17, $p = 0.516$) or categorical (3 or more biopsies HR 1.07, 95% CI 0.72–1.61, $p = 0.727$) variable (table 2). Kaplan-Meier estimates of freedom from BCR were similar among the groups with a median followup of 37 months (log rank $p = 0.211$, see figure). Median time to recurrence was 150 months for 1 biopsy, and was not reached for 2 or for 3 or more biopsies.

DISCUSSION

In the current study we found no independent association between the number of biopsy sessions and