Original Study

Racial Variation in the Outcome of Subsequent Prostate Biopsies in Men With an Initial Diagnosis of Atypical Small Acinar Proliferation

Robert Scott Libby,[1,2] Jordan J. Kramer,[1,2] Hoang Minh Tue Nguyen,[1,2] Allison Feibus,[1,2] Raju Thomas,[1] Jonathan L. Silberstein[1,2]

Abstract

African American (AA) men often have more aggressive prostate cancer (PCa) than Caucasian American men. We sought to determine predictive factors for subsequent PCa detection after an initial biopsy showing atypical small acinar proliferation (ASAP). Retrospective analysis of data from 106 men with ASAP showed no racial variation in subsequent PCa detection; therefore, AA and non-AA with ASAP should be managed similarly.

Background: African American (AA) men are known to have more aggressive prostate cancer (PCa) compared with Caucasian American men. We sought to determine predictors of subsequent detection and risk stratification of PCa in a racially diverse group of men with atypical small acinar proliferation (ASAP) on initial prostate biopsy. **Materials and Methods:** A retrospective analysis was conducted on data from men with ASAP on initial prostate biopsy who subsequently received confirmatory biopsies between September 2000 and July 2015. Biopsies with more than 3 years between initial and confirmatory biopsies were excluded. Race, age, body mass index, transrectal ultrasound volume, serum prostate-specific antigen (PSA), PSA velocity, PSA density, and elapsed time between biopsies were assessed for predictive value in subsequent PCa diagnosis after an initial finding of ASAP. **Results:** Of 106 men analyzed, 75 (71%) were AA and 31 (29%) were non-AA. Baseline variables revealed AA men had higher PSA levels, PSA velocity, and PSA density (all $P < .05$). PCa was diagnosed in subsequent biopsy in 42 (40%) patients without significant racial variation; 30 (40%) AA versus 12 (39%) non-AA. Of the 42 PCa patients, 25 (24%) met Epstein criteria for significant disease without racial variation; 18 (24%) AA versus 7 (23%) non-AA. Only 10 (9%) patients had any component of Gleason 4; 7 (9%) AA versus 3 (10%) non-AA. In multivariate analysis, increasing age, PSA level, and PSA density were significant predictors of PCa. **Conclusion:** AA men diagnosed with ASAP on initial prostate biopsy do not have increased risk of PCa on confirmatory biopsy compared with non-AA men.

Clinical Genitourinary Cancer, Vol. ■, No. ■, ■-■
Keywords: African American, Atypia, Prostate cancer, PSA, Race

Introduction

Prostate cancer is the most commonly diagnosed nonskin solid organ malignancy and the second leading cause of mortality by cancer among American men.[1] African American (AA) men have shown a 2.5 times greater mortality from prostate cancer than Caucasian men, making prostate cancer the greatest disparity in mortality between black and white race of any cancer in the United States.[2,3] AA men are diagnosed with prostate cancer, on average, 2 years before non-AA men and are 3 times more likely to have advanced disease; however, treatment has been less aggressive compared with treatment in Caucasian men.[4] Although prostate cancer is more common in adults older than age 40 years, approximately 37% of men from African descent have latent prostate cancer by the age of 40 years.[5]

Atypical small acinar proliferation (ASAP), or simply, atypia, is a pathological diagnosis when pathologists identify small foci in the prostate that are suspected to be, but are not diagnostic of, adenocarcinoma. Approximately 1% to 5% of prostate biopsies show atypia,[6-8] and, of those with atypia who undergo subsequent

R.S.L. and J.J.K. are both considered first authors.

[1]Department of Urology, Tulane University School of Medicine, New Orleans, LA
[2]Southeast Louisiana Veterans Health Care Services, New Orleans, LA

Submitted: Mar 10, 2017; Revised: Apr 6, 2017; Accepted: Apr 14, 2017

Address for correspondence: Jonathan L. Silberstein, MD, Department of Urology, Tulane University, School of Medicine, 1430 Tulane Ave., Rm 3518 New Orleans, LA 70112
E-mail contact: jsilbers@tulane.edu

1558-7673/$ - see frontmatter
http://dx.doi.org/10.1016/j.clgc.2017.04.018

biopsy, approximately 30% to 40% receive a diagnosis of prostate cancer on repeat biopsy within a 5-year period, although it has been reported to range from 17% to 60%.[9] Current guidelines recommend rebiopsy within 3 to 6 months of finding ASAP on previous biopsy, and these recommendations do not differ with regard to race or ethnicity.[10] With a previous biopsy not showing benign glands only, 23% of selected men were found to have prostate cancer on subsequent biopsy.[11] As active surveillance gains momentum as the most appropriate treatment strategy for low-risk prostate cancer, it must be reconsidered how aggressively a diagnosis of prostate cancer should be pursued in those with ASAP, and if race should influence the decision-making process.

We sought to determine if race is an indicator for finding prostate cancer upon repeat biopsy in a diverse group of men with a previous biopsy showing ASAP. In addition, we investigated the clinical significance of prostate cancer found in these men as defined by the previously established Epstein criteria.[12]

Materials and Methods

Upon receiving institutional review board approval, a retrospective analysis was performed on the data of men from one institution in New Orleans, who presented with ASAP on initial prostate biopsy and subsequently received confirmatory prostate biopsies between September 2000 and July 2015.

We identified 267 patients with $>$ 1 prostate biopsy. Patients who did not meet inclusion criteria included 12 patients with positive initial biopsies, 20 patients with a $>$ 3-year interval between consecutive biopsies, and 129 patients without ASAP on initial biopsy. Of those 267 patients, 106 patients were eligible, had an initial biopsy showing ASAP, and subsequently underwent repeat biopsy. AA and non-AA men were compared for body mass index (BMI), number of cores with ASAP, transrectal ultrasound (TRUS) volume, serum prostate-specific antigen (PSA) at initial biopsy, PSA velocity (PSAV; defined as PSA divided by the time in years elapsed between measurements), PSA density (PSAD; defined as PSA divided by TRUS volume of prostate), and time elapsed between consecutive biopsies.

Data were analyzed on the basis of 2 representative biopsies from each patient. The "initial biopsy" was the first biopsy in which ASAP was detected. The "repeat biopsy" was the first biopsy after the "initial biopsy" that was indicative of the final diagnosis. Final diagnoses were categorized as benign, low-grade prostate cancer defined according to the Epstein criteria, or non−low-grade prostate cancer. The Epstein criteria used defined clinically insignificant cancer as prostate cancer with no Gleason pattern $>$ 3% or $<$ 50% involvement in any core.[12] Final diagnoses of high-grade prostatic intraepithelial neoplasia (HGPIN) were categorized as benign. Biopsy specimens with more than 1 diagnosis were assigned to the highest category present in descending order from high-grade prostate cancer, low-grade prostate cancer, to benign.

Racial differences were only analyzed between AA and non-AA patients because of a limited number of patients from groups other than AA and Caucasian. Of the patients who met initial inclusion criteria, 1 patient was excluded from the study because of a lack of TRUS recordings on initial as well as repeat biopsy. Univariate and multivariate regression analyses were performed to assess the correlation between the presence of prostate cancer and independent variables such as age, BMI, number of cores with ASAP, and PSAD on repeat biopsy. In our models, an AA patient is assigned the value of 1 for race whereas a non-AA patient is assigned the value of 0. Regression models with correlation coefficients were more appropriate than odds ratios because most of our variables are not discrete but continuous variables. Statistical analysis was performed using STATA version 9 (STATA Corp, College Station, TX).

Results

Of the 106 men in the analysis cohort, 75 (71%) were AA and 31 (29%) were non-AA. Descriptive statistics for all patients with ASAP are shown in Table 1. On average, AA men showed higher values for PSA, PSAV, PSAD, and time intervals between biopsies whereas age, BMI, and TRUS volume were not significantly different between AA and non-AA men. Forty-two men (40%) had prostate cancer on repeat biopsy without significant racial variation (Table 2). In our study, 40% of AA men were found to have subsequent positive biopsies and 39% of non-AA men were found to have subsequent positive biopsies. Of the 42 with prostate cancer, only 10 patients (9%) displayed a Gleason component of $\geq$ 4 with 7 being AA, or 9% of all AA men with cancer, and 3 non-AA, or 10% of non-AA men with cancer. Most of the positive biopsies (76%) showed clinically insignificant cancer defined according to the Epstein criteria (Table 3).

Univariate analysis showed PSAD on repeat biopsy, number of ASAP cores found on initial biopsy, and age to positively correlate with finding any prostate cancer on repeat biopsy. PSA, PSAD on initial biopsy, and TRUS volume were not significant predictors of detecting prostate cancer on subsequent biopsy.

When high-grade cancer, as defined according to the Epstein criteria, was used as the dependent variable, univariate analysis showed age, PSA on repeat biopsy, PSAV, and PSAD on repeat biopsy to be statistically significant predictors of finding high-grade cancer on repeat biopsy after an initial biopsy showing ASAP (Table 4). Race, BMI, PSA on initial biopsy, TRUS volume on initial biopsy, and PSAD on initial biopsy were not shown to be statistically significant predictors of finding high-grade prostate cancer on subsequent biopsy. Number of ASAP cores, PSA, and TRUS volume on repeat biopsy were not significant predictors of finding high-grade prostate cancer on that biopsy.

In multivariate analysis, PSAD on repeat biopsy (P = .005), number of ASAP cores on initial biopsy (P = .001), and age

Table 1 Descriptive Statistics of All Patients (n = 106) With Atypical Small Acinar Proliferation on Initial Biopsy

Characteristic	Median
Age	66
Body Mass Index	28.05
Atypical Small Acinar Proliferation, Number of Cores	2
Prostate-Specific Antigen, ng/mL	6.01
Prostate Volume, cc	42.6
Prostate-Specific Antigen Density, ng/mL/cc	0.15
Time Gap, y	1.08
Prostate-Specific Antigen Velocity, ng/mL/y	0.28