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Does larger tumor volume explain the higher prostate specific antigen levels in black men with prostate cancer—Results from the SEARCH database

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ABSTRACT

Objectives: To assess whether larger tumor volume in black men explains higher presurgical PSA levels versus white men with prostate cancer.
Methods: We retrospectively analyzed 1904 men from the Shared Equal Access Regional Cancer Hospital database who underwent radical prostatectomy from 1990 to 2013. Geometric mean of tumor volume and preoperative PSA for each race were estimated from multivariable linear regression models.
Results: There were 1104 (58%) white men and 800 (42%) black men. Black men were younger (60.2 vs. 62.9 years, $p < 0.001$) had a higher PSA (6.7 vs. 6.0 ng/mL, $p < 0.001$), more positive margins (47 vs. 38%, $p < 0.001$), and seminal vesicle invasion (13 vs. 9%, $p = 0.007$). White patients had higher clinical stage ($p < 0.001$) and greater median tumor volume (6.0 vs. 5.3 gm, $p = 0.011$). After multivariable adjustment (except for PSA), white men had smaller mean tumor volumes (5.2 vs. 5.8 gm, $p = 0.011$). When further adjusted for PSA, there was no racial difference in mean tumor volume ($p = 0.34$). After multivariable adjustment, black men had higher mean PSAs vs. white men (7.5 vs. 6.1 ng/mL, $p < 0.001$). Results were similar after further adjusting for tumor volume: black men had 16% higher mean PSAs versus white men (7.4 vs. 6.2 ng/mL, $p < 0.001$).
Conclusions: In this study of men undergoing radical prostatectomy at multiple equal access medical centers, racial differences in tumor volume did not explain higher presurgical PSA levels in black versus white men. The exact reason for higher PSA values in black men remains unclear.

1. Introduction

Multiple previous population-based studies have demonstrated that black men have higher prostate-specific antigen (PSA) values than white men [1,2]. Similar results have been seen among men with prostate cancer [3] and specifically among men undergoing radical prostatectomy [4–6]. There are multiple potential explanations for a higher serum PSA including larger prostate size and

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larger tumor size [7]. We previously showed that the inherent racial serum PSA differences in men undergoing radical prostatectomy were not explained by racial differences in prostate size [8].

An alternative explanation for higher serum PSA values among black men with prostate cancer may be increased tumor volume. Increasing tumor volume is associated with higher serum PSA [9–11]. Several studies have shown that among men with low-grade (Gleason $\leq$6) prostate cancer, black men had higher tumor volume compared to non-black men [12,13]. Furthermore, black men with cT1c prostate cancer undergoing radical prostatectomy had greater mean tumor volume and tumor per ng/mL of serum PSA compared to white men [14]. We hypothesized that larger tumor volume in black men may explain all or part of the higher presurgical PSA levels in black versus white men with prostate cancer. To test this hypothesis, we used a radical prostatectomy database of men treated at equal access centers with a large proportion of black patients to assess whether larger tumor volumes explains the inherent higher PSA levels in black versus white men.

2. Materials and methods

2.1. Study population

After obtaining Institutional Review Board approval, data on patients treated with radical prostatectomy from 1990 to 2013 at Veterans Affairs Medical Centers in West Los Angeles, San Diego and Palo Alto, California; Durham and Asheville, North Carolina; and Augusta, Georgia, were combined into the Shared Equal Access Regional Cancer Hospital (SEARCH) database [15]. This database includes information on patient age at the time of surgery, race, height, weight, clinical stage, grade of cancer on diagnostic biopsies, preoperative serum PSA value, surgical specimen pathology (specimen weight, tumor grade, tumor volume, stage and surgical margin status), and follow-up serum PSA data. Patients treated with either preoperative androgen deprivation therapy or radiation therapy were excluded from analysis. Of the 5062 patients in the SEARCH Database, we excluded 2733 patients with missing data for tumor volume, 27 patients with missing data for PSA, and 128 patients who were neither white nor black because of limited numbers of men from other races. An additional 18 men diagnosed from a transurethral resection specimen (clinical stage T1a/T1b) were also excluded because this affects prostate size, tumor volume and serum PSA value. Finally, patients with missing data for pathologic Gleason sum (n = 5), pathologic features (n = 52), or BMI (n = 195) were excluded. This resulted in a study population of 1904 patients.

Prostatectomy specimens were sectioned per each institution's protocol. All institutions determined prostate weight by measurement of the gross weight of the entire specimen, including seminal vesicles and tips of the vasa. In the pathology reports, we abstracted data for percent of the total prostatectomy specimen involved with cancer. This value was then used to calculate tumor volume as follows: tumor volume (gm) = [prostate weight (gm) $\times$ percent of prostate with tumor]/100. Preoperative BMI was calculated as weight in kg divided by height in m^2 (kg/ m^2).

2.2. Statistical analysis

The distribution of clinicopathologic characteristics was compared between races using Chi-square analysis for categorical variables and Wilcoxon rank-sum or t-tests for continuous variables. The associations between race and the outcome variables of tumor volume and preoperative serum PSA values were examined using linear regression. Both tumor volume and serum PSA value were examined as continuous variables after logarithmic transformation. In the models, we mutually adjusted for age (continuous), year of surgery (continuous), pathologic Gleason sum (2 to 6, 3 + 4, 4 + 3, and 8 to 10), BMI (continuous, log-

Table 1
Clinical and pathologic features of men undergoing radical prostatectomy.

Characteristic	White	Black	p value*
Patients, n (%)	1104 (58)	800 (42)	
Age at surgery, mean ± SD	62.9 ± 5.5	60.2 ± 6.4	<0.001[b]
Median yr surgery	2008	2009	<0.001[c]
BMI (kg/m^2), median (Q1–Q3)	28.0 (25.3–31.1)	28.1 (25.2–31.6)	0.93[c]
PSA (ng/mL), median (Q1–Q3)	6.0 (4.4–8.3)	6.7 (5.0–10.4)	<0.001[c]
Biopsy Gleason sum, n (%)			0.025
2 – 6	496 (45)	327 (41)	
3 + 4	293 (27)	264 (33)	
4 + 3	147 (14)	103 (13)	
8 – 10	157 (14)	101 (13)	
Clinical stage, n[a] (%)			<0.001
T1	625 (62)	550 (72)	
T2/T3	391 (38)	213 (28)	
Pathologic Gleason sum, n (%)			<0.001
2 – 6	297 (27)	143 (18)	
3 + 4	441 (40)	414 (52)	
4 + 3	191 (17)	157 (20)	
8 – 10	175 (16)	86 (11)	
Prostate weight (gm), median (Q1–Q3)	41.0 (32.5–53.2)	41.0 (32.6–53.0)	0.81[c]
Tumor volume (gm), median (Q1–Q3)	6.0 (3.0–11.8)	5.3 (2.8–9.9)	0.011[c]
Positive surgical margins, n (%)	416 (38)	379 (47)	<0.001
Extracapsular extension, n (%)	210 (19)	154 (19)	0.90
Seminal vesicle invasion, n (%)	103 (9)	106 (13)	0.007
Positive lymph nodes, n (%)	37 (3)	25 (3)	0.94

Values are number (percentage) unless otherwise stated.
SD = standard deviation; BMI = body mass index; PSA = prostate specific antigen; Q1 = 25th percentile; Q3 = 75th percentile.
* p value from Chi-square comparing black vs. white, except when noted.
[a] Clinical stage analyzed from 1779 patients with available data.
[b] p value from t-test.
[c] p value from Wilcoxon rank-sum.