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Pathologic and Biochemical Outcomes among African-American and Caucasian Men with Low-Risk Prostate Cancer in the SEARCH Database: Implications for Active Surveillance Candidacy

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ABSTRACT

Background: Racial disparities in the incidence and risk profile of prostate cancer (PCa) at diagnosis among African-American (AA) men are well reported, however it remains unclear whether AA race is independently associated with adverse outcomes among men with clinical low risk disease.

Methods: We conducted a retrospective analysis among 895 men with clinical low risk PCa treated with radical prostatectomy within the Shared Equal Access Regional Cancer Hospital (SEARCH) database. Associations between AA versus Caucasian race with pathologic biochemical recurrence outcomes were examined using chi-square, logistic regression, log-rank, and Cox proportional hazards analyses.

Results: We identified 355 AA and 540 Caucasian men with low-risk tumors within the SEARCH cohort followed for a median of 6.3 years. Following adjustment for relevant covariates, AA race was not significantly associated with pathological upgrade (OR 1.33, p=0.12), major upgrade (OR 0.58, p=0.10), upstaging (OR 1.09, p=0.73), or positive surgical margins (OR 1.04, p=0.81). The 5-year recurrence-free survival rates were 73.4% for AA and 78.4% for Caucasian men (log-rank p=0.18). In a Cox proportional hazards analysis model, AA race was not significantly associated with BCR (HR 1.11, p=0.52).

Conclusions: In a cohort of clinical low-risk patients treated with prostatectomy within an equal access health system with a high representation of AA men, we observed no significant differences in the rates of pathologic upgrade, upstage or biochemical recurrence. These data support continued use of AS in AA. Upgrading and upstaging remain concerning possibilities for all men regardless of race.

Introduction

The suitability of active surveillance (AS) for African-American (AA) men with otherwise clinically favorable prostate cancer (PCa) at presentation has been questioned on the presumption of more aggressive disease. This assertion has been difficult to validate given marked under-representation of AA men in the landmark cohorts that have established the viability of surveillance in the low-risk state[1 2]. Indeed, AA men bear a comparatively greater burden from PCa relative to other major U.S. demographic groups, including increased PCa rates, higher proportions of high-grade and advanced-stage disease at presentation, and greater risk for cancer-specific mortality [3 4 5]**.** However, it is unclear whether these disparities persist following adjustment for disease characteristics, therapeutic selection, socio-economic status and access to care as conflicting studies addressing this issue exist [6 7].

Among those studies that directly address outcomes of AA patients during AS, most indicate higher rates of disease reclassification and treatment compared with Caucasians, though are limited by smaller sample sizes and relative under-representation of AA patients within these cohorts [8 9 10 11]. In the absence of larger studies, concordance between clinical grade and stage with pathologic parameters at radical prostatectomy (RP) has been offered as a proxy for evaluating candidacy for AS in men with low-risk disease. Several studies with disproportionately low participation rates of AA men relative to the U.S. population have offered contrasting results: single institution and cross-sectional data from the National Cancer Database have shown higher rates of upgrading and upstaging, while others including a multi-institutional study from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) showed no significant differences by race [12 13 14 15]. In this context, we sought to evaluate rates of pathological upgrading, upstaging, and recurrence-free survival among a racially diverse cohort

of clinically low-risk men receiving surgical treatment for PCa within the United States Veterans Affairs system, an equal access health system with a high representation of AA men.

Materials and Methods

Under institutional review board supervision, data from men who underwent RP between 1989 and 2011 at six U.S. Department of Veterans Affairs medical centers (West Los Angeles, CA; San Diego, CA; Palo Alto, CA; Durham, NC; Asheville, NC, and Augusta, GA) were combined into the Shared Equal Access Regional Cancer Hospital (SEARCH) database. Data collected in SEARCH included socio-demographic parameters, clinical tumor characteristics, surgical pathology, follow-up PSA and disease recurrence. Details regarding SEARCH methodology have been reported previously[16 17].

The primary study objective was to examine the effect of AA versus Caucasian race in occurrence of any adverse pathological characteristics among men with clinical low risk PCa treated with prostatectomy. We identified low-risk patients, defined as Gleason pattern ≤3+3 on diagnostic biopsy, PSA ≤10 ng/mL, and clinical stage ≤T2a. Men of other races, including missing or undefined responses, were excluded from analysis, as Asian, Latino, or Pacific Islander status represented a small proportion of the cohort (n=46). Clinical and demographic characteristics were compared across AA and Caucasian strata using frequency tables, the Kruskall-Wallis, Wilcoxon, Mann-Whitney rank sum, chi-square t and t-tests as appropriate. We further described postoperative risk status using the Cancer of the Prostate Risk Assessment post-Surgical (CAPRA-S) score based on pre-treatment PSA and pathological characteristics[18].

We examined several definitions of adverse pathology, including the presence of any Gleason upgrade (≥3+4), major Gleason upgrade (≥4+3), upstage (≥ pT3a, or N1), or positive

surgical margins. These endpoints were selected on the basis of an association with adverse longitudinal oncologic outcomes, and are often regarded as surrogates—albeit intermediate ones—for AS candidacy. We constructed multivariable logistic regression models examining the impact of race adjusted for other relevant clinical and pathological characteristics including age, PSA, clinical stage (T2 versus T1), percentage of cores positive for cancer, year of treatment, body mass index (BMI, kg/m^2) and treatment center. Covariates included in the analysis of positive margin status included prostate weight and surgical technique (open retropubic, perineal, laparoscopic, or robotic-assisted). We tested for interaction terms between covariates that may modify the response variables within the multivariable logistic regression models. Two-sided P-values <0.05 were regarded as significant. All statistical analysis was performed using STATA version 13 (Stata Corp., College Station, TX).

Sub-analyses were conducted using more restrictive definitions of AS candidacy, including the Johns Hopkins University (JHU) and University of California San Francisco (UCSF) criteria. The JHU criteria include Gleason grade ≤3+3, PSA density ≤0.15 ng/ml/ml, clinical stage ≤T1c, ≤2 cores positive, and no single core involvement of cancer ≥50%; and the UCSF criteria include Gleason ≤3+3, clinical stage ≤T2c, ≤33% of cores positive, and no single core involvement of cancer ≥50% [19,20]. PSA density was calculated using pathological specimen weight for those without available volume calculations at biopsy (n=853, 95.3%) as we have previously shown a strong correlation between pre-operative ultrasound measured volume and pathological prostate weight in SEARCH[21]. Core-specific data, including the maximum percentage of tissue involved with tumor, was lacking for individual treatment centers (as low as 25.3%) yet relatively complete in others (highest 92.3%). Complete clinical and pathological

data allowing calculation of strict AS definitions were available for 532 (59.4%) for JHU and 544 (60.8%) for UCSF criteria.

Recurrence was defined as a single post-operative PSA value greater than 0.2 ng/mL, two values at 0.2 ng/mL (biochemical recurrence, BCR) or the receipt of any salvage PCa therapy administered for an elevated PSA. Time to recurrence was compared between AA and Caucasian groups using Kaplan-Meier plots and the log-rank test. We examined the role of AA versus Caucasian race using Cox proportional hazards adjusted for significant clinical and pathological characteristics including age, pathologic Gleason score, pre-operative PSA, margin status, presence or absence of seminal vesicle invasion, extra-capsular extension, year of treatment, treatment center and BMI. Patients who received adjuvant radiation for an undetectable post-operative PSA were censored at that time as not having recurred.

Results:

Clinical and Demographic Characteristics

We identified 895 men with clinical low risk tumors treated with surgery including 355 (39.7%) AA and 540 (60.3%) Caucasian from a cohort of 3,492 patients. Among all patients, the median PSA was 5.2 ng/mL (IQR 4.2-6.9) and mean age 61.0 years. Compared with Caucasian men, AAs were younger at diagnosis (mean age 59.5 versus 62.0 years, $p<0.01$), had significantly higher PSA (median 5.5 versus 5.1, $p<0.01$) and PSA density (median 0.134 versus 0.126, $p=0.02$). A higher proportion of AA men were clinical stage T1c at diagnosis (78.3.4% versus 69.3%, $p<0.01$). A total of 344 men met strict UCSF AS criteria, as did 204 by Johns Hopkins criteria (63% and 38% of those with sufficient clinical data for calculation, respectively). The complete clinical and demographic characteristics are outlined in Table 1.

Pathological Findings

At radical prostatectomy, Gleason score was concordant with biopsy (3+3) in 523 (58.4%) men. A higher proportion of AA men (46.8%) experienced any upgrade from diagnostic biopsy (≥3+4) compared with (38.2%) of Caucasians, p=0.01. Unadjusted rates of major upgrade (≥4+3), however, were significantly higher in Caucasian compared with AA patients (11.9% versus 7.3%, p=0.03). Positive surgical margins occurred in 41.5% of AA men compared with 35.2% of Caucasians, p=0.06. No significant differences were observed between AA and Caucasian men in the occurrence of pathologic upstaging, seminal vesicle invasion, or extra-capsular extension. One (Caucasian) patient had positive lymph nodes at surgery, while node status was not assessed in 58% of patients. Post-surgical CAPRA-S scores were similar between both groups. Complete pathological outcomes are demonstrated in Table 2.

On multivariable logistic regression analysis adjusted for clinical and pathological characteristics, AA race was not significantly associated pathological upgrade ≥3+4, (OR 1.33 95% CI 0.92-1.93, p=0.12), major upgrade (OR 0.58, 95% CI 0.31-1.10, p=0.10), upstaging (OR 1.09, 95% CI 0.65-1.83, p=0.73), or positive surgical margins (OR 1.04, 95% CI 0.73-1.49, p=0.81), (Table 3). In separate sub-set analyses of men meeting strict JHU (p=0.50) and UCSF strict AS criteria (p=0.75), AA status was not significantly associated with pathologic upgrade ≥3+4. Moreover, there was no significant association between AA versus Caucasian race and major pathologic upgrade, upstaging, or surgical margin status within these subsets (Table 4).

Recurrence Free Survival

Among patients who did not experience BCR, the median follow-up was 6.3 years (IQR 3.8-8.9). Median follow was shorter for AA patients: 5.7 years (IQR 3.2-8.6) versus 6.6 (IQR

4.2-9.2), p=0.03. A total of 209 men experienced BCR, including 89 AA (22.3%) and 120 Caucasian (25.2%), p=0.32. The five-year freedom from BCR rates were 73.4% and 78.4% for AA and Caucasian men, respectively (log-rank p=0.18), Figure 1. After adjustment for clinical and pathological characteristics, AA race was not significantly associated with time to BCR (HR 1.11, 95% CI 0.81-1.50, p=0.52), Table 5. In multivariable Cox proportional hazards analysis there was no association between race and time to BCR upon further restriction to men meeting JHU (p=0.95) or UCSF (p=0.56) AS criteria.

Discussion:

Whether or not AA men are at greater risk of adverse outcomes during surveillance for clinically low risk PCa is a matter of significant clinical importance. As AA men endure a higher burden of PCa in relation to Caucasian men, exclusion from AS will expose a considerable proportion of AA men to treatment and therefore warrants closer scrutiny[6]. Presently, discordance exists in the literature with some studies indicating higher risks of pathologic upstaging and biochemical recurrence among AA, while others showing equivalence when adjusting for relevant factors. Unifying limitations among these studies, however, are disproportionately low participation rates of AA patients and unmeasured influences of socioeconomic status and access to care[1,12,14]. We evaluated the role of AA versus Caucasian race within a large, diverse cohort of clinically low-risk men receiving treatment within six U.S. Veteran's Affairs medical centers and observed no significant association between AA race and pathological upgrading, upstaging, positive margin status or biochemical recurrence following treatment.

Prior studies examining the incidence of pathologic upgrade and upstage among AA men have yielded conflicting results. Sundi et al. described 1,801 very-low risk men treated with prostatectomy at Johns Hopkins, among whom 256 (14%) AA men were significantly more likely to experience adverse pathological findings, even given highly restrictive criteria for low-risk disease[12]. Higher rates of upgrading and upstaging within the Hopkins cohort have been attributed, in part, to a higher incidence of anterior tumors among AA men that resulted in clinical under-staging [22]. In contrast, Jalloh et al. evaluated similar endpoints among 273 (6.5%) AA and 3,771 (89.1%) Caucasian men derived from UCSF and the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry, a national disease registry drawing from 43 sites, in which no differences were observed in rates of upgrading or upstaging by race[14].

We observed higher unadjusted rates of positive surgical margins among AA men however on multivariable analysis incorporating relevant clinical and pathological features at diagnosis this relationship was not statistically significant. These findings are supportive of those published by Witte et al. examining 260 AA men compared with 347 Caucasians, which found that race was not an independent predictor of margin status[23]. Other studies, including Jalloh et al's., have detected persistent differences in margin status associated with race, even when adjusted for relevant clinical factors including prostate size, year of treatment, nerve-sparing technique and surgical approach[14]. Notably, high rates of positive margins were observed in both AA and Caucasian patients relative to many published open and robotic series. Although consistent with prior analyses within the SEARCH database, these findings highlighting technical and patient-related factors which may contribute to higher rates of positive margins [24] [25]. Among AA patients, variations in pelvic anatomy between AA and Caucasian men, including

steeper symphysis pubis angles and more narrow mid-pe lvic areas have been described that may impart greater technical challenge, particularly during apical dissection [26 27].

Prior studies examining disparities in recurrence free survival outcomes among risk-stratified AA men have demonstrated inconsistent results with several studies indicating an independent association of race and recurrence[1 28]. In this updated study restricted to low risk patients, we did not detect significant differences in the rates of clinical recurrence among AA men. Our findings are in agreement with an earlier SEARCH analysis examining pathologic outcomes among men who were candidates for AS—including 140 AA, comprising 42.5% of the cohort—where AA race was not significantly associated with time to BCR at median 43 month follow[29]. Our present results, within a restricted cohort of clinically low-risk men, are also consistent in direction with prior publications from the broader SEARCH experience, which have shown a small but consistently increased risk of recurrence in AA men in multivariable analysis that have not reached thresholds for statistical significance[17 30] . Greater statistical power may be required to definitively address this question within a longitudinally followed surgical cohort, however if present, such an effect would likely be small.

There are limitations of this analysis that require discussion. Improvements in biopsy with routine use of extended sextant sampling may not be well reflected among participants in earlier study years, factors that may exaggerate discordance between biopsy and prostatectomy. To account for this, we adjusted for year of surgery in our analyses. In addition, we observed differences in the length of follow between AA and Caucasian participants of nearly one year, which introduces the possibility of follow up bias in our analysis of recurrence free survival. To address this, we used time to event analysis, which accounts for differential follow-up. In addition, pathologic specimens were not reviewed centrally, a limitation which may affect the

relationship between biopsy and surgical pathologic assignment. Lastly, a subset of SEARCH participants were lacking complete clinical and demographic information, particularly among early study year participants. Such limitations also impacted the description of biopsy characteristics including the percentage of cores involved with tumor as well as the greatest single core tumor volume within treatment sites, variables that prevented the description of Johns Hopkins University or UCSF strict criteria for approximately 40% of the study population.

We studied the role of AA versus Caucasian race on immediate pathologic and distant biochemical outcomes in a cohort of clinical low-risk men treated with prostatectomy. AA men were diagnosed at younger age and higher PSA, however when controlling for relevant disease characteristics, AA race was not independently associated with pathologic upgrading, upstaging, positive surgical margins or clinical recurrence. These findings may be directly impactful on the management of AA men with newly diagnosed PCa with low-risk features by demonstrating parity in surgical outcomes, which may offer a valuable surrogate inclusion criteria for AS candidacy. Ultimately, greater racial diversity within longitudinal surveillance cohorts is required to explicitly study the outcome of AA patients with favorable disease over time however these results support the validity of clinical risk stratification within AA men with localized PCa.

Conclusions:

Within a diverse, multi-centered multi-ethnic cohort of clinical low-risk men in an equal access medical system, African-American race was not associated with pathologic upgrading, upstaging, positive surgical margins, or clinical recurrence. Active surveillance for African-American men with clinically favorable-risk prostate cancer should not be withheld on the basis of higher risks of adverse pathological features at prostatectomy.

Figure Legend: Biochemical recurrence free survival stratified by African-American (dotted blue line) versus Caucasian race (solid green line).

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Table 1. Patient characteristics at diagnosis among 895 men treated between 1990 and 2011.

Variable	Caucasian (N=540)	African-American (N=355)	*P*
Age at diagnosis, mean (SD)	62.0 (5.8)	59.5 (6.7)	<0.01
PSA at diagnosis, ng/mL, median (IQR)	5.1 (4.0-6.6)	5.5 (4.5-7.2)	<0.01
PSA density, ng/mL/g, median (IQR)	0.126 (0.088-0.177)	0.134 (0.096-0.192)	0.02
Biopsy cores sampled, mean (SD)	9.1 (3.0)	9.3 (3.1)	0.40
Positive cores, mean (SD)	2.5 (1.8)	2.5 (1.7)	0.75
Positive cores, %, mean (SD)	0.30 (0.21)	0.28 (0.19)	0.28
Prostate volume, ml, median* (IQR)	33 (26-44)	33 (25-44)	0.99
Clinical stage (%)			<0.01
T1c	374 (69.3)	278 (78.3)	
T2a	166 (30.7)	77 (27.2)	
Year of treatment (%)			0.03
1990-1996	59 (10.9)	38 (10.7)	
1997-2003	248 (45.9)	133 (37.5)	
2004-2011	233 (43.2)	184 (51.8)	

PSA=prostate-specific antigen; SD=standard deviation; IQR=interquartile range; UCSF=University of California San Francisco; CAPRA=Cancer of the Prostate Risk Assessment
*Diagnostic TRUS volume unavailable for 479 patients

Table 2. Pathological characteristics among men 895 men treated with radical prostatectomy for low clinical risk Gleason 3+3 prostate cancer.

Clinical Variable	**Caucasian (N=540)**	**AA (N=355)**	***P***
Surgical Approach			0.001
Open Retropubic	367 (69.0)	275 (77.5)	
Perineal	143 (26.9)	54 (15.2)	
Laparoscopic	14 (2.6)	11 (3.1)	
Robotic	8 (1.5)	13 (3.7)	
Unknown	8 (1.5)	2 (0.6)	
Pathological Gleason Grade (%)			<0.01
3+3	334 (61.9)	189 (53.2)	
3+4	142 (26.3)	140 (39.4)	
4+3	39 (7.2)	14 (3.9)	
≥4+4	25 (4.6)	12 (3.4)	
Pathological T Stage			0.46
T2	455 (87.0)	306 (86.9)	
T3	58 (11.1)	35 (9.9)	
T4	10 (1.9)	11 (3.1)	
Lymph Node Status			0.55
pN1	1 (0.2)	0 (0)	
pN0	217 (40.5)	153 (43.1)	
pNx	317 (59.3)	202 (56.9)	
Positive Surgical Margin	179 (35.2)	144 (41.5)	0.06
Extracapsular extension	50 (9.3)	33 (9.3)	0.99
Seminal Vesicle Invasion	12 (2.2)	12 (3.4)	0.29
Any Gleason upgrade ≥3+4	206 (38.2)	166 (46.8)	0.01
Major upgrade ≥4+3	64 (11.9)	26 (7.3)	0.03
Mean Pathologic Weight in grams, (SD)	41.9 (18.1)	42.8 (19.8)	0.49
Pathologic Upstage (≥pT3, or N1)	68 (13.0)	46 (13.1)	0.98
Any Upgrade or Upstage	233 (43.2)	182 (51.3)	0.02
CAPRA-S Grouping			0.16
0-2	387 (71.7)	234 (65.9)	
3-5	142 (26.3)	110 (31.0)	
6-10	11 (2.0)	11 (3.1)	

CAPRA-S = Cancer of the Prostate Risk Assessment following surgery; SD = standard deviation

Table 3. Logistic regression models for histopathologic outcomes among men treated with radical prostatectomy.

Outcome	Independent Variable	Odds Ratio	95% CI, Lower	95% CI, Upper	*P*
Any Pathologic Upgrade (≥3+4)	Race: AA vs. Caucasian	1.33	0.92	1.93	0.12
	Age at diagnosis, years	1.03	1.00	1.06	0.04
	PSA level at diagnosis, ng/mL	1.04	0.93	1.16	0.48
	PSA density (ng/mL/g)	1.99	1.45	2.72	<0.01
	Clinical stage: T2 vs. T1	1.48	0.97	2.27	0.07
	% of biopsy cores positive (per 10%)	1.10	1.00	1.20	0.05
	Year of treatment	1.13	1.07	1.19	<0.01
	Body mass index, kg/m^2 (per 5 units)	1.29	1.08	1.56	0.01
Major Upgrade (≥4+3)	Race: AA vs. Caucasian	0.58	0.31	1.10	0.10
	Age at diagnosis, years	1.04	0.99	1.09	0.16
	PSA level at diagnosis, ng/mL	1.00	0.84	1.19	0.98
	PSA density (ng/mL/g)	1.81	1.17	2.78	0.01
	Clinical stage: T2 vs. T1	2.13	1.12	4.04	0.02
	% of biopsy cores positive (per 10%)	0.87	0.74	1.03	0.11
	Year of treatment	1.02	0.94	1.11	0.65
	Body mass index, kg/m^2 (per 5 units)	1.38	1.04	1.84	0.03
Upstage (≥pT3a)	Race: AA vs. Caucasian	1.09	0.65	1.83	0.73
	Age at diagnosis, years	1.04	1.00	1.09	0.04
	PSA level at diagnosis, ng/mL	1.00	0.87	1.16	0.99
	PSA density (ng/mL/g)	1.77	1.23	2.53	<0.01
	Clinical stage: T2 vs. T1	1.66	0.95	2.90	0.08
	% of biopsy cores positive (per 10%)	1.02	0.90	1.15	0.80
	Year of treatment	0.91	0.85	0.98	0.01
	Body mass index, kg/m^2 (per 5 units)	1.22	0.95	1.56	0.11
Positive Margins	Race: AA vs. Caucasian	1.04	0.73	1.49	0.81
	Age at diagnosis, years	1.02	0.99	1.05	0.25
	PSA level at diagnosis, ng/mL	1.13	0.96	1.34	0.15
	PSA density (ng/mL/g)	1.22	0.73	2.04	0.45
	Clinical stage: T2 vs. T1	1.20	0.80	1.82	0.38
	% of biopsy cores positive (per 10%)	1.05	0.96	1.15	0.29
	Year of treatment	0.97	0.92	1.02	0.23
	Body mass index, kg/m^2 (per 5 units)	1.21	1.01	1.44	0.04
	Surgery type (perineal vs. others)	1.02	0.60	1.72	0.95
	Prostate weight, g	0.98	0.96	1.00	0.04

PSA=prostate-specific antigen; AA=African-American
*All models adjusted for treatment center; Odds Ratio for PSA density reporter per 0.1 unit increase

Table 4. Multivariable logistic regression results among subsets of patients meeting strict active surveillance inclusion by the University of California San Francisco (UCSF) and Johns Hopkins University (JHU) criteria.

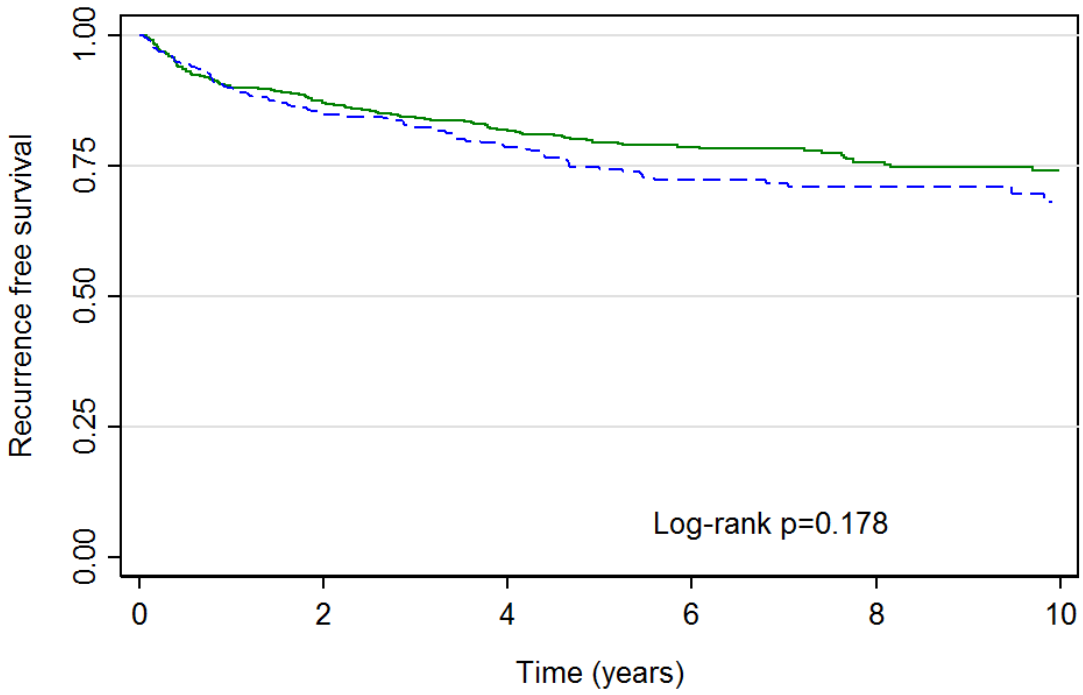
		UCSF AS Criteria (n=344)				***JHU AS Criteria (n=204)***			
Outcome	**Independent Variable**	**Odds Ratio**	**95% CI, Lower**	**95% CI, Upper**	***P***	**Odds Ratio**	**95% CI, Lower**	**95% CI, Upper**	***P***
Any Pathologic Upgrade (≥3+4)	Race: AA vs. Caucasian	1.19	0.71	1.99	0.50	0.89	0.43	1.85	0.75
	Age at diagnosis, years	0.99	0.95	1.03	0.61	1.02	0.96	1.08	0.60
	PSA level at diagnosis, ng/mL	1.34	1.17	1.53	<0.01	1.14	0.93	1.40	0.20
	Clinical stage: T2 vs. T1	2.13	1.13	4.02	0.02	2.51	0.99	6.33	0.05
	% of biopsy cores positive (per 10%)	1.35	0.97	1.90	0.08	1.06	0.60	1.86	0.84
	Year of treatment	1.12	1.03	1.22	0.01	1.20	1.05	1.36	0.01
	Body mass index, kg/m^2 (per 5 units)	1.07	0.82	1.40	0.62	1.55	1.06	2.26	0.03
Major Upgrade (≥4+3)	Race: AA vs. Caucasian	0.49	0.21	1.11	0.09	0.50	0.11	2.24	0.37
	Age at diagnosis, years	1.03	0.97	1.10	0.37	1.11	0.99	1.24	0.08
	PSA level at diagnosis, ng/mL	1.21	1.00	1.48	0.06	1.04	0.74	1.46	0.84
	Clinical stage: T2 vs. T1	1.39	0.55	3.54	0.49	1.12	0.22	5.78	0.89
	% of biopsy cores positive (per 10%)	1.41	0.84	2.37	0.19	0.53	0.17	1.60	0.26
	Year of treatment	0.95	0.84	1.08	0.43	0.75	0.59	0.93	0.01
	Body mass index, kg/m^2 (per 5 units)	1.26	0.84	1.88	0.27	0.91	0.44	1.91	0.81
Upstage	Race: AA vs. Caucasian	1.43	0.65	3.11	0.38	0.51	0.11	2.33	0.39
	Age at diagnosis, years	1.03	0.97	1.09	0.31	1.09	0.95	1.24	0.22
	PSA level at diagnosis, ng/mL	1.19	0.98	1.43	0.08	0.60	0.37	0.98	0.04
	Clinical stage: T2 vs. T1	1.53	0.63	3.75	0.35	0.13	0.01	1.52	0.10
	% of biopsy cores positive (per 10%)	1.63	0.98	2.69	0.06	1.02	0.29	3.59	0.97
	Year of treatment	0.87	0.77	0.98	0.02	0.76	0.60	0.96	0.02
	Body mass index, kg/m^2 (per 5 units)	0.98	0.67	1.43	0.91	0.91	0.39	2.11	0.82
Positive Margins	Race: AA vs. Caucasian	1.22	0.71	2.08	0.47	0.73	0.33	1.61	0.43
	Age at diagnosis, years	1.03	0.98	1.07	0.26	1.01	0.95	1.09	0.70
	PSA level at diagnosis, ng/mL	1.31	1.14	1.51	<0.01	1.18	0.88	1.59	0.28
	Clinical stage: T2 vs. T1	1.51	0.80	2.84	0.21	2.90	1.05	8.01	0.04
	% of biopsy cores positive (per 10%)	1.05	0.74	1.50	0.78	0.84	0.45	1.58	0.59
	Year of treatment	0.95	0.86	1.03	0.21	1.03	0.90	1.18	0.65
	Body mass index, kg/m^2 (per 5 units)	1.36	1.02	1.81	0.04	1.94	1.25	3.01	<0.01
	Surgery type (perineal vs. others)	0.69	0.30	1.60	0.39	0.67	0.17	2.69	0.57
	Prostate weight, g	0.96	0.94	0.98	<0.01	0.98	0.95	1.01	0.18

Abbreviations: UCSF=University of California San Francisco; JHU=Johns Hopkins University; CI=Confidence Interval; PSA=prostate-specific antigen; AA=African-American

*All models adjusted for treatment center

Table 5. Cox proportional hazards analysis modeling recurrence free survival among 895 men treated with radical prostatectomy.

Independent Variable	Hazard Ratio	95% CI, Lower	95% CI, Upper	P-value
Race: AA vs. Caucasian	1.105	0.814	1.501	0.521
Age at diagnosis, years	0.998	0.975	1.021	0.865
Pathological Gleason Score				
3+3 (reference)	1.357	0.975	1.889	0.071
3+4	1.459	0.787	2.704	0.230
4+3	2.022	1.071	3.817	0.030
≥4+4				
PSA level at diagnosis, ng/mL	1.107	1.029	1.191	0.006
Margin status	2.134	1.563	2.913	0.000
Seminal Vesicle Invasion	1.854	0.900	3.821	0.094
Extra-capsular extension	1.096	0.702	1.711	0.687
Year of treatment	0.980	0.945	1.017	0.286
Body mass index, kg/m^2 (per 5 units)	1.107	0.953	1.286	0.183



No. at risk						
Caucasian	538	431	353	243	159	87
AA	353	266	199	132	90	43

Key of Definitions and Abbreviations

AA=African-American
SEARCH=Shared Equal Access Regional Cancer Hospital
AS=Active Surveillance
PCa=prostate cancer
PSA=prostate-specific antigen
BCR=biochemical recurrence
IQR=interquartile range
OR=odds ratio
HR=hazard ratio