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Pathological outcome and biochemical recurrence-free survival after radical prostatectomy in African-American, Afro-Caribbean (Jamaican) and Caucasian-American men: an international comparison

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OBJECTIVE

- To compare pathological and biochemical outcomes of radical prostatectomy (RP) among African-American (AA), Afro-Caribbean (AC; Jamaican) and Caucasian-American (CA) men using an international cohort of patients who underwent RP in the USA and Jamaica.

MATERIALS AND METHODS

- A retrospective review was performed of men who underwent RP for clinically organ-confined (OC) prostate cancer between 2000 and 2011 at Columbia University Medical Center (New York, USA) and the University Hospital of the West Indies (Kingston, Jamaica) between 2000 and 2007.
- Men who had received neoadjuvant or adjuvant (within 3 months) therapy were excluded.
- Clinicopathological variables were compared among the three groups, focusing on age, stage, PSA level, Gleason sum (GS) and margin status.
- Multivariate analysis was performed to determine the predictors of biochemical recurrence (BCR; PSA >0.2 ng/mL), and Kaplan–Meier analysis was performed to determine BCR-free survival rates in AA, AC and CA men.

What's known on the subject? and What does the study add?
It is known that men of African descent in the USA and Jamaica have both a higher incidence of prostate cancer and higher mortality than Caucasian men, but it is unclear whether they have worse pathological and biochemical recurrence (BCR) outcome than their Caucasian counterparts after radical prostatectomy (RP) for prostate cancer.

We found that African-American (AA) men present at a younger age and have a higher mean PSA level than Caucasian-American (CA) men and that Afro-Caribbean (AC; Jamaican) men present with the highest mean PSA level, Gleason score and tumour stage of the three groups. In addition, we showed that AA and AC men have a higher likelihood of 5-year BCR than CA men and that AA and AC race are both independent predictors of BCR after RP.

RESULTS

- A total of 483 men underwent RP for clinically OC disease (CM, $n = 309$, AA, $n = 93$ and AC, $n = 81$).
- The mean patient age was 59 years, with AA men being younger than CA men (58 vs 60 years, $P < 0.05$). The mean (range) follow-up was 49 (13–133) months with no significant difference among the groups.
- The men in the AC cohort had a higher mean PSA level than AA and CA men (8.8 vs 6.2 and 5.0 ng/mL, respectively, $P < 0.05$) and more clinical GS ≥7 (44%) tumours than AA (8%) and CA men (0%; $P < 0.01$).
- On multivariate analysis, controlling for stage, grade, PSA level and margins, AA and AC race were independent predictors of BCR.
- AA and AC men had significantly lower 5-year BCR-free survival (76 and 74%, respectively) than CA men (98% [$P < 0.001$]).

CONCLUSIONS

- This international comparison of clinicopathological outcomes in AA, AC and CA men undergoing RP shows that AA and AC men present similarly with more aggressive disease features than CA men and have lower 5-year BCR-free survival.

- Both AA and AC race are significant predictors of BCR, independently of stage, grade, PSA level and margin status.

Further research is needed to elucidate and correct the mechanisms behind the observed difference in outcome among these populations.

KEYWORDS

radical prostatectomy, African-American, Jamaica, prostate cancer

INTRODUCTION

In the USA, African-American (AA) men have a higher incidence of prostate cancer than Caucasian- American (CA) men (232 vs 146 per 100 000) [1]. AA men also tend to present with more aggressive disease characteristics, including higher PSA levels and Gleason sums (GS) [2–4]. Mortality rates for prostate cancer are 2.4 times higher in AA men than in CA men [1]. These disparities may be attributable to a combination of socio-economic, environmental and genetic outcomes [5,6]. Similarly to AA men, studies suggest that Afro-Caribbean (AC) men (specifically Jamaican men) may have a higher incidence of prostate cancer than CA men [7]. Furthermore, prostate cancer is the leading cause of cancer death among Jamaican men in contrast to AA and CA men where lung cancer is the most fatal malignancy [1,8]. The higher mortality rate for AC (Jamaican) men is probably attributable to limited screening and therefore later stage at presentation and this is supported by studies that show a high median PSA level at the time of diagnosis in this population [9]. Genetic and environmental factors may also play a role in the high incidence and mortality rates but evidence supporting these hypotheses is inconclusive [10–12].

Data comparing clinical outcomes between AA, AC and CA men with clinically organ-confined (OC) prostate cancer are limited. Some studies suggest that disease recurrence is worse for AA men than CA men [4]. Recent data from a cohort of AC men at the University Hospital of the West Indies (Kingston, Jamaica) who underwent radical prostatectomy (RP) suggest that 5-year biochemical recurrence (BCR)-free survival rates are relatively low (78%) when compared with those published in the literature for AA men (87%) [13,14]. To our knowledge, there are few studies directly comparing RP outcomes in these three distinct racial/ethnic groups. An international collaboration, incorporating patients from all three groups, was therefore developed with the goal of analysing clinical and pathological features after RP in men with clinically OC prostate cancer from both the USA and Jamaica. The objective of the current study was, therefore, to compare PSA levels, GS, clinical and pathological stage and 5-year biochemical recurrence-free survival among AA, AC and CA men.

MATERIALS AND METHODS

A retrospective review was performed on the medical records of 1389 patients from the institutional-review-board-approved Columbia University Comprehensive Urologic Oncology Database who self-identified as either Caucasian- or African-American (CA, $n = 1154$ and AA, $n = 235$) and 116 AC patients from the database approved by the Faculty of Medical Sciences Ethics Committee, University Hospital of the West Indies, who underwent RP for clinically OC (T1c–T2c) prostate cancer. The US (AA, CA) cohort of patients had surgery performed between 2001 and 2011 and the Jamaican (AC) cohort between 2000 and 2007. Men undergoing neoadjuvant or adjuvant (within 3 months) hormone therapy or adjuvant (within 3 months) radiotherapy were excluded. Men with insufficient clinicopathological data and <1 year of follow-up were also excluded. Preoperative staging and evaluation were performed using history and physical examination, DRE and serum PSA measurement. All men were diagnosed via standard 12-core TRUS-guided prostate biopsy before RP. RP was performed by multiple surgeons at the two institutions and pelvic lymph node dissection was performed at the discretion of the surgeon. AA and CA men underwent either retropubic or laparoscopic/robotic prostatectomy and AC patients were exclusively treated via retropubic prostatectomy. Several pathologists from each institution performed histological analysis of the RP specimen. A total of 483 men (CA, $n = 309$, AA, $n = 93$ and AC, $n = 81$) were included in the final analysis based on the exclusion criteria.

We used ANOVA to compare age, clinical stage, GS, PSA level and pathological findings (margin status, extracapsular extension [ECE], seminal vesicle invasion [SVI]) and GS upgrading among the three different cohorts. GS upgrading was defined as an increase in pathological GS compared with clinical GS before surgery. BCR was defined as PSA ≥0.2 ng/mL after a previously undetectable PSA. Univariate and multivariate Cox proportional hazards models were created to determine the association between age, race (AA, AC and CA), stage, PSA level, GS, margin status and BCR. Kaplan–Meier survival analysis was performed to determine the 5-year BCR-free survival rate after RP in AA, AC and CA men. All data were analysed using STATA SE software version 9.0 (StatCorp LE, College Station, TX, USA).

RESULTS

From the available patients who underwent RP at Columbia University Medical Center, a total of 402 men (CA, $n = 309$ and AA, $n = 93$) were included and 81 AC men from the Jamaican cohort were included in the final analysis (total, $N = 483$; Table 1) The AA cohort was significantly younger (58 years) than the CA cohort (60 years) and the AC cohort (61 years; $P < 0.05$ [Table 1]) The median PSA level for all men was 5.5 ng/mL and the AC cohort had a significantly higher median PSA level (8.8 ng/mL) compared with the AA cohort (6.2 ng/mL) and CA cohort (5 ng/mL [Table 1]). The mean (median; range) follow-up for the entire group was 49 (39; 13–133) months with no significant differences between the three groups (Table 1). With respect to clinicopathological features, the most common stage was T1c for all groups and AC men had a higher proportion of cT2 tumours (32%) and GS ≥7 (44%) prostate cancers than CA men (20 and 0%, respectively) and AA men (4 and

TABLE 1 Demographic and clinicopathological features of AA, AC and CA men undergoing RP

	AA	AC	CA	*P*
N	93	81	309	
Mean age, years	58	60	61	<0.05
Mean follow-up, months	49	42	50	NS
Median PSA level, ng/mL	6.2	8.8	5.0	<0.01
Clinical stage, *n* (%)				
T1c	89 (96)	55 (68)	245 (80)	NS
T2	4 (4)	26 (32)	64 (20)	<0.05
Clinical GS, *n* (%)				
Median GS <7	86 (92)	45 (56)	309 (100)	NS
Median GS ≥7	7 (8)	36 (44)	0 (0)	<0.01
Pathological stage, *n* (%)				
T2	74 (80)	73 (90)	281 (91)	NS
≥ T3	19 (20)	8 (10)	28 (9)	NS
Pathological GS, *n* (%)				
Median GS <7	26 (28)	35 (43)	161 (52)	NS
Median GS ≥7	67 (72)	46 (57)	148 (48)	<0.05
ECE, *n* (%)	18 (19)	7 (9)	28 (9)	<0.01
SVI, *n* (%)	9 (10)	3 (4)	3 (1)	<0.05
PSM, *n* (%)	31 (33)	12 (15)	37 (12)	<0.05
GS upgrade, *n* (%)	61 (66)	20 (25)	148 (48)	<0.05
BCR, *n* (%)	15 (16)	19 (23)	9 (3)	<0.05

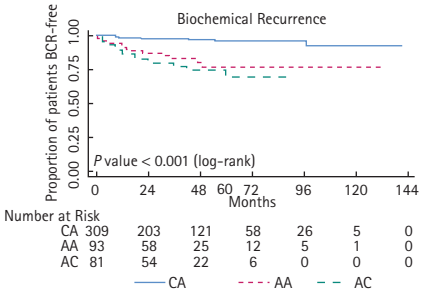
NS, nonsignificant.

TABLE 2 Multivariate analysis of BCR after RP in AA, AC and CA men

	Hazard ratio	*P*
Age	0.99	NS
Race		
AA	6.5	<0.01
AC	7.1	<0.01
Log PSA	1.6	<0.05
Pathological stage	2.51	<0.05
Pathological GS	1.23	NS
Positive surgical margin	1.71	NS

NS, nonsignificant.

FIG. 1. Kaplan–Meier curve for BCR-free survival after RP in AA, AC and CA men.



8%, respectively; $P < 0.01$ [Table 1]). The most common pathological stage was pT2 for the entire cohort; however, AA men had a higher proportion of pT3 tumours (20%) compared with AC (10%) and CA men (9%) although this difference was not significant (Table 1). There was a significantly higher proportion of pathological GS ≥7 prostate cancer in AA men (72%) than in AC and CA men (57 and 48%, respectively; $P < 0.01$) and AA men had a greater percentage (66%) of GS upgrading compared with AC (25%) and CA men (48%; $P < 0.01$ [Table 1]). With respect to pathological findings, AA men treated in the USA had a higher rate of positive margins, ECE and SVI (33, 19 and 10%, respectively compared with AC men (15, 9 and 4%, respectively) and CA men (12, 9 and 1%, repectively; $P < 0.05$ [Table 1]).

A total of 42 patients experienced BCR during the follow-up period, with AC men having the highest proportion of BCR among all three groups (23 vs 16% for AA and 3% for CA men; $P < 0.05$ [Table 1]). Kaplan–Meier survival analysis showed significantly lower 5-year BCR-free survival for AC (74%) and AA men (76%) compared with CA men (98% [Fig. 1]). When controlling for age, stage, GS, PSA level and margin status, both AA and AC race were independent predictors of BCR on multivariate analysis (hazard ratios 6.5 and 7.1, respectively; $P < 0.01$ [Table 2]) when compared with the CA cohort.

DISCUSSION

Several studies have addressed the question of AA race and the impact on treatment outcome for clinically OC prostate cancer but the results are contradictory [2,4,15,16]. While some studies suggest that AA men do worse with respect to BCR-free and disease-specific survival, others have found no independent association between race and outcome [15–17]. In Jamaica, where the majority of the population (>90%) is of sub-Saharan West-African descent, and the incidence and mortality of prostate cancer have been reported to be high, one would suspect the outcomes for treatment of clinically OC prostate cancer to be similar to those of AA men in the USA and possibly worse than those of CA men [7,8,14]; however, to our knowledge, there are currently no published data directly comparing these distinct ethnic populations. The present study sought to compare clinicopathological outcomes and BCR-free survival after RP for OC prostate cancer in AA, CA and AC men.

Consistent with several other studies, the present findings show that AA men present slightly younger and with more aggressive features such as higher PSA level and GS than CA men [2,13,18]. Interestingly, AC men presented at a slightly older age (61 years) compared with CA and AA men (60 and 59 years, respectively). These findings, in conjunction with the higher median PSA level (8.8 ng/mL) in the present study in AC men compared with AA (6.1 ng/mL) and CA men (5.0 ng/mL), probably represent less prevalent screening practices and therefore later presentation of prostate cancer in AC men in Jamaica and this is supported by other published studies [8,9]. With respect to stage, adverse pathological features and GS upgrading, both AA and AC men had worse

outcomes than CA men but this difference was significantly greater in the AA group. Socio-economic factors and screening behaviour may explain to some extent our adverse findings in AA men compared with CA men [5]. Pelvic anatomic variation may also contribute to the significantly higher positive surgical margin rate seen in AA and AC men [19]. Interestingly, von Bodman *et al.* [19] found using preoperative MRI that there was a more pronounced adverse impact on positive margins of a deep pelvis (as measured by apical prostatic depth) in AA men undergoing RP.

It is widely accepted that BCR is affected by stage, GS, preoperative serum PSA level and surgical margin status; therefore, when considering BCR-free survival, multivariate analysis controlling for these factors is of critical importance. In the present study, after controlling for these variables, both AA and AC race were independent predictors of BCR. These findings suggest that in addition to presenting at a younger age and with more advanced disease, men of sub-Saharan West African descent in the USA and Jamaica do worse with respect to oncological outcome compared with CA men. Furthermore, as hypothesized because of similarities in genetic background from their respective African ancestry, we have shown that both AA and AC men have similar 5-year BCR-free survival rates after RP for clinically OC disease (76 and 74%, respectively). These results contrast with other studies, which have found no association between AA race and BCR [16,20].; however, recent data reported by Chu *et al.* [21] from an equal access healthcare setting showed that AA men still have a higher risk of BCR than CA men. In addition, even after controlling for socio-economic status, AA men were significantly more likely to experience BCR than CA men, despite equal access to care [21]. It is possible that in this cohort of AA and AC men, molecular/genetic and environmental influences may play a role in the increased risk of BCR. With respect to genetics/molecular biology, it is accepted that the androgen receptor (AR) plays an important role in prostate growth and studies suggest that in AA men, AR density is higher in benign and malignant prostate tissue [22]. In addition, young AA men may have higher androgen levels than their CA counterparts. A recent study by Kim *et al.* [23] showed that prostate biopsies in AA men exhibit increased expression of aggressive biomarkers such as AR and Ki-67 compared with CA men. With respect to environmental influences, particularly diet, evidence suggests that certain fatty acids in the Jamaican diet may be associated with increased tumour grade and risk of prostate cancer, but these data are inconclusive [10–12].

The current study is limited as a result of the inherent biases associated with a retrospective review of a single treatment method and a relatively short follow-up. Given that risk stratification may influence prognosis, the lower 5-year BCR-free survival of AA and AC men may largely be attributable to a disproportionate number of high-risk patients in those cohorts compared with CA men, but the number of AA and AC men included in the study was too low to allow clinically meaningful subanalysis. Another limiting factor is the inability to assess the surgical selection bias that is certain to influence the proportion of patients undergoing surgical intervention for prostate cancer in these two distinct healthcare systems. Finally, owing to the fact that multiple pathologists analysed the biopsy and surgical specimens, the difference in GS, as well as rates of upgrading, should be interpreted with caution as this may reflect some degree of interobserver variability.

In conclusion, this international collaboration has provided a unique opportunity directly to compare clinicopathological and biochemical outcome in AA, AC and CA men after RP for clinically OC disease. Based on our findings, both AA and AC men present with more aggressive disease than CA men at the time of RP. In addition we have shown that AA and AC men had similar rates of BCR-free survival after RP for clinically OC disease at 5 years (76 and 74%, respectively) and these rates were significantly lower than BCR-free survival in CA men (98%). Furthermore, AA and AC race are independent predictors of BCR and this may contribute to the worse BCR-free survival compared with CA men observed in the current study. American and Caribbean men of sub-Saharan West-African descent should be counselled on the likelihood of having aggressive prostate cancer and their potential increased risk of BCR after RP for clinically OC prostate cancer.

CONFLICT OF INTEREST

None declared.

REFERENCES

1 **Jemal A, Siegel R, Xu J, Ward E.** Cancer statistics, 2010. *CA Cancer J Clin* 2010; **60**: 277–300

2 **Kang JS, Maygarden SJ, Mohler JL, Pruthi RS.** Comparison of clinical and pathological features in African-American and Caucasian patients with localized prostate cancer. *BJU Int* 2004; **93**: 1207–10

3 **Sanchez-Ortiz RF, Troncoso P, Babaian RJ, Lloreta J, Johnston DA, Pettaway CA.** African-American men with nonpalpable prostate cancer exhibit greater tumor volume than matched white men. *Cancer* 2006; **107**: 75–82

4 **Hamilton RJ, Aronson WJ, Presti JC Jr *et al*.** Race, biochemical disease recurrence, and prostate-specific antigen doubling time after radical prostatectomy: results from the SEARCH database. *Cancer* 2007; **110**: 2202–9

5 **Vijayakumar S, Weichselbaum R, Vaida F, Dale W, Hellman S.** Prostate-specific antigen levels in African-Americans correlate with insurance status as an indicator of socioeconomic status. *Cancer J Sci Am* 1996; **2**: 225–33

6 **Reichardt JK, Makridakis N, Henderson BE, Yu MC, Pike MC, Ross RK.** Genetic variability of the human SRD5A2 gene: implications for prostate cancer risk. *Cancer Res* 1995; **55**: 3973–5

7 **Glover FE Jr, Coffey DS, Douglas LL *et al*.** The epidemiology of prostate cancer in Jamaica. *J Urol* 1998; **159**: 1984–6; discussion 1986–7

8 **Blake G, Hanchard B, Mitchell K *et al*.** Jamaica cancer mortality statistics, 1999. *West Indian Med J* 2002; **51**: 64–7

9 **Coard KC, Skeete DH.** A 6-year analysis of the clinicopathological profile of patients with prostate cancer at the University Hospital of the West Indies, Jamaica. *BJU Int* 2009; **103**: 1482–6

10 **Ritch CR, Brendler CB, Wan RL, Pickett KE, Sokoloff MH.** Relationship of erythrocyte membrane polyunsaturated fatty acids and prostate-specific antigen levels in Jamaican men. *BJU Int* 2004; **93**: 1211–5

11 **Ritch CR, Wan RL, Stephens LB *et al*.** Dietary fatty acids correlate with

prostate cancer biopsy grade and volume in Jamaican men. *J Urol* 2007; **177**: 97–101
12 **Jackson MD, Walker SP, Simpson-Smith CM *et al*.** Associations of whole-blood fatty acids and dietary intakes with prostate cancer in Jamaica. *Cancer Causes Control* 2012; **23**: 23–33
13 **Cross CK, Shultz D, Malkowicz SB *et al*.** Impact of race on prostate-specific antigen outcome after radical prostatectomy for clinically localized adenocarcinoma of the prostate. *J Clin Oncol* 2002; **20**: 2863–8
14 **Morrison BF, Coard K, Strachan G, Miller R, Aiken W, Mayhew R.** Radical prostatectomy outcomes at the University Hospital of the West Indies: 2000–2007. *West Indian Med J* 2011; **60**: 68–72
15 **Moul JW, Douglas TH, McCarthy WF, McLeod DG.** Black race is an adverse prognostic factor for prostate cancer recurrence following radical prostatectomy in an equal access health care setting. *J Urol* 1996; **155**: 1667–73
16 **Freedland SJ, Jalkut M, Dorey F, Sutter ME, Aronson WJ.** Race is not an independent predictor of biochemical recurrence after radical prostatectomy in an equal access medical center. *Urology* 2000; **56**: 87–91
17 **Laudano MA, Badani KK, McCann TR *et al*.** Significant change in predicted risk of biochemical recurrence after radical prostatectomy more common in black than in white men. *Urology* 2009; **74**: 660–4
18 **Powell IJ, Dey J, Dudley A *et al*.** Disease-free survival difference between African Americans and whites after radical prostatectomy for local prostate cancer: a multivariable analysis. *Urology* 2002; **59**: 907–12
19 **von Bodman C, Matikainen MP, Yunis LH *et al*.** Ethnic variation in pelvimetric measures and its impact on positive surgical margins at radical prostatectomy. *Urology* 2010; **76**: 1092–6
20 **Nielsen ME, Han M, Mangold L *et al*.** Black race does not independently predict adverse outcome following radical retropubic prostatectomy at a tertiary referral center. *J Urol* 2006; **176**: 515–9
21 **Chu DI, Moreira DM, Gerber L *et al*.** Effect of race and socioeconomic status on surgical margins and biochemical outcomes in an equal-access health care setting: results from the Shared Equal Access Regional Cancer Hospital (SEARCH) database. *Cancer* 2012 [Epub ahead of print]. DOI:10.1002/cncr.27456
22 **Gaston KE, Kim D, Singh S, Ford OH 3rd, Mohler JL.** Racial differences in androgen receptor protein expression in men with clinically localized prostate cancer. *J Urol* 2003; **170**: 990–3
23 **Kim HS, Moreira DM, Jayachandran J *et al*.** Prostate biopsies from black men express higher levels of aggressive disease biomarkers than prostate biopsies from white men. *Prostate Cancer Prostatic Dis* 2011; **14**: 262–5

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Abbreviations: **RP**, radical prostatectomy; **AA**, African-American; **AC**, Afro-Caribbean; **CA**, Caucasian-American; **OC**, organ-confined; **GS**, Gleason sum; **BCR**, biochemical recurrence; **ECE**, extracapsular extension, SVI, seminal vesicle invasion; **AR**, androgen receptor.