JACC: CARDIOONCOLOGY VOL. 6, NO. 3, 2024

Letters

RESEARCH LETTER

Black-White Disparities in Submaximal Exercise Capacity Reductions in Breast Cancer Survivors

A Prospective Cohort Study

Breast cancer survivors (BCS) experience improved survival, in part because of treatment advances; however, chemotherapy-treated BCSs experience a 20% reduction in exercise capacity, which threatens to offset those gains.[1] Black BCSs experience greater treatment-induced cardiotoxicity than White BCSs, possibly because of less equitable delivery of cardioprotective treatments, but no study has investigated whether a disparity exists in exercise capacity.[2] Examining such a disparity is critical because reduced exercise capacity substantially impacts quality of life and mortality. Thus, we investigated racial differences in submaximal exercise capacity changes in the first 3 months postdiagnosis in a prospective BCS cohort.

This analysis included women with stage I to III breast cancer with a mean age of 55.9 ± 11.1 years from the UPBEAT (Understanding and Predicting Fatigue, Cardiovascular Decline, and Events After Breast Cancer) (NCT02791581) study in whom the 6-minute walk distance (6MWD), a measure of submaximal exercise capacity, was calculated using standard protocols.[3] The outcome was the change from baseline to 3-month 6MWD, a time point when BCSs were receiving (70%) or completed with chemotherapy (30%). Missing data were imputed using imputation by random forest. This study (Wake Forest NCI Community Oncology Research Program Research Base [UG1CA189824]) received Institutional Review Board approval.

Unadjusted mean differences in 6MWD were compared with *t*-tests. Linear regression was used to investigate the association between race and changes in 6MWD. Next, we conducted logistic regression dichotomizing 6MWD at a minimal clinically important difference (MCID) threshold of 41.0 m.[4] In sensitivity analysis, we examined a threshold of 58.9 m.[4] Confounders included baseline levels of 6MWD, age, left ventricular ejection fraction, body mass index, diabetes, income, education, and receipt of anthracycline and trastuzumab.

Black BCSs experienced lower submaximal exercise capacity before cancer treatment than White BCSs and subsequently experienced a greater reduction in exercise capacity at 3 months post-treatment initiation. Before breast cancer treatment, the mean 6MWD was lower for Black women (420.7 m; 95% CI: 403.6-438.4) than White women (476.0 m; 95% CI: 457.7-494.3; $P = 0.011$). Furthermore, Black BCSs experienced a greater mean decline from baseline to 3 months (−53.0 m; 95% CI: −33.9 to −72.2) than White BCSs (−22.9 m; 95% CI: −12.7 to −22.2). After adjustment for confounders, Black race was associated with a 23-m shorter 6MWD at 3 months (β coefficient: −22.8; 95% CI: −0.07 to −45.46; $P = 0.049$). A greater proportion of Black BCSs had clinically meaningful declines >41 m (42.6% in Black BCSs vs 31.5% in White BCSs). After adjustment for confounders, Black BCSs experienced 2.9-fold increased odds of an MCID of 41 m in 6MWD (OR: 2.87; 95% CI: 1.26-6.71; $P = 0.013$) relative to White BCSs (**Figure 1**). In a sensitivity analysis using a larger MCID reference value (58.9 m), after adjustment for confounders, the estimate was not significantly different from 1.0 (OR: 1.33; 95% CI: 0.49-3.42; $P = 0.56$).

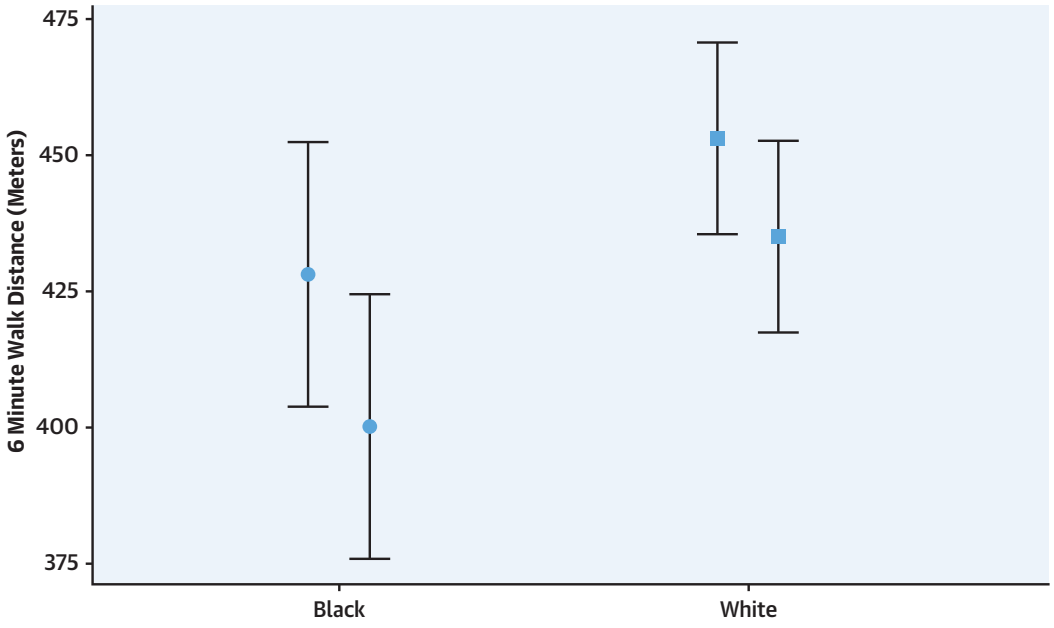
To our knowledge, this is the first report of Black-White differences in submaximal exercise capacity after cancer treatment initiation. Our finding that Black BCSs experienced lower submaximal exercise capacity than White BCSs at diagnosis and also a greater reduction by 3 months is striking; a pretreatment disparity was increased over the course of early cancer treatment. This may indicate a pretreatment cardiovascular vulnerability for Black BCSs that warrants deeper investigation as well as an opportunity to reduce disparities with tailored intervention. Given that exercise interventions can improve exercise capacity among BCSs,[5] the development of culturally relevant interventions to support improvements in exercise capacity, guided by the involvement of Black BCSs, is of high priority. We

ISSN 2666-0873 https://doi.org/10.1016/j.jaccao.2024.05.003

JACC: CARDIOONCOLOGY, VOL. 6, NO. 3, 2024
JUNE 2024:467–469

FIGURE 1 Examination of Black-White Difference in Submaximal Exercise Capacity in Breast Cancer Survivors

A Adjusted Change in 6MWD From Baseline (Left) to 3-Months (Right) in BCS by Race*



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	≥41 Meter Decrease in 6 Six-Minute Walk Distance		
	OR	*95% CI*	*P*
Baseline 6MWD (m)	1.01	1.01-1.02	<0.001
Age	1.06	1.03-1.11	0.001
Black Race	2.87	1.26-6.71	0.013
Baseline LVEF	1.04	0.98-1.11	0.19
Baseline BMI	1.08	1.02-1.14	0.011
Baseline Diabetes	2.49	0.79-7.83	0.12
Income: $35K-$75K	0.98	0.39-2.43	0.96
Income: $75K+	0.88	0.39-1.99	0.77
Education: College	1.55	0.70-3.43	0.28
Education: Post-college	1.26	0.54-2.94	0.59
Receipt of anthracycline	2.57	1.22-5.61	0.015
Receipt of trastuzumab	2.18	0.94-5.15	0.072

* Analytic dataset limited to Black (n = 47) and White (n = 185) BCS with 6MWD at both timepoints (n = 232)

(A) The adjusted change in 6-minute walk distance (6MWD) by race from the linear regression model: Black breast cancer survivors (BCS) (circle) and White BCSs (square). (B) Results from the multivariable logistic regression examining the change in the 6MWD minimal clinically important difference (MCID) in Black BCSs and White BCSs. BMI = body mass index; LVEF = left ventricular ejection fraction.

previously reported in this BCS population that physical activity during treatment helped maintain exercise capacity and reduce cardiac dysfunction.[3] However, if women at breast cancer diagnosis have lower exercise capacity, the ability to engage in exercise during treatment may be limited, resulting in greater declines.

The mean pretreatment 6MWD for White women (476 m) in this study was comparable to the pooled mean of post-treatment 6MWD (477 m) from a meta-analysis of 21 studies of BCSs, whereas the mean pretreatment 6WMD found here for Black women (421 m) was roughly 30 m less than the pooled lower bound (454 m).[6] This difference may reflect poor representation of Black BCSs in studies and further highlights the need for high-quality studies with ample enrollment of Black BCSs.

A study limitation is the challenge in making direct comparisons to the reference study from which MCID thresholds were determined.[4] That study used a treadmill 6MWD rather than the standard 30-m corridor, had a younger age of BCSs, and lacked representation of Black BCSs. Direct investigation of MCID for Black BCSs is an important next step so that a meaningful change in 6MWD may be directly estimated. Lastly, our results may not generalize to other minoritized racial and ethnic groups because our study had too few women in other minoritized groups to allow for investigation.

The drivers of racial disparities in outcomes after breast cancer are multifaceted. Our study found that the Black-White disparity in exercise capacity reduction persisted after controlling for factors such as left ventricular ejection fraction, body mass index, and income, suggesting that differences in individual-level factors are not sufficient to account for the observed differences in 6MWD decline. Thus, unmeasured factors related to structural racism and social determinants of health may contribute to this disparity.[2] Here, race was measured with self-classification and likely represents a marker of multiple exposures impacting Black women's health. The growing recognition of social determinants of health as a fundamental driver of racial disparities[2] and the elucidation of racial disparities in a variety of health outcomes, such as exercise capacity during breast cancer treatment, point to the imperative to prioritize action-oriented work in clinical and research settings to address these factors.

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Husam Abdel-Qadir, MD, PhD, served as Guest Associate Editor for this paper. Paaladinesh Thavendiranathan, MD, MSc, served as Guest Editor-in-Chief for this paper.
This study received funding by NCI (grant R01CA199167) and was supported by ECOG-ACRIN (grant UG1CA189828) and NCI Community Oncology Research Program (grant UG1CA189824). The authors have reported that they have no relationships relevant to the contents of this paper to disclose. The authors wish to thank the participants of UPBEAT (Understanding and Predicting Fatigue, Cardiovascular Decline, and Events After Breast Cancer) for their involvement in this study and the UPBEAT staff for their work on this study.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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