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Hispanic Ethnicity as a Moderator of the Effects of Aerobic and Resistance Exercise in Survivors of Breast Cancer

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Abstract

BACKGROUND: Metabolic syndrome (MSY) is associated with an increased risk of cardiovascular disease, type 2 diabetes, and recurrence in breast cancer survivors (BCS). MSY is 1.5 times more common in Hispanic women compared with non-Hispanic women. Although

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CONFLICT OF INTEREST DISCLOSURES

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exercise mitigates MSY in BCS, to the best of the authors' knowledge, few studies to date have focused on minorities. This secondary analysis examined ethnicity as a moderator of the effects of a 16-week aerobic and resistance exercise intervention on MSY, sarcopenic obesity, and serum biomarkers in BCS.

METHODS: A total of 100 eligible BCS were randomized to exercise (50 BCS) or usual care (50 BCS). The exercise intervention promoted moderate to vigorous aerobic and resistance exercise 3 times a week for 16 weeks. MSY z scores, sarcopenic obesity, and serum biomarkers were measured at baseline, after the intervention, and at the 28-week follow-up (exercise group only). Linear mixed models adjusted for baseline values of the outcome, age, disease stage, adjuvant treatment, and recent physical activity were used to evaluate effect modification by ethnicity.

RESULTS: The study sample was 57% Hispanic BCS (HBCS) and 43% non-Hispanic BCS (NHBCS). HBCS were younger, of greater adiposity, and had been diagnosed with more advanced cancers compared with NHBCS ($P<.001$). Ethnicity was found to moderate the mean differences in exercise training on triglycerides (-36.4 mg/dL; 95% confidence interval [95% CI], -64.1 to -18.8 mg/dL), glucose (-8.6 mg/dL; 95% CI, -19.1 to -3.0 mg/dL), and C-reactive protein (-3.3 mg/L; 95% CI, -7.3 to -0.9 mg/L).

CONCLUSIONS: HBCS appear to have poorer metabolic profiles and therefore may derive relatively larger metabolic changes from exercise compared with NHBCS. Clinical exercise interventions may attenuate existing health disparities across diverse groups of BCS.

Keywords

exercise; Hispanic breast cancer survivors; metabolic syndrome; obesity

INTRODUCTION

Hispanics comprise the largest and fastest growing ethnic minority group in the United States. Currently reported to be 53 million (approximately 17.8% of the population),¹⁻³ the number of Hispanics is projected to be 128 million by 2060.^{1,2} Thus, the need to understand relevant ethno-specific health disparities among the increasing number of Hispanic cancer survivors is paramount.

An advanced stage of disease at the time of diagnosis, poorer prognosis, and increased mortality are well documented among Hispanic breast cancer survivors (HBCS) when compared with non-Hispanic breast cancer survivors (NHBCS).^{1,4-6} HBCS have the lowest 5-year survival rate compared with non-Hispanic ethnic groups (83.8% vs 89.7%).^{7,8} It has been purported that this disparity may be due to decreased levels of physical activity and increased adiposity and weight gain during adulthood among HBCS.¹ Therefore, the importance of investigating modifiable lifestyle interventions, such as exercise, to mitigate such differences is vital. Across all US ethnic groups, Hispanic women report the highest rates of physical inactivity and therefore are at greater risk of cardiovascular disease, obesity, diabetes,⁹ and metabolic syndrome (MSY). MSY is 1.5 times more prevalent in Hispanic individuals compared with non-Hispanic whites or blacks.¹⁰ MSY also is a long-term complication of curative treatment for many cancers, including breast cancer.¹¹ MSY due to

heightened adipose and systemic inflammation and increased cell proliferation may influence cancer recurrence and mortality.^{12,13}

As breast cancer survival rates continue to improve worldwide, there is an increasing focus on the role of modifiable risk factors in prognosis. For example, obesity and related markers of MSY and insulin resistance at the time of diagnosis and hyperinsulinemia after treatment are associated with an increased risk of breast cancer mortality, all-cause mortality, and breast cancer recurrence.^{12,14,15} Taken together, there is a critical need to investigate the role of modifiable lifestyle interventions in deterring obesity-related MSY and related biomarkers in higher-risk HBCS. However, to the best of our knowledge, few studies have been published to date.^{16,17} Of the 51 exercise trials for BCS successfully completed since 1989, few have specifically involved Hispanic patients.^{18,19}

We previously reported that a 16-week intervention of moderate to vigorous combined aerobic and resistance exercise led to significant improvements in MSY, sarcopenic obesity, and circulating biomarkers that were sustained at the 28-week follow-up among sedentary, overweight, and obese BCS.²⁰ In the current study, we report the secondary analysis related to the ethnocentric differences in response to our exercise intervention. To our knowledge, the current study is the first study to date to target specific health disparities in obesity-related comorbidities with a clinical exercise intervention in HBCS compared with NHBCS. We hypothesized that HBCS have worse metabolic profiles, and therefore may derive significantly greater metabolic benefit from exercise than NHBCS.

MATERIALS AND METHODS

Participants

Detailed methods have been published previously.²⁰ Eligible participants were <6 months posttreatment for chemotherapy or radiotherapy for stage 0 to III breast cancer and were nonsmokers and sedentary (<60 minutes of structured exercise/week), with a body mass index ≥ 25.0 kg/m² (or body fat >30%) and a waist circumference >88 cm. Participants self-identified as Hispanic or non-Hispanic. All study methods were conducted in English or Spanish as needed.

Recruitment occurred between August 1, 2012, and December 31, 2016, from the University of Southern California (USC) Norris Comprehensive Cancer Center and Los Angeles County Hospital during routine medical oncology clinic visits. Women self-referred via study brochures (available in English and Spanish) from the Norris Comprehensive Cancer Center and Los Angeles County Hospital in addition to the USC Physical Therapy Associates Clinic and Keck Medicine of USC in Pasadena, California. The protocol and informed consent were approved by the institutional review board (HS-12-00141) and registered ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01140282) identifier NCT01140282). Signed informed consent was obtained from each participant. Participants were randomized to exercise or usual care after the completion of baseline testing using concealed randomization lists.

Experimental Design

The current 2-arm randomized controlled trial compared the effects of an aerobic and resistance exercise intervention versus usual care on changes in MSY, body composition, and circulating biomarkers between baseline and 16 weeks after the intervention. Endpoints were assessed at baseline, after the intervention (16 weeks), and at the 28-week follow-up (exercise group only). Primary outcomes for the entire study sample were published previously.²⁰ To enhance participation, participants receiving usual care were offered the exercise program after the study period.

Metabolic Syndrome

The primary outcome was the MSY *z* score calculated from modified *z* scores of each MSY variable, namely waist circumference, systolic blood pressure (SBP)/diastolic blood pressure (DBP), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and glucose using National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria, and standard deviations (denominator of each factor in the formulas) using individual participant baseline data of the entire study cohort (100 participants): $[(50-\text{HDL})/5.5]+[(\text{TG}-15)/25.5]+[(\text{glucose}-100)/15.9]+[(\text{waist circumference}-88)/8.8]+[(\text{SBP}-130)/11.4]+[(\text{DBP}-85)/10.8]$.^{21,22} Based on the ATP III definition,²³ MSY constituted 3 of the following risk factors: waist circumference ≥ 88 cm, SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg or treatment with blood pressure medication, fasting levels of HDL-C <50 mg/dL, TG ≥ 150 mg/dL, and glucose ≥ 100 mg/dL or treatment with diabetes medication. The ATP III score for each participant was calculated by summing the ATP III criteria met at each timepoint.

Serum biomarkers—Fasting blood was obtained by trained phlebotomists. Methods for analyzing glucose, HDL-C, low-density lipoprotein cholesterol, total cholesterol, triglycerides, glycosylated hemoglobin (hemoglobin A1c), high-sensitivity C-reactive protein, insulin, interleukin 6, interleukin 8, tumor necrosis factor α , leptin, and adiponectin are detailed elsewhere.²⁰ Homeostasis model assessment—insulin resistance estimated insulin resistance using the validated equation of fasting plasma insulin multiplied by fasting plasma glucose in mmol/L/22.5.²⁴

Anthropometrics/dual-energy X-ray absorptiometry—Weight was measured to the nearest 0.1 kg on an electronic scale with the patient wearing a hospital gown and no shoes. Height was measured to the nearest 0.5 cm with a fixed stadiometer. Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the iliac crest. Hip circumference was measured around the widest portion of the buttocks. Whole-body dual-energy X-ray absorptiometry (DXA) scans were performed to assess percentage body fat, fat mass, appendicular skeletal mass, and lean mass (Lunar iDXA; GE Healthcare, Chicago, Illinois). Sarcopenic obesity was defined as an appendicular skeletal mass index <5.45 kg/m²²⁵ and a body mass index ≥ 30.0 kg/m².

Blood pressure—After 5 minutes of quiet sitting, blood pressure was measured using the arm contralateral to the affected breast with an automated sphygmomanometer (Welch Allyn Inc, Skaneateles Falls, New York).

Covariate Measures

Physical activity history was assessed at baseline using an interviewer-administered, validated questionnaire.²⁶ Three-day dietary records (2 weekdays and 1 weekend day) were completed at baseline, after the intervention, and at the 28-week follow-up (exercise group only) within 1 week of each assessment and were analyzed using Nutritionist Pro (Axxya Systems LLC, Redmond, Washington). Participants were asked to maintain dietary behaviors throughout the trial.

Participants completed the Charlson Comorbidity Index questionnaire.²⁷ Cancer-related information (stage of disease, hormone receptor status, receipt of endocrine therapy, type/duration of chemotherapy, duration of radiotherapy, and receipt of surgery) was abstracted from medical records.

Physical Fitness

A single-stage, submaximal treadmill test estimated maximal oxygen uptake. Participants first performed a 4-minute warmup by walking on a treadmill (Desmo Treadmill; Woodway USA Inc, Waukesha, Wisconsin) at a speed (2.0 miles per hour [mph], 3.0 mph, 4.0 mph, or 4.5 mph) that increased their heart rate (HR) between 50% to 70% of the HR maximum. This was followed by a 4-minute test at the same speed with a 5% grade; HR was measured during the final 30 seconds of the test. Using HR, speed, age, and sex, the maximal oxygen uptake was calculated using the test-specific formula.²⁸

Maximal voluntary strength (1 repetition maximum [RM]) was assessed for the chest press, latissimus pulldown, knee extension, and knee flexion using the 10-RM method (Tuff Stuff Fitness Equipment, Pomona, California).²⁹ Participants completed a warmup load of approximately 5-RM to 8-RM before attempting 10-RM. A 2-minute rest period was given between attempts and 3 to 5 attempts were performed. Results were used to quantify fitness and to prescribe exercise intensity for the intervention.

Exercise Intervention

As per American Cancer Society (ACS)/American College of Sports Medicine (ACSM) exercise guidelines for cancer survivors, 150 minutes of aerobic exercise and 2 to 3 days of resistance exercise training per week was promoted (and tracked) via 2 supervised 1-on-1 sessions per week with a certified ACS/ACSM Cancer Exercise Trainer.³⁰ Days 1 and 3 consisted of aerobic and resistance exercise for approximately 80 minutes and day 2 included approximately 50 minutes of aerobic exercise. Each session began with a 5-minute aerobic exercise warmup at 40% to 50% of the estimated maximal oxygen consumption. Sequenced resistance exercise followed in a circuit training fashion with no rest periods between exercises (leg press ⇔ chest press ⇒ lunges ⇔ seated row ⇒ leg extensions ⇔ triceps extensions ⇒ leg flexion ⇔ biceps curl, in which “⇔” indicates the 2 exercises that alternated until all sets were completed, and then the following pair of exercises was performed). Initial resistance was set at approximately 80% of the estimated 1-RM for lower body exercises and 60% of the estimated 1-RM for upper body exercises. When the participant was able to complete 3 sets of 10 repetitions at the set weight in 2 consecutive sessions, the weight then was increased by 10%. Repetitions increased from 10 (week 4) to

12 (week 8) to 15 (week 12) every 4 weeks to safely build muscular endurance. Compression garments were required during the exercise sessions for all participants who held prescriptions.

Resistance exercises were followed by self-selected aerobic exercise (ie, treadmill walking/running, rowing machine, or stationary bicycle). HR was monitored throughout the aerobic sessions to maintain a HR at 65% to 80% of the maximum HR. The duration of the aerobic sessions was increased from 30 minutes (week 1) to 50 minutes (week 16) as cardiorespiratory fitness increased. Participants ended each session with a 5-minute cool down at 40% to 50% of the estimated maximal oxygen consumption.

Follow-Up Period (Exercise Group Only)

Participants were encouraged to exercise on their own without supervision and to log their activity during the 12 weeks that followed.³¹ Sustainability was assessed in this group at the 28-week follow-up by 7-day accelerometer monitoring (Model GT3X Actigraph; Actigraph, Fort Walton Beach, Florida). Participants were asked to wear the accelerometer during waking hours for 7 consecutive days; to perform their normal or usual activity; and to remove the device while bathing, showering, or swimming. Participants received verbal and written instructions and a wear time log to encourage adherence. Devices were returned at the time of follow-up testing. Accelerometer data were used to estimate the minutes and intensity of physical activity performed according to the manufacturer's directions.

Statistical Analyses

The parent trial was powered based on projected changes in insulin.³² The enrollment of 100 women provided 80% statistical power ($\alpha=.05$) to detect a difference of 2.6 uU/mL (SD, 4.0 uU/mL) in mean insulin levels assuming 20% dropout using a 2-group Student *t* test.

Baseline characteristics of the 2 ethnic groups were compared using independent-sample Student *t* tests for continuous variables and Pearson chi-square or Fisher exact tests for categorical variables. Within-group differences in mean changes for individual outcomes measured at 4 months and at the 3-month follow-up (exercise group only) were evaluated using general linear models repeated-measures analyses of variance. Linear regression was used to assess effect modification of the intervention by ethnicity. A priori covariates that were explored included age, stage of disease, adjuvant treatment, and recent physical activity. We adjusted our final models for baseline values of the outcome, age, and recent physical activity. Analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc, Cary, North Carolina).

RESULTS

The Consolidated Standards Of Reporting Trials (CONSORT) diagram has been presented elsewhere.²⁰ The overall sample included 56 HBCS and 41 NHBCS (Table 1); the 3 African American women in the study were excluded. Compared with NHBCS, HBCS were younger (with a higher percentage being premenopausal), were obese, had a higher stage of disease (and hence were treated with both radiotherapy and chemotherapy), and were less physically

active ($P<.001$). Both groups had high rates of session attendance (96%) and adherence to the intensity or volume of aerobic and resistance exercise (95%).

Metabolic Syndrome

At baseline, approximately 85% of the HBCS and 69% of the NHBCS presented with MSY. Table 2 shows the changes from baseline to after the intervention with regard to MSY variables and the interaction by ethnicity. Both HBCS and NHBCS who were assigned to exercise experienced significant improvements in all MSY variables when compared with baseline ($P<.01$) and usual care ($P<.001$). At the 28-week follow-up, all MSY variables remained significantly improved for both ethnic groups assigned to exercise when compared with baseline ($P<.001$). Ethnicity was found to moderate the effect of exercise on HDL-C (11.3 mg/dL; 95% confidence interval [95% CI], 18.7 to 6.2 mg/dL), TG (−36.4 mg/dL; 95% CI, −64.1 to −18.8 mg/dL), glucose (−8.6 mg/dL; 95% CI, −19.1 to −3.0 mg/dL), and MSY z scores (−3.0; 95% CI, −7.0 to −0.8). In all cases, HBCS demonstrated more favorable improvements compared with NHBCS.

Body Composition

At baseline, approximately 96% of the HBCS and 92% of the NHBCS presented with sarcopenic obesity. After the intervention, sarcopenic obesity and body composition measures were found to be significantly improved in the exercise group (both HBCS and NHBCS) when compared with baseline ($P=.01$) and usual care ($P<.001$) (Table 3). At the 28-week follow-up, all body composition variables remained significantly improved for both ethnic groups assigned to exercise compared with baseline ($P<.001$). There was some evidence that ethnicity moderated the effect of the exercise intervention on fat mass (−3.2 kg; 95% CI, −8.8 to −0.3 kg) and the percentage of body fat (−3.0%; 95% CI, −7.6% to −0.5%).

Circulating Biomarkers

Table 4 shows changes between baseline and after the intervention and interactions in circulating biomarkers. After the intervention, HBCS and NHBCS assigned to exercise experienced significant reductions in all biomarkers when compared with baseline ($P<.01$) and usual care ($P<.01$). At the 28-week follow-up, all biomarkers remained significantly improved in the exercise group when compared with baseline ($P<.01$). Again, there was some evidence that ethnicity moderated the effect of exercise on insulin (−9.8 uU/mL; 95% CI, −18.0 to −3.5 uU/mL), homeostasis model assessment–insulin resistance (−5.7; 95% CI, −5.7 to 1.1), IGF-1 (−22.7 ng/mL; 95% CI, −38.4 to 16.9 ng/mL), high-sensitivity C-reactive protein (−3.3 mg/L; 95% CI, −7.3 to −0.9 mg/L), adiponectin (3.8 μg/mg; 95% CI, 1.0–7.5 μg/mg), and total cholesterol (−25.2 mg/dL; 95% CI, −35.3 to −19.0 mg/dL).

DISCUSSION

At baseline, HBCS participants demonstrated significantly poorer metabolic health and body composition, and were less physically active when compared with NHBCS. Ethnicity moderated the effects of the 16-week supervised aerobic and resistance exercise intervention on the majority of MSY indicators, body composition, and circulating biomarkers. To our

knowledge, the current study is the first to explore racial/ethnic disparities in MSY and sarcopenic obesity between HBCS and NHBCS and to document differential response to exercise.

Hispanic women in the United States are more likely to be obese and physically inactive compared with their non-Hispanic counterparts,⁹ effectively rendering them at greater risk of MSY and obesity-related comorbidities.^{33,34} Ervin et al¹⁰ reported that Hispanic women are up to 150% more likely to have MSY compared with non-Hispanic women. In the current study, HBCS also were found to have significantly higher adiposity at baseline compared with NHBCS. In addition, HBCS were less active than NHBCS, thereby corroborating these epidemiologic findings.

To the best of our knowledge, the current study is the first to explore exercise as a means of directly attenuating ethnic differences in the presence of MSY and obesity-related comorbidities. In related research and in a sample comprised of 79% HBCS, Greenlee et al¹⁷ explored the impact of the Curves weight loss and low-intensity exercise program (Curves North America, Woodway, Texas). At 6 months, they found a 3.3% decline in body weight, although the study was not powered to address differences by ethnicity. The scope of the current trial extends beyond weight status to encompass the variable domains of MSY and circulating biomarkers. The current study results suggest that exercise is effective beyond weight loss to mitigate clinically significant, obesity-related, circulating biomarkers. This relatively unexplored area bears great potential for explaining racial and ethnic disparities across diverse populations of cancer survivors.

The current study is unique in that our adherence rate of 96% exceeds the rate of 70% to 80% noted in similar exercise trials,³⁵⁻³⁷ and may have been due to flexible session timing (5 AM-8 PM, 7 days/week), 1-on-1 supervision in a clinical setting, or the provision of parking permits or bus passes to overcome common transportation barriers. Adherence is particularly important because minority recruitment across cancer trials is low, and to the best of our knowledge there is scarce evidence regarding minority participation and adherence with lifestyle-modifiable interventions.¹⁶ Spector et al³⁸ found that, in addition to globally lower participation in physical activity, Hispanic women reported more perceived barriers to exercise compared with white women. Hispanic women more often related a lack of knowledge regarding how to exercise, a lack of enjoyment from exercise, and discouragement as barriers to their participation, further explicating the significance of our 1-on-1, directly supervised trial in motivating participants and maintaining adherence to the study protocol. We purport that by providing individual clinical expertise in guiding our participants through the exercise protocols, in addition to offering bilingual trainers, flexible hours, and multiple follow-up telephone calls regarding attendance, we engendered a supportive and engaging environment for HBCS.

The strengths of the current study include the focus on an ethnically diverse, high-risk sample of BCS; the comprehensive assessment of MSY components and markers; the use of continuous MSY scores replicating those used in cancer²¹ and noncancer populations²²; the randomized controlled design; the high adherence rate; the incorporation of bilingual exercise training staff; and the modest rate of patients lost to follow-up. Limitations include

limited power for interaction analyses, possible recruitment bias, a lack of intervention reproducibility with high adherence outside of a supervised setting, and the lack of an attention control group.

Although the results of the current study suggest that ethnicity moderated obesity-related outcomes in response to our exercise intervention, we cannot assume that these differences are related to racially oriented phenotypic differences between HBCS and NHBCS. As per the US Census Bureau's ordinal nomenclature for distinguishing between these groups,² the self-reported identity of "Hispanic" or "Latino" remains separate from that of a racial composition because Hispanic Americans have broad ethnic origins ranging from Latin America, the Caribbean, Spain, and Portugal. Thus, future work is needed to ascertain factors contributing to such profound dissimilarities between these unique ethnic groups (ie, etiological factors contributing to poorer breast cancer prognosis and response to modifiable lifestyle interventions, such as exercise, presented in the current study). Relevant future work includes investigating the etiology, covariates, and precipitating factors that contribute to baseline physiological differences specific to the HBCS population and addressing said factors in the design and implementation of successful exercise programs to improve cancer survivorship.

The results of the exploratory secondary analysis of our randomized controlled trial presented in the current study suggest that ethnicity moderates the effects of exercise participation when comparing HBCS with NHBCS. Although the results suggest that MSY and obesity-related biomarkers are improved by exercise, it is important to determine whether specific modifications would be more successful within the identified high-risk HBCS population. Due to the limited exercise trials conducted in HBCS, it is important to determine whether certain exercise regimens are more effective than others in altering MSY and whether these improvements are maintained after the exercise intervention. In an upcoming trial ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03120390) identifier [NCT03120390](https://clinicaltrials.gov/ct2/show/study/NCT03120390)), we plan to investigate the effects of 2 different exercise mechanisms, clinical and community-based, in deterring metabolic dysregulation specifically in HBCS. The goal is to explore further the potential impact of ethnically appropriate, modifiable lifestyle interventions in improving prognosis and engendering sustainable behaviors and attitudes toward participation in exercise.

In the current study, HBCS improved their relative metabolic profile more than NHBCS from a supervised, structured, combined aerobic and resistance exercise intervention. The results presented herein demonstrated the potential of exercise interventions in attenuating ethnocentric disparities across diverse groups of BCS. These results support the implementation of a clinically structured exercise intervention in the continuum of breast cancer care across Hispanic and non-Hispanic populations.

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TABLE 1.

Baseline Characteristics of the Study Participants

Variable	Exercise N = 48			Usual Care N = 49		
	HBCS Mean (SD) N = 29	NHBCS Mean (SD) N = 19	P	HBCS Mean (SD) N = 27	NHBCS Mean (SD) N = 22	P
Age, y	46.9 (10.2)	55.6 (10.5)	<.001	46.7 (10.0)	55.9 (10.3)	<.001
Postmenopausal, no. (%)	14 (49)	12 (62)	.01	13 (48)	13 (60)	.001
Weight, kg	87.0 (13.5)	84.0 (13.8)	.12	87.5 (13.2)	84.5 (13.9)	.10
Height, cm	157.0 (5.9)	159.3 (6.2)	.34	157.5 (6.2)	160.2 (5.8)	.46
BMI, kg/m ²	35.1 (6.1)	33.2 (5.9)	.5	34.7 (6.4)	33.0 (5.5)	.06
BMI category, no. (%)						
Overweight, BMI <30	10 (35)	13 (68)	<.001	9 (33)	15 (68)	<.001
Obese, BMI ≥ 30	19 (65)	6 (32)	<.001	18 (66)	7 (32)	<.001
Educational level, no. (%)						
High school degree	22 (76)	6 (32)	<.001	21 (78)	7 (32)	<.001
Some college/college degree	7 (24)	13 (68)	<.001	6 (22)	15 (68)	<.001
Time since diagnosis, mo	6.0 (2.0)	6.4 (2.1)	.45	6.2 (2.1)	6.3 (2.4)	.65
AJCC stage of disease, no. (%)						
I	12 (42)	10 (52)	.06	12 (44)	12 (55)	.03
II	8 (28)	8 (43)	.08	7 (24)	10 (45)	.04
III	9 (30)	1 (5)	<.001	8 (32)	0 (0)	<.001
Treatment in addition to surgery, no. (%)						
Radiotherapy only	2 (7)	3 (16)	.45	3 (11)	2 (10)	.69
Chemotherapy only	4 (14)	5 (26)	.36	4 (15)	6 (30)	.06
Radiotherapy and chemotherapy	23 (79)	11 (58)	<.001	20 (74)	13 (60)	.001
Current endocrine therapy, no. (%)						
None	4 (12)	1 (10)	.65	2 (10)	0 (0)	.70
Tamoxifen	13 (46)	9 (45)	.78	13 (50)	12 (48)	.84
Aromatase inhibitor	12 (42)	9 (45)	.69	12 (40)	10 (45)	.63
Recent physical activity, min/wk of moderate to vigorous intensity recreational activity	7.4 (5.3)	9.5 (7.4)	<.001	7.3 (5.1)	9.6 (7.0)	<.001

Abbreviations: BMI, body mass index; HBCS, Hispanic breast cancer survivors; NHBCS, non-Hispanic breast cancer survivors; SD, standard deviation.

Ethnicity as a Moderator of Exercise Effects on Metabolic Syndrome in Survivors of Breast Cancer

TABLE 2.

		Baseline		Postintervention		Mean Change		Adjusted Subgroup		Adjusted Interaction	
		No.	Mean (SD)	No.	Mean (SD)	Mean (95% CI) ^a	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b
Waist circumference, cm											
HBCS											
Exercise	29	105.2 (9.8)	28	92.1 (8.0)		-13.0 (-16.9 to -9.3)	-13.2 (-18.0 to -6.9); .001			-4.1 (-14.4 to 1.0); .45	
Usual care	27	106.1 (9.3)	24	106.2 (9.5)		0.2 (-1.9 to 2.1)					
NHBCS											
Exercise	19	94.8 (8.5)	19	86.9 (7.5)		-8.1 (-11.5 to -5.5)	-9.1 (-17.0 to -4.5); .010				
Usual care	22	95.0 (8.0)	22	95.8 (8.8)		0.8 (-1.3 to 2.3)					
Systolic blood pressure, mm Hg											
HBCS											
Exercise	29	140.1 (11.2)	28	122.9 (9.9)		-17.1 (-23.4 to -10.5)	-16.9 (-20.2 to -11.5); .003			-1.7 (-15.4 to 2.5); .65	
Usual care	27	138.9 (11.6)	24	138.0 (10.4)		-0.1 (-1.5 to 2.1)					
NHBCS											
Exercise	19	134.2 (11.9)	19	119.3 (9.7)		-15.0 (-19.4 to -9.3)	-15.2 (-19.0 to -9.6); .001				
Usual care	22	133.7 (11.0)	22	133.9 (11.5)		0.2 (-0.8 to 1.8)					
Diastolic blood pressure, mm Hg											
HBCS											
Exercise	29	96.5 (10.7)	28	82.4 (8.5)		-14.1 (-21.4 to -10.4)	-13.3 (-19.0 to -8.5); .001			-3.0 (-3.5 to 6.6); .45	
Usual care	27	97.0 (10.3)	24	97.8 (10.4)		-0.8 (-3.2 to 2.2)					
NHBCS											
Exercise	19	92.6 (10.8)	19	81.9 (8.0)		-10.7 (-16.5 to -6.2)	-10.4 (-15.5 to -5.3); .012				
Usual care	22	92.7 (9.6)	22	93.0 (9.8)		0.3 (-1.1 to 2.0)					
HDL-C, mg/dL											
HBCS											
Exercise	29	38.7 (7.1)	28	63.7 (7.7)		25.0 (40.0 to 16.8)	27.2 (38.8 to 15.3); .001			11.3 (18.7 to 6.2); .05	
Usual care	27	37.9 (6.8)	24	35.7 (7.1)		-2.2 (-4.0 to 2.5)					
NHBCS											
Exercise	19	45.1 (7.8)	19	54.3 (8.6)		9.2 (16.2 to 3.5)	15.9 (26.2 to 5.4); .005				

	No.	Baseline Mean (SD)	No.	Postintervention Mean (SD)	Mean Change Mean (95% CI) ^a	Adjusted Subgroup Difference in Mean Change Mean (95% CI); <i>P</i> ^b	Adjusted Interaction Effect Mean (95% CI); <i>P</i> ^b
Usual care	22	44.6 (7.0)	22	37.9 (6.8)	-6.7 (-11.5 to -1.4)		
Triglycerides, mg/dL							
HBCS							
Exercise	29	269.1 (31.7)	28	150.7 (24.3)	-118.4 (-170.3 to -80.1)	-120.3 (-164.3 to -65.7); <.001	-36.4 (-64.1 to -18.8); .03
Usual care	27	276.2 (29.5)	24	278.1 (29.4)	-1.9 (-4.2 to 3.9)		
NHBCS							
Exercise	19	233.4 (25.6)	19	152.0 (21.5)	-81.4 (-114.5 to -46.6)	-83.9 (-109.9 to -34.6); .002	
Usual care	22	248.3 (31.6)	22	250.8 (31.1)	2.5 (-2.9 to 4.4)		
Glucose, mg/dL							
HBCS							
Exercise	29	115.6 (14.3)	28	93.6 (13.7)	-22.0 (-45.1 to -9.2)	-21.3 (-45.5 to -8.5); .001	-8.6 (-19.1 to -3.0); .05
Usual care	27	117.3 (14.9)	24	118.0 (15.5)	0.7 (-3.0 to 3.1)		
NHBCS							
Exercise	19	105.7 (12.4)	19	92.5 (14.6)	-13.2 (-22.1 to -6.5)	-12.7 (-18.8 to -5.2); .010	
Usual care	22	103.4 (14.0)	22	103.9 (14.5)	0.5 (-2.9 to 3.1)		
Metabolic syndrome z score							
HBCS							
Exercise	29	9.0 (1.5)	28	4.5 (0.8)	-4.5 (-10.4 to -2.0)	-4.3 (-11.6 to -1.9); <.001	-3.0 (-7.0 to -0.8); .07
Usual care	27	9.1 (1.7)	24	9.3 (1.4)	0.2 (-2.0 to 2.1)		
NHBCS							
Exercise	19	6.5 (1.3)	19	4.7 (0.6)	-1.8 (-6.6 to 3.3)	-1.3 (-4.2 to 3.9); .010	
Usual care	22	6.0 (1.3)	22	6.5 (0.9)	0.5 (-3.2 to 3.0)		
ATP III score							
HBCS							
Exercise	29	5.0 (0.8)	28	1.0 (0.8)	-4.0 (-6.0 to -1.0)	-4.1 (-7.0 to -0.1); <.001	-2.5 (-5.0 to -1.5); .14
Usual care	27	5.0 (0.8)	24	5.0 (0.8)	-0.1 (-1.0 to 1.0)		
NHBCS							
Exercise	19	3.0 (1.0)	19	1.0 (0.6)	-2.0 (-5.0 to -0.5)	-1.5 (-3.0 to 2.5); .012	
Usual care	22	3.0 (1.5)	22	3.5 (1.5)	0.5 (1.0 to 1.5)		

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Abbreviations: 95% CI, 95% confidence interval; ATP III, Adult Treatment Panel III; HBCS, Hispanic breast cancer survivors; HDL-C, high-density lipoprotein cholesterol; NHBCS, non-Hispanic breast cancer survivors; SD, standard deviation.

^aEstimated based on general linear models repeated-measures analysis of variance.

^bEstimated based on linear regression analysis and adjusted for baseline values of the outcome, age, and recent physical activity.

TABLE 3.
Ethnicity as a Moderator of Exercise Effects on Sarcopenic Obesity and Body Composition in Survivors of Breast Cancer

	No.	Baseline Mean (SD)	No.	Postintervention Mean (SD)	Mean Change Mean (95% CI) ^a	Adjusted Subgroup		Adjusted Interaction Effect Mean (95% CI); <i>p</i> ^b
						Difference in Mean Change	Mean (95% CI); <i>p</i> ^b	
Appendicular skeletal muscle index, kg/m ²								
HBCS								
Exercise	29	4.4 (0.5)	28	6.4 (0.5)	2.0 (0.8 to 8.1)	2.1 (0.5 to 5.1); <.001		0.5 (−1.9 to 5.0); .75
Usual care	27	4.6 (0.4)	24	4.7 (0.6)	−0.1 (−1.9 to 2.0)			
NHBCS								
Exercise	19	5.1 (0.6)	19	6.6 (0.4)	1.5 (−1.1 to 5.5)	1.6 (0.4 to 5.2); .010		
Usual care	22	5.1 (0.4)	22	5.0 (0.4)	−0.1 (−1.8 to 2.0)			
BMI, kg/m ²								
HBCS								
Exercise	29	35.1 (6.1)	28	28.9 (3.5)	−6.2 (−12.4 to −2.4)	−6.5 (−11.8 to −1.0); .005		−1.7 (−4.0 to 3.4); .34
Usual care	27	34.7 (6.4)	24	35.0 (5.9)	0.3 (−1.1 to 3.0)			
NHBCS								
Exercise	19	33.2 (5.9)	19	27.7 (3.7)	−5.5 (−8.4 to −1.9)	−4.8 (−7.2 to −2.8); .008		
Usual care	22	33.0 (5.5)	22	32.3 (4.1)	−0.7 (−2.5 to 1.8)			
Weight, kg								
HBCS								
Exercise	29	87.0 (11.0)	28	82.5 (10.5)	−4.5 (−9.5 to −1.0)	−4.8 (−9.0 to −1.8); .005		−3.2 (−6.6 to 0.1); .11
Usual care	27	87.5 (11.5)	24	87.8 (10.3)	0.3 (−2.0 to 1.9)			
NHBCS								
Exercise	19	84.0 (10.8)	19	81.9 (9.7)	−2.1 (−6.6 to −0.8)	−1.6 (−5.5 to −0.5); .007		
Usual care	22	84.5 (9.6)	22	85.0 (9.8)	0.5 (−1.8 to 1.8)			
Hip circumference, cm								
HBCS								
Exercise	29	45.3 (5.0)	28	41.9 (4.9)	−3.4 (−9.1 to −0.5)	−4.0 (−9.0 to −0.5); .007		−0.1 (−2.9 to 3.1); .89
Usual care	27	44.9 (5.4)	24	45.5 (5.5)	0.6 (−2.1 to 2.4)			
NHBCS								

	No.	Baseline Mean (SD)	No.	Postintervention Mean (SD)	Mean Change Mean (95% CI) ^a	Adjusted Subgroup Difference in Mean Change		Adjusted Interaction Effect Mean (95% CI); <i>p</i> ^b
						Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	
Exercise	19	39.8 (4.7)	19	36.4 (4.4)	-3.4 (-6.3 to -0.4)	-4.1 (-7.9 to -0.7); .007		
Usual care	22	39.5 (4.9)	22	40.2 (4.8)	0.7 (-3.2 to 3.1)			
Lean mass, kg								
HBCS								
Exercise	29	52.0 (7.1)	28	55.3 (8.0)	3.3 (0.2 to 10.1)	3.8 (0.2 to 9.6); .005	1.1 (-0.1 to 7.0); .29	
Usual care	27	52.5 (7.5)	24	52.0 (7.3)	-0.5 (-3.0 to 2.9)			
NHBCS								
Exercise	19	55.1 (7.8)	19	57.3 (8.2)	2.2 (0.2 to 9.5)	2.7 (0.3 to 8.4); .012		
Usual care	22	55.5 (7.2)	22	55.0 (7.8)	-0.5 (-3.8 to 3.7)			
Fat mass, kg								
HBCS								
Exercise	29	34.8 (5.4)	28	28.7 (5.0)	-6.1 (-13.5 to -2.0)	-6.7 (-13.1 to -1.5); .001	-3.2 (-8.8 to -0.3); .08	
Usual care	27	35.0 (6.1)	24	35.6 (6.0)	0.6 (-2.9 to 3.0)			
NHBCS								
Exercise	19	30.2 (4.1)	19	26.8 (4.6)	-3.4 (-7.5 to -0.5)	-3.5 (-6.3 to -1.3); .006		
Usual care	22	30.5 (4.0)	22	30.6 (4.0)	0.1 (-1.3 to 1.1)			
Body fat, %								
HBCS								
Exercise	29	40.2 (4.9)	28	35.8 (3.7)	-4.4 (-8.0 to -0.1)	-4.8 (-9.5 to -1.3); .003	-3.0 (-7.6 to -0.5); .09	
Usual care	27	40.6 (5.0)	24	41.0 (5.6)	0.4 (-2.5 to 2.7)			
NHBCS								
Exercise	19	36.4 (3.7)	19	34.7 (3.3)	-1.7 (-5.3 to 3.1)	-1.9 (-4.0 to -0.9); .010		
Usual care	22	36.0 (4.0)	22	36.2 (4.0)	0.2 (-2.0 to 1.9)			
Trunk fat, kg								
HBCS								
Exercise	29	24.6 (5.5)	28	20.4 (4.3)	-4.2 (-9.5 to -1.1)	-4.4 (-9.5 to -0.8); <.001	-1.9 (-6.5 to -0.5); .16	
Usual care	27	24.0 (5.1)	24	24.2 (4.6)	0.2 (-2.0 to 2.4)			
NHBCS								
Exercise	19	20.9 (4.4)	19	18.9 (3.4)	-2.0 (-5.1 to -0.5)	-2.5 (-6.5 to -0.8); .018		

Baseline		Postintervention		Mean Change		Adjusted Subgroup Difference in Mean Change		Adjusted Interaction Effect	
No.	Mean (SD)	No.	Mean (SD)	Mean (95% CI) ^a	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b	Mean (95% CI); <i>p</i> ^b
22	21.3 (4.1)	22	21.5 (4.0)	0.5 (−0.0 to 1.2)					
Usual care									

Abbreviations: 95% CI, 95% confidence interval; BMI, body mass index; HBCS, Hispanic breast cancer survivors; NHBCS, non-Hispanic breast cancer survivors; SD, standard deviation.

^aEstimated based on general linear models repeated-measures analysis of variance.

^bEstimated based on linear regression analysis and adjusted for baseline values of the outcome, age, and recent physical activity.

TABLE 4.
Ethnicity as a Moderator of Exercise Effects on Circulating Biomarkers in Survivors of Breast Cancer

	No.	Baseline Mean (SD)	No.	Postintervention Mean (SD)	Mean Change Mean (95% CI) ^a	Adjusted Subgroup Difference in Mean Change Mean (95% CI); <i>p</i> ^b	Adjusted Interaction Effect Mean (95% CI); <i>p</i> ^b
Insulin, uU/mL							
HBCS							
Exercise	29	39.5 (19.5)	28	21.7 (9.9)	-14.0 (-23.0 to -9.5)	-19.4 (-25.5 to -13.9); <.001	-9.8 (-18.0 to -3.5); .08
Usual care	27	39.7 (18.9)	24	45.1 (11.3)	5.4 (1.5 to 8.0)		
NHBCS							
Exercise	19	32.9 (16.0)	19	25.5 (8.5)	-7.4 (-16.8 to -1.9)	-9.6 (-17.5 to -4.6); .009	
Usual care	22	33.4 (15.5)	22	35.6 (8.8)	2.2 (1.0 to 3.6)		
HOMA-IR							
HBCS							
Exercise	29	14.9 (6.4)	28	7.1 (2.0)	-7.8 (-13.7 to -3.5)	-8.4 (-11.5 to -3.9); <.001	-5.7 (-8.5 to -1.1); .05
Usual care	27	14.0 (6.0)	24	14.6 (5.9)	0.6 (-1.9 to 2.1)		
NHBCS							
Exercise	19	9.7 (3.7)	19	8.0 (2.9)	-1.7 (-2.5 to 1.9)	-2.7 (-4.1 to -0.5); .007	
Usual care	22	8.9 (2.9)	22	9.9 (3.5)	1.0 (-0.9 to 1.8)		
IGF-1, ng/mL							
HBCS							
Exercise	29	135.3 (35.7)	28	105.7 (22.5)	-29.6 (-55.3 to -12.5)	-38.5 (-19.2 to -8.4); .003	-22.7 (-38.4 to -16.9); .10
Usual care	27	138.7 (36.0)	24	147.6 (36.8)	8.9 (3.5 to 13.7)		
NHBCS							
Exercise	19	118.3 (29.9)	19	106.4 (19.0)	-11.9 (-18.5 to -6.0)	-15.8 (-22.0 to -8.8); .008	
Usual care	22	119.4 (33.6)	22	123.3 (19.8)	3.9 (0.8 to 5.8)		
IGFBP-3, ng/mL							
HBCS							
Exercise	29	36.7 (3.4)	28	45.4 (4.5)	8.7 (3.0 to 12.6)	9.1 (15.9 to 5.0); .002	4.4 (0.9 to 8.5); .11
Usual care	27	35.1 (3.1)	24	34.7 (3.0)	-0.4 (-3.0 to 3.1)		
NHBCS							
Exercise	19	41.2 (3.7)	19	48.4 (4.0)	7.2 (2.6 to 12.7)	4.7 (1.1 to 10.3); .009	

	No.	Baseline Mean (SD)	No.	Postintervention Mean (SD)	Mean Change Mean (95% CI) ^a	Adjusted Subgroup Difference in Mean Change Mean (95% CI); <i>P</i> ^b	Adjusted Interaction Effect Mean (95% CI); <i>P</i> ^b
Usual care	22	39.5 (3.9)	22	41.5 (4.3)	2.5 (0.1 to 5.5)		
hs-CRP, mg/L							
HBCS							
Exercise	29	5.5 (1.1)	28	2.9 (0.5)	-2.6 (-4.9 to -0.1)	-3.6 (-5.2 to -0.9); <.001	-3.3 (-7.3 to -0.9); .04
Usual care	27	5.6 (1.3)	24	5.7 (1.6)	1.0 (-1.9 to 1.7)		
NHBCS							
Exercise	19	3.0 (0.7)	19	2.5 (0.3)	-0.5 (-1.9 to 1.7)	-0.7 (-1.9 to 2.9); .04	
Usual care	22	2.8 (0.9)	22	3.0 (0.7)	0.2 (-2.0 to 2.3)		
Leptin, ng/mL							
HBCS							
Exercise	29	37.8 (2.6)	28	26.4 (2.0)	-11.4 (-19.3 to -8.5)	-12.3 (-19.0 to -5.9); .002	-6.6 (-13.5 to -2.0); .11
Usual care	27	37.0 (2.0)	24	37.9 (3.3)	0.9 (-2.0 to 2.1)		
NHBCS							
Exercise	19	31.6 (2.0)	19	27.1 (2.1)	-4.5 (-9.0 to -1.6)	-5.7 (-11.5 to -1.4); .007	
Usual care	22	32.0 (2.5)	22	33.2 (2.7)	1.2 (-2.5 to 2.1)		
Adiponectin, ug/mg							
HBCS							
Exercise	29	9.6 (1.0)	28	19.2 (2.6)	9.6 (3.9 to 14.5)	10.1 (3.5 to 15.5); <.001	3.8 (1.0 to 7.5); .06
Usual care	27	9.0 (1.3)	24	8.5 (1.2)	-0.5 (-1.5 to 1.6)		
NHBCS							
Exercise	19	14.1 (2.0)	19	19.7 (2.0)	5.6 (6.5 to 1.3)	6.3 (2.5 to 8.7); .005	
Usual care	22	14.7 (2.5)	22	14.0 (2.7)	-0.7 (-2.0 to 1.9)		
Total cholesterol, mg/dL							
HBCS							
Exercise	29	216.7 (59.6)		161.1 (39.0)	-55.6 (-87.0 to -32.3)	-57.4 (-92.1 to -30.2); <.001	-25.2 (-35.3 to -19.0); .09
Usual care	27	218.4 (60.2)		220.2 (61.3)	1.8 (-2.0 to 2.6)		
NHBCS							
Exercise	19	189.4 (53.7)		160.2 (35.4)	-29.2 (-55.0 to -18.0)	-32.2 (-50.0 to -21.7); .002	
Usual care	22	192.2 (50.5)		195.2 (52.0)	3.0 (0.8 to 5.3)		

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Abbreviations: 95% CI, 95% confidence interval; HBCS, Hispanic breast cancer survivors; HOMA-IR, homeostasis model assessment–insulin resistance; hs-CRP, high-sensitivity C-reactive protein; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor-binding protein 3; NHBCS, non-Hispanic breast cancer survivors; SD, standard deviation.

^aEstimated based on general linear models repeated-measures analysis of variance.

^bEstimated based on linear regression analysis and adjusted for baseline values of the outcome, age, and recent physical activity.