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Metabolic Syndrome, Exercise, and Cardiovascular Fitness in Breast Cancer Survivors

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

Comorbid illness contributes to poorer cancer outcomes and higher mortality. Metabolic syndrome (MetS) includes a cluster of risk factors that are associated with an increased risk of comorbidities. Routine physical activity represents a risk reduction strategy for cancer survivors. From 148 participants in a 12-month randomized control trial (RCT) of a fitness center exercise intervention compared to home physical activity group, a subset analysis was conducted to explore the effect of exercise on MetS risk factors. There were 32 (21.6%) breast cancer survivors who met the criteria for MetS at baseline. Over the 12 months, there were significantly fewer participants who met the criteria for MetS ($p < .01$), and there was significant improvement in individual risk factors, specifically fasting blood sugar ($p = .01$), and high-density lipoprotein (HDL; $p = .02$). Cardiovascular fitness was evaluated and greater heart recovery rate (HRR) was negatively associated with waist circumference, triglycerides, systolic blood pressure, fasting blood sugar, and MetS risk ($p < .02$) and positively associated with HDL ($p = .03$). Oncology advanced practitioners are uniquely qualified to integrate risk reduction into the management of at-risk oncology patients.

The role of the advanced practitioner in oncology is to provide high-quality, patient-centered care to complex patients with unique needs (Ewing, 2015; Wall & Rawson, 2016). One aspect of oncology care is the challenge of managing cancer survivors who are at risk for or have comorbid illness (Edgington & Morgan, 2011). For breast cancer survivors, being overweight or obese significantly contributes to a higher risk for recurrence (Ligibel et al., 2014) and comorbid illness (O'Neill & O'Driscoll, 2015). A higher overall mortality has also been reported (American Society of Clinical Oncology [ASCO], 2014; Ligibel et al., 2014).

Nearly two thirds of breast cancer survivors are overweight or obese (Butross et al., 2012; Calip et al., 2014; Simon et al., 2018), which contributes to an increased risk of develop-

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ing metabolic syndrome (MetS) and other comorbid illnesses (Edgington & Morgan, 2011; O'Neill & O'Driscoll, 2015). Metabolic syndrome has been identified in 20% to 58% of breast cancer survivors (Berrino et al., 2014; Buttros et al., 2012; Calip et al., 2014; Dieli-Conwright et al., 2016; Lohmann, Ennis, Taylor, & Goodwin, 2017; Maiti, Kundranda, Spiro, & Daw, 2010). Metabolic syndrome in breast cancer survivors is associated with an increased risk of cardiovascular disease and higher all-cause mortality (Alberti et al., 2009; Coviello, Knobf, Laclergue, 2013; Simon et al., 2018).

Lifestyle behavior interventions, specifically exercise, healthy eating, and weight loss–designed nutrition counseling, have been shown to reduce the risk for cardiovascular disease, cancer, and diabetes. The purpose of this study was to evaluate the effect of exercise in a subsample of breast cancer survivors with MetS from a larger randomized control year-long exercise clinical trial.

METHODS

Parent Study

We conducted a 12-month randomized control trial (RCT), called The Yale Fitness Intervention Trial (Yale FIT), comparing a fitness center aerobic resistance exercise intervention to a home-based physical activity group. The fitness center intervention consisted of 30 minutes of aerobic activity in the participant's target heart range and 30 minutes of resistance exercises three times weekly. During the first 6 months, the fitness center participants were supervised in small groups by a study-trained interventionist. The second 6 months were unsupervised. The fitness center group was also encouraged to engage in moderate activity on other days of the week. The home-based group received the American Cancer Society "Smart Steps" booklet that provided examples of moderate intensity physical activity. The most common moderate activity among participants was walking. Instructions to the home-based group were based on national recommendations of 30 minutes of moderate activity most days of the week.

Data were collected at baseline, 6, and 12 months. Details on recruitment, enrollment, intervention protocol, and primary outcome of bone mineral density (BMD) have been previously published (Knobf et al., 2016), but of note, the effects of the exercise on bone mineral density were influenced by endocrine therapy. Participants on aromatase inhibitors had significantly decreased BMD at all sites compared to little or no change for participants on no endocrine therapy or those on tamoxifen. Secondary outcomes of Yale FIT were cardiovascular fitness, body composition, and metabolic risk factors (Knobf et al., 2017). Cardiovascular fitness improved in both groups (time on treadmill, $p < .001$) but there was significantly greater improvement for the fitness center group ($p = .03$). Heart rate recovery at 1 minute was significantly improved for the fitness center group compared to the home group after controlling for peak heart rate and age at baseline ($p = .02$). Nearly two thirds of the participants were overweight or obese in the Yale FIT trial. Body mass index at baseline was a predictor of higher insulin ($p < .01$) and insulin resistance ($p = .01$). At 12 months, fasting insulin was significantly higher in the home group compared with the fitness center group ($p = .04$; Knobf et al., 2016).

Metabolic Syndrome Study

We conducted a secondary data analysis to identify participants with risk factors for MetS and evaluate if exercise and type of exercise influenced outcomes over the 1 year of Yale FIT. Metabolic syndrome is defined as having 3 of 5 cardiometabolic risk factors: increased waist circumference (WC), elevated triglycerides, elevated fasting blood glucose, hypertension, and reduced high-density lipoprotein (HDL) cholesterol (Table 1).

In Yale FIT, 21.6% (N = 32) met the criteria for MetS at baseline (Alberti et al., 2009; Dieli-Conwright et al., 2016; Table 2). Of the 32 participants with MetS at baseline, there were more participants in the home group with MetS (n = 22) compared with the fitness center group (n =

Table 1. Risk Factors for Metabolic Syndrome

Waist circumference ≥ 80 cm in women, ≥ 94 cm in men
Triglycerides ≥ 150 mg/dL
HDL cholesterol < 40 mg/dL
Blood pressure ≥ 130 and/or diastolic > 85 mm Hg
Fasting blood glucose ≥ 100 mg/dL

Note. HDL = high-density lipoprotein. Information from Alberti et al. (2009).

Table 2. Changes of Metabolic Syndrome and Risk Factors Over 12-Month Exercise Intervention Among 32 Participants With Metabolic Syndrome at Baseline

Risk factors for metabolic syndrome	Baseline	6 months	12 months	*p* value (GEE)
Waist circumference (cm), mean (SD)	100.0 (13.7)	98.2 (12.6)	95.5 (13.5)	
≥ 80 cm, n/N[a] (%)	25/26 (96.1%)	28/30 (93.3%)	30/32 (93.7%)	.4304
Triglyceride (mg/dL), mean (SD)	163.5 (78.6)	171.0 (94.3)	154.0 (77.6)	
≥ 150 mg/dL, n/N (%)	16/32 (50.0%)	17/31 (54.8%)	14/32 (43.7%)	.4142
HDL cholesterol (mg/dL), mean (SD)	39.6 (10.8)	43.6 (10.8)	44.6 (14.8)	
< 40 mg/dL, n/N (%)	23/32 (71.9%)	10/31 (32.3%)	15/32 (46.9%)	.0209
Systolic BP (mm Hg), mean (SD)	128.1 (14.9)	126.7 (12.3)	122.2 (11.9)	
Diastolic BP (mm Hg), mean (SD)	76.0 (10.8)	73.2 (7.4)	72.8 (7.4)	
Hypertension (≥ 130 or 85 mm Hg), n/N (%)	16/32 (50.0%)	15/32 (46.9%)	12/32 (37.5%)	.1573
Fasting blood sugar (mg/dL), mean (SD)	127.5 (45.9)	125.1 (55.3)	120.9 (57.1)	
≥ 100 mg/dL, n/N (%)	28/32 (87.5%)	23/31 (74.2%)	20/32 (62.5%)	.0114
Metabolic syndrome > 3/5, no. (%)	32/32 (100.0%)	23/31 (74.2%)	20/32 (62.5%)	.0005

Note. GEE = generalized estimating equations; HDL = high-density lipoprotein; BP = blood pressure.
[a]n/N indicates the number of cases/the number of observed samples.

10; p = .01). The mean age was 51.7 years (standard deviation: 6.4), the majority were white (85.8%), and 4.7% were African American and 4.7% Latino. Both groups resulted in fewer participants meeting the criteria for MetS at 12 months, but only the home-based group had a significant change over time (odds ratio = .66 [0.44–0.98]; p = .04). For adjuvant endocrine therapy, more breast cancer survivors who were taking tamoxifen had MetS (30.9%) compared to those on an aromatase inhibitor (17.1%) or no endocrine therapy (20.7%), but these were not statistically different. Among 32 subjects with MetS at baseline, the percentage of participants with MetS at 12 months decreased significantly (p < .01). The decrease of MetS was not statistically significant for all participants (p = .09) but was significant in those who were overweight or obese at baseline (p = .05). Metabolic syndrome in overweight and obese patients on tamoxifen (52.2%) at baseline significantly decreased to 30.4% at 12 months (p = .01).

Cardiovascular fitness as measured by heart rate recovery was negatively associated with waist circumference, triglycerides, fasting blood sugar, blood pressure, and overall MetS risk (p < .02), and positively associated with HDL cholesterol (p = .03).

DISCUSSION

Moderate routine physical activity is an important nonpharmacologic risk reduction strategy for all cancer survivors, especially for those who are overweight or obese, both of which are associated with poorer outcomes (ASCO, 2014; Edgington & Morgan, 2011; O'Neill & O'Driscoll, 2015). Our findings support the benefit of routine physical activity on metabolic risk factors, especially those at higher risk, as defined by criteria for MetS.

Three pilot studies were conducted to evaluate the effects of an exercise intervention compared to usual care in breast cancer survivors on risk factors for MetS (Guinan et al., 2013; Nuri et al., 2012; Travier et al., 2018). Two of the studies reported decreases in components of MetS, specifically lower triglycerides, waist circumference, insulin, and glucose (Nuri et al., 2012; Travier et al., 2018). Limitations of the pilots include small sample sizes (N = 26–37), varying types of exercise (aerobic only vs. aerobic + resistance), and length of the intervention (8–12 weeks).

One RCT was conducted that compared a 16-week supervised aerobic-resistance intervention (one-on-one 3 days a week) with usual care in 100 survivors (Dieli-Conwright et al., 2018). There were significant changes in all risk factors and in MetS over time. However, it is important to note

that this study reported that 77% of subjects met the criteria for MetS at baseline, which is significantly higher than our sample (21.6%) and also that reported from two of the pilot studies (34%–46%; Guinan et al., 2013; Travier et al., 2018). Adherence rate to the RCT supervised intervention was 96%, which likely influenced the significant improvement in the intervention group (Dieli-Conwright et al., 2018). Despite the limitations of the pilot studies, those findings combined with our study results and those of the larger RCT strongly suggest that a routine program of exercise, even if only moderate activity such as walking, can decrease the risk factors for MetS, especially for breast cancer survivors at higher risk for cardiovascular disease and diabetes due to being overweight or obese and who have a sedentary lifestyle.

IMPLICATIONS FOR PRACTICE

Oncology advanced practitioners, specifically oncology nurse practitioners, have been identified as adding value to oncology care because of the holistic perspective of the nursing discipline (Wall & Rawson, 2016). From a survey of 759 breast cancer survivors, nurse practitioners discussed physical activity, nutrition, and weight more frequently than their physician colleagues (Kenison, Silverman, Sustin, Thompson, 2015). However, it was noted that such discussions did not routinely translate into actual change in lifestyle behavior. Thus, innovative strategies are needed to follow up with survivors to reinforce recommendations and assess adoption of those recommendations. Oncology advanced practitioners are uniquely positioned to intervene over time with risk reduction counseling for survivors, especially for those at higher risk for comorbid illness. ●

Disclosure

The authors have no conflicts of interest to disclose.

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