Original Article

An Observational Study to Examine Changes in Metabolic Syndrome Components in Patients With Breast Cancer Receiving Neoadjuvant or Adjuvant Chemotherapy

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BACKGROUND: The authors sought to determine the effect of chemotherapy on the development of metabolic syndrome (MetS) in premenopausal and postmenopausal women undergoing (neo)adjuvant therapy for early-stage breast cancer. **METHODS:** A total of 86 women with early-stage (AJCC stage I-III) breast cancer who were free from clinically diagnosed MetS (defined as 3 of 5 components of MetS) were prospectively tested for the presence of the 5 components of MetS within 1 week before initiating and after completing (neo)adjuvant chemotherapy. The 5 components of MetS measured were waist circumference; blood pressure; and fasting levels of blood glucose, triglycerides, and high-density lipoprotein cholesterol. Anthropometrics (body weight, percentage body fat, fat mass), lipid profile (total cholesterol, low-density lipoprotein cholesterol), glucose metabolism (insulin, homeostatic model assessment of insulin resistance, glycated hemoglobin), and inflammation (C-reactive protein) also were examined before initiating and after completing treatment. **RESULTS:** The current study included 46 premenopausal and 40 postmenopausal women. All individual MetS components and the overall MetS score were found to be statistically significantly increased ($P<.01$) after chemotherapy. Body weight, percentage body fat, fat mass, lipids, glucose metabolism, and inflammation also were found to be statistically significantly increased ($P<.01$). **CONCLUSIONS:** A 12-week to 18-week course of chemotherapy appears to statistically significantly increase MetS and related anthropometrics, biomarkers of glucose metabolism, and inflammation in patients with early-stage breast cancer with no preexisting MetS. Lifestyle interventions such as diet and exercise may be preventive approaches for use during chemotherapy to reduce the onset of MetS in patients with breast cancer. ***Cancer* 2016;122:2646-53**.

KEYWORDS: body composition, breast cancer, chemotherapy, glucose metabolism, metabolic syndrome.

INTRODUCTION

Survivors of breast cancer comprise the largest subgroup of cancer survivors in the United States. Improvements in screening and adjuvant therapies are credited with improving survival from breast cancer. These individuals experience many treatment-associated changes, including weight gain,[1] reduced physical activity levels,[2] and worsening metabolic profiles leading to metabolic syndrome (MetS).[3] MetS includes a cluster of factors such as hypertension, dyslipidemia, and central obesity.[4] It is a highly prevalent disorder, affecting approximately 25% of adults,[5] and is associated with a 2-fold greater risk of diabetes and cardiovascular disease.[6] Specifically, MetS is diagnosed when a woman has any 3 of the 5 following components: 1) a waist circumference $\geq$80 cm (32 inches); 2) an elevated triglyceride (TRI) level $\geq$150 mg/dL or currently receiving drug treatment for an elevated TRI level; 3) reduced high-density lipoprotein cholesterol (HDL-C) $<$40 mg/dL; 4) elevated blood pressure $\geq$130/85 mm Hg or currently receiving antihypertensive drug treatment; or 5) elevated fasting blood glucose $\geq$100 mg/dL or currently receiving drug treatment for elevated glucose.[7] MetS and associated factors, including obesity, physical inactivity, hyperinsulinemia, insulin resistance, elevated inflammatory biomarkers, and altered adipokines, also are associated with an increased risk of breast cancer, all-cause mortality, and an increased risk of disease recurrence.[8,9]

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Postmenopausal patients with breast cancer experience negative changes in their MetS risk factors after chemotherapy, thereby placing them at an increased risk of mortality from cardiovascular and metabolic diseases.[10,11] It is interesting to note that a high rate of MetS-related comorbidities was observed in women who recently completed treatment of breast cancer, with obesity present in 51% of cases, hypertension in 34% of cases, peripheral vascular disease in 26% of cases, and diabetes in 13% of cases.[12] Premenopausal patients with breast cancer also experience detrimental effects from chemotherapy on conditions contributing to MetS; in particular, their body weight may increase, leading to a higher body mass index (BMI) and larger measures of central obesity.[1] Furthermore, chemotherapy in premenopausal patients with breast cancer may induce premature menopause, which is associated with increases in body fat and cholesterol and TRI levels.[1,13] Therefore, it is important to monitor changes in MetS components in both premenopausal and postmenopausal patients with breast cancer during chemotherapy. Understanding the potential detrimental effects of chemotherapy on MetS components and metabolic health is critical to controlling future chronic health problems, improving survival, and enhancing quality of life as clinicians develop survivorship care plans for patients with breast cancer.

The purpose of the current study was to investigate the immediate effects of (neo)adjuvant chemotherapy on MetS components and related anthropometric and metabolic biomarkers among premenopausal and postmenopausal patients with early-stage breast cancer with no preexisting MetS.

MATERIALS AND METHODS

Patients

We developed a prospective observational study that recruited both premenopausal women and postmenopausal women with newly diagnosed, early-stage breast cancer from the medical oncology clinics at City of Hope (COH) National Medical Center. This study was approved by the Institutional Review Board at COH. We obtained informed consent from each participant before the baseline visit (within 1 week before the first treatment visit). A research nurse screened all new patients with breast cancer for the following eligibility criteria: 1) women with newly diagnosed, stage I to III breast cancer; 2) age $\geq$18 years; 3) planned adjuvant chemotherapy after lumpectomy or mastectomy or planned neoadjuvant chemotherapy; and 4) ability to provide informed consent. Participation in this outcome study did not influence the treatment regimens the women received. All patients received chemotherapy as determined by their treating oncologist.

Patients were excluded if they had MetS at the time of chemotherapy. A woman was determined to have MetS if she had any 3 of the following 5 components: 1) a waist circumference $\geq$80 cm (32 inches); 2) a TRI level $\geq$150 mg/dL or currently receiving drug treatment for an elevated TRI level; 3) HDL-C $<$40 mg/dL; 4) blood pressure $\geq$130/85 mm Hg or currently receiving antihypertensive drug treatment; or 5) fasting blood glucose $\geq$100 mg/dL or currently receiving drug treatment for elevated blood glucose.[7] Additional exclusion criteria included $\geq$10% weight loss within the past 6 months or the diagnosis of distant metastatic disease.

Study Measurements

All study measurements were performed on a single day at baseline and after the final treatment visit (within 1 week after the completion of chemotherapy) by trained research staff at COH.

Blood pressure

Blood pressure was measured under resting conditions (participants were seated for 5 minutes) using an automated blood pressure device (Connex ProBP; Welch Allyn Inc, Skaneateles Falls, NY) and was performed twice to ensure accuracy in measures.

Body composition

BMI measured in kg/m^2 was calculated from height and weight measurements. Body composition (lean body mass, fat mass, and percentage body fat) was measured using a portable hand-held bioelectrical impedance device (Omron Healthcare, Hoffman Estates, Ill). Waist and hip circumferences were measured using a fabric measuring tape to determine the circumference of the waist (centered at the navel) and hip (centered on the greater trochanter) for each participant, and used to calculate the waist/hip ratio.

Biomarkers

A 12-hour fasting blood sample was obtained for glucose, insulin, lipid profile (total cholesterol, HDL-C, low-density lipoprotein cholesterol, and TRI levels), glycated hemoglobin (HbA1c), and C-reactive protein (CRP). Insulin resistance was calculated using the homeostatic model assessment (HOMA-IR) as fasting glucose in mg/dL multiplied by fasting insulin in mg/dL divided by 405.[14] Blood samples were analyzed at the clinical pathology laboratory at COH. Lipids, glucose, insulin, and

TABLE 1. Baseline Patient Characteristics (N = 86)

Characteristic N (%)		No. (%)
Mean age (± SD), y	48.2 (10.1)	
Menopausal status	Premenopausal	46 (53)
	Postmenopausal	40 (47)
Race/ethnicity	White	38 (44)
	Asian	6 (7)
	Hispanic	26 (30)
	African American	7 (8)
	Other	9 (11)
Tobacco use	Never	42 (49)
	Current	4 (4)
	Past	40 (47)
Partner status	Married	68 (79)
	Single/divorced	13 (15)
	Widowed	5 (6)
Educational level	High school or equivalent	30 (35)
	College or postgraduate degree	47 (55)
	Other	8 (10)
Employment status	Full time	57 (66)
	Part time	16 (19)
	Retired	13 (15)
Stage (AJCC) of disease	I	34 (40)
	II	42 (49)
	III	10 (11)
Surgery type	Mastectomy	39 (45)
	Lumpectomy	29 (34)
	NA (neoadjuvant chemotherapy)	18 (21)
Chemotherapy type	Doxorubicin and cyclophosphamide plus paclitaxel	36 (42)
	Docetaxel and cyclophosphamide	31 (36)
	Carboplatin plus paclitaxel	8 (9)
	Doxorubicin and cyclophosphamide	6 (7)
	Docetaxel, cyclophosphamide, and trastuzumab	5 (6)

Abbreviations: NA, not applicable; SD, standard deviation.

CRP assays were analyzed on the Vitros 4600 Analyzer (Ortho Clinical Diagnostics, Rochester, NY) using microslide technology. HbA1c was determined using high-performance liquid chromatography (Diazyme, Poway, Calif).

Physical activity assessment

Physical activity history[15] was assessed to capture varying levels of physical activity throughout the patient's lifetime including current levels, quantified as the average number of minutes per week per year over each 5-year period from school age (aged 5-9, 10-14, and 15-19 years) through adulthood (aged 20-24, 25-29, 30-34, 35-39 years and onward to diagnosis).

Statistical Analysis

Sample size estimation

The recruitment of 50 evaluable patients (25 premenopausal and 25 postmenopausal women) would provide 80% power to detect an effect size of 0.584 (58% of the standard deviation of the difference) using a Student *t* test for paired data with a 2-sided significance level of .05 for premenopausal and postmenopausal women. The decision to overenroll was made in the event that there were meaningful differences in MetS between premenopausal and postmenopausal women.

All data were analyzed using SPSS statistical software (version 18.0; IBM Corporation, Armonk, NY). Standard methods were used to compute means, standard deviations, and frequencies. Student *t* tests for paired samples were used to compare MetS, anthropometric, and metabolic biomarkers before the initiation of and after the completion of chemotherapy. One-way analysis of covariance was used to compare means adjusting for age, race, type of chemotherapy, duration of chemotherapy, BMI at baseline, and menopausal status. Bonferroni multiple comparison post hoc tests were used to compare mean values. All statistical tests were conducted with 2-sided alternative hypotheses, and P values $<.05$ were considered to be statistically significant.

RESULTS

Patient Population

Over 36 months, a total of 963 women were screened for study participation; 153 (16%) were eligible. Among the

TABLE 2. Changes in MetS After Chemotherapy Among Patients With Early-Stage Breast Cancer

Variable Post-treatment	Pretreatment[a]	Posttreatment[a]	% Change	*P*
Waist circumference, cm	86.7 (12.9)	90.7 (11.2)	4.7	<.01
Blood pressure, mm Hg				
Systolic	122 (25)	128 (27)	5.1	<.01
Diastolic	83 (13)	90 (18)	8.6	<.01
Fasting blood glucose, mg/dL	97.2 (19.8)	117.0 (37.0)	20.3	<.01
Triglycerides, mg/dL	108.7 (47.6)	128.7 (58.9)	18.4	<.01
HDL-C, mg/dL	57.9 (12.0)	50.6 (14.9)	−12.6	<.01
No. of MetS components	1.0 (0.5)	4.0 (1.0)	275.0	<.01

Abbreviations: HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome.
[a] Shown as the mean (± standard deviation).

TABLE 3. Changes in Anthropometrics After Chemotherapy Among Patients With Early-Stage Breast Cancer

Variable Post-treatment	Pretreatment[a]	Posttreatment[a]	% Change	*P*
Height, cm	161.2 (7.4)	-	-	-
Weight, kg	69.2 (17.1)	74.7 (17.9)	7.7	<.001
BMI, kg/m^2	25.9 (6.3)	29.0 (7.0)	11.5	<.001
Lean body mass, kg	45.8 (9.7)	47.1 (9.6)	2.9	.29
Fat mass, kg	23.6 (10.3)	27.6 (9.5)	16.9	<.001
Body fat, %	33.1 (8.2)	36.0 (5.1)	8.9	<.001
Hip circumference, cm	40.8 (4.3)	41.5 (7.4)	1.8	.41
Waist/hip ratio	0.84 (0.07)	1.1 (0.1)	30.3	.28

Abbreviation: BMI, body mass index.
[a] Shown as the mean (± standard deviation).

eligible women, 86 women (56%) consented to participate in the study, 46 of whom (53%) were premenopausal at the time of diagnosis. The primary reason for ineligibility was the presence of MetS at the time of diagnosis. Baseline characteristics are presented in Table 1. The mean age of the patients was 48.2 years (±10.1 years). The majority of patients were white (38 patients; 44%) or Hispanic (26 patients; 30%), nonsmoking (82 patients; 95%), employed (73 patients; 85%), and well-educated (77 patients; 90%). Overall, the population was sedentary, averaging 7.2 minutes (±5.8 minutes) of physical activity per week within the previous 12 months. Initial mastectomy was performed in 39 patients (45%) and lumpectomy was performed in 29 patients (34%). Neoadjuvant therapy was administered in 18 patients (21%). The chemotherapy regimens included dose-dense cyclophosphamide and doxorubicin followed by paclitaxel in 36 patients (42%); docetaxel and cyclophosphamide in 31 patients (36%); carboplatin and paclitaxel in 8 patients (9%); cyclophosphamide and doxorubicin in 6 patients (7%); or docetaxel, carboplatin, and trastuzumab in 5 patients (6%). The average duration of chemotherapy was 15.3 weeks (±2.7 weeks). The duration and regimen of chemotherapy did not appear to influence the results.

MetS Components

The individual components of MetS before and after chemotherapy are shown in Table 2. After chemotherapy, a new diagnosis of MetS was made in 72.5% of the patients. Each individual component of MetS was found to be statistically significantly worsened by the completion of chemotherapy ($P<.01$). The individual MetS components remained significant when adjusted for age, race, type/duration of chemotherapy, and BMI. The percentage changes observed in components of MetS varied from 4.7% (waist circumference) to 20.3% (blood glucose) over the approximately 4-month duration of chemotherapy. No statistically significant differences were observed between premenopausal and postmenopausal patients ($P>.01$).

Pretreatment and posttreatment anthropometric values are shown in Table 3. Before the initiation of chemotherapy, patients had a mean body weight of 69.2 kg (±17.1 kg) and a BMI of 25.9 kg/m^2 (±6.3 kg/m^2). Patients demonstrated a high percentage of body fat (33.1%±8.2%) despite the BMI classification of normal-overweight. Body weight, BMI, fat mass, and percentage body fat were all found to be statistically significantly higher after the completion of chemotherapy when compared with prechemotherapy values ($P<.01$). The mean

TABLE 4. Changes in Metabolic Biomarkers After Chemotherapy Among Patients With Early-Stage Breast Cancer

Variable Post-treatment	Pretreatment[a]	Posttreatment[a]	% Change	*P*
Lipid profile				
Total cholesterol, mg/dL	185.5 (48.3)	201.9 (45.5)	8.8	<.001
LDL-C, mg/dL	100.5 (34.4)	111.1 (43.7)	10.5	<.001
Glucose metabolism				
Fasting insulin, mIU/mL	18.9 (21.8)	32.6 (17.3)	73.1	.05
HOMA-IR	4.52 (1.1)	9.4 (1.5)	108.3	<.001
HbA1c, %	5.4 (0.4)	5.9 (0.6)	8.6	<.001
Inflammation				
CRP, mg/L	0.37 (0.36)	0.49 (0.21)	31.9	.04

Abbreviations: CRP, C-reactive protein; HbA1c, glycosylated hemoglobin; HOMA-IR, homeostatic model assessment-insulin resistance; LDL-C, low-density lipoprotein cholesterol.
[a] Shown as the mean (± standard deviation).

weight gain was 5.5 kg (±17.4 kg). Lean body mass was not found to be statistically significantly changed ($P>.05$), whereas the mean percentage body fat increased by 8.9%. Adverse changes in these anthropometric values remained statistically significant when adjusted for age, race, and type/duration of chemotherapy. The percentage changes observed in anthropometrics varied from 1.8% (hip circumference) to 30.3% (waist/hip ratio) over the approximately 4-month duration of chemotherapy. No statistically significant differences were observed between premenopausal and postmenopausal patients ($P>.01$).

Metabolic biomarkers, including lipid profile, glucose metabolism, and inflammation before and after chemotherapy are shown in Table 4. It is interesting to note that despite the exclusion of patients with diagnosed MetS or elevated singular components of MetS at baseline, biomarkers of glucose metabolism, including fasting insulin and HOMA-IR, were found to be clinically elevated before treatment (18.9 mIU/mL and 4.52, respectively). Total cholesterol, low-density lipoprotein cholesterol, HOMA-IR, insulin, HbA1c, and CRP were found to be statistically significantly higher after the completion of chemotherapy when compared with prechemotherapy values ($P<.05$). Furthermore, these changes in metabolic biomarkers remained statistically significantly elevated when adjusted for age, race, and type/duration of chemotherapy. The percentage changes in metabolic biomarkers observed varied from 8.6% (HbA1c) to 108.3% (HOMA-IR) over the approximately 4-month duration of chemotherapy. No statistically significant differences were observed between premenopausal and postmenopausal patients ($P>.01$).

DISCUSSION

To the best of our knowledge, the current study is the largest study to date to systematically address the effect of (neo)adjuvant chemotherapy alone on MetS and its components in both premenopausal and postmenopausal women. Smaller studies have reported MetS or its components after the completion of all treatments for breast cancer.[3,16,17]

Of critical importance in the current study is how quickly metabolic changes occurred in patients with breast cancer who were free from any serious comorbidities at the time of diagnosis. Within 4 months, newly diagnosed MetS occurred in >70% of the current study population. In combination with the weight gain, hypercholesterolemia, hyperinsulinemia, and insulin resistance that we also observed, these patients are now susceptible to additional health-related concerns, including diabetes, cardiovascular diseases, and cancer recurrence.

A significant number of women treated at the study institution had at least 3 of the 5 criteria for MetS at the time of diagnosis. We screened 963 patients, of whom only 153 (16%) were eligible. This is by itself particularly striking because MetS is recognized as negatively affecting overall survival in patients with breast cancer.[18-20] The current study provides insight not only into the potential metabolic changes after the completion of (neo)adjuvant chemotherapy but also into the preexisting metabolic disturbances present at the time of chemotherapy initiation. This emphasizes the need to focus research efforts on large randomized controlled trials of modifiable lifestyle factors such as body size, physical activity, and diet to offset these metabolic disturbances and improve prognosis.[21]

Weight gain after treatment has been previously reported by numerous investigators. Although others have reported changes in weight at 1 year, we documented an increase in body weight of approximately 8% (approximately 5 kg) at the time of the completion of chemotherapy. This surpasses the previously documented average of

approximately 2 to 3 kg after chemotherapy.[1,22] The results of the current study indicated a significant increase in waist circumference, averaging 90.7 cm after treatment, indicating the development of or progression of central obesity during the course of treatment, which may drive the additional metabolic disturbances observed in the current study population.

One of the most interesting findings from the current study was the effect of chemotherapy on glucose metabolism. Fasting insulin increased by approximately 73% and HOMA-IR more than doubled, increasing approximately 108% over the 4-month duration of the current study. These are profound changes, yet it is interesting to note that both insulin and HOMA-IR were elevated at baseline (18.9 mIU/mL and 4.52, respectively). The duration of these disturbances in glucose metabolism before diagnosis in the current study population is unknown, as is their potential effect on carcinogenesis. Similar to the current study, Guinan et al reported a significant increase in fasting insulin, HOMA-IR, and HbA1c in 61 women with breast cancer after adjuvant treatment, which included chemotherapy, radiotherapy or anti-human epidermal growth factor receptor 2 (HER2)-directed therapy (ie, trastuzumab).[3]

Many investigations have followed glucose metabolism in patients with breast cancer at different time points in the disease trajectory. Overall, elevated fasting insulin is associated with distant disease recurrence and death in patients with early-stage breast cancer,[23] elevated insulin levels are associated with a 2-fold increase in the risk of postmenopausal breast cancer,[24] patients with a more advanced stage of disease (stage II-IV) are more likely to be hyperinsulinemic,[11] and elevated HOMA-IR scores are associated with reduced breast cancer survival and all-cause survival.[9] Furthermore, hyperinsulinemia in women with breast cancer reflects the presence of insulin resistance, as indicated by a significant correlation of hyperinsulinemia with HOMA-IR.[25] It is important to note that although the index of insulin resistance (HOMA-IR) more than doubled, the rise in HbA1c was marginal (an 8.6% change from baseline). The lack of a clinically significant change in HbA1c demonstrates its limited value in assessing the degree of deterioration in glucose metabolism during weight gain; because of the capacity of beta cells for insulin secretion and masking hyperglycemia, it further increases the importance of using HOMA-IR or other measures of insulin sensitivity in MetS rather than HbA1c. Collectively, these observations support the need to design interventions that target hyperinsulinemia and insulin resistance in patients with breast cancer for long-term survivorship, perhaps by using metformin, which lowers insulin and improves insulin resistance in nondiabetic women with breast cancer.[26,27]

The current study also is unique in that it reported CRP levels before and after chemotherapy in this population, which to our knowledge has not been previously investigated. CRP is among the many circulating biomarkers of inflammation that have been evaluated as potential mediators of the association between obesity and cancer. CRP concentrations are elevated with obesity[28] and insulin resistance,[29] and may be an important independent biomarker for long-term survival in survivors of breast cancer.[30-32] In the current study, a 32% increase in CRP after chemotherapy was observed, suggesting an increase in systemic inflammation. Previous studies have characterized CRP levels at different time points in the disease trajectory. CRP was found to be moderately to severely elevated (5.1±5.3 mg/dL) in 91% of overweight survivors of breast cancer (42 survivors) who were using adjuvant hormone therapy[33] and was found to be significantly elevated (5.0±4.2 mg/dL) in obese, insulin-resistant survivors of breast cancer (18 survivors) when compared with normal-weight, non-insulin-resistant survivors (19 survivors); obese, non-insulin-resistant survivors (16 survivors); or normal-weight, insulin-resistant survivors of breast cancer (16 survivors).[34] Collectively, previous studies assessing CRP in patients with breast cancer indicated that CRP is an important link between inflammation, prognosis, and metabolic presentation that should be closely monitored throughout survivorship.

The lack of differences observed at baseline and after chemotherapy among premenopausal and postmenopausal patients with breast cancer across all outcomes is surprising based on previous literature that suggested that, before the initiation of chemotherapy, premenopausal patients are leaner, have a lower BMI, and have a smaller waist circumference.[35] Regardless, premenopausal patients experience similar detrimental changes to metabolic dysfunction and anthropometrics as postmenopausal patients during adjuvant therapy.[35] In fact, a recent observational study noted greater increases in BMI in premenopausal patients compared with postmenopausal patients after chemotherapy.[36] It is possible that due to the sedentary behavior of all of the patients in the current study at baseline that they were similarly experiencing an energy imbalance favoring weight gain and metabolic dysfunction that was exacerbated further by chemotherapy. Long-term follow-up of the current study cohort would allow for the examination of changes in metabolic dysfunction by menopausal status.

Potential mechanisms exist to explain the metabolic deterioration after chemotherapy observed in the current study. Weight gain may be one of the critical driving factors because the current study participants experienced, on average, an approximately 8% gain in body weight, an approximately 17% gain in fat mass, and an approximately 12% increase in BMI. Thus, a group with an overall normal BMI before chemotherapy was reclassified as overweight/obese after chemotherapy. Waist circumference, which is used to characterize metabolically active, visceral adipose tissue, increased by approximately 5%. Visceral adipose tissue has been proposed to promote the development of inflammation[37] and insulin resistance.[38,39] This could explain the increased insulin resistance observed in the population in the current study. Overall, weight gain leading to obesity is associated with elevated levels of glucose, TRI, and blood pressure, and reduced HDL-C, thus predisposing women to MetS.[40]

The current study has limitations. First, we were unable to capture self-reported dietary intake from the patients. We initially set out to collect such information from all of the participants before treatment, weekly during the course of treatment, and at the completion of treatment to determine whether dietary habits had changed. However, this task appeared to be too burdensome for the majority of study participants due to the time and effort required to document dietary habits on a weekly or even sporadic basis. We were able to collect dietary caloric intake for 7 of the 86 patients; among these women, we observed no statistically significant change in the average amount of calories consumed (data not shown) from before the initiation of treatment to after its completion. Second, although to the best of our knowledge the sample size in the current study is the largest to date to study MetS, it is a small representation of patients with breast cancer undergoing chemotherapy. Third, despite our efforts to include a racially diverse population, the current study sample did not include a large representation of Asian or African American patients. Fourth, our original study protocol did not allow for an extended follow-up period and therefore we do not know whether the changes in components of MetS persisted over time or if they resolved. We are currently in the process of incorporating a follow-up period to reexamine metabolic dysfunction at 1, 3, and 5 years after the completion of chemotherapy. Last, the current study lacks a control group with which to assess whether the patients would have experienced these changes in the absence of chemotherapy.

Conclusions

Patients with breast cancer who undergo (neo)adjuvant chemotherapy experience an impaired metabolic presentation, as noted by worsened components of MetS, anthropometrics, and biomarkers of glucose metabolism. The findings of the current study contribute to the growing body of literature that suggests the need to strategize appropriate interventions to offset these detrimental metabolic effects or, when possible, to initiate them as preventive measures before the start of treatment.

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CONFLICT OF INTEREST DISCLOSURES

Behrouz Salehian has received personal fees from Eisai Inc for work performed outside of the current study.

AUTHOR CONTRIBUTIONS

Christina M. Dieli-Conwright conceived the study, designed the methods, and analyzed the data. **Christina M. Dieli-Conwright**, **Louise Wong**, and **Sarah Waliany** collected and entered the data. **Christina M. Dieli-Conwright**, **Leslie Bernstein**, **Behrouz Salehian**, and **Joanne E. Mortimer** wrote the article.

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