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Exercise after diagnosis and Metabolic Syndrome among Breast Cancer Survivors: A report from the Shanghai Breast Cancer Survival Study

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Abstract

Metabolic syndrome (MetS) is an established risk factor for cardiovascular diseases and mortality. Limited data are available on the prevalence of MetS and its association with exercise among breast cancer survivors. The present study included 1696 breast cancer survivors from the Shanghai Breast Cancer Survival Study, a population-based prospective cohort study conducted between April 2002 and October 2011 in Shanghai, China. All women had a physical examination taken at study clinic approximately 60 months post-diagnosis. Exercise was assessed at approximately 6, 18, 36, and 60 months post-diagnosis. Information on medical history, tumor characteristics, cancer treatment, anthropometrics, and lifestyle were collected at study enrollment. Associations between exercise and MetS at 60 months post-diagnosis were evaluated with multivariable logistic regression models. The mean age of the study population was 56.68 at 60-month survey and the mean follow-up since cancer diagnosis was 63.66 months. The prevalence of MetS using NCEP-ATPIII criteria at approximately 60 months after diagnosis was 33.14%. Among overweight and obesity breast cancer survivors (BMI≥25 kg/m^2 at baseline), the prevalence was 55.18%. The most common type of exercise in this population was walking (45.40%) at baseline. Exercise participation between 6 and 60 months post-diagnosis was inversely associated with the prevalence of MetS with the adjusted OR for exercise participation of ≥3.5 hours/week (30 minutes/day) being 0.69 (95% CI: 0. 0.48–0.98). In addition consistent exercise participation reduced the prevalence of MetS (adjusted OR 0.70 (95%CI: 0.50–1.00). Associations of exercise with MetS were not modified by baseline WC, BMI, comorbidity, baseline menopausal status, TNM stage, cancer treatment, or ER/PR status (*P* interactions >0.05). Regular and persistent exercise after cancer diagnosis, even at low-to-moderate intensity level, decrease the prevalence of MetS among long-term breast cancer survivors.

Keywords

Breast cancer; Metabolic Syndrome; Exercise; Survivorship

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Conflict of interest The authors declare they have no conflict interest.

Introduction

The number of breast cancer survivors has continued to grow with advances in early diagnosis and cancer treatment (1–3). With the improvement of survival rate, the impact of comorbidity on survival and quality of life among long-term breast cancer has becoming an important issue (4).

Metabolic syndrome (MetS) is characterized as a cluster of conditions including hyperglycemia, abdominal obesity, dyslipidemia, and high blood pressure, and is associated with cardiovascular diseases and death (5–6). Emerging evidence implicates MetS as a long-term risk factor for cancer, but also suggests that certain cancer therapies might increase risk of developing MetS among cancer survivors (7–9). One recent meta-analyses of cross-sectional studies found that adult cancer survivors with hematologic malignancies were at an increased risk of MetS (10). The issue for MetS and related risk factors among breast cancer survivors has attracted growing attention (8). Anti-estrogen hormonal therapy may be associated with the development of MetS among breast cancer survivors. Use of aromatase inhibitors (AIs) agents in women with breast cancer can worsen lipid profiles, increase hypercholesterolemia, and increase risk of adverse cardiovascular outcomes (11). Lifestyle changes after cancer diagnosis and treatment may also play a role in the development of MetS (12). Previous studies have shown that high levels of exercise are inversely correlated with the prevalence of MetS in the general population (13–15). However, whether exercise participation can reduce the risk of MetS among cancer survivors has been less studied. Exercise was found to associated with the development of MetS childhood cancer survivors (16). However, data among breast cancer survivors is scant. We only found one previous report which shown that MetS was diagnosed in 54.8% of overweight postmenopausal breast cancer survivors (17). To our knowledge, no study has specifically evaluated the association between exercise and MetS among breast cancer survivors. As metabolic and hormonal parameters related to MetS may affect breast cancer prognosis (18–20) and MetS is associated with increased risk of CVD disease and mortality (21–22), it is of particular importance to identify modifiable factors related to MetS among breast cancer survivors so that proper preventive measurements can be taken.

Using data from the Shanghai Breast Cancer Survival Study (SBCSS), a prospective cohort of female breast cancer survivors, we examined the prevalence of MetS approximately 5 years after cancer diagnosis, and evaluated the association of exercise after diagnosis with the risk of MetS and its components.

Materials and Methods

The study was approved by the institutional review boards of all participating institutions: the Shanghai Municipal Center for Disease Control and Prevention and Vanderbilt University. Written, informed consent was obtained from all study participants.

Study Participants

Study participants were female breast cancer survivors enrolled in the SBCSS, a population-based prospective cohort study conducted in Shanghai, China. Details of the study design and methods have been previously described (23–24). In short, a total of 6299 women diagnosed with breast cancer between March 2002 and April 2006 were identified from the Shanghai Cancer Registry, and 5042 were enrolled (participation rate, 80.0%) and completed baseline interviews at approximately 6 months after cancer diagnosis. The cohort has been followed up by in-person interviews at 18 months, 36 months, and 60 months after cancer diagnosis. The 60-month interview was completed for 3640 patients out of 4439 surviving patients (response rate, 82.0%). A subset of women who completed the 60-month in-person interview participated in a physical health examination at a designated study clinic, which included assessment of MetS components (n=1696) and they were included in the current analysis. The MetS components tested include waist circumference (WC), blood pressure (BP), fasting plasma glucose (FBG), triglycerides (TG), and high density lipoprotein (HDL-C).

Data Collection

Structured questionnaires were used to collect data during in-person survey took place at approximately at 6-, 18-, 36- and 60- months after cancer diagnosis. The survey questionnaire at the 6-month post-diagnosis baseline interview covered socio-demographic characteristics, disease history, menstrual and reproductive history, diet, lifestyle (such as exercise, smoking), medication use, CAM use, as well as quality of life (QOL). Clinical information collected included TNM stage at diagnosis, estrogen receptor (ER) and progesterone receptor (PR) status, type of surgery, chemotherapy, radiation therapy, chemotherapy, and hormonal therapy at baseline. Medical charts were reviewed to verify clinical and treatment information. Anthropometric measurements of height, weight, and waist and hip circumference were measured at 6 and 60 months survey. Exercise was updated at each follow-up surveys (i.e., 18, 36, and 60 months post-diagnosis). Anthropometric measurements were taken according to a standard protocol. Body mass index (BMI) at baseline and the 60-month post-diagnosis survey were calculated. A Charlson comorbidity index was created for each woman based on a validated comorbidity scoring system (25) and the diagnostic codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*.

Exercise assessment

Using a validated exercise questionnaire (26), participants were asked whether they participated in exercise regularly (at least twice a week) at of each the 6, 18, 36, and 60-month interview. If the woman answered “Yes”, she was further asked to report up to 5 of the most common activities in which she participated. At the baseline, 6-month post-diagnosis interview, women reported activities that took place during the 6 months preceding the interview. At subsequent interviews, women reported activities since the last interview (i.e., for the preceding 12 or 18 months or 24 months). No women reported participating in more than 4 types of exercise during the first 18 months after diagnosis, and only 4 cases of women reported participating in 5 types of exercise at the 36-month post-diagnosis interview, and 1 case reported participating in 5 types of exercise at 60-month post-diagnosis interview. Patients were asked how many hours per week they spent exercise (eg. walking, jogging, and swimming). Given that exercise during the first 6 month post-diagnosis interview may be influenced by cancer treatments, a variable combining exercise participation between 6 months and 60 months (18, 36, and 60-month interview) after diagnosis among breast cancer survivors was created as a cumulative level of exercise. According to the exercise recommendation “a half-hour of exercise every day” (27), all patients were classified into one of the following categories: no exercise (0 hours per week), ≤3.5 hours per week, and >3.5 hours per week. We derived patterns of exercise participation according to information collected at the post-diagnosis surveys as follows: 1) “never participation refers to those with no exercise participation reported at any survey; 2)”consistent participation” refers to participants who reported exercise participation all four relevant follow-up surveys; and 3) “non-consistent participation” refers to those who reported to have exercised in some but not all surveys. The two latter patterns were included in the “ever participation” category. A variable combining exercise participation over the entire 60 months after diagnosis was also created as a cumulative level of exercise.

Furthermore, each activity was assigned a metabolic equivalent (MET) score, based on the method proposed by Ainsworth (28). The score for MET-hours per week for each activity was calculated from the hours per week the participant reported engaging in that activity multiplied by the assigned MET score. The MET score for individual activities were summed to derive a total exercise MET score.

MetS evaluation

The following MetS components were assessed at the 60-month, post-diagnosis interview during a physical examination at the Health Physical Examination Center of the Shanghai Municipal Center for Disease Prevention & Control: anthropometric measurements (waist circumference (WC), height, weight); blood pressure; and clinical laboratory assessments, including FBG, lipids (total cholesterol (TC), TG, HDL-C, and low density lipoprotein (LDL-C)). Blood pressure was measured using a sphygmomanometer. Abdominal circumference was evaluated at midway between the iliac crest and the last rib. Blood samples for fasting glucose, triglycerides, and cholesterol tests were obtained after overnight fasting.

MetS was defined using two approaches: the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) definition (modified in 2005) (27) and the International Diabetes Federation (IDF) definition (revised in 2006) (29). According to the NCEP-ATPIII definition, participants who met at least three of the following five criteria were considered to have MetS: waist circumference (WC) ≥ 88 cm; fasting blood glucose level ≥6.1 mmol/L; fasting TG level ≥1.7 mmol/L; fasting HDL-C <1.295 mmol/L; and blood pressure ≥ 130/85 mmHg. According to the 2006 IDF definition, the same five criteria were used, but the presence of central adiposity (WC≥80 cm) as a required component to define MetS. The NCEP-ATPIII definition of MetS is the most widely used and clinically relevant guideline (30).

In this analyses of the association of exercise and MetS, patients who reported a diagnosis of diabetes mellitus at baseline interview were excluded (n=80).

Statistical Analysis

The primary outcome of this study was prevalence of MetS at approximately 5-years post-diagnosis. Analyses of variance (ANOVA) and χ^2 tests were conducted to examine differences between women included in the present study and all women who completed the 60-month interview. Logistic regression model was used to evaluate the association of exercise participation during the 60 months post-diagnosis and the prevalence of MetS. Women reporting no exercise participation after breast cancer diagnosis served as the reference group. Odds ratios (ORs) and 95% confidence intervals (CIs) were adjusted for age at diagnosis, education at baseline, BMI at baseline, menopausal status at baseline, TNM status and Charlson comorbidity index at baseline. BMI was categorized as normal (BMI <25 kg/m^2), overweight (BMI ≥25-<30 kg/m^2), and obese (BMI ≥30 kg/m^2). Analyses of the association of exercise and MetS were further stratified by BMI and WC at baseline, menopausal status at baseline, cormorbidity at baseline, TNM stage, ER/PR status, and cancer treatment. Multiplicative interaction was tested by using the log-likelihood test in the logistic models by introducing interaction. Tests for trend were performed by entering the categorical variables as continuous parameters in the models. A p-value of <0.05 was be used to define statistical significance. All tests were conducted by using SAS version 9.2 (SAS Institute, Cary, NC).

Results

Among the 1696 study participants, the mean age at the 60-month post-diagnosis survey was 56.68 (SD=7.79) and the mean months of follow-up after cancer diagnosis was 63.66 (range: 59.04–87.89). The demographic and clinical features of the study population, and the comparison of these characteristics between women in the present study and women who completed the 60-month survey (n=3640) are presented in Table 1. Compared with women who completed the 60-month survey, those in the current study were younger, had higher education, were more likely to have received chemotherapy, and were less likely to be postmenopausal at study enrollment. Women in the present study also had a lower comorbidity index, BMI, and WC at the baseline survey, compared to all women who completed the 60-month interview. Regular participation in exercise was not significantly different between the study population and women who completed the 60-month interview.

At 6-month post-diagnosis survey, 65.92% of women reported regular exercise participation. The corresponding percentages were 74.59%, 74.82%, and 66.75% at 18, 36 and 60 months post-diagnosis, respectively. The major types of exercise in this population included walking (48.12%), gentle gymnastics (15.74%), body building using fitness equipment (6.53%) and traditional Chinese exercises (5.72%, including Tai Chi and Qigong) at baseline survey. Similar results were observed at 18, 36 and 60 months post-diagnosis among this study participants, but more participants were involved in the traditional Chinese exercises (20.43%, 20.52%, and 18.83%, respectively).

The duration of exercise participation increased with time since diagnosis. Among women who reported exercise participation, the percent who spent longer than 3.5 hours per week was 32.65%, 58.18%,62.57% and 64.49% at 6-, 18-, 36- and 60-month survey, respectively. The mean duration of exercise participation was 3.11 hours per week (median 8.87 MET-hr/wk). at 6-month post-diagnosis survey and increased to 4.87 (median 16.00 MET-hr/wk), 5.13 (median 18.00 MET-hr/wk) and 5.18 hours per week (median 18.10 MET-hr/wk) at 18-, 36-, and 60-month post-diagnosis survey.

As shown in Table 2, according to NCEP-ATP III and IDF definitions, the prevalence of MetS among breast cancer survivors at 5 years post-diagnosis was 33.14% and 36.56%, respectively. Older age at diagnosis (≥60 years) was associated with a higher prevalence of MetS. The prevalence of MetS using NCEP-ATP III criteria by BMI category was 22.27% among normal/underweight participants, 51.43% among overweight participants, and 80.56% among obese participants. The prevalence of each MetS component was as follows: WC≥88cm (19.34%), high triglycerides (42.81%), high blood pressure (59.91%), low HDL (36.73%) and high blood glucose (31.60%) (data not shown in tables).

Table 3 presents associations of cumulative exercise over the entire 60 months after diagnosis and between 6 and 60 months post-diagnosis with the prevalence of MetS among breast cancer survivors at 60 months post-diagnosis. According to the NCEP-ATP III definition, prevalence of MetS was significantly lower for survivors who reported exercise participation of at least 3.5 hours/week (30 minutes/day) between 6 and 60 months post-diagnosis, compared to women who reported no exercise participation during this time (adjusted OR: 0.69, 95% CI: 0.48–0.98, P for trend =0.005). Consistent exercise participation reduced the risk of MetS (adjusted OR: 0.70, 95%CI: 0.50–1.00, P for trend =0.005). Similar results were found for cumulative exercise over the first 60 months after diagnosis, but the P for trend for duration of exercise was not statistical significant (P=0.09).

Table 4 displays results for the association of cumulative exercise between 6 months and 60 months post-diagnosis and each of the specific components of MetS, and the number of

MetS components. We found that exercise was significantly associated with only one specific MetS component, i.e., abdominal obesity (WC≥88cm).

As Table 5 shows, associations of exercise with risk of MetS were not modified by baseline WC, BMI, menopausal status, Tamoxifen use, radiotherapy use (*P* for interactions >0.05 for all), although significant associations were only observed for breast cancer survivors using Tamoxifen and those with BMI< 25. Vast majority of our study participants received chemotherapy (93.9%) prevented a stratified analysis by this treatment, while the results suggested that a statistically significant inverse association was seen in that subgroup received chemotherapy. Similarly, no significant interactions were observed for associations of exercise and MetS by comorbidity, TNM stage, or ER/PR status (data not shown).

Discussion

In this longitudinal population-based cohort study of breast cancer survivors, we found that regular exercise at least 30 minutes a day and consistent exercise participation for approximately five years after diagnosis was significantly associated with reduced prevalence of MetS at 5-years post-diagnosis of breast cancer. This association varied little by WC, BMI, menopausal status, comorbidity, TNM stage, ER/PR status, and cancer treatment. Exercise was also associated with reduced WC at 5-years post-diagnosis.

Because cancer treatments may lead to lifestyle changes through physical complications or psychological stress, exercise participation of breast cancer patients receiving cancer treatments may be reduced (31–32), and this was confirmed in the present study. Specifically, exercise participation was lowest within the first 6 months post-diagnosis, and after 6 months post-diagnosis, the median duration increased, which is consistent with exercise change patterns observed in previous studies (33–34). Due to the concern that exercise in the first 6 months post-diagnosis are confounded by cancer related treatments, we focus on the discussion on results generated based on exercise participation during 6 and 60 months post-diagnosis.

The findings in the present study are consistent with previous studies conducted in the general population indicating that the regular physical activity is associated with reduces risk of MetS (35–37). The musculoskeletal, endocrine, cardiovascular, immune and neurological system of the body are all influenced to some degree when a person participates in exercise (38). A study of survivors of childhood cancer found that reduced exercise was involved in the development of metabolic syndrome (16) We identified only one study to date of the association of exercise and the risk of Mets among breast cancer survivors. This study of 29 cases showed that combination exercise training can improve metabolic syndrome parameters in postmenopausal breast cancer patients (39).

Weight gain is common among breast cancer survivors in Western countries (40) and this also has been confirmed in our study population (41). The presence of visceral adipose tissue may directly lead to metabolic syndrome, because of its hyperlipolytic state and the contribution of excess free fatty acids to insulin resistance (5). In our study we found that exercise was associated with reduced WC at 5-years post-diagnosis. Similar results were reported by investigators using data from the National Health and Nutrition Examination Survey (42), which showed that increasing physical activity was negatively associated with adiposity among breast cancer survivors. An intervention study among African American breast cancer survivors reported that regular moderate exercise, such as walking, appears to improve BMI and anthropometric measurements (43). These data suggest that the beneficial of exercise on MetS is likely to be mediated through the weight reduction and reduced central adiposity.

A working group of the American College of Sports Medicine published a major review and update on physical activity and cancer survivors in 2010 in MSSE (44). There was consensus that exercise was safe and appropriate during and after cancer treatments and resulted in improvement in physical functioning and quality of life for cancer survivors. This review also indicated that the benefits for cancer survivors were sufficient for the recommendation to avoid inactivity following the 2008 Physical Activity Guidelines(45), which stated that physical activity can significant reduce the risk of some cancers and benefits the quality of life for cancer survivors. The majority of women in our study participated in low to moderate levels of exercise, such as walking, and our results indicated that approximately 30 minutes of participant in low and moderate activities daily may achieve the same goal of reducing the risk of MetS among breast cancer survivors.

Our study has several strengths. To our knowledge, it is the first population-based, longitudinal study to prospectively evaluate the effect of post-diagnosis exercise on the prevalence of MetS among long-term breast cancer survivors. The population-based study design and the high response and follow-up rates largely minimized selection bias. Multiple exercise assessments were implemented and the detailed exercise information was collected. This improved the exposure assessment. The data on socio-demographic, lifestyle and medical factors, and anthropometrics collected using structured and/or validated questionnaires allowed a detailed adjustment for potential confounding factors and stratified analyses for evaluation of potential interactions.

Several limitations of this study should be mentioned. First, exercise information was self-reported, which can be subject to recall bias or over-reporting. However, our validation study indicated that the self-reported exercise questionnaire has high validity (26). Second, our study included only one assessment of MetS, and MetS status at baseline was unknown. However, we had collected detailed information on disease history (including diabetes, hypertension, heart disease and so on) at baseline. We excluded those cases with diabetes history at diagnosis when assessing the association between post-diagnosis exercise and the prevalence of MetS. We also adjusted for the baseline comorbidy index in our analysis. Nevertheless, because our study design did not allow identification of the onset of MetS, temporality between exercise participation and development of MetS cannot be determined. Lastly, the participants of current study differ from the entire cohort in several demographic and clinical characteristics which may influence the generaliziblity of the study results.

In conclusion, our results indicate MetS is highly prevalent in long-term overweight breast cancer survivors and regular exercise at least 30 minutes a day may decrease the risk of MetS. Given the negative health consequences of MetS, further studies are warranted to evaluate the strategies for screening, monitoring, and treating MetS, and development of exercise programs for breast cancer survivors. Addressing the healthy lifestyle practices to reduce the risk of MetS and other comorbidities should be encouraged and it will reduce the risk for non-cancer-related mortality among breast cancer survivors.

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Table 1

Comparison of selected demographics and clinical characteristics at study enrollment for subjects who were included the current study and all eligible subjects [a]

	All subjects for 60-month interview	Subjects in this study(n=1696)	*P* [b]
Age at 60 month interview, mean ± SD	58.97 ±9.78	56.68± 7.80	<0.01
Age at diagnosis, mean ± SD	53.66± 9.79	51.38±7.80	<0.01
Education, %			
No formal education or Elementary or middle school	46.89	42.75	
High school	37.99	43.16	
College or higher	15.11	14.09	<0.01
Post-menopausal women,%	51.54	43.09	<0.01
Body mass index, kg/m^2, mean ± SD	24.15 ± 3.35	23.96 ± 3.17	<0.01
Waist circumference, cm, mean ± SD	81.36 ± 8.95	80.42 ± 8.37	<0.01
Regular exercise, %	66.07	65.98	0.95
Charlson comorbidity index (≥1) %	20.14	15.98	<0.01
TNM stage %			
0–I	39.59	41.57	
IIa	33.93	34.14	
IIb	15.30	14.62	
III	6.62	5.13	
Unknown	4.56	4.54	0.22
ER/PR status,%			
Positive(ER+/PR+)	52.34	51.36	
Negative(ER−/PR−)	26.07	26.83	
Mixed(ER+/PR−or ER−/PR+)	20.30	20.34	
Unknown	1.29	1.47	0.86
Tamoxifen use %	54.09	54.54	0.76
Chemotherapy use,%	91.15	93.87	<0.01
Radiotherapy use, %	29.62	30.66	0.44

[a] All subjects who were successfully interviewed at 60-month survey.

[b] From χ^2 test (categorical variables) or ANOVA test (continuous variables), *P* values for women who were in the present study versus cases who completed the 60-month interview but did not involved in physical examination.

Abbreviations: ER, estrogen receptor; PR, progesterone receptor

Table 2

Prevalence of the MetS according to NCEP-ATP III [a] and IDF definition at 60 months after breast cancer diagnosis by demographic, lifestyle, and medical characteristics, SBCSS, 2002–2006 (N=1696)

	No. of Subjects	NCEP-ATP III criteria		IDF criteria	
Characteristics		No. of MetS	%	No. of MetS	%
Overall	1696	562	33.14	620	36.56
Age at diagnosis					
< 40	69	7	10.14	8	11.59
40–49	785	222	28.28	238	30.32
50–59	587	212	36.12	232	39.52
≥ 60	255	121	47.45*	142	55.69*
Educational level					
No formal education or Elementary or middle school	725	272	37.52	293	40.41
High school	732	224	30.60	252	34.43
College or higher	239	66	27.62*	75	31.38*
WC					
< 88	1381	354	25.63	390	28.24
≥ 88	315	208	66.03*	230	73.02*
BMI					
< 25	1136	253	22.27	251	22.10
25–29.9	488	251	51.43	311	63.73
≥ 30	72	58	80.56*	58	80.56*
Menopausal status					
Premenopausal	965	271	28.08	293	30.36
Postmenopausal	731	291	39.81*	327	44.73*
TNM stage					
0–I	705	214	30.35	225	31.91
IIa	579	206	35.58	228	39.38
IIb	248	91	36.69	102	41.13

	No. of Subjects	NCEP-ATP III criteria		IDF criteria	
Characteristics		No. of MetS	%	No. of MetS	%
III–IV	87	32	36.78	35	40.23
Unknown	77	19	26.78	30	38.96
ER/PR status					
Positive(ER+/PR+)	871	275	31.57	308	35.36
Negative(ER−/PR−)	455	163	35.82	167	36.70
Mixed(ER+/PR−or ER−/PR+)	345	115	33.33	133	38.55
Unknown	25	9	36.00	12	48.00
Tamoxifen use					
No	771	264	34.24	287	37.22
Yes	925	298	32.22	333	36.00
Chemotherapy					
No	104	39	37.50	34	32.69
Yes	1592	523	32.85	586	36.81
Radiotherapy					
No	1176	391	33.25	423	35.97
Yes	520	171	32.88	197	37.88
Charlson comorbidity index					
0	1425	442	31.02	473	33.19
≥1	271	120	44.28*	147	54.24*

[a]NCEP-ATP III criteria using WC ≥ 88 cm.

*$P < 0.05$, from χ^2 test.

Abbreviations: WC, waist circumference; BMI, body mass index; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; IDF, International Diabetes Federation.

Table 3

Association of exercise after diagnosis with MetS using NCEP-ATPIII criteria at 60 months post-diagnosis among breast cancer survivors, SBCSS, 2002–2006 (N=1616)[a]

	Exercise between 6 and 60 months after diagnosis (18-, 36- and 60-month survey)			Exercise over the first 60 months after diagnosis (6-, 18-, 36- and 60-month survey)		
	All	**N. MetS**	**OR (95%CI)** [b]	**All**	**N. MetS**	**OR (95%CI)** [b]
Exercise						
Never	209	72	1.00	131	46	1.00
Ever	1407	438	0.81(0.58–1.14)	1485	464	0.80(0.53–1.20)
Duration of exercise (h/week)						
Never	209	72	1.00	131	46	1.00
<3.5	656	221	0.98(0.69–1.40)	830	261	0.86(0.57–1.30)
≥3.5	751	217	0.69(0.48–0.98)	655	203	0.73(0.48–1.12)
P for trend			0.005			0.094
Exercise participation pattern[c]						
Never	209	72	1.00	131	46	1.00
Non-consistent participation	516	181	1.03(0.71–1.48)	795	263	0.90(0.59–1.36)
Consistent participation	891	257	0.70(0.50–1.00)	690	201	0.70(0.46–1.07)
P for trend			0.005			0.025

[a] Those cases with diabetes before diagnosis at baseline survey were excluded.

[b] ORs from logistic regression models adjusted for age at diagnosis, education, BMI at baseline, menopausal status at baseline, history of chronic disease (Charlson comorbidity score 0/≥1), and TNM stage.

[c] "never participation" refers to those with no exercise participation reported at any survey (6- and/or 18-, 36-, 60-month post-diagnosis); "consistent participation" refers to participants who reported exercise participation all four relevant follow-up surveys; and "non-consistent participation" refers to those with exercise participation, but not consistent participation. The two latter patterns were also defined as "ever participation".

Abbreviations: NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III

Table 4

Associations of exercise between 6 and 60 months after diagnosis with components of MetS at 60-months post-diagnosis among breast cancer survivors, SBCSS, 2002–2006 (N=1616)[a]

	No exercise		Duration of exercise, per week, h<3.5		Duration of exercise, per week, h≥3.5		
Components of MetS	**N. MetS/non-MetS**		**N MetS/non-MetS**	**OR(95%CI)[b]**	**N MetS/non-MetS**	**OR(95%CI)[b]**	**P for trend**
WC ≥ 88cm	47/162	1.00	132/524	0.87(0.55–1.39)	122/629	0.52(0.33–0.84)	<0.001
BP≥130/85 mmHg	121/88	1.00	384/272	1.01(0.72–1.42)	446/305	0.94(0.67–1.31)	0.56
TG≥1.7 mmol/l	89/120	1.00	283/373	1.02(0.74–1.41)	315/436	0.93(0.68–1.28)	0.47
HDLC<1.3 mmol/l	75/134	1.00	246/410	1.10(0.79–1.53)	269/482	1.01(0.73–1.40)	0.80
FPG≥5.6 mmol/l	54/155	1.00	199/457	1.27(0.88–1.83)	205/546	1.01(0.70–1.46)	0.46

[a]Those cases with diabetes before diagnosis at baseline survey were excluded.

[b]ORs from logistic regression models adjusted for age at diagnosis, education, BMI at baseline, menopausal status at baseline, history of chronic disease (Charlson comorbidity score 0/≥1), and TNM stage.

Table 5

Associations of exercise after diagnosis with MetS at 60-months post-diagnosis (NCEP-ATPIII criteria) among breast cancer survivors, stratified by waist circumference at baseline, BMI at baseline, menopausal status, Tamoxifen use, and radiotherapy, SBCSS, 2002–2006 (N=1614)[a]

	No exercise		Duration of exercise, per week, h<3.5		Duration of exercise, per week, h≥3.5			
	N. MetS/non-MetS	OR	N. MetS/non-MetS	OR (95% CI)[b]	N. MetS/non-MetS	OR (95% CI)[b]	*P* for trend	*P* for interaction[b]
Stratified by waist circumference at baseline								
WC<88cm	42/122	1.00	138/392	1.00(0.66–1.51)	142/488	0.72(0.48–1.09)	0.03	
WC≥88cm	30/15	1.00	83/43	0.96(0.45–2.08)	75/46	0.75(0.35–1.62)	0.37	0.83
Stratified by BMI at baseline								
BMI<25 kg/m^2	34/108	1.00	107/344	0.98(0.63–1.54)	89/410	0.63(0.40–0.99)	0.01	
BMI≥25 kg/m^2	38/29	1.00	114/91	1.02(0.57–1.84)	128/124	0.77(0.44–1.36)	0.18	0.60
Stratified by menopausal status at baseline								
Premenopausal	42/99	1.00	116/287	1.09(0.68–1.72)	98/302	0.69(0.43–1.10)	0.03	
Postmenopausal	30/38	1.00	105/148	0.84(0.47–1.50)	119/232	0.62(0.35–1.09)	0.04	0.85
Stratified by Tamoxifen use								
Tamoxifen use	47/71	1.00	108/242	0.75(0.47–1.20)	119/299	0.57(0.36–0.91)	0.01	
No Tamoxifen use	25/66	1.00	113/193	1.44(0.83–2.53)	98/235	0.90(0.51–1.57)	0.15	0.59
Stratified by radiotherapy								
Radiotherapy	26/42	1.00	64/132	0.84(0.44–1.59)	68/163	0.60(0.32–1.13)	0.07	
No radiotherapy	46/95	1.00	157/303	1.07(0.69–1.65)	149/371	0.74(0.48–1.15)	0.04	0.76
Stratified by chemotherapy								
Chemotherapy	68/130	1.00	203/407	0.95(0.66–1.38)	206/504	0.67(0.47–0.97)	0.01	
No chmotherapy	7/4	1.00	28/18	1.66(0.59–4.68)	30/11	0.91(0.43–1.93)	0.52	-[c]

[a]Those cases with diabetes before diagnosis at baseline survey were excluded.

[b]ORs from logistic regression models and adjusted for age at diagnosis, education, BMI at baseline, menopausal status at baseline, history of chronic disease (Charlson comorbidity score 0/≥1), TNM stage, and *P*-interaction across subgroups by the stratified factors.

[c]Number of breast cancer patients without chemotherapy was very small (n=98).