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Modifiable lifestyle factors and triple-negative breast cancer survival: a population-based prospective study

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Abstract

Background—Very little is known about the effect of modifiable lifestyle factors on outcomes of triple-negative breast cancer. We examined this association in a population-based prospective cohort study of patients with triple-negative breast cancer.

Methods—A total of 518 women with confirmed triple-negative breast cancer with breast cancer, recruited by the Shanghai Breast Cancer Survival Study, completed 6-month, 18-month, 36-month, and 60-month post-diagnosis surveys. We applied Cox proportional hazard models to evaluate the associations.

Results—The mean age at diagnosis was 53.4 (SD=10.6) years old. After a median follow-up of 9.1 years (range: 0.6–11.8), 128 deaths and 112 recurrences were documented. Exercise during the first 60 months post-diagnosis was inversely associated with total mortality and recurrence/disease-specific mortality with adjusted hazard ratios (HRs) of 0.67 (95% CI: 0.46, 0.96) and 0.58(95% CI: 0.39, 0.86), respectively. Women with higher exercise-metabolic equivalent(MET) scores (7.6 MET-hours/wk) and longer duration of exercise (2.5 h/wk) had lower risk of total and recurrence/disease-specific mortality than did non-exercisers. Compared with non-tea drinkers, survival was better among women who were regular tea drinkers during the first 60 months for all-cause (HR= 0.57, 95% CI: 0.34, 0.93) and recurrence/disease-specific mortality (HR=0.54, 95% CI: 0.31, 0.96). There was no dose-response pattern for tea consumption. No interactions were observed for body mass index, menopausal status, and comorbidity.

Conclusions—These findings show that post-diagnosis exercise and tea intake were associated with improved survival among women with triple-negative breast cancer.

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Disclosure

The authors declare no conflict of interest to disclose.

Keywords

triple-negative breast cancer; lifestyle factors; exercise; tea consumption; survival outcomes

Introduction

The prognosis of breast cancer in general is good, with estimated five-year survival rates of 89% and 10-year survival rates of 82% in the United States¹. However, triple-negative breast cancer [TNBC], a subset of breast cancers characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and no overexpression of human epidermal growth factor receptor 2 (HER-2)], has a much worse prognosis compared to hormonal receptor positive breast cancer due to its aggressive behavior and lack of effective targeted therapies. Triple-negative breast cancer accounts for 10%–20% of all breast cancer subtypes and women with triple-negative breast cancer experience the peak risk of recurrence and mortality within 3 to 5 years after diagnosis². Given the limited treatment options and the little information on prognostic factors for triple-negative breast cancer identification of potential modifiable lifestyle factors that may improve survival is particularly important to triple-negative breast cancer patients as well as their care givers.

There is a growing body of epidemiologic evidence suggesting that exercise after a diagnosis of breast cancer can improve mortality, morbidity, and health-related quality of life^{3–4}. Many randomized controlled trials have also shown that exercise interventions for breast cancer patients can improve their quality of life, cardiorespiratory fitness, and physical functioning^{5–6}. However, the few studies that have stratified on ER/PR status have shown inconsistent findings^{7–11}. A meta-analysis published in 2011 demonstrated strong effects of exercise participation among those with ER positive tumors⁸. A recent study by Bradshaw et al.¹¹ showed that the inverse association was more pronounced among women with tumors that were estrogen/progesterone receptor-positive (ER+ and PR+) compared to either negative. However, two previous studies^{7,10} reported that the reduced risk of mortality for exercise participation after breast cancer diagnosis was restricted to ER– and PR– cases. To our knowledge, no data are available on the effects of exercise on triple-negative breast cancer subtype and its effects at different time points after cancer diagnosis. With respect to the prognostic effect of other modifiable lifestyle factors, including alcohol consumption, cigarette smoking, and tea consumption on breast cancer survival, previous studies have been limited and have reported mixed findings^{12–19}. Only one study to date has examined their association with prognosis of triple-negative breast cancer so far, finding that pre-diagnostic smoking behavior was associated with poorer outcomes, with HR of 1.93 (95%CI: 1.02–3.65) for all-cause mortality²⁰. The association of modifiable lifestyle factors with prognosis may be particularly relevant for triple-negative breast cancer patient outcomes and the knowledge may provide a chance to improve the survival rate through lifestyle modification.

To address the limitations of previous studies, we carried out an analysis of modifiable lifestyle factors (including exercise, tea consumption, alcohol consumption, and cigarette smoking) after breast cancer diagnosis with all-cause and recurrence/disease-specific

mortality of triple-negative breast cancer, using data from the Shanghai Breast Cancer Survival Study, a population-based prospective cohort study of 5042 breast cancer patients in Shanghai, China. With detailed information on patient socio-demographic and medical characteristics and lifestyle factors collected over time, our study design enabled us to perform a comprehensive evaluation of their effects on survival from triple-negative breast cancer, both prospectively and at different time points.

Methods

Study Population

Study participants were female breast cancer survivors enrolled in the Shanghai Breast Cancer Survival Study, a population-based prospective cohort study conducted in Shanghai, China. Details of the study design and methods have been previously described^{21–22}. Briefly, women aged 20–75 years who were newly diagnosed with breast cancer between March 2002 and April 2006 were identified from the Shanghai Cancer Registry and approached for study participation. Of 6299 eligible cases, 5042 were enrolled (participation rate, 80%) and completed baseline interviews approximately 6 months after cancer diagnosis. Ten tumor sections were collected for each participant from the diagnostic hospitals. HER-2 status was assessed in the Vanderbilt Molecular Epidemiology Laboratory as described in details elsewhere²³. Among these cases, 532 patients were diagnosed with triple-negative breast cancer. We excluded women with non-invasive breast cancer (TNM stage 0, n=13) and stage IV breast cancer (n=1) leaving a final sample size of 518 women for the current study.

Data Collection

Baseline interviews were conducted by trained interviewers who were mostly retired medical professionals. Information was collected on cancer treatment, tumor characteristics, reproductive history, habitual dietary intake, medical history, selected lifestyle factors, complementary and alternative medicine use, socio-demographics, and quality of life using a standardized questionnaire. Medical records were reviewed to abstract detailed information on tumor characteristics and treatment information for 98% of the cohort. The agreement between self-reported and medical chart information for tumor-related variables was 94%–98%²⁴.

The cohort has been followed up by in-person interviews at 18, 36, 60 and 120 months after cancer diagnosis to collect data on vital status and recurrence, and update information on selected diet and lifestyle factors, anthropometry, and medical history. After excluding those women who refused to participate and those who could not be contacted, there remained 4572 women who completed the 18-month post-diagnosis interview (participation rate, 91%), 4149 (participation rate, 84 %) who completed the 36-month post-diagnosis interview, and 3641 (participation rate, 77 %) who completed the 60-month post-diagnosis interview. The 120-month interview is ongoing, with 2156 cases having completed the interview to date. The cohort has also been periodically linked to the Shanghai Vital Statistics Registry to ascertain deaths that occurred between surveys and among women missing one or more in-person follow-up surveys. The Shanghai Breast Cancer Survival

Study was approved by the institutional review boards of all institutions involved in this study.

Details of exercise assessments have been described previously¹⁰. In short, information on regular exercise frequency and duration was obtained for up to five types of the most common exercises at each of the 6, 18, 36, and 60-month interviews using a validated questionnaire. The 120-month post-diagnosis survey is still ongoing; thus, the current analyses only include information from the first 60 months post-diagnosis. Each activity was assigned a metabolic equivalent score based on the method proposed by Ainsworth and colleagues²⁵. The score for metabolic equivalent-hours per week (MET hours/wk) for each activity was derived from the hours per week the participant reported engaging in that activity multiplied by the assigned metabolic equivalent score. Scores for individual activities were summed to derive a total exercise metabolic equivalent score.

At the baseline survey, information on tea consumption was obtained and participants were asked whether they regularly drank tea and at what age they started regularly drinking, followed by questions on the type and the amount of tea (in dry weight of dried tea leaves) consumed per month during the year before the interview as well as currently. Former tea drinkers were additionally asked about the age at which they stopped regularly drinking tea. At subsequent interviews, women reported the following information: duration of tea consumption since the last interview, the type, and the amount consumed per month. Details regarding the assessment questionnaire have been described previously²⁶.

Information about other lifestyle factors, including alcohol consumption and cigarette smoking, was also collected, including data on the starting age, the amount of consumption, and the age of quitting if the participants had stopped smoking or drinking.

Statistical Analysis

The endpoints for the analysis were any death for total mortality (overall survival, OS) and cancer recurrence/metastasis or death related to breast cancer for recurrence/disease-specific mortality (disease-free survival, DFS). Survival status was censored at the date of last in-person contact or December 31, 2013 (the most recent for linkage to the Vital Statistics Registry). For disease-free analysis, censoring occurred at the date of last in-person contact or date of death for non-breast cancer death.

We estimated survival distributions using the Kaplan–Meier method and differences in survival rates for women with different socio-demographic and clinical characteristics were evaluated by the log-rank tests. Multivariable Cox proportional hazards models were applied to derive the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for breast cancer outcomes in association with lifestyle factors using age as time scale²⁷. Entry time was defined as age at diagnosis and exit time was defined as age at the event or censoring. Exercise was categorized by 7.6 metabolic equivalent-hours per week, the median for exercise-metabolic equivalent score at baseline, and by 2.5 hours per week for exercise duration according to the recommendations from Physical Activity Guidelines for Americans²⁸. The amount of tea consumption was categorized by 100 grams per month, the median for tea consumption at the 18-month, 36-month and 60-month interviews. Exercise

and tea consumption were treated as time-dependent variables. In the multivariate analysis, we adjusted for known clinical factors (tumor-node-metastasis [TNM] stage, chemotherapy, radiotherapy), age at diagnosis, education level, menopausal status, intake of soy protein (quartiles), body mass index (BMI) at baseline (<18, 18–24.99, 25–29.99, ≥30), and Charlson comorbidity index (created for each participant on the basis of a validated comorbidity scoring system²⁹). Further adjustment of exercise was conducted when we evaluated the effects of tea consumption on survival. Analyses of mortality and exercise and tea consumption were further stratified by BMI, menopausal status, comorbidity, and radiotherapy.

Tests for trend were performed by entering the category variable as continuous parameters in the models. Tests for multiplicative interactions were conducted using –2 log likelihood ratio test statistics, which compared models with and without the interaction terms. All analyses were performed using SAS version 9.3.

Results

Over a median of 9.1 years of follow-up (range: 0.6–11.8 years), 128 deaths and 112 recurrences or breast cancer deaths were observed. The mean age at breast cancer diagnosis was 53.4 years (standard deviation, SD: 10.6). Older age at diagnosis, advanced TNM stage, postmenopausal status, low education level, presence of comorbidity, and receiving radiotherapy were inversely related to the survival rate, while use of chemotherapy was positively associated with survival rate (Table 1).

At 6 months post-diagnosis, 66% of participants (343 cases) were engaged in exercise. Walking was the most common type of exercise among our study population (50% among exercisers). The percent who reported regular exercise participation was 72% (334 cases), 73% (293 cases), and 65% (225 cases) at the 18-, 36- and 60-month surveys, respectively. Among women who reported exercise participation, the median duration of exercise participation was 2.0 hours per week (median 7.6 metabolic equivalent-hours/wk) at the 6-month post-diagnosis survey and increased to 4.0 (median 15.2 metabolic equivalent-hours/wk), 4.0 (median 15.2 metabolic equivalent-hours/wk) and 4.5 hours per week (median 18.3 metabolic equivalent-hours/wk) at the 18-, 36-, and 60-month post-diagnosis surveys, respectively.

Overall, 12% of women (62 cases) reported tea drinking regularly after diagnosis (among women with tea consumption, 89% drank green tea) with a median of 15 grams per month of dried tea leaves at the baseline survey. At the 18-, 36-, and 60-month follow-up, the proportions drinking tea was 28% (130 cases), 31% (124 cases), 27% (91 cases), respectively, all with median of 100 grams of dried tea leaves.

As shown in Table 2, compared with non-exercisers, women who engaged in exercise regularly during the first 6 months post-diagnosis had a lower risk of total mortality and recurrence/disease-specific mortality, with adjusted HRs of 0.58(95% CI: 0.40–0.84) and 0.54(95% CI: 0.36–0.81), respectively. A longer duration of exercise participation and higher exercise-metabolic equivalents were inversely associated with total mortality and

recurrence/disease-specific mortality: an exercise duration of 2.5 h/wk was associated with adjusted HRs of 0.60(95% CI: 0.38–0.95) for total mortality and 0.56(95% CI: 0.34–0.92) for recurrence/disease-specific mortality when compared with non-exercisers, and women who exercised 7.6 metabolic equivalent-hours/wk had a reduced risk of all-cause (HR=0.59, 95% CI: 0.38–0.93) and recurrence/disease-specific mortality (HR=0.57, 95% CI: 0.35–0.92), compared with non-exercisers (0 metabolic equivalent-hours/wk). Similarly, inverse associations of exercise over the first 18, 36 and 60 months post-diagnosis with mortality were observed.

Table 3 presents associations of tea consumption over the first 60 months after diagnosis with the outcome of triple-negative breast cancer patients. After adjustment for clinical and other confounders, the HRs were 0.58(95% CI: 0.29, 1.16) for total mortality and 0.60 (95% CI: 0.29, 1.27) for recurrence/disease-specific mortality for those who drank tea regularly during the first 6 months post-diagnosis compared with non-drinkers. When tea consumption during the first 18-, 36-, and 60-month post-diagnosis periods were taken into consideration, a reduced risk of total mortality and recurrence/disease-specific mortality was observed. The HRs for the first 60-month post-diagnosis period were 0.57(95% CI: 0.34, 0.93) and 0.54(95% CI: 0.31, 0.96), respectively. We further explored the amount of tea consumption and did not find a dose-response relationship. Compared with women who never drank tea, the women who drank less than 100 grams per month had a lower risk of total mortality, with an adjusted HR of 0.36(95% CI: 0.16, 0.83), while the women who drank more than 100 gram evidenced no measured effect, with HR of 0.76(95% CI: 0.42, 1.36) during the first 60-month post-diagnosis survey.

While additional analysis stratified by baseline BMI suggested that the inverse association of exercise and tea consumption with risk of death was more pronounced among women with higher BMI (≥ 25 kg/m²) than among women with lower BMI (<25 kg/m²), no modified effects were observed (data not shown). Menopausal status, comorbidity, and radiotherapy did not affect the relationship between regular exercise, tea consumption and outcome of patients with triple-negative breast cancer (data not shown).

Of the total participants, only one woman was currently a regular alcohol drinker, while 14 cases reported a history of regular alcohol consumption at the baseline survey. For cigarette smoking, the number of current smokers and former smokers was 2 and 6, respectively.

Discussion

In this population-based prospective cohort of Chinese triple-negative breast cancer survivors diagnosed at age 20–75 years, we found that regular exercise after cancer diagnosis was associated with reduced risk of all-cause mortality and recurrence/disease-specific mortality. The triple-negative breast cancer patients with tea consumption over the first 60 months after cancer diagnosis evidenced better rates of survival. The associations were not modified by BMI, although the inverse association appeared more evident for women with higher BMI (≥ 25 kg/m²).

The effect of post-diagnosis modifiable lifestyle factors on breast cancer has attracted increasing attention in recent years. Accumulating evidence from prospective observational studies has demonstrated that exercise after breast cancer diagnosis is associated with a 24%–67% reduction in the risk of total death and a 35%–83% reduction in the risk of breast cancer death when compared to a sedentary lifestyle^{11,30–36}. A recent review published in 2014 suggested that exercise was not merely safe but feasible for breast cancer patients, who could benefit from rehabilitation programs combining both strengthening and aerobic exercises³. The mechanism underlying exercise and breast cancer prognosis is considered to be related to enhancement of immune functions, reducing inflammation, angiogenesis, and apoptosis, as well as maintaining an ideal weight³.

However, most previous studies on exercise^{3–4} included patients with all subtypes of breast cancer. Only a few of them have investigated the association between exercise and the risk of mortality/recurrence for certain subgroups based on ER/PR status, among which some positive but inconsistent findings were reported^{7–11}. We have previously reported that regular exercise post-diagnosis was not associated with improved outcomes for ER+ and PR+ breast cancer: the favorable association was restricted to ER– and PR– cases¹⁰, which accorded with another study published by Schmidt⁷. To our knowledge, no study has specifically evaluated the association of exercise with triple-negative breast cancer prognosis. Furthermore, very limited data on changing patterns of exercise over time and the effects of such change on survival of any type of breast cancer are available. In this study, exercise was assessed at multiple time points after cancer diagnosis. The consistency of the association over 60 months post-diagnosis we observed has provided the strongest epidemiologic evidence to date that exercise after diagnosis is related to the reduced risk of mortality in triple-negative breast cancer survivors, although we cannot completely rule out chance findings caused by residual confounding. As a comparison group, we also examined the associations of regular exercise and ER+/PR+ tumors with an extended follow-up period on the same cohort study. The results showed that exercise during the first 60 months post-diagnosis was not associated with total mortality and recurrence/disease-specific mortality of ER+PR+ breast cancer with HRs of 1.01(95% CI: 0.82,1.24) and 0.99(95% CI: 0.80,1.23), respectively, similar to the previous report¹⁰. The reverse association, on the other hand, supports the idea that the 2008 Physical Activity Guidelines for the general population, in which engaging in at least 2.5 hours of moderate intensity physical activity per week is recommended to reduce risk of mortality, can be extended to triple-negative breast cancer patients.

Recent experimental data have shown strong chemopreventive and possibly cancer chemotherapeutic effects of green tea polyphenols against cancer¹³. Green tea catechins, the major component of polyphenols, have been shown to inhibit proliferation of breast cancer cells and to block carcinogenesis³⁷. Few observational studies have investigated the association between green tea consumption and breast cancer survival, and findings have been inconsistent. Among the two studies that focused on the association of breast cancer recurrence with green tea, both found green tea consumption may be associated with a reduced risk in recurrence of breast cancer in early stage cases^{38–39}. A meta-analysis for these two studies suggested a reduction of 27% in recurrence among heavy green tea drinkers (> 3 cups a day) (summary RR = 0.73, 95% CI: 0.56–0.96)³⁷. With respect to other

types of tea consumption, one Swedish cohort study reported that black tea consumption was not associated with breast cancer-specific or overall mortality¹⁶. Tea is the most common beverage consumed by our study participants, and among tea drinkers, 89% drank green tea regularly after diagnosis. Our study found that tea consumption over the first 60 months after diagnosis may be associated with a reduced risk of total mortality and recurrence/disease-specific mortality among triple-negative breast cancer survivors. Compared with non-tea drinkers, those patients who regularly drank tea during the first 60-month period after their cancer diagnosis posted a 43% decreased risk of all-cause death and a 46% decreased risk of recurrence/disease-specific death. The reduced risk of total mortality and recurrence/disease-specific mortality for tea consumption was observed during the 18-, 36-, and 60-month post-diagnosis periods, but not at baseline. The possible reason is that compared with the three sequential follow-up surveys, the amount of tea consumption at the 6-month post-diagnosis baseline survey (15 grams per month) was very low. Of note, we did not find a dose-response relationship between tea consumption and triple-negative breast cancer outcome. More studies are warranted to address the possible beneficial effect of tea consumption on survival of this specific subtype.

The few studies that have examined the influence of other lifestyle factors, including alcohol consumption and cigarette smoking, on breast cancer outcomes, have reported inconsistent findings^{14–16,18–19}. Only one study has reported that pre-diagnostic smoking behavior was associated with poorer outcomes for triple-negative breast cancer and luminal A-like tumors with HRs of 1.93 (95%CI: 1.02–3.65) and 2.08 (95%CI: 1.40–3.10) for all-cause mortality, respectively, but not for other tumor subtypes²⁰. No study has examined whether alcohol consumption influences survival outcomes in triple-negative breast cancer. In our study, fewer than 5% of participants were regular alcohol drinkers or smokers, and the statistical power was limited to examine the association of alcohol consumption or smoking with triple-negative breast cancer outcome.

Our study has several strengths. First, this was a large, population-based cohort study on the effect of modifiable lifestyle factors on triple-negative breast cancer outcome. The design and ability to adjust for a wide range of potential confounders increased the validity of the study findings. Second, detailed information on exercise and tea consumption was collected at study recruitment and in the follow-up surveys, which allowed us to take into account the change of exposure in our analysis. Last is the relatively long follow-up time we had for this cohort of triple-negative breast cancer patients. It also should be noted that our study has some limitations. We collected information on recreational exercise activities only, and could not evaluate physical activity from other sources, such as daily living and employment. Further, the prevalence of some specific lifestyle factors, including smoking and alcohol consumption, in our study subjects was low, which prevented us from evaluating the association of these factors with triple-negative breast cancer survival. An additional limitation is the potential for reverse confounding to influence these results (i.e. those who are near death are more likely to be inactive or suspend tea consumption). Furthermore, statistical power was limited when exploring interactions by BMI and other factors (especially for the recurrence/disease-specific mortality outcome).

In summary, our findings provide evidence that regular participation in exercise and tea consumption during the first 60 months after cancer diagnosis may be associated with the long-term survival of triple-negative breast cancer patients. Additional studies with larger sample sizes are warranted to confirm our findings, as well as future research focusing on the development of effective programs to promote healthy lifestyle behavior among triple-negative breast cancer patients.

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Demographic and clinical predictors for 5-year and 10-year overall survival for triple-negative breast cancer patients in the Shanghai Breast Cancer Survival Study

Table 1

Characteristic	No.	%	Deaths, No.	5-year Overall Survival Rate, %	10-year Overall Survival Rate, %
Total	518	100	128	82.1	74.6
Age at diagnosis, y					
< 50	230	45	45	83.9	80.0
50–59	141	27	28	84.4	79.5
60	147	28	55	76.9	61.4
Education					
None/Elementary	72	14	31	73.6	57.2
Middle school	180	35	36	83.9	79.7
High School	190	37	38	85.3	78.2
College	76	14	23	77.6	69.5
Income (Yuan/person/month)					
<700	152	29	43	77.6	71.5
700–999	153	30	42	81.6	71.2
1000	213	41	43	85.5	78.9
Menopausal status					
Premenopausal	243	47	45	84.8	81.2
Postmenopausal	275	53	83	79.6	68.6
BMI at baseline					
<18	17	3	3	88.2	73.5
18–24.99	319	62	73	83.1	76.6
25–29.99	152	29	40	80.3	73.8
30	30	6	12	73.3	56.6
Charlson comorbidity index					
0	409	79	94	82.6	76.2
1	109	21	34	78.9	68.4
TNM stage*					
I	160	31	22	90.0	86.4

Characteristic	No.	%	Deaths, No.	5-year Overall Survival Rate, %	10-year Overall Survival Rate, %
II	288	56	77	81.3	71.9
III	53	10	26	60.4	50.9
Unknown	17	3	3	88.2	82.4
Chemotherapy					
No	29	7	12	69.0	62.1
Yes	489	94	116	82.8	75.3
Radiotherapy					
No	376	73	75	87.0	79.2
Yes	142	27	53	69.0	62.2
Radical mastectomy					
No	23	4	6	78.3	73.9
Yes	498	96	122	82.2	74.6
Tamoxifen use					
No	406	78	101	82.3	74.0
Yes	112	22	27	81.3	76.4

Note: Abbreviation: TNM, tumor-node-metastasis

Association of exercise over the first 60 months after triple-negative breast cancer diagnosis with total mortality and recurrence/disease-specific mortality

Table 2

Characteristics	Total ^a	Events ^a	HR(95%CI)		
			First 6 months post-diagnosis ^b	First 18 months post-diagnosis ^c	First 36 months post-diagnosis ^c
Total mortality					
Exercise participation					
No	175	56	1.0	1.0	1.0
Yes	343	72	0.58(0.40,0.84)	0.66(0.45,0.96)	0.67(0.46,0.96)
Duration of exercise (h/wk)					
No exercise	175	56	1.0	1.0	1.0
<2.5	185	39	0.56(0.37,0.87)	0.79(0.50,1.24)	0.80(0.51,1.26)
2.5	158	33	0.60(0.38,0.95)	0.57(0.38,0.88)	0.64(0.42,0.98)
P for trend			0.02	0.01	0.04
MET-hours per week (MET-hours/wk)					
No exercise	175	56	1.0	1.0	1.0
<7.6	165	35	0.56(0.36,0.88)	0.78(0.48,1.24)	0.79(0.50,1.27)
7.6	178	37	0.59(0.38,0.93)	0.60(0.39,0.91)	0.61(0.41,0.91)
P for trend			0.02	0.02	0.05
Recurrence/disease-specific mortality					
Exercise participation					
No	175	49	1.0	1.0	1.0
Yes	343	63	0.54(0.36,0.81)	0.58(0.39,0.86)	0.58(0.39,0.86)
Duration of exercise (h/wk)					
No exercise	175	49	1.0	1.0	1.0
<2.5	185	34	0.52(0.33,0.83)	0.64(0.39,1.03)	0.64(0.40,1.04)
2.5	158	29	0.56(0.34,0.92)	0.53(0.34,0.84)	0.53(0.34,0.84)
P for trend			0.02	0.01	0.01
MET-hours per week (MET-hours/wk)					
No exercise	175	49	1.0	1.0	1.0
<7.6	165	30	0.51(0.32,0.82)	0.60(0.36,1.00)	0.64(0.39,1.07)
7.6	178	33	0.57(0.35,0.92)	0.56(0.36,0.87)	0.54(0.35,0.84)

Characteristics	Total ^a	Events ^a	HR(95%CI)			
			First 6 months post-diagnosis ^b	First 18 months post-diagnosis ^c	First 36 months post-diagnosis ^c	First 60 months post-diagnosis ^c
P for trend			0.02	0.01	0.01	0.01

Note: Abbreviations: CI, confidence interval; HR, hormone receptor; MET, metabolic equivalent; TNM, tumor-node-metastasis

^aThe numbers of total and events refer to baseline survey.

^b Adjusted for age at diagnosis (continuous variable), education (<middle school, middle school, high school, >high school), marital status, Charlson comorbidity index (0, 1), menopausal status (yes, no), BMI at baseline(<18,18–24,25–29,30), soy protein intake(Q1–Q4), tea consumption at baseline (yes, no), chemotherapy (yes, no), radiotherapy (yes, no), and TNM stage (I, II, III, unknown).

^c Adjusted for the same variables as above, but exercise was treated as a time-dependent variable.

Adjusted hazard ratios for triple-negative breast cancer total mortality and recurrence/disease-specific mortality and tea consumption over the first 60 months after diagnosis

Table 3

Characteristics	Total ^a	Events ^a	HR(95%CI)			
			First 6 months post-diagnosis ^b	First 18 months post-diagnosis ^c	First 36 months post-diagnosis ^c	First 60 months post-diagnosis ^c
Total mortality						
Tea consumption						
No	456	119	1.0	1.0	1.0	1.0
Yes	62	9	0.58(0.29,1.16)	0.76(0.47,1.21)	0.47(0.29,0.79)	0.57(0.34,0.93)
Tea consumption amount, gram per month						
No	456	119	1.0	1.0	1.0	1.0
<100	48	6	0.48(0.21,1.11)	0.38(0.16,0.89)	0.31(0.13,0.71)	0.36(0.16,0.83)
100	14	3	0.99(0.30,3.25)	1.17(0.67,2.02)	0.63(0.35,1.16)	0.76(0.42,1.36)
P for trend			0.24	0.76	0.02	0.10
Recurrence/disease-specific mortality						
Tea consumption						
No	456	104	1.0	1.0	1.0	1.0
Yes	62	8	0.60(0.29,1.27)	0.58(0.33,1.02)	0.46(0.26,0.83)	0.54(0.31,0.96)
Tea consumption amount, gram per month						
No	456	104	1.0	1.0	1.0	1.0
<100	48	5	0.44(0.17,1.10)	0.56(0.28,1.11)	0.30(0.12,0.75)	0.40(0.17,0.93)
100	14	3	1.55(0.47,5.05)	0.92(0.43,1.95)	0.66(0.32,1.36)	0.72(0.35,1.47)
P for trend			0.42	0.33	0.04	0.10

Note: Abbreviations: CI, confidence interval; HR, hormone receptor; MET, metabolic equivalent; TNM, tumor-node-metastasis

^aThe numbers of total and events refer to baseline survey.

^b Adjusted for age at diagnosis (continuous variable), education (<middle school, middle school, high school, >high school), marital status, Charlson comorbidity index (0, 1), menopausal status(yes, no), BMI at baseline (<18,18–24,99,25–29,99, 30), exercise participation at baseline (yes, no), soy protein intake (Q1–Q4), chemotherapy (yes, no), radiotherapy (yes, no), and TNM stage (I, II, III, unknown).

^c Adjusted for the same variables as above, but tea consumption was treated as a time-dependent variable.