

Higher Level of Sports Activities Participation During the Five-year Survival Was Associated With Better Quality of Life Among Chinese Breast Cancer Survivors

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Abstract

Background

To investigate the association between level of sports activities participation at post-diagnosis and quality of life (QoL) among Chinese women with early-stage breast cancer patients during the first five years of survival.

Methods

A validated modified Chinese Baecke questionnaire was used to prospectively measure sports activities among a breast cancer cohort at four time-points: baseline (sports activities during the previous 12 months before cancer diagnosis), 18-, 36- and 60-month after diagnosis (sports activities during the previous 12 months before each interview); QoL was measured at the same time.

Results

In total, 1289, 1125 and 1116 patients were included into the analyses at 18-, 36- and 60-month follow-up, respectively. The percentages of patients who belonged to no [0 metabolic equivalent of task (MET)-hours per week], low-level (<10 MET-hours/week) and high-level (≥ 10 MET-hours/week) sports activities group were 20.7%, 45.5% and 33.8% at 18-month follow-up, respectively; the corresponding figures at 36- (29.4%, 38.9% and 31.6%, respectively) and 60-month (32.8%, 36.7% and 30.5%, respectively) differed slightly. Using data from the three follow-ups, Generalized Estimating Equations (GEE) analyses showed that higher level of sports activities participation was associated with better QoL in several items, including global health status/QoL, physical functioning, role functioning and emotional functioning (P for trend < 0.05 for all), as well as less symptoms in fatigue, pain, loss of appetite and constipation (P for trend < 0.05 for all).

Conclusions

The present findings in Chinese women with breast cancer provided another important evidence on the beneficial effect of regularly participation in sports activities following cancer diagnosis and patients' QoL. Health promotion programs should be encouraged with the inclusion of regular sports activities after breast cancer diagnosis.

Background

Survival analysis based on cancer registry data indicated that the incidence of breast cancer has increased steadily; in the other hand, in recent decades in Hong Kong the mortality rate has only increased slightly over the same period.[44] These trends have resulted in a rising number of women who would live longer as breast cancer survivors. According to the American Cancer Society (ACS), a cancer survivor is defined as any individual who has been diagnosed with cancer.[39] As the survival rate have quantitatively increased, the improvement of quality of life (QoL) has become a critical long-term management issue for breast cancer survivors.[34, 36] Previous studies have reported that both newly diagnosed breast cancer patients and long-term breast cancer survivors had worse QoL than healthy female controls.[15, 26] As such, identifying effective strategies, especially by adoption of healthy lifestyles, to improve QoL have been explored among breast cancer survivors.

Among modifiable lifestyle habits after breast cancer diagnosis, participation in sports activities is one of the factors that has been associated with reduced risk of mortality as well as enhanced QoL.[40, 46] A large body of short-term, structured exercise interventional programs and several meta-analyses have supported the beneficial effect of exercise on QoL.[8, 25, 45, 46] There have also been some evidence from observational studies, including cohort studies and cross-sectional studies, suggesting the association between regular sports activities engagement and better QoL.[9, 10, 12, 18, 35, 41] Although evidence supporting the beneficial effect of sports activity on QoL have been strong in the West, data from Chinese breast cancer patients has been limited, with only one prospective study having been reported.[12]

The present study aimed to evaluate the association between the level of sports activities and QoL among Chinese women with early-stage breast cancer during the first five years of their survival. It hypothesized that higher level of sports activities was associated with better QoL.

Methods

Patients

The Hong Kong NTEC-KWC Breast Cancer Survival Study (HKNKBCSS) was a prospective study among Chinese women with early-stage breast cancer that was initiated in 2011. It aimed to evaluate the associations between lifestyle factors, especially soy isoflavones intake, and outcomes of breast cancer.[27-31] The study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee and the KWC Research Ethics Committee of the Chinese University of Hong Kong and the Hong Kong Hospital Authority.

The enrollment of this cohort took place between January 2011 and February 2014 in two regional cancer centers in Hong Kong. Consecutive breast cancer patients who attended outpatient clinics were identified for the study; eligible patients were invited to participate in the study. Inclusion criteria included Chinese females who were of any age, had histologically confirmed breast cancer with American Joint Committee on Cancer (AJCC) stage 0-III disease, [16] were mentally stable, were able to read Chinese, and did not have prior history of breast or other cancers. These patients should have a diagnosis of breast cancer no more than 12-month from study entry. A written informed consent was obtained from each individual prior to study entry. Each participant was interviewed at four time-points according to the study protocol: baseline at study entry, 18-, 36- and 60-month post-diagnosis.

Data collection of socio-demographic characteristics and clinical information

Each participant had face-to-face assessment by trained interviewers at baseline and during the three follow-ups. During the assessment, patients' socio-demographics were collected. The clinical records were retrieved for details of breast tumor characteristics and anti-cancer treatment. In addition, disease recurrence and survival status were updated periodically by reviewing medical records during follow-ups, or by asking patients or family contacts through face-to-face interviews or telephone calls.

Data collection of lifestyle factors

Standardized questionnaires were used to collect lifestyle factors, such as habits of dietary intake and physical activity. Anthropometric measurements included body weight and height. Body mass index (BMI) classification was based on criteria in Asia-Pacific region, and included four groups as follow: underweight $<18.5 \text{ kg/m}^2$, normal $18.5\text{-}22.9 \text{ kg/m}^2$, overweight $23\text{-}24.9 \text{ kg/m}^2$ and obese $\geq 25 \text{ kg/m}^2$. [2]

Measurements of sports activity

A validated modified Chinese Baecke questionnaire (Supplementary table 1) was used to measure the level of physical activities, which consisted of four parts: at work, in doing housework, at leisure time (time excluding working and playing sports or exercise) and in doing sports. [19] At baseline assessment, patients were asked to report their physical activities in the previous year before cancer diagnosis. During the 18-, 36- and 60-month follow-ups, patients recalled habitual physical activities involvement over the previous 12 months before interviews.

Among the four parts of physical activities, sports activity was the one recommended by World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) cancer survivor guideline and has been extensively explored by previous studies. In order to be more comparable with available evidence in the literature, the present study only analyzed data from one part of Chinese Baecke questionnaire, namely sport activities that contribute to the overall physical activities. In the questionnaire, each individual who did sports was asked to specify the activities they had involved in categorically (up to 2 types of sports activities), and also to recall the number of hours per week and months per year they have engaged in each activity. The Ainsworth compendium of physical activity provided a MET code for each sports. [5] Based on these data, a score of metabolic equivalent of task (MET)-hours per week could be calculated by multiplying the corresponding MET value of the activity by the time (hours per week) engaged in a particular sports activity. [5] Subsequently, each individual would get a final level of sports activities by summing the score of MET-hours per week of the one or two sports activities they were engaged in.

The recommendation from ACS and WCRF/AICR have suggested that cancer survivors should be moderately physically active, equivalent to brisk walking, for at least 30 minutes every day. [3, 39] This recommended level of sports activity could be operationalized as being engaged in fast walking or other moderate activities for about 30 minutes per day for at least 5 days per week. According to the above-mentioned methods for calculation, such recommended level of sports activities equaled to 10 MET-hours/week (calculated as follow: $4.0 \text{ METs/hour} * 0.5 \text{ hours/day} * 5 \text{ days/week}$). As such, patients in the present study were divided into three groups according to their level of sports activities, as follow: no (0 MET-hours/week), low-level ($<10 \text{ MET-hours/week}$) and high-level ($\geq 10 \text{ MET-hours/week}$) sports activities. Patients in high-level sports activities group belonged to those who met the recommendations for cancer survivors. [3, 39]

Measurement of QoL using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

At each assessment, a globally accepted questionnaire, EORTC QLQ-C30, was used to measure patients' QoL. [13] EORTC QLQ-C30 was developed to assess a range of cancer-specific QoL issues. [4] Consisting of thirty cancer-specific questions with multiple-point scales, it included a global health status, five functional domains (physical, role, emotional, cognitive and social), and nine symptom profiles (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties). In the analyses, the multiple-point scale in each item would be transformed into standard score, ranging from 0 to 100. Higher scores for global health status and five functioning domains indicated better QoL, while lower scores for symptom items suggested less symptoms or problems. [17]

Statistical analysis

Characteristics of participants were compared among patients who engaged in different levels of sports activity using ANOVA for continuous data and chi-squared test for categorical data. Univariate and multivariate linear regression analyses were used to investigate the association between levels of sports activities and QoL at 18-, 36- and 60-month follow-up cross-sectionally. As patients were longitudinally followed up at 18-, 36- and 60-month, this study further used Generalized Estimating Equations (GEE) model to evaluate the longitudinal association between sports activities and QoL over the three follow-ups, which enable the analyses to address the within-subject correlation. [38] In such analyses, each QoL item was a dependent variable as a function of time and level of sports activities, as well as other covariates, which included age at follow-up, education level, household income, AJCC stage, histology, human epidermal-growth-factor receptor 2 (HER 2) status, chemotherapy, endocrine therapy, BMI at follow-up and presence of menopausal symptoms at follow-up. All statistical analysis was performed using SPSS 26.0; and P values <0.05 based on two-sided analysis were considered statistically significant.

Results

Demographic, clinical and lifestyle characteristics of patients by level of sports activities at 18-, 36- and 60-month follow-up

Up to January 2019, the 60-month follow-up has been completed. A total of 1462 patients completed the baseline assessment, and 1310 (89.6%), 1162 (79.5%), 1173 (80.2%) patients completed 18-, 36- and 60-month follow-up assessment, respectively. In the present study, patients who had disease recurrence, metastasis, other primary cancers, or had incomplete data on sports activities or QoL were excluded; this resulted in 1289, 1125 and 1116 patients included

into the analyses at 18-, 36- and 60-month follow-up, respectively. The demographic and clinical characteristics of patients who were included into the present analysis were comparable to the whole cohort. The median intervals between the diagnosis of breast cancer and 18-, 36-, 60-month follow-up were 19.0 months (range: 12.1-35.8), 37.9 months (range: 30.1-41.8) and 59.7 months (range: 54.1-66.0), respectively.

At 18-month assessment, the proportions of patients who belonged to no, low-level and high-level sports activities groups were 20.7%, 45.5% and 33.8%, respectively, with the mean levels of sports activities being 0, 4.2 and 23.4 MET-hours/week, respectively (Table 1). Compared to patients who did not participate in any sports activities, those who engaged in low- or high-level of sports activities were more likely to have college or above education, be post-menopausal, had a histology of invasive ductal carcinoma (IDC), had tumor with HER 2 positive, had received chemotherapy and had normal BMI. Other demographic and clinical characteristics showed no significant difference between patients participating in different levels of sports activities.

Similar analyses were conducted at 36-month follow-up. The proportions of patients having no, low-level and high-level sports activities were 29.4%, 38.9% and 31.6%, respectively. The observed differences in education level, menopausal status at 18-month follow-up were also significant at 36-month follow-up. In addition, patients who were involved in high-level of sports activities at 36-month follow-up tended to be older and had higher household income than those who did not engage in any sports activities. Moreover, patients who had low-level of sports activities at 36-month follow-up were more likely to have endocrine therapy and reported menopausal symptoms more than those who did not engage in any sports activities or those who were engaged in high-level of sports activities.

At 60-month follow-up, the proportions of patients who belonged to no, low-level and high-level of sports activities were similar to those during the 36-month follow-up, with corresponding figures being 32.8%, 36.7% and 30.5%, respectively. When compared to patients who did not engage in any sports activity, those who were engaged in low- or high-level of sports activities were also more likely to have college or above education and be post-menopausal. No significant differences were found regarding other characteristics.

Linear regression model to investigate the associations between level of sports activities participation and QoL scores at 18-, 36- and 60-month follow-up based on cross-sectional analyses

At 18-month follow-up, 1289 patients were included in the analysis. Multivariate linear regression models with adjustment for socio-demographic, clinical and lifestyle variables indicated that, when compared to patients who had no sports activity, patients in higher level of sports activities had significantly better QoL in global health status/QoL (P for trend <0.001, Table 2), physical functioning (P for trend =0.008), role functioning (P for trend =0.037) and emotional functioning (P for trend =0.013), as well as less symptoms in fatigue (P for trend <0.001) and dyspnea (P for trend =0.014).

At 36-month follow-up, 1125 patients were included in the analysis. Similar to the associations noted at 18-month follow-up, when compared to patients who had no sports activity, women with higher level of sports activities reported better global health status/QoL (P for trend =0.028, table 3), physical functioning (P for trend =0.003) and emotional functioning (P for trend =0.006), when compared to those who had no sports activity. In addition, higher participation in sports activities was significantly related to less symptoms in fatigue (P for trend <0.001) and constipation (P for trend =0.002).

A total of 1116 patients were included in the analyses at 60-month follow-up. Similar associations were noted at this follow-up. Compared with those who had no sports activity, those having participated in higher level of sports activities reported higher scores in global health status/QoL (P for trend <0.001, table 4) and physical functioning (P for trend =0.020); on the other hand, they also had higher scores (more severe symptoms) in insomnia (P for trend =0.034).

GEE analyses to investigate the association between level of sports activity and QoL sports over the three follow-ups longitudinally

Based on the GEE analysis, after controlling for three follow-up time-points and other covariables, when compared to those who had no sports activity, higher level of sports activities was associated with better global health status/QoL, physical functioning, role functioning and emotional functioning (Table 5). For instance, compared to patients who did not participate in sports activity, patients who participated in low-level and high-level of sports activities reported higher score in global health status/QoL (mean difference: 0.97 and 4.53, respectively; P for trend <0.0001). In terms of symptom items, higher level of sports activities was associated with lower symptom scores (less severe symptoms) in fatigue, pain, loss of appetite and constipation. For instance, compared to patients who did not participate in sports activity, patients who participated in low-level and high-level of sports activities reported lower score in fatigue score (mean difference: -0.73 and -3.52, respectively; P for trend <0.0001). In addition, interactions between level of sports activities and follow-up time-points were also tested in the GEE models, and no significant interaction was noted (P for interaction >0.05 for all).

Discussion

Based on a cohort study, the present report found that regular participation in sports activities after breast cancer diagnosis was significantly associated with better general health status/QoL and physical functioning during the first five years of survival. Furthermore, the positive association between sports activities and QoL persisted over time. Using GEE model to control for the follow-up time-points, the findings indicated that women engaged in higher-level of sports activities, especially meeting the sports activities recommendation for cancer survivors (≥ 10 MET-hours/week) tended to have better QoL general health status/QoL, physical functioning, role functioning and emotional functioning, as well as less symptoms in fatigue, pain, loss of appetite and constipation.

There has been a series of interventional studies investigating whether short-term, structured sports activities interventions could improve QoL of breast cancer patients. A systematic review by Bicego et al. included 9 randomized controlled trials involving 373 patients who involved in structured sports activities programs that lasted for at least 4 weeks.[8] There was strong evidence supporting the notion that sports activities positively impact QoL of women with breast cancer.[8] In 2014, Zeng et al. published a meta-analysis which included 25 trials involving 2,927 women with breast cancer.[45] Compared to the controls, women in various sports activities groups had better overall QoL.[45] Another meta-analysis assessed the benefit of sports activities interventions after adjuvant therapy for breast cancer patients.[25] Sixty-three trials involving 5761 women were included and well randomized to exercise or control groups;

while studies only included aerobic sports activities or resistance training, others adopted both. The results suggested that interventions with sports activities might have small-to-moderate benefit on overall QoL, emotional, physical and social function as well as reduction in anxiety.[25] Another recently published systematic review by Zhang et al. included 36 studies and 3914 participants, the type of sports activities were categorized into three modes: aerobic, resistance, and a combination of aerobic and resistance. All three modes of sports activities intervention showed a significant positive effect on QoL between groups.[46]

In addition to evidence obtained from interventional studies, observational studies have also evaluated the beneficial effects of sports activities on QoL in breast cancer survivors. The Health, Eating, Activity and Lifestyle (HEAL) study enrolled a multi-ethnic cohort of 729 early-stage breast cancer survivors in the United States (US).[41] Participation in sports activities was evaluated around 2.5 years after diagnosis, with QoL being assessed 6-12 months thereafter using Medical Outcomes Study Short Form Survey (SF-36). Breast cancer survivors who partook in ≥ 2.5 hours/week of moderate to vigorous sports activities were categorized as meeting recommendations by the American College of Sports Medicine. The results showed that women who met the recommendation had better vitality, social functioning, emotional roles and global QoL.[41] Chen et al. investigated the association between post-diagnosis sports activities and QoL among Chinese breast cancer survivors who participated in the Shanghai Breast Cancer Survival Study (SBCSS). Participants reported their level of sports activities at 3 time-points, i.e. 6, 18 and 36 months after diagnosis.[12] The General Quality of Life Inventory-74 (GQOLI-74) was used to assess QoL at 6- and 36-month follow-up after diagnosis. Patients were categorized into three groups according to their level of sports activities: no sports activity group, low-level group (< 8.3 MET-hours/week) and high-level group (≥ 8.3 MET-hours/week) based on the US Department of Health and Human Services national recommendation for recreational physical activity.[1] At 6-month follow-up, higher level of sports activities was associated with better physical, psychological, and social well-being, as well as total QoL. Further, the average level of sports activities over the 36 months after diagnosis was positively associated with total QoL as well as physical, psychological and social well-being.[12] Additionally, a few cross-sectional studies have also investigated the association between sports activities and QoL among breast cancer survivors.[9, 10] Blanchard et al. reported that US women who met the ACS recommendations on sports activities had better QoL than those who did not.[9, 10] In another study, 3344 Chinese women with breast cancer were included.[18] Patients who were engaged in moderate-intensity sports activities for at least 30 minutes once every week in the past month were defined as exercisers, and the others were non-exercisers. Compared to non-exercisers, exercisers had significantly higher scores of physical, role and emotional functioning as well as global health status; they also reported milder symptoms of nausea and vomiting, pain, dyspnea and appetite loss.[18] More recently, a cross-sectional study among 214 breast and colorectal cancer survivors in Korea also supported the association between higher level of sports activities and better QoL.[35]

Compared to interventional studies, observational studies evaluated patients' participation in sports activities engagement in unsupervised condition, which has the advantage of capturing patients' real-life participation in sports activities as part of their routine daily lifestyle. The present study used prospective data from a cohort study and investigated the association between participation of sports activities and QoL during an important time-window, namely the first five years of survival. During this stage, breast cancer patients would adapt from an immediate to a long-term cancer survivorship. The finding in the present study supports previous evidence that breast cancer patients who were engaged in regular sports activities, especially those who met the recommendation for cancer survivors and general public, appeared to have better QoL.

There are a few possible biological mechanisms which mediate potential beneficial effects on QoL with the engagement of sports activities. These include cardiovascular and pulmonary adaptations, improved musculoskeletal strength, maintenance of mobility and independence.[14, 43] In addition, sports activities could indirectly influence psychosocial well-being, via self-efficacy and health status indicators.[37] Further, a growing number of studies have shown that higher participation in sports activities is associated with better long-term outcome in women with breast cancer.[7, 11, 20-24, 42] A number of proposed mechanisms have been raised to explain the role of sports activities in modifying disease progression, these include changes in insulin-like growth factor (IGF) levels, immune regulation and changes in metabolic hormone levels.[6, 32, 33] Follow-up of the cohort in the present study would provide important evidence about the potential benefit of regular engagement in sports activities on long-term outcomes among Chinese breast cancer survivors.

The present study has several strengths. It was based on a prospective study with relatively large sample size. During each assessment, interviewers collected detailed socio-demographic, clinical and lifestyle factors, and potential confounders have been adjusted in multivariate analyses. Moreover, this study investigated the association between participation of sports activities and QoL in a longitudinal manner at three time-points during the first five years of survival among Chinese women with breast cancer. The GEE model used in this study allows the control for follow-up time-points, and strengthen the reliability of the findings that regular sports activities is beneficial. However, a few limitations exist in the present study. Firstly, while the modified Chinese Baecke questionnaire included physical activity at work, in doing housework, at leisure time and in doing sports, the present study only used one part of the data. Secondly, the modified Chinese Baecke questionnaire has been validated in a random sample of Hong Kong adult population and has not specifically been validated in cancer patients. Additionally, this questionnaire was based on self-reporting, and it may result in potential bias in overestimation or underestimation. Wearable instruments, such as sports bracelet, could help assess the measure of sports activities in a more objective manner in future studies.

Conclusions

The association of adopting a healthy lifestyle and improvement in QoL is an important issue in the long-term management of cancer survivors. The present findings among Chinese women after their breast cancer diagnosis provided another important piece of evidence on the beneficial effect of regular participation in sports activities on QoL. Hence, health promotion programs after breast cancer diagnosis should aim to encourage regular participation in sports activities. In addition, continual follow-up of the studied cohort will provide information on the potential benefit of engagement in regular sports activities on outcomes of breast cancer.

Declarations

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Conflicts of interest statement

The authors declare no potential conflicts of interest.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Authors' contributions

YYL, SCH and WY designed the study and performed the statistical analysis. KLC, VY, RL, AC, CK, collected data. FM participated in statistical analysis. YYL, SCH and WY wrote the first draft of the manuscript, to which all authors subsequently contributed. All authors read and approved the final manuscript.

Ethics approval

The study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee and the KWC Research Ethics Committee of the Chinese University of Hong Kong and the Hong Kong Hospital Authority.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent to publication

Patients signed informed consent regarding publishing their data.

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Tables

Table 1. Demographic, clinical and lifestyle characteristics of patients by level of sports activities at 18-, 36- and 60-month follow-up

Characteristics	Level of sports activities at 18-month FU, (N=1289)				Level of sports activities at 36-month FU, (N=1125)				Level of sports activities at 60-month FU, (N=1116)			
	No (N=267, 20.7%)	Low- level group (N=586, 45.5%)	High-level group (N=436, 33.8%)	P	No (N=331, 29.4%)	Low- level group (N=438, 38.9%)	High- level group (N=356, 31.6%)	P	No (N=366, 32.8%)	Low- level group (N=410, 36.7%)	High-level group (N=340, 30.5%)	P
Level of sports activity, MET-hour/week, mean±SD	0	4.2±2.8	23.4±14.0		0	4.3±2.8	25.8±16.1		0	4.6±2.8	25.3±17.2	
Age at FU, mean±SD, year	53.5±9.3	53.3±9.1	54.3±8.6	0.240	54.9±8.9	54.7±9.1	56.4±8.1	0.019	56.4±8.8	56.7±9.2	58.3±8.5	0.209
Education level, %				0.003				0.026				0.004
High school or below	91.0	82.1	84.6		89.4	82.9	83.4		89.3	81.0	82.6	
Collage or above	9.0	17.9	15.4		10.6	17.1	16.6		10.7	19.0	17.4	
Marital status, %				0.081				0.106				0.569
Married or cohabitating	70.8	68.1	74.5		68.9	70.8	75.8		69.9	73.4	71.8	
Unmarried or divorced or widowed	29.2	31.9	25.5		31.1	29.2	24.2		30.1	26.6	28.2	
Household income, HKD/month				0.054				0.009				0.109
<15,000	54.3	44.7	44.3		51.7	43.8	43.5		50.0	43.9	43.2	
15,000-29,999	28.5	31.2	32.1		31.1	33.3	28.4		31.7	30.7	31.5	
≥30,000	17.2	24.1	23.6		17.2	22.8	28.1		18.3	25.4	25.3	
Employment status				0.086				0.133				0.229
Full time	34.1	35.7	40.8		34.4	36.1	42.4		36.1	33.9	42.1	
Part time	16.1	12.1	14.7		14.5	11.4	12.4		12.8	13.7	11.2	
Not working	49.8	52.2	44.5		51.1	52.5	45.2		51.1	52.4	46.8	
No. of comorbidity, %				0.273				0.528				0.629
0	55.4	61.9	62.6		59.2	62.8	61.5		60.7	62.7	61.5	
1	28.5	25.3	25.9		25.7	24.0	27.2		24.6	26.3	25.0	
≥2	16.1	12.8	11.5		15.1	13.2	11.2		14.8	11.0	13.5	
Menopausal status at FU, %				0.027				0.039				0.259
Pre-menopausal	25.1	22.5	17.2		24.5	22.4	16.9		17.5	18.0	13.8	
Post-menopausal	74.9	77.5	82.8		75.5	77.6	83.1		82.5	82.0	86.2	
AJCC stage, %				0.518				0.472				0.059
0-I	36.3	35.0	36.9		35.0	38.6	35.1		38.8	37.3	38.2	
II	43.1	45.7	46.8		46.5	46.1	48.9		41.5	48.0	48.8	
III	19.9	18.6	16.3		17.5	15.3	15.4		18.3	14.6	12.4	
Missing	0.7	0.7	0		0.9	0	0.6		1.4	0	0.6	
Histology, %				0.043				0.591				0.789

IDC	79.8	85.7	85.1	84.3	83.1	84.3	83.9	84.4	83.2
ILC	1.9	2.7	3.9	1.5	3.7	3.7	1.9	3.4	3.2
DCIS	9.7	4.9	5.0	7.3	6.2	5.3	7.1	5.6	5.6
Others	8.6	6.7	6.0	6.9	7.1	6.7	7.1	6.6	7.9
ER status, %				0.267			0.993		0.664
Positive	73.1	73.1	73.4	72.8	72.8	72.5	75.1	71.2	73.8
Negative	23.2	23.5	25.2	24.2	24.2	25.0	21.3	25.6	23.5
Missing	3.7	3.4	1.4	3.0	3.0	2.5	3.6	3.2	2.6
PR status, %				0.050			0.838		0.924
Positive	59.2	55.8	54.8	55.3	57.5	42.4	56.0	55.6	55.9
Negative	37.1	39.9	43.8	41.1	39.3	55.1	39.9	41.2	41.2
Missing	3.7	4.3	1.4	3.6	3.2	2.5	4.1	3.2	2.9
HER 2 status, %				<0.001			0.599		0.084
Positive	21.0	28.5	26.8	29.0	27.2	24.4	24.9	27.8	23.8
Negative	66.3	66.9	68.1	63.7	66.4	69.7	65.6	67.3	70.0
Missing	12.7	4.6	5.0	7.3	6.4	5.9	9.6	4.9	6.2
Type of surgery				0.403			0.904		0.511
Mastectomy	65.9	61.6	61.2	62.2	61.0	60.7	62.0	61.0	57.9
Conservation	34.1	38.4	38.8	37.8	39.0	39.3	38.0	39.0	42.1
Chemotherapy, %				0.027			0.826		0.607
Yes	70.0	78.2	77.5	75.5	76.5	77.5	72.4	75.4	75.0
No	30.0	21.8	22.5	24.5	23.5	22.5	24.6	24.6	25.0
Radiotherapy, %				0.181			0.470		0.811
Yes	67.4	73.4	70.2	69.2	72.8	71.3	69.9	69.0	71.2
No	32.6	26.6	29.8	30.8	27.2	28.7	30.1	31.0	28.8
Endocrine therapy, %				0.227			0.018		0.784
Yes	76.4	72.2	76.4	71.0	78.8	71.3	75.4	74.9	73.2
No	23.6	27.8	23.6	29.0	21.1	28.7	24.6	25.1	26.8
BMI at FU, kg/m ²				0.001			0.153		0.007
Underweight (<18.5)	5.2	6.3	3.9	3.6	4.8	4.5	3.0	6.3	3.8
Normal (18.5-22.9)	41.9	42.3	53.0	41.1	40.9	46.3	37.4	38.8	41.8
Overweight (23-24.9)	19.9	20.5	22.0	19.3	22.4	23.3	16.9	23.9	25.0
Obese (≥25)	33.0	30.9	21.1	36.0	32.0	25.8	42.6	31.0	29.4
Presence of menopausal symptoms, %				0.677			0.017		0.311
Yes	64.0	65.7	63.1	60.7	70.1	63.2	62.8	66.6	61.5
No	36.0	34.3	36.9	39.3	29.9	36.8	37.2	33.4	38.5

Abbreviations: FU, follow-up, SD, standard deviation; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; BMI, body mass index; MET, metabolic equivalent of task.

Table 2. Univariate and multivariate linear regression analyses to investigate the associations of level of sports activities and QoL scores at 18-month follow-up cross-sectionally (N=1289)

EORTC QLQ-C30	Crude					Adjusted				
	Low-level group (N=438)		High-level group (N=356)		P for trend	Low-level group (N=438)		High-level group (N=356)		P for trend
	Mean difference	95%CI	Mean difference	95%CI		Mean difference	95%CI	Mean difference	95%CI	
Global Health status/QoL	1.43	1.08 to 3.95	5.44	2.79 to 8.09	<0.001	1.32	1.06 to 3.69	5.07	2.56 to 7.57	<0.001
Functioning										
Physical Functioning	-0.31	-1.98 to 1.37	2.21	0.46 to 3.97	0.004	-0.38	-1.93 to 1.16	1.86	0.23 to 3.50	0.008
Role Functioning	-0.32	-2.43 to 1.78	1.71	-0.50 to 3.93	0.076	-0.05	-2.11 to 2.00	2.02	-0.15 to 4.19	0.037
Emotional Functioning	2.41	-0.27 to 5.10	3.22	0.39 to 6.05	0.033	2.97	0.57 to 5.38	3.48	0.94 to 6.02	0.013
Cognitive Functioning	0.18	-2.56 to 2.92	1.06	-1.82 to 3.94	0.432	0.14	-2.48 to 2.75	0.81	-1.96 to 3.57	0.531
Social Functioning	0.41	-1.79 to 2.61	0.44	-1.87 to 2.76	0.730	0.70	-1.45 to 2.86	0.40	-1.87 to 2.68	0.805
Symptoms										
Fatigue	-0.56	-3.14 to 2.30	-4.79	-7.80 to -1.79	<0.001	-0.90	-3.53 to 1.73	-4.31	-7.09 to -1.54	<0.001
Nausea and vomiting	-0.15	-1.07 to 0.78	-0.54	-1.52 to 0.43	0.242	-0.10	-1.03 to 0.84	-0.30	-1.28 to 0.69	0.530
Pain	1.19	-2.12 to 4.50	-3.59	-7.07 to -0.11	0.015	1.58	-1.44 to 4.61	-2.36	-5.56 to 0.83	0.060
Dyspnea	-0.60	-3.05 to 1.85	-3.41	-5.99 to -0.83	0.005	-0.88	-3.28 to 1.52	-2.98	-5.51 to -0.48	0.014
Insomnia	3.41	-0.71 to 7.52	0.79	-3.54 to 5.13	0.958	3.05	-0.84 to 6.94	0.57	-3.55 to 4.68	0.962
Loss of appetite	-0.83	-2.76 to 1.10	-2.05	-4.08 to -0.02	0.040	-0.46	-2.39 to 1.47	-1.42	-3.47 to 0.62	0.148
Constipation	-1.94	-4.81 to 0.92	-2.58	-5.59 to 0.44	0.109	-1.82	-4.72 to 1.09	-2.54	-5.61 to 0.54	0.119
Diarrhea	1.57	-0.22 to 3.35	-0.51	-2.39 to 1.37	0.329	1.15	-0.64 to 2.94	-0.66	-2.56 to 1.23	0.286
Financial impact	0.35	-3.05 to 3.75	0.14	-3.44 to 3.71	0.968	1.28	-2.01 to 4.57	1.67	-1.81 to 5.15	0.372

Univariate and multivariate linear regression models were used to investigate the associations between level of sports activities and QoL scores. The adjusted variables included age at follow-up, education level, household income, menopausal status at follow-up, total number of comorbidities, AJCC stage, histology, HER 2 status, chemotherapy, endocrine therapy, BMI at follow-up, presence of menopausal symptoms at follow-up. Patients in the no sports activity group were treated as the reference in calculating the mean difference of QoL.

Abbreviations: 95%CI, 95% confidence intervals; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; AJCC, American joint Committee on cancer; HER 2, human epidermal-growth-factor receptor 2; BMI, body mass index.

Table 3. Univariate and multivariate linear regression analyses to investigate the associations of level of sports activities and QoL scores at 36-month follow-up cross-sectionally (N=1125)

EORTC QLQ-C30	Crude				P for trend	Adjusted				
	Low-level group (N=586)		High-level group (N=436)			Low-level group (N=586)		High-level group (N=436)		P for trend
	Mean difference	95%CI	Mean difference	95%CI		Mean difference	95%CI	Mean difference	95%CI	
Global Health status/QoL	-0.59	-3.20 to 2.02	3.17	0.43 to 5.91	0.021	-0.05	-2.50 to 2.40	2.85	0.27 to 5.43	0.028
Functioning										
Physical Functioning	-0.61	-2.40 to 1.18	3.05	1.17 to 4.93	0.001	-0.39	-2.08 to 1.30	2.67	0.90 to 4.45	0.003
Role Functioning	-0.32	-2.52 to 1.87	2.08	-0.23 to 4.38	0.072	0.28	-1.88 to 2.44	1.97	-0.31 to 4.24	0.087
Emotional Functioning	-0.16	-2.78 to 2.47	3.11	0.36 to 5.86	0.002	1.60	-0.75 to 3.95	3.46	0.99 to 5.93	0.006
Cognitive Functioning	-0.43	-3.22 to 2.36	0.76	-2.16 to 3.69	0.598	0.69	-1.88 to 3.26	0.46	-2.25 to 3.17	0.748
Social Functioning	-0.65	-2.71 to 1.42	1.68	-0.49 to 3.84	0.119	-0.23	-2.28 to 1.82	1.37	-0.79 to 3.52	0.205
Symptoms										
Fatigue	0.05	-2.94 to 3.04	-5.19	-8.32 to -2.05	0.001	-1.24	-3.91 to 1.44	-5.05	-7.86 to -2.23	<0.001
Nausea and vomiting	0.52	-0.86 to 1.89	-0.38	-1.82 to 1.06	0.587	0.42	-0.96 to 1.80	-0.24	-1.70 to 1.21	0.726
Pain	1.08	-2.04 to 4.20	-3.48	-6.75 to -0.21	0.033	0.66	-2.26 to 3.57	-2.86	-5.93 to 0.22	0.063
Dyspnea	0.83	-1.92 to 3.57	-0.46	-3.34 to 2.42	0.739	0.43	-2.21 to 3.07	0.22	-2.56 to 3.00	0.881
Insomnia	0.99	-3.20 to 5.18	-2.05	-6.44 to 2.34	0.347	-0.85	-4.77 to 3.07	-2.60	-6.73 to 1.53	0.214
Loss of appetite	0.23	-1.94 to 2.39	-1.86	-4.14 to 0.41	0.102	-0.09	-2.26 to 2.07	-1.83	-4.11 to 0.44	0.109
Constipation	-3.06	-6.15 to 0.04	-5.25	-8.49 to -2.00	0.002	-3.75	-6.83 to -0.68	-5.13	-8.34 to -1.88	0.002
Diarrhea	0.23	-1.91 to 2.37	-1.02	-3.26 to 1.22	0.362	-0.19	-2.33 to 1.94	-1.15	-3.41 to 1.10	0.309
Financial impact	2.12	-0.77 to 5.00	0.55	-2.47 to 3.57	0.746	2.34	-0.44 to 5.12	1.43	-1.50 to 4.37	0.356

Univariate and multivariate linear regression models were used to investigate the associations between level of sports activity and QoL scores. The adjusted variables included age at follow-up, education level, household income, menopausal status at follow-up, total number of comorbidities, AJCC stage, histology, HER 2 status, chemotherapy, endocrine therapy, BMI at follow-up, presence of menopausal symptoms at follow-up. Patients in the no sports activity group were treated as the reference in calculating the mean difference of QoL.

Abbreviations: 95%CI, 95% confidence intervals; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; AJCC, American joint Committee on cancer; HER 2, human epidermal-growth-factor receptor 2; BMI, body mass index.

Table 4. Univariate and multivariate linear regression analyses to investigate the associations of level of sports activities and QoL scores at 60-month follow-up cross-sectionally (N=1116)

EORTC QLQ-C30	Crude				P for trend	Adjusted				P for trend
	Low-level group		High-level group			Low-level group		High-level group		
	(N=410)		(N=340)			(N=410)		(N=340)		
	Mean difference	95%CI	Mean difference	95%CI	Mean difference	95%CI	Mean difference	95%CI		
Global Health status/QoL	1.13	-1.35 to 3.61	6.20	3.60 to 8.80	<0.001	1.43	-0.92 to 3.78	5.74	3.26 to 8.21	<0.001
Functioning										
Physical Functioning	-0.13	-1.90 to 1.63	2.58	0.73 to 4.43	0.007	-0.22	-1.87 to 1.43	2.07	0.33 to 3.81	0.020
Role Functioning	0.49	-1.65 to 2.64	0.60	-1.65 to 2.85	0.597	0.97	-1.18 to 3.12	0.44	-1.82 to 2.71	0.697
Emotional Functioning	0.06	-2.45 to 2.56	1.92	0.71 to 4.54	0.157	0.62	-1.66 to 2.91	1.40	-1.01 to 3.80	0.253
Cognitive Functioning	-0.34	-3.08 to 2.40	0.66	-2.21 to 3.53	0.661	-0.04	-2.61 to 2.52	-0.05	-2.75 to 2.65	0.971
Social Functioning	-0.53	-2.43 to 1.36	-0.18	-2.16 to 1.81	0.852	-0.53	-2.39 to 1.34	-0.95	-2.92 to 1.02	0.342
Symptoms										
Fatigue	0.55	-2.25 to 3.34	-1.79	-4.72 to 1.13	0.240	-0.03	-2.56 to 2.50	-0.95	-3.62 to 1.71	0.483
Nausea and vomiting	0.27	-0.90 to 1.43	-0.26	-1.48 to 0.96	0.692	0.37	-0.81 to 1.55	0.09	-1.15 to 1.33	0.886
Pain	1.06	-2.08 to 4.21	-0.98	-4.27 to 2.32	0.577	1.22	-1.69 to 4.14	0.09	-2.98 to 3.17	0.949
Dyspnea	-0.26	-2.79 to 2.27	-1.14	-3.79 to 1.51	0.402	-0.13	-2.59 to 2.33	0.10	-2.49 to 2.70	0.938
Insomnia	4.56	0.45 to 8.67	3.69	-0.61 to 8.00	0.086	4.07	0.20 to 7.94	4.40	0.32 to 8.48	0.034
Loss of appetite	0.42	-1.49 to 2.34	-2.19	-4.20 to -0.19	0.036	0.43	-1.47 to 2.33	-1.62	-3.62 to 0.38	0.115
Constipation	-0.93	-4.07 to 2.22	-3.54	-6.84 to -0.25	0.036	-1.63	-4.79 to 1.53	-3.32	-6.64 to 0.01	0.050
Diarrhea	0.22	-1.88 to 2.32	-1.38	-3.58 to 0.81	0.225	0.23	-1.88 to 2.34	-0.85	-3.08 to 1.37	0.455
Financial impact	-0.31	-2.99 to 2.37	-1.38	-4.19 to 1.43	0.340	0.14	-2.48 to 2.75	0.01	-2.75 to 2.76	0.997

Univariate and multivariate linear regression models were used to investigate the associations between level of physical activity and QoL scores. The adjusted variables included age at follow-up, education level, household income, menopausal status at follow-up, total number of comorbidities, AJCC stage, histology, HER 2 status, chemotherapy, endocrine therapy, BMI at follow-up, presence of menopausal symptoms at follow-up. Patients in the no sports activity group were treated as the reference in calculating the mean difference of QoL.

Abbreviations: 95%CI, 95% confidence intervals; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; AJCC, American joint Committee on cancer; HER 2, human epidermal-growth-factor receptor 2; BMI, body mass index.

Table 5. Generalized Estimating Equations (GEE) analyses to investigate the associations between level of sports activities and QoL scores longitudinally

EORTC QLQ-C30	Model 1					Model 2				
	Low-level group (N=410)		High-level group (N=340)		P for trend	Low-level group (N=410)		High-level group (N=340)		P for trend
	Mean difference	95%CI	Mean difference	95%CI		Mean difference	95%CI	Mean difference	95%CI	
Global Health status/QoL	0.67	-1.0 to 2.34	4.9	3.03 to 6.80	<0.001	0.97	-0.51 to 2.45	4.53	2.85 to 6.20	<0.001
Functioning										
Physical Functioning	-0.33	-1.52 to 0.86	2.61	1.38 to 3.83	<0.001	-0.27	-1.35 to 0.80	2.25	1.16 to 3.34	<0.001
Role Functioning	-0.09	-1.50 to 1.32	1.49	-0.01 to 3.00	0.042	0.29	-1.09 to 1.66	1.53	0.09 to 2.97	0.030
Emotional Functioning	0.78	-0.98 to 2.53	1.92	0.68 to 4.62	0.007	1.77	0.27 to 3.28	2.75	1.10 to 4.40	0.001
Cognitive Functioning	-0.20	-2.06 to 1.66	0.88	-1.27 to 2.88	0.419	0.26	-1.42 to 1.94	0.54	-1.31 to 2.38	0.567
Social Functioning	-0.24	-1.52 to 1.04	0.60	-0.85 to 2.05	0.389	-0.02	-1.23 to 1.19	0.30	-1.05 to 1.66	0.644
Symptoms										
Fatigue	0.08	-1.90 to 2.07	-3.90	-6.03 to -1.77	<0.001	-0.73	-2.42 to 0.97	-3.52	-5.28 to -1.75	<0.001
Nausea and vomiting	0.21	-0.49 to 0.91	-0.37	-1.08 to 0.33	0.261	0.22	-0.48 to 0.92	-0.14	-0.82 to 0.54	0.631
Pain	1.19	-0.89 to 3.28	-2.71	-4.94 to -0.48	0.011	1.17	-0.66 to 3.00	-1.74	-3.67 to 0.19	0.011
Dyspnea	0.08	-1.57 to 1.73	-1.68	-3.43 to 0.07	0.049	-0.05	-1.59 to 1.50	-0.91	-2.55 to 0.73	0.051
Insomnia	3.05	0.37 to 5.72	0.82	-2.16 to 3.80	0.682	2.06	-0.32 to 4.44	0.64	-1.99 to 3.27	0.713
Loss of appetite	-0.08	-1.37 to 1.20	-1.98	-3.22 to -0.75	0.001	-0.13	-1.38 to 1.12	-1.62	-2.83 to -0.40	0.006
Constipation	-2.04	-4.14 to 0.06	-3.74	-6.02 to -1.47	0.001	-2.45	-4.49 to -0.42	-3.64	-5.83 to -1.44	0.001
Diarrhea	0.66	-0.57 to 1.90	-1.02	-2.26 to 0.21	0.078	0.44	-0.77 to 1.64	-0.98	-2.19 to 0.22	0.082
Financial impact	0.67	-1.28 to 2.62	-0.22	-2.33 to 1.90	0.798	1.17	-0.67 to 3.02	1.09	-0.88 to 3.06	0.302

Generalized estimating equations were used to investigate the associations between level of physical activity and QoL scores. Model 1, adjusted for follow-up time-points; Model 2, further adjusted for age at follow-up, education level, household income, menopausal status at follow-up, total number of comorbidities, AJCC stage, histology, HER 2 status, chemotherapy, endocrine therapy, BMI at follow-up, presence of menopausal symptoms at follow-up. Patients in the no sports activity group were treated as the reference in calculating the mean difference of QoL.

Abbreviations: 95%CI, 95% confidence intervals; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; QoL, quality of life; AJCC, American joint Committee on cancer; HER 2, human epidermal-growth-factor receptor 2; BMI, body mass index.

Supplementary Files

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- [Supplementarytable.docx](#)