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Influence of Prediagnostic Recreational Physical Activity on Survival from Breast Cancer

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Abstract

OBJECTIVES—Recreational physical activity (RPA) is associated with a reduced risk of developing breast cancer, but there is limited research on whether prediagnostic RPA influences survival after breast cancer diagnosis.

METHODS—We evaluated the association between prediagnostic RPA and risk of death in 1,508 women with a first breast cancer diagnosis between 1996 and 1997 in the population-based Long Island Breast Cancer Study Project. Five-year mortality through the end of 2002 was assessed using the National Death Index (N=196). An in-person interview was completed shortly after diagnosis to obtain information on lifetime RPA, which was expressed as metabolic equivalent task hours per week (MET-h/wk).

RESULTS—A lower risk of all-cause death was observed for women who engaged in an average of ≥9 MET-h/wk of RPA from menarche to diagnosis compared with women who did not exercise (age and BMI adjusted hazard ratio [HR]=0.57; 95% confidence interval [CI]=0.39–0.83), an association that was similar when evaluated according to menopausal status. Decreased all-cause mortality was found for women with any moderate intensity lifetime RPA (>0 MET-h/wk) (HR=0.62; 95% CI=0.46-0.84) and breast cancer-specific mortality (HR=0.64; 95% CI=0.43-0.93) risk than women who engaged in no moderate RPA. Among postmenopausal women, RPA that took place after menopause resulted in a decrease in overall mortality, whereas no association was observed for RPA which took place prior to menopause (>0 MET-h/wk of RPA vs. no RPA: HR=0.61; 95% CI=0.39-0.94; and HR=1.00; 95% CI=0.65-1.54, respectively).

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CONCLUSIONS—This study provides support that RPA prior to breast cancer diagnosis improves survival.

Keywords

Physical activity; exercise; breast cancer; survival; prevention; epidemiology

INTRODUCTION

There is convincing evidence for an inverse relationship between physical activity and breast cancer with many studies reporting a 20% to 30% decreased risk of developing breast cancer for those who are physically active, and most reporting a dose-response relationship [1, 2]. The inverse relationship of breast cancer with physical activity has been consistently observed in both cohort and case-control studies and across many subgroups including both pre- and postmenopausal women, intensity of physical activity, and appears to be independent of obesity and hormone receptor status [3, 4]. Further, a recent review suggests that recreational physical activity, rather than occupational, household, and transportation, is associated with the greatest decreases in risks observed for physical activity on breast cancer occurrence [4]. Similar mechanisms for breast cancer risk and survival are thought to be involved, including direct reduction in exposure to sex steroid hormones, reduced insulin and insulin-like growth factors, modulation of inflammation and indirectly through reduced adiposity [5]. Therefore, increasing physical activity is a promising preventive measure for reducing risk of death after a breast cancer diagnosis.

While there is ample evidence supporting a reduction in breast cancer risk for higher levels of physical activity, fewer studies have examined whether exercise influences mortality among breast cancer survivors. Both case-control and cohort studies have investigated this association, most finding an inverse association between physical activity and survival [6-11]. However, only a few studies have investigated intensity of recreational physical activity on breast cancer survival [9, 11, 12], and to our knowledge, no studies have evaluated the effect of the timing of physical activity during the lifetime on survival after breast cancer diagnosis.

The purpose of this study was to examine whether the amount, intensity, duration and timing of prediagnostic physical activity influences risk of death after a breast cancer diagnosis in the Long Island Breast Cancer Study Project, population-based cohort of women with breast cancer.

METHODS

Study Population

This study draws on data that were collected from participants as part of the Long Island Breast Cancer Study Project (LIBCSP), a population-based study of English-speaking residents of Nassau and Suffolk counties of Long Island, New York [13]. LIBCSP participants were women newly diagnosed with a first, primary *in situ*, or invasive breast cancer between August 1, 1996, and July 31, 1997. Women were identified using a rapid reporting system established specifically for the LIBCSP and were confirmed by physician's and medical records. The attending physician was contacted to confirm study eligibility and to seek permission to contact the patient. Institutional review board approval of the study protocol was obtained from each collaborating institution and participating hospital and written informed consent was obtained from each participant before the interview. A total of 1,508 women with breast cancer, of which 1,273 had invasive breast cancer, participated in the LIBCSP baseline, case-control study interview, which was administered shortly after

diagnosis. As part of the LIBCSP follow-up of the case women, vital status through the end of 2002 was determined through the National Death Index (NDI).

Data Collection

Baseline Data—The lifetime physical activity and most of the covariate data used in this analysis were collected as part of the LIBCSP baseline interview. The main questionnaire was administered in-home by a trained interviewer and took ~2 hours to complete. Information obtained from the main questionnaire includes reproductive and menstrual history, exogenous hormone use, family history of cancer, body size, physical activity, smoking history, alcohol intake, and demographic characteristics. Nearly two thirds of baseline case interviews occurred before initiation of chemotherapy [13]. Descriptive characteristics for the entire LIBCSP study have been previously published [13].

As part of the baseline interview, participants reported participation in recreational physical activity (RPA) using an instrument which was a modification of that developed by Bernstein and colleagues [14, 15]. Participants were asked about all recreational physical activities in which they had engaged for at least one hour per week for at least three months or more in any year over their entire lifetime, but prior to the breast cancer diagnosis. Activity information recorded was the name of the activity, the ages the activity was started and stopped, the total years of participation in the activity, the number of months per year and the number of hours per week the activity was usually performed.

Treatment and Tumor Characteristic Data—Information on treatment undergone for the first primary breast cancer is based on response at baseline and during follow-up. Nearly two-thirds of participants with breast cancer completed their baseline interview prior to the initiation of chemotherapy, therefore additional treatment information was obtained by trained interviewer via telephone from 1,098 case participants or their proxy in 2002 to 2004 and by re-abstracting medical records. There were 410 cases without follow-up interview data due to non-response, refusal, untraceability, or death without an identifiable proxy.

Data on estrogen receptor (ER) and progesterone receptor (PR) status were gathered from medical records of 1,402 women who signed a medical release form. Treatment and tumor characteristic data were abstracted for 598 women. A high concordance was found between information abstracted from records and self-reported radiation therapy ($\kappa = 0.97$), chemotherapy ($\kappa = 0.96$), and hormone therapy ($\kappa = 0.92$). Thus, for this study, the analysis is based on self-reported treatment at the baseline and follow-up interviews.

Study Outcome—For the LIBCSP follow-up study, the NDI was used to ascertain all-cause and breast cancer-specific mortality among study participants. Because most women who die from their breast cancer will do so within five years of diagnosis [16], we are reporting survival after 5 years of follow-up. Participants were followed from diagnosis until December 31, 2002. Among the 1,508 women diagnosed with breast cancer, 198 (13.1%) deaths occurred. Based on International Classification of Diseases (ICD) codes 174.9 and C-50.9 listed as a primary or secondary code on the death certificate, 128 (64.6%) deaths were due to breast cancer. Cases without a death record in the NDI database were determined to be alive as of December 31, 2002.

Variable Definitions

Recreational Physical Activity—Among participants classified as ever having participated in recreational physical activity, a duration-frequency measure was calculated using the reported number of hours per week of participation summed across all activities for each year of a woman's life. This combination duration and frequency measure was

calculated as hours per week of activity and examined among all women. This variable was then further divided among subcategories of specific time periods during the lifecourse including RPA over the lifetime (expressed as hours per week of RPA from menarche to diagnosis), premenopausal RPA (for postmenopausal women only, RPA from menarche up to menopause), RPA from onset of menopause to diagnosis, and recent RPA (within 10 years prior to diagnosis). There were 1,504 case women who had a valid response for physical activity.

Metabolic equivalent task (MET) scores were assigned to each reported activity using a published database as a guide [17]. One MET is defined as the energy expended when sitting quietly, which is equal to 3.5 milliliters of oxygen per kilogram of body weight per minute, or one kilocalorie per kilogram of body weight per hour [17]. This MET score was then multiplied by the number of hours per week the subject reported engaging in the activity to derive MET-hours per week (MET-h/wk) that were averaged for annual activity levels (MET-h/wk) for the specific lifecourse time periods described above. Use of this measure in analyses allowed for simultaneous examination of activity duration, and frequency in relation to risk of breast cancer. Total RPA was further classified according to intensity, where low intensity activities were defined as those expending <3 MET, moderate intensity activities expending ≥3 - <6 MET, and high intensity activities expending ≥6 MET [18].

Covariates—Self-reported data on potential covariates were gathered through interviewer-administered questionnaires at baseline (in person) and at follow-up (by telephone) and included prediagnostic factors related to demography (race, income, education, marital status), reproduction (parity, age at first live birth, breast feeding), and menstruation (age at menarche, age at menopause). Prediagnostic exogenous hormone use was also considered (hormonal birth control, hormone replacement) as was prediagnostic medical history (benign breast disease, family history of breast cancer), lifestyle factors (lifetime average alcohol consumption, dietary fat (grams/day) and total caloric intake (kilocalories/day), and cigarette smoking, history of co-morbidities reported at the baseline interview (high cholesterol, history of blood clots, diabetes, hypertension, previous myocardial infarction and stroke), as well as the tumor characteristics (tumor stage, tumor size and nodal status), and treatment undergone (chemotherapy, radiation, tamoxifen) for the original breast cancer diagnosis.

Menopausal status was derived using information provided on the baseline questionnaire [13]. Postmenopausal status was defined as having a last menstrual period >6 months before the date of diagnosis or if both ovaries were removed before the date of diagnosis. Women with unknown menopausal status were categorized as postmenopausal based on the 90th percentile for age at menopause in the control population from the baseline study, and calculated according to smoking status (≥54.8 yrs for smokers and ≥55.4 yrs for non-smokers).

Statistical Methods

Lifetime RPA was defined as RPA from menarche to diagnosis. RPA analyses were also carried out for the life periods from menarche to menopause; menopause to diagnosis; and recent RPA (within 10 years prior to diagnosis). To reduce the possibility that RPA by life period associations we observed were due to the differences in sample size, the analyses for timing of RPA was restricted to women who had a reported RPA measure at each time point. Physical activity variables were classified as MET-h/wk in categories defined as 0, >0 to 8.9, and 9 or more MET-h/wk. These cutpoints were selected based on Centers for Disease Control and Prevention and the American College of Sports Medicine recommendations for physical activity [18] as well as for consistency with other

investigations by Holmes et al. (<3, 3 to 8.9, 9 to 14.9, 15 to 23.9, and 24 or more MET-h/wk) [19] and Irwin et al. (0, >0 to 8.9, and 9 or more MET-h/wk) [7].

Kaplan-Meier methods [20] were used to generate survival curves by RPA category (data not shown). Cox proportional hazards regression [20] was used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for the risk of all-cause and breast cancer-specific mortality. Participants with *in situ* disease were excluded when calculating breast cancer-specific mortality estimates. Proportional hazards assumptions were verified with Schoenfield residuals. No violation of this assumption was found. The results for overall and 5-year survival were similar; therefore, only overall survival is reported. Tests of trend were conducted using the continuous values for RPA.

Effect measure modification on the multiplicative scale between categorical RPA variables and other covariates was evaluated using the log likelihood ratio test to compare proportional hazards regression models with and without the cross-product terms [20]. To assess for potential heterogeneity, we evaluated effects stratified by variables, which included exogenous hormone use (never used hormones, ever used hormones), body mass index (median BMI = weight in meters/height in meters squared), menopausal status (premenopausal, postmenopausal), and family history of breast cancer in a first-degree relative (no family history, family history). Associations were also evaluated by stratification on the tumor characteristics ER status (negative, positive), PR status (negative, positive), tumor stage (*in situ*, invasive), nodal status (node-negative, node-positive), and tumor size (<2cm, ≥2cm).

For assessment of confounding, variables were included in multivariate models if they were related to either the exposure (RPA) or the outcome (death). Using backward elimination, potential confounders were removed from models beginning with those with the highest P value. Variables remained in the final models if their inclusion changed the estimate of effect by >10% [21]. Adjustment for most factors did not substantially alter the estimates of effect therefore all models include only age at diagnosis and BMI in the year prior to the diagnosis. Models including both pre- and postmenopausal women were also adjusted for menopausal status.

To further explore possible confounding by tumor characteristics and treatment, we conducted separate analyses restricted to women for whom we have complete tumor characteristic and tumor treatment data. There were no differences in effects or evidence of confounding by these variables for the relationship between RPA and mortality. All analyses were carried out using SAS version 9.1 [22].

RESULTS

There were 196 deaths identified, 128 due to breast cancer. Mean follow up was 66.7 months (range, 2.7-88.6). Distributions of select characteristics by total MET-h/wk of RPA from menarche up to diagnosis among women with breast cancer are shown in Table 1. Women who engaged RPA during this time tended to be younger at diagnosis, more likely to have completed high school, had a lower BMI and were more likely to have taken exogenous hormones than those who were inactive. There was little difference in estrogen receptor or progesterone receptor status in physically active women compared with inactive women.

Results for analyses that examined the association between overall lifetime physical activity and intensity of lifetime physical activity are shown in Table 2. Each category of lifetime RPA over 0 MET h/wk showed a modest decreased risk of both all-cause and breast cancer-specific mortality. Compared with women who never participated in RPA, those with high

levels of RPA (≥9 MET-h/wk) had improved survival from all causes for total lifetime RPA (HR=0.57; 95% CI=0.39-0.83). The results for No RPA vs. Any RPA, regardless of MET-h/wk, were similar to those seen for the highest levels of activity (≥9 MET h/wk) for both all-cause and breast cancer-specific mortality, where women who engaged in any lifetime RPA had a 42% decrease in risk of death due to all causes (HR= 0.58, 95% CI=0.43-0.91) and a 37% reduced risk of death due to breast cancer (HR=0.63; 95% CI=0.43-0.91). No significant trends were observed for reduced mortality with increasing MET h/wk of RPA (data not shown).

We also investigated the effect of intensity of RPA on death outcomes. Moderate intensity lifetime RPA also resulted in decreased mortality, where those who reported ever regularly engaging in moderate RPA had lower risk of death attributed to breast cancer RPA (HR=0.64; 95% CI=(0.43-0.93) and all-causes (HR=0.62; 95% CI=0.46-0.84) compared to those who never engaged in moderate RPA. There was no decreased association with mortality observed for those who engaged in vigorous intensity physical activity.

The 5-year survival for premenopausal women who engaged in any lifetime RPA was 93% and 85% for inactive women (Figure 1a). Similarly, among postmenopausal breast cancer participants the 5-year survival from any cause was 90% for active women and 83% for inactive women (Figure 1b). Associations were similar, although slightly attenuated, for breast cancer-specific mortality. We further evaluated the association of lifetime RPA stratified by menopausal status and found no evidence of statistically significant interaction (*P* for interaction = 0.48). Lifetime RPA among premenopausal women was associated with modest decreases in all-cause and breast cancer-specific mortality regardless of MET h/wk of activity (any RPA vs. no RPA: HR =0.53; 95% CI=0.28-0.97; HR =0.54; 95% CI=0.27-1.05, respectively), although there were no apparent trends for reduced risk of death with increasing RPA (Table 3). Similar, although attenuated, reduced associations that approached statistical significance were seen for low levels of RPA up to 8.9 MET-h/wk and high levels greater than 9.0 MET-h/wk among postmenopausal women.

When considering the timing of physical activity among postmenopausal women, we observed that engaging in exercise after menopause was associated with a reduced risk of death due to all causes, whereas there was no effect for physical activity which took place before menopause (Table 4). Compared with inactive women, those who engaged in 9 MET-h/wk or more of RPA after menopause had a 67% lower risk of death (HR=0.33; 95% CI=0.17-0.63, *P* for trend = 0.002). Results for breast cancer-specific mortality were similar, but not as strong as those seen for deaths from all causes. Postmenopausal women who engaged in physical activity in the 10 years prior to diagnosis showed similar results for all-cause mortality as those seen for RPA after menopause (≥9 MET-h/wk vs. no RPA: HR = 0.33; 95% CI=0.18-0.61).

Analyses of overall and breast cancer mortality stratified by BMI is shown in Table 5. We observed no decreasing trend in overall or breast cancer-specific mortality observed for those with increasing levels of RPA in either normal weight or overweight/obese women. Similar associations for breast cancer-specific mortality were seen for women who were normal weight and those who were overweight/obese. However, when examining the effects of any lifetime RPA vs. no RPA on all-cause mortality, women with a BMI<25 had a 56% decrease in risk of death whereas the protective effect of RPA on all-cause death for women with a BMI≥25 was not as strong (HR=0.44, 95% CI=0.27-0.70; HR=0.66; 95% CI=0.46-0.96, respectively; *P* for interaction=0.08).

Examination of effect modification of the association of RPA on breast cancer survival by other factors such as hormone receptor status, tumor stage and exogenous hormone use did not reveal any differential associations, and are not reported here.

DISCUSSION

We evaluated the association of breast cancer survival with prediagnostic recreational physical activity based on frequency, intensity, duration and timing. We found that women with who reported being ever being physically active prior to diagnosis had a reduced risk of mortality from any cause. These findings were observed among women diagnosed with both pre- and postmenopausal breast cancer, and regardless of their hormone receptor status. The risk reduction in mortality was stronger – near 50% reduction – among those postmenopausal women who reported engaging in any pre-diagnostic RPA vs no RPA during their postmenopausal years, rather than their premenopausal years. There was also evidence that moderate intensity RPA, but not vigorous, improved both all-cause and breast cancer-specific survival. Additionally, postmenopausal women had greater survival with increased RPA during the postmenopausal years. We did not, however, observe any effect measure modification by BMI, although the observed reduced mortality was somewhat stronger in women with a normal BMI (<25).

Our results are consistent with the population studies that have been previously published on this issue to date [6, 9, 19], even though different exposure assessment methods and study populations were utilized. For example, Abrahamson et al. [6] also focused on self-reported, pre-diagnostic levels of moderate and vigorous RPA only among younger women, which were assessed at three different time periods (ages 12 to 13 years, age 20, and in the year prior to the breast cancer diagnosis), rather than the lifetime assessment we included here. Abrahamson et al. found that the 22% risk reduction in mortality among young women was limited to the most recent pre-diagnostic RPA, which is more attenuated, but still fairly consistent with our findings reported here of a 30-50% reduction associated with activity in the past 10 years among postmenopausal women. Thus, both of these studies suggest a recency effect – that more activity undertaken in the years leading up to a breast cancer diagnosis may exert stronger beneficial effects on mortality risk than activity undertaken in the distant past. Alternatively, our results may indicate that recent prediagnostic RPA levels are strongly correlated with post-diagnostic RPA levels, which have been reported to also be associated with a modest reduction in the risk of death in two recent studies [19, 23]. Unfortunately, neither reported findings on whether women who were consistently active both prior to and subsequent to a breast cancer diagnosis had the best survival advantage, or whether women who reported being active after their breast cancer diagnosis were also those who were most active prior to their diagnosis. Another recent study examined change in physical activity from 1 year before to 3 years after diagnosis and found that those who decreased their physical activity more than 3 MET-h/wk had an increased risk of death compared to those who were inactive both before and after diagnosis [7]. However, it was not reported whether the women who had decreased their physical activity were in the lowest or highest physical activity group before diagnosis. Thus, whether the beneficial effects on mortality associated with pre- and post-diagnostic levels of RPA actually reflect the same optimal time period, or two different time periods that are each associated with its own beneficial effects on survival remains unknown at this time. Similarly, it is also unclear whether breast cancer survival is affected by the change in the amount of RPA from before to after diagnosis. There are some studies that have shown that post-diagnosis physical activity levels briefly decline, but return to similar levels within three years [24]. Future studies should focus on elucidating the effects of timing of the physical activity, and whether the RPA must have been initiated prior to the diagnosis of breast cancer to fully benefit from its positive effects on survival, or whether activity initiated after diagnosis is sufficient.

Although moderate activity levels were associated with a better survival advantage, associations for intense activity levels were weaker, an observation which is consistent with findings from animal studies [25]. Our results for intensity of physical activity on survival after breast cancer are also similar to those found in two recent studies of prediagnostic RPA and breast cancer survival and another investigating post-diagnosis physical activity, both reporting a lower risk of death for moderate activity and while finding no association of vigorous-intensity activity [9, 23, 26]. Similarly, several studies have found no decreased risk for breast cancer development with vigorous intensity of activities [27-29]. However, a recent study found greater survival from breast cancer, but not all causes, with vigorous activity [9] and the Nurse's Health Study found that vigorous exercise after diagnosis also lowered risk of breast cancer death [19]. We are unsure why vigorous intensity exercise did not improve survival in our study, however one possible explanation could be due to the low reporting of vigorous activities and lack of adequate variation of vigorous intensity activities in our population, where only one third of the population had ever engaged in vigorous RPA.

There are several limitations to this study that warrant mention. As with all studies that rely on self-reported measures of physical activity, measurement error, and the accompanying attenuation in the effect estimate, is of concern [30]. We attempted to minimize the effects of poor measurement by relying on the instrument developed by Bernstein and colleagues [14, 15] which considers activity type, duration, intensity, and frequency. To optimize Bernstein's method, we linked it to a life events calendar, a memory aid that is used to enhance recall of dates and activities. Given the limited number of outcome events, our observed risk reductions in mortality associated with RPA were strongest for all-cause, rather than breast cancer-specific mortality. Although the hazards ratios for breast cancer-specific mortality were consistently below the null, we could not rule out an effect size of 1, as was often observed for all-cause mortality. Additionally, in this study we had limited power to detect effect modification, therefore our stratified analyses should be interpreted as exploratory, and should be confirmed by other studies.

Many investigators have speculated on the biologic mechanism linking physical activity to the risk of developing breast cancer, including the insulin resistance pathway, inflammation, and DNA repair [5, 31-33]. Or, perhaps, the beneficial effects of RPA may simply be accomplished through avoiding weight gain [34, 35]. However, the precise mechanism remains elusive. For example, as we discussed above, controlling for prediagnostic body size did not substantially affect our effect estimates reported here. Similarly, previous studies have been unable to detect a strong and consistent association between RPA and levels of insulin-like-growth factor-1 [36-38]. Thus, whether these same potential mechanisms also underlie the RPA-breast cancer survival link is currently unknown. A recent review, however, attempted to elucidate these mechanisms and summarized the literature for proposed common biomarkers in relation to breast cancer risk and physical activity separately. This review reported that after evaluating BMI, estrogens, androgens, sex hormone binding globulin, leptin, adiponectin, markers of insulin resistance, tumor necrosis factor-A, interleukin-6, and C-reactive protein, only BMI and estrone showed convincing evidence of an association with both breast cancer and physical activity [39]. Future studies should focus on understanding the underlying biologic mechanisms, which would strengthen our evidence linking RPA to risk reductions in breast cancer incidence and mortality.

In conclusion, this population-based study of women with breast cancer provides some evidence for a modest beneficial effect of lifetime RPA on survival outcomes. The beneficial effect was even stronger for postmenopausal women who engaged in RPA during their postmenopausal years, rather than their premenopausal years suggesting that there is a

particular period during adulthood when RPA could be most beneficial for prognosis. Whether this survival advantage is due to activity undertaken prior to diagnosis, as we and Abrahamson [6] report, or whether it reflects activity undertaken after diagnosis, as reported by others [19, 23], or both, currently remains unclear. Nevertheless, RPA appears to be a promising strategy to reduce the risk of mortality among breast cancer survivors.

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Abbreviations

LIBCSP	Long Island Breast Cancer Study Project
RPA	Recreational physical activity
BMI	Body mass index
NDI	National Death Index
ICD	International Classification of Diseases
MET	Metabolic equivalent task
ER	Estrogen receptor
PR	Progesterone receptor
HR	Hazard ratio
CI	Confidence interval

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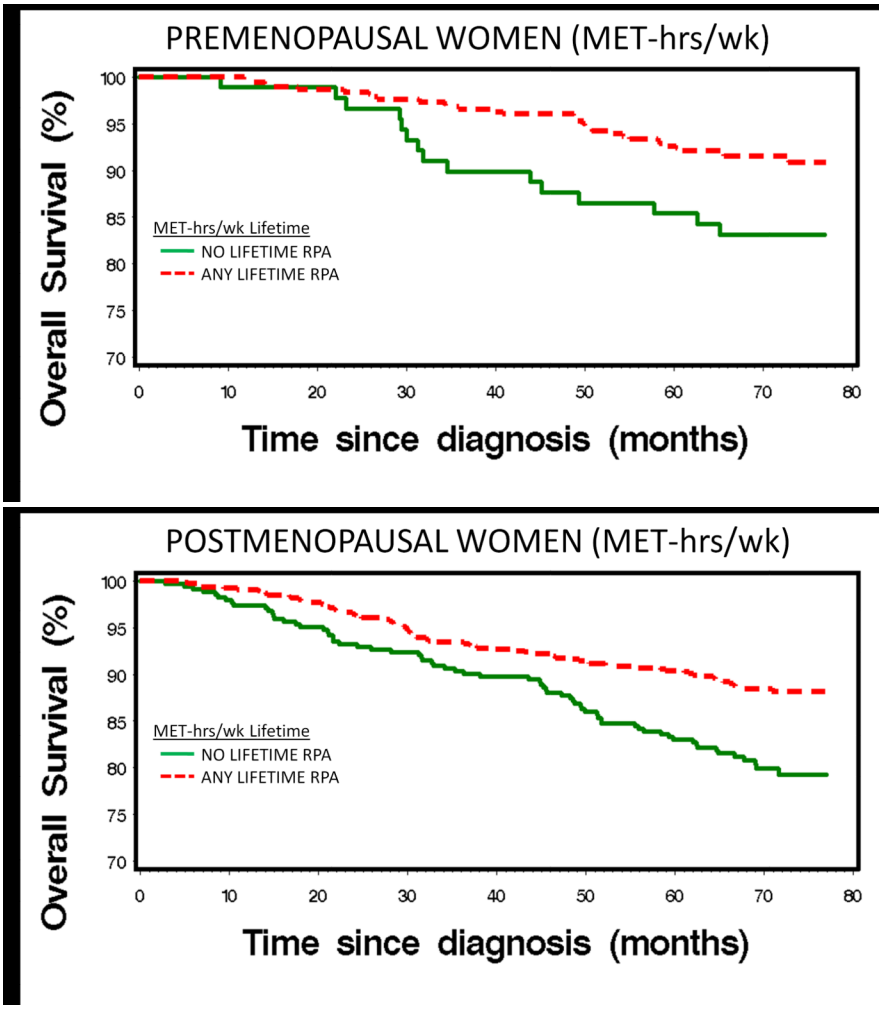

FIGURE 1.

Kaplan-Meier survival curves for mortality due to all-causes after a breast cancer diagnosis, stratified by prediagnosis lifetime RPA. The solid line represents no lifetime RPA, and the dashed line represents any lifetime RPA. Hazard ratio (HR) and 95% confidence interval (CI) are adjusted for age and body mass index. (A) Premenopausal breast cancer diagnosis. (B) Postmenopausal breast cancer diagnosis.

Table 1

Selected characteristics of women diagnosed with a first primary breast cancer in 1996-1997, Long Island Breast Cancer Study Project, by categories of total lifetime recreational physical activity undertaken prior to diagnosis.

Characteristics	Total lifetime recreational physical activity (MET-hrs/wk)		
	0 (*n* = 444)	>0 to <9 (*n* = 607)	≥9 (*n* = 446)
Mean age at diagnosis	62.1	58.1	56.6
Race (% Caucasian)	91.7	94.2	95.1
Education ≥ 12 yrs (%)	79.5	89.5	94.2
Parity (% Nulliparous)	11.9	13.2	14.4
BMI, mean	27.5	26.7	25.4
Energy intake (Kcal/day), mean	1270	1324	1370
Ever exogenous hormones (%)	49.1	68.1	75.2
Family history of breast cancer (%)	21.2	18.7	21.3
Breast cancer stage (% invasive)	87.2	83.9	82.5
ER + tumor (%)	75.1	71.9	73.1
PR + tumor (%)	62.7	63.0	67.3

Table 2

HR (95% CI) for mortality through 2002 among women diagnosed with breast cancer in 1996-1997 according to categories of total, moderate-intensity, or vigorous intensity recreational physical activity undertaken before diagnosis, Long Island Breast Cancer Study Project

Level of RPA (MET-h/wk)	Breast cancer-specific mortality		All-cause mortality	
	Deaths/Cohort	HR (95% CI) [§]	Deaths/Cohort	HR (95% CI) [§]
Total lifetime[*] recreational physical activity				
0	48/369	Referent	84/425	Referent
>0 - <9	41/499	0.61 (0.40-0.92)	65/594	0.59 (0.42-0.82)
≥9	31/357	0.66 (0.42-1.06)	43/432	0.57 (0.39-0.83)
0	48/369	Referent	84/425	Referent
>0	72/856	0.63 (0.43-0.92)	108/1026	0.58 (0.43-0.78)
Moderate intensity[**] lifetime recreational physical activity [†]				
0	54/430	Referent	91/496	Referent
>0 - <9	41/520	0.60 (0.39-0.91)	65/631	0.59 (0.42-0.83)
≥9	25/275	0.73 (0.44-1.20)	36/324	0.66 (0.44-0.99)
0	54/430	Referent	91/496	Referent
>0	66/795	0.64 (0.43-0.93)	101/955	0.62 (0.46-0.84)
Vigorous intensity[¥] lifetime recreational physical activity [¶]				
0	80/801	Referent	138/925	Referent
>0 - <9	34/341	1.16 (0.75-1.79)	47/419	1.02 (0.71-1.47)
≥9	6/83	0.83 (0.35-1.97)	7/107	0.68 (0.31-1.50)
0	80/801	Referent	138/925	Referent
>0	40/424	1.12 (0.74-1.70)	54/526	0.97 (0.69-1.38)

[§] Multivariable HR (95% CI) adjusted for age at diagnosis, BMI and menopausal status

[*] Lifetime recreational physical activity defined as being from menarche to reference date; reference date is date of diagnosis for cases

[**] Moderate intensity recreational physical activity includes activities that expend ≥3.0 or < 6.0 MET

[†] Additionally adjusted for vigorous physical activity (activities that expend ≥6.0 MET)

[¥] Vigorous intensity recreational physical activity includes activities that expend ≥6.0 MET

[¶] Additionally adjusted for moderate physical activity (activities that expend ≥3.0 or < 6.0 MET)

Table 3

HR (95% CI) for mortality through 2002 according to lifetime* recreational physical activity before breast cancer diagnosis among pre- and postmenopausal women diagnosed with breast cancer in 1996-1997, Long Island Breast Cancer Study Project

Level of RPA (MET-h/wk)	Breast cancer-specific mortality		All-cause mortality	
	Deaths/Cohort	HR (95% CI) §	Deaths/Cohort	HR (95% CI) §
Premenopausal women				
0	13/73	Referent	15/89	Referent
>0 - <9	15/165	0.52 (0.25-1.10)	20/206	0.56 (0.28-1.09)
≥9	12/45	0.56 (0.25-1.25)	13/173	0.49 (0.23-1.03)
0	13/73	Referent	15/89	Referent
>0	27/310	0.54 (0.27-1.05)	33/379	0.53 (0.28-0.97)
Postmenopausal women				
0	35/296	Referent	69/336	Referent
>0 - <9	26/334	0.66 (0.40-1.10)	45/388	0.61 (0.42-0.89)
≥9	19/212	0.79 (0.45-1.39)	30/259	0.65 (0.42-1.00)
0	35/296	Referent	69/336	Referent
>0	45/546	0.71 (0.45-1.11)	75/647	0.62 (0.45-0.87)

§ Multivariable HR (95% CI) adjusted for age at diagnosis and BMI

* Lifetime recreational physical activity defined as being from menarche to reference date; reference date is date of diagnosis for cases and interview date for control

Table 4

HR (95% CI) for mortality through 2002 according to timing of recreational physical activity before breast cancer diagnosis among postmenopausal women diagnosed with breast cancer in 1996-1997, Long Island Breast Cancer Study Project

Level of RPA (MET-h/wk)	Breast cancer-specific mortality		All-cause mortality	
	Deaths/Cohort	HR (95% CI) [§]	Deaths/Cohort	HR (95% CI) [§]
Recreational physical activity before menopause[†]				
0	39/354	Referent	76/407	Referent
>0 - <9	16/233	0.77 (0.41-1.46)	27/269	0.91 (0.56-1.46)
≥9	18/167	1.64 (0.74-3.63)	27/203	1.98 (1.09-3.62)
0	39/354	Referent	76/407	Referent
>0	34/400	0.91 (0.52-1.61)	54/472	1.00 (0.65-1.54)
Recreational physical activity after menopause[¶]				
0	40/353	Referent	79/407	Referent
>0 - <9	17/193	0.82 (0.44-1.54)	31/216	0.65 (0.41-1.03)
≥9	16/208	0.60 (0.27-1.36)	20/256	0.33 (0.17-0.63)
0	40/353	Referent	79/407	Referent
>0	33/401	0.87 (0.49-1.56)	51/472	0.61 (0.39-0.94)
Recent[¥] recreational physical activity				
0	38/359	Referent	82/411	Referent
>0 - <9	18/175	1.07 (0.53-2.18)	26/201	0.67 (0.39-1.14)
≥9	17/220	0.90 (0.37-2.21)	22/267	0.45 (0.23-0.89)
0	38/359	Referent	82/411	Referent
>0	35/395	1.13 (0.53-2.42)	48/468	0.62 (0.36-1.06)

[§] Multivariable HR (95% CI) adjusted for age at diagnosis and BMI

[†] Additionally adjusted for recreational physical activity after menopause

[¶] Additionally adjusted for recreational physical activity before menopause

[¥] Recent recreational physical activity includes activities within the 10 years preceding diagnosis

Table 5

HR (95% CI) for mortality through 2002 according to timing of lifetime* recreational physical activity before breast cancer diagnosis according to BMI among women diagnosed with breast cancer in 1996-1997, Long Island Breast Cancer Study Project

Level of RPA (MET-h/wk)	Breast cancer-specific mortality		All-cause mortality	
	Deaths/Cohort	HR (95% CI) §	Deaths/Cohort	HR (95% CI) §
BMI < 25				
0	17/147	Referent	34/175	Referent
>0 - <9	13/227	0.49 (0.23-1.04)	21/267	0.43 (0.25-0.74)
≥9	15/189	0.67 (0.32-1.40)	18/226	0.45 (0.25-0.80)
0	17/147	Referent	34/175	Referent
>0	28/416	0.57 (0.30-1.09)	39/493	0.44 (0.27-0.70)
BMI ≥ 25				
0	34/235	Referent	50/250	Referent
>0 - <9	28/278	0.65 (0.39-1.08)	44/327	0.68 (0.45-1.03)
≥9	16/174	0.59 (0.32-1.08)	25/206	0.62 (0.38-1.02)
0	34/235	Referent	50/250	Referent
>0	44/452	0.63 (0.40-0.99)	69/533	0.66 (0.46-0.96)

§ Multivariable HR (95% CI) adjusted for age at diagnosis and menopausal status

* Lifetime recreational physical activity defined as being from menarche to reference date; reference date is date of diagnosis for cases and interview date for control