Breast Cancer Res Treat (2011) 129:521–529
DOI 10.1007/s10549-011-1483-5

EPIDEMIOLOGY

Associations of physical activity with quality of life and functional ability in breast cancer patients during active adjuvant treatment: the Pathways Study

Jeanne S. Mandelblatt · Gheorghe Luta · Marilyn L. Kwan · Solomon B. Makgoeng · Isaac J. Ergas · Janise M. Roh · Barbara Sternfeld · Lucile L. Adams-Campbell · Lawrence H. Kushi

Received: 16 March 2011 / Accepted: 17 March 2011 / Published online: 8 April 2011
© Springer Science+Business Media, LLC. 2011

Abstract Physical activity can improve quality of life (QOL) in breast cancer survivors but little is known about associations of physical activity and QOL during active cancer therapy. We examine associations between activity levels and QOL in a large cohort of breast cancer patients. Women with invasive, non-metastatic breast cancer ($n = 2{,}279$) were enrolled between 2006 and 2009 from a managed care organization; assessment were done during active therapy. A physical activity frequency questionnaire was used to calculate the average weekly metabolic equivalent task (MET) hours spent in moderate and vigorous activity during active treatment. QOL was measured by the Functional Assessment of Cancer Therapy-Breast Cancer. Linear regression models tested cross-sectional associations of QOL and functional well-being with physical activity and covariates [socio-demographics, comorbidity, body mass index (BMI), clinical variables, social support, and assessment timing]. Physical activity had a significant positive unadjusted association with all QOL sub-scales (except emotional well-being) (all P values < 0.01). Overall QOL was 4.6 points higher for women in the highest quartile of moderate and vigorous activity versus women in the lowest quartile ($P < 0.001$). In regression models, higher activity was associated with better overall QOL and functional well-being, controlling for covariates ($P < 0.05$). Increasing BMI was also independently but inversely associated with overall QOL ($P < 0.001$) but did not explain the relationship of activity and QOL. White women reported the higher levels of activity than minority women and activity was associated with QOL for Whites but not for minority women. Greater physical activity is associated with small but clinically meaningful increases in QOL during active breast cancer care therapy for Whites but this effect is not seen for minority women. If confirmed in longitudinal analyses, these differences may have implications for disparities research.

Keywords Breast cancer · Physical activity · Quality of life

J. S. Mandelblatt (✉) · S. B. Makgoeng
Cancer Control Program, Lombardi Cancer Center and Department of Oncology, Georgetown University Medical Center, 3300 Whitehaven St. NW, Ste 4100, Washington, DC 20007, USA
e-mail: mandelbj@georgetown.edu

G. Luta
Department of Biostatistics, Bioinformatics and Biomathematics and Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC, USA

M. L. Kwan · I. J. Ergas · J. M. Roh · B. Sternfeld · L. H. Kushi
Division of Research, Kaiser Permanente, Oakland, CA, USA

L. L. Adams-Campbell
Carcinogenesis, Biomarkers and Epidemiology Program, Lombardi Cancer Center and Department of Oncology, Georgetown University Medical Center, Washington, DC, USA

Introduction

Breast cancer treatment can have a considerable impact on women's short-term quality of life (QOL) and functional capacity [1–5]. Physical activity can improve oxygen consumption, reduce fatigue, and improve QOL among breast cancer survivors [6]. As a result, physical activity has been suggested as an important component of cancer rehabilitation [7]. However, almost all of these studies were done among survivors after the completion of active treatment.

In this article, we use cross-sectional baseline data from an on-going cohort of women newly diagnosed with breast cancer to examine whether self-reports of physical activity during the active treatment period is associated with better overall QOL and functional well-being. The results are intended to inform future interventions to improve QOL during the active treatment phase of care.

Methods

The Pathways Study is a prospective cohort study designed to assess the effects of lifestyle factors on breast cancer recurrence and mortality. Women with invasive breast cancer have been recruited from the Kaiser Permanente Northern California (KPNC) patient population since January 2006 [8]. Briefly, cases are ascertained rapidly by scanning of electronic pathology reports. Eligibility criteria for the parent study include current KPNC membership, being at least 21 years of age at diagnosis, and having a first primary invasive breast cancer with no prior history of cancer other than non-melanoma skin cancer. Participants must speak English, Spanish, Cantonese, or Mandarin and reside within a 65-mile radius of a field interviewer. Passive consent was obtained from the patient's physician of record to contact the patient for study recruitment. Written informed consent was obtained from all participants. The study was approved by all Institutional Review Boards.

Recruitment is ongoing, and as of December 31, 2009, a total of 2,828 patients have been enrolled. We excluded some women from the current analysis for the following reasons: 97 women with missing stage information or stage 4 cancers, 90 with missing information on treatment or hormone receptor status, one who died before treatment, one with inconsistent treatment dates, and 7 who indicated "other race/ethnicity". Some women were ineligible for more than one reason; total of 183 were excluded. Among the remaining 2,645 women, we further excluded 366 (14%) women who did not complete key measures. The remaining 2,279 women constitute the final analytic sample. With one exception, there were no differences between excluded women and those included in the final sample: women who were excluded were less likely than those included to have received hormonal therapy at baseline. The mean time from pathology-confirmed diagnosis to baseline interview was 2.24 months (SD 0.88). Thus, the baseline time point corresponded to the period of active adjuvant therapy.

Data collection

Baseline data were collected by the trained staff. Staff conducted in-home interviews lasting 2–4 h. Information was collected on socio-demographics, QOL, social support, and physical activity. Body mass index (BMI) was based on self-reported height and weight.

Measures

We used the Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B) Version 4 to assess health-related QOL from the baseline interview as our primary outcome measure [9]. The instrument has been extensively validated in different race/ethnic groups and languages. It has a total of 36 statements asking respondents to rate how true each statement is for the last 7 days. Responses range from 0 (not at all) to 4 (very much). Statements represent five subscales: physical well-being (PWB, Cronbach's alpha = 0.88), functional well-being (FWB, Cronbach's alpha = 0.84), emotional well-being (EWB, Cronbach's alpha = 0.77), social/family well-being (SWB, Cronbach's alpha = 0.72), and breast cancer-specific concerns (BCS, Cronbach's alpha = 0.67). A general score is calculated by summing all subscales except the BCS (FACT-G, Cronbach's alpha = 0.90); the total FACT-B score is calculated by including BCS in the sum (Cronbach's alpha = 0.91).

Independent variable

The primary correlate of QOL of interest is baseline physical activity encompassing the active treatment period. We used an activity frequency questionnaire based on the Arizona Activity Questionnaire that asked about frequency and duration of different physical activities and sedentary behaviors during the prior 6 months, amount of time spent doing the activities, and how strenuous the activity was; the original asked about the past 1 month, otherwise the tools were the same [10, 11]. Activities include job or work-related activities, recreational activities (e.g., sports, exercise, dance, and sedentary recreation such as reading or socializing), transportation, and activities not related to paid or volunteer work (e.g., household chores, care giving, and home repairs).

Each activity is assigned a standard *metabolic equivalent task* (MET) value according to the Compendium by Ainsworth et al. [12]. To examine moderate–vigorous physical activity, the primary exposure of interest, a summary variable in MET-hours/week was created by multiplying the MET value of each activity by frequency and duration and summing over all activities with MET value of 3 or more. In sensitivity analyses, we also examined total activity in MET-hours/week, including mild activity. Since the results were qualitatively similar to those with moderate–vigorous physical activity, we present the data for moderate–vigorous physical activity.

Covariates

There are several variables that could confound the relationships between physical activity and QOL, including age (continuous), BMI (continuous), comorbidity, smoking status (current, former and never), clinical factors, timing of assessment, race [Black, White, Hispanic, and Asian American or Pacific Islander (AAPI)], education (less than high school vs. high school+), marital status (married vs. other), depression, and social support. For pre-cancer comorbidity we abstracted common conditions by ICD-9 codes from the electronic medical record (EMR) and used these data to calculate the Charlson score [13]. Based on the distribution of scores, we dichotomized comorbidity scores as 0–1 versus two or more.

Clinical variables include surgical and adjuvant treatment received, stages 1–3, and hormonal receptor status. Using the EMR, data on breast surgery (lumpectomy, mastectomy) were obtained using ICD-9 (85.20–85.23, 85.33–85.48) diagnostic and CPT-4 (19120–19240, 19301–19307, and 19340–19342) procedural codes. Adjuvant therapies were defined from a combination of registry and EMR data. Data on estrogen receptor (ER) and progesterone receptor (PR) status were obtained from the Cancer Registry [14].

Since physical activity may vary by the timing of adjuvant therapy, we used the actual start and projected stop dates of chemotherapy, radiation therapy, and/or hormonal therapy and the dates of the survey to calculate whether the patient was interviewed during adjuvant therapy (yes vs. no or did not receive adjuvant treatment). The CES-D was used to assess depression. We used continuous scores but note that a cut-point of 16 and above is used to define potentially depressed patients [15]. We used the 19-item Medical Outcomes Study (MOS) Social Support Survey to assess perceived social support that might affect activity including emotional/informational support, tangible support, positive social interaction, and affectionate support [16]. The reliability for each of the sub-scales and overall index were excellent (Cronbach's alpha 0.92–0.96) in our sample.

Statistical analysis

We examined unadjusted bivariate associations between physical activity grouped into quartiles of METs per week of moderate or vigorous activity and study variables using χ^2 tests. Next, we compared the QOL sub-scale scores and overall QOL by physical activity quartile using *t* tests and one-way analysis of variance. We then constructed preliminary linear regression models for the continuous outcomes of interest using physical activity as our primary predictor and controlling for covariates that were significantly associated with QOL in bivariate analysis. Variables that were not significant in the preliminary models were not included in the final model except that comorbidity was retained in final models for face validity purposes. Finally, we conducted a sensitivity analysis, via interactions, to test if conclusions varied based on race or comorbidity level (based on bivariate results). We also explored the possibility of including a higher order functional form for physical activity and BMI; since these were not significant they were not included in the final models. The R^2 statistic was used as an estimate of the variation in QOL explained by the variables in the final regression models. All analyses were conducted using SAS software Version 9.2 (SAS Institute, Inc., Cary, NC).

Results

Women were interviewed a median of 2 months post-diagnosis. Ninety-two percent of women were interviewed during active treatment (chemotherapy, radiation, or hormonal treatment); 37% while actually on-treatment, 55% who had just completed treatment, and 8% received no treatment beyond surgery.

These breast cancer patients were very active, reporting a median of 20.2 MET-hours of moderate or vigorous activity per week during the period just before and including the active treatment phase of care. Activity levels were inversely and linearly related to age with younger women reporting higher levels of activity, $P = <0.0001$ (Table 1). Interestingly, there were also race/ethnicity variations in activity with 27.1% of White patients reporting the highest quartiles of activity versus 18.7% of Blacks, 21.4% of Hispanics, and 17.2% of AAPIs ($P = <0.0001$). Women taking aromatase inhibitors as their type of hormonal therapy were significantly less likely to be in the highest activity quartile than women on tamoxifen (21.7 vs. 29.8%, $P = 0.0026$). Finally, there was a non-significant trend for smokers to be less likely to be in the highest quartile of activity (16.8 vs. 25.3 and 24.7% for current, former, and never smokers, respectively).

In unadjusted analyses, physical activity was associated with all QOL sub-scales, except for emotional well-being. The absolute differences from the least to the greatest amount of activity were small (2–5 points increase in QOL per sub-scale) (Table 2). Cumulatively, QOL was 4.6 points higher for women in the highest quartile of moderate and vigorous activity compared to women in the lowest quartile ($P = <0.0001$).

Physical activity remained significantly associated with overall QOL after considering other covariates, with women in the highest quartile of physical activity reporting significantly higher adjusted QOL than women in the lowest quartile ($P = 0.010$) (Table 3). As BMI increased,

Table 1 Breast cancer patient characteristics by activity level

	Overall % (*N*)	Quartiles of moderate–vigorous activity (in MET-hours/week)				*P* value
		1 (<7.8) % (*N*)	2 (7.8 to <20.2) % (*N*)	3 (20.2 to <39.7) % (*N*)	4 (≥39.7) % (*N*)	
Age, mean (SD)	59.7 (11.6)	62.0 (12.1)	60.6 (11.6)	58.8 (11.0)	57.2 (11.2)	<0.0001
Race/ethnicity						
White	73.3 (1671)	21.1 (352)	24.7 (413)	27.1 (453)	27.1 (453)	<0.0001
Black	6.6 (150)	40.7 (61)	26.0 (39)	14.7 (22)	18.7 (28)	
Hispanic	8.6 (196)	34.7 (68)	22.5 (44)	21.4 (42)	21.4 (42)	
Asian-PI	11.5 (262)	34.4 (90)	27.9 (73)	20.6 (54)	17.2 (45)	
Education						
<High school	3.4 (78)	51.3 (40)	29.5 (23)	12.8 (10)	6.4 (5)	<0.0001
≥High school	84.6 (1929)	24.8 (478)	24.6 (474)	25.4 (489)	25.3 (488)	
Missing	11.9 (272)	53	72	72	75	
Marital status						
Married	55.2 (1259)	23.4 (294)	24.8 (312)	25.7 (324)	26.1 (329)	0.0066
Not married	32.7 (746)	29.9 (223)	24.8 (185)	23.5 (175)	21.9 (163)	
Missing	12.0 (274)	54	72	72	76	
Employment						
No	38.4 (876)	27.1 (237)	26.0 (228)	24.1 (211)	22.8 (200)	0.1144
Yes	61.6 (1403)	23.8 (334)	24.3 (341)	25.7 (360)	26.2 (368)	
AJCC stage						
I	54.3 (1238)	24.3 (301)	24.2 (300)	25.5 (316)	25.9 (321)	0.6768
II	35.5 (809)	25.6 (207)	25.6 (207)	24.2 (196)	24.6 (199)	
III	10.2 (232)	27.2 (63)	26.7 (62)	25.4 (59)	20.7 (48)	
ER status						
Negative	17.2 (391)	23.5 (92)	26.1 (102)	26.1 (102)	24.3 (95)	0.8132
Positive	82.8 (1888)	25.4 (479)	24.7 (467)	24.8 (469)	25.1 (473)	
Surgery						
Breast conserving	60.3 (1375)	26.0 (357)	24.4 (335)	25.2 (347)	24.4 (336)	0.8548
Mastectomy	38.8 (885)	23.7 (210)	26.0 (230)	24.6 (218)	25.7 (227)	
None	0.8 (19)	21.1 (4)	21.1 (4)	31.6 (6)	26.3 (5)	
Hormonal therapy						
Aromatase inhibitors	43.1 (982)	26.2 (257)	27.5 (270)	24.6 (242)	21.7 (213)	0.0133
Tamoxifen	20.5 (467)	21.6 (101)	22.9 (107)	25.7 (120)	29.8 (139)	
None	35.4 (807)	25.7 (207)	23.2 (187)	25.4 (205)	25.8 (208)	
Unknown	1.0 (23)	6	5	4	8	
Chemotherapy						
No	53.8 (1225)	27.1 (332)	24.4 (299)	24.7 (302)	23.8 (292)	0.1028
Yes	46.2 (1054)	22.7 (239)	25.6 (270)	25.5 (269)	26.2 (276)	
Radiation						
No	63.8 (1453)	24.7 (359)	24.8 (360)	24.8 (360)	25.7 (374)	0.6942
Yes	36.2 (826)	25.7 (212)	25.3 (209)	25.5 (211)	23.5 (194)	
Comorbidity						
0, 1	92.4 (2105)	23.7 (499)	24.5 (516)	25.8 (542)	26.0 (548)	<0.0001
2+	7.6 (174)	41.4 (72)	30.5 (53)	16.7 (29)	11.5 (20)	
Smoking						
Current	4.4 (101)	36.6 (37)	27.7 (28)	18.8 (19)	16.8 (17)	0.1489
Former	35.7 (814)	25.2 (205)	24.6 (200)	24.9 (203)	25.3 (206)	

Table 1 continued

	Overall % (*N*)	Quartiles of moderate–vigorous activity (in MET-hours/week)				*P* value
		1 (<7.8) % (*N*)	2 (7.8 to <20.2) % (*N*)	3 (20.2 to <39.7) % (*N*)	4 (≥39.7) % (*N*)	
Never	47.9 (1091)	25.3 (276)	24.6 (268)	25.4 (277)	24.8 (270)	
Missing	12.0 (273)	53	73	72	75	
Mean CES-D score (SD)	11.1 (9.0)	12.0 (10.1)	11.0 (8.2)	11.0 (8.9)	10.6 (8.5)	0.0688
Mean BMI (SD)	28.4 (6.6)	31.1 (7.6)	28.8 (6.7)	27.2 (5.6)	26.4 (5.0)	<0.0001
Social support						
Mean (SD)						
Emotion/info	78.8 (18.7)	76.8 (21.1)	78.4 (19.5)	78.7 (16.9)	81.5 (16.6)	<0.0001
Tangible	78.8 (22.8)	76.9 (24.9)	79.1 (21.7)	79.0 (21.9)	80.2 (22.7)	0.003
Affectionate	86.4 (20.8)	84.0 (23.5)	86.6 (19.8)	86.6 (19.6)	88.3 (19.8)	<0.0001
Social interaction	82.8 (21.0)	80.5 (24.3)	82.1 (19.9)	82.3 (20.5)	86.5 (18.8)	<0.0001
Overall	80.8 (17.6)	78.6 (20.2)	80.5 (17.1)	80.7 (16.2)	83.3 (16.3)	<0.0001

Missing data are not used in calculation of *P* values

Table 2 QOL sub-scales by physical activity quartile during active breast cancer treatment [Mean (SD)]

	Overall sample	Moderate–vigorous activity				*P* value[a]
		Quartiles of MET-hours/week				
		1 *N* (%) (<7.8)	2 *N* (%) (7.8 to <20.2)	3 *N* (%) (20.2 to <39.7)	4 *N* (%) (≥39.7)	
Physical well being	22.1 (5.8)	21.6 (6.1)	22.1 (5.6)	22.4 (5.6)	22.3 (5.8)	0.006
Social well being	24.4 (4.0)	23.9 (4.5)	24.7 (3.8)	24.4 (3.8)	24.8 (3.9)	0.003
Emotional well being	19.1 (4.1)	18.8 (4.8)	19.3 (3.7)	19.1 (4.1)	19.2 (4.0)	0.371
Functional well being	20.6 (5.5)	19.8 (6.1)	20.5 (5.3)	20.9 (5.2)	21.4 (5.3)	<0.0001
Breast cancer well being	25.6 (5.8)	25.1 (5.8)	25.4 (5.8)	25.8 (5.6)	26.1 (5.8)	0.004
General well being	86.3 (14.6)	84.2 (16.2)	86.8 (13.4)	86.8 (14.4)	87.7 (14.2)	<0.0001
Overall QOL score	111.8 (18.8)	109.2 (20.3)	112.0 (17.8)	112.5 (18.6)	113.7 (18.4)	<0.0001

[a] *P* values from 1-way ANOVAs

QOL decreased ($P < 0.001$). BMI did not explain the relationship between physical activity and QOL, however, since both activity and BMI were independently associated with QOL. As age increased QOL increased ($P < 0.001$), despite the fact that older women reported lower activity levels. As expected, women who were actively undergoing chemotherapy, radiation, or hormonal therapy had lower QOL scores than those who has not yet started or had recently completed these modalities. The model explained 53% of the variation in QOL.

In race-stratified models (not shown), physical activity was significantly associated with QOL for Whites but not for minorities. In analyses examining FACT-B subscales, results for functional well-being during active treatment mirrored those for overall QOL (Table 4), except that BMI was not related to functional well-being.

Discussion

It is widely accepted that physical activity improves QOL in cancer survivors [6, 17–19]. This study uses a large and racially/ethnically diverse cohort to extend our knowledge about physical activity to the early phases of active adjuvant treatment. We found that women who reported the highest levels of moderate and vigorous activity had the highest QOL in this period. Increasing BMI was also independently but inversely associated with QOL, but did not explain the physical activity findings. There were some differences between activity levels and race/ethnicity and relationship to QOL but differences by type of hormonal agent were eliminated after considering age.

This group of breast cancer patients had a higher level of moderate and vigorous activity than reported in other past

Table 3 Adjusted estimates of the associations between physical activity (and other covariates) and overall QOL among breast cancer patients during active therapy

	Beta	Std. error	*P* value
Age (per 1 year increase in age)	0.21	0.02	<0.001
Activity level (quartiles)			
1 (referent)			
2	0.72	0.68	0.286
3	1.50	0.69	0.030
4	1.81	0.71	0.010
BMI (per kg/m^2 unit increase)	−0.14	0.04	<0.001
Depression (per 1 point increase)[a]	−1.43	0.03	<0.001
Summary social support (per 1 point increase)	0.15	0.01	<0.001
Race/ethnicity			
White (referent)			
Asian-PI	−3.45	0.79	<0.001
Black	0.84	0.99	0.394
Hispanic	−4.91	0.87	<0.001
ER status			
Positive (referent)			
Negative	−1.35	0.64	0.035
Comorbidity score			
0, 1 (referent)			
2+	−1.73	0.93	0.062
AJCC stage			
III (referent)			
I	6.12	0.82	<0.001
II	3.49	0.85	<0.001
On adjuvant treatment (no vs. yes)	1.18	0.51	0.020
Time from diagnosis to interview (months)	−0.40	0.28	0.158

Each variable is adjusted for the effects of the other variables in the table in a linear regression model

Model R^2 53%

[a] Higher depression score indicates greater depression

studies of breast cancer patients [10, 20, 21]. This is likely due to the more detailed physical activity assessment in our study, resulting in possible overestimation of energy expenditure. Also, since activity levels have increased over time, our cohort may have been more physically active than groups reported in the past. Increasing awareness of the benefits of exercise may have also led to higher self-reported activity levels. Our sample was comparable to other similar breast cancer populations, however, in ratings of QOL during treatment [22].

The magnitude of observed differences in QOL scores between the lowest and highest quartile of physical activity was small but in the range reported as important clinically in other studies (2 points on sub-scales and 5 points for the overall score) [22–24]. Similar magnitude of benefits have been observed in the few published [1, 18, 25–27] studies; a few clinical trials [28, 29] and observational studies [30] of exercise during active treatment are currently in process and shown provide additional evidence to support using active treatment as a "teachable moment" for lifestyle changes in the lives of breast cancer patients [31].

The association of physical activity was not explained by BMI, although BMI was also associated with QOL. Higher BMI may be associated with poorer body image, although we did not measure this construct [32]. High BMI, especially BMI of 30 or more, has been linked to increased risk of breast cancer, diminished treatment effectiveness and lower survival [33–35]. It is thought that these effects are in part mediated through insulin-like growth factor-1 (IGF-1) axis and altered production of proinflammatory cytokines [36]. These same paths have been linked to cancer fatigue [37], which could, in turn, lower QOL. These biological mechanisms are also postulated to partially explain the pathways whereby physical activity improves QOL [38]. We will be examining inflammatory markers in this cohort in our future study to better understand these pathways in breast cancer QOL and prognosis.

In this sample, White women were more likely to report the highest levels of activity and better QOL compared to minority women. A similar result has been noted in other breast cancer studies [39]. Of note, physical activity was associated with QOL for Whites but not for minority women. Moreover, even after considering activity level, social support, comorbidity, and clinical factors, Whites maintained a higher QOL during active treatment than minority women. These results suggest that minority women may have different experiences during active therapy than Whites, or that there are unmeasured differences in correlates of QOL by race/ethnicity. Alternatively, minority women may be judging their cancer diagnosis against a different contextual backdrop that leads them to rate QOL at lower levels during the active treatment phase of care (e.g., feeling that "cancer is like a death sentence") [40]. Others have noted poorer QOL in Blacks (vs. Whites) among longer-term survivors [41]. It will be important to explore treatment experiences further, especially when considering physical activity interventions for minority groups.

While aromatase inhibitors have equivalent or better survival benefits than tamoxifen [42], they have different side-effect profiles, many with the potential to affect physical activity, and QOL. For instance, aromatase inhibitors have been noted to cause greater fatigue, arthralgias, and myaglias than tamoxifen, side effects that could affect both activity level and QOL [43]. We noted that women on aromatase inhibitors were less active than women on tamoxifen, but this effect disappeared after

Table 4 Adjusted estimates of the associations between physical activity and functional well-being among breast cancer patient during the active phase of therapy

	Beta	Std. error	*P* value
Age (per 1 year increase in age)	0.02	0.01	0.026
Activity level (quartiles)			
1 (referent)			
2	0.33	0.25	0.189
3	0.88	0.26	<0.001
4	0.95	0.26	<0.001
BMI (per kg/m^2 unit increase)	−0.00	0.01	0.938
Depression (per 1 point increase)[a]	−0.36	0.01	<0.001
Summary social support (per 1 point increase)	0.04	0.01	<0.001
Race/ethnicity			
White (referent)	–	–	–
Asian-PI	0.07	0.29	0.801
Black	0.05	0.37	0.900
Hispanic	−1.30	0.32	<0.001
ER status			
Positive (referent)	–	–	–
Negative	−0.13	0.24	0.572
Comorbidity score			
0, 1 (referent)	–	–	–
2+	−0.79	0.34	0.021
AJCC stage			
III (referent)	–	–	–
I	1.41	0.30	<0.001
II	0.92	0.31	0.003
On adjuvant treatment (no vs. yes)	0.22	0.19	0.231
Time from diagnosis to interview (months)	0.00	0.10	0.999

Each variable is adjusted for the effects of the other variables in the table in a linear regression model

Model R^2 36%

[a] Higher score on depression scale indicates greater depression

considering age and the activity-QOL association did not differ by type of hormonal therapy received. It is possible, however, that activity levels were affected by side effects of specific non-hormonal agents (e.g., taxanes and muscle pain and neuropathy). Unfortunately, we do not have data on specific agents and doses or self-reported toxicities; this will be important to consider in future investigations. Although, depression may influence both activity levels and QOL; depression did not alter the association of physical activity with QOL.

Surprisingly, while they had lower levels of activity, older women reported *higher* QOL during active therapy than younger women despite having higher risks of toxicity and decreased functional status during chemotherapy than younger women [31, 44]. It is possible that older women were more accustomed to chronic illness so that health decrements during treatment were viewed less negatively than by younger women. It is unclear, however, if increasing activity levels can enhance physiological reserve and QOL in those with comorbidities (e.g., by diminishing fatigue or increasing oxygen consumption). This will be an important area for future research.

There are several caveats that should be noted in considering our results. First, we measured activity and QOL at the same time, so we cannot make any inferences about causality. It is logical that greater activity levels would lead to improved QOL, yet it is also plausible that women with greater QOL felt more energetic or had greater exercise self-efficacy and, thus, were able to be more active [45, 46]. Also, a related issue is that our measure of activity asks about the past 6 months, a period that spans the treatment period, but may be skewed toward higher activity levels from pre-diagnosis and does not capture decrements due to breast cancer. We are collecting follow-up assessments of both physical activity and QOL, and will be able to examine temporal relationships in future analyses. Next, we rely on self-reported activity levels, although the instrument that our tool was based on has been validated against doubly labeled water [11]. Our sample was drawn from a managed care population and findings may therefore be limited in generalizability to other care settings or the uninsured. However, it is unlikely that type of health care coverage affects physical activity patterns per se, although there may be effects on QOL. In addition, women who are diagnosed with breast cancer in this setting appear to be largely similar demographically and diagnostically to the breast cancer population overall. Despite these limits, the study has several strengths, including the very large and diverse sample, use of standard, validated measures of QOL and physical activity, and assessment of important covariates that captured a very high proportion of variance in QOL.

Physical activity, improves QOL for survivors, may decrease breast cancer mortality [36, 47, 48] and diminishes all-cause mortality rates [10, 49, 50]. Our study demonstrates that physical activity is also associated with QOL during the active treatment phase of breast cancer care. If causal relationships are demonstrated in future research, our results suggest that physical activity "prescriptions" might be considered early in cancer therapy and continue into survivorship care planning [48]. Value for minorities and for the growing older population with comorbidities remains to be established and should receive priority for future investigation.

Acknowledgments This research was supported, in part by National Cancer Institute Grants R01 CA105274 and R01 CA124924

to LK; BC043120 (Department of Defense) to LK; National Cancer Institute Grants RO1 CA 127617, U10 CA 84131, RO1 CA124924, and KO5 CA96940 to JSM; R21 CA 149996 to LAC, and the Biostatistics and Bioinformatics Shared Resources at Lombardi Comprehensive Cancer Center under National Cancer Institute Grant #P30 CA51008 covering GL.

Conflict of interest None.

References

1. Kwan ML, Ergas IJ, Somkin CP, Quesenberry CP Jr, Neugut AI, Hershman DL et al (2010) Quality of life among women recently diagnosed with invasive breast cancer: the Pathways Study. Breast Cancer Res Treat 123(2):507–524
2. Lu W, Cui Y, Chen X, Zheng Y, Gu K, Cai H et al (2009) Changes in quality of life among breast cancer patients three years post-diagnosis. Breast Cancer Res Treat 114(2):357–369
3. Avis NE, Crawford S, Manuel J (2005) Quality of life among younger women with breast cancer. J Clin Oncol 23(15): 3322–3330
4. Hayes SC, Rye S, Battistutta D, DiSipio T, Newman B (2010) Upper-body morbidity following breast cancer treatment is common, may persist longer-term and adversely influences quality of life. Health Qual Life Outcomes 8:92−98
5. Carling M, Goodare H, Ironside A, Millington J, Rogers C (2010) Quality of life after breast radiotherapy. Lancet Oncol 11(7): 612–613
6. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS (2006) Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ 175(1):34–41
7. Galvao DA, Newton RU (2005) Review of exercise intervention studies in cancer patients. J Clin Oncol 23(4):899–909
8. Kwan ML, Ambrosone CB, Lee MM, Barlow J, Krathwohl SE, Ergas IJ et al (2008) The Pathways Study: a prospective study of breast cancer survivorship within Kaiser Permanente Northern California. Cancer Causes Control 19(10):1065–1076
9. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR et al (1997) Reliability and validity of the functional assessment of cancer therapy-breast quality-of-life instrument. J Clin Oncol 15(3):974–986
10. Sternfeld B, Weltzien E, Quesenberry CP Jr, Castillo AL, Kwan M, Slattery ML et al (2009) Physical activity and risk of recurrence and mortality in breast cancer survivors: findings from the LACE study. Cancer Epidemiol Biomarkers Prev 18(1):87–95
11. Staten LK, Taren DL, Howell WH, Tobar M, Poehlman ET, Hill A et al (2001) Validation of the Arizona activity frequency questionnaire using doubly labeled water. Med Sci Sports Exerc 33(11):1959–1967
12. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ et al (2000) Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 32(9 Suppl):S498–S504
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5): 373–383
14. Oehrli M, Quesenberry C, Leyden W (2006) Annual report on trends, incidence, and outcomes. Kaiser Permanente NCCR
15. Radloff LS (1977) The CES-D scale: a self-report depression scale for research in the general population. Appl Pscyhol Meas 1:385–401
16. Sherbourne CD, Stewart AL (1991) The MOS social support survey. Soc Sci Med 32(6):705–714
17. Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G (2005) Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. J Clin Oncol 23(16):3830–3842
18. Bicego D, Brown K, Ruddick M, Storey D, Wong C, Harris SR (2009) Effects of exercise on quality of life in women living with breast cancer: a systematic review. Breast J 15(1):45–51
19. Kendall AR, Mahue-Giangreco M, Carpenter CL, Ganz PA, Bernstein L (2005) Influence of exercise activity on quality of life in long-term breast cancer survivors. Qual Life Res 14(2): 361–371
20. Caan B, Sternfeld B, Gunderson E, Coates A, Quesenberry C, Slattery ML (2005) Life After Cancer Epidemiology (LACE) Study: a cohort of early stage breast cancer survivors (United States). Cancer Causes Control 16(5):545–556
21. Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA (2005) Physical activity and survival after breast cancer diagnosis. JAMA 293(20):2479–2486
22. Humpel N, Iverson DC (2007) Depression and quality of life in cancer survivors: is there a relationship with physical activity? Int J Behav Nutr Phys Act 4:65−75
23. Brucker PS, Yost K, Cashy J, Webster K, Cella D (2005) General population and cancer patient norms for the Functional Assessment of Cancer Therapy-General (FACT-G). Eval Health Prof 28(2):192–211
24. Eton DT, Cella D, Yost KJ, Yount SE, Peterman AH, Neuberg DS et al (2004) A combination of distribution- and anchor-based approaches determined minimally important differences (MIDs) for four endpoints in a breast cancer scale. J Clin Epidemiol 57(9):898–910
25. Ligibel JA, Partridge A, Giobbie-Hurder A, Campbell N, Shockro L, Salinadri T, Winer EP (2010) Physical and psychological outcomes among women in a telephone-based exercise intervention during adjuvant therapy for early stage breast cancer. J Womens Health 19(8):1553–1559
26. Spence RR, Heesch KC, Brown WJ (2010) Exercise and cancer rehabilitation: a systematic review. Cancer Treat Rev 36(2): 185–194
27. Markes M, Brockow T, Resch KL (2006) Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev 4:CD005001
28. van Waart H, Stuiver MM, van Harten WH, Sonke GS, Aaronson NK (2010) Design of the Physical exercise during Adjuvant Chemotherapy Effectiveness Study (PACES): a randomized controlled trial to evaluate effectiveness and cost-effectiveness of physical exercise in improving physical fitness and reducing fatigue. BMC Cancer 10:673−683
29. Velthuis MJ, May AM, Koppejan-Rensenbrink RA, Gijsen BC, van Breda E, de Wit GA et al (2010) Physical Activity during Cancer Treatment (PACT) Study: design of a randomised clinical trial. BMC Cancer 10:272−281
30. Speck RM, Courneya KS, Masse LC, Duval S, Schmitz KH (2010) An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv 4(2):87–100
31. Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM (2005) Riding the crest of the teachable moment: promoting long-term health after the diagnosis of cancer. J Clin Oncol 23(24): 5814–5830
32. Schwartz MB, Brownell KD (2004) Obesity and body image. Body Image 1(1):43–56
33. Ewertz M, Jensen MB, Gunnarsdottir KA, Hojris I, Jakobsen EH, Nielsen D et al (2011) Effect of obesity on prognosis after early-stage breast cancer. J Clin Oncol 29(1):25–31

34. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. N Engl J Med 348(17):1625–1638
35. Majed B, Moreau T, Senouci K, Salmon RJ, Fourquet A, Asselain B (2008) Is obesity an independent prognosis factor in woman breast cancer? Breast Cancer Res Treat 111(2):329–342
36. Carmichael AR, Daley AJ, Rea DW, Bowden SJ (2010) Physical activity and breast cancer outcome: a brief review of evidence, current practice and future direction. Eur J Surg Oncol 36(12): 1139–1148
37. Brown JC, Huedo-Medina TB, Pescatello LS, Pescatello SM, Ferrer RA, Johnson BT (2011) Efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: a meta-analysis. Cancer Epidemiol Biomarkers Prev 20(1): 123–133
38. McTiernan A (2008) Mechanisms linking physical activity with cancer. Nat Rev Cancer 8(3):205–211
39. Smith AW, Alfano CM, Reeve BB, Irwin ML, Bernstein L, Baumgartner K et al (2009) Race/ethnicity, physical activity, and quality of life in breast cancer survivors. Cancer Epidemiol Biomarkers Prev 18(2):656–663
40. Sheppard VB, Christopher J, Nwabukwu I (2010) Breaking the silence barrier: opportunities to address breast cancer in African-born women. J Natl Med Assoc 102(6):461–468
41. Bowen DJ, Alfano CM, McGregor BA, Kuniyuki A, Bernstein L, Meeske K et al (2007) Possible socioeconomic and ethnic disparities in quality of life in a cohort of breast cancer survivors. Breast Cancer Res Treat 106(1):85–95
42. Baum M, Buzdar A, Cuzick J, Forbes J, Houghton J, Howell A et al (2003) Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early-stage breast cancer: results of the ATAC (arimidex, tamoxifen alone or in combination) trial efficacy and safety update analyses. Cancer 98(9):1802–1810
43. Garreau JR, Delamelena T, Walts D, Karamlou K, Johnson N (2006) Side effects of aromatase inhibitors versus tamoxifen: the patients' perspective. Am J Surg 192(4):496–498
44. Demark-Wahnefried W, Morey MC, Sloane R, Snyder DC, Cohen HJ (2009) Promoting healthy lifestyles in older cancer survivors to improve health and preserve function. J Am Geriatr Soc 57(Suppl 2):S262–S264
45. Emery CF, Yang HC, Frierson GM, Peterson LJ, Suh S (2009) Determinants of physical activity among women treated for breast cancer in a 5-year longitudinal follow-up investigation. Psychooncology 18(4):377–386
46. Perkins HY, Baum GP, Taylor CL, Basen-Engquist KM (2009) Effects of treatment factors, comorbidities and health-related quality of life on self-efficacy for physical activity in cancer survivors. Psychooncology 18(4):405–411
47. Patterson RE, Cadmus LA, Emond JA, Pierce JP (2010) Physical activity, diet, adiposity and female breast cancer prognosis: a review of the epidemiologic literature. Maturitas 66(1):5–15
48. Patterson RE, Saquib N, Natarajan L, Rock CL, Parker BA, Thomson CA, Pierce JP (2010) Improvement in self-reported physical health predicts longer survival among women with a history of breast cancer. Breast Cancer Res Treat. doi:10.1007/s10549-010-1236-x
49. Braithwaite D, Satariano WA, Sternfeld B, Hiatt RA, Ganz PA, Kerlikowske K et al (2010) Long-term prognostic role of functional limitations among women with breast cancer. J Natl Cancer Inst 102(19):1468–1477
50. Saquib N, Pierce JP, Saquib J, Flatt SW, Natarajan L, Bardwell WA et al (2011) Poor physical health predicts time to additional breast cancer events and mortality in breast cancer survivors. Psychooncology 20:252–259