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EPIDEMIOLOGY

Associations between health-related fitness and quality of life in newly diagnosed breast cancer patients

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Abstract

Purpose Newly diagnosed breast cancer patients face substantial stress and uncertainty that may undermine their quality of life (QoL). The purpose of the present study was to examine the associations between health-related fitness (HRF) and QoL in newly diagnosed breast cancer patients from the Alberta Moving Beyond Breast Cancer Study.

Methods Newly diagnosed breast cancer patients with early-stage disease ($n = 1458$) were recruited between 2012 and 2019 in Edmonton and Calgary, Canada to complete baseline HRF and QoL assessments within 90 days of diagnosis. HRF assessments included cardiorespiratory fitness (VO_{2peak} treadmill test), muscular fitness (upper and lower body strength and endurance tests), and body composition (dual x-ray absorptiometry). QoL was assessed by the Medical Outcomes Study Short Form 36 (SF-36) version 2. We used logistic regression analyses to examine the associations between quartiles of HRF and poor/fair QoL (bottom 20%) after adjusting for key covariates.

Results In multivariable analysis, the least fit groups compared to the most fit groups for relative upper body strength (OR = 3.19; 95% CI = 1.98–5.14), lean mass percentage (OR = 2.31; 95% CI = 1.37–3.89), and relative VO_{2peak} (OR = 2.08; 95% CI = 1.21–3.57) were independently at a significantly higher risk of poor/fair physical QoL. No meaningful associations were found for mental QoL.

Conclusions The three main components of HRF (muscular fitness, cardiorespiratory fitness, and body composition) were independently associated with physical QoL in newly diagnosed breast cancer patients. Exercise interventions designed to improve these components of HRF may optimize physical QoL and help newly diagnosed breast cancer patients better prepare for treatments and recovery.

Keywords Body composition · Breast cancer · Cardiorespiratory fitness · Muscular strength · Physical fitness · Quality of life

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Introduction

In Canada and the United States, there are over 300,000 combined new breast cancer diagnoses every year [1, 2]. Newly diagnosed breast cancer patients face substantial stress and uncertainty related to their diagnosis, prognosis, and treatment decisions that can undermine quality of life (QoL) and potentially affect treatment-related outcomes and survival [3–5]. Understanding the determinants of QoL in newly diagnosed breast cancer patients may help to identify early intervention targets to improve QoL and better prepare patients for treatments and recovery.

Health-related fitness (HRF) refers to the components of physical fitness that exhibit a strong relationship with health status and generally includes cardiorespiratory (aerobic) fitness, muscular fitness (strength and endurance), body composition, and flexibility [6]. HRF is emerging as an important consideration in clinical oncology, however, current research is limited. Specifically, few studies have provided a comprehensive assessment of HRF [7] and most studies have relied on easily administered measures of HRF such as body mass index (BMI) [8], handgrip strength [9], and submaximal tests of cardiovascular fitness [10]. Furthermore, most studies have had small sample sizes and/or included mixed cancer patient groups during and after treatments [7, 9]. Small sample sizes and limited assessments of HRF have made it difficult to directly compare the relative importance of different components of HRF and inform clinical exercise prescriptions for improving QoL. Moreover, no study to date has focused on the setting of newly diagnosed breast cancer patients.

The purpose of the present study was to examine the associations between a comprehensive set of high quality HRF measures and QoL in a large sample of newly diagnosed breast cancer patients from the Alberta Moving Beyond Breast Cancer (AMBER) Cohort Study [11–13]. Given the distinct fitness dimensions represented by the different components of HRF, we hypothesized that all three main components of HRF (cardiorespiratory fitness, muscular fitness, and body composition) would be independently associated with QoL. Moreover, given the physical basis of HRF components, we hypothesized that HRF would be more strongly associated with physical QoL than mental QoL.

Methods

Ethical approval was obtained through the Health Research Ethics Board of Alberta: Cancer Committee (HREBA. CC-17-0576) and each participant completed a signed consent form. We have previously described the AMBER study design and methods [11] as well as the baseline characteristics of the full cohort [13].

Study design, participants, and procedures

AMBER is a prospective cohort study examining the role of physical activity, sedentary behavior, and HRF in breast cancer treatment, recovery, and survivorship [11, 12]. Assessments are performed at baseline (within 90 days of diagnosis) and at 1, 3, and 5-years postdiagnosis. Participants were recruited between July 2012 and July 2019 in Edmonton and Calgary, Alberta, Canada. Women with newly diagnosed breast cancer were eligible if they had histologically confirmed stage I ($\geq$T1c) to stage IIIc breast cancer, were 18 to 80 years old, proficient in English, and not pregnant.

Timing and order of baseline assessments

Our goal was to complete baseline assessments within 90 days of surgery and/or prior to initiating neoadjuvant or adjuvant therapy, however, participants were allowed to complete baseline assessments until the third cycle of chemotherapy or tenth fraction of radiation therapy. Baseline testing generally occurred over two separate days about 1 week apart. On Day 1, participants completed a fasted blood draw followed by body composition assessments (dual x-ray absorptiometry, height, weight, and waist and hip circumference), lymphedema and range of motion testing, muscular fitness and flexibility testing (partial curl-ups, sit-and-reach, and handgrip strength), and cardiorespiratory fitness testing (graded exercise treadmill test). At the end of Day 1, we gave participants questionnaires (including the QoL measures) and accelerometers to return the following week at Day 2 testing. Day 2 testing included the upper and lower body muscular strength and endurance tests with a 10-min rest between tests. If two separate days were not feasible for participants, we conducted single day testing with appropriate rest between cardiorespiratory fitness testing and strength testing.

Health-related fitness measures

Certified exercise physiologists conducted HRF assessments using standardized testing protocols and the same equipment at both sites as described previously [11]. Cardiorespiratory fitness was assessed by a graded treadmill exercise test using the modified Bruce protocol with gas exchange measurements to determine the peak volume of oxygen consumed (VO_{2peak}) in absolute (L/min) and relative (mL/kg/min) terms based on meeting at least two of the following criteria: (a) respiratory exchange ratio > 1.05, (b) heart rate within 5 beats/minute of age-predicted maximum, (c) rating of perceived exertion ≥ 7 on the 10 point scale, and (d) plateau in VO_2 (defined as < 0.150 L/min over the final minute of exercise) [11]. Muscular fitness was assessed by combined right and left handgrip strength using a dynamometer, abdominal endurance (number of consecutive partial curl-ups), and upper and lower body (chest press and leg press) muscular strength and endurance tests [11]. Maximal strength was assessed by an 8–10 repetition maximum test used to predict one repetition maximum (1-RM). Muscular endurance was assessed as a multiple repetition maximum based on 50% of predicted 1-RM for the chest press and 70% of predicted 1-RM for the leg press, and calculated as the number of repetitions x weight lifted. Muscular strength and endurance were expressed in absolute (kg lifted) and relative (kg lifted/kg body weight) terms. Body composition was assessed by dual x-ray absorptiometry (DXA) and expressed as fat mass, lean mass, body fat percentage, lean mass percentage, and lean mass/fat mass ratio. Height and weight were used to calculate body mass index (BMI). Flexibility was assessed by the sit-and-reach test.

Quality of life measure

Quality of life was measured using the SF-36 Version 2 (SF-36v2) [14, 15] which is a 36-item generic measure of health status used extensively in both healthy and clinical populations. The measure yields eight health domain scales that can be aggregated into two distinct summary measures: physical component summary (PCS) and mental component summary (MCS). The PCS and MCS were scored using a *T*-score metric standardized to a population mean of 50 and a standard deviation of 10 based on 2009 United States norms. A single item from the SF-36v2, asking about general health with response options of poor, fair, good, very good, and excellent, was also used as a separate QoL indicator.

Patient characteristics

Participants self-reported sociodemographic characteristics and lifestyle behaviors such as smoking, alcohol consumption, and dietary intake using the Canadian Diet History Questionnaire-II [16]. Clinical information about their cancer and treatments was extracted from medical charts.

Statistical analyses

We used logistic regression to examine the associations between quartiles of HRF and binary QoL outcomes. For the PCS and MCS, we used the bottom 20% of the distribution as an indicator of poor/fair QoL given there is no clinical threshold for this measure. For the single general health item, we compared poor/fair versus good/very good/excellent. For HRF variables with < 5% missing data (handgrip strength, partial curl-ups, sit-and-reach, and body composition), we replaced the missing data with multivariable imputations through chained equations using all correlated baseline variables before computing quartiles [17]. Two HRF tests incurred substantial missing data of approximately 25% because of safety reasons or physical limitations [13]: cardiorespiratory fitness (absolute and relative VO_{2peak}) and upper and lower body strength (absolute and relative maximal strength and endurance). For these HRF variables, we used the inability to complete VO_{2peak} or maximal strength testing as an indicator of the worst fitness category (quartile). We then computed tertiles for the remaining approximately 75% that achieved VO_{2peak} or maximal strength, which resulted in roughly four equal quartiles of HRF.

Our primary reason for categorizing our exposures and outcomes was to generate more clinically interpretable results for patients and clinicians (both oncologists and exercise physiologists) using odds ratios rather than correlations or regression coefficients. A second reason for categorizing our exposures and outcomes was the substantial missing data (about 25%) for the VO_{2peak} test and maximal muscular strength test. We would have had to exclude these patients from any analysis of continuous data but we were able include them as their own category in our logistic regression analysis (i.e., unable to perform test). Finally, we did examine the associations of continuous HRF variables (per a given measurement unit) with binary QoL for participants without missing data.

We compared baseline characteristics across quartiles of relative VO_{2peak} (our primary exposure) using analyses of variance. We examined multivariable associations between each HRF variable and each QoL indicator adjusting for age, education, comorbidity, family history, disease stage, surgery type, kilocalorie intake, location, and smoking as described in a previous publication [18]. We conducted an additional sensitivity analysis that also adjusted for whether HRF testing occurred (a) before or after surgery and (b) before/no chemotherapy or after starting chemotherapy. Adjusting for the timing of surgery and chemotherapy in relation to HRF testing did not materially change the statistical significance or magnitude of our results, therefore, we have reported our original adjusted analysis. HRF variables that were statistically significant in the multivariable adjusted analyses were further evaluated in a multivariable model where the covariates above were forced into the model followed by stepwise forward consideration of all statistically significant HRF exposures. We chose stepwise forward consideration over forced entry for the statistically significant HRF exposures because of the high multi-collinearity among the HRF variables. In addition to statistical significance, we interpreted odds ratios (ORs) of < 0.50 or > 2.0 as clinically significant and meaningful [19].

Results

Flow of participants through the baseline assessment has been reported elsewhere [13]. Of 3673 eligible patients, 1528 (42%) were recruited. For the present analysis, 70 participants were excluded because of missing QoL data. Of the 1458 participants analyzed in the present report, 110 (7.5%) were scheduled for neoadjuvant chemotherapy. Across all participants, Day 1 and Day 2 HRF assessments were completed a median of 88 (IQR = 73—106) and 96 (IQR = 80—115) days postdiagnosis, respectively. For participants who received surgery first ($n = 1338$), the Day 1 and Day 2 HRF assessments were completed a median of 50 (IQR = 41–63) and 57 (IQR = 48–72) days postsurgery, respectively. For participants scheduled to receive adjuvant/neoadjuvant chemotherapy ($n = 833$), 260 (31.2%) and 458 (55.0%) completed Day 1 and Day 2 HRF assessments after starting chemotherapy, respectively.

Baseline patient characteristics

Table 1 reports the descriptive information for sociodemographic, clinical, and QoL variables, overall and by relative VO_{2peak} quartile. Relative VO_{2peak} was significantly associated with most demographic, behavioral, and QoL variables. Table 2 presents descriptive information for the HRF variables, overall and by quartiles.

Multivariable adjusted associations between physical fitness and QoL

Statistically significant associations were found between all physical fitness variables and the PCS (Table 3). The strongest associations were with the relative upper body muscular fitness measures (i.e., relative upper body muscular strength, relative upper body muscular endurance, and relative handgrip strength). For example, for relative upper body strength (p for trend < 0.001), breast cancer patients who were unable to achieve a maximal strength score were almost five times more likely to report poor/fair physical QoL than breast cancer patients in the highest relative upper body strength group (OR = 4.88; 95% CI = 3.12–7.64). For the 1107 (75.9%) breast cancer patients who were able to achieve a maximal upper body strength score, the OR for having poor/fair physical QoL per 0.1 kg/kg increase in relative upper body strength was 0.60 (95% CI = 0.51–0.70).

Relative VO_{2peak} was also strongly associated with physical QoL (p for trend < 0.001). Specifically, breast cancer patients who were unable to attempt or reach VO_{2peak} were over four times more likely to report poor/fair physical QoL than the high fit group (OR = 4.46; 95% CI = 2.81–7.09). For the 1119 (76.7%) breast cancer patients who were able to complete the VO_{2peak} test, the OR for having poor/fair physical QoL per 1 ml/kg/min increase in relative VO_{2peak} was 0.88 (95% CI = 0.85–0.91).

For the MCS, there were no statistically significant multivariable associations with any physical fitness variables. For the single general health item, there were statistically significant multivariable adjusted associations between relative handgrip strength ($p < 0.001$), relative VO_{2peak} ($p = 0.013$), absolute VO_{2peak} ($p = 0.021$), and relative upper body endurance ($p = 0.05$) with poor/fair QoL (Table 3).

Multivariable adjusted associations between body composition and QoL

Statistically significant associations were found between all body composition variables and the PCS except for total lean mass (Table 4). The strongest association was with lean mass percentage (p for trend < 0.001) where breast cancer patients with the lowest lean mass percentage were over four times more likely to report poor/fair physical QoL than patients with the highest lean mass percentage (OR = 4.13; 95% CI = 2.69–6.35). The OR for having poor/fair physical QoL per 1% increase in lean mass percentage was 0.92 (95% CI = 0.90–0.94).

For the MCS, the only statistically significant association between body composition and poor/fair mental QoL was for lean/fat ratio ($p = 0.027$), however, the pattern was not clear. For the single general health item, there were statistically significant adjusted associations between body fat percentage ($p = 0.005$), lean/fat ratio ($p = 0.009$), lean mass percentage ($p = 0.011$), and BMI ($p = 0.029$) with poor/fair QoL.

Multivariable associations between significant HRF variables and QoL

For the PCS, relative upper body strength, lean mass percentage, and relative VO_{2peak} entered the model and independently demonstrated dose–response associations culminating in the least fit groups being 2–3 times more likely to report poor/fair physical QoL compared to the high fit groups (Fig. 1). For the MCS, only lean/fat ratio entered the model and, therefore, it demonstrated the same nonlinear and modest association as in the original multivariable analysis (see Table 4). For the general health item, only relative handgrip strength entered the model, and it exhibited the same dose–response association as in the original multivariable analysis (see Table 3).

Table 1 Baseline characteristics of 1458 newly diagnosed breast cancer patients in the AMBER cohort study, overall and by relative VO_{2peak} (2012–2019)

	Overall (N = 1458)	High fit (n = 374)	Mid fit (n = 380)	Low fit (n = 365)	No VO_2 peak (n = 339)	*p* value
Age at diagnosis (year)	55.5 ± 10.7	49.8 ± 9.4	53.9 ± 9.1	58.6 ± 10.4	60.5 ± 10.9	< 0.001
Race						
White	1279 (87.7)	347 (92.8)	336 (88.4)	314 (86)	282 (83.2)	< 0.001
Non-white	179 (12.3)	27 (7.2)	44 (11.6)	51 (14)	57 (16.8)	
Education						
High school/below/college	794 (54.5)	155 (41.4)	206 (54.2)	225 (61.6)	208 (61.4)	< 0.001
University/graduate school	664 (45.5)	219 (58.6)	174 (45.8)	140 (38.4)	131 (38.6)	
Marital status						
Married/common-law	1091 (74.8)	287 (76.7)	295 (77.6)	278 (76.2)	231 (68.1)	0.013
Not married/common-law	367 (25.2)	87 (23.3)	85 (22.4)	87 (23.8)	108 (31.9)	
Income						
< 100 K	699 (47.9)	126 (33.7)	153 (40.3)	205 (56.2)	215 (63.4)	< 0.001
≥ 100 K	759 (52.1)	248 (66.3)	227 (59.7)	160 (43.8)	124 (36.6)	
Location						
Calgary	831 (57.0)	205 (54.8)	202 (53.2)	211 (57.8)	213 (62.8)	0.050
Edmonton	627 (43.0)	169 (45.2)	178 (46.8)	154 (42.2)	126 (37.2)	
Smoking status						
Never/past	1361 (93.3)	360 (96.3)	356 (93.7)	334 (91.5)	311 (91.7)	0.036
Current	97 (6.7)	14 (3.7)	24 (6.3)	31 (8.5)	28 (8.3)	
Alcohol consumed (g/day)	7.1 ± 16.2	8.8 ± 14.9	7.8 ± 13.7	5.2 ± 13.4	6.7 ± 21.8	0.015
Kilocalorie intake (kcal/day)	1716 ± 745	1777 ± 682	1734 ± 734	1678 ± 750	1667 ± 814	0.16
Weight (kg)	73.7 ± 15.8	63.3 ± 9.2	71.4 ± 11.9	83.8 ± 17.0	76.9 ± 16.3	< 0.001
Body mass index (kg/m^2)	27.5 ± 5.6	23.3 ± 2.9	26.4 ± 3.9	31.4 ± 5.6	29.1 ± 6.0	< 0.001
< 25	550 (37.7)	276 (73.8)	145 (38.2)	42 (11.5)	87 (25.7)	
≥ 25	908 (62.3)	98 (26.2)	235 (61.8)	323 (88.5)	252 (74.3)	
Disease stage						
I	657 (45.1)	171 (45.7)	164 (43.2)	158 (43.3)	164 (48.4)	0.64
II	675 (46.3)	176 (47.1)	183 (48.2)	172 (47.1)	144 (42.5)	
III	126 (8.6)	27 (7.2)	33 (8.7)	35 (9.6)	31 (9.1)	
Tumor grade						
1	186 (12.8)	46 (12.3)	54 (14.2)	53 (14.5)	33 (9.7)	0.044
2	625 (42.9)	163 (43.6)	146 (38.4)	146 (40.0)	170 (50.1)	
3	647 (44.4)	165 (44.1)	180 (47.4)	166 (45.5)	136 (40.1)	
Surgery status[a]						
Presurgery	120 (8.2)	35 (9.4)	34 (8.9)	31 (8.5)	20 (5.9)	0.36
Lumpectomy	818 (56.1)	198 (52.9)	210 (55.3)	217 (59.5)	193 (56.9)	
Mastectomy	520 (35.7)	141 (37.7)	136 (35.8)	117 (32.1)	126 (37.2)	
Chemotherapy status[a]						
None/before	1198 (82.2)	314 (84.0)	304 (80.0)	303 (83.0)	277 (81.7)	0.52
After 1 or 2 cycles	260 (17.8)	60 (16.0)	76 (20.0)	62 (17.0)	62 (18.3)	
PCS	49.2 ± 7.5	51.9 ± 6.4	49.8 ± 6.9	48.0 ± 7.5	47.0 ± 8.3	< 0.001
Bottom 20%	292 (20)	51 (13.6)	61 (16.3)	79 (21.3)	101 (29.8)	< 0.001
MCS	47.8 ± 10.0	47.9 ± 9.7	46.7 ± 9.9	48.6 ± 9.8	48.2 ± 10.8	0.06
Bottom 20%	292 (20)	75 (20.1)	81 (21.7)	69 (18.6)	67 (19.8)	0.78
General Health	2.3 ± 0.8	2.0 ± 0.7	2.3 ± 0.8	2.5 ± 0.8	2.6 ± 0.8	< 0.001
Poor/fair %	96 (6.6)	12 (3.2)	25 (6.7)	26 (7.0)	33 (9.7)	0.006

[a]At time of baseline fitness testing. *PCS* physical component summary; *MCS* mental component summary

Table 2 Baseline descriptive statistics for health-related fitness of 1458 newly diagnosed breast cancer patients in the AMBER cohort study, overall and by fitness quartiles (2012–2019)

Health related fitness measures	Overall	Quartile 1	Quartile 2	Quartile 3	Quartile 4[a]	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	*n* (%)
Aerobic fitness						
Relative VO_{2peak} (mL/kg/min)	26.6 ± 6.0	33.3 ± 4.0	26.1 ± 1.5	20.4 ± 2.3		339 (23.3)
Absolute VO_{2peak} (L/min)	1.89 ± 0.37	2.30 ± 0.22	1.86 ± 0.09	1.50 ± 0.16		339 (23.3)
Muscular strength						
Upper body strength (kg)	36.7 ± 9.8	47.6 ± 6.9	35.8 ± 2.2	26.6 ± 3.6		351 (24.1)
Relative upper body strength (kg/kg)	0.51 ± 0.14	0.66 ± 0.10	0.49 ± 0.03	0.37 ± 0.05		351 (24.1)
Lower body strength (kg)	98.9 ± 31.4	130.7 ± 24.6	92.4 ± 6.3	67.0 ± 11.4		358 (24.6)
Relative lower body strength (kg/kg)	1.39 ± 0.41	1.85 ± 0.29	1.34 ± 0.09	0.97 ± 0.16		358 (24.6)
Handgrip Strength (kg)	55.2 ± 12.1	70.6 ± 7.0	58.5 ± 2.3	50.7 ± 2.3	39.8 ± 5.5	
Relative handgrip strength (kg/kg)	0.77 ± 0.21	1.05 ± 0.11	0.83 ± 0.04	0.69 ± 0.04	0.52 ± 0.08	
Muscular endurance						
Upper body endurance (kg)	490 ± 211	721 ± 179	453 ± 46	291 ± 63		387 (26.5)
Relative upper body endurance(kg/kg)	6.8 ± 3.1	10.2 ± 2.8	6.2 ± 0.7	4.0 ± 0.8		387 (26.5)
Lower body endurance (kg)	1271 ± 776	2085 ± 783	1118 ± 145	603 ± 180		393 (27.0)
Relative lower body endurance(kg/kg)	17.8 ± 10.7	29.0 ± 10.9	15.6 ± 2.0	8.8 ± 2.6		393 (27.0)
Curl ups (reps)	28 ± 28	64 ± 31	31 ± 4	16 ± 5	0.1 ± 0.6	
Flexibility						
Sit and reach (cm)	27.4 ± 9.8	40.0 ± 3.9	31.0 ± 2.0	24.1 ± 2.0	14.5 ± 4.3	
Body Composition						
Body weight (kg)	73.7 ± 15.8	56.4 ± 4.6	66.6 ± 2.5	76.5 ± 3.3	95.1 ± 11.7	
Body mass index (kg/m^2)[b]	27.5 ± 5.6	22.3 ± 1.8	27.4 ± 1.4	32.0 ± 1.4	38.9 ± 3.4	
Total lean mass (kg)	37.7 ± 5.4	44.9 ± 3.6	39.0 ± 1.0	35.6 ± 0.9	31.4 ± 2.1	
Total fat mass (kg)	31.6 ± 11.5	18.6 ± 3.1	26.8 ± 2.1	34.0 ± 2.3	47.2 ± 8.2	
Lean mass percentage (%)	52.2 ± 6.4	60.9 ± 3.8	53.6 ± 1.3	49.6 ± 1.1	44.6 ± 2.3	
Body fat percentage (%)	43.0 ± 7.2	33.3 ± 3.9	41.2 ± 1.4	45.9 ± 1.3	51.6 ± 2.5	
Lean/fat ratio	1.32 ± 0.45	1.95 ± 0.43	1.35 ± 0.08	1.11 ± 0.06	0.89 ± 0.08	

[a]Quartile 4 provides the mean (SD) for fitness measures with complete data or n (%) for measures with missing data

[b]Body mass index quartiles are < 25, 25–29.9, 30–34.9, and ≥ 35

Discussion

Our results suggest that inferior HRF was significantly and meaningfully associated with a higher risk of poor/fair physical QoL in newly diagnosed breast cancer patients. Moreover, the three primary HRF components of cardiorespiratory fitness (relative VO_{2peak}), muscular fitness (relative upper body strength), and body composition (lean mass percentage) were all independently associated with physical QoL in multivariable analysis that considered all other significant HRF exposures. Conversely, no HRF variables were significantly and meaningfully associated with mental QoL. Finally, worse scores on most HRF variables were associated with a higher risk of poor/fair general health in multivariable analyses, however, only relative handgrip strength was independently associated with general health.

One novel finding of our study was that measures of all three main components of HRF—muscular fitness, body composition, and cardiorespiratory fitness—were independently associated with physical QoL in newly diagnosed breast cancer patients. To our knowledge, no previous observational study or randomized controlled trial has demonstrated this important finding in any cancer patient group at any phase of the cancer trajectory. Moreover, the three independent associations all demonstrated dose–response patterns and remained clinically meaningful (ORs > 2.0) even after adjusting for each other. This finding has important implications for the exercise prescription that may optimize physical QoL in newly diagnosed breast cancer patients. Specifically, exercise interventions that increase relative VO_{2peak}, relative upper body strength, and lean mass percentage may maximize improvements in physical QoL.

Another novel finding from our study was that the strongest associations between HRF and physical QoL were for measures of relative upper body muscular fitness (i.e., relative upper body muscular strength, relative upper body

Table 3 Multivariable associations between physical fitness and poor/fair quality of life in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012–2019)

	Poor/fair PCS (bottom 20%) OR (95% CI)	Poor/fair MCS (bottom 20%) OR (95% CI)	Poor/fair general health (bottom 6.6%) OR (95% CI)
Relative VO_2peak			
High fit	1.0	1.0	1.0
Mid fit	1.91 (1.21–3.03)	1.42 (0.98–2.06)	1.45 (0.68–3.10)
Low fit	4.04 (2.58–6.34)	1.45 (0.97–2.15)	2.74 (1.34–5.61)
No VO_2peak	4.46 (2.81–7.09)	1.53 (1.01–2.32)	2.62 (1.24–5.50)
P for trend	< 0.001	0.15	0.013
OR per 1 ml/kg/min	0.88 (0.85–0.91)	0.98 (0.95–1.01)	0.92 (0.87–0.97)
Absolute VO_2peak			
High fit	1.0	1.0	1.0
Mid fit	1.29 (0.85–1.95)	1.39 (0.96–2.01)	2.23 (1.08–4.60)
Low fit	1.80 (1.18–2.75)	1.39 (0.94–2.07)	2.68 (1.27–5.65)
No VO_2peak	2.63 (1.72–4.01)	1.49 (0.99–2.25)	2.88 (1.37–6.06)
P for trend	< 0.001	0.20	0.021
OR per 1 L/min	0.49 (0.30–0.82)	0.74 (0.47–1.16)	0.38 (0.16–0.90)
Upper body strength			
High fit	1.0	1.0	1.0
Mid fit	1.32 (0.87–2.01)	0.91 (0.63–1.32)	1.35 (0.72–2.56)
Low fit	1.40 (0.92–2.14)	0.90 (0.61–1.32)	0.85 (0.42–1.74)
No RM	2.76 (1.87–4.08)	1.06 (0.72–1.55)	1.79 (0.97–3.30)
P for trend	< 0.001	0.82	0.08
OR per 1 kg	0.89 (0.74–1.07)	1.08 (0.92–1.27)	0.93 (0.69–1.24)
Relative upper body strength			
High fit	1.0	1.0	1.0
Mid fit	2.25 (1.41–3.60)	0.81 (0.56–1.18)	0.92 (0.46–1.86)
Low fit	3.54 (2.22–5.65)	0.94 (0.63–1.38)	1.43 (0.74–2.78)
No RM	4.88 (3.12–7.64)	1.03 (0.71–1.51)	1.91 (1.01–3.59)
P for trend	< 0.001	0.61	0.08
P per 0.1 kg/kg	0.60 (0.51–0.70)	1.02 (0.91–1.15)	0.83 (0.66–1.03)
Lower body strength			
High fit	1.0	1.0	1.0
Mid fit	1.25 (0.84–1.88)	0.88 (0.60–1.27)	1.11 (0.57–2.15)
Low fit	1.57 (1.06–2.35)	1.08 (0.74–1.56)	1.41 (0.75–2.68)
No RM	2.25 (1.53–3.32)	1.12 (0.77–1.64)	1.63 (0.89–3.00)
P for trend	< 0.001	0.63	0.38
OR per 1 kg	0.95 (0.90–1.01)	1.01 (0.96–1.06)	0.99 (0.90–1.07)
Relative lower body strength			
High fit	1.0	1.0	1.0
Mid fit	1.66 (1.07–2.56)	1.07 (0.74–1.56)	1.33 (0.64–2.75)
Low fit	2.46 (1.60–3.77)	1.06 (0.72–1.56)	2.22 (1.12–4.40)
No RM	3.07 (2.00–4.71)	1.19 (0.81–1.77)	2.17 (1.10–4.30)
P for trend	< 0.001	0.84	0.50
P per 0.1 kg/kg	0.89 (0.85–0.94)	1.00 (0.96–1.04)	0.94 (0.88–1.01)
Upper body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.68 (1.08–2.60)	1.12 (0.76–1.64)	0.91 (0.46–1.80)
Low fit	1.74 (1.13–2.68)	1.18 (0.80–1.73)	1.14 (0.59–2.19)
No max reps	3.06 (2.04–4.58)	1.26 (0.87–1.84)	1.66 (0.91–3.04)
P for trend	< 0.001	0.67	0.20
OR per 100 kgs	0.89 (0.81–0.97)	0.96 (0.89–1.04)	0.875 (0.75–1.02)
Relative upper body endurance			
High fit	1.0	1.0	1.0
Mid fit	2.34 (1.44–3.79)	1.05 (0.71–1.54)	1.20 (0.58–2.49)
Low fit	3.29 (2.05–5.28)	1.35 (0.92–2.00)	1.85 (0.93–3.68)

Table 3 (continued)

	Poor/fair PCS (bottom 20%) OR (95% CI)	Poor/fair MCS (bottom 20%) OR (95% CI)	Poor/fair general health (bottom 6.6%) OR (95% CI)
No max reps	4.59 (2.91–7.26)	1.30 (0.89–1.92)	2.23 (1.14–4.34)
P for trend	< 0.001	0.32	0.05
P per 1 kg/kg	0.83 (0.77–0.89)	0.97 (0.92–1.02)	0.88 (0.78–0.98)
Lower body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.22 (0.81–1.85)	0.89 (0.61–1.31)	1.07 (0.55–2.09)
Low fit	1.20 (0.79–1.82)	1.01 (0.69–1.48)	1.19 (0.61–2.32)
No max reps	1.95 (1.31–2.89)	1.08 (0.74–1.58)	1.41 (0.76–2.62)
P for trend	0.004	0.82	0.71
OR per 100 kgs	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.98 (0.94–1.02)
Relative lower body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.23 (0.79–1.89)	1.13 (0.77–1.64)	1.33 (0.67–2.64)
Low fit	1.75 (1.16–2.66)	1.01 (0.68–1.50)	1.48 (0.74–2.94)
No max reps	2.28 (1.52–3.42)	1.16 (0.79–1.71)	1.65 (0.86–3.17)
P for trend	< 0.001	0.82	0.49
P per 1 kg/kg	0.98 (0.96–1.00)	0.99 (0.98–1.01)	0.98 (0.95–1.01)
Handgrip strength			
Highest 25%	1.0	1.0	1.0
50–75%	1.06 (0.72–1.58)	1.15 (0.80–1.66)	1.16 (0.60–2.28)
25–50%	1.36 (0.92–2.02)	0.93 (0.63–1.37)	1.52 (0.78–2.94)
Lowest 25%	1.82 (1.21–2.73)	1.30 (0.87–1.95)	2.24 (1.15–4.36)
P for trend	0.016	0.35	0.08
OR per 1 kg	0.98 (0.97–0.99)	0.99 (0.98–1.01)	0.97 (0.95–0.99)
Relative handgrip strength			
Highest 25%	1.0	1.0	1.0
50–75%	2.07 (1.32–3.25)	1.30 (0.90–1.88)	1.12 (0.51–2.46)
25–50%	2.90 (1.86–4.54)	1.11 (0.75–1.63)	1.76 (0.85–3.64)
Lowest 25%	4.88 (3.13–7.62)	1.18 (0.79–1.77)	3.67 (1.85–7.28)
P for trend	< 0.001	0.57	< 0.001
P per 0.1 kg/kg	0.75 (0.70–0.81)	0.95 (0.89–1.02)	0.78 (0.69–0.88)
Curl up			
Highest 25%	1.0	1.0	1.0
50–75%	1.22 (0.81–1.83)	0.88 (0.61–1.28)	0.93 (0.48–1.83)
25–50%	1.87 (1.27–2.76)	1.05 (0.72–1.52)	1.79 (0.97–3.29)
Lowest 25%	1.54 (1.02–2.33)	1.08 (0.72–1.60)	1.24 (0.64–2.42)
P for trend	0.010	0.75	0.13
OR per 1 rep	0.99 (0.99–1.00)	1.00 (0.99–1.00)	0.99 (0.98–1.00)
Sit and reach			
Highest 25%	1.0	1.0	1.0
50–75%	1.25 (0.83–1.89)	0.71 (0.48–1.04)	0.79 (0.40–1.57)
25–50%	1.75 (1.18–2.60)	0.97 (0.67–1.40)	1.35 (0.74–2.47)
Lowest 25%	1.77 (1.19–2.64)	1.19 (0.82–1.72)	1.40 (0.76–2.59)
P for trend	0.009	0.07	0.24
OR per 1 cm	0.98 (0.97–0.99)	0.99 (0.98–1.01)	0.98 (0.96–1.00)

All analyses adjusted for age, education, comorbidity, family history, disease stage, surgery, kilocalorie intake, location, and smoking

PCS physical component summary; *MCS* mental component summary; *OR* odds ratio; *CI* confidence interval

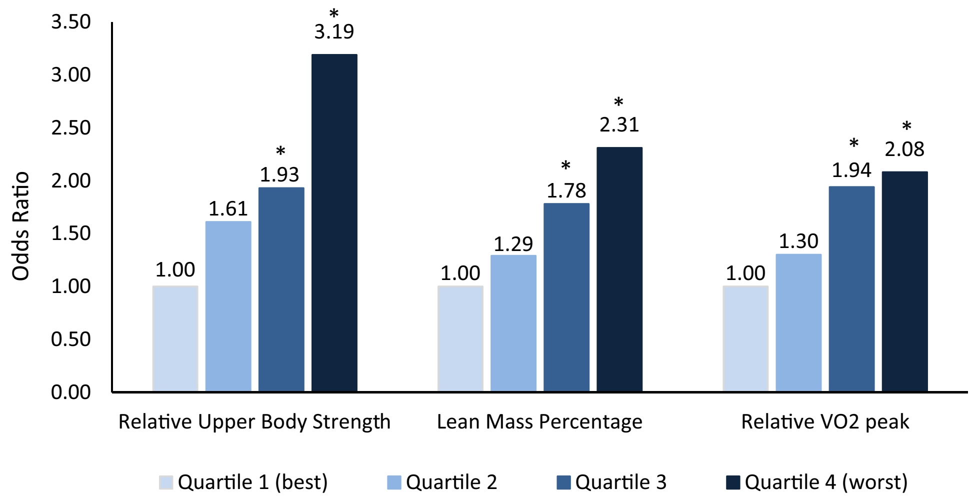
Table 4 Multivariable associations between body composition and poor/fair quality of life in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012–2019)

	Poor/fair PCS (bottom 20%) OR (95% CI)	Poor/fair MCS (bottom 20%) OR (95% CI)	Poor/fair general health (bottom 6.6%) OR (95% CI)
Body weight			
Lowest 25%	1.0	1.0	1.0
25–50%	1.83 (1.20–2.80)	0.96 (0.66–1.40)	0.92 (0.45–1.88)
50–75%	2.24 (1.47–3.40)	0.95 (0.65–1.39)	1.33 (0.69–2.56)
Highest 25%	2.71 (1.80–4.09)	0.97 (0.67–1.41)	1.82 (0.99–3.37)
P for trend	< 0.001	0.99	0.10
OR per 1 kg	1.02 (1.02–1.03)	1.00 (0.99–1.01)	1.02 (1.00–1.03)
Body mass index			
< 25	1.0	1.0	1.0
25–29.9	1.92 (1.36–2.70)	0.84 (0.61–1.16)	1.44 (0.81–2.55)
30–34.9	2.05 (1.36–3.09)	0.97 (0.65–1.45)	1.92 (1.01–3.66)
≥ 35	3.96 (2.56–6.11)	1.05 (0.68–1.65)	2.63 (1.36–5.10)
P for trend	< 0.001	0.66	0.029
OR per 1 kg/m^2	1.07 (1.05–1.10)	1.01 (0.98–1.03)	1.05 (1.02–1.09)
Total lean mass			
Highest 25%	1.0	1.0	1.0
50–75%	0.76 (0.53–1.11)	0.97 (0.67–1.41)	1.18 (0.66–2.11)
25–50%	0.76 (0.52–1.11)	1.10 (0.76–1.61)	1.22 (0.67–2.20)
Lowest 25%	0.72 (0.49–1.05)	1.17 (0.80–1.71)	0.86 (0.45–1.64)
P for trend	0.30	0.76	0.69
OR per 1 kg	1.03 (1.01–1.06)	0.99 (0.97–1.02)	1.01 (0.98–1.05)
Total fat mass			
Lowest 25%	1.0	1.0	1.0
25–50%	2.10 (1.36–3.26)	1.28 (0.88–1.85)	0.96 (0.47–1.95)
50–75%	2.35 (1.52–3.65)	1.03 (0.70–1.53)	1.49 (0.78–2.87)
Highest 25%	3.76 (2.46–5.76)	1.14 (0.77–1.67)	1.83 (0.98–3.44)
P for trend	< 0.001	0.57	0.11
OR per 1 kg	1.04 (1.03–1.05)	1.00 (0.99–1.02)	1.03 (1.01–1.04)
Lean mass percentage			
Highest 25%	1.0	1.0	1.0
50–75%	1.57 (1.00–2.47)	1.44 (0.99–2.08)	1.14 (0.56–2.33)
25–50%	2.54 (1.65–3.92)	1.07 (0.72–1.59)	1.33 (0.66–2.68)
Lowest 25%	4.13 (2.69–6.35)	1.37 (0.92–2.03)	2.49 (1.30–4.78)
P for trend	< 0.001	0.17	0.011
OR per 1%	0.92 (0.90–0.94)	0.99 (0.97–1.01)	0.94 (0.91–0.98)
Body fat percentage			
Lowest 25%	1.0	1.0	1.01
25–50%	1.53 (0.98–2.38)	1.52 (1.05–2.20)	0.66 (0.31–1.38)
50–75%	2.15 (1.40–3.32)	1.07 (0.72–1.59)	1.35 (0.71–2.58)
Highest 25%	3.85 (2.53–5.87)	1.28 (0.86–1.90)	2.01 (1.08–3.72)
P for trend	< 0.001	0.11	0.005
OR per 1%	1.08 (1.06–1.11)	1.01 (0.99–1.03)	1.05 (1.02–1.09)
Lean/fat ratio			
Highest 25%	1.0	1.0	1.0
50–75%	1.58 (1.01–2.46)	1.68 (1.16–2.43)	0.71 (0.34–1.47)
25–50%	2.27 (1.47–3.50)	1.08 (0.72–1.61)	1.29 (0.67–2.48)
Lowest 25%	3.95 (2.58–6.03)	1.32 (0.89–1.97)	1.99 (1.07–3.69)
P for trend	< 0.001	0.027	0.009
OR per 1 unit	0.87 (0.83–0.90)	0.98 (0.95–1.01)	0.94 (0.88–1.00)

All analyses adjusted for age, education, comorbidity, family history, stage, surgery, kilocalorie intake, location, and smoking

PCS physical component summary; *MCS* mental component summary; *OR* odds ratio; *CI* confidence interval

Fig. 1 Health-related fitness variables independently associated with poor/fair physical quality of life in newly diagnosed breast cancer patients. *significantly different from reference group



muscular endurance, and relative handgrip strength) which demonstrated steep dose–response associations and ORs exceeding of 3.0 and 4.0. Most previous studies examining the associations between muscular fitness and QoL in cancer survivorship have relied on handgrip strength alone [9]. A recent systematic review and meta-analysis [9] summarized the association between relative handgrip strength and QoL from five studies involving 587 breast cancer survivors and reported significant positive correlations with total QoL, physical/functional QoL, and emotional QoL; however, no associations were reported for social QoL or mental QoL. Only one small study ($n = 93$) focused on newly diagnosed postsurgical breast cancer patients and it showed positive associations between relative handgrip strength and physical/functional QoL but not mental QoL [20]. Our study demonstrates that relative upper body strength is superior to handgrip strength for predicting physical QoL but not general health.

Another important finding from our study was that cardiorespiratory fitness was significantly and meaningfully associated with physical QoL and general health but not mental QoL. Few studies have examined the association between cardiorespiratory fitness and QoL in breast cancer patients [10, 21–23] and have been limited by very small sample sizes of < 100 [10, 21–23] and the use of submaximal measures of VO_{2peak} [10, 22]. Additionally, only one study focused on newly diagnosed breast cancer patients [10]. The findings overall have been mixed, perhaps because of small sample sizes, suboptimal measures of cardiorespiratory, and different phases of the cancer continuum.

Another main finding from our study was that almost all body composition variables were associated with physical QoL and general health but not mental QoL. The most commonly used body composition measures in the cancer survivorship literature are BMI [8] and skeletal muscle mass assessed by computed tomography [7]. Smits et al. [8] conducted a systematic review and meta-analysis of the association between BMI and QoL in four studies of 1362 endometrial cancer survivors and found that obese survivors had significantly poorer physical functioning, social functioning, and role functioning, but not emotional functioning or cognitive functioning. Hanna et al. [7] conducted a systematic review and meta-analysis summarizing the association between skeletal muscle mass and QoL from 14 studies involving 2776 cancer survivors and reported that low muscle mass was significantly associated with poorer global QoL and poorer physical functioning; but not social, role, emotional, or cognitive functioning. Only one small study focused on newly diagnosed breast cancer patients [24] and it involved 99 early-stage breast cancer patients scheduled for adjuvant chemotherapy. That study showed that lower skeletal muscle index was significantly associated with better general QoL and physical QoL whereas lower BMI was borderline significantly associated with better physical QoL. Our study demonstrates that body composition, especially the relative amount of lean mass, is more important than BMI for physical QoL.

HRF may be associated with better physical QoL and general health in newly diagnosed breast cancer patients for several reasons. First, greater relative upper body muscular fitness may be an indicator of fewer surgical complications and/or a better recovery from surgery although we adjusted for timing and type of surgery in the analysis. Second, greater relative upper body muscular fitness may improve performance of activities of daily living and recreational activities that require upper body strength such as shoveling snow, mowing the lawn, vacuuming, gardening, grocery shopping, bowling, curling, golfing, and yoga. Third, greater relative cardiovascular fitness and relative muscle mass may be associated with fewer comorbidities although we adjusted for comorbidities in our analyses. Finally, greater relative cardiorespiratory fitness and relative muscle mass may be associated with better physical QoL because they may provide greater capacity to perform physically demanding activities of daily living and recreational activities with less perceived effort, dyspnea, and fatigue.

Interestingly, no HRF variables were significantly and meaningfully associated with mental QoL in our study, which is consistent with the general literature [7–9]. These data suggest that HRF does not buffer breast cancer patients against the mental distress of a new cancer diagnosis, surgical recovery, and pending/initiating treatments. These results should not be construed, however, to suggest that exercise does not improve mental QoL in breast cancer patients. Exercise may improve mental QoL in newly diagnosed breast cancer patients [25] but not through mechanisms related to HRF [26, 27]. Mental QoL improvements from exercise are more likely due to biological and psychosocial mechanisms such as chemical changes in the brain, pleasant outdoor environments, social interactions, distraction from daily stressors, enjoyment, a sense of accomplishment, and improved self-esteem [28].

Our study has important strengths and limitations. The key strengths of our study include the understudied cancer phase, the large sample size, the comprehensive assessment of HRF using high quality measures, and the validated measure of QoL assessing both physical and mental QoL. Some key limitations of our study include the cross-sectional design, the failure to assess all participants after surgery and before adjuvant treatments, the inability of almost 25% of participants to complete VO_{2peak} or maximal strength testing, and a healthier sample which limits the generalizability of our findings.

In conclusion, we reported the largest and most comprehensive assessment of the associations between HRF and QoL in any cancer patient group. Our results suggest that HRF is strongly associated with physical QoL, but not mental QoL, in newly diagnosed breast cancer patients. Our study is the first to show that the three primary components of HRF—muscular fitness, body composition, and cardiorespiratory fitness—are independently associated with physical QoL in newly diagnosed breast cancer patients. These findings highlight the value of a comprehensive assessment of HRF in breast cancer patients and the potential for a more evidence-based exercise prescription to maximize physical QoL [29, 30]. Moreover, our results also demonstrated that relative HRF (i.e., relative to body weight) is more important than absolute HRF for physical QoL. This finding is encouraging because it suggests that exercise interventions may improve physical QoL in breast cancer patients regardless of body size.

Author contributions Conceptualization: KSC, KYA, FZA, GJB, ARM, JM, QW, SJA, SMN, MLM, JKV, SNCR, KK, LY, CEM, MF, LD, JRM, CMF. Data curation: QW, KK. Formal analysis: KYA, FZA, QW, KK. Funding acquisition: KSC, GJB, MLM, JKV, SNCR, CEM, JRM, CMF. Investigation: KYA, FZA, GJB, ARM, SJA, SMN, MLM, MF, LD. Methodology: KSC, GJB, MLM, JKV, SNCR, CEM, CMF. Project administration: KSC, LD, MLM, CMF. Resources: KSC, JRM, CMF. Supervision: KSC, CMF. Writing—original draft: KSC, FZA, SJA, SMN. Writing—review and editing: KSC, KYA, FZA, GJB, ARM, JM, QW, SJA, SMN, MLM, JKV, SNCR, KK, LY, CEM, MF, LD, JRM, CMF.

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Data availability The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

References

1. Brenner DR, Poirier A, Woods RR, Ellison LF, Billette JM, Demers AA, Zhang SX, Yao C, Finley C, Fitzgerald N, Saint-Jacques N, Shack L, Turner D, Holmes E; Canadian Cancer Statistics Advisory Committee (2022) Projected estimates of cancer in Canada in 2022. CMAJ 2022 May 2; 194(17):E601–7. https://doi.org/10.1503/cmaj.212097
2. Siegel RL, Miller KD, Wagle NS, Jemal A (2023) Cancer statistics, 2023. CA Cancer J Clin 2023; 73:17–48.
3. Montgomery M, McCrone SH (2010) Psychological distress associated with the diagnostic phase for suspected breast cancer: systematic review. J Adv Nurs 66(11):2372–2390
4. Mai TTX, Choi JH, Lee MK, Chang YJ, Jung SY, Cho H, Lee ES (2019) Prognostic value of post-diagnosis health-related quality of life for overall survival in breast cancer: findings from a 10-year prospective cohort in Korea. Cancer Res Treat 51(4):1600–1611
5. Quinten C, Coens C, Mauer M, Comte S, Sprangers MA, Cleeland C, Osoba D, Bjordal K, Bottomley A, Groups EC (2009) Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials. Lancet Oncol 10(9):865–871
6. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, George SM, Olson RD (2018) The physical activity guidelines for Americans. JAMA 320 (19):2020–2028
7. Hanna L, Nguo K, Furness K, Porter J, Huggins CE (2022) Association between skeletal muscle mass and quality of life in adults with cancer: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle 13(2):839–857
8. Smits A, Lopes A, Bekkers R, Galaal K (2015) Body mass index and the quality of life of endometrial cancer survivors–a systematic review and meta-analysis. Gynecol Oncol 137(1):180–187
9. Campos E, Silva AC, Bergmann A, Araujo CM, Montenegro AKS, Tenorio ADS, Dantas D (2022) Association of handgrip strength

with quality of life in breast cancer survivors: a systematic review and meta-analysis. Asian Pac J Cancer Prev 23(10):3237–3245
10. Bortolozo HI, Derchain S, Vechin FC, Maginador GF, Santos IS, Torresan R, de Nazare Silva Dos Santos P, Sarian LO, Conceicao MS (2021) Aerobic fitness is a predictor of body composition in women with breast cancer at diagnosis. Clin Breast Cancer 21(3):e245–e251
11. Courneya KS, Vallance JK, Culos-Reed SN, McNeely ML, Bell GJ, Mackey JR, Yasui Y, Yuan Y, Matthews CE, Lau DC et al (2012) The Alberta moving beyond breast cancer (AMBER) cohort study: a prospective study of physical activity and health-related fitness in breast cancer survivors. BMC Cancer 12:525
12. Courneya KS, McNeely ML, Culos-Reed SN, Vallance JK, Bell GJ, Mackey JR, Matthews CE, Morielli AR, Cook D, MacLaughlin S et al (2016) The Alberta moving beyond breast cancer (AMBER) cohort study: recruitment, baseline assessment, and description of the first 500 participants. BMC Cancer 16:481
13. Friedenreich CM, Vallance JK, McNeely ML, Culos-Reed SN, Matthews CE, Bell GJ, Mackey JR, Kopciuk KA, Dickau L, Wang Q et al (2022) The Alberta moving beyond breast cancer (AMBER) cohort study: baseline description of the full cohort. Cancer Causes Control 33(3):441–453
14. Maruish M (2011) User's Manual for the SF36v2 Health Survey. 3rd ed. Quality Metric Incorporated, RI, US
15. Ware JKM, Dewey J (2000) How to score version two of the SF-36® health survey. Spine. https://doi.org/10.1097/00007632-200012150-00008
16. Csizmadi I, Kahle L, Ullman R, Dawe U, Zimmerman TP, Friedenreich CM, Bryant H, Subar AF (2007) Adaptation and evaluation of the national cancer institute's diet history questionnaire and nutrient database for Canadian populations. Public Health Nutr 10(1):88–96
17. van Buuren S, Groothuis-Oudshoorn K (2011) Mice: multivariate imputation by chained equations in R. J Stat Softw 45(3):1–67
18. Vallance JK, Friedenreich CM, Wang Q, Matthews CE, Yang L, McNeely ML, Culos-Reed SN, Bell GJ, Morielli AR, McNeil J et al (2023) Associations of device-measured physical activity and sedentary time with quality of life and fatigue in newly diagnosed breast cancer patients: baseline results from the AMBER cohort study. Cancer 129(2):296–306
19. Streiner DL, Norman GR (2012) Mine is bigger than yours: measures of effect size in research. Chest 141(3):595–598
20. Buyukakincak O, Akyol Y, Ozen N, Ulus Y, Canturk F, Tander B, Buyukakincak S, Bilgici A, Kuru O (2014) Quality of life in patients with breast cancer at early postoperative period: relationship to shoulder pain, handgrip strength, disability, and emotional status. Turk J Phys Med Rehab 60:1–6
21. Herrero F, Balmer J, San Juan AF, Foster C, Fleck SJ, Perez M, Canete S, Earnest CP, Lucia A (2006) Is cardiorespiratory fitness related to quality of life in survivors of breast cancer? J Strength Cond Res 20(3):535–540
22. Kim DY, Kim JH, Park SW (2019) Aerobic capacity correlates with health-related quality of life after breast cancer surgery. Eur J Cancer Care (Engl) 28(4):e13050
23. Tolentino GP, Battaglini CL, Araujo SS, Otano AS, Conde DM, Evans ES, de Oliveira RJ (2010) Cardiorespiratory fitness and quality-of-life analysis posttreatment in breast cancer survivors. J Psychosoc Oncol 28(4):381–398
24. Aleixo GFP, Deal AM, Nyrop KA, Muss HB, Damone EM, Williams GR, Yu H, Shachar SS (2020) Association of body composition with function in women with early breast cancer. Breast Cancer Res Treat 181(2):411–421
25. Aune D, Markozannes G, Abar L, Balducci K, Cariolou M, Nanu N, Vieira R, Anifowoshe YO, Greenwood DC, Clinton SK et al (2022) Physical activity and health-related quality of life in women with breast cancer: a meta-analysis. JNCI Cancer Spectr. https://doi.org/10.1093/jncics/pkac072
26. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS (2003) Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol 21(9):1660–1668
27. Courneya KS, Sellar CM, Stevinson C, McNeely ML, Peddle CJ, Friedenreich CM, Tankel K, Basi S, Chua N, Mazurek A et al (2009) Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 27(27):4605–4612
28. Mikkelsen K, Stojanovska L, Polenakovic M, Bosevski M, Apostolopoulos V (2017) Exercise and mental health. Maturitas 106:48–56
29. An KY, Morielli AR, Kang DW, Friedenreich CM, McKenzie DC, Gelmon K, Mackey JR, Reid RD, Courneya KS (2020) Effects of exercise dose and type during breast cancer chemotherapy on longer-term patient-reported outcomes and health-related fitness: a randomized controlled trial. Int J Cancer 146(1):150–160
30. Courneya KS, McKenzie DC, Mackey JR, Gelmon K, Friedenreich CM, Yasui Y, Reid RD, Cook D, Jespersen D, Proulx C et al (2013) Effects of exercise dose and type during breast cancer chemotherapy: multicenter randomized trial. J Natl Cancer Inst 105(23):1821–1832