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Original article

Associations between health-related fitness and patient-reported symptoms in newly diagnosed breast cancer patients

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Abstract

Background: Newly diagnosed breast cancer patients experience symptoms that may affect their quality of life, treatment outcomes, and survival. Preventing and managing breast cancer-related symptoms soon after diagnosis is essential. The purpose of this study was to investigate the associations between health-related fitness (HRF) and patient-reported symptoms in newly diagnosed breast cancer patients.

Methods: This study utilized baseline data from the Alberta Moving Beyond Breast Cancer Cohort Study that were collected within 90 days of diagnosis. HRF measures included peak cardiopulmonary fitness (peak volume of oxygen consumption (VO_{2peak})), maximal muscular strength and endurance, flexibility, and body composition. Symptom measures included depression, sleep quality, and fatigue. Adjusted multivariable logistic regression was performed for analyses.

Results: Of 1458 participants, 51.5% reported poor sleep quality, 26.5% reported significant fatigue, and 10.4% reported moderate depression. In multivariable-adjusted models, lower relative VO_{2peak} was independently associated with a greater likelihood of all symptom measures, including moderate depression ($p < 0.001$), poor sleep quality ($p = 0.009$), significant fatigue ($p = 0.008$), any symptom ($p < 0.001$), and multiple symptoms ($p < 0.001$). VO_{2peak} demonstrated threshold associations with all symptom measures such that all 3 lower quartiles exhibited similar elevated risk compared to the highest quartile. The strength of the threshold associations varied by the symptom measure with odds ratios ranging from ~1.5 for poor sleep quality to ~3.0 for moderate depression and multiple symptoms. Moreover, lower relative upper body muscular endurance was also independently associated with fatigue in a dose-response manner ($p = 0.001$), and higher body weight was independently associated with poor sleep quality in an inverted U pattern ($p = 0.021$).

Conclusion: Relative VO_{2peak} appears to be a critical HRF component associated with multiple patient-reported symptoms in newly diagnosed breast cancer patients. Other HRF parameters may also be important for specific symptoms. Exercise interventions targeting different HRF components may help newly diagnosed breast cancer patients manage specific symptoms and improve outcomes.

Keywords: Breast cancer; Fatigue; Depression; Sleep quality; Cardiorespiratory fitness

1. Introduction

Breast cancer is the most common cancer worldwide with almost 2.3 million new diagnoses each year, accounting for 11.7% of all new cancer cases.[1] In women, breast cancer

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accounts for 24.5% of all new cancer diagnoses and 15.5% of all cancer deaths, ranking first in incidence and mortality in the vast majority of countries around the world.[1] A breast cancer diagnosis may cause emotional distress marked by a period of uncertainty and a loss of control.[2] Previous studies have shown that most newly diagnosed breast cancer patients report moderate or severe distress,[3,4] as well as psychiatric syndromes such as depression and post-traumatic stress disorder.[4] Depression, sleep disturbance, and fatigue are common symptoms in breast cancer patients[5] that often form a symptom cluster.[6] Moreover, these symptoms in newly diagnosed patients may persist for years[5] and are associated with a lower quality of life,[2,5] disruption of cancer treatment,[7] and increased risk of cancer recurrence and mortality.[7–9]

Health-related fitness (HRF) refers to the components of physical fitness that exhibit a strong relationship with health status. HRF may be one of the key underlying factors contributing to the depression–poor sleep–fatigue symptom cluster. Several studies have examined the associations between HRF and breast cancer-related symptoms;[10–17] however, most studies have utilized simple measures of HRF, such as body mass index (BMI), handgrip strength, sit and stand, or submaximal treadmill tests. Moreover, these studies have examined only a limited number of HRF measures in small samples (<100) of breast cancer patients during and after treatments. Currently, there is a gap in the literatures concerning the relative importance of HRF in managing breast cancer-related symptoms in newly diagnosed patients. If research is able to identify key HRF components associated with specific symptoms, it may be possible to develop more targeted exercise interventions to improve specific symptoms in newly diagnosed breast cancer patients.

The purpose of the present study was to investigate the associations between a comprehensive set of high quality HRF measures and patient-reported symptoms in a large sample of newly diagnosed breast cancer patients using data from the Alberta Moving Beyond Breast Cancer (AMBER) cohort study.[18–20] We focused on the key symptom cluster of depression, poor sleep quality, and fatigue. Our primary objective was to determine which HRF components were most strongly associated with each individual symptom as well as the experience of multiple symptoms. In general, we hypothesized that breast cancer patients with lower levels of HRF would be more likely to report depressive symptoms, poor sleep quality, and significant fatigue as well as multiple symptoms. More specifically, based on previous smaller and limited studies,[10–17] we expected that worse cardiovascular fitness, muscular fitness, and body composition would each be associated with higher rates of symptom experience.

2. Methods

2.1. Study design and participants

The AMBER study design and methods[18] and baseline characteristics of the cohort[19] have been described elsewhere. The AMBER study was approved by the Health Research Ethics Board of Alberta: Cancer Committee (HREBA.CC-17-0576), and written consent was obtained from all participants. Participants were recruited between July 2012 and July 2019 in Edmonton and Calgary, Alberta, Canada. Inclusion criteria included women with newly diagnosed breast cancer who (a) had histologically confirmed Stage I (≥T1c) to Stage IIIc breast cancer, (b) were 18–80 years old, (c) were fluent in English, and (d) were not pregnant. Assessments were conducted at baseline, 1 year, 3 years, and 5 years (questionnaires only) after diagnosis. The current study is a cross-sectional design, which included the baseline data of the AMBER study.

2.2. Baseline assessment

Our goal was to complete baseline assessments within 90 days of diagnosis and *prior to* initiating neoadjuvant or adjuvant therapy. Adjuvant patients who completed surgery first were allowed 4–6 weeks recovery after surgery. Participants were allowed to complete baseline assessments before the third cycle of chemotherapy or the tenth fraction of radiation therapy. Participants were asked to come to the study site on 2 separate days for the baseline HRF assessments. On Day 1, participants completed anthropometric and body composition assessments, lymphedema and range of motion testing, and other HRF testing (abdominal endurance, flexibility, handgrip strength, and graded exercise treadmill test). Participants were also provided with questionnaires (including the symptoms measures) and accelerometers. The Day 2 assessment was conducted after about 1 week. Participants returned the questionnaires and accelerometers and completed upper and lower body muscular strength and endurance tests using chest press and leg press machines. If participants were not available to come on 2 separate days, all assessments were completed on a single day with appropriate rest between physical fitness tests.

2.3. HRF measures

HRF measures included a graded treadmill exercise test with metabolic and cardiorespiratory measurements, handgrip dynamometer isometric strength, partial curl-ups, chest and leg press strength and endurance, sit-and-reach flexibility, body composition using dual x-ray absorptiometry, and anthropometric measurements of waist and hip circumference. Aerobic and muscular fitness were expressed as absolute scores and relative to body mass.

The graded treadmill exercise test was performed using the modified Bruce protocol with gas exchange measurements to assess cardiopulmonary fitness. Expired gases during exercise were analyzed using an automated metabolic measurement cart (Parvo Medics TrueOne 2400, Parvo Medics Inc, Sandy, UT, USA). The peak oxygen consumption (VO_{2peak}) in absolute (L/min) and relative (mL/kg/min) terms was collected.[18] Muscular fitness was assessed by different tests, such as combined right and left handgrip strength using a dynamometer, abdominal endurance using partial curl-ups, upper and lower body strength, and endurance using chest press and leg press. Upper and lower body strength was assessed by a predicted 1 repetition maximum using an 8–10 repetition maximum test with a validated equation (100 × weight/

(101.3−2.67123 × repetitions)).[21] Upper and lower body endurance were assessed by the number of repetitions × 50% of the predicted 1 repetition maximum for the chest press and 70% of the predicted 1 repetition maximum for the leg press. Hand grip strength and upper and lower body strength were expressed in absolute (kg lifted) and relative (kg lifted/kg body weight) terms. Flexibility was assessed by the sit-and-reach test. Body composition was assessed by dual x-ray absorptiometry using a Lunar Prodigy (General Electric Company, Madison, WI, USA) and includes fat mass, lean mass, body fat percentage, lean mass percentage, and lean mass/fat mass ratio. For anthropometric measurements, height and weight were assessed and used to calculate BMI. All HRF assessments were conducted by certified exercise physiologists using standardized testing protocols and the same equipment at both the Edmonton and the Calgary sites.

2.4. Symptoms

We assessed depression, sleep quality, and fatigue using reliable and validated self-report measures with previously established cut-points identifying possible clinical thresholds. Depression was assessed using the Patient Health Questionnaire-9.[22] Participants were asked, "Over the last 2 weeks, how often have you been bothered by any of the following problems?". The Patient Health Questionnaire-9 has 9 "Diagnostic and Statistical Manual of Mental Disorders", 4th edition, criteria, and each criteria has response options ranging from 0 (*not at all*) to 3 (*nearly every day*). The summed score from the 9 items provides a provisional assessment of depression severity that can be categorized into 5 severity groups (i.e., none to minimal: 0−4; mild: 5−9; moderate: 10−14; moderately severe: 15−19; and severe: 20−27).

Sleep quality was measured using the Pittsburgh Sleep Quality Index, which has been validated in cancer patients.[23,24] The Pittsburgh Sleep Quality Index assesses 7 components of sleep consisting of subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component is rated on a 0−3 scale with higher scores indicating worse sleep quality. The 7 components can be summed to calculate a global sleep quality score, which ranges from 0 to 21. Scores of ≤5 indicate good sleep quality, while scores of >5 indicate poor sleep quality.[23]

Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue scale,[25] which includes 13 items to measure fatigue over the previous 7 days. Each item is scored on a 0−4 response scale, and all items are summed to calculate a single fatigue score ranging from 0 to 52, with higher scores indicating less fatigue. A threshold score of <34 indicates significant fatigue.[26]

2.5. Participant characteristics

Participant characteristics, including sociodemographic characteristics, medical history, and smoking and alcohol drinking histories, were assessed using the Baseline Health Questionnaire. Dietary intake was assessed using the Canadian version of the U.S. National Cancer Institute's Diet History Questionnaire.[27] Clinical information about the cancer and treatments was collected from medical charts.

2.6. Statistical analyses

For variables with <5% missing data (i.e., handgrip strength, partial curl-ups, sit-and-reach, and body composition), we used multivariable imputations through chained equations using all correlated baseline variables before computing quartiles.[28] For several HRF variables (i.e., absolute and relative VO_{2peak}, absolute and relative maximal strength and endurance) with substantial missing data (i.e., approximately 25%) due to participant limitations in safely completing exercise assessments,[19] we coded this group as the lowest fitness category (e.g., no VO_{2peak} or no maximum strength test). We then computed tertiles for the approximately 75% of patients who completed the tests, which resulted in roughly 4 equal quartiles of HRF.

We used analyses of variance for continuous variables and the χ^2 test for categorical variables to compare baseline characteristics across quartiles of relative VO_{2peak}. To examine the associations between quartiles of HRF and binary symptom outcomes, we used logistic regression. For depression, we compared moderate/severe *vs*. none/mild; for sleep quality, we compared poor *vs.* good; and for fatigue we compared significant *vs.* not significant fatigue. We also computed a composite symptom score by summing the prevalence of the 3 individual symptoms (i.e., 0, 1, 2, or 3 symptoms)[29] and compared any symptom *vs*. no symptom and multiple (≥2 symptoms) *vs.* none/single symptom.

We categorized our exposures and outcomes for analyses to generate more clinically interpretable results for patients and clinicians by using odds ratios (ORs) rather than correlations or regression coefficients. We also wanted to include the 25% of participants who were unable to achieve VO_{2peak} or maximal muscular strength by coding them as their own category in our logistic regression analysis (i.e., unable to perform test) rather than excluding them. For comparison, we also examined the associations of continuous HRF variables (per a given measurement unit) with binary symptoms for all participants with available data.

We investigated multivariable associations between lower levels of HRF and the presence of each symptom adjusting for age, education, comorbidity, family history, disease stage, surgery type (i.e., no surgery *vs.* lumpectomy *vs.* mastectomy), kilocalorie intake, location, treatment status (i.e., started chemotherapy *vs.* not), and smoking as described in a previous publication.[30] We then examined multivariable associations, including all HRF variables that were statistically significantly associated with each symptom in a second multivariable model. In that multivariable model, the covariates above were forced into the model and all statistically significant HRFs were examined by stepwise forward analysis. We chose stepwise forward consideration over forced entry for the statistically significant HRF exposures because of the high multicollinearity among the HRF variables. We interpreted ORs of <0.50 or >2.00 as clinically meaningful.[31]

3. Results

The AMBER study flow chart for the baseline assessment has been reported elsewhere.[19] Briefly, a total of 14,680 newly diagnosed breast cancer patients were screened, 3673 (25%) were eligible, and 1528 (42%) were recruited. In the current study, 1458 participants who completed symptom assessments were included in the analysis. Of the 1458 participants, 120 (8.2%) had not yet had surgery and 260 (17.8%) had started chemotherapy at the time of the Day 1 HRF assessments.

3.1. Baseline participant characteristics

Baseline demographic and clinical characteristics of the sample have been reported elsewhere.[19] The mean age of the 1458 participants was 56 years, 87.7% were white, 93.3% were currently not smoking, and 62.3% had a BMI of ≥25 kg/m^2. Most participants had Stage I (45.1%) or Stage II (46.3%) disease, had surgery before the baseline assessment (i.e., lumpectomy 56.1% and mastectomy 35.7%), and were assessed before starting chemotherapy (82.2%). Baseline HRF of the sample has also been reported elsewhere.[30] Briefly, the overall mean and SD were 26.6 ± 6.6 mL/kg/min for relative VO_{2peak}, 36.7 ± 9.8 kg for upper body strength, 98.9 ± 31.4 kg for lower body strength, 37.7 ± 5.4 kg for lean mass, 31.6 ± 11.5 kg for fat mass, and 43.0 ± 7.2% for body fat percentage.

Table 1 shows the descriptive information for the symptom variables for the entire sample and across relative VO_{2peak} quartiles. Overall, 152 (10.4%) participants reported at least moderate depression, 751 (51.5%) reported poor sleep quality, and 386 (26.5%) reported significant fatigue. Moreover, 602 (41.3%) participants reported no symptoms, 529 (36.3%) reported 1 symptom, 221 (15.2%) reported 2 symptoms, and 106 (7.3%) reported all 3 symptoms. Supplementary Table 1 reports descriptive information for HRF variables across the number of symptoms experienced by participants.

3.2. Associations between physical fitness and symptoms

Multivariable adjusted associations of physical fitness with depression, sleep quality, and fatigue are presented in Table 2. For depression, the significant HRF correlates were relative VO_{2peak} ($p < 0.001$) and relative handgrip strength ($p = 0.049$), with both variables demonstrating a threshold association with higher rates of depression for the 3 lower

Table 1
Breast cancer related symptoms in 1458 newly diagnosed breast cancer patients in the AMBER cohort study, overall and by relative VO_{2peak}.

	Overall (n = 1458)	High fit (n = 374)	Mid fit (n = 380)	Low fit (n = 365)	No VO_{2peak} (n = 339)	p
Depression (Pittsburgh Sleep Quality Index and the Functional Assessment of Chronic Illness Therapy-Fatigue)	4.3 ± 4.1	3.8 ± 3.7	4.7 ± 4.1	4.2 ± 4.1	4.5 ± 4.5	0.014
None/minimal	916 (62.8)	253 (67.6)	220 (57.9)	235 (64.4)	208 (61.4)	0.003
Mild	390 (26.7)	99 (26.5)	105 (27.6)	94 (25.8)	92 (27.1)	
Moderate	109 (7.5)	16 (4.3)	46 (12.1)	22 (6.0)	25 (7.4)	
Moderately severe	31 (2.1)	2 (0.5)	7 (1.8)	12 (3.3)	10 (2.9)	
Severe	12 (0.8)	4 (1.1)	2 (0.5)	2 (0.5)	4 (1.2)	
None/mild combined	1306 (89.6)	352 (94.1)	325 (85.5)	329 (90.1)	300 (88.5)	<0.001
Moderate + combined	152 (10.4)	22 (5.9)	55 (14.5)	36 (9.9)	39 (11.5)	
None	916 (62.8)	253 (67.6)	220 (57.9)	235 (64.4)	208 (61.4)	0.039
Any	542 (37.2)	121 (32.4)	160 (42.1)	130 (35.6)	131 (38.6)	
Sleep (Pittsburgh Sleep Quality Index)	6.3 ± 5.7	5.4 ± 3.5	6.6 ± 3.6	6.8 ± 9.4	6.6 ± 3.8	0.004
Good	707 (48.5)	217 (58.0)	166 (43.7)	171 (46.8)	153 (45.1)	<0.001
Poor	751 (51.5)	157 (42.0)	214 (56.3)	194 (53.2)	186 (54.9)	
Fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue)	39.2 ± 9.8	41.6 ± 9.1	38.9 ± 9.8	38.7 ± 9.8	37.7 ± 10.3	<0.001
Less fatigue	1072 (73.5)	302 (80.7)	276 (72.6)	264 (72.3)	230 (67.8)	<0.001
Significant fatigue	386 (26.5)	72 (19.3)	104 (27.4)	101 (27.7)	109 (32.2)	
Symptom clustering						
No symptom	602 (41.3)	196 (54.2)	137 (36.1)	143 (39.2)	126 (37.2)	<0.001
Depression only	3 (0.2)	0 (0.0)	1 (0.3)	0 (0)	2 (0.6)	
Poor sleep only	438 (30.0)	103 (27.5)	121 (31.8)	118 (32.3)	96 (28.3)	
Fatigue only	88 (6.0)	20 (5.3)	23 (6.1)	25 (6.8)	20 (5.9)	
Depression + poor sleep	29 (2.0)	3 (0.8)	17 (4.5)	3 (0.8)	6 (1.8)	
Depression + fatigue	14 (1.0)	1 (0.3)	5 (1.3)	3 (0.8)	5 (1.5)	
Poor sleep + fatigue	178 (12.2)	33 (8.8)	44 (11.6)	43 (11.8)	58 (17.1)	
All 3 symptoms	106 (7.3)	18 (4.8)	32 (8.4)	30 (8.2)	26 (7.7)	
Symptom number						
No symptom	602 (41.3)	196 (32.6)	137 (36.1)	143 (39.2)	126 (37.2)	<0.001
1 symptom	529 (36.3)	123 (32.9)	145 (38.2)	143 (39.2)	118 (34.8)	
2 symptoms	221 (15.2)	37 (9.9)	66 (17.4)	49 (13.4)	69 (20.4)	
3 symptoms	106 (7.3)	18 (4.8)	32 (8.4)	30 (8.2)	26 (7.7)	

Note: Data are present as mean ± SD or n (%). Percentages may not add up to 100% due to rounding.
Abbreviations: AMBER = Alberta Moving Beyond Breast Cancer; PHQ-9 = Patient Health Questionnaire-9; VO_{2peak} = peak volume of oxygen consumption.

Table 2
Multivariable associations between physical fitness and breast cancer-related symptoms in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012−2019).

	Depression (moderate/severe)	Sleep quality (poor)	Fatigue (significant)
Relative VO_{2peak}			
High fit	1.00	1.0	1.0
Mid fit	3.15 (1.84−5.41)	1.75 (1.30−2.36)	1.82 (1.27−2.61)
Low fit	2.29 (1.27−4.13)	1.52 (1.11−2.08)	2.10 (1.44−3.07)
No VO_{2peak}	2.88 (1.58−5.26)	1.53 (1.10−2.13)	2.61 (1.76−3.87)
p for trend	<0.001	0.002	<0.001
OR per 1 mL/kg/min	0.94 (0.90−0.98)	0.97 (0.95−0.99)	0.93 (0.90−0.96)
Absolute VO_{2peak}			
High fit	1.0	1.0	1.0
Mid fit	1.39 (0.86−2.27)	1.01 (0.82−1.48)	1.42 (0.99−2.02)
Low fit	1.28 (0.75−2.17)	1.20 (0.88−1.65)	1.84 (1.27−2.66)
No VO_{2peak}	1.62 (0.95−2.76)	1.19 (0.85−1.66)	2.25 (1.53−3.29)
p for trend	0.330	0.680	<0.001
OR per 0.1 L/min	0.98 (0.92−1.04)	0.97 (0.94−1.01)	0.94 (0.90−0.98)
Upper body strength			
High fit	1.0	1.0	1.0
Mid fit	0.81 (0.49−1.32)	1.18 (0.88−1.59)	1.04 (0.73−1.47)
Low fit	1.06 (0.65−1.73)	1.33 (0.98−1.81)	1.03 (0.72−1.48)
No max test	0.84 (0.51−1.40)	1.18 (0.87−1.62)	1.64 (1.15−2.33)
p for trend	0.660	0.330	0.015
OR per 1 kg	1.00 (0.81−1.22)	0.88 (0.77−1.00)	0.91 (0.78−1.06)
Relative upper body strength			
High fit	1.0	1.0	1.0
Mid fit	1.00 (0.61−1.64)	1.24 (0.92−1.67)	1.12 (0.78−1.60)
Low fit	1.20 (0.72−1.98)	1.32 (0.97−1.80)	1.45 (1.01−2.10)
No max test	0.94 (0.56−1.57)	1.20 (0.88−1.64)	1.90 (1.33−2.72)
p for trend	0.800	0.340	0.002
OR per 0.1 kg/kg	0.83 (0.70−0.97)	0.88 (0.80−0.97)	0.82 (0.73−0.92)
Lower body strength			
High fit	1.0	1.0	1.0
Mid fit	1.13 (0.70−1.81)	1.24 (0.93−1.67)	0.88 (0.62−1.25)
Low fit	0.89 (0.53−1.49)	1.09 (0.81−1.46)	1.31 (0.93−1.85)
No max test	1.25 (0.77−2.03)	1.08 (0.80−1.46)	1.53 (1.09−2.16)
p for trend	0.600	0.530	0.010
OR per 1 kg	1.03 (0.97−1.10)	0.98 (0.94−1.02)	0.98 (0.93−1.02)
Relative lower body strength			
High fit	1.0	1.0	1.0
Mid fit	1.32 (0.82−2.14)	1.35 (1.00−1.82)	1.05 (0.74−1.50)
Low fit	0.90 (0.52−1.53)	1.24 (0.92−1.68)	1.34 (0.94−1.91)
No max test	1.33 (0.80−2.20)	1.17 (0.86−1.60)	1.65 (1.15−2.37)
p for trend	0.320	0.240	0.024
OR per 0.1 kg/kg	1.00 (0.95−1.05)	0.97 (0.94−1.00)	0.96 (0.93−1.00)
Upper body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.38 (0.85−2.25)	1.08 (0.80−1.45)	1.53 (1.06−2.20)
Low fit	1.30 (0.79−2.15)	1.24 (0.92−1.68)	1.94 (1.34−2.79)
No max test	0.97 (0.58−1.64)	1.15 (0.85−1.56)	2.22 (1.55−3.18)
p for trend	0.400	0.540	<0.001
OR per 100 kgs	0.94 (0.85−1.04)	0.96 (0.90−1.01)	0.87 (0.81−0.94)
Relative upper body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.39 (0.84−2.32)	1.15 (0.85−1.55)	1.33 (0.92−1.94)
Low fit	1.75 (1.05−2.92)	1.24 (0.92−1.68)	2.28 (1.58−3.30)
No max test	1.11 (0.64−1.90)	1.18 (0.87−1.60)	2.30 (1.59−3.31)
p for trend	0.120	0.550	<0.001
OR per 1 kg/kg	0.91 (0.84−0.98)	0.96 (0.92−1.00)	0.88 (0.83−0.93)
Lower body endurance			
High fit	1.0	1.0	1.0
Mid fit	0.97 (0.58−1.60)	1.01 (0.75−1.37)	0.96 (0.67−1.38)
Low fit	0.99 (0.59−1.65)	1.21 (0.89−1.64)	1.24 (0.87−1.78)
No max test	1.15 (0.70−1.88)	1.13 (0.83−1.54)	1.53 (1.07−2.17)

(*continued on next page*)

Table 2 (Continued)

	Depression (moderate/severe)	Sleep quality (poor)	Fatigue (significant)
p for trend	0.900	0.560	0.037
OR per 100 kg	1.00 (0.98−1.03)	0.99 (0.98−1.01)	0.98 (0.97−1.00)
Relative lower body endurance			
High fit	1.0	1.0	1.0
Mid fit	1.13 (0.69−1.85)	1.10 (0.82−1.49)	0.97 (0.67−1.38)
Low fit	0.93 (0.55−1.57)	1.22 (0.90−1.66)	1.24 (0.87−1.78)
No max test	1.19 (0.72−1.96)	1.17 (0.86−1.59)	1.53 (1.07−2.18)
p for trend	0.770	0.620	0.038
OR per 1 kg/kg	0.99 (0.97−1.02)	0.99 (0.98−1.00)	0.98 (0.97−1.00)
Handgrip strength			
High fit	1.0	1.0	1.0
Mid fit	0.90 (0.56−1.46)	1.08 (0.80−1.45)	1.19 (0.85−1.67)
Low fit	0.92 (0.56−1.52)	1.15 (0.85−1.55)	0.95 (0.67−1.36)
Poor fit	1.22 (0.73−2.06)	0.95 (0.69−1.31)	1.39 (0.96−2.02)
p for trend	0.660	0.610	0.150
OR per 1 kg	1.00 (0.98−1.01)	1.00 (0.99−1.01)	0.99 (0.98−1.00)
Relative handgrip strength			
High fit	1.0	1.0	1.0
Mid fit	1.86 (1.11−3.11)	1.38 (1.02−1.86)	1.31 (0.92−1.87)
Low fit	1.67 (0.98−2.85)	1.41 (1.04−1.91)	1.20 (0.83−1.72)
Poor fit	1.96 (1.14−3.38)	1.08 (0.79−1.48)	1.97 (1.37−2.85)
p for trend	0.0490	0.050	0.002
OR per 0.1 kg/kg	0.89 (0.81−0.98)	0.96 (0.91−1.02)	0.88 (0.82−0.94)
Curl up			
High fit	1.0	1.0	1.0
Mid fit	1.02 (0.63−1.67)	1.14 (0.85−1.53)	1.04 (0.74−1.46)
Low fit	1.13 (0.69−1.85)	1.20 (0.88−1.62)	1.22 (0.87−1.73)
Poor fit	1.31 (0.77−2.21)	1.09 (0.80−1.48)	1.28 (0.89−1.85)
p for trend	0.740	0.680	0.450
OR per 1 rep	0.99 (0.99−1.00)	1.00 (0.99−1.00)	1.00 (0.99−1.00)
Sit and reach			
High fit	1.0	1.0	1.0
Mid fit	1.01 (0.61−1.66)	1.00 (0.74−1.34)	0.89 (0.62−1.26)
Low fit	0.97 (0.59−1.61)	0.81 (0.61−1.09)	1.03 (0.73−1.46)
Poor fit	1.30 (0.80−2.13)	0.98 (0.73−1.33)	1.43 (1.01−2.01)
p for trend	0.620	0.430	0.043
OR per 1 cm	0.99 (0.97−1.01)	1.00 (0.99−1.01)	0.99 (0.98−1.00)

Notes: Data are presented as OR(95%CI). All analyses were adjusted for age, education, comorbidity, family history, disease stage, surgery type and timing, chemotherapy status, kilocalorie intake, location, and smoking.

Abbreviations: 95%CI = 95% confidence interval; AMBER = Alberta Moving Beyond Breast Cancer; OR = odds ratio; VO_{2peak} = peak volume of oxygen consumption.

fitness groups compared to the highest fitness group. For sleep quality, the significant HRF correlates were relative VO_{2peak} ($p = 0.002$) and relative handgrip strength ($p = 0.050$). Relative VO_{2peak} demonstrated a threshold association of higher rates of poor sleep quality for the 3 lower fitness groups compared to the highest fitness group, whereas relative handgrip strength demonstrated an inverted U association of higher rates of poor sleep quality for the middle 2 fitness groups compared to the highest and lowest fitness groups. For fatigue, there were significant dose−response associations of higher rates of fatigue with worse scores for almost all fitness variables. The strongest association was with relative VO_{2peak} ($p < 0.001$).

3.3. Associations between body composition and symptoms

Table 3 reports multivariable adjusted associations between body composition and the 3 symptoms. For depression, statistically significant dose−response associations of higher rates of depression were identified for lean percent ($p = 0.010$), body fat percent ($p = 0.015$), and lean/fat ratio ($p = 0.008$). For sleep quality, most body composition variables demonstrated significant threshold associations of higher rates of poor sleep quality. For fatigue, there were significant dose−response associations of higher rates of fatigue with BMI ($p = 0.024$), fat mass ($p = 0.008$), lean percent ($p = 0.001$), body fat percent ($p < 0.001$), and lean/fat ratio ($p = 0.001$).

3.4. Associations between HRF variables and number of symptoms

Tables 4 and 5 report the associations of physical fitness and body composition, respectively, with the number of symptoms experienced. When comparing any symptom *vs.* no symptoms, the statistically significant HRF correlates were relative VO_{2peak} ($p < 0.001$), absolute VO_{2peak} ($p = 0.040$), upper body endurance ($p = 0.030$), relative upper body endurance ($p = 0.012$), and relative handgrip strength ($p = 0.041$) among physical fitness variables (Table 4); and body weight

Table 3
Multivariable associations between body composition and breast cancer-related symptoms in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012−2019).

	Depression (moderate/severe)	Sleep quality (poor)	Fatigue (significant)
Body weight			
Lowest 25%	1.0	1.0	1.0
25%−50%	1.07 (0.63−1.82)	1.60 (1.19−2.15)	1.09 (0.76−1.56)
50%−75%	1.33 (0.78−2.24)	1.56 (1.16−2.10)	1.29 (0.91−1.84)
Highest 25%	1.63 (0.99−2.68)	1.22 (0.90−1.65)	1.52 (1.08−2.15)
p for trend	0.200	0.005	0.080
OR per 1 kg	1.01 (1.00−1.02)	1.00 (0.10−1.01)	1.01 (1.01−1.02)
Body mass index			
<25	1.0	1.0	1.0
25−29.9	1.30 (0.84−2.00)	1.25 (0.97−1.60)	1.00 (0.74−1.34)
30−34.9	1.54 (0.92−2.59)	1.17 (0.86−1.60)	1.28 (0.89−1.84)
≥35	1.99 (1.45−3.45)	1.02 (0.71−1.48)	1.75 (1.17−2.61)
p for trend	0.090	0.330	0.024
OR per 1 kg/m^2	1.04 (1.01−1.07)	1.01 (0.99−1.03)	1.04 (1.01−1.06)
Lean mass			
Highest 25%	1.0	1.0	1.0
50%−75%	0.92 (0.57−1.51)	0.97 (0.72−1.31)	0.87 (0.62−1.21)
25%−50%	1.18 (0.73−1.90)	1.09 (0.81−1.47)	0.80 (0.57−1.13)
Lowest 25%	1.05 (0.64−1.73)	1.05 (0.78−1.42)	0.90 (0.64−1.27)
p for trend	0.81	0.87	0.64
OR per 1 kg	1.01 (0.98−1.04)	1.00 (0.98−1.02)	1.02 (1.00−1.04)
Fat mass			
Lowest 25%	1.0	1.0	1.0
25%−50%	1.43 (0.84−2.43)	1.57 (1.16−2.11)	1.37 (0.96−1.96)
50%−75%	1.65 (0.97−2.82)	1.69 (1.25−2.29)	1.42 (0.99−2.05)
Highest 25%	2.01 (1.20−3.36)	1.38 (1.02−1.87)	1.85 (1.30−2.64)
p for trend	0.060	0.004	0.008
OR per 1 kg	1.02 (1.01−1.04)	1.01 (1.00−1.02)	1.02 (1.01−1.03)
Lean percent			
Highest 25%	1.0	1.0	1.0
50%−75%	1.43 (0.83−2.47)	1.37 (1.02−1.85)	1.62 (1.14−2.32)
25%−50%	1.94 (1.15−3.29)	1.47 (1.09−1.99)	1.42 (0.98−2.05)
Lowest 25%	2.31 (1.36−3.93)	1.47 (1.08−2.01)	2.08 (1.44−3.00)
p for trend	0.010	0.040	0.001
OR per 1 %	0.95 (0.92−0.97)	0.98 (0.96−1.00)	0.96 (0.94−0.98)
Body fat percent			
Lowest 25%	1.0	1.0	1.0
25%−50%	1.60 (0.94−2.73)	1.54 (1.14−2.07)	1.54 (1.08−2.19)
50%−75%	1.84 (1.08−3.13)	1.46 (1.08−1.97)	1.26 (0.87−1.82)
Highest 25%	2.32 (1.37−3.95)	1.49 (1.09−2.03)	2.08 (1.45−2.99)
p for trend	0.015	0.018	<0.001
OR per 1 %	1.05 (1.02−1.08)	1.02 (1.00−1.04)	1.04 (1.02−1.06)
Lean/fat ratio			
Highest 25%	1.0	1.0	1.0
50%−75%	1.82 (1.07−3.10)	1.56 (1.16−2.10)	1.55 (1.09−2.21)
25%−50%	1.76 (1.02−3.04)	1.40 (1.03−1.89)	1.26 (0.87−1.83)
Lowest 25%	2.46 (1.45−4.20)	1.51 (1.11−2.05)	2.03 (1.42−2.92)
p for trend	0.008	0.017	0.001
OR per 0.1 kg/kg	0.91 (0.87−0.96)	0.96 (0.94−0.99)	0.94 (0.91−0.97)

Notes: Data are presented as OR(95%CI). All analyses were adjusted for age, education, comorbidity, family history, disease stage, surgery type and timing, chemotherapy status, kilocalorie intake, location, and smoking.
Abbreviations: 95%CI = 95% confidence interval; AMBER = Alberta Moving Beyond Breast Cancer; OR = odds ratio.

($p = 0.011$), fat mass ($p = 0.001$), lean percent ($p = 0.003$), body fat percent ($p = 0.001$), and lean/fat ratio ($p = 0.001$) among body composition variables (Table 5). The strongest association was with relative VO_{2peak} ($p < 0.001$).

When comparing multiple symptoms to single/no symptoms, there were significant dose−response associations of higher rates of multiple symptoms with relative VO_{2peak} ($p < 0.001$), absolute VO_{2peak} ($p = 0.007$), upper body endurance ($p = 0.007$), relative upper body endurance ($p = 0.001$), and relative handgrip strength ($p = 0.025$) among physical fitness variables (Table 4); and fat mass ($p = 0.013$), lean percent ($p = 0.003$), body fat percent ($p = 0.002$), and lean/fat ratio ($p = 0.001$) among body composition variables (Table 5). The strongest HRF correlate was relative VO_{2peak} ($p < 0.001$).

Table 4
Multivariable associations between physical fitness and number of breast cancer−related symptoms in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012−2019).

	Symptom number (any *vs.* 0)	Symptom number (2−3 *vs.* 0−1)
Relative VO_{2peak}		
High fit	1.00	1.0
Mid fit	2.03 (1.50−2.76)	2.30 (1.57−3.38)
Low fit	1.85 (1.34−2.55)	2.02 (1.34−3.05)
No VO_{2peak}	1.91 (1.36−2.68)	2.90 (1.90−4.41)
p for trend	<0.001	<0.001
OR per 1 mL/kg/min	0.95 (0.93−0.97)	0.94 (0.92−0.97)
Absolute VO_{2peak}		
High fit	1.0	1.0
Mid fit	1.28 (0.95−1.73)	1.30 (0.90−1.88)
Low fit	1.54 (1.12−2.14)	1.40 (0.94−2.07)
No VO_{2peak}	1.53 (1.09−2.15)	2.00 (1.35−2.97)
p for trend	0.040	0.007
OR per 0.1 L/min	0.95 (0.91−0.98)	0.97 (0.93−1.02)
Upper body strength		
High fit	1.0	1.0
Mid fit	1.13 (0.84−1.54)	1.06 (0.73−1.54)
Low fit	1.28 (0.93−1.75)	1.23 (0.84−1.79)
No max test	1.33 (0.96−1.83)	1.52 (1.05−2.20)
p for trend	0.30	0.13
OR per 1 kg	0.89 (0.77−1.01)	0.87 (0.74−1.03)
Relative upper body strength		
High fit	1.0	1.0
Mid fit	1.22 (0.90−1.65)	1.19 (0.82−1.73)
Low fit	1.42 (1.03−1.95)	1.40 (0.95−2.06)
No max test	1.41 (1.03−1.95)	1.66 (1.14−2.42)
p for trend	0.11	0.06
OR per 0.1 kg/kg	0.86 (0.78−0.95)	0.80 (0.70−0.90)
Lower body strength		
High fit	1.0	1.0
Mid fit	1.14 (0.85−1.54)	0.94 (0.65−1.35)
Low fit	1.16 (0.86−1.58)	1.13 (0.78−1.62)
No max test	1.24 (0.91−1.69)	1.42 (0.99−2.04)
p for trend	0.58	0.14
OR per 1 kg	0.97 (0.93−1.01)	1.00 (0.95−1.05)
Relative lower body strength		
High fit	1.0	1.0
Mid fit	1.46 (1.08−1.97)	0.95 (0.66−1.38)
Low fit	1.36 (1.00−1.84)	1.14 (0.79−1.66)
No max test	1.43 (1.03−1.96)	1.45 (1.00−2.10)
p for trend	0.06	0.13
OR per 0.1 kg/kg	0.97 (0.94−1.00)	0.97 (0.94−1.01)
Upper body endurance		
High fit	1.0	1.0
Mid fit	1.13 (0.84−1.53)	1.52 (1.04−2.23)
Low fit	1.53 (1.12−2.09)	1.65 (1.12−2.42)
No max reps	1.41 (1.03−1.92)	1.88 (1.29−2.75)
p for trend	0.030	0.007
OR per 100 kg	0.92 (0.86−0.98)	0.90 (0.83−0.97)
Relative upper body endurance		
High fit	1.0	1.0
Mid fit	1.17 (0.87−1.59)	1.30 (0.88−1.92)
Low fit	1.62 (1.19−2.22)	1.92 (1.31−2.83)
No max reps	1.46 (1.07−1.99)	1.92 (1.31−2.82)
p for trend	0.012	0.001
OR per 1 kg/kg	0.93 (0.89−0.97)	0.90 (0.85−0.95)
Lower body endurance		
High fit	1.0	1.0
Mid fit	1.09 (0.81−1.48)	0.90 (0.62−1.32)
Low fit	1.26 (0.93−1.73)	1.17 (0.80−1.70)
No max reps	1.29 (0.94−1.77)	1.45 (1.01−2.10)
p for trend	0.33	0.07
OR per 100 kg	0.99 (0.97−1.01)	0.99 (0.97−1.01)
Relative lower body endurance		
High fit	1.0	1.0
Mid fit	1.12 (0.83−1.52)	0.96 (0.65−1.40)
Low fit	1.23 (0.90−1.68)	1.19 (0.82−1.74)
No max reps	1.29 (0.94−1.77)	1.50 (1.03−2.17)
p for trend	0.40	0.07
OR per 1 kg/kg	0.99 (0.98−1.00)	0.98 (0.97−1.00)
Handgrip strength		
Highest 25%	1.0	1.0
50%−75%	1.34 (0.99−1.82)	0.95 (0.67−1.35)
25%−50%	1.31 (0.96−1.78)	0.82 (0.57−1.19)
Lowest 25%	1.27 (0.91−1.76)	1.04 (0.71−1.54)
p for trend	0.23	0.60
OR per 1 kg	0.99 (0.98−1.00)	0.99 (0.98−1.01)
Relative handgrip strength		
Highest 25%	1.0	1.0
50%−75%	1.46 (1.07−1.97)	1.51 (1.05−2.19)
25%−50%	1.48 (1.09−2.03)	1.25 (0.85−1.83)
Lowest 25%	1.41 (1.02−1.94)	1.74 (1.18−2.56)
p for trend	0.041	0.025
OR per 0.1 kg/kg	0.92 (0.87−0.98)	0.89 (0.84−0.96)
Curl up		
Highest 25%	1.0	1.0
50%−75%	1.05 (0.78−1.41)	1.01 (0.71−1.46)
25%−50%	1.27 (0.93−1.74)	1.10 (0.76−1.59)
Lowest 25%	1.04 (0.76−1.43)	1.33 (0.91−1.94)
p for trend	0.42	0.44
OR per 1 rep	1.00 (0.99−1.00)	0.99 (0.99−1.00)
Sit and reach		
Highest 25%	1.0	1.0
50%−75%	0.98 (0.73−1.33)	1.04 (0.72−1.50)
25%−50%	0.85 (0.63−1.14)	0.99 (0.69−1.43)
Lowest 25%	1.11 (0.82−1.51)	1.31 (0.91−1.88)
p for trend	0.36	0.38
OR per 1 cm	1.00 (0.99−1.01)	0.99 (0.98−1.01)

Notes: Data are presented as OR(95%CI). All analyses adjusted for age, education, comorbidity, family history, disease stage, surgery type and timing, chemotherapy status, kilocalorie intake, location, and smoking.
Abbreviations: 95%CI = 95% confidence interval; AMBER = Alberta Moving Beyond Breast Cancer; OR = odds ratio; VO_{2peak} = peak oxygen consumption.

3.5. *Independent associations of statistically significant HRF variables with symptoms*

Fig. 1 summarizes the stepwise multivariable adjusted associations between the significant HRFs and the individual and composite symptom scores. In the stepwise model including all statistically significant HRF variables, only relative VO_{2peak} ($p < 0.001$) was independently associated with depression, and it exhibited a threshold association. In the stepwise model for sleep quality, including all significant HRF variables, significant independent associations were identified for relative VO_{2peak} ($p = 0.009$) and body weight ($p = 0.021$). Specifically, relative VO_{2peak} demonstrated a threshold association whereas body weight exhibited an inverted U association

Table 5
Multivariable associations between body composition and number of breast cancer−related symptoms in 1458 newly diagnosed breast cancer patients in the AMBER cohort study (2012−2019).

	Symptom number (any *vs.* 0)	Symptom number (2−3 *vs.* 0−1)
Body weight		
Lowest 25%	1.00	1.0
25%−50%	1.50 (1.11−2.03)	1.30 (0.89−1.90)
50%−75%	1.61 (1.19−2.18)	1.41 (0.97−2.06)
Highest 25%	1.32 (0.97−1.79)	1.55 (1.07−2.24)
p for trend	0.011	0.120
OR per 1 kg	1.01 (1.00−1.01)	1.01 (1.00−1.01)
Body mass index		
<25	1.0	1.0
25−29.9	1.20 (0.93−1.54)	1.12 (0.82−1.53)
30−34.9	1.26 (0.91−1.73)	1.24 (0.85−1.82)
≥35	1.20 (0.82−1.76)	1.68 (1.11−2.55)
p for trend	0.41	0.11
OR per 1 kg/m^2	1.02 (1.00−1.04)	1.03 (1.01−1.06)
Lean mass		
Highest 25%	1.0	1.0
50%−75%	0.95 (0.70−1.29)	0.83 (0.58−1.18)
25%−50%	1.01 (0.74−1.37)	0.90 (0.63−1.29)
Lowest 25%	1.04 (0.77−1.42)	0.91 (0.64−1.31)
p for trend	0.95	0.78
OR per 1 kg	1.00 (0.98−1.02)	1.02 (0.99−1.04)
Fat mass		
Lowest 25%	1.0	1.0
25%−50%	1.63 (1.21−2.21)	1.54 (1.05−2.26)
50%−75%	1.78 (1.31−2.42)	1.66 (1.13−2.44)
Highest 25%	1.63 (1.20−2.23)	1.81 (1.23−2.64)
p for trend	0.001	0.013
OR per 1 kg	1.01 (1.00−1.02)	1.02 (1.01−1.03)
Lean percent		
Highest 25%	1.0	1.0
50%−75%	1.57 (1.16−2.13)	1.43 (0.98−2.11)
25%−50%	1.54 (1.13−2.10)	1.75 (1.20−2.57)
Lowest 25%	1.71 (1.25−2.36)	2.00 (1.36−2.96)
p for trend	0.003	0.003
OR per 1 %	0.97 (0.95−0.99)	0.96 (0.94−0.98)
Body fat percent		
Lowest 25%	1.0	1.0
25%−50%	1.73 (1.27−2.34)	1.60 (1.10−2.34)
50%−75%	1.48 (1.09−2.02)	1.55 (1.05−2.28)
Highest 25%	1.75 (1.28−2.41)	2.10 (1.43−3.09)
p for trend	0.001	0.002
OR per 1 %	1.03 (1.01−1.05)	1.04 (1.02−1.06)
Lean/fat ratio		
Highest 25%	1.0	1.0
50%−75%	1.73 (1.27−2.35)	1.71 (1.17−2.49)
25%−50%	1.46 (1.07−1.98)	1.54 (1.04−2.27)
Lowest 25%	1.75 (1.28−2.41)	2.12 (1.44−3.13)
p for trend	0.001	0.001
OR per 0.1 kg/kg	0.95 (0.93−0.98)	0.94 (0.91−0.97)

Notes: Data are presented as OR(95%CI). All analyses adjusted for age, education, comorbidity, family history, disease stage, surgery type and timing, chemotherapy status, kilocalorie intake, location, and smoking.
Abbreviations: 95%CI = 95% confidence interval; AMBER = Alberta Moving Beyond Breast Cancer; OR = odds ratio.

with poor sleep quality. For fatigue, there were significant independent dose−response associations with relative VO_{2peak} ($p = 0.008$) and relative upper body endurance ($p = 0.001$). For the composite symptom score, only relative VO_{2peak} was significantly independently associated with the number of symptoms reported; however, the association was different depending on the comparison. Specifically, relative VO_{2peak} was significantly independently associated with a higher rate of any *vs.* no symptom in a threshold manner ($p < 0.001$), whereas it was associated with a higher rate of multiple *vs.* single/no symptom in a dose−response manner ($p < 0.001$).

4. Discussion

In the present study, approximately 60% of newly diagnosed breast cancer patients reported at least 1 symptom consisting of poor sleep quality (51.5%), fatigue (26.5%), and/or depression (10.5%). The most prevalent symptom cluster was the combination of poor sleep quality and fatigue (12.2%), while the presence of all 3 symptoms was the second most common symptom cluster (7.3%). These findings are consistent with previous studies, which have reported 38%−65% of breast cancer patients experienced poor sleep quality,[32−34] 24%−25% experienced fatigue,[35,36] and 7%−13.7% experienced depression.[37−39] Many participants in previous studies, however, were breast cancer patients during or after treatment. Our study shows that more than half of newly diagnosed breast cancer patients experience at least 1 key breast cancer−related symptom soon after diagnosis (and surgery). Effectively managing symptoms soon after diagnosis may be crucial given that pre-adjuvant treatment symptoms are significantly associated with post-treatment and long-term symptoms. For example, fatigue experienced before treatment may influence not only post-treatment fatigue levels but also the development of depression during and after treatment.[40]

Among all HRF variables examined, relative VO_{2peak} demonstrated the strongest and most consistent associations with individual symptoms and the number of symptoms. These findings are contrary to previous findings. Padin et al.[10] reported that VO_{2peak} assessed using a cycle ergometer was not correlated with depression in 106 postsurgical breast cancer patients prior to starting adjuvant therapy; however, it was unclear whether absolute or relative aerobic fitness was examined. Winters-Stone et al.[16] reported that a submaximal measure of aerobic fitness (12-min walk) was not associated with fatigue in 47 older long-term breast cancer survivors. In contrast, our study consisted of a direct VO_{2peak} assessment with metabolic measurement and examined absolute and relative VO_{2peak} in almost 1500 newly diagnosed breast cancer patients.

Interestingly, the pattern of associations with relative VO_{2peak} differed by symptom. For depression, sleep quality, and experiencing any symptom, there were threshold associations with relative VO_{2peak}. More specifically, participants who did not attempt/achieve a VO_{2peak} or who had low (20.4 ± 2.3 mL/kg/min) or mid (26.1 ± 1.5 mL/kg/min) were found to be 1.5−3.0 times more likely to experience those symptoms compared to those with the highest level of cardiopulmonary fitness (33.3 ± 4.0 mL/kg/min). The magnitude of the association was much stronger with depressive symptoms (ORs, ~3.0) than for experiencing any symptom (ORs, ~2.0) or

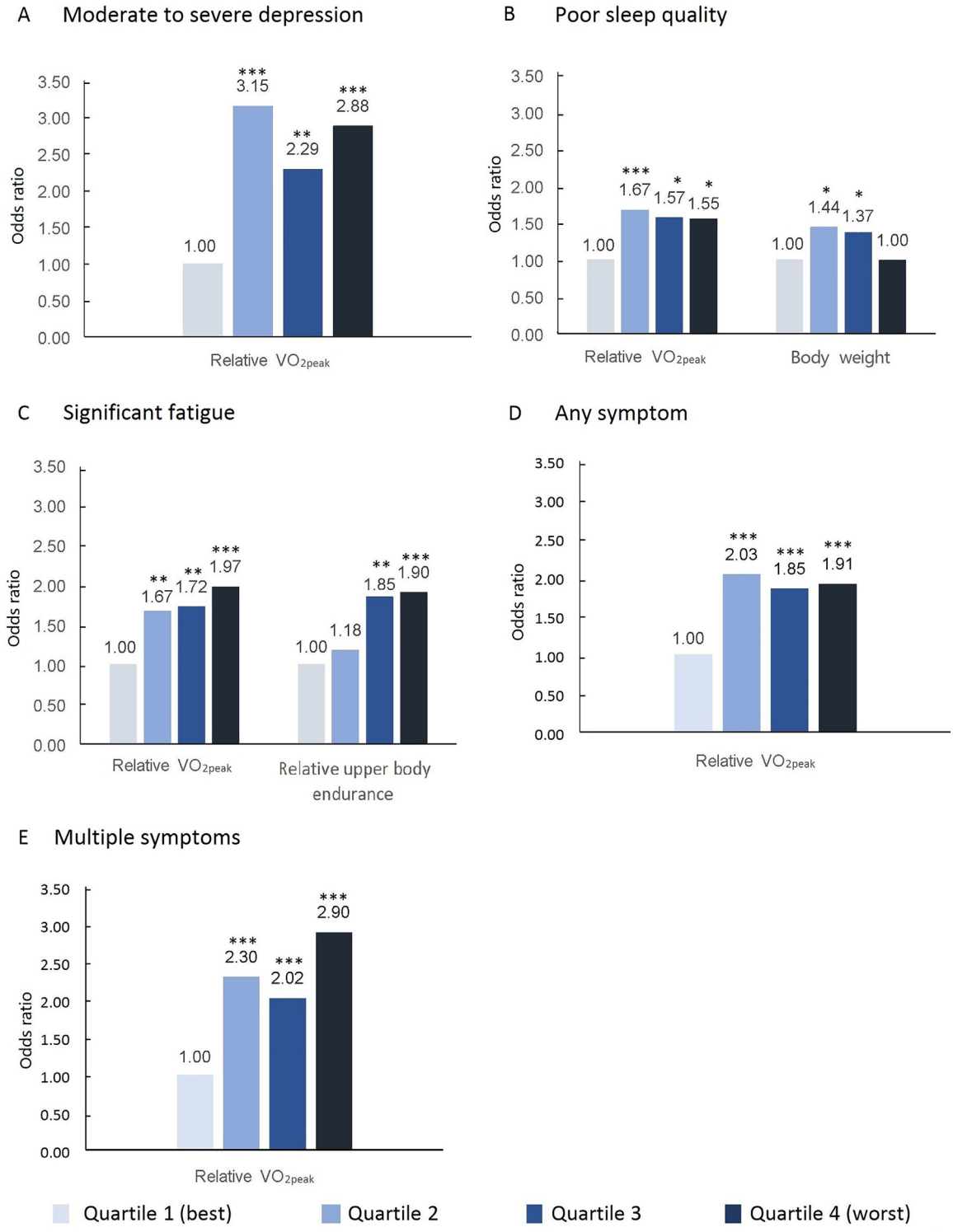

Fig. 1. Independent associations between health-related fitness variables and breast cancer-related symptoms in newly diagnosed breast cancer patients. (A) Moderate/severe depression, (B) poor sleep quality, (C) significant fatigue, (D) any symptom, and (E) multiple symptoms. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, compared with Quartile 1. VO_{2peak} = peak oxygen consumption.

having poor sleep quality (ORs, ~1.5). On the other hand, there were dose–response associations for VO_{2peak} with fatigue and multiple symptoms, although the magnitude of the association was stronger with multiple symptoms (ORs between 2.0 and 3.0) than with fatigue (ORs between 1.7 and 2.0). These findings suggest that an exercise intervention targeting relative cardiopulmonary fitness may help breast cancer patients to effectively manage all 3 symptoms, especially depressive symptoms, and prevent the occurrence of multiple symptoms.

Sleep quality and fatigue exhibited independent associations with other HRF variables in addition to relative VO_{2peak}. Sleep quality was associated with body weight while fatigue was associated with relative upper body endurance. These findings align with previous research, which reported significant relationships of BMI and waist circumference with sleep disturbance and duration[11,15] as well as a relationship between lower body strength and fatigue[16] in breast cancer survivors. These findings highlight the importance of maintaining a healthy body weight as an essential strategy for managing sleep quality; they also suggest that upper body muscular endurance, in addition to cardiopulmonary fitness, may play a crucial role in managing fatigue. Consequently, the optimal exercise prescription for symptom management in newly diagnosed breast cancer patients may vary depending on the specific symptom.

The current study has important strengths and limitations. The strengths include the understudied cancer phase of newly diagnosed breast cancer patients, the large sample size, the comprehensive high quality HRF measurements, validated symptom measures with established clinical cut-points, and the focus on a key symptom cluster. Limitations include the cross-sectional design, the inclusion of some participants who had not had surgery yet (8.2%) or who had initiated adjuvant treatment (17.8%), the substantial number of participants who were unable to complete the maximal fitness tests, the lack of objective measures and/or clinical diagnoses of symptom experience, and the highly correlated HRF variables that may mask important associations with multiple HRF variables.

5. Conclusion

Our large and comprehensive study of HRF and symptoms in newly diagnosed breast cancer patients demonstrates that the majority of patients experience ≥ 1 symptoms of poor sleep quality, fatigue, and depression soon after diagnosis and surgery. Moreover, our study showed that relative VO_{2peak} is the most critical HRF component associated with all 3 individual symptoms as well as the experience of multiple symptoms. Consequently, improving relative cardiopulmonary fitness may be an effective strategy for preventing or managing all 3 symptoms in newly diagnosed patients. These data suggest that vigorous-intensity aerobic exercise or high-intensity interval training, which maximize VO_{2peak} improvements, may be optimal for symptom management compared to light or moderate-intensity exercise such as walking. Furthermore, improving upper body muscular endurance may provide additional benefits for fatigue, suggesting that combined aerobic and resistance exercise programs may be optimal for managing fatigue. Randomized controlled trials are needed to confirm the optimal exercise interventions for symptom management in newly diagnosed breast cancer patients.

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Authors' contributions

KYA and FZA contributed to conceptualization, formal analysis, investigation, and writing (original draft, review and editing); MF, SJA, and SMN contributed to conceptualization, investigation, and writing (original draft, review, and editing); GJB contributed to conceptualization, funding acquisition, investigation, methodology, and writing (review and editing); JM and LY contributed to conceptualization and writing-review and editing; QW contributed to conceptualization, data curation, formal analysis, and writing (review and editing); MLM contributed to conceptualization, funding acquisition, investigation, methodology, project administration, and writing (review and editing); JKV and SNCR contributed to conceptualization, funding acquisition, methodology, and writing (review and editing); LD contributed to conceptualization, investigation, project administration, and writing (review and editing); JRM contributed to conceptualization, funding acquisition, resources, and writing (review and editing); CMF contributed to conceptualization, funding acquisition, methodology, project administration, resources, supervision, and writing (review and editing); KSC contributed to conceptualization, funding acquisition, methodology, project administration, resources, supervision, and writing (original draft, review and editing). All authors read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials associated with this article can be found in the online version at doi:10.1016/j.jshs.2024.04.012.

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