ORIGINAL ARTICLE

An Investigation on Body Composition, Bone Parameters, Physiological Function, Quality of Life, And Cancer-Related Fatigue in Malaysian Breast Cancer Survivors

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ABSTRACT

INTRODUCTION: The aim of the study is to determine the correlation of body composition, bone parameters, physiological functions, with the quality of life (QoL) and cancer-related fatigue (CRF) among Malaysian breast cancer survivors. **MATERIALS AND METHODS:** Eighty-three female breast cancer survivors participated. Assessments of body composition, bone speed of sound (SOS), and T-score. Physiological functions consisted of handgrip strength, shoulder and lower body flexibility, and peak expiratory flow rate (PEFR) were performed on the participants. The Breast Cancer Functional Assessment of Cancer Therapy questionnaire was used for determining their QoL, while the Brief Fatigue Inventory scale questionnaire was used for assessing the CRF.Descriptive statistics and Pearson correlation were performed for statistical analysis. **RESULTS:** The mean T-score value for the right and left radius and tibia of the participants ranged between -1 and -2.5 SD, i.e., under the osteopenia category. There was no significant correlation between the percentage of body fat and fat-free mass with components of QoL and CRF, respectively. In addition, statistically significant positive correlations of bone SOS with components of QoL were not evidenced. A significant negative correlation was found between left handgrip strength and CRF ($r=-0.240$, $p=0.032$). However, no statistically significant correlations were observed between shoulder and lower body flexibility or PEFR with components of QoL and CRF, respectively. **CONCLUSION:** Higher handgrip strength of participants was related to lower CRF. Thus, the aspect of improvement of muscular strength of the arm should be emphasized while designing interventions for rehabilitation among breast cancer survivors.

Keywords
Body composition, bone health, physiological function, cancer-related fatigue, quality of life

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INTRODUCTION

Breast cancer is a major health problem worldwide, including Malaysia, with a rising incidence rate. The incidence rate of breast cancer in Malaysia shows an increasing rate from 34.1 to 38.9 per 100,000 population.[1,2] With the advancement of cancer treatment, breast cancer survivors who had undergone primary cancer treatments are expected to return to their daily life and work at their levels like before the cancer diagnosis.[3] However, it is important to be aware that the treatments received by cancer patients also lead to prolonged side effects and complications that hinder them from returning to their normal daily life. It has been reported that cancer and its treatments lead to physical and psychosocial health problems.[4]

Poor body composition, such as the presence of visceral adipose tissue and skeletal muscle density, are associated with body function, which can affect treatment tolerability

and cancer outcomes.[5] In addition, it has been reported that higher abdominal body fat may be associated with a higher risk of breast cancer recurrence and death.[6]

Breast cancer treatment can have negative effects on bone health.[7] In breast cancer patients, treatment-associated bone loss can be caused by adjuvant endocrine therapy such as aromatase inhibitors (AIs), surgery, or chemotherapy.[8] One of the challenging comorbidities faced by cancer survivors is osteoporosis, which can increase the risk of bone fracture.[9]

Secondary to cancer illness, cancer survivors face changes in physiological functions which negatively affect their quality of life (QoL). It has been reported that cancer survivors may experience physiological side effects such as muscular atrophy, weight changes, reduced aerobic capacity, decreased muscular strength, and flexibility loss.[10]

Cancer-related fatigue (CRF) is one of the major problems among cancer survivors[11], which is described as a distressing, permanent feeling of tiredness or exhaustion related to cancer.[12] It is multifactorial and can be influenced by various demographic, medical, psychosocial, behavioural, and biological factors.[13] Additionally, it is partly induced by cancer treatments such as chemotherapy, radiation, and endocrine therapy, which can be further exacerbated by physically inactive lifestyle.[14]

QoL refers to a person's perception and satisfaction with life and their general appraisal of their level of functional well-being.[15] Given the evolving norms, values, lifestyle, and changing conceptualization of QoL over time, studies on QoL in the breast cancer population are warranted.[16]

Breast cancer survivors are at high risk of developing comorbid conditions such as osteoporosis, sarcopenia, and cardiovascular disease, which lead to a decline in bone health, muscular strength, cardiorespiratory fitness, and QoL.[17] To date, there are limited studies, especially on the association of bone health, QoL and CRF among breast cancer survivors in Malaysia. A previous study showed inconclusive results on CRF due to several factors such as homogeneity of the participants and strict inclusion criteria.[18]

Therefore, the present study was carried out to explore body compositions, bone speed of sound, physiological functions and their correlation with QoL and CRF among breast cancer survivors among Malaysian.

MATERIALS AND METHODS

Study Participants and Experimental Design

This study applied a cross-sectional study design. A total of 83 participants were selected by purposive sampling. The inclusion criteria for the participants were: Malaysian females diagnosed with breast cancer (stage 1-4) more than one year prior to the study and who had completed primary treatment, were between 25 and 70 years old, and possessed normal cognitive function and communication abilities. Those with a history of other types of cancer were excluded.

Participants were recruited from two hospitals and one primary clinic in Malaysia. Data collection procedures were conducted by the researcher at the above-mentioned hospitals and primary clinic. During the visit, participants were required to fill up a basic information form. Brief Fatigue Inventory (BFI) scale questionnaire and Breast Cancer Functional Assessment of Cancer Therapy (FACT-B) questionnaire were answered by the participants to assess their basic information, level of CRF and QoL, respectively. The participants also performed physical tests: 1. Anthropometric and body composition measurements, 2. Bone speed of sound and T-score assessment for bilateral radius and tibia bones of arms and legs, 3. Physiological function tests consisted of a handgrip strength test for both upper limbs, shoulder and lower body flexibility tests, and a peak expiratory flow rate test.

Basic information of the participants

All participants basic information, such as age, ethnicity, category of breast cancer stages and breast cancer affected side were obtained.

Body weight, body height, and body composition measurements

Body height of participants was assessed by using a stadiometer (Seca 220, Hamburg, Germany) and their body weight and body composition, comprised of percent body fat and fat-free mass were measured by using a body composition analyser (Tanita model TBF-140, Japan).

Bone speed of sound (SOS) and T-score assessment

The bone SOS and T-scores of both upper and lower limbs were assessed at the mid-shaft of the tibia and radius using a bone sonometer (Sunlight Mini Omni™, Petah Tikva, Israel) as described in previous studies.[19, 20]

Physiological function assessments

Handgrip strength test

Handgrip strength was assessed using a handgrip dynamometer (Jamar J00105, USA). Participants were instructed to squeeze the dynamometer as forcefully as possible for approximately 5 seconds. Three attempts were conducted for each hand, and the highest value was recorded

Back scratch test for assessing shoulder flexibility

Back scratch test was conducted to reflect the overall shoulder range of motion by measuring the distance between (or overlap of) the middle fingers of both hands as they moved towards each other behind the back. The test was conducted three times for both arms and the final score in centimetres (cm) was calculated as the mean value of the best attempt for both arms.

Sit and reach test for assessing lower body flexibility

The flexibility of participants was tested via the sit and reach test. They were instructed to sit with their feet placed against the sit-and-reach testing box, then reach forward as far as possible by pushing the marker on top of the box. The highest score from three attempts was recorded as the final score.

Peak expiratory flow rate (PEFR) test

A Wright handheld peak flow meter was used to measure the participants' PEFR. The participants were instructed to take a deep breath and blow into the peak flow meter as fast, powerfully, and fully as possible in a single exhalation. This test was repeated three times for each participant, and the highest recorded value was used for analysis.

Quality of life (QoL) assessment

QoL was assessed using the Breast Cancer Functional Assessment of Cancer Therapy (FACT-B) questionnaire. The FACT-B was developed by the Functional Assessment of Chronic Illness Therapy authority (FACIT.org) to measure the QoL of breast cancer survivors. The tool consisted of five sub-dimensions, which are: physical well-being, social/family well-being, emotional well-being, functional well-being, and a subscale on additional concerns for breast cancer survivors. A higher score indicates a better QoL.

Cancer-related fatigue (CRF) assessment

The Brief Fatigue Inventory (BFI) scale questionnaire was used to determine the CRF levels among the participants in this study.[21] The validity and reliability of BFI has been established with internal consistency reported at 0.96.[22] The higher score of CRF obtained from the BFI scale questionnaire reflects higher severity of the CRF.

Data Analysis

Statistical Package for Social Science (SPSS) version 24.0 was used for the statistical analysis. Data are presented in percentage (%) and mean (standard deviation) (SD). Correlation analysis was conducted to evaluate the magnitude and direction of the relationship between the variables by using Pearson correlation. A 'p' value of <0.05 was considered statistically significant.

RESULTS

Basic information of the participants

A total of 83 breast cancer survivors diagnosed with either of cancer stages 1, 2, 3, or 4 completed this study. The age of the participants ranged from 35 to 72 years, with a mean of 52.8 (8.7) years. Participants consisted of

90.4% (n=75) Malays, 7.2% (n=6) Chinese, and 2.4% (n=2) Indians. It was found that 39.8% (n=33) of participants were diagnosed with breast cancer stage 2, followed by 34.9% (n=29) with stage 3, 15.7% (n=13) with stage 1, and 9.6% (n=8) diagnosed with stage 4. A total of 60.2% (n=50) participants had breast cancer on the left side of the breast, 36.2% (n=30) on the right side of the breast, whereas 3.6% (n=3) were affected on both breasts.

Body composition, bone speed of sound, physiological functions, components of quality of life (QoL) and cancer-related fatigue (CRF) of the participants

Table I shows the results of body composition, i.e., percentage of body fat and fat-free mass, bone speed of sound, bone T score value, and physiological functions. It was found that the mean bone T-scores of the participants were ranged between -1 and -2.5 SD, i.e., under the osteopenia category. It was also found that the mean total score of QoL was 110.44 (2.68). The mean subscale total scores of physical, social, emotional, functional well-being, and additional concerns were 20.55 (0.83), 23.84 (0.68), 18.15 (0.67), 23.2 (0.67), and 25.11 (0.79), respectively. The mean CRF score was 3.20(2.69).

Table I: Body composition, bone speed of sound, bone T scores, and physiological functions of breast cancer survivors in Malaysia.

Variables		Mean (SD)
Body height (cm)		154.0 (0.68)
Body weight (kg)		67.2 (1.61)
Body Mass Index (kg/m²)		28.15 (0.62)
Body composition:		
Percent of Body Fat (%)		39.8. (0.75)
Fat Free Mass (kg)		37.2 (0.48)
Bone Parameters:		
Bone Speed of Sound (m/s) :	Right radius bone	3750.7 (975.8)
	Left radius bone	3750.0(960.5)
	Right tibia bone	3768.2 (163.5)
	Left tibia bone	3720.5 (309.1)
Bone T score value	Right radius bone	-1.84 (1.56)
	Left radius bone	-1.80 (1.95)
	Right tibia bone	-1.98 (1.48)
	Left tibia bone	-1.82 (1.75)
Physiological Functions:		
Handgrip strength (kg)		
Right side		26.25 (5.11)
Left side		24.71 (5.05)
Shoulder flexibility (cm)		
Right side		7.02 (7.32)
Left side		13.47(9.90)
Lower body flexibility (cm)		29.12 (6.70)
Pulmonary function, PEFR (L/min)		350.36 (74.5)

Abbreviations:
PEFR: Peak expiratory flow rate which indicates pulmonary function Note: A lower value obtained from the back scratch test indicates higher shoulder flexibility

Correlations of body weight, percentage of body fat, fat-free mass, and bone speed of sound (SOS) with quality of life (QoL) and cancer-related fatigue (CRF)

As presented in Table II, there was no significant correlation between percentage of body fat, fat-free mass, with total QoL score and CRF score, respectively. There were also no statistically significant positive correlations of bone SOS of right and left arms and legs with components of QoL of the participants. Meanwhile, statistically significant negative correlation of all the bone SOS values with CRF was also not observed.

Table II Correlation of body weight, percentage of body fat, fat-free mass, and bone speed of sound with QoL and CRF (B)

Variables	Total QoL score				CRF Score		
Body weight	r=0.046 p=0.68				r=0.107 p=0.33		
Percent body fat	r=0.110 p=0.33				r=-0.02 p=0.881		
Fat free mass	r=-0.017 p=0.88				r=0.077 p=0.49		
	Components of QoL						CRF score
	Physical wellbeing	Social wellbeing	Emotional wellbeing	Functional wellbeing	BCS	Total QOL score	
Bone SOS							
R arm	r=-0.199 p=0.101	r=0.051 p=0.679	r=-0.331** p=0.005	r=-0.101 p=0.409	r=-0.107 p=0.381	r=-0.189 p=0.120	r=0.083 p=0.496
L arm	r=-0.026 p=0.847	r=0.080 p=0.542	r=-0.235 p=0.071	r=-0.066 p=0.617	r=-0.061 p=0.642	r=-0.090 p=0.493	r=-0.084 p=0.522
R leg	r=-0.140 p=0.229	r=0.058 p=0.616	r=-0.064 p=0.582	r=-0.196 p=0.091	r=-0.092 p=0.427	r=-0.135 p=0.244	r=0.137 p=0.238
L leg	r=-0.139 p=0.236	r=0.157 p=0.178	r=-0.099 p=0.398	r=-0.195 p=0.094	r=-0.122 p=0.298	r=-0.126 p=0.282	r=0.105 p=0.371

Abbreviations:
Bone SOS; Bone speed of sound, R arm: Right arm, L arm: Left am, R leg: Right leg, L leg: Left leg, BCS: Additional concern for breast cancer survivors; QoL: Quality of life; CRF: cancer-related fatigue
*Pearson correlations (r) were performed to explore the correlation between measured parameters. P<0.05 was considered as statistically significant. Bold numbers and ** indicate statistically significant at p<0.001.*

Correlations of handgrip strength with quality of life (QoL) and cancer-related fatigue (CRF)

As shown in Figure 1, there was a significant negative correlation between the handgrip strength of the left hand and CRF score (r=-0.240, p=0.032). As shown in Table III, statistically significant positive correlations between right-handgrip strength and left handgrip strength with components of QoL were not evidenced.

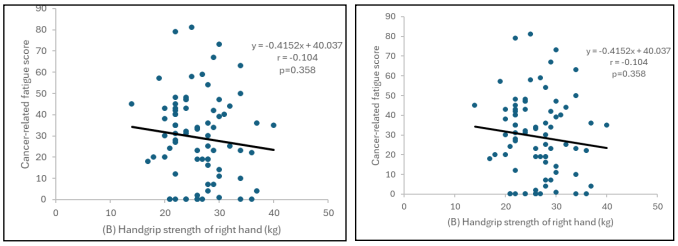

Figure 1: Correlations of handgrip strength (A) of left hand and (B) right hand with cancer -related fatigue

Table III Correlation matrix of handgrip strength with QoL

Variables	Components of QoL					
	Physical wellbeing	Social wellbeing	Emotional wellbeing	Functional wellbeing	BCS	Total QoL score
Right handgrip strength (kg)	r=-0.107 p=0.346	r=0.107 p=0.344	r=-0.234* p=0.037	r=0.063 p=0.582	r=-0.062 p=0.582	r=-0.103 p=0.365
Left handgrip strength (kg)	r=-0.110 p=0.331	r=0.093 p=0.413	r=-0.132 p=0.243	r=0.077 p=0.500	r=-0.108 p=0.339	r=-0.093 p=0.409

Abbreviations:
BCS: additional concern for breast cancer survivors; QoL: Quality of life

Correlation of shoulder and lower body flexibility and peak expiratory flow rate (PEFR) with quality of life (QoL) and cancer-related fatigue (CRF)

The correlations of right and left shoulder flexibility, lower body flexibility, and pulmonary function reflected by PEFR values with components of QoL and CRF are shown in **Table IV**. Results showed that there were no statistically significant correlations of the above-mentioned physiological function parameters with QoL and CRF.

Table IV: Correlations of shoulder and lower body flexibility and pulmonary function with QoL and CRF

Variables	Components of QoL,						CRF score
	Physical wellbeing	Social wellbeing	Emotional wellbeing	Functional wellbeing	BCS	Total QoL score	
R Sh flexibility (cm)	r=0.195 p=0.108	r=-0.038 p=0.758	r=0.136 p=0.266	r=0.092 p=0.450	r=0.131 p=0.282	r=0.159 p=0.191	r=-0.115 p=0.345
L Sh flexibility (cm)	r=0.114 p=0.360	r=0.086 p=0.491	r=0.230 p=0.061	r=0.142 p=0.252	r=0.013 p=0.915	r=0.163 p=0.188	r=0.003 p=0.983
SRT	r=-0.029 p=0.795	r=0.061 p=0.586	r=-0.074 p=0.507	r=-0.087 p=0.433	r=-0.153 p=0.167	r=-0.137 p=0.218	r=-0.029 p=0.795
PEFR (L/min)	r=-0.154 p=0.182	r=-0.060 p=0.606	r=-0.173 p=0.133	r=0.088 p=0.447	r=-0.140 p=0.224	r=-0.142 p=0.217	r=0.100 p=0.389

Abbreviations:
R Sh flexibility: Right shoulder flexibility; L Sh flexibility: Left shoulder flexibility; SRT: Lower body flexibility; PEFR: Peak expiratory flow rate indicates the pulmonary function; BCS: Additional concern for breast cancer survivors; QoL: Quality of life

DISCUSSION

Breast cancer patients experience weight gain and changes in body composition during and after breast cancer treatment. This weight gain occurs due to several factors, including side effects of treatment, hormonal changes, as well as a reduction in physical activity.[23] Higher abdominal body fat may be associated with a higher risk of breast cancer recurrence and death.[24] The average percentage of body fat of the participants in this study was 39.8% (0.75), and fat-free mass was 37.2 (0.48) kg. The BMI and body composition data indicate that the participants in the study are generally overweight, with high body fat percentage and substantial fat-free mass. A recent JAMA study reported that obesity was associated with an increased risk of breast cancer recurrence among postmenopausal patients with HR+ early-stage breast cancer treated with aromatase inhibitors.[25]

The present study shows that there was no significant correlation between the percentage of body fat and fat-free mass with CRF and QoL, respectively. These findings are inconsistent with a study that reported that higher fat mass and lower muscle mass were associated with worse CRF, and physical domain of QoL.[26] Thus, we would like to speculate that the discrepancy between the findings of these previous studies and the present study could be due to differences in the general physical conditions of the breast cancer survivors, variability in clinical characteristics of the breast cancer, age, and stages of cancer.

Regarding bone health and cancer treatments, previous studies found that cancer treatment, such as chemotherapy, can negatively affect bone health and lead to osteoporosis, and hence affecting their physical activity and increasing the level of fatigue.[27,28] The bone health status of the participants identified in this study was categorised under the osteopenia category. This finding implies that breast cancer survivors are at the borderline of osteoporosis and may have a risk of having osteoporosis in the future. Unexpectedly, the current finding indicates that there was no statistically significant positive correlation between bone SOS and components of QoL. In addition, a statistically significant negative linear correlation between bone SOS and CRF was also not evidenced. To date, there is a lack of studies on the relationship between bone health status, QoL, and CRF. Therefore, direct comparison could not be performed.

Regarding muscular strength, the present study found that the right handgrip strength of the participants was higher, with 26.25(5.11) kg compared to the left side, with 24.71(5.05) kg. This finding was supported by the fact that majority of the participants were diagnosed with breast cancer at the left side of breast (60.2%) compared to right side of breast (36.2%), hence, it is not surprising to observe higher handgrip strength at the right side compared to the left side. Besides, 92.8% of the participants were right-handed compared only 7.2% who were left-handed; this may contribute to the fact that the right hand is stronger compared to the left hand among the participants. In contrast to a study conducted in Malaysia[29] with findings on handgrip strength among breast cancer patients was very much lower, i.e., 9.60 (4.89) kg compared to the findings of the present study. This indicates good handgrip strength with reference to 27.6(6.58) kg as reported in a previous study[30]. In this study, we found a weak negative linear correlation between right handgrip strength and emotional well-being among breast cancer survivors. One possible explanation could be that breast cancer survivors with stronger physical capabilities may have higher expectations for their recovery. Unmet expectations could lead to emotional distress.

The most notable finding in the present study is that there was a significant negative relationship between left handgrip strength and CRF score (r=-0.240, p=0.032), which reflects that higher muscular strength of the upper limb could be related to lower level of CRF **(**Figure 1A). Previous study reported that higher CRF was linked to reduced physical function including the handgrip strength[31]. In addition, it was also reported that higher handgrip strength was associated with better cognitive function, indicating a potential inverse relationship between muscular strength and CRF, as cognitive function can be a component of overall fitness.[32] Nevertheless, another study found that CRF levels were not significantly related to muscular strength or fatigability, suggesting that cancer patients can benefit from following standard exercise guidelines regardless of their self-reported fatigue levels.[33]

Shoulder muscle activity is significantly affected by breast cancer surgery through altered muscle activation patterns due to muscular inactivity and muscle tightness, and different surgical techniques, such as axillary surgery, which leads to muscle dysfunction.[34] The alterations in muscular activity lead to functional impairments such as pain, weakness, and limitation in range of motion, impacting daily activity and overall QoL of the breast cancer survivors.

The normal value for shoulder flexibility measured via the back scratch test, regardless of right and left side and age, is −2.3 (8.5) cm in the healthy female population.[35] The present study observed that there was low shoulder flexibility on both sides compared to the healthy female population. Comparison between right and left side shoulder flexibility of the participants in this study showed that the participants had higher shoulder flexibility at the right side compared to the left side. This finding is also supported by the fact that the majority of the participants' affected side was on the left side of the breasts compared to the right side. The current study also found that participants exhibited good lower body flexibility, with a mean score of 29.12 cm (SD = 6.70), compared to the healthy population, where a score of 24.3 cm (SD=13.2) is considered indicative of good lower body flexibility.[35]

PEFR is the reflection of the functioning of the larger airways, and the normative value of PEFR for females was reported as 320-470 L/min in adults.[36] The mean PEFR value of the participants in this study was 350.36 (74.5) L/min, which can be categorised as normal pulmonary function. Conventional radiotherapy causes a restrictive pattern of the lungs, causing inability to fully expand hence resulting in an abnormal pattern of breathing which can impact the pulmonary function.[37]

The present study showed that there were no significant correlations between shoulder and lower body flexibility and pulmonary function with QoL and CRF, respectively. This might be due to the participants of this study were relatively healthy breast cancer survivors, with minimal physical impairment. As a result, the variability in

flexibility and pulmonary function may not have been substantial enough to demonstrate a significant association with QoL and CRF.

CONCLUSION

Bone health status of the participants in this study is categorized as osteopenia. It was also evidenced that body composition, flexibility, and pulmonary function showed no significant correlations with QoL nor CRF in breast cancer survivors of this study. Notably, there was a significant negative relationship between the handgrip strength of the left hand and CRF among the participants, implying that higher handgrip strength was linked to lower fatigue levels. These findings have practical implications, as they may assist healthcare providers and breast cancer survivors in addressing the importance of bone health, and the relationship between muscular strength with CRF. Furthermore, it is hoped that this study provides evidence-based insights that may strengthen the theoretical framework for cancer rehabilitation in Malaysia.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

INSTITUTIONAL REVIEW BOARD (ETHIC COMMITTEE)

This study was approved by Human Research Ethics Committee of Universiti Sains Malaysia (USM) (JEPeM code: USM/JEPeM/20040233) and Medical Research and Ethics Committee (MREC) of Malaysia Ministry of Health (NMRR ID: NMRR ID-21-02047-QRK(IRR).

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