



Differences in the Relationships Between Muscle Strength, Muscle Mass, Balance Function, and Quality of Life for Middle-Aged and Older Breast Cancer Survivors

Integrative Cancer Therapies
Volume 21: 1–11
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/15347354221138574
journals.sagepub.com/home/ict


Shinichiro Morishita, PhD¹ , Ryuichi Kasahara, MSc², Yuichi Yamamoto, BSc², Ryohei Jinbo, BSc², Aya Takano, BSc², Mitsuhiko Yasuda, MD², Atsuhiko Tsubaki, PhD³, Osamu Aoki, PhD⁴, Jack B. Fu, MD⁵, and Tetsuya Tsuji, MD⁶

Abstract

Purpose: The purpose of this study was to investigate the differences in muscle strength, muscle mass, balance function, and quality of life (QOL) among middle-aged breast cancer survivors (BCSs) and older BCSs. **Methods:** The study included 53 middle-aged (<65 years old) BCSs and 49 older (≥65 years old) BCSs. Muscle strength was evaluated via handgrip and knee extensor strength, and muscle mass was assessed using a body composition test. Balance function was assessed using the Timed Up and Go test and the body sway test. QOL was assessed using the Medical Outcome Study 36-item Short-Form Health Survey. **Results:** The older BCSs had significantly lower right grip strength, right knee extension strength, and muscle mass ($P < .05$) than the middle-aged BCSs. In addition, the body sway test showed that older BCSs had a significant increase in the length of center of pressure compared to middle-aged BCSs ($P < .05$). Older BCSs showed significantly lower physical functioning subscales in QOL compared to middle-aged BCSs ($P < .05$). The associations among muscle strength, muscle mass and QOL were more significantly observed in the older BCSs ($P < .05$). Furthermore, a significant correlation between QOL and balance function was observed in the older BCSs, but not in the middle-aged BCSs ($P < .05$). **Conclusion:** There may be associations among muscle strength, muscle mass, balance and QOL in older BCSs, but not in middle-aged BCSs. We believe that the findings of this study will be relevant in the context of planning rehabilitation for older BCSs.

Keywords

breast cancer survivors, older, muscle strength, muscle mass, balance function, QOL

Submitted June 26, 2022; revised October 11, 2022; accepted October 27, 2022

Introduction

The number of older cancer survivors is continuing to rise due to population growth and aging, as well as advances in early detection and treatment.¹ Cancer survivors may experience musculoskeletal problems. Breast cancer survivors (BCSs) after completing cancer treatment have been reported to exhibit lower muscle strength (20%-30% loss) in 7 types of upper body muscle strength, compared to healthy controls.² It has also been reported that older cancer patients have more muscle weakness, and that this weakness is associated with overall survival.³ Another study reported that 75 of 471 BCSs had sarcopenia with muscle atrophy.⁴ They also reported that the percentage of BCSs in the sarcopenia group aged over 50 years was significantly

higher than that of the group under 50 years of age.⁴ Muscle weakness is a common problem in BCSs and is reported to be caused by abnormal protein metabolic turnover balance

¹Fukushima Medical University, Fukushima, Japan

²Kita-Fukushima Medical Center, Fukushima, Japan

³Niigata University of Health and Welfare, Niigata, Japan

⁴Shijonawate Gakuen University, Osaka, Japan

⁵University of Texas MD Anderson Cancer Center, Houston, TX, USA

⁶Keio University School of Medicine, Tokyo, Japan

Corresponding Author:

Shinichiro Morishita, Department of Physical Therapy, School of Health Sciences, Fukushima Medical University, 10-6 Sakaemachi, Fukushima City 960-8516, Japan.

Email: ptmorishin@yahoo.co.jp



and mitochondrial changes after chemotherapy.⁵ It has also been reported to negatively affect quality of life (QOL).⁵ In addition, BCSs may have poorer balance function compared to healthy individuals of the same age. BCSs also performed worse than non-BCSs in difficult balance exercises, such as reduced sensory information and altered support bases.⁶

In terms of QOL, BCSs were comparable in general health and overall QOL when compared to healthy participants of the same age. BCSs reported significantly more limitations on most functional and symptom measures at long-term follow-up.⁷ Disability on various QOL subscales (eg, physical and social functioning, pain, economic hardship) worsened from year 5 to year 10. Moreover, young BCSs have more the degree of limitation compared to age-matched people without a history of cancer.⁷ BCSs may have worse muscle strength, muscle mass, and balance function compared to healthy controls. In addition, QOL may tend to be lower as well.

Previous studies have examined age-segmented characteristics of BCSs. BCSs diagnosed at older ages (>65) reported significantly worse QOL in the physical domain than the other age groups, and BCSs diagnosed at younger ages (27-44) reported worse QOL in the social domain than the middle age (45-65) and older age (>65) groups.⁸ In patients with type 2 diabetes mellitus, older (aged ≥ 65 years) patients reported lower physical component summary scores of QOL than younger (aged <65 years).⁹ As described above, older BCSs may have decreased muscle strength and muscle mass, and decreased balance function compared to middle-aged BCSs. QOL may also be reduced in older BCSs. Physical function and QOL are closely related in cancer survivors; poor physical function leads to poor QOL.¹⁰ Therefore, muscle strength, muscle mass, and balance function are likely to be related to QOL in BCSs, but this is not yet clearly understood.

The purpose of this study was to investigate the differences in muscle strength, muscle mass, balance function, and QOL among middle-aged BCSs and older BCSs.

Methods

Study Design

This study was a prospective, observational investigation of muscle strength, body composition, balance function, and QOL among middle-aged BCSs aged under 65 years and older BCSs aged over 65 years. Conventionally, “elderly” has been defined as a chronological age of 65 years old or older¹¹; according to a cancer elderly definition, elder was more than 65 years of age, and thus have been defined in the same way.¹² Therefore, the BCSs in the present study were divided into middle-aged (<65 years old) and older (≥ 65 years old) groups at age 65.

Participants and Methods

BCSs were recruited in Kita-Fukushima Medical Center BCSs meetings in November 2018, June 2019, and November 2019 using a poster describing the study aim regarding muscle strength, body composition, balance function, and QOL. BCSs aged ≥ 18 years with an Eastern Cooperative Oncology Group Performance Status Score of 0 or 1 were enrolled.¹³ Finally, 53 middle aged (<65 years old) BCSs and 49 older (≥ 65 years old) BCSs were included in the study (Table 1). The BCSs each participated in one assessment session in our study. The mean ages were significantly different: 55.6 years (\pm SD 6.8) for the middle-aged BCSs and 71.8 years (\pm SD 4.9) for the older BCSs ($P < .05$) (Table 1). Similarly, height and weight were significantly higher in the middle-aged BCSs than in the older BCSs. No significant difference was observed regarding body mass index (BMI), affected side, type of breast cancer, mastectomy, lymph node removal, pathologic stage, chemotherapy, hormonal therapy, or time from breast cancer surgery (Table 1). Middle-aged BCSs were found to have undergone significantly more radiation therapy than older BCSs ($P < .05$) (Table 1).

Ethical Approval Statement

The Kita-Fukushima Medical Center Institutional Committee on Human Research approved the study, and written informed consent was obtained from each participant (Approval No. 72).

Muscle Strength

Handgrip strength. Handgrip strength (kilogram of force [kgf]) was measured as an index for upper limb strength using a digital dynamometer (TKK5101; TAKEI Scientific Instruments Co. Ltd., Niigata, Japan) that measures between 5.0 and 100.0 kgf with a precision of 0.1 kg. The dynamometer was adjusted to each participant’s hand size. During the assessment, the participants were instructed to stand upright with their feet shoulder-width apart and to look forward, with their elbows fully extended. The dynamometer was held in the testing hand with the grip meter indicator facing outward and away from any part of the body. The participants performed 2 trials for each hand alternatively, always starting with their dominant hand. The participants were instructed to squeeze the grip with full force continuously for at least 2 seconds.^{14,15} The maximum handgrip strength for each hand was recorded as “Handgrip strength,” and was measured bilaterally.

Knee-extensor muscle strength. Knee-extensor muscle strength (kgf) was measured as an index for lower limb strength using a hand-held dynamometer (μ -TAS F1; Anima, Tokyo, Japan). For all measurements, a stabilizing belt was used to aid the tester in applying resistance. Knee extension force was tested

Table 1. Clinical and Demographic Characteristics Between Middle-Aged and Older Breast Cancer Survivors.

Characteristics	Middle-aged breast cancer survivors (n=53)	Older breast cancer survivors (n=49)	P-value
Age, years	55.6 ± 6.8	71.8 ± 4.9	<.001
Height, cm	158.0 ± 5.3	153.2 ± 7.2	<.001
Body weight, kg	58.4 ± 8.7	53.8 ± 8.3	.008
BMI	23.3 ± 2.9	22.9 ± 3.4	.52
Affected side			
Right	28 (52.8)	26 (53.1)	.981
Left	25 (47.2)	23 (46.9)	
Types of breast cancer			
Invasive	39 (73.6)	43 (87.8)	.072
Non-invasive	14 (26.4)	6 (12.2)	
Surgical procedure			
Mastectomy	12 (22.6)	19 (38.8)	.077
Breast conserving surgery	41 (77.4)	30 (61.2)	
Lymph node removed			
Without removed	1 (1.9)	1 (2.0)	.776
Axillary lymph node dissection	16 (30.2)	18 (36.7)	
Sentinel lymph node biopsy	36 (67.9)	30 (61.2)	
Pathologic stage			
0	7 (13.2)	2 (4.1)	.317
I	24 (45.3)	19 (38.8)	
II	14 (26.4)	17 (34.7)	
III	8 (15.1)	10 (20.4)	
IV	0 (0)	1 (2.0)	
Adjuvant therapy			
Chemotherapy			
Yes	30 (56.6)	28 (57.1)	.956
No	23 (43.4)	21 (42.9)	
Radiation therapy			
Yes	41 (77.4)	26 (53.1)	.01
No	12 (22.6)	23 (46.9)	
Hormonal therapy			
Yes	39 (73.6)	39 (79.6)	.475
No	14 (26.4)	10 (20.4)	
Time from breast cancer surgery	1507.6 ± 1500.2	2058.1 ± 1812.8	.1

Values are presented as means ± standard deviations or numbers and percentages. Statistical testing at baseline was performed using independent Student's *t*-tests or Pearson's χ^2 tests.

with participants sitting with their knee flexed at approximately 60°. The dynamometer was applied to the anterior surface of the tibia, proximal to the malleoli. The maximum force exerted during 10 seconds of static effort was recorded.

Handgrip strength and knee-extensor muscle strength were normalized according to body weight, and these measurements were expressed as a percentage of each patient's body weight.

Body composition. Fat free mass and skeletal muscle mass were measured by bioelectrical impedance analysis (BIA) using InBody S10 (InBody Co. Ltd, Seoul, Korea). After height and weight were measured, 4 electrodes were attached, one each to both the upper and lower extremities

with the participant in the supine position. Skeletal muscle index (SMI) was calculated by dividing the appendicular muscle mass by squared height in meters.¹⁶ Based on the resistance and reactance obtained when measuring muscle mass with the InBody S10, the phase angle (PhA) was calculated using the following formula: PhA (°) = arctangent (Xc/R) * (180/π). Reactance and resistance values measured at a current of 50 kHz were used to calculate the PhA.¹⁷

Balance function

Timed up and go (TUG) test. The TUG test is a reliable and widely-accepted test for quantifying functional mobility.¹⁸ We instructed the participants to "Stand up, walk as quickly

and safely as possible.”¹⁹ The time taken to complete the test was recorded. Participants performed the TUG test twice, and the faster of the 2 measurements was used for analysis.

Body sway testing. Body sway was measured using a gravicorder force platform (GS-10, Anima Inc, Tokyo, Japan) to investigate postural stability among the participants. The participants stood on both feet in the Romberg stance for 30 seconds while looking at a 3-cm-diameter round mark, placed 2 m away, at eye level. The center of pressure (CoP), as the index for postural stability, was measured once using the gravicorder at a 20-Hz sampling rate, which was in accordance with Japanese Industrial Standards (JIS). The data was filtered with 10-Hz low pass filtering by an analog amplifier. Tasks were performed with eyes both opened and closed. The total CoP length (cm), environmental CoP area (cm²), and rectangle CoP area (cm²) were calculated as parameters of conventional stationary analysis.

Health-related QOL. General health-related QOL was assessed using the Medical Outcome Study 36-item Short-Form Health Survey (SF-36), which assesses physical and mental health components across the following 8 domains: physical functioning (PF), physical role function (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), emotional role functioning (RE), and mental health (MH). The SF-36 measures multidimensional properties of health-related QOL on a 0 to 100 scale, with higher scores indicating better QOL. This self-administered questionnaire is widely used, particularly among cancer survivors.²⁰

Statistical Analysis

The results are presented as means \pm standard deviations (SDs). We compared demographic and clinical characteristics between middle and older BCSs using Student's *t*-tests for continuous variables and Pearson's chi-squared tests for ordinal variables. Two-tailed unpaired *t*-tests (continuous) were used to compare handgrip and knee extensor muscle strength, body composition, balance function, and QOL between the 2 BCSs groups. Pearson's correlation coefficients were used to evaluate the associations among muscle strength, body composition, balance function, and QOL. Statistical analysis was performed using SPSS 25 (SPSS Japan Inc., Tokyo, Japan). *P*-values of $<.05$ were considered statistically significant.

Results

Table 2 shows the mean values for muscle strength, body composition, and balance function for all participants. Right hand grip strength and right knee strength were significantly

decreased in the older BCSs compared with the middle-aged BCSs ($P < .05$). However, left grip strength and left knee strength were not significantly different between the 2 groups. Body composition, fat free mass, skeletal muscle mass, PhA, SMI were significantly lower in the older BCSs than in the middle-aged BCSs ($P < .05$). In balance function, only the length of COP with eyes open was significantly longer in the older BCSs compared to the middle-aged BCSs ($P < .05$). However, there were not significant differences regarding TUG or other body sway parameters between middle-aged and older BCSs.

Table 3 shows the mean SF-36 values for both groups. PF was significantly lower in the older BCSs. No significant differences were found in other subscales of QOL between the 2 groups.

Table 4 presents the correlation coefficients between muscle strength, body composition, and QOL in the middle-aged and older BCSs. In the middle-aged BCSs, a correlation was not found between the muscle strength and QOL subscales. The PhA was found to be significantly negatively related to SF ($P < .05$). In the older BCSs, right handgrip was significantly positively related to PF, RP, BP, SF, and RE ($P < .05$). Left handgrip was significantly positively related to PF, BP, and SF ($P < .05$). Right knee extension was significantly positively related to PF, RP, BP, GH, and RE ($P < .05$). Right knee extension was significantly positively related to BP ($P < .05$). The fat free mass was significantly positively related to VT ($P < .05$). Skeletal muscle mass was significantly positively related to RP, VT, and RE ($P < .05$), and the PhA was significantly positively related to PF, RP, VT, and RE ($P < .05$).

Table 5 presents the correlation coefficients between balance function and QOL in the middle-aged BCSs and older BCSs. The middle-aged BCSs indicated that TUG was significantly positively related to BP ($P < .05$). There was no significant correlation between other balance function tests and QOL in middle-aged BCSs. In older BCSs, TUG was significantly negatively related to PF, RP, BP, GH, VT, and RE ($P < .05$). The environmental CoP area (cm²) and rectangle CoP area (cm²) with eyes open were significantly negatively related to VT, and SF ($P < .05$). The environmental CoP area (cm²) and rectangle CoP area (cm²) with eyes closed were significantly negatively related to VT ($P < .05$).

Discussion

The present study showed that older BCSs had significantly lower right grip strength, right knee extension strength, fat free mass, skeletal muscle mass, PhA, and SMI than middle-aged BCSs. In addition, the body sway test showed that the older BCSs had a significantly increased length of COP compared to the middle-aged BCSs, and showed significantly lower PF subscales in QOL. The associations among

Table 2. Differences in Muscle Strength, Body Composition and Balance Function Between Middle-Aged and Older Breast Cancer Survivors.

Variables	Middle-aged breast cancer survivors (n=53)	Older breast cancer survivors (n=49)	P-value
Muscle strength			
Right hand grip (kgf/BW)	0.42 ± 0.08	0.38 ± 0.08	.022
Left hand grip (kgf/BW)	0.39 ± 0.08	0.36 ± 0.08	.069
Right knee extensor (kgf/BW)	0.52 ± 0.13	0.47 ± 0.12	.032
Left knee extensor (kgf/BW)	0.48 ± 0.13	0.44 ± 0.13	.123
Body composition			
Fat free mass	40.5 ± 4.2	37.2 ± 4.5	<.001
Skeletal muscle mass	21.6 ± 2.4	19.6 ± 2.7	<.001
Phase angle	5.0 ± 0.5	4.6 ± 0.5	<.001
Skeletal muscle mass index	6.5 ± 0.5	6.2 ± 0.8	.021
Balance function			
Timed up and go test (s)	6.6 ± 1.5	7.3 ± 2.3	.064
Eyes open condition			
Length of CoP (cm)	51.0 ± 20.2	60.8 ± 24.8	.029
Environmental area of CoP (cm ²)	2.9 ± 2.9	2.9 ± 2.3	.988
Rectangle area of CoP (cm ²)	10.3 ± 10.8	9.6 ± 8.7	.700
Eyes closed condition			
Length of CoP (cm)	79.2 ± 47.7	86.0 ± 36.1	.422
Environmental area of CoP (cm ²)	6.4 ± 15.8	4.9 ± 4.8	.526
Rectangle area of CoP (cm ²)	21.9 ± 65.5	15.4 ± 14.5	.501

Values are presented as mean ± SD unless. Statistical testing was performed using unpaired t-test. Abbreviations: BW, body weight; CoP, center of pressure.

Table 3. Differences in Health Related QOL Between Middle-Aged and Older Breast Cancer Survivors.

Variables	Middle-aged breast cancer survivors (n=53)	Older breast cancer survivors (n=49)	P-value
Physical functioning	85.2 ± 12.7	74.4 ± 20.4	.002
Role-physical	79.7 ± 21.9	74.5 ± 24.6	.259
Bodily pain	64.9 ± 20.9	70.1 ± 25.6	.263
General health	54.2 ± 13.7	54.7 ± 17.1	.874
Vitality	58.5 ± 18.4	61.1 ± 20.0	.503
Social functioning	85.4 ± 19.6	76.5 ± 27.3	.065
Role-emotional	78.5 ± 23.4	79.3 ± 22.8	.863
Mental health	69.6 ± 17.1	68.0 ± 19.1	.644

Values are presented as mean ± SD unless. Statistical testing was performed using unpaired t-test. Abbreviations: QOL=quality of life.

muscle strength, body composition, and QOL were more frequently observed in older BCSs than in middle-aged BCSs. Furthermore, we examined the relationship between the balance function and QOL, and we found a correlation between QOL and balance function more frequently in older BCSs than in middle-aged BCSs.

A previous study reported that the grip strength of older adults with an average age of 69.5 years was significantly lower than that of a group of younger adults with an average age of 23.3 years.²¹ Similarly, in a study measuring grip

strength in Japanese people, the grip strength of older women, with an average age of 72.9 years, was 22.7 kg, while that of the younger group, with an average age of 20.9 years, was 32.9 kg.²² In the present study, BCSs were divided into older ≥ 65 and middle-aged < 65. Since the mean body weight of the 2 groups was different, grip strength was adjusted for body weight to enable an accurate comparison between the 2 groups. Right grip strength was lower in the older BCSs than in the middle-aged BCSs; however, left grip strength did not differ between the 2

Table 4. Correlations Between Muscle Strength, Body Composition and Quality of Life Among Middle-Aged and Older Breast Cancer Survivors.

	Group	Physical functioning	Role-physical	Bodily pain	General health	Vitality	Social functioning	Role-emotional	Mental health
Right hand grip (kgf/BW)	Middle-aged breast cancer survivors (n = 53)	0.49**	0.41**	0.32*			0.30*	0.39**	
	Older breast cancer survivors (n = 49)								
Left hand grip (kgf/BW)	Middle-aged breast cancer survivors (n = 53)	0.44**		0.33*			0.30*		
	Older breast cancer survivors (n = 49)								
Right knee extensor (kgf/BW)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)	0.47**	0.46**	0.49**	0.29*			0.36**	
Left knee extensor (kgf/BW)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)			0.31*					
Fat free mass	Middle-aged breast cancer survivors (n = 53)					0.34*			
	Older breast cancer survivors (n = 49)								
Skeletal muscle mass	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)		0.29*			0.35*		0.30*	
Phase angle	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)	0.40**	0.31*				-0.29*	0.29*	
Skeletal Muscle mass Index	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)								

Statistical analysis using Pearson correlation coefficient. Only significant correlation coefficients are presented.

**p < .01. *p < .05.

Table 5. Correlations Between Balance Function and Quality of Life Among Middle-Aged and Older Breast Cancer Survivors.

	Group	Physical functioning	Role-physical	Bodily pain	General health	Vitality	Social functioning	Role-emotional	Mental health
Timed up and go test (sec)	Middle-aged breast cancer survivors (n = 53)			0.33*					
	Older breast cancer survivors (n = 49)	-0.70**	-0.52**	-0.33*	-0.31*	-0.43**		-0.50**	
Body Sway Testing Eyes open condition Length of CoP (cm)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)								
Environmental area of CoP (cm ²)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)					-0.42**	-0.37**		
Rectangle area of CoP (cm ²)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)					-0.44**	-0.37**		
Body Sway Testing Eyes closed condition Length of CoP (cm)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)								
Environmental area of CoP (cm ²)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)								
Rectangle area of CoP (cm ²)	Middle-aged breast cancer survivors (n = 53)								
	Older breast cancer survivors (n = 49)								

Statistical analysis using Pearson correlation coefficient. Only significant correlation coefficients are presented.

Abbreviation: CoP = center of pressure.

** $p < .01$. * $p < .05$.

groups. In the present study, the groups were separated by the age of 65 years, resulting in an average age of 56 years for the middle-aged group and 72 years for the older group. The average age of the middle-aged group in this study was higher than that of the younger group in the previous study. Therefore, we believe that differences between the groups were less likely to occur, and did not reach significance in terms of left hand grip strength.

A previous study compared knee extension, leg press and squat muscle strength in 16 younger women, an average age of 27.1 years old, and older women, an average age of 62.9 years old, and reported that the older women had significantly lower values in all categories.²³ However, another study compared knee extension strength in 12 middle-aged women (50-58 years) and 13 older women (70-76 years), and reported no significant differences.²⁴ Other studies have reported that the cross-sectional area of the quadriceps muscle decreases significantly with age in healthy Japanese women.²⁵ The time required to stand up for 10 repetitions and maximum knee extension muscle strength were measured in 285 young female participants (aged 65-74 years) and 89 older female participants (aged 75-90 years), and the time required was significantly higher in the older participants than in the young participants.²⁶ This study showed that the older BCSs' right knee extension muscle strength was lower than that of middle-aged BCSs. However, the older BCSs' left knee extension muscle strength did not significantly differ from that of the middle-aged BCSs. This study separates age at 65 years of age; the average age of the older BCSs was 72 years old, and that of the middle-aged BCSs was 56. Hence, we believe that because the age difference was small, it was difficult to make a difference as with left grip strength.

Muscle mass generally decreases with age, and is also significantly associated with cancer.²⁷ The cancer survivors reported significantly lower muscle mass compared to the healthy controls, along with duration of disease after cancer diagnosis.²⁸ In the present study, all values indicating muscle mass were significantly lower in the older BCSs than in the middle-aged BCS. Thus, the older BCS may have had more muscle atrophy than the middle-aged BCSs. Both muscle weakness and muscle atrophy in BCSs are associated with aging, malnutrition, inactivity, and treatment toxicity.²⁹ In addition, older BCSs often have overlapping symptoms such as nausea, vomiting, pain, depression, fatigue, insomnia, loss of appetite, decreased libido, and increased anxiety.³⁰ These factors may also be associated with muscle atrophy and muscle weakness in older BCSs.

Although cancer survivors may also have impaired balance function, there are few reports on balance function in BCSs. In our results, only length of COP was higher in the older BCSs when compared to the middle-aged BCSs. This indicates that the center of gravity sway is increased, and the balance function is impaired. Of the 511 cancer

survivors in the prior study by Medina et al,³¹ 282 (48.3%) had balance disorders, primarily due to vestibular dysfunction. A previous study reported that there were no significant differences in the tests of gravimetric sway in older cancer survivors compared to age-matched healthy controls. However, TUG test results were significantly higher in the cancer survivors.³² In our previous study, cancer survivors and healthy participants underwent the TUG test and body sway testing. The TUG test results were significantly higher in the cancer survivors than in the healthy participants, and environmental CoP area (cm²) was also higher.³³ The current study showed that TUG test results were also higher in older BCSs than in middle-aged BCSs (7.3 vs 6.6 seconds; $P = .064$). Only 1 item in the current study showed a significant difference in the body sway test. It is possible that balance function may be getting worse with older age in BCSs. Previous studies have reported that BCSs aged >50 years had significantly poorer physical well-being, social/family well-being, functional well-being, and subjective QOL compared to those aged <50 years.³⁴ Cancer patients have reported worse HRQOL with increasing age in regard to physical and cognitive functioning and constipation.³⁵ Another study compared the quality of life of 46 breast cancer patients divided into younger and older groups at age 65. They reported that there were no significant differences in overall QOL and physical and pain QOL between the younger and older breast cancer groups.³⁶ In our study, the PF subscale and muscle strength, muscle mass, and balance function were found to be lower in older BCSs than middle-aged BCSs. Thus, QOL may also be associated with a tendency to decline in items related to physical function in BCSs. On the other hand, a previous study reported that social functioning increased significantly with increasing age when comparing quality of life in 18 to 49, 50 to 70, and 71 to 80 years age groups in colorectal cancer patients.³⁵ In the present study, of BCSs, social functioning was higher in the middle-age group than in the older age group, although this difference did not reach statistical significance. Quality of life score may vary depending on the type of cancer.

An association between muscle strength, muscle mass, and QOL in cancer survivors has also been reported. Male cancer survivors' hand grip strength is significantly associated with QOL of self-care and QOL of usual activities, with lower QOL as grip strength decreases.³⁷ Female cancer survivors have reported that QOL in terms of mobility problems, usual activities, pain/discomfort, and anxiety/depression were associated with low grip strength. In healthy controls, there was no significant relationship between low grip strength and QOL.³⁷ In 1037 cancer survivors (60.7% female, mean age 62.2 years), those with weak grip strength were reported to show statistically significant worsening in all 5 EuroQoL-5 dimensions (EQ-5D) compared to cancer survivors with normal grip strength.³⁸ Other studies have

similarly reported that grip strength correlated with physical function and physical pain in QOL among cancer survivors.³⁹ As noted in previous studies, grip strength in cancer survivors may be more likely to be associated with QOL. Although the middle-aged BCSs in this study showed no correlations between hand grip strength and all subscales of QOL, the older BCSs had more subscales of QOL associated with grip strength. This indicates that grip strength is linked to QOL and may be more reflective of QOL in older BCSs than in middle-aged BCSs. There are a few reports on the relationship between knee extensor strength and QOL in cancer survivors. A previous study reported that knee extensor strength in cancer survivors correlated with PF of QOL.³⁹ In the present study, extension strength was significantly correlated with QOL in the older BCSs, although no correlation was found in the middle age group. In particular, knee extension strength was found to be closely related to mobility including walking and may be more significantly related to QOL in older BCSs.

Weight loss and muscle wasting have a negative impact on the QOL of cancer patients.⁴⁰ Metastatic colorectal cancer patients with increased skeletal muscle mass were significantly associated with improved global health status compared with metastatic colorectal cancer patients who lost skeletal muscle mass. Increased skeletal muscle mass was found to be significantly and clinically associated with improved role function, less fatigue, and less pain in metastatic colorectal cancer patients.⁴¹ Low SMI values are associated with low PF and RF of QOL in non-small cell lung cancer patients.⁴² Our results revealed no association between muscle mass and QOL in middle-aged BCSs, but there were correlations between skeletal muscle mass and QOL items in older BCSs. This indicates that muscle mass may be closely linked to QOL in older BCSs.

PhA score has been reported to be significantly associated with muscle strength in breast cancer survivors⁴³; it is attracting attention as a prognostic indicator of survival and QOL in cancer patients.⁴⁴ Higher PhA may be found in individuals with high muscle mass in athletes.⁴⁵ In the present study, PhA was positively correlated with 4 subscales of QOL in older BCSs. PhA is independently associated with muscle mass, strength, and sarcopenia in patients undergoing peritoneal dialysis.⁴⁶ Thus, high PhA may be positively correlated with QOL in older BCSs.

In terms of balance function, TUG was correlated with 6 subscales of QOL in older BCSs. Previous studies have also reported that QOL worsened significantly with increasing TUG values in Parkinson's disease patients.⁴⁷ In the present study, older BCSs showed a negative correlation with TUG and QOL. This result suggests that QOL decreases with increasing TUG values, which is consistent with the results of previous studies.⁴⁷ Few studies have investigated the association between gravimetric sway testing and QOL in cancer survivors. Previous studies have reported a negative

correlation between body sway test results and QOL in cancer survivors.⁴⁸ Therefore, the older BCSs results in the current study are similar to those of previous studies. Physical ability has been reported to be strongly associated with QOL in older cancer survivors.⁴⁹ Physical well-being, health functional limitations, disability, mobility, physical health status, and ability to perform activities of daily living have been reported to be important and affect to QOL in older survivors.⁴⁹ In the present study, the older BCSs had stronger associations between muscle strength and muscle mass and QOL than that of the middle-aged BCSs, indicating not only physical limitations that have been reported in previous studies,⁴⁹ but also that actual muscle weakness in older BCSs may cause a decline in QOL.

The present study has some limitations. First, we compared strength, muscle mass, balance and QOL between the 2 groups. A multivariate analysis adjusted for age to identify factors related to QOL may be more appropriate. Secondly, the current study was had a relatively small study population; we hope to resolve this problem by using a larger sample size in future. Thirdly, the 2 BCS age groups in our study have significant differences in body weight and history of radiation therapy. Body weight tended to be related to muscle strength; therefore, we adjusted grip strength and knee extension muscle strength for body weight. However, we did not adjust for history of radiation therapy; this may have affected muscle strength, muscle mass, and QOL with radiation therapy in the middle-aged group. Finally, we did not compare our data with those of cancer patients using age-matched standards values. Therefore, it is difficult to determine whether the differences between the 2 age groups were due to natural aging or their cancer and treatment.

Conclusion

In conclusion, older BCSs have significantly lower muscle strength, muscle mass, and PF in QOL than middle-aged BCSs. Additionally, older BCSs have significantly longer length of COP than middle-aged BCSs. Furthermore, muscle strength, muscle mass, TUG, and the body sway test were related to QOL in older BCSs more than in middle-aged BCSs. Breast cancer survivors may differ in strength, muscle mass, balance, and QOL characteristics according to their age. We believe that the current findings contribute to the understanding of muscle strength, muscle mass, balance function and QOL in older breast cancer survivors. Additionally, we believe that the findings of this study will be relevant in the context of planning rehabilitation for older breast cancer survivors.

Acknowledgments

The authors are grateful to the study participants and physical therapists in the Department of Rehabilitation, as well as the

physicians in the Department of Breast surgery, in Kita-Fukushima Medical Center.

Author contributions

S.M and R.K made substantial contributions to the conception and design. S.M, R.K, Y.Y, R.J, and A.T were accountable for the collection and assembly of data. S.M, O.A, A.T, J.F, and T.T drafted and wrote the manuscript. All authors have read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was partly supported by a Grant-in-Aid for Fukushima Medical University as well as the M.D. Anderson Cancer Center Support Grant CA 016672.

Ethics Approval

This study was approved by the Kita-Fukushima Medical Center Institutional Committee on Human Research (No. 72). The research was conducted in accordance with the Declaration of Helsinki, 1964.

Consent to Participate

Written informed consent was obtained from all participants.

Consent for Publication

Written informed consent was obtained from the patients regarding publishing their data.

ORCID iD

Shinichiro Morishita  <https://orcid.org/0000-0002-4841-948X>

References

1. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. *CA Cancer J Clin.* 2019;69:363-385.
2. Harrington S, Padua D, Battaglini C, et al. Comparison of shoulder flexibility, strength, and function between breast cancer survivors and healthy participants. *J Cancer Surviv.* 2011;5:167-174.
3. Versteeg KS, Blauwhoff-Buskermolen S, Buffart LM, et al. Higher muscle strength is associated with prolonged survival in older patients with advanced cancer. *Oncologist.* 2018;23:580-585.
4. Villaseñor A, Ballard-Barbash R, Baumgartner K, et al. Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. *J Cancer Surviv.* 2012;6:398-406.
5. Mallard J, Hucteau E, Hureau TJ, Pagano AF. Skeletal muscle deconditioning in breast cancer patients undergoing chemotherapy: current knowledge and insights from other cancers. *Front Cell Dev Biol.* 2021;9:719643.
6. Hsieh KL, Wood TA, An R, Trinh L, Sosnoff JJ. Gait and balance impairments in breast cancer survivors: A systematic review and meta-analysis of observational studies. *Arch Rehabil Res Clin Transl.* 2019;1:100001.
7. Koch L, Jansen L, Herrmann A, et al. Quality of life in long-term breast cancer survivors - a 10-year longitudinal population-based study. *Acta Oncol.* 2013;52:1119-1128.
8. Cimprich B, Ronis DL, Martinez-Ramos G. Age at diagnosis and quality of life in breast cancer survivors. *Cancer Pract.* 2002;10:85-93.
9. Sari Y, Isworo A, Upoyo AS, et al. The differences in health-related quality of life between younger and older adults and its associated factors in patients with type 2 diabetes mellitus in Indonesia. *Health Qual Life Outcomes.* 2021;19:124.
10. van Leeuwen M, Husson O, Alberti P, et al. Understanding the quality of life (QOL) issues in survivors of cancer: towards the development of an EORTC QOL cancer survivorship questionnaire. *Health Qual Life Outcomes.* 2018;16:114.
11. Ouchi Y, Rakugi H, Arai H, et al. Redefining the elderly as aged 75 years and older: proposal from the Joint Committee of Japan Gerontological Society and the Japan Geriatrics Society. *Geriatr Gerontol Int.* 2017;17:1045-1047.
12. Cinar D, Tas D. Cancer in the elderly. *North Clin Istanb.* 2015;2:73-80.
13. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5:649-655.
14. Malhotra R, Ang S, Allen JC, et al. Normative values of hand grip strength for elderly Singaporeans aged 60 to 89 years: a cross-sectional study. *J Am Med Dir Assoc.* 2016;17:864.e1-867.
15. Yu R, Ong S, Cheung O, Leung J, Woo J. Reference values of grip strength, prevalence of low grip strength, and factors affecting grip strength values in Chinese adults. *J Am Med Dir Assoc.* 2017;18:551.e9-551.e16.
16. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol.* 1998;147:755-763.
17. Bosy-Westphal A, Danielzik S, Dörhöfer RP, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. *JPEN J Parenter Enteral Nutr.* 2006;30:309-316.
18. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 1991;39:142-148.
19. Isles RC, Choy NL, Steer M, Nitz JC. Normal values of balance tests in women aged 20-80. *J Am Geriatr Soc.* 2004;52:1367-1372.
20. Kiecolt-Glaser JK, Bennett JM, Andridge R, et al. Yoga's impact on inflammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial. *J Clin Oncol.* 2014;32:1040-1049.
21. Lee SC, Wu LC, Chiang SL, et al. Validating the capability for measuring age-related changes in grip-force strength using a digital hand-held dynamometer in healthy young and elderly adults. *Biomed Res Int.* 2020;2020:1-9.
22. Kubota H, Demura S, Kawabata H. Laterality and age-level differences between young women and elderly women in

- controlled force exertion (CFE). *Arch Gerontol Geriatr.* 2012; 54:e68-e72.
23. Petrella JK, Kim JS, Tuggle SC, Hall SR, Bamman MM. Age differences in knee extension power, contractile velocity, and fatigability. *J Appl Physiol.* 2005;98:211-220.
 24. Pääsuke M, Ereline J, Gapeyeva H. Age-related differences in knee extension rate of isometric force development and vertical jumping performance in women. *J Sports Med Phys Fitness.* 2003;43:453-458.
 25. Mizuno T, Matsui Y, Tomida M, et al. Differences in the mass and quality of the quadriceps with age and sex and their relationships with knee extension strength. *J Cachexia Sarcopenia Muscle.* 2021;12:900-912.
 26. Yanagawa N, Shimomitsu T, Kawanishi M, Fukunaga T, Kanehisa H. Sex difference in age-related changes in knee extensor strength and power production during a 10-times-repeated sit-to-stand task in Japanese elderly. *J Physiol Anthropol.* 2015;34:40.
 27. Williams GR, Rier HN, McDonald A, Shachar SS. Sarcopenia & aging in cancer. *J Geriatr Oncol.* 2019;10:374-377.
 28. Williams GR, Chen Y, Kenzik KM, et al. Assessment of sarcopenia measures, survival, and disability in older adults before and after diagnosis with cancer. *JAMA Netw Open.* 2020;3:e204783.
 29. Christensen JF, Jones LW, Andersen JL, Dugaard G, Rorth M, Hojman P. Muscle dysfunction in cancer patients. *Ann Oncol.* 2014;25:947-958.
 30. Rao A, Cohen HJ. Symptom management in the elderly cancer patient: fatigue, pain, and depression. *J Natl Cancer Inst Monographs.* 2004;32:150-157.
 31. Medina HN, Liu Q, Cao C, Yang L. Balance and vestibular function and survival in US cancer survivors. *Cancer.* 2021;127:4022-4029.
 32. Ihira H, Mizumoto A, Makino K, et al. Physical functions, health-related outcomes, nutritional status, and blood markers in community-dwelling cancer survivors aged 75 years and older. *Asian Pac J Cancer Prev.* 2014;15:3305-3310.
 33. Morishita S, Mitobe Y, Tsubaki A, et al. Differences in balance function between cancer survivors and healthy subjects: a pilot study. *Integr Cancer Ther.* 2018;17:1144-1149.
 34. Park BW, Lee S, Lee AR, Lee KH, Hwang SY. Quality of life differences between younger and older breast cancer patients. *J Breast Cancer.* 2011;14:112-118.
 35. Quinten C, Coens C, Ghislain I, et al. The effects of age on health-related quality of life in cancer populations: A pooled analysis of randomized controlled trials using the European Organisation for research and Treatment of Cancer (EORTC) QLQ-C30 involving 6024 cancer patients. *Eur J Cancer.* 2015;51:2808-2819.
 36. Takada K, Kashiwagi S, Asano Y, et al. Significance of age-associated quality of life in patients with stage IV breast cancer who underwent endocrine therapy in Japan. *Oncol Lett.* 2020;20:180.
 37. Kim H, Yoo S, Kim H, Park SG, Son M. Cancer survivors with low hand grip strength have decreased quality of life compared with healthy controls: the Korea National Health and Nutrition Examination Survey 2014-2017. *Korean J Fam Med.* 2021;42:204-211.
 38. Paek J, Choi YJ. Association between hand grip strength and impaired health-related quality of life in Korean cancer survivors: a cross-sectional study. *BMJ Open.* 2019;9:e030938.
 39. Morishita S, Tsubaki A, Fu JB, Mitobe Y, Onishi H, Tsuji T. Cancer survivors exhibit a different relationship between muscle strength and health-related quality of life/fatigue compared to healthy subjects. *Eur J Cancer Care.* 2018;27:e12856.
 40. Ryan AM, Prado CM, Sullivan ES, Power DG, Daly LE. Effects of weight loss and sarcopenia on response to chemotherapy, quality of life, and survival. *Nutrition.* 2019;67-68:110539.
 41. Derksen JWG, Kurk SA, Peeters PHM, et al. The association between changes in muscle mass and quality of life in patients with metastatic colorectal cancer. *J Cachexia Sarcopenia Muscle.* 2020;11:919-928.
 42. Bye A, Sjøblom B, Wentzel-Larsen T, et al. Muscle mass and association to quality of life in non-small cell lung cancer patients. *J Cachexia Sarcopenia Muscle.* 2017;8:759-767.
 43. Matias CN, Cavaco-Silva J, Reis M, et al. Phase angle as a marker of muscular strength in breast cancer survivors. *Int J Environ Res Public Health.* 2020;17:4452.
 44. Arab A, Karimi A, Vingrys E, Shirani F. Is phase angle a valuable prognostic tool in cancer patients' survival? A systematic review and meta-analysis of available literature. *Clin Nutr.* 2021;40:3182-3190.
 45. Matias CN, Campa F, Nunes CL, et al. Phase angle is a marker of muscle quantity and strength in overweight/obese former athletes. *Int J Environ Res Public Health.* 2021;18:6649.
 46. Do JY, Kim AY, Kang SH. Association between phase angle and sarcopenia in patients undergoing peritoneal dialysis. *Front Nutr.* 2021;8:742081.
 47. Stegemöller EL, Nocera J, Malaty I, Shelley M, Okun MS, Hass CJ. Timed up and go, cognitive, and quality-of-life correlates in Parkinson's disease. *Arch Phys Med Rehabil.* 2014;95:649-655.
 48. Morishita S, Hirabayashi R, Tsubaki A, et al. Relationship between balance function and QOL in cancer survivors and healthy subjects. *Medicine.* 2021;100:e27822.
 49. Fitch MI, Nicoll I, Newton L, Strohschein FJ. Challenges of survivorship for older adults diagnosed with cancer. *Curr Oncol Rep.* 2022;24:763-773.