Online Exclusive Article

Frailty in Older Breast Cancer Survivors: Age, Prevalence, and Associated Factors

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Older women (aged 65 years and older) constitute the largest group of breast cancer survivors (BCSs) in the United States (Howlader et al., 2012). More than 1.6 million U.S. women aged 65 years and older are BCSs (Centers for Disease Control and Prevention, 2011). Long-term problems reported by BCSs, such as cognitive difficulty, neuropathy, osteoporosis, muscle weakness, weight loss, slow walking speed, and fatigue, may be similar to those of older women without cancer, but may begin at an earlier age (Clough-Gorr, Stuck, Thwin, & Silliman, 2010; Klepin et al., 2010; Maccormick, 2006). A useful approach may be to consider the long-term effects of cancer and cancer treatment as *accelerated aging*, or early-onset frailty (Maccormick, 2006).

Frailty is an overall weakened physiologic state usually associated with advanced age (Fried et al., 2001). A measurable frailty phenotype model was proposed by Fried et al. (2001) that has been widely adopted in geriatric research and practice. The frailty phenotype is a conceptual cycle of inactivity and increasing weakness that cascades into eventual disability and dependence. Fried et al. (2001) proposed five criteria to measure frailty (unintentional weight loss, exhaustion, weakness, slow walking speed, and low physical activity) and demonstrated that older adults with at least three of the five criteria were at increased risk for worsening mobility, hospitalization, and death. Frailty, as measured by the frailty phenotype, has been strongly associated with older age, hospitalization, development of disability, reduced cardiac and pulmonary function, and reduced exercise capacity in older adults without cancer (Avila-Funes et al., 2008; Bandeen-Roche et al., 2006; Boyd, Xue, Simpson, Guralnik, & Fried, 2005; Fernandez-Bolanos et al., 2008; Santos-Eggimann, Cuénoud, Spagnoli, & Junod, 2009; Szanton, Seplaki, Thorpe, Allen, & Fried, 2010; Weiss, Hoenig, Varadhan, Simonsick, & Fried, 2010; Wong et al., 2010; Woo, Chan, Leung, & Wong, 2010).

Cancer survivors are not yet known to be measurably more frail than other adults of the same age because frailty

Purpose/Objectives: To describe frailty and associated factors in breast cancer survivors (BCSs) and evaluate whether BCSs are frail at an earlier age than female participants from in two large epidemiological studies.

Design: Descriptive, cross-sectional.

Setting: School of Nursing at Oregon Health and Science University.

Sample: 216 BCSs aged 53–87 years who were a mean 5–7 years post-treatment and not currently participating in exercise.

Methods: Performance tests, clinical measures, and self-reported questionnaires provided baseline data on five criteria for frailty.

Main Research Variables: Frailty was defined as meeting three of the five criteria of the frailty phenotype: shrinking, exhaustion, low activity, slowness, and weakness. Data were compared to published data from women in the Cardiovascular Health Study (CHS) and Women's Health and Aging Study (WHAS).

Findings: Eighteen percent of BCSs aged 70–79 years were frail compared to 11% of women of the same age in the CHS and WHAS. Frailty was more common at a younger age in BCSs, and more BCSs were frail in all age groups compared to women in the CHS study until about age 80 years, when prevalence of frailty was similar in the two groups. Fifty percent of BCSs were classified as prefrail because they met one or two of the five frailty criteria. Higher body mass index increased the odds of frailty, and higher physical activity decreased the odds of frailty (odds ratio [OR] = 1.12, $p = 0.003$, and OR = 0.99, $p = 0.000$, respectively).

Conclusions: Frailty and prefrailty may be common in BCSs and may occur at an earlier age than in adults without a history of breast cancer.

Implications for Nursing: Nurses should be alert to prefrailty or frailty at a younger age in BCSs. Awareness and early intervention may delay or prevent frailty.

Knowledge Translation: BCSs may be frail even when they are not yet considered older adults. Prefrailty in BCSs is important to recognize because it suggests impending frailty that could lead to reduced physical functioning or poor health. Prefrailty and frailty could be assessed in BCSs aged 50 years and older in a clinical setting using a few questions about weight, fatigue, and activity levels, in addition to simple tests of walking speed and grip strength, if warranted.

rarely has been measured in cancer studies. However, researchers have called on peers to include assessment of frailty in research studies and clinical care of patients with cancer and survivors (Audisio & van Leeuwen, 2011; Bylow, Mohile, Stadler, & Dale, 2007; Maccormick, 2006; Monfardini & Basso, 2007; Pal, Katheria, & Hurria, 2010; Retornaz et al., 2008). To the authors' knowledge, only one published study has reported frailty in cancer survivors. In that study, 8% of 71 men on androgen deprivation therapy (ADT) were frail, and 56% were prefrail (had one or two criteria for frailty) (Bylow et al., 2011).

The purpose of the current study was to measure frailty in 216 older BCSs using the five criteria of the frailty phenotype. To provide a context for the findings, the authors present published data on frailty from older women in the Cardiovascular Health Study (CHS) and Women's Health and Aging Study (WHAS) and a regression model of the current study's BCSs data to evaluate characteristics associated with frailty.

Methods

Participants and Procedures

For this cross-sectional descriptive study, data of older adult BCSs from two exercise intervention trials were analyzed. Data were collected from 2006–2010 in BCSs prior to beginning the exercise intervention. Women for both trials were recruited through the Oregon State Cancer Registry, referral by clinical providers, recruitment at breast cancer events, advertisements, and community information sessions. Detailed descriptions of the samples and procedures have been published elsewhere (Loprinzi, Cardinal, Si, Bennett, & Winters-Stone, 2012; Winters-Stone et al., 2011). Both samples consisted of BCSs older than 50 years and interested in participation in an exercise study but not currently participating in resistance exercise (Winters-Stone et al., 2011) or not currently participating in both resistance and aerobic exercise (Loprinzi et al., 2012). BCSs in both studies were screened for eligibility and invited to an appointment at the study site where they were enrolled, completed a self-report questionnaire, and underwent performance tests of physical functioning and other clinical measures.

Baseline data were combined because both studies used the same measures of criteria for frailty and other variables and both samples consisted of older BCSs. Some differences existed between the two samples, as shown in Table 1, but combining the samples was advantageous because it broadened the range of some variables, such as age, physical activity, and survival time in the combined sample. The combined sample of 216 BCSs were aged 53–87 years, were generally healthy but inactive, and reported few difficulties in activities of daily living. Most breast cancers were stages I and II, with mean completion of chemotherapy or radiation 5–7 years earlier.

Measures of Frailty

Frailty was measured using the components of the frailty phenotype (Fried et al., 2001), which consists of five criteria: shrinking, exhaustion, low activity, slowness, and weakness. BCSs with three or more criteria were classified as frail, those with one or two criteria were classified as prefrail (Fried et al., 2001), and those with no criteria were classified as robust. The criteria were measured as follows.

Shrinking: Shrinking was determined by low muscle mass as measured by appendicular lean mass using dual energy x-ray absorptiometry, adjusted for height and fat mass using linear regression residual –1.73 or less. Muscle mass was considered low if it was in the lowest 20th percentile of well-functioning older adults. The cut point for lowest 20th percentile was from 2,984 well-functioning older adults in the Health, Aging and Body Composition Study (HABC) study (Newman et al., 2003).

Exhaustion: Exhaustion was measured by a self-reported score on the SF-36® vitality scale (Ware, Kosinski, & Gandek, 2000) of less than 45.85 (normed) for BCSs aged 50–74 years or less than 42.73 (normed) for BCSs aged 75 years or older. Cut points were the lowest quartile of the scale in the general U.S. population (Ware, 2005).

Low activity: Activity was measured by the number of kcals expended per week in moderate-to-vigorous intensity activity measured by the Community Healthy Activities Model Program for Seniors (CHAMPS) physical activity questionnaire (Stewart et al., 2001). Less than 270 kcal per week was selected as the cut point to conform to the cut point used by Fried et al. (2001) for the frailty phenotype.

Slowness: Slowness was determined if patients walked four meters at less than 1 m per second using fastest time recorded from two attempts. The cut point was chosen based on findings in the HABC study of older adults that a walking speed less than 1 m per second predicted mortality (Cesari et al., 2005).

Weakness: Weakness was determined by low grip strength, as measured by handgrip dynamometry. Grip strength was considered low if dynamometer measure was 17 kg or less for BCSs with a body mass index (BMI) of 23 or lower, 17.3 kg or less for BCSs with a BMI of 23.1–26, 18 kg or less for BCSs with a BMI of 26.1–29, or 21 kg or less for BCSs with a BMI greater than 29. Cut points were selected to conform to the cut points used by Fried et al. (2001) and Bandeen-Roche et al. (2006).

Measures

Participant characteristics (e.g., age, race, education, marital status) were reported by written answers to items on the study questionnaire. Cancer stage, dates, treatments, and current use of an aromatase inhibitor or a selective estrogen receptor modulator also were

self-reported. Comorbidity was measured by self-reported items on the **Charlson Comorbidity Index** (Charlson, Pompei, Ales, & MacKenzie, 1987). Cancer was included in the comorbidity measure only if it was treated fewer than five years prior or had metastasized. Comorbidity was categorized according to the Charlson weighted scores as 0–2 (not or mildly ill), 3–4 (moderately ill), or greater than 4 (severely ill). Validity and reliability of the Charlson Comorbidity Index were shown in Katz, Chang, Sangha, Fossel, and Bates (1996). Disability was measured by difficulty in activities of daily living measured by a sum of "yes" answers to difficulty in six items on the Personal Role Domain Scale, part of the disability component of the **Late-Life Function and Disability Instrument** (Jette et al., 2002). The items asked about ability to take care of one's house, finances, health, personal care, local errands, and meal preparation. The validity and reliability of the Late-Life Function and Disability Instrument were shown in Jette et al. (2002). Physical activity was measured by the self-report **CHAMPS questionnaire** (Stewart et al., 2001) of frequency and duration of various activities, and answers were transposed to kcal per week using CHAMPS protocols. Validity and reliability of the CHAMPS questionnaire were shown by Harada, Chiu, King, and Stewart (2001).

Table 1. Characteristics of Two Samples of Breast Cancer Survivors From Prior Studies and the Combined Sample (N = 216)

	Sample 1 (n = 105)		Sample 2 (n = 111)		Combined Sample	
Characteristic	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
Age (years)*	62	6.7	71	5.1	66.7	7.4
Body mass index (kg/m^2)	29	5.7	29.2	5.8	29.4	5.8
Usual physical activity*	1,632.3	1,643.3	895.3	1,045	1,255.2	1,415.2
Months since cancer diagnosis*	60.6	37.9	87.1	45.3	74.1	44
Months since chemotherapy completion*	52	34.1	92.8	46	70.1	44.6
Months since radiation completion*	53.5	36.1	83.6	42.4	68.6	42.1
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Race						
Caucasian	101	96	108	97	209	97
African American or Black	1	1	–	–	1	< 1
Other	3	3	2	2	5	2
Missing	–	–	1	1	1	< 1
Education						
Less than high school	–	–	1	1	1	< 1
High school graduate or GED	24	23	32	29	56	26
Associate or technical degree	8	8	20	18	28	13
Bachelor's degree	35	33	30	27	65	30
Advanced degree	24	23	27	24	51	24
Missing	14	13	1	1	15	7
Marital status						
Married or partnered	59	56	65	59	124	57
Divorced or separated	28	27	24	22	52	24
Widowed	10	10	17	15	27	13
Single	8	8	4	4	12	6
Missing	–	–	1	1	1	< 1
Comorbidity						
0–2 (not to mildly ill)	78	74	71	64	149	69
3–4 (moderately ill)	20	19	30	27	50	23
More than 4 (severely ill)	7	7	9	8	16	7
Missing	–	–	1	1	1	< 1
Difficulty in one or more ADLs	5	5	7	6	12	6
Breast cancer stage						
0	6	6	14	13	20	9
I	42	40	53	48	95	44
II	44	42	32	29	76	35
III	5	5	9	8	14	7
Missing	8	8	3	3	11	5
Treatment[a]						
Received chemotherapy*	63	60	50	45	113	52
Received radiation therapy	93	89	95	86	188	87
Currently taking AI	43	41	30	27	73	34
Currently taking SERM	16	15	2	2	18	8

* P values reported for significant differences between samples 1 and 2 are $p < 0.05$.

[a] Participants could select more than one, if applicable.

ADLs—activities of daily living; AI—aromatase inhibitor; SERM—selective estrogen receptor modulator

Note. Because of rounding, percentages may not total 100.

Note. Age ranges (years) are: sample 1 = 53–83, sample 2 = 64–87, combined sample = 53–87.

Note. Samples 1 and 2 were participants from previous trials who were non-exercisers. The samples were combined for analysis in the current study. Refer to Loprinzi et al. (2012) for more information about sample 1 and Winters-Stone et al. (2012) for more information about sample 2.

Comparison to Published Data

Participants in the CHS study were a large sample (N = 5,317) of community-dwelling older adults whose data, collected in 1989–1990, were used to validate the original frailty phenotype (Fried et al., 2001). Subsequently, a subsample of 1,741 older women aged 70–79 years from CHS was assessed for frailty criteria and compared with a sample of 786 older women

aged 70–79 years from WHAS (Bandeen-Roche et al., 2006). Those two samples of older community-dwelling women had a broad range of socioeconomic, functional, and health statuses, and thus provide a reasonable comparison for frailty status with older BCSs. CHS and WHAS data were previously published (Bandeen-Roche et al., 2006; Fried et al., 2001).

Statistical Analysis

Descriptive statistics were used to characterize the sample and compare BCSs with CHS and WHAS data. Robust, prefrail, and frail groups in the BCS sample were compared using analysis of variance with least significant difference post-hoc analysis between pairs. Logistic regression models using SPSS®, version 20, were constructed to evaluate associations among sample characteristics and frailty status. Independent variables were entered in one block (age, BMI, physical activity, disability, comorbidity, prior chemotherapy, prior radiation treatment, current aromatase inhibitor therapy, and current selective estrogen receptor modulator therapy) in a logistic regression model with frailty as the condition of interest, compared to robust and prefrail combined. Physical activity was included as an independent variable in logistic regression models in its full continuous variation because it was not collinear with the dependent variable frailty (r = –0.25), although a low cut point of physical activity was one of the five criteria of frailty.

Table 2. Baseline Characteristics of Breast Cancer Survivors in Three Frailty Groups (N = 216)

	Robust (n = 81)		Prefrail (n = 108)		Frail (n = 27)		
Characteristic	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**p**
Age (years)	66.7	7.1	67.6	7.6	69.3	6.1	< 0.01[a, b]
Body mass index (kg/m^2)	27.4	4.8	29.6	5.2	34.5	7.4	< 0.01[a, b, c]
Usual physical activity (kcals/week)	2,033	1,357.5	901.9	1,316.4	299.7	631.7	< 0.01[a, b, c]
Months since cancer diagnosis	80.2	48.8	68.9	38	76.8	48.6	–
Months since chemotherapy completion	73.2	47.4	65.9	42.1	74.6	45	–
Months since radiation completion	73.8	46	64.3	37.1	71.9	49.5	–
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**p**
Comorbidity (Charlson Comorbidity Index)							< 0.01[a, b]
0–2 (not to mildly ill)	68	84	69	64	12	44	–
3–4 (moderately ill)	8	10	31	29	11	41	–
More than 4 (severely ill)	5	6	8	7	3	11	–
Missing	–	–	–	–	1	4	–
Difficulty in one or more ADLs	1	1	10	9	1	4	–
Breast cancer stage							
0	4	5	13	12	3	11	–
I	42	52	45	42	8	30	–
II	31	38	35	32	10	37	–
III	2	3	8	7	4	15	–
Missing	2	3	7	7	2	7	–
Treatment[d]							
Received chemotherapy	49	61	51	47	13	48	–
Received radiation therapy	68	84	97	90	23	85	–
Currently taking AI	28	35	39	36	6	22	–
Currently taking SERM	11	14	7	7	–	–	–

[a] Signifies p value of significant difference between robust and prefrail
[b] Signifies p value of significant difference between robust and frail
[c] Signifies p value of significant difference between prefrail and frail
[d] Participants could select more than one, if applicable.
ADLs—activities of daily living; AI—aromatase inhibitor; SERM—selective estrogen receptor modulator
Note. Because of rounding, percentages may not total 100.

Results

The criteria for frailty were met by almost 13% (n = 27) and the criteria for prefrailty were met by 50% (n = 108) of the 216 BCSs. Table 2 shows personal characteristics and cancer variables in BCSs who were robust (no frailty criteria), prefrail, and frail. The prefrail and frail BCSs were similar in most characteristics, although frail BCSs had significantly higher BMI and lower levels of usual activity compared to prefrail and robust BCSs. The age of robust BCSs was significantly younger than the ages of both prefrail and frail BCSs. Categories of comorbidity were in an expected direction, with least illness in robust BCSs, followed by prefrail and frail BCSs.

The measures of each frailty criterion in the three groups (BCSs, women in CHS, and women in WHAS) are shown in Tables 3 and 4, along with the proportion of women in each group who met each criterion. The BCSs were younger (65% were younger than 70 years) than CHS and WHAS women (aged 70–79 years), yet

the proportion of BCSs who were frail (13%) is similar to the proportions in CHS and WHAS (12% and 11%, respectively). In the 66 BCSs who were the same age as the CHS and WHAS participants (70–79 years), frailty was higher in BCSs (18%) than in CHS and WHAS women (12% and 11%, respectively). Prefrail status in women aged 70–79 years was similar in the three groups—lowest in WHAS women (44%), followed by BCSs (50%) and CHS women (55%).

Age may be an important factor in many aspects of cancer survivorship, including onset of frailty (Lichtman, 2012). To describe the data more fully in terms of age, prefrail and frail status are shown in five-year age ranges in Figure 1 for BCSs (age range = 53–87 years) compared to women in CHS (age range = 65–90 years) (Fried et al., 2001). Data were not available in five-year increments for WHAS women. Frailty was more common at a younger age (18% of BCSs aged 65–70 years were frail compared to 3% of CHS women), whereas the percentage of frail CHS women began to increase at an older age and increased gradually with age. BCSs had higher proportions of frailty in all age groups until aged 80–84 years, when proportion of frailty in BCSs and CHS were almost equal. The BCS sample only had nine women older than 80 years, so comparisons at older ages are not likely to be accurate. Prefrailty was high in BCSs, but comparison data on prefrailty in CHS were not available in five-year increments.

In a logistic regression model to predict odds of being frail or prefrail compared to robust, BCSs with a higher BMI (odds ratio [OR] = 1.12, p = 0.003, 95% confidence interval [CI] [1.04, 1.19]) and lower physical activity levels (OR = 0.99, p = 0.000, 95% CI [0.99, 1]) were more likely to be frail or prefrail. All other variables in the model (i.e., age, disability, comorbidity, chemotherapy, radiation therapy, current selective estrogen receptor modulator, current aromatase inhibitor) were not significantly associated with likelihood to be frail or prefrail.

Discussion

Using criteria for a phenotype of frailty developed and validated in older adults (Fried et al., 2001), the current study's findings suggest that BCSs may become frail at an earlier age than older women without cancer. In this study, a greater proportion of younger BCSs were frail than similarly aged women without cancer (18% of BCSs aged 65–70 years were frail, compared to 3% of CHS women) and frailty affected more BCSs aged 70–79 years (18% compared to 11%–12% of CHS and WHAS women). That finding is remarkable in the context of this particular sample of BCSs, a healthy group

Table 3. Comparison of Prefrailty and Frailty Among Women in WHAS and CHS (N = 2,527)

	WHAS[a] (n = 786)		CHS[a] (n = 1,741)	
Characteristic	**Definition**	**%**	**Definition**	**%**
Shrinking	Weight at age 60 minus weight at examination is 10% or more of age 60 weight *or* BMI at examination is less than 18.5 kg/m^2	13	Lost more than 10 lbs unintentionally in last year	7
Exhaustion	Self-report of any of the following: low usual energy level (3 or lower on 0–10 scale), felt unusually tired in last month, or felt unusually weak in the past month	14	Self-report of either "Felt that everything I did was an effort in the last week," or "Could not get going in the last week"	21
Low activity	90 on activity scale (6 items)	20	270 on activity scale (18 items)	24
Slowness	Walking 4 m: less than 4.57 m in 7 seconds for height of 159 cm or less or less than 4.57 in 6 seconds for height of more than 159 cm	31	Walking 15 feet (4.57 m): 7 seconds or more for height of 159 cm or less or 6 seconds or more for height of more than 159 cm	38
Weakness	Grip strength of 17 or more for BMI of 23 or less, 17.3 or less for BMI from 23.1–26, 18 or less for BMI from 26.1–29, or 21 or less for BMI greater than 29 kg/m^2	21	Grip strength of 17 or more for BMI of 23 or less, 17.3 or less for BMI from 23.1–26, 18 or less for BMI from 26.1–29, or 21 or less for BMI greater than 29 kg/m^2	26
Overall frailty status	Robust Prefrail Frail	45 44 11	Robust Prefrail Frail	33 55 12

[a] Women aged 70–79 years

BMI—body mass index; CHS—Cardiovascular Health Study; WHAS—Women's Health and Aging Study

Note. From "Phenotype of Frailty: Characterization in the Women's Health and Aging Studies," by K. Bandeen-Roche, Q.L. Xue, L. Ferrucci, J. Walston, J.M. Guralnik, P. Chaves, . . . L.P. Fried, 2006, *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 61,* p. 263. Copyright 2006 by Oxford University Press. Reprinted with permission.

that signed up to begin a 12-month exercise study and that reported low levels of comorbidity and disability in activities of daily living. Frailty may be even more prevalent in BCSs who are less healthy.

An important finding was the high level of prefrailty across the age ranges of BCSs, particularly the continuous increase in prevalence of prefrailty after age 70 years. Prefrailty, measured as having one or two frailty criteria, may be an early sign of impending frailty (Bylow et al., 2007). The authors do not know if the age of onset of prefrailty or the steep increase in prevalence in older BCSs is unusual because age data on prefrailty in WHAS and CHS have not been published. However, 20% prefrailty in BCSs aged 50–54 years—increasing to 45% prefrailty in BCSs aged 71–74 years—warrants additional investigation. Longitudinal data on frailty and age would be clinically useful; if prefrailty predicts later frailty and occurs at an earlier age in cancer survivors, reasonably simple performance tests, such as walking speed, may predict early-onset frailty that could be prevented by early intervention.

Frailty describes a seriously debilitated physical state or syndrome shown to increase with age in older adults without cancer (Rockwood, 2005). Prior studies have shown a strong association of frailty, albeit measured in different ways, with adverse outcomes for older adults without cancer, including falls, fractures, hospitalization, disability, nursing home admission, reduced mobility, and shorter time until death (Bandeen-Roche et al., 2006; Boyd et al., 2005; Ensrud et al., 2008; Fried et al., 2001; Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Rockwood et al., 2004). If frailty occurs sooner or more frequently in BCSs, the same adverse effects may likely occur more frequently or at a younger age. This study provides the first data showing that frailty and prefrailty may indeed be common in BCSs and may occur at an earlier age than in adults without a history of cancer.

Exhaustion, low activity, and shrinking were the most frequent criteria of frailty found in BCSs in this study, whereas slowness and weakness were the most frequent criteria of frailty in women in WHAS or CHS. The differences in these components may be related to symptoms of cancer treatment. For example, fatigue often is reported as a long-term symptom by BCSs, and may be the reason for the exhaustion component being more common in BCSs than in women without cancer. However, the study data did not show an association between cancer treatments and frailty in regression models. Future studies of frailty in cancer survivors could measure other potential factors associated with early frailty, such as persistent neuropathies, reduced voluntary activity because of habits formed during illness, fear of lymphedema, or other factors.

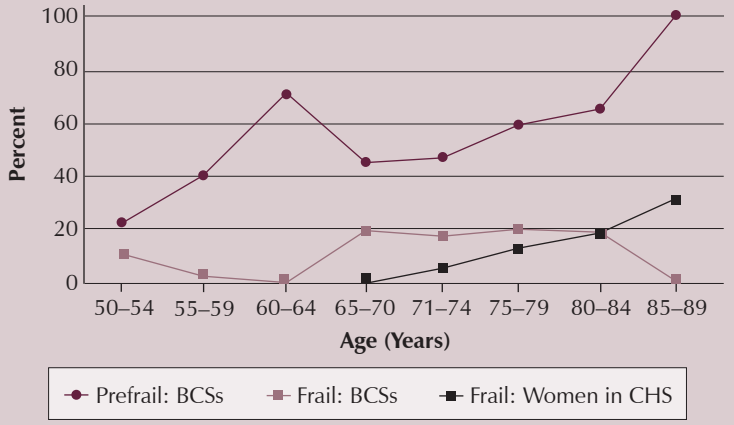
The finding that 19% of BCSs had evidence of shrinking may be a result of actual reduced muscle mass (i.e., sarcopenia) in BCSs or from more accurate measurement of sarcopenia in this study than in WHAS or CHS. In this study, sarcopenia was measured by lean mass adjusted for height and fat mass, a more accurate measure than a simple self-report of lost weight as in the WHAS and CHS studies. Adjusted lean mass was shown to be more accurate in detecting sarcopenia, particularly in obese individuals, in the HABC study (Newman et al., 2003). The accuracy of adjusted lean mass to measure sarcopenia may be particularly important in cancer survivors. In a study of 71 prostate cancer survivors on ADT, self-reported weight loss did not indicate frailty, but when BMI greater than 30 was substituted for shrinking, 9% of survivors were "obese frail" and 56% were "obese prefrail" (Bylow et al., 2011). The current study's finding that frail BCSs had significantly higher mean BMI ($\overline{X} = 34.5$) than prefrail or robust BCSs indicates that obesity, as well as shrinking or weight loss, may be a risk factor for frailty in cancer survivors (Bylow et al., 2011). The logistic regression model in this study showed that each one-unit increase in BMI increased the odds of being frail by 12%. Sarcopenic obesity, which develops when fat mass

Table 4. Prefrailty and Frailty Among Breast Cancer Survivors in the Current Study (N = 216)

Characteristic	Definition	% Total	%[a]
Shrinking	Appendicular lean mass adjusting for height and fat mass using linear regression residual of –1.73 or less	19	23
Exhaustion	Self-report on SF-36® vitality scale: less than 45.85 (normed) score for those aged 50–74 years or less than 42.73 (normed) score for those aged 75 years and older	31	26
Low activity	Less than 270 kcals per week on CHAMPS	31	41
Slowness	Walking 4 m in less than 1 m per second	20	30
Weakness	Grip strength of 17 or more for BMI of 23 or less, 17.3 or less for BMI from 23.1–26, 18 or less for BMI from 26.1–29, or 21 or less for BMI greater than 29 kg/m^2	13	14
Overall frailty status	Robust	38	32
	Prefrail	50	50
	Frail	13	18

[a] 66 women aged 70–79 years

BMI—body mass index; CHAMPS—Community Healthy Activities Model Program for Seniors



BCSs—breast cancer survivors; CHS—Cardiovascular Health Study

Note. Frail was defined as meeting 3 of 5 frailty criteria; prefail was defined as meeting 1–2 of the 5 frailty criteria.

Note. Data in five-year increments were not available for prefrail women in CHS or for frail or prefrail women in the Women's Health and Aging Study.

Note. Six BCSs were aged 80–84, and three were aged 85–89.

Figure 1. Proportion of Frailty and Prefrailty by Age in BCSs and Women in the CHS

is disproportionate to muscle mass, has been associated with chemotherapy, chemotherapy-induced ovarian failure, and tamoxifen therapy in women cancer survivors, including premenopausal women (Costa, Varella, & del Giglio, 2002; Demark-Wahnefried et al., 2001; Demark-Wahnefried, Rimer, & Winer, 1997; Demark-Wahnefried, Winer, & Rimer, 1993; Hoskin, Ashley, & Yarnold, 1992). Consideration of shrinking and obesity in the context of sarcopenia may be important in future studies of frailty and functioning among cancer survivors.

The finding that increased physical activity reduced the odds of frailty is expected. A one-unit increase in caloric expenditure per week is very small, with a correspondingly small (less than 1%) decrease in odds of frailty. The significant OR should be interpreted with caution because self-report of physical activity is only generally accurate. Therefore, the small association shown by the OR may not be valid. Instead, the general finding that physical activity reduced the risk for frailty when other variables were controlled may provide a rationale for future studies focused on this potentially protective factor.

This study was limited by the characteristics of the samples from the two prior studies. In general, BCSs in this study were healthy and willing to undertake a lengthy exercise study. Frailty may be even more common in BCSs who are not as healthy and well-functioning. On the other hand, frailty may be less common in BCSs who exercise regularly. Some have proposed that cancer treatments and cancer symptoms may cause early-onset frailty in survivors of cancer (Bylow et al., 2007; Maccormick, 2006), but perhaps the long-term survivors in this study were too far beyond treatment to show an association with particular risk factors, such as type of treatment. The associations between frailty, obesity, and low physical activity may be particularly relevant to cancer survivors and warrant additional study. Although the data only describe and do not establish cause, this study is among the first to measure criteria for frailty in cancer survivors. The findings provide preliminary evidence that early-onset frailty as a result of cancer treatment, hypothesized by Maccormick (2006), may be a reality for many BCSs.

Implications for Nursing

Gerontological nurses are familiar with the multicomponent syndrome of frailty and usually assess for signs of frailty in older women without cancer, particularly those older than 80 years. However, oncology nurses may not be thinking about frailty when evaluating the well-being of BCSs, particularly those who are younger than age 80. The study's findings suggest that nurses should consider the possibility of frailty, and particularly prefrailty, at a younger-than-expected age in BCSs. Recognition of prefrailty may be particularly important because awareness and early intervention may delay or prevent frailty. More knowledge about the prevalence and causes of frailty in BCSs, and perhaps in survivors of other cancers, could be gained if nurse scientists include measures of the components of the frailty phenotype in future research among cancer survivors, even if frailty is not the focus of the study.

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